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# Preparation of Polyfunctional Arylmagnesium, or Arylzinc Reagents Bearing a Triazene Moiety and Their Applications in Organic Synthesis

von

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## Erklärung

Diese Dissertation wurde im Sinne von § 13 Abs. 3 bzw. 4 der Promotionsordnung vom 29. Januar 1998 von Herrn Prof. Dr. Paul Knochel betreut.

## Ehrenwörtliche Versicherung

Diese Dissertation wurde selbständig, und ohne unerlaubte Hilfe erarbeitet.

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1. **C.-Y. Liu**, P. Knochel, "Preparation of Polyfunctional Aryl Azides from Aryl Triazenes. A New Synthesis of Ellipticine, 9-Methoxyellipticine, Isoellipticine, and 7-Carbethoxyisoellipticine", *J. Org. Chem.* **2007**, *submitted for publication*.

2. **C.-Y. Liu**, H. Ren, P. Knochel, "Magnesiated Unsaturated Silylated Cyanohydrins as Synthetic Equivalents of Aromatic and Heterocyclic Grignard Reagents Bearing a Ketone or an Aldehyde", *Org. Lett.* **2006**, *8*, 617-619.

3. **C.-Y. Liu**, P. Knochel, "Preparation of Polyfunctional Arylmagnesium Reagents Bearing a Triazene Moiety. A New Carbazole Synthesis", *Org. Lett.* **2005**, *7*, 2543-2546.

4. **C.-Y. Liu**, P. Knochel, "A Direct Insertion Reaction of Zn·LiCl into Functionalized Iodo- or Bromophenyl Triazenes", *manuscript in preparation*.

5. **C.-Y. Liu**, A. Gavryushin, P. Knochel, "Synthesis of Functionalized *o*-, *m*-, or *p*-Terphenyls *via* Consecutive Cross-Coupling Reactions of Arylboronic Esters Bearing a Triazene Moiety", *manuscript in preparation*.

*To my family, especially Xiaofang,*
*with love.*

## ABBREVIATIONS

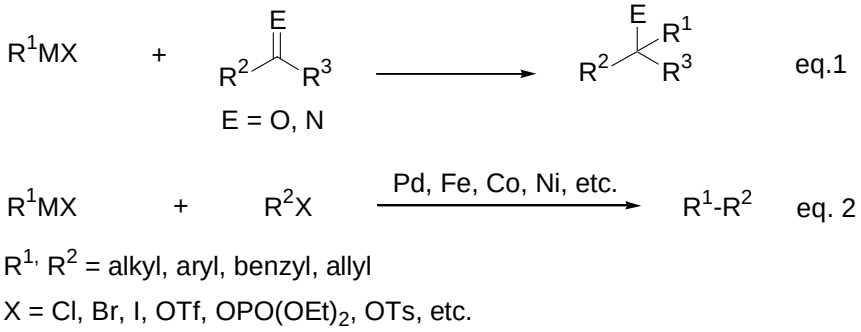
| | |
|---|---|
| Ac | acetyl |
| AcOH | acetic acid |
| Ar | aryl |
| Bn | benzyl |
| Boc | *tert*-butoxycarbonyl |
| br. | broad |
| calcd. | calculated |
| $CH_2Cl_2$ | dichloromethane |
| Cy | cyclohexyl |
| d | double |
| dba | *trans*,*trans*-dibenzylideneacetone |
| dec. | decomposition |
| DMAP | 4-dimethylaminopyridine |
| DME | 1,2-dimethoxyethane |
| DMF | *N*,*N*-dimethylformamide |
| DMSO | dimethyl sulfoxide |
| equiv. | equivalent |
| EI | electron-impact |
| Et | ethyl |
| FAB | fast-atom bombardment |
| FG | functional group |
| GC | gas chromatography |
| h | hour |
| HMPT | hexamethylphosphorous triamide |
| HRMS | high resolution mass spectroscopy |
| *n*-Bu | *n*-butyl |
| *i*-Pr | isopropyl |
| IR | infra-red |
| *J* | coupling constant (NMR) |
| LG | leaving group |
| M | molarity |
| *m* | meta |
| m | multiplet |

| | |
|---|---|
| Me | methyl |
| Met | metal |
| min | minute |
| mol. | mole |
| mp. | melting point |
| MS | mass spectroscopy |
| NBS | *N*-bromosuccinimide |
| NMR | nuclear magnetic resonance |
| Nu | nucleophile |
| *o* | ortho |
| *p* | para |
| Pent | pentyl |
| PG | protecting group |
| Ph | phenyl |
| Piv | pivaloyl |
| q | quartet |
| quint | quintet |
| rt | room temperature |
| s | singlet |
| sept | septet |
| t | triplet |
| *t*-Bu | *tert*-butyl |
| TBAF | tetrabutylammonium fluoride |
| TBS | *tert*-butyldimethylsilyl |
| TES | triethylsilyl |
| Tf | triflate |
| TFA | trifluoroacetic acid |
| tfp | *tri*-(2-furyl)phosphine |
| THF | tetrahydrofuran |
| TLC | thin layer chromatography |
| TMEDA | *N*,*N*,*N'*,*N'*-tetramethylethylenediamine |
| TMS | trimethylsilyl |
| TP | typical procedure |
| Ts | 4-toluenesulfonyl |

# THEORETICAL PART

# 1. Overview

Carbon-carbon bond formation is one of the most important processes in chemistry because it represents the key step for building more complex molecules from simple precursors. For instance, the addition of organometallic reagents to electrophiles, such as aldehydes or ketones, is a versatile method for the carbon-carbon bond formation (eq. 1, Scheme 1). Indeed, preparation of lithium, magnesium, zinc, boron and aluminium reagents has played an important role since the Grignard reagents were first employed more than one hundred years ago.[1] Besides, in the past 30 years, a wide variety of cross-coupling methodologies using organometallic reagents have been developed and become the most powerful and useful synthetic tools for C-C bond formation (eq. 2, Scheme 1).[2] Therefore, the development of synthetically useful methods for the preparation of polyfunctional organometallic reagents, such as Grignard and organozinc reagents, is attracting much research interest of organic chemists.




**Scheme 1**: Carbon-carbon formation by using organometallic reagents.

## 1.1 Preparation of organomagnesium and organozinc reagents

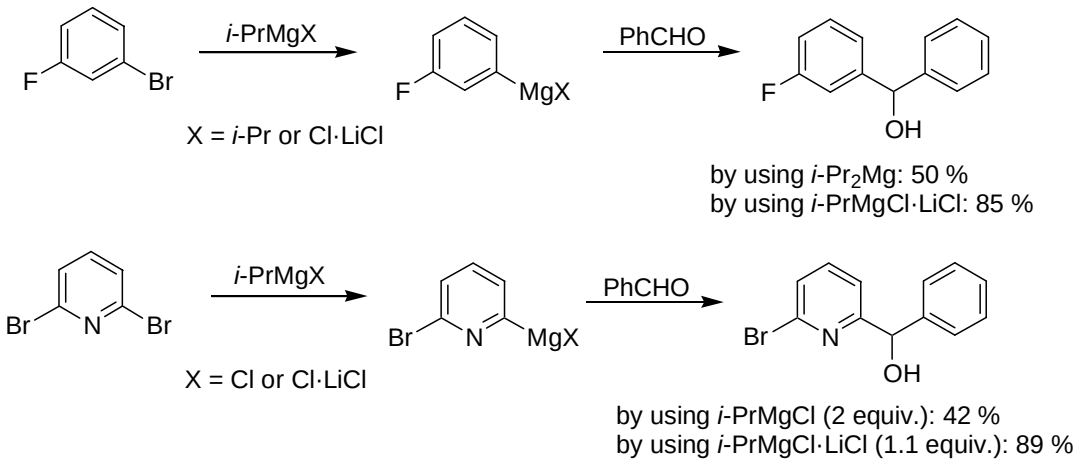
### 1.1.1 Halogen/magnesium or halogen/zinc exchange reactions

2

[1] a) *Handbook of Functionalized Organometallics*, Ed.: P. Knochel, Wiley-VCH, Weinheim, **2005**; b) *Main Group Metals in Organic Synthesis***,** Ed.: H. Yamamoto and K. Oshima, Wiley-VCH, Weinheim, **2004**; c) G. S. Silverman, P. E. Eds Rakita, *Handbook of Grignard Reagents*; Marcel Dekker: **1996**; d) Richey, Jr. H. G., Ed. *Grignard Reagents: New developments*; Wiley, New York: **1999**; e) P. Knochel, W. Dohle, N. Gommermann, F. F. Kneisel, F. Kopp, T. Korn, I. Sapountzis, V. A. Vu, *Angew. Chem.* **2003**, *115*, 4438; *Angew. Chem. Int. Ed.* **2003**, *42*, 4302; f) *Organolithiums: Selectivity for Synthesis*, Ed.: J. Clayden, Elsevier Science/Pergamon, Amsterdam, **2003**.

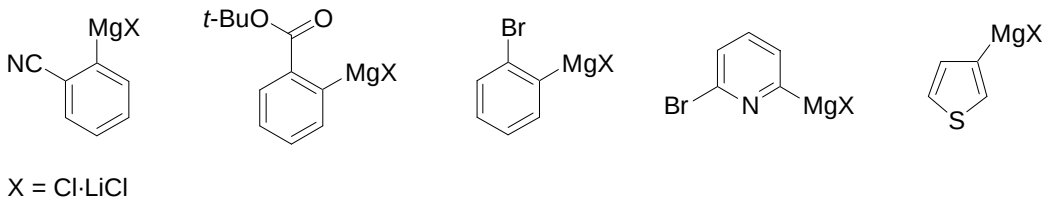
[2] For reviews on this topic, see a) *Metal-catalyzed Cross-coupling Reactions*; F. Diederich, P. J. Stang, Eds. Wiley-VCH: New York, 1998; b) J. Hassa, M. Sevignon, C. Gozzi, E. Schulz, M. Lemaire, *Chem. Rev.* **2002**, *102*, 1359; c) Metal-Catalyzed Cross-Coupling Reactions, 2nd ed. (Eds: A. de Meijere, F. Diederich), wiley-VCH, Weinheim, **2004**; d) *Palladium Reagents and Catalysts*, Ed.: J. Tsuji, John Wiley & Sons, Ltd, **2004.**

P. Knochel and co-workers have reported that highly functionalized aryl- and heteroaryl-magnesium halides can be readily prepared by using an iodine-magnesium exchange reaction.[3] It is worth noting that *i*-PrMgX (X = Cl, Br) has been proved to be the most convenient exchange reagent. Recently, Knochel developed a general halogen-magnesium exchange reaction using a super Grignard reagent: *i*-PrMgCl·LiCl.[4] Both aryl iodides and bromides undergo a halogen-magnesium exchange under very mild reaction conditions. By using this new Grignard reagent, preparation of organomagnesium reagents obtained *via* the bromine-magnesium exchange reaction is easily achieved (Scheme 2).




**Scheme 2.** Br/Mg exchange reactions with various magnesium reagents.

A number of aryl- and heteroaryl bromides with functional groups such as nitrile, *tert*-butyl ester, or bromine groups were readily converted to the corresponding magnesium reagents at room temperature using *i*-PrMgCl·LiCl (Scheme 3).



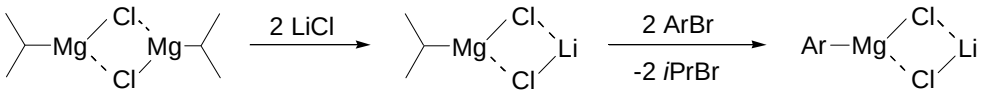

**Scheme 3.** Preparation of functionalized Grignard reagents *via* Br/Mg exchange reaction using *i*-PrMgCl·LiCl.

3

[3] a) L. Boymond, M. Rottländer, G. Cahiez, P. Knochel, *Angew. Chem.* **1998**, *110*, 1801; *Angew. Chem. Int. Ed*. **1998**, *37*, 1701; b) G. Varchi, A. E. Jensen, W. Dohle, A. Ricci, P. Knochel, *Synlett* **2001**, 477.

[4] A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed*. **2004**, *43*, 3333.

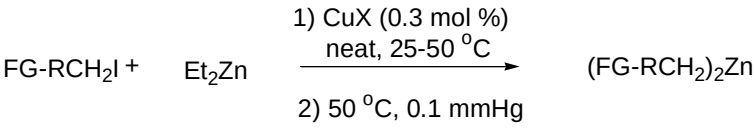
It is noteworthy that the necessity of using the stoichiometric complex *i*-PrMgCl·LiCl led the author to postulate that the addition of LiCl breaks the polymeric aggregates **1** of *i*-PrMgCl, producing the reactive complex **2**. The magnesiate character of **2** [*i*-PrMgCl$_2^-$Li$^+$] may be responsible for the enhanced reactivity of this reagent. Interestingly, the magnesiate character of the resulting organometallic complexes **3** is similar to that of a dimeric or oligomeric magnesium reagent prepared in the absence of LiCl (standard Grignard reagent), but the former displays higher reactivity towards electrophiles (Scheme 4).[5]

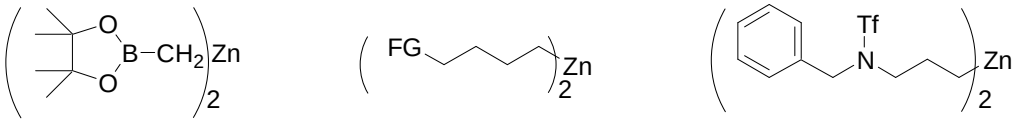



**1** **2** **3**

**Scheme 4.** Catalysis of the Br/Mg exchange reaction with LiCl.

It is well known that the iodine-zinc exchange reaction is also a practical way for preparing polyfunctional diorganozincs. This method provides a general and easy access to functionalized dialkylzincs (**4a-c,** Scheme 5).[6]




**4a** **4b** **4c**

**Scheme 5.** Preparation of polyfunctional dialkylzincs using an iodine-zinc exchange reaction.

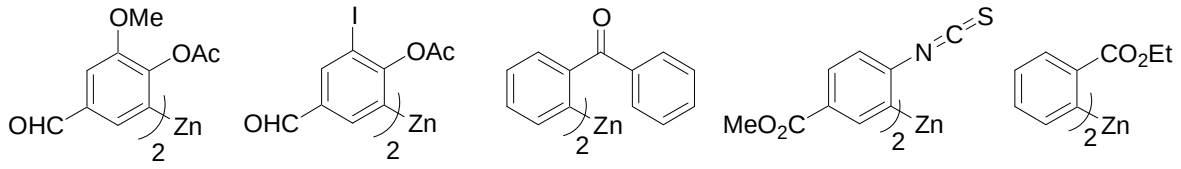
In 2004, P. Knochel and co-workers found that Li(acac) can dramatically accelerate the exchange reaction. These mild reaction conditions allow its compatibility with a range of sensitive functionalities such as aldehyde, ketone and isothiocyanate (Scheme 6).[7]

4

[5] The heterometallic organomagnesium complex RMgBr·LiBr·3THF (R=(Me$_3$Si)$_3$C) has been structurally characterized: N. H. Buttrees, C. Eaborn, M. N. A. E-Khely, P. B. Hitchcock, J. D. Smith, K. Tavakkoli, *J. Chem. Soc. Dalton Trans.* **1988**, 381.

[6] L. Micouin, P. Knochel, *Synlett* **1997**, 327.

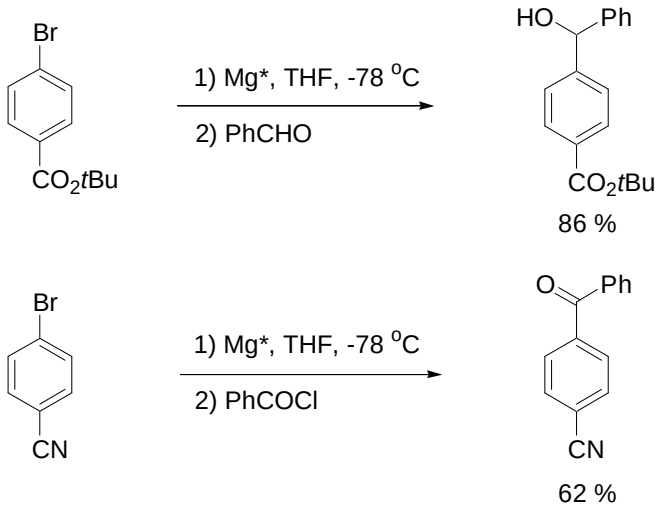
[7] F. F. Kneisel, M. Dochnahl, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 1017.




**Scheme 6.** Preparation of polyfunctional diarylzinc reagents in the presence of Li(acac).

### 1.1.2 Direct magnesium or zinc insertion into organic halides

Preparation of functionalized Grignard reagents *via* a direct magnesium insertion is extremely difficult to achieve due to the high reductive reactivity of magnesium towards many functional groups. However, using highly active magnesium (such as Rieke Magnesium), a direct Mg insertion into aryl bromides containing a nitrile or ester group can be carried out at low temperature (Scheme 7).[8]




**Scheme 7.** Preparation of functionalized Grignard reagents using Rieke Magnesium.

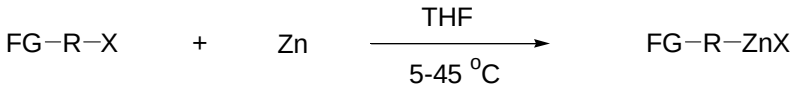
In addition, the direct insertion of zinc dust into organic halides has become the most attractive and simplest method for the preparation of functionalized organozinc halides. Functional groups such as ester, ether, acetate, ketone, nitrile, halide, primary and second amines, amide, sulfoxide, sulfide, sulfone and boronic acid are tolerated during the formation of alkylzinc halides (Scheme 8).[9] However, the preparation of arylzinc iodides in THF from

5

[8] a) R. D. Rieke, *Science* **1989**, *246*, 1260; b) T. P. Burns, R. D. Rieke, *J. Org. Chem.* **1987**, *52*, 3674; c) J. Lee, R. Velarde-Ortiz, A. Guijarro, J. R. Wurst, R. D. Rieke, *J. Org. Chem.* **2000**, *65*, 5428; d) R. D. Rieke, T. –J. Li, T. P. Burns, S. T. Uhm, *J. Org. Chem.* **1981**, *54*, 4323; e) R. D. Rieke, M. S. Sell, T. Chen, J. D. Brown, M. V. Hansan, in *Active Metals*, A. Fuerstner, Ed., Wiley-VCH, Weinheim, **1995**.

[9] *Handbook of Functionalized Organometallics: Applications in Synthesis*, Ed.: P. Knochel, Wiley-VCH, Weinheim, **2005**.

aryl iodides can only be achieved by using highly activated zinc powder (Rieke Zn)[10] or requiring the presence of electron-withdrawing groups in the *ortho*- position of the aryl iodides, as well as by elevated temperatures.[11]



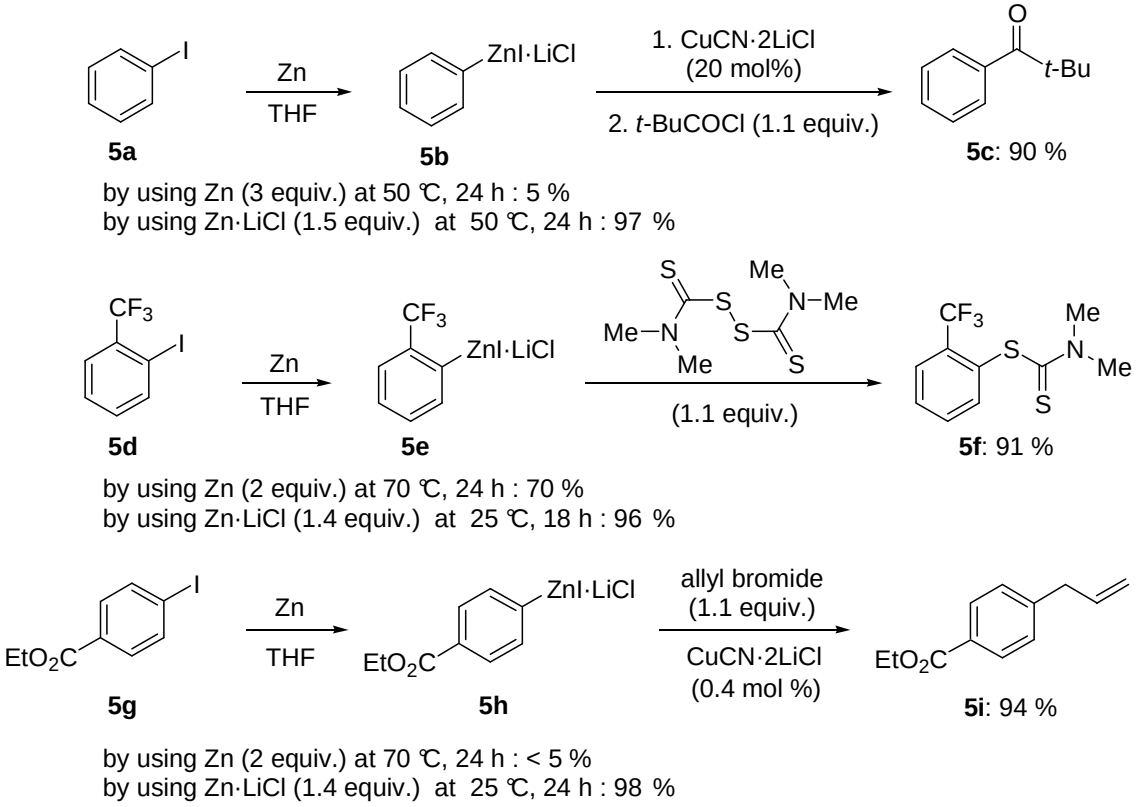

X = I, Br;

FG = $CO_2R$, CN, halide, $(RCO)_2N$, $(TMS)_2N$, RCONH, $(RO)_3Si$, RSO, $RSO_2$

R = alkyl, aryl, benzyl, allyl

**Scheme 8.** Preparation of functionalized organozinc reagents by a direct zinc insertion.

Recently, P. Knochel and co-workers have reported a new protocol for the preparation of functionalized aryl- and alkylzinc compounds by the direct insertion of commercially available Zn powder in the presence of LiCl in THF (Scheme 9).[12]

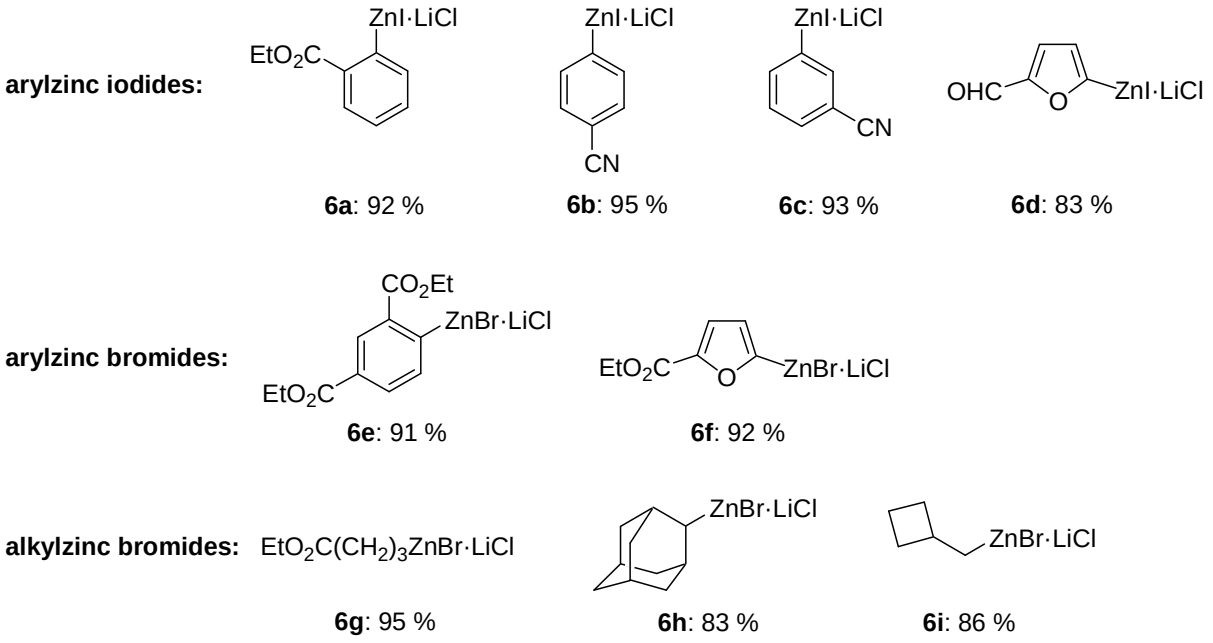



**Scheme 9.** Insertion of Zn in the presence and absence of LiCl.

6

[10] a) *Organozinc Reagents*, Editors: P. Knochel, P. Jones, Oxford University press, New York, **1999**; b) R. D. Rieke, P. T. Li, T. P. Burns, S. T. Uhm, *J. Org. Chem.* **1981**, *46*, 4323; c) R. T. Arnold, S. T. Kulenovic, *Synth. Commun.* **1977**, *7*, 223.
[11] R. Ikegami, A. Koresawa, T. Shibata, K. Takagi, *J. Org. Chem.* **2003**, *68*, 2195.
[12] A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem. Int. Ed.* **2006**, *45*, 6040.

A broad range of functionalized arylzinc iodides **6a-6d** (Scheme 10) bearing functional groups such as aldehyde, ester, nitrile or amide have been synthesized in excellent yields (83-95 %). Interestingly, the insertion of Zn into C-Br bond is also possible in the case of activated aryl- and heteroaryl compounds (**6e**, **6f**). Surprisingly, the unactivated primary alkyl bromides can also be converted to the corresponding alkylzinc reagents by using Zn·LiCl (**6g-6i**, Scheme 10).[12]




**Scheme 10.** Preparation of functionalized organozinc halides using Zn·LiCl.

## 1.2 Preparation of triazene as a versatile compound in organic synthesis

### 1.2.1 Introduction

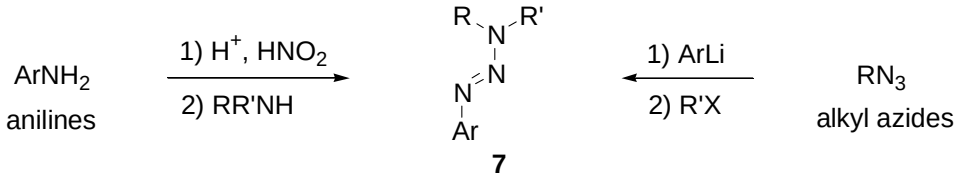
Triazenes (RN=N−NR'R'') are useful and versatile compounds in preparative chemistry because they are stable and adaptable to numerous synthetic transformations. They have been studied for their potential anticancer properties,[13,14] used as protecting group in natural product synthesis [15] and combinatorial chemistry, [16] incorporated into polymer [17] and

7

[13] C. A. Rouzer, M. Sabourin, T. L. Skinner, E. J. Thompson, T. O. Wood, G. N. Chmurny, J. R. Klose, J. M. Roman, R. H. Smith, Jr., C. J. Michejda, *Chem. Res. Toxicol*. **1996**, *9*, 172-178.
[14] T. A. Connors, P. M. Goddard, K. Merai, W. C. J. Ross, D. E. V. Wilman, *Biochem. Pharmacol*. **1976**, *25*, 241-246.
[15] K. C. Nicolaou, C. N. C. Boddy, H. Li, A. E. Koumbis, R. Hughes, S. Natarajan, N. F. Jain, J. M. Ramanjulu, S. Bräse, M. E. Solomon, *Chem. Eur. J.* **1999**, *5*, 2602-2621.
[16] S. Bräse, S. Dahmen, M. Pfefferkorn, *J. Comb. Chem*. **2000**, *2*, 710-715.
[17] L. Jones II, J. S. Schumm, J. M. Tour, *J. Org. Chem*. **1997**, *62*, 1388-1410.

oligomer[18] synthesis, and used to prepare some heterocycles.[19] Furthermore, triazenes can be also converted into different functional groups after treatment with the appropriate reagents. Take aryl triazenes as an example, iodomethane-induced decomposition affords an iodoarene, which can undergo cross-coupling reactions. In the presence of Lewis acids, both a diazonium and an ammonium species are generated and each can be used depending on the desired application.[20] Disubstituted triazenes can also form anions which are useful as ligands in organometallic chemistry.[21]

Triazenes of type **7** are easily prepared from readily available anilines or alkyl azides (Scheme 11). Treatment of anilines with nitrite ion under acidic conditions to form a diazonium salt, which is quenched with a primary or secondary amine to give the desired triazenes in excellent yields. Alternatively, dialkyl triazenes can be also produced from the reaction of an alkyl azide with a Grignard or alkyllithium reagent.




**Scheme 11**. Preparation of triazenes.

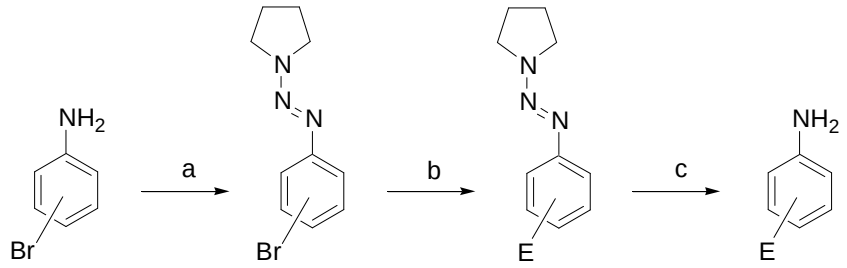
### 1.2.2 Protection/Generation of an amine from a triazene

Using a triazene can be an easy access to protect or generate an amine. Although the formation of an amine by the acid-induced decomposition of aryl triazenes has been known,[22] this particular use is not as many as other protecting groups.[23] However, triazenes have shown to be indeed useful for this purpose and they are fairly stable to a variety of conditions.[24] For instance, triazenes are particularly useful protecting groups for anilines when undergoing halogen-metal exchanges. Gross, Blank, and Welch used a series of triazene-protected

8

[18] J. S. Moore, *Acc. Chem. Res*. **1997**, *30*, 402-413, and references therein.
[19] W.Wirshun, M.Winkler, K. Lutz, J. C. Jochims, *J. Chem. Soc. Perkin Trans.* **1998**, *2*, 1755-1762.
[20] H. Zollinger, *Diazo Chemistry, Vol. I*, VCH, Weinheim, **1994**.
[21] H. G. Ang, L. L. Koh, G. Y. Yang, *J. Chem. Soc. Dalton Trans*. **1996**, 1573-1581
[22] K. H. Saunders, *The Aromatic Diazo Compounds*, 2nd ed., Longmans, Green and Co., New York, **1949**, pp. 157-179, and references therein.
[23] *Protective Groups in Organic Synthesis*, 3nd ed. (Eds.: T. W. Greene, P. G. M. Wuts), Wiley, New York, **1999**, pp. 494-653.
[24] E. B. Merkushev, *Synthesis* **1988**, 923-937.

bromoanilines for Br/Li exchange and followed by the reaction with electrophiles (Scheme 12).[25]




E = $CO_2$, PhCOPh, PhSSPh, $Me_3SiCl$, $D_2O$, MeCOMe, $Bu_3SnCl$, etc

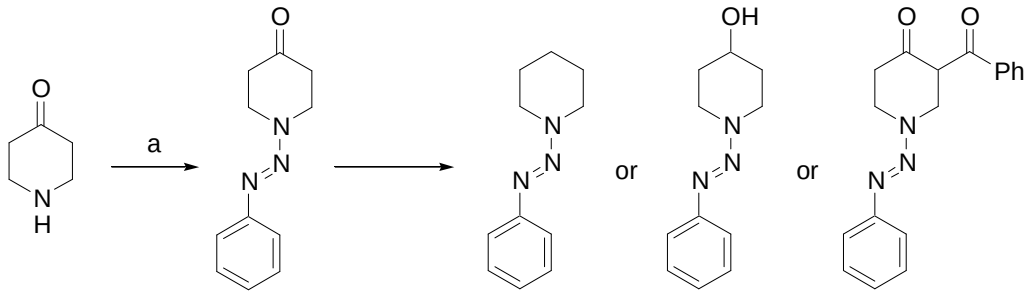
**Scheme 12.** a) 1. HCl, $NaNO_2$; 2. KOH, pyrrodine; b) 1. *s*BuLi or *t*BuLi; 2. electrophile ($E^+$); c) Ni/Al, KOH, MeOH.

The triazene moiety was stable to electrophilic reagents and its compatibility with *meta*- and *para*-carbanion formation. The readily available bromoanilines were converted into the triazenes and metalated with *sec*- or *tert*-butyllithium to generate aryl carbanions which reacted smoothly with carbon, sulfur, and silicon electrophiles, or with deuterium oxide. The corresponding anilines were regenerated using nickel-aluminum alloy in methanolic hydroxide solution. Generally speaking, triazenes are quantitatively transformed to anilines in almost all cases.[26]

Non-aromatic amines can also be protected efficiently as triazenes. Lazny *et al*. used the triazene group to protect 4-piperidone **8**.[27] After 4-piperidone reacted with phenyldiazonium salt, the resulting triazene **9** was stable to $LiAlH_4$, chromium-based oxidants, $NaBH_4$, and other reagents to provide several useful products (**10a-c**, Scheme 13). The amines were regenerated in good yield using 50 % trifluoroacetic acid (TFA) in $CH_2Cl_2$ at room temperature. Other secondary amines protected as triazenes for similar purposes include piperazine derivatives, [28] proline derivatives,[28] 3-alkoxy-4-aryl piperidines, [29] and nortropanes.[28]

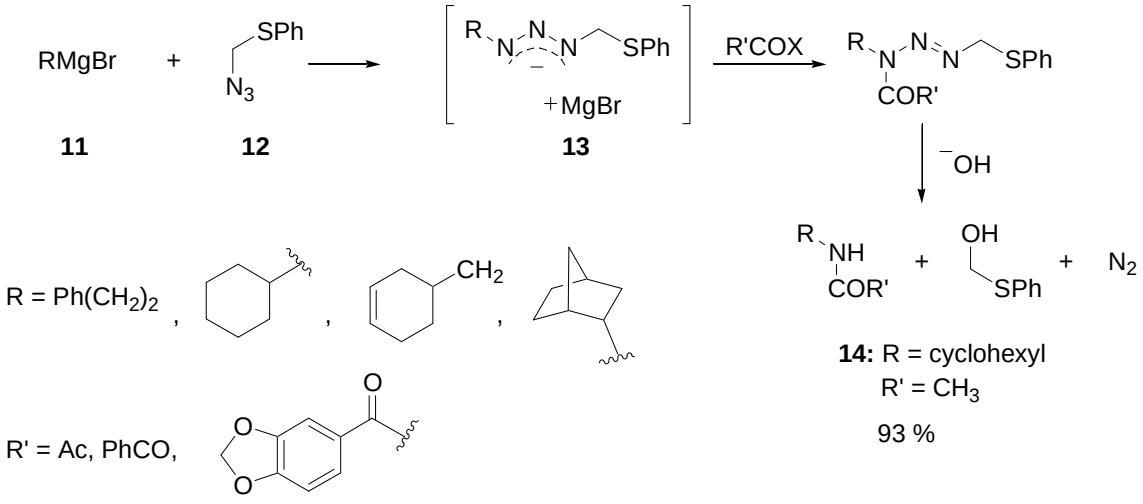
9

[25] M. L. Gross, D. H. Blank, W. M. Welch, *J. Org. Chem.* **1993**, *58*, 2104-2109.
[26] G. Lunn, E. B. Sansone, *Synthesis* **1985**, 1104-1108.
[27] R. Lazny, J. Poplawski, J. Köbberling, D. Enders, S. Bräse, *Synlett* **1999**, 1304-1306.
[28] R. Lazny, M. Sienkiewicz, S. Bräse, *Tetrahedron* **2001**, *57*, 5825-5832
[29] M. G. Bursavich, D. H. Rich, *Org. Lett*. **2001**, *3*, 2625-2628.




**Scheme 13.** a) $PhN_2BF_4$, $Et_3N$.

It is interesting that triazenes can be also used as intermediates to prepare useful amines. Unlike typical syntheses, however, the amine is not used to form the triazene. Instead, an alkyl or aryl anion reacts with an azide. Trost and Pearson showed that alkyl or aryl bromides can be readily converted into amines by using this method.[30,31] The bromide compounds were first converted into the Grignard reagents **11** and then treated with azidomethylphenyl sulfide **12** (Scheme 14). The triazene anion **13** formed could be quenched either with a proton or an acyl source, depending on the substituent desired on the final amine. The methylphenyl sulfide substituent on the azide dictates this configuration and promotes initial triazene formation. The sulfur atom also promotes decomposition to the desired amines **14** by various nucleophiles. The authors found that aqueous formic acid would also release the amine or amide from the triazene.

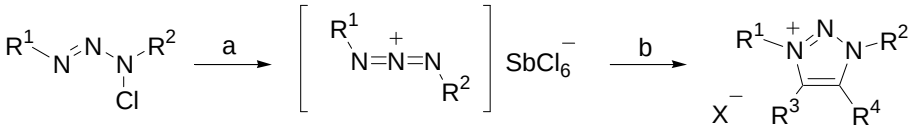



**Scheme 14.** Amide synthesis *via* acylated triazenes.

[30] B. M. Trost,W. H. Pearson, *J. Am. Chem. Soc*. **1981**, *103*, 2483-2485.
[31] B. M. Trost,W. H. Pearson, *J. Am. Chem. Soc*. **1983**, *105*, 1054-1056.

### 1.2.3 Triazenes used to synthesize heterocycles

Heterocycle synthesis is an important and interesting area in organic chemistry. Triazene chemistry reflects this by showing a remarkable and sometimes unexpected tendency to produce new heterocycles. Indeed, triazenes could be used as synthetic precursors for heterocycles which are unattainable by other routes. For example, N-chloro-substituted triazenes of type **15** can react with dipolarophiles to give heterocyclic products of type **16**. Jochims and co-workers have observed [3+2] cycloadditions between 1,3-diaza-2-azoniaallene ions (**17**, Scheme 15) and dipolarophiles such as alkenes,[32] 1,3-butadienes,[33] alkynes, carbodiimides, and cyanamides.[34]




**15** **17** **16:** $R_3 = R_4 = H$, 83 %

$R^1$, $R^2$ = 2,4,6-$Cl_3C_6H_2$

$R_3$ = H, Bu, *t*Bu, $CH_2OH$, Et, $CH_2Cl$, Me, Ph, $CO_2Me$

$R_4$ = H, Et, $CH_2Cl$, Ph, $CO_2Me$

**Scheme 15.** a) $SbCl_5$, $CH_2Cl_2$, -60 °C; b) $R^3C{\equiv}CR^4$, $CH_2Cl_2$, -60 to 23 °C.

The dipolar ions were prepared by the reaction of N-chlorotriazenes with Lewis acids, usually $SbCl_5$. Cycloadditions were carried out at low temperatures because of instability of the chlorotriazenes and its corresponding dipolar ions.

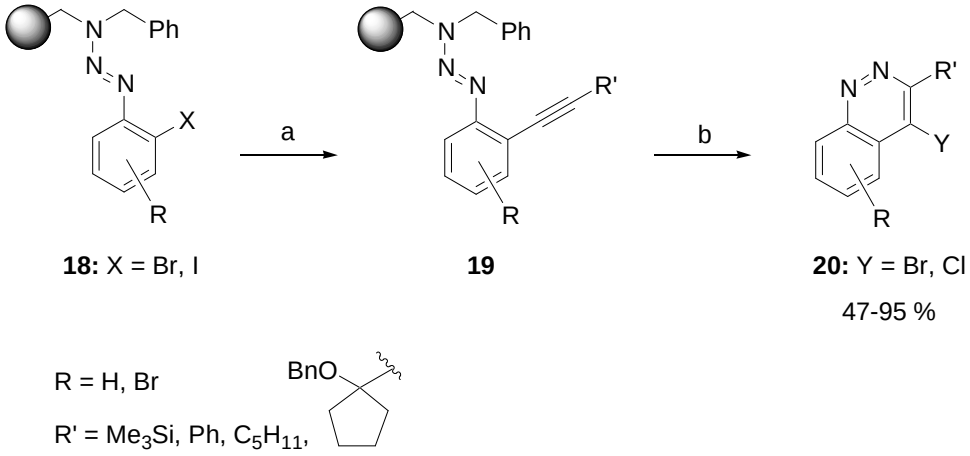
The Richter cyclization of an aromatic diazonium ion *ortho* to an acetylene functionality to give a cinnoline has been utilized extensively since its discovery in 1883.[35] The cinnolines produced are substituted at the 4-position as a result of nucleophilic attack on the acetylene to start the cyclization.

In 1999, Bräse *et al*. modified the Richter cyclization to include triazenes as protected diazonium species (Scheme 16).[36] This modification also allows the triazenes to be attached

11

[32] W. Wirschun, J. C. Jochims, *Synthesis* **1997**, 233-241.
[33] W. Wirschun, G.-M. Maier, J. C. Jochims, *Tetrahedron* **1997**, *53*, 5755-5766.
[34] W.Wirschun, M.Winkler, K. Lutz, J. C. Jochims, *J. Chem. Soc. Perkin Trans. 1* **1998**, 1755-1762.
[35] V. von Richter, *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 677-683.
[36] S. Bräse, S. Dahmen, J. Heuts, *Tetrahedron Lett*. **1999**, *40*, 6201-6203.

to a solid support, benzylaminomethyl polystyrene, which significantly simplifies the purification of starting materials. Using anilines substituted at the *ortho* and *para* positions, formation of the diazonium ion followed by quenching with the solid-supported amine provides the aryl triazenes of type **18**. Sonogashira coupling[37,38] was performed with the halogenated aryl triazenes to give the required *ortho*-alkyne precursors of type **19**. Cleavage of the resin under acidic conditions generates the diazonium species which cyclizes to the cinnolines **20** in moderate to good yields. However, the Richter cyclization produces only 4-substituted cinnolines, which could be a limitation of this method.

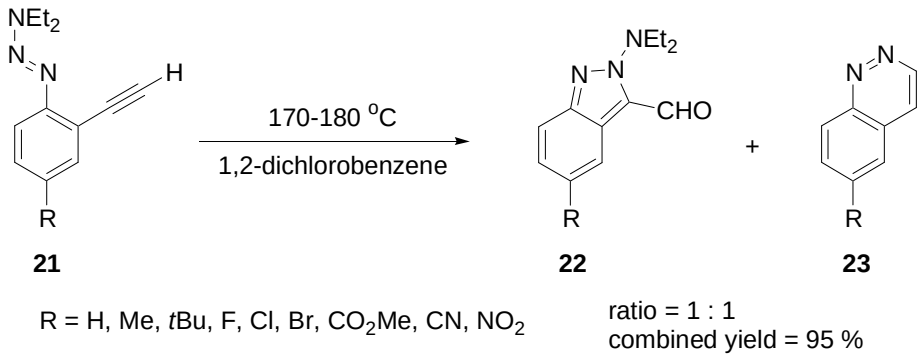



**Scheme 16.** A modified Richter cyclization used to synthesize cinnolines. a) HC≡CR', $Pd(OAc)_2$, $NEt_3$, DMF, 80 $^oC$, 12 h; b) HY, acetone/$H_2O$.

It is noteworthy that a new method for the preparation of cinnolines as well as isoindazoles from aryl triazene moieties *ortho* to alkyne has been developed by Haley and co-workers in 2000.[39] 1-(2-Ethynylphenyl)-3,3-diethyltriazenes (**21**) was heated to 170-180 $^oC$ in 1,2-dichlorobenzene gaving a mixture of isoindazole (**22**) and cinnoline (**23**). A wide range of functional groups were tolerated under the neutral conditions. High yields (>90%) of **23** were obtained by heating the starting triazenes to 190-200 $^oC$. Comparable yields and exclusive formation of **22** could be achieved at much lower temperatures (≈50 $^oC$) when these cyclizations were performed in the presence of CuCl (Scheme 17).[40]

12

[37] K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, 4467-4470.
[38] K. Sonogashira in *Metal-catalyzed Cross-coupling Reactions* (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, **1998**, pp. 203-230.
[39] D. B. Kimball, A. G. Hayes, M. M. Haley, *Org. Lett.* **2000**, *2*, 3825-3827.
[40] D. B. Kimball, R. Herges, M. M. Haley, *J. Am. Chem. Soc.* **2002**, *124*, 1572-1573.




**Scheme 17.** Synthesis of isoindazoles and cinnolines.

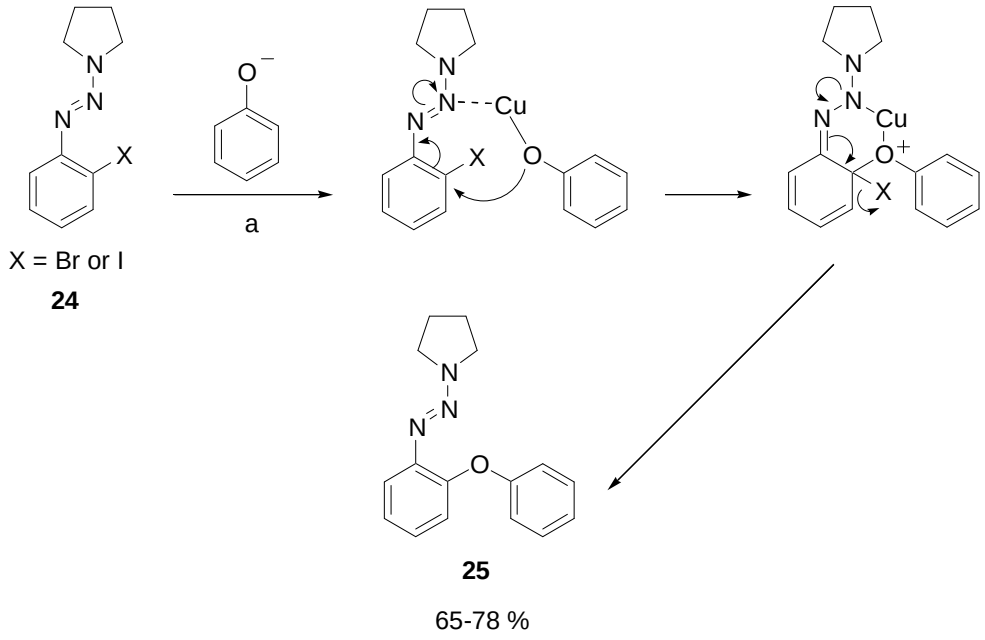
### 1.2.4 Converting triazenes into other functional groups

Triazenes have been used to produce many different types of functional groups other than amines and heterocycles. The synthesis of halides is a notable example. In other words, triazenes can be decomposed to give aryl fluorides[41] and aryl iodides.[42] Other functional groups which can be generated from triazenes include phenols,[22] alkenes,[43] biaryls,[44,45] and products resulting from aryne intermediates.[46]

In 1997, Nicolaou and co-workers reported an interesting use of aryl triazenes in the total synthesis of vancomycin.[47] The triazene functionality served a dual purpose: to protect a reactive site for later conversion into a phenol and to aid in the construction of *ortho* biaryl ether functionalities (Scheme 18). The (*ortho*-haloaryl)triazene **24** was treated with phenolic counterparts in the presence of base and CuBr to give the desired ether **25**. Sequential reaction of the 2,6-dihalogenated aryl triazene backbone with phenols installed the necessary regiochemistry for each macrocyclic ring system.

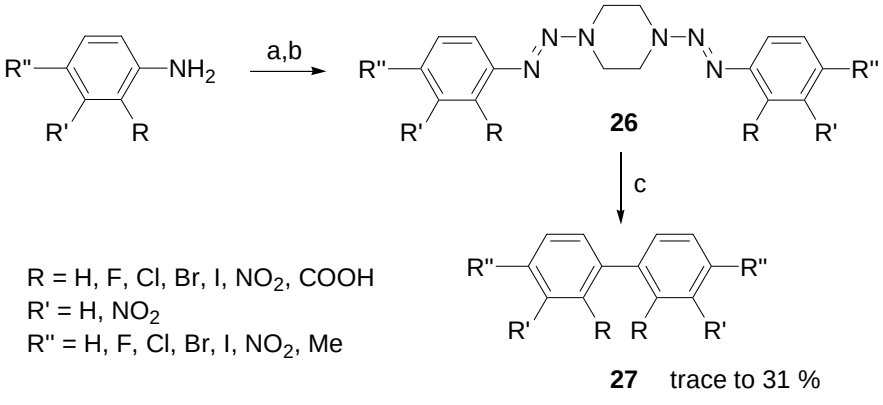
13

[41] T. Pages, B. R. Langlois, D. Le Bars, P. Landais, *J. Fluorine Chem*. **2001**, *107*, 329-335.
[42] A. Khalaj, D. Beiki, H. Rafiee, R. Najafi, *J. Labelled Compd. Radiopharm.* **2001**, *44*, 235-240.
[43] S. Bhattacharya, S. Majee, R. Mukherjee, S. Sengupta, *Synth. Commun*. **1995**, *25*, 651-657.
[44] E. Yanarates, A. Disili, Y. Yildirir, *Org. Prep. Proced. Int.* **1999**, *31*, 429-433.
[45] T. B. Patrick, R. P. Willaredt, D. J. DeGonia, *J. Org. Chem.* **1985**, *50*, 2232-2235.
[46] P. C. Buxton, H. Heaney, *Tetrahedron* **1995**, *51*, 3929-3938.
[47] a) K. C. Nicolaou, C. N. C. Boddy, S. Natarajan, T. Y. Yue, H. Li, S. Bräse, J. M. Ramanjulu, *J. Am. Chem. Soc*. **1997**, *119*, 3421-3422.; b) K. C. Nicolaou, S. Natarajan, H. Li, N. F. Jain, R. Hughes, M. E. Slolomon, J. M. Ramanjulu, C. N. C. Boddy, M. Takayanagi, *Angew. Chem*. **1998**, *110*, 2872-2878; *Angew. Chem. Int. Ed*. **1998**, *37*, 2708-2714.; c) K. C. Nicolaou, N. F. Jain, S. Natarajan, R. Hughes, M. E. Solomon, H. Li, J. M. Ramanjulu, M. Takayanagi, A. E. Koumbis, T. Bando, *Angew. Chem*. **1998**, *110*, 2879-2881; *Angew. Chem. Int. Ed*. **1998**, *37*, 2714-2716.; d) K. C. Nicolaou, M. Takayanagi, N. F. Jain, S. Natarajan, A. E. Koumbis, T. Bando, J. M. Ramanjulu, *Angew. Chem*. **1998**, *110*, 2881-2883; *Angew. Chem. Int. Ed*. **1998**, *37*, 2717-2719.




**Scheme 18.** a) $CuBr \cdot Me_2S$, $K_2CO_3$, pyridine, MeCN, 75 $^oC$, 3 h

A variety of methods can be used for biaryl synthesis. Using transition-metal catalysis is the most reliable and practical way to achieve this goal, and Suzuki coupling reaction is a typical example.[48] However, triazenes also provide an alternative route to biaryls, which is mild and avoids using expensive catalysts. Patrick, Willaredt, and DeGonia have shown that TFA-promoted decomposition of aryl triazenes in benzene affords the corresponding heterocoupled biaryl compounds in good yields.[45] Interestingly, Yildirir and co-workers prepared a similar series of homocoupled biaryls starting from bistriazenes of type **26** obtained by quenching aryl diazonium compounds with piperazine (Scheme 19).[44] Decomposition of the triazenes and biaryl coupling reaction occurred under acidic conditions at 90 $^oC$. Unfortunately, the yields of biaryls of type **27** ranged from trace amounts to 31 %.



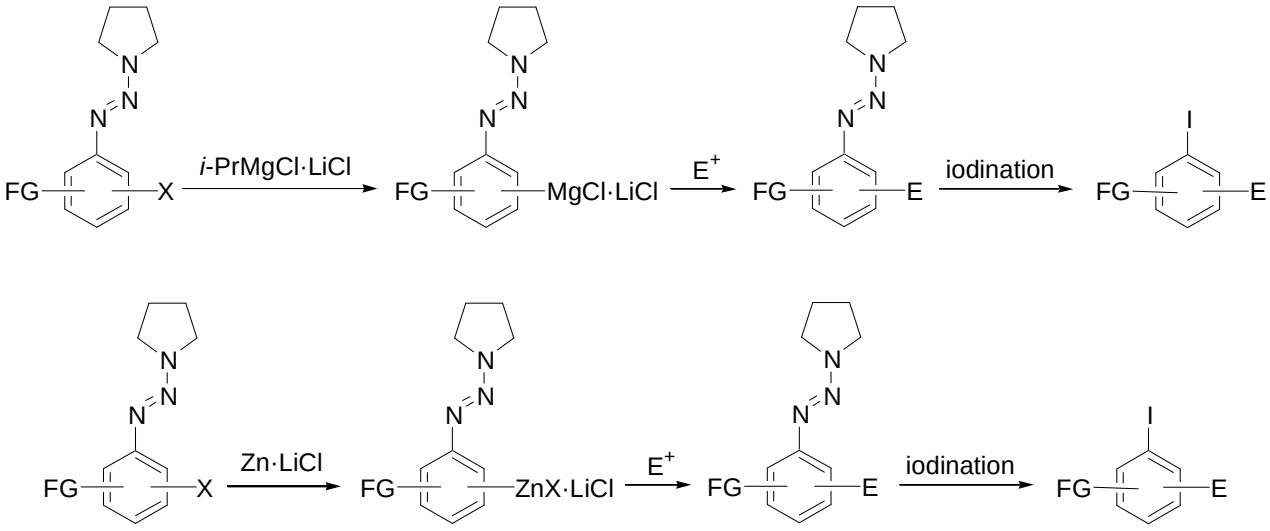

**Scheme 19.** a) HCl, $NaNO_2$; b) piperazine; c) AcOH, 85-90 $^oC$.

[48] U. C. Dyer, P. D. Shapland, P. D. Tiffin, *Tetrahedron Lett.* **2001**, *42*, 1765-1767.

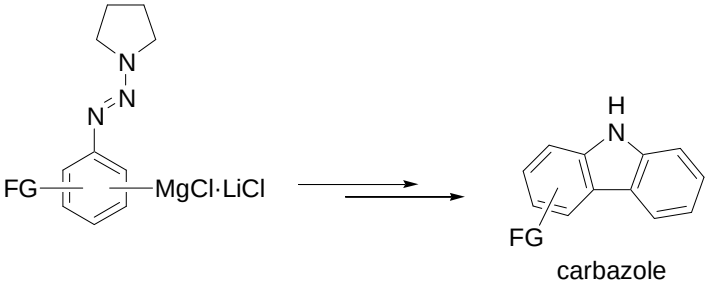
## 2. Objectives

Since the successful development of a mild I/Mg- or Br/Mg-exchange reaction and a direct zinc insertion procedure, it would be interesting to apply these methodologies to the functionalization of halogenated aryl triazenes (Scheme 20, 21). The objectives are presented as followed:

- an easy access to polyfunctional arylmagnesium reagents bearing a triazene moiety *via* I/Mg- or Br/Mg-exchange reactions.
- an easy access to polyfunctional arylzinc reagents bearing a triazene moiety *via* direct zinc insertion reactions.
- preparation of polyfunctional iodoarenes *via* the conversion of a triazene to an iodide.
- development of a new carbazole synthesis starting from the arylmagnesium reagents.



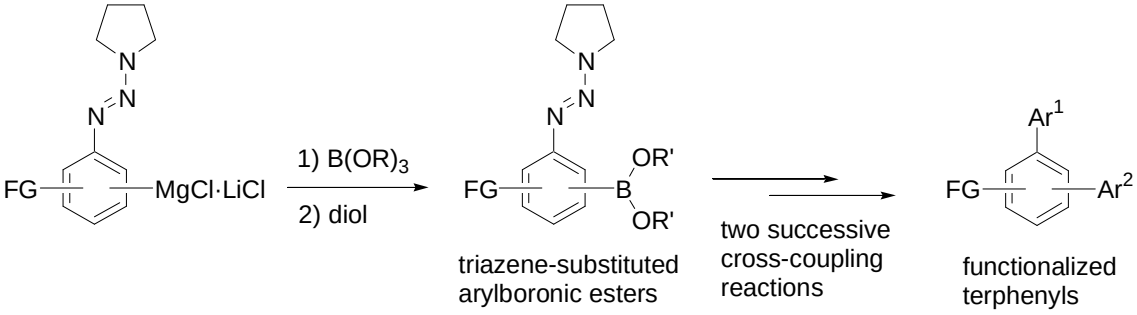

**Scheme 20.** Generation of polyfunctional arylmagnesium or arylzinc reagents bearing a triazene moiety.



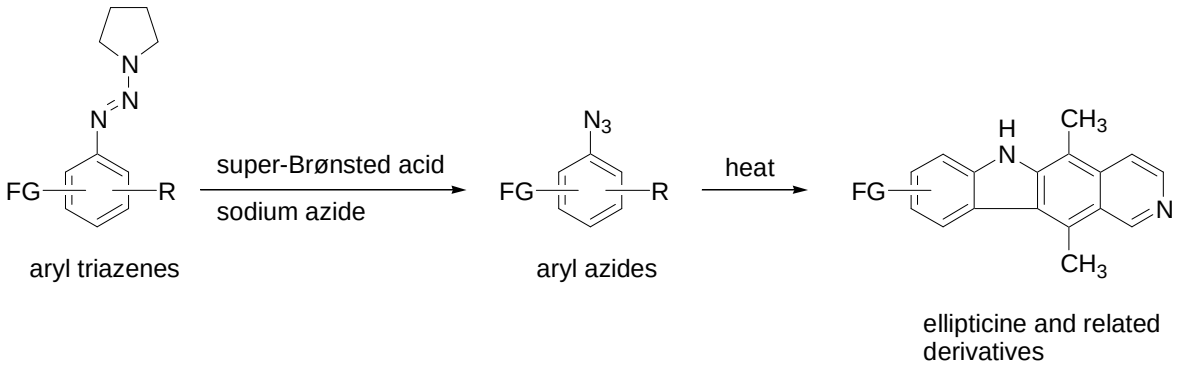

**Scheme 21.** A new carbazole synthesis.

In the second part, we would like to use the methodology mentioned above to prepare arylboronic esters bearing a triazene moiety and to synthesize polyfunctional aryl azides from the corresponding aryl triazenes (Scheme 22, 23). The objectives are:

- preparation of functionalized terphenyls from triazene-substituted arylboronic esters *via* two successive cross-coupling reactions.
- an easy access to polyfunctional aryl azides *via* a super-Brønsted acid induced decomposition of aryl triazenes in the presence of sodium azide.
- the conversion from a triazene to an azide would be used as a key-transformation in the total synthesis of ellipticine and related derivatives.




**Scheme 22.** Synthesis of functionalized terphenyls.

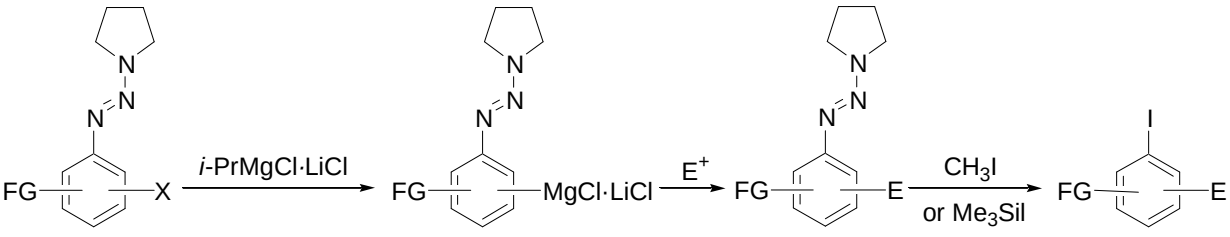



**Scheme 23.** Preparation of polyfunctional aryl azides and a new ellipticine synthesis.

# 3. Preparation of Polyfunctional Arylmagnesium Reagents Bearing a Triazene Moiety

## 3.1 Introduction

Using the triazene functionality ($ArN=N-NR_2$) is a convenient way to protect a diazonium salt and to carry this reactive functionality through several steps. It has also proved its utility as a linker in solid phase combinatorial synthesis.[49] Of special synthetic interest is its conversion to an iodide function under mild conditions.[50] Recently, we have developed a general halogen-magnesium exchange reaction using the mixed Mg/Li-reagent: *i*-PrMgCl·LiCl.[51] Both aryl iodides and bromides undergo a halogen/magnesium exchange under mild conditions. Since this exchange reaction tolerates many functional groups, we envisioned the compatibility of a halogen/magnesium exchange with a triazene moiety. Reaction of halogenated aryl triazenes of type **28** with *i*-PrMgCl·LiCl would generate the polyfunctional arylmagnesium reagents of type **29**, which might react with a number of electrophiles to give polyfunctional triazenes of type **30**. Furthermore, we have also envisaged that these triazenes **30** would be converted the corresponding aryl iodides of type **31** (Scheme 24).




**Scheme 24.** General reaction sequence.



[49] For reviews, see: (a) D. B. Kimball, M. M. Haley, *Angew. Chem. Int. Ed.* **2002**, *41*, 3338; (b) J. S. Moore, *Acc. Chem. Res.* **1997**, *30*, 402; (c) S. Bräse, *Acc. Chem. Res.* **2004**, *37*, 805. See also: (d) K. C. Nicolaou, H. Li, C. N. C. Boddy, J. M. Ramanjulu, T. Y. Yue, S. Natarajan, X. J. Chu, S. Bräse, F. Rübsam, *Chem. Eur. J.* **1999**, *5*, 2584; (e) D. Enders, C. Rijksen, E. Bremus-Köbberling, A. Gillner, J. Köbberling, *Tetrahedron Lett.* **2004**, *45*, 2839; (f) M. E. P. Lormann, S. Dahmen, F. Avemaria, F. Lauterwasser, S. Bräse, *Synlett*, **2002**, 915; (g) D. B. Kimball, R. Herges, M. M. Haley, *J. Am. Chem. Soc.* **2002**, *124*, 1572; (h) D. B. Kimball, T. J. R. Weakley, M. M. Haley, *J. Org. Chem.* **2002**, *67*, 6395; (i) M. L. Gross, D. H. Blank, W. M. Welch, *J. Org. Chem.* **1993**, *58*, 2104.

[50] (a) J. S. Moore, E. J. Weinstein, Z. Wu, *Tetrahedron Lett*. **1991**, *32*, 2465; (b) Z. Wu, J. S. Moore, *Tetrahedron Lett*. **1994**, *35*, 5539; (c) H. Ku, J. R. Barrio, *J. Org. Chem.* **1981**, *46*, 5239; (d) W. B. Wan, R. C. Chiechi, T. J. R. Weakley, M. M. Haley, *Eur. J. Org. Chem*. **2001**, 3485.

[51] (a) A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed*, **2004**, *43*, 3333; (b) F. Kopp, A. Krasovskiy, P. Knochel, *Chem. Commum*. **2004**, 2288; (c) H. Ren, A. Krasovskiy, P. Knochel, *Org. Lett*. **2004**, *6*, 4215; See also: (d) P. Knochel, W. Dohle, N. Gommermann, F. F. Kneisel, F. Kopp, T. Korn, I. Sapountzis, V. A. Vu, *Angew. Chem. Int. Ed*. **2003**, *42*, 4302.

## 3.2 Preparation of polyfunctional aryl triazenes

We have found that in the case of the reaction of iodotriazene with *i*-PrMgCl, the triazene group reacted, and no arylmagnesium reagent was formed. However, by using the more reactive exchange reagent *i*-PrMgCl·LiCl, this exchange reaction proceeds smoothly. Therefore, we have developed a novel method for the preparation of polyfunctional arylmagnesium reagents bearing a triazene functionality of type **29** starting from the aromatic halides of type **28** (X = I or Br) and leading to polyfunctional triazenes such as **30** which can be converted to the polyfunctional iodides **31,** allowing an effective functionalization of aromatic derivatives (Scheme 24).[52]

Thus, 1-(2,6-dibromophenylazo)pyrrolidine (**28a**) obtained from 2,6-dibromoaniline in 95 % yield reacts with *i*-PrMgCl·LiCl (1.1 equiv, -40 $^{o}$C to -15 $^{o}$C, 5 h) affording the expected arylmagnesium derivative **29a** (see entries 1-4 of Table 1). After a transmetalation with CuCN·2LiCl,[53] the resulting copper reagent is readily allylated giving the triazene **30a** (78 %; entry 1 of Table 1). Acylation of the copper derivatives of **29a** or **29b** (obtained from 1-(2,6-dibromo-4-methylphenylazo)pyrrolidine (**28b**) *via* the reaction with *i*-PrMgCl·LiCl under similar conditions) with acyl, heteroaryl or aliphatic acid chlorides furnishes the expected ketones **30b** (82 %; entry 2), **30c** (85 %; entry 3) or **30e** (82 %; entry 5). An addition-elimination reaction with 3-iodo-2-cyclohexen-1-one leads to the triazene **30d** in 80 % yield (entry 4). Starting with 1-(2-iodo-4-carboethoxyphenylazo)pyrrolidine (**28c**), the reaction with *i*-PrMgCl·LiCl is complete within 40 min at -40 $^{o}$C leading to the polyfunctional magnesiated triazene (**29c**; entries 6-8) which reacts with electrophiles leading to the ester-substituted triazenes **30f**, **30g**, and **30h** in 78-86 %. A similar transformation is also achieved for a cyano-substituted iodoaryltriazene (**28d**) providing the Grignard reagent (**29d**) and the acylated products **30i** (86 %; entry 9) and **30j** (85 %; entry 10). Finally, not only triazenes bearing a halogen in the *ortho*-position undergo a halogen/magnesium exchange smoothly, but also 1-(4-iodophenylazo)pyrrolidine (**28e**) reacts with *i*-PrMgCl·LiCl (-40 $^{o}$C, 40 min) affording the corresponding magnesiated triazene **29e**. Its direct reaction with EtCHO provides the benzylic alcohol **30k** (90 %; entry 11). A copper-catalyzed acylation leads to the ketone **30l** (88 %; entry12).

18

[52] C. Y. Liu, P. Knochel, *Org. Lett*. **2005**, *7*, 2543.
[53] P. Knochel, M. C. P. Yeh, S. C. Berk, J. Talbert, *J. Org. Chem*. **1988**, *53*, 2390.

**Table 1.** Polyfunctional aryl triazenes of type **30** obtained by the reaction of the Grignard Reagents **29** with electrophiles.

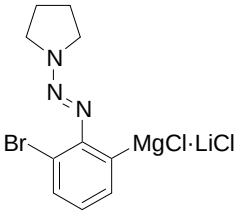
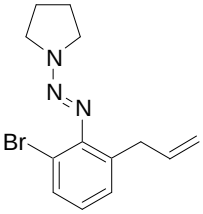
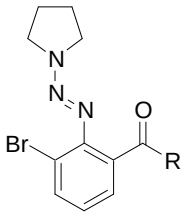
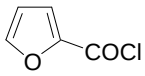
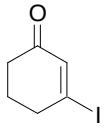
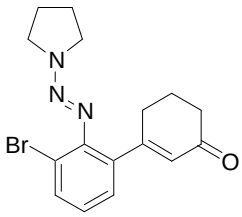
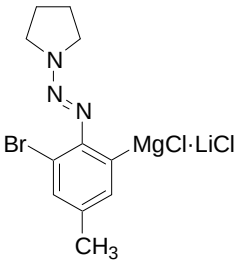
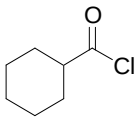
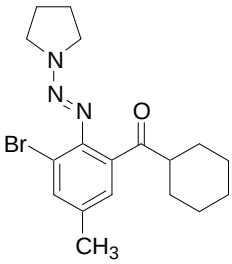
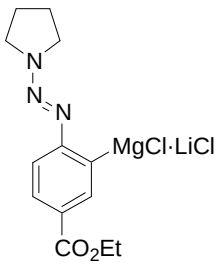
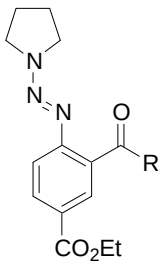
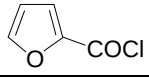
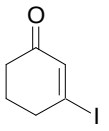
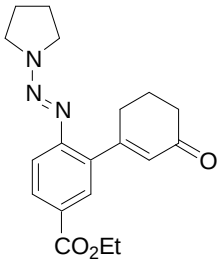
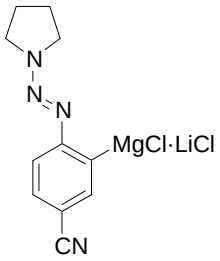
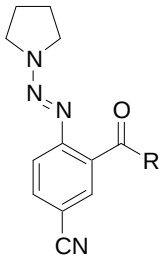
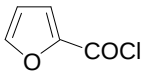
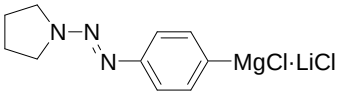
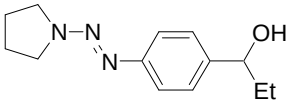
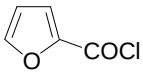
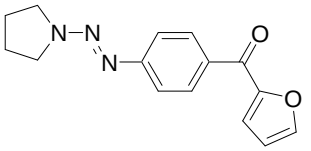
| entry | Grignard reagent of type **29** | electrophile | product of type **30** | yield (%)[a] |
|---|---|---|---|---|
| 1 |  **29a** | allyl-bromide |  **30a** | 78 |
| 2 | **29a** | PhCOCl |  **30b**: R = Ph | 82 |
| 3 | **29a** |  | **30c**: R = 2-furyl | 85 |
| 4 | **29a** |  |  **30d** | 80 |
| 5 |  **29b** |  |  **30e** | 82 |
| 6 |  **29c** | PhCOCl |  **30f**: R = Ph | 78 |
| 7 | **29c** |  | **30g**: R = 2-furyl | 86 |

**Table 1.** (continued)

| | | | | |
|---|---|---|---|---|
| 8 | **29c** |  |  **30h** | 80 |
| 9 |  **29d** | PhCOCl |  **30i**: R = Ph | 86 |
| 10 | **29d** |  | **30j**: R = 2-furyl | 85 |
| 11 |  **29e** | EtCHO |  **30k** | 90 |
| 12 | **29e** |  |  **30l** | 88 |

[a] Isolated yield of analytically pure product.

## 3.3 Preparation of polyfunctional aryl iodides

### 3.3.1 $CH_3I$ or TMSI used to convert a triazene to an iodide

The triazenes of type **30** are readily converted to the corresponding aryl iodides of type **31** using either a reaction in a sealed-tube with MeI[50] (15 equiv, 120 °C, 24-48 h; Method A) or in refluxing $CH_2Cl_2$ with TMSI (2 equiv, 4-6 h; Method B) in 70-90 % yield (Table 2). Various functional groups such as ketones, enones or an ester are tolerated. In the case of a benzylic alcohol such as **30k**, a dehydration is observed leading to the iodostyrene **31j** in 85 % yield (entry 10).

**Table 2.** Polyfunctional aryl iodides of type **31** obtained by the iodolysis of triazenes of type **30** with $CH_3I$ (Method A) or TMSI (Method B).

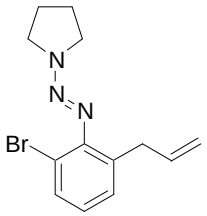
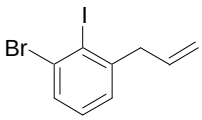
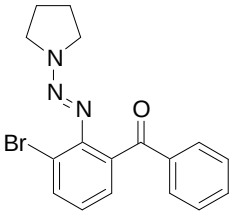
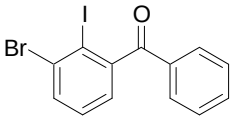
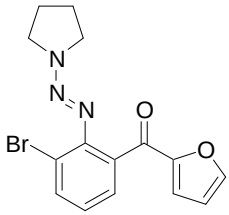
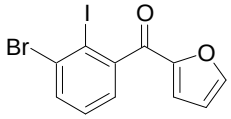
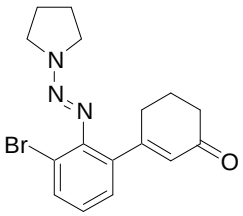
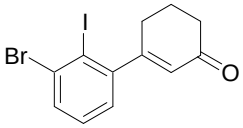
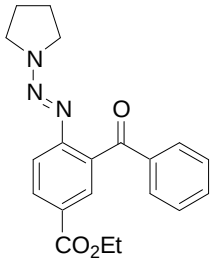
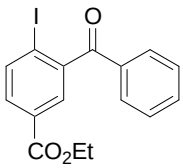
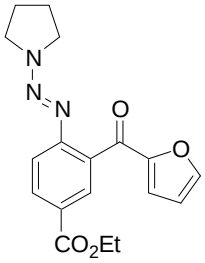
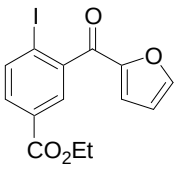
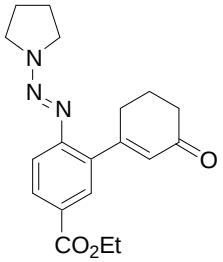
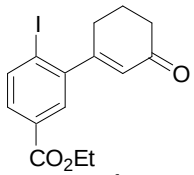
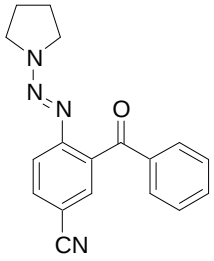
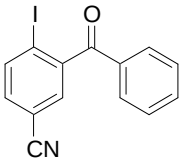
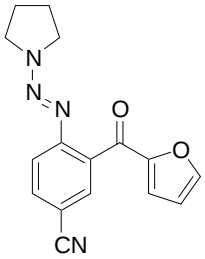
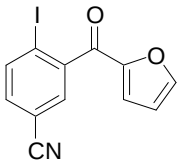
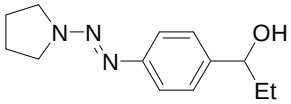
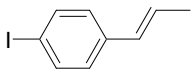
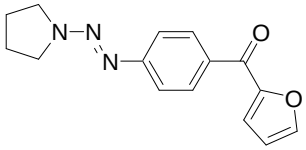
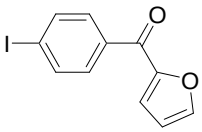
| entry | triazenes of type **30** | aryl iodides of type **31** | yield (%)[a] |
|---|---|---|---|
| 1 |  **30a** |  **31a**[b] | 83 |
| 2 |  **30b** |  **31b**[c] | 88 |
| 3 |  **30c** |  **31c**[c] | 78 |
| 4 |  **30d** |  **31d**[b] | 87 |
| 5 |  **30f** |  **31e**[c] | 72 |
| 6 |  **30g** |  **31f**[c] | 78 |

**Table 2.** (continued)

| | | | |
|---|---|---|---|
| 7 |  **30h** |  **31g**[b] | 76 |
| 8 |  **30i** |  **31h**[c] | 70 |
| 9 |  **30j** |  **31i**[c] | 82 |
| 10 |  **30k** |  **31j**[b] | 85 |
| 11 |  **30l** |  **31k**[b] | 90 |

[a] Isolated yield of analytically pure product. [b]Prepared according to Method A: $CH_3I$, 120 °C, 24-48 h. [c]Prepared according to Method B: $(CH_3)_3SiI$, $CH_2Cl_2$, reflux, 4-6 h.

### 3.3.2 Application of the iodoarenes

#### 3.3.2.1 Introduction

The preparation of aromatic organomagnesium reagents bearing a reactive functionality such as a ketone[54] or an aldehyde is rather difficult to achieve in the absence of a protecting

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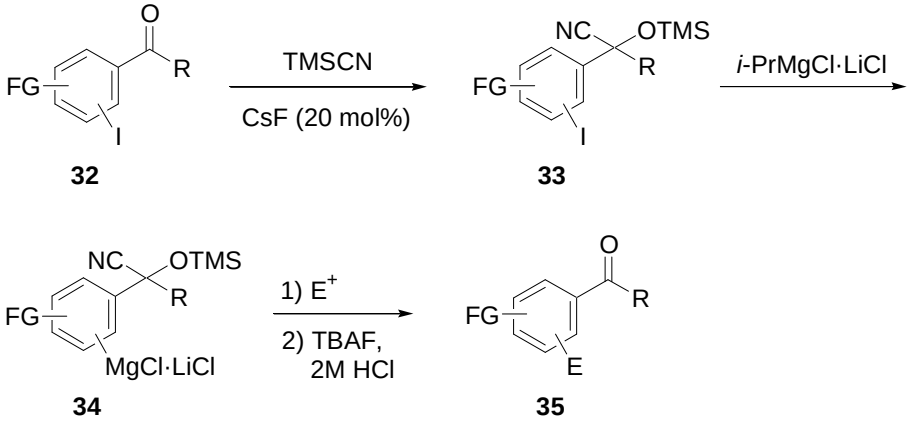
[54] F. F. Kneisel, P. Knochel, *Synlett* **2002**, 179.

group.[55] As potential protecting group for iodoketones of type **32**, we envisioned using silylated cyanohydrins[56] of type **33**, which are available by a CsF catalyzed silylcyanation with trimethylsilyl cyanide. We wish these silylated cyanohydrins **33** could be converted to the corresponding Grignard reagents **34** by using the powerful exchange reagent: *i*-PrMgCl·LiCl.[51,52] A direct reaction of **34** with various electrophiles ($E^+$) or in the presence of CuCN·2LiCl[53] would provide a range of silylated cyanohydrins which might be easily converted to the polyfunctional ketones of type **35** (Scheme 25). In other words, the magnesiated silylated cyanohydrins could be used as synthetic equivalents of aromatic or heterocyclic Grignard reagents bearing a ketone or an aldehyde.[57]




**Scheme 25.** Preparation and reaction of silylated cyanohydrins (**33**).

### 3.3.2.2 Preparation of polyfunctional ketones

In general, the silylated cyanohydrins of type **33** can be readily prepared by using TMSCN (1.2 equiv), CsF (20 mol %) in $CH_3CN$ (rt, 2 h), starting from the corresponding ketones of type **32**.[56] Thus, unsaturated 3-iodocyclohexenones was readily converted to the expected silylated cyanohydrins **33a-b** in almost quantitative yield. Their reactions with *i*-PrMgCl·LiCl in THF at -40 °C for 1 h produced the Grignard reagents **34a-b** in high yields. Copper(I)-catalyzed acylation with furoyl chloride affords after deprotection (1 M TBAF, 2 M HCl) the unsaturated diketones **35a** and **35b** in 81-87 % yield (entries 1 and 2, Table 3).[57]

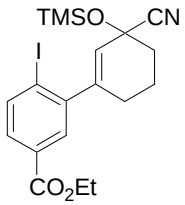
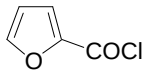
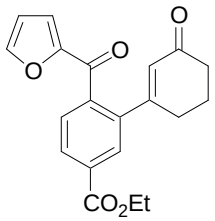
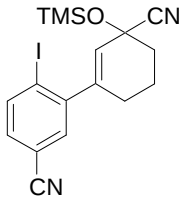
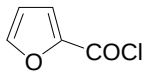
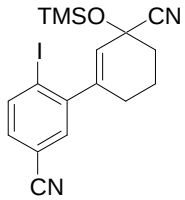
23

[55] *Protective Groups in Organic Synthesis*, T. W. Greene, and P. G. M. Wuts, John Wiley & Sons Inc, 3rd edition, **1999**. 293-369. S. S.;

[56] (a) S. S. Kim, G. Rajagopal, D. H. Song, *J. Organomet. Chem.* **2004**, *689*, 1734; (b) M. North, *Synlett* **1993**, 807; (c) H. Deng, M. P. Ister, M. L. Snapper, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2002**, *41*, 3333; (d) K. Tanaka, A. Mori, S. Inoue, *J. Org. Chem.* **1990**, *55*, 181; (e) M. Hayashi, Y. Miyamoto, S. Inoue, N. Oguni, *J. Org. Chem.* **1993**, *58*, 1515; (f) S. Kobayashi, Y. Tsuchiya, T. Mukaiyama, *Chem. Lett.* **1991**, 537; (g) Y. Hanashima, D. Sawada, H. Nogami, M. Kanai, M. Shibasaki, *Tetrahedron* **2001**, *57*, 805.

[57] C. Y. Liu, H. Ren, P. Knochel, *Org. Lett*. **2006**, *8*, 617.

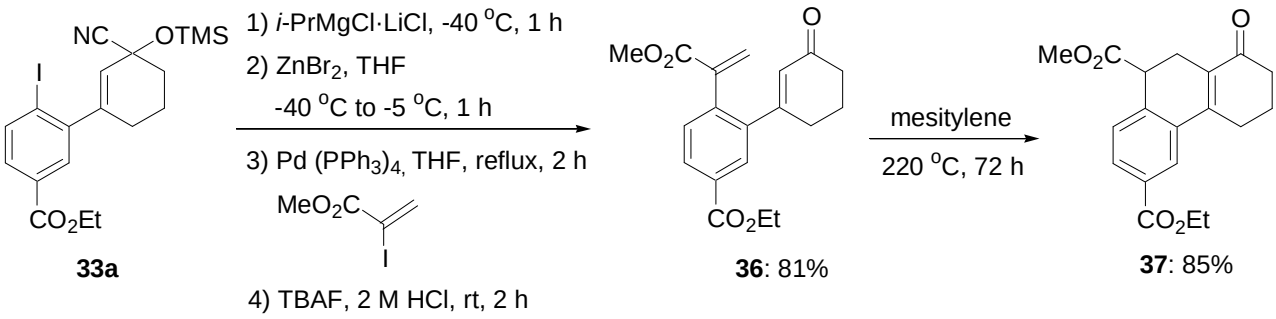
**Table 3.** Polyfunctional ketones obtained by the reaction of the silylated cyanohydrins **33** with *i*-PrMgCl·LiCl leading to the functionalized Gignard Reagents **34**, followed by the transmetalation with CuCN·2LiCl and then the reaction with an electrophile and deprotection.

| entry | silylated cyanohydrins of type **33** | T, t (°C, h)[a] | electrophiles | product of type **35** | yield (%)[b] |
|---|---|---|---|---|---|
| 1 |  **33a** | -40, 1 |  |  **35a** | 87 |
| 2 |  **33b** | -40, 1 |  |  **35b** | 81 |

[a] Reaction conditions for performing the I/Mg-exchange. [b] Overall yield (being from the cyanohydrin) after reaction with an electrophile and deprotection.

### 3.3.2.3 Preparation of a tricyclic ketone

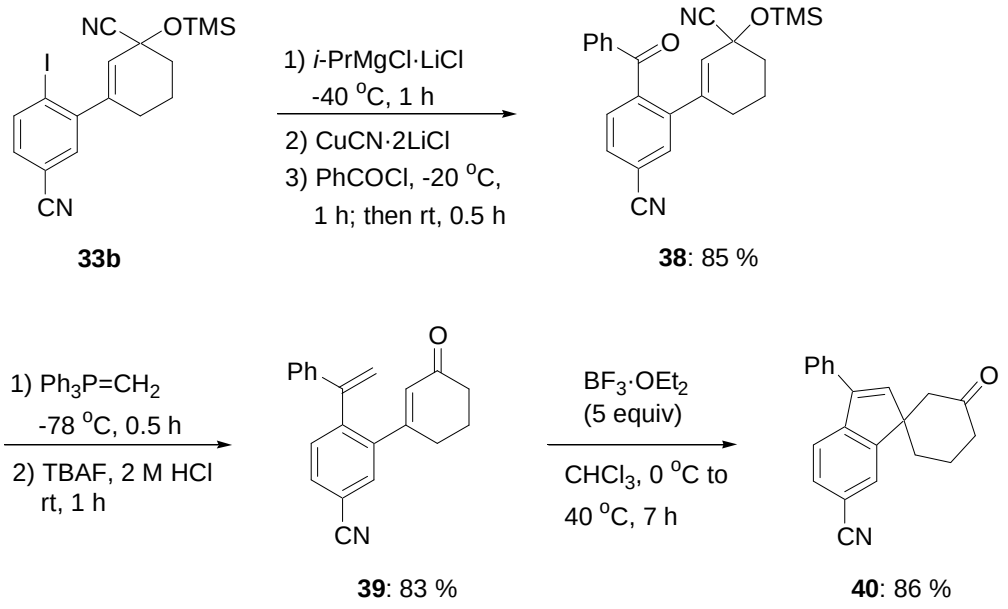
Starting from the silylated cyanohydrin **33a**, we performed after magnesiation a Negishi cross-coupling with methyl 2-iodoacrylate. The usual deprotection is leading to the dienic ketone **36** in 81 % yield. A solution of **36** in mesitylene was heated (220 °C, 72 h) and underwent an electrocyclic ring closing followed by a double bond isomerization, affording the tricyclic ketone **37** in 85 % yield (Scheme 26).




**Scheme 26.** Electrocyclic ring closing of **36**.

### 3.3.2.4 Preparation of a spiroketone

Interestingly, the silylated cyanohydrin **33b** reacts after magnesiation with PhCOCl leading to the ketone **38** which after Wittig olefination and deprotection furnishes dienic ketone **39** in 83 % yield. The treatment of the functionalized diene **39** with $BF_3 \cdot OEt_2$ (5 equiv; 0 °C to 40 °C, 7 h) triggers an intramolecular Michael-addition, providing the annelated spiroketone **40** in 86 % yield (Scheme 27).[58]




**Scheme 27.** Synthesis of the annelated spiroketone **40**.

## 3.4 A new carbazole synthesis

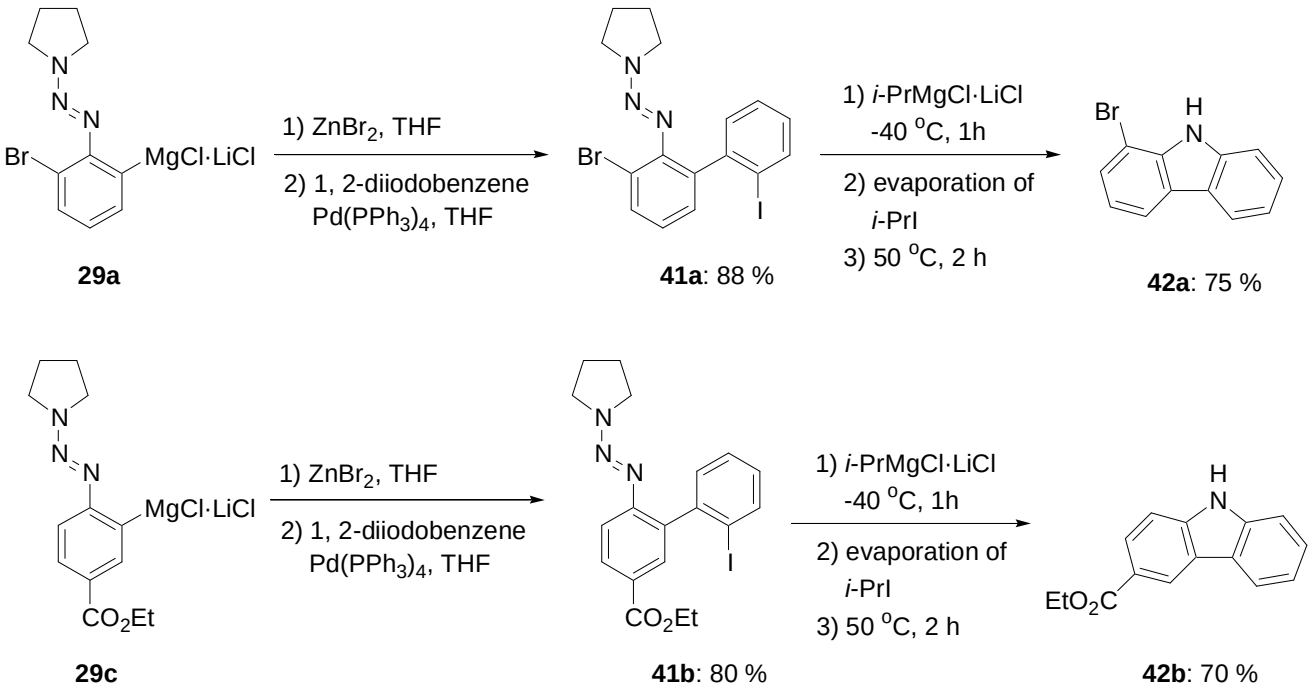
Using our method, we have developed a new carbazole synthesis.[59] Starting from the Grignard reagents **29a** and **29c**, we performed Negishi cross-coupling reactions[60] with 1,2-diiodobenzene leading to the derived polyfunctional biphenyls **41a** (88 %) and **41b** (80 %). Reactions of compound type **41** with *i*-PrMgCl·LiCl (1.1 equiv, -40 °C, 1 h) provides the functionalized carbazoles **42a** (75 %) and **42b** (70 %). Evaporation of *i*-PrI resulting from the I/Mg-exchange is important before heating (50 °C, 2 h). Otherwise, unwanted cross-coupling products with *i*-PrI are observed (Scheme 28).

25

[58] T. Lomberget, E. Bentz, D. Bouyssi, G. Balme, *Org. Lett.* **2003**, *5*, 2055.

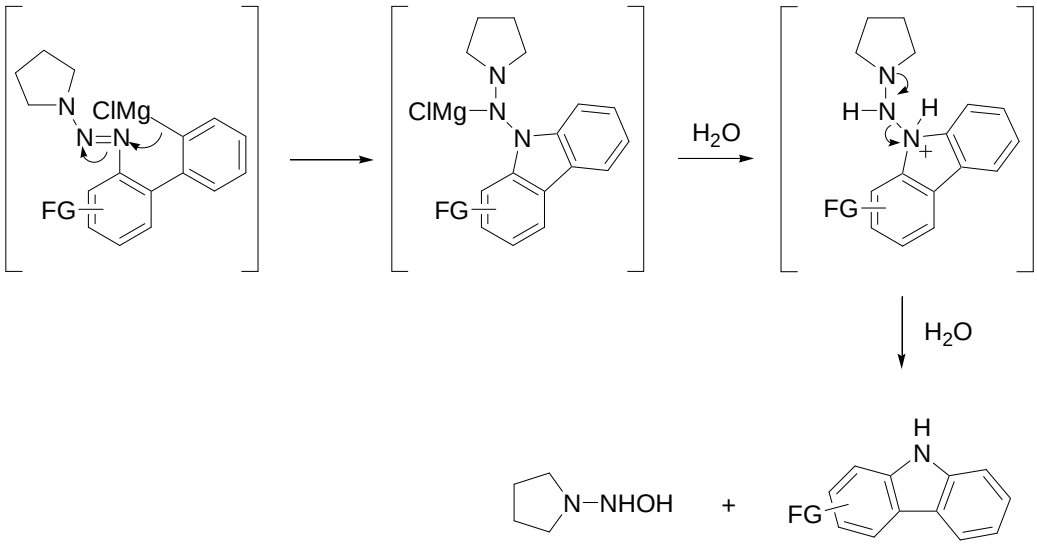
[59] H. S. Knölker, K. R. Reddy, *Chem. Rev*. **2002**, *102*, 4303.

[60] (a) L. Green, B. Chauder, V. Snieckus, *J. Heterocycl. Chem*. **1999**, *36*, 1453; (b) E. Negishi, L. F. Valente, M. Kobayashi, *J. Am. Chem. Soc*. **1980**, *102*, 3298; (c) M. Kobayashi, E. Negishi, *J. Org. Chem*. **1980**, *45*, 5223; (d) E. Negishi, *Acc. Chem. Res*. **1982**, *15*, 340; (e) Y. Tamaru, H. Ochiai, T. Nakamura, Z. Yishida, *Tetrahedron Lett*, **1986**, *27*, 955; (f) I. Klement, M. Rottländer, C. E. Tucker, T. N. Majid, P. Knochel, P. Venegas, G. Cahiez, *Tetrahedron* **1996**, *52*, 7201.




**Scheme 28.** Synthesis of functionalized carbazoles **42a** and **42b**.

A tentative mechanism of the cyclization involving the formation of a hydroxylamine derivative as side-product is described in Scheme 29.

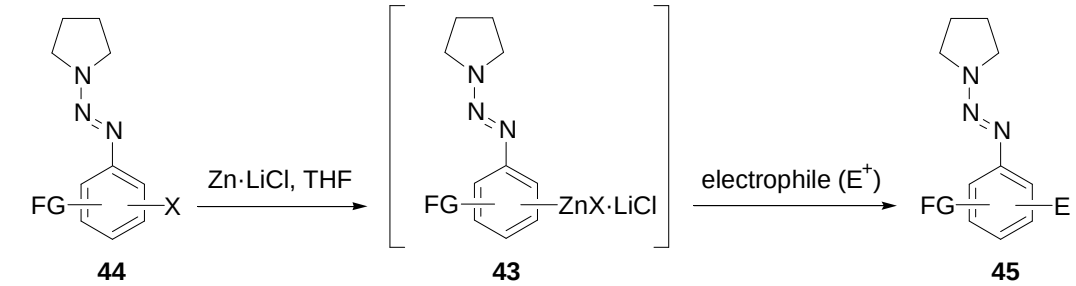



**Scheme 29.** A plausible mechanism of the cabazole formation.

# 4. Preparation of Polyfunctional Arylzinc Reagents Bearing a Triazene Moiety

## 4.1 Introduction

The triazene moiety has shown to exhibit a variety of interesting applications in organic synthesis.[49a] It has also proved its utility as a convenient protecting group for a diazonium salt to bear this reactive functionality through a halogen/magnesium exchange reaction under mild conditions.[52] Recently, Knochel and co-workers have developed an efficient synthesis of functionalized organozinc compounds by the direct insertion of zinc into organic iodides and bromides.[12] Since this zinc insertion can be successfully performed and tolerates many functional groups, we envisioned the preparation of polyfunctional arylzinc reagents of type **43** starting from the corresponding bromo- or iodoaryl triazenes of type **44**. Polyfunctional aryl triazenes of type **45** would be obtained after the reaction of organozinc reagents with electrophiles ($E^+$) (Scheme 30).




**Scheme 30.** Zinc insertion into functionalized bromo- or iodoaryl triazenes.

## 4.2 A direct zinc insertion into iodophenyl triazenes

Recently, our group has found that the mixed Zn/Li reagent Zn·LiCl can be easily prepared and used for the preparation of functionalized aryl- and alkylzinc compounds.[12] Thus, the arylzinc iodide (**43a**) was prepared in 92 % yield from the corresponding iodophenyl triazene (**44a**) by the insertion of zinc (2 equiv.) in the presence of LiCl (2 equiv.) in THF (50 $^oC$, 7 h). The resulting zinc reagent was treated with allyl bromide and catalytic amounts of CuCN·2LiCl (3 mol%) to give the triazene **45a** (76 %; entry 1, Table 4). Acylation of the

copper derivative of **43a** with benzoyl chloride furnishes the expected ketone **45b** (81 %; entry 2). Interestingly, a direct reaction of the arylzinc iodide (**43b**) with 4-iodo-diazobenzene tetrafluoroborate leads to a new triazene-diazene compound **45c** in 66 % yield (entry 3). Similar acylation reactions are observed when the copper species of **43b** or **43c** reacts with aliphatic or heteroaryl acid chlorides to afford the ketones **45d** (73 %; entry 4) or **45e** (43 %; entry 5), respectively. Starting from the arylzinc reagent **43c**, we can perform a Negishi cross-coupling reaction with 2-iodobenzaldehyde in the presence of $Pd(PPh_3)_4$ (3 mol%) leading to the biphenyl triazene **45f** in 71 % yield (entry 6). The cyano-substituted arylzinc iodide **43d** can undergo either a copper-catalyzed acylation or a palladium-catalyzed cross-coupling to give the desired polyfunctional triazenes **45g** and **45h** in yields of 58 % and 75 %, respectively (entry 7 and 8, Table4). Finally, a selective formation of the corresponding monometalated species **43e** is possible in the case of diiodoaryl triazene **44e**. Preparation of the arylzinc reagent **43e** (97 %; entry 9 and 10) is easily achieved after 15 h at 50 $^{o}$C. A copper-catalyzed acylation with benzoyl chloride or a direct reaction with toluenesulfonyl cyanide (TsCN, 1.5 equiv.) provides the ketone **45i** (83 %; entry 9) or the expected nitrile **45j** (70 %, entry 10).

**Table 4.** Preparation and reaction of functionalized arylzinc iodides bearing a triazene moiety.

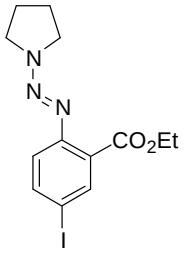
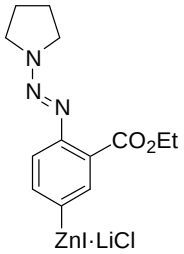
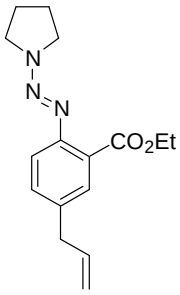
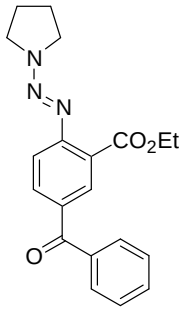
| entry | iodophenyl triazene of type **44** | T, t [°C, h] | zinc reagent of type **43** yield [%][a] | electrophile | product of type **45**, yield [%][b] |
|---|---|---|---|---|---|
| 1 |  **44a** | 50, 7 |  **43a:** 92 | AllBr[c] |  **45a:** 76 |
| 2 | **44a** | 50, 7 | **43a:** 92 | PhCOCl[d] |  **45b:** 81 |

**Table 4.** (continued)

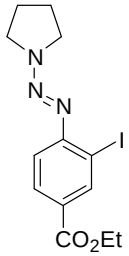
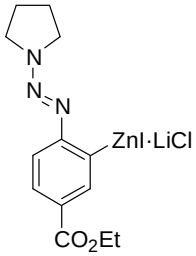
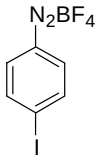
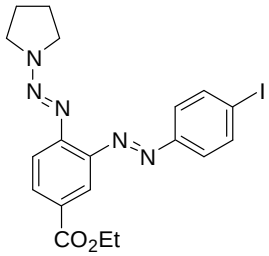
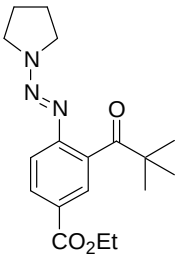
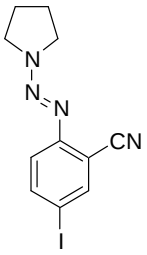
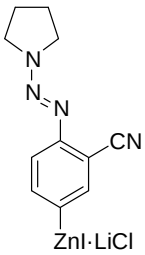
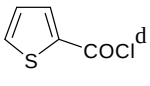
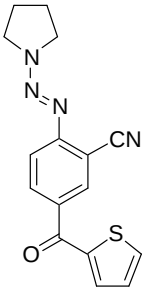
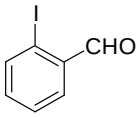
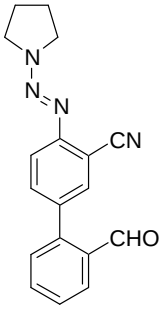
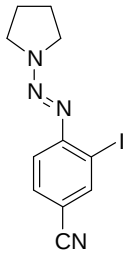
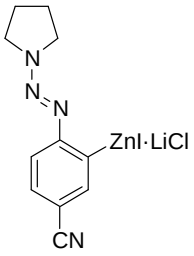
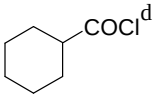
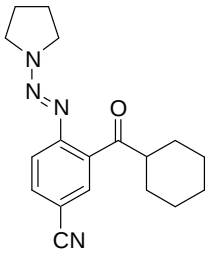
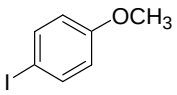
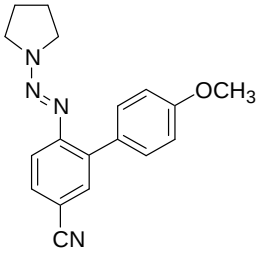
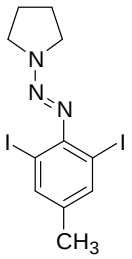
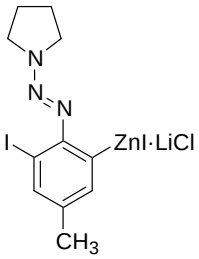
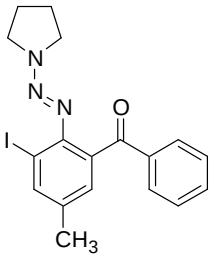
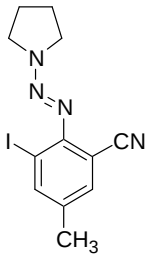
| | | | | | |
|---|---|---|---|---|---|
| 3 |  **44b** | 50, 30 |  **43b:** 85 |  |  **45c:** 66 |
| 4 | **44b** | 50, 30 | **43b:** 85 | *t*BuCOCl[d] |  **45d:** 73 |
| 5 |  **44c** | 50, 8 |  **43c:** 93 |  |  **45e:** 43 |
| 6[e] | **44c** | 50, 8 | **43c:** 93 |  |  **45f:** 71 |
| 7 |  **44d** | 50, 24 |  **43d:** 88 |  |  **45g:** 58 |
| 8[e] | **44d** | 50, 24 | **43d:** 88 |  |  **45h:** 75 |

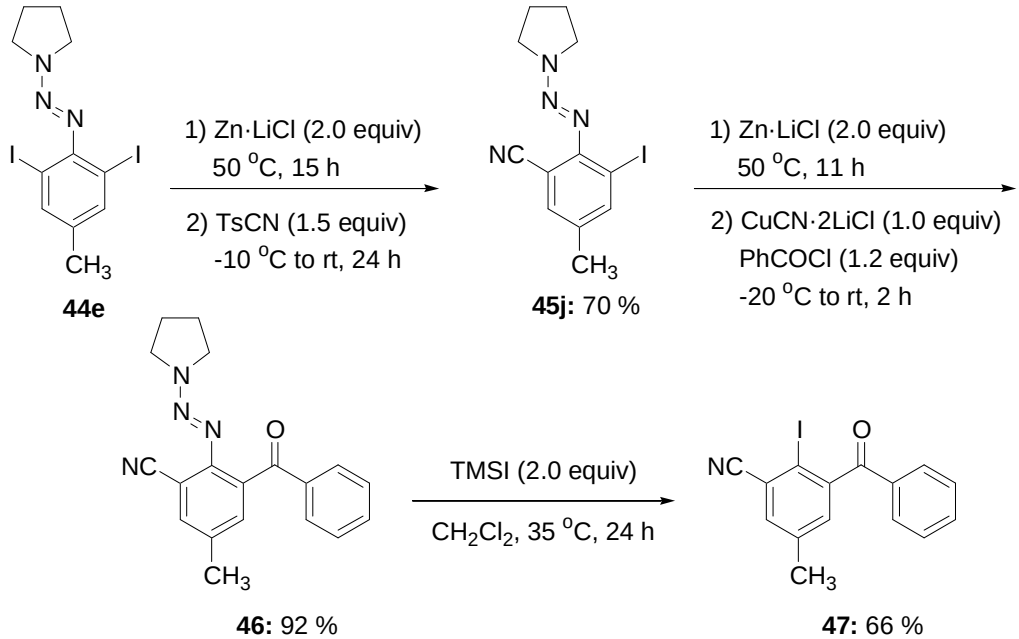
**Table 4.** (continued)

| | | | | | |
|---|---|---|---|---|---|
| 9 |  **44e** | 50, 15 |  **43e:** 97 | PhCOCl[d] |  **45i:** 83 |
| 10 | **44e** | 50, 15 | **43e:** 97 | TsCN |  **45j:** 70 |

[a] Yield estimated after titration with $I_2$. [b] Isolated yield of analytically pure product based on the molarity of the zinc reagent. [c] 3 mol% of CuCN·2LiCl was added. [d] 1 equivalent of CuCN·2LiCl was added. [e] 3 mol% of $[Pd(PPh_3)_4]$ was added.

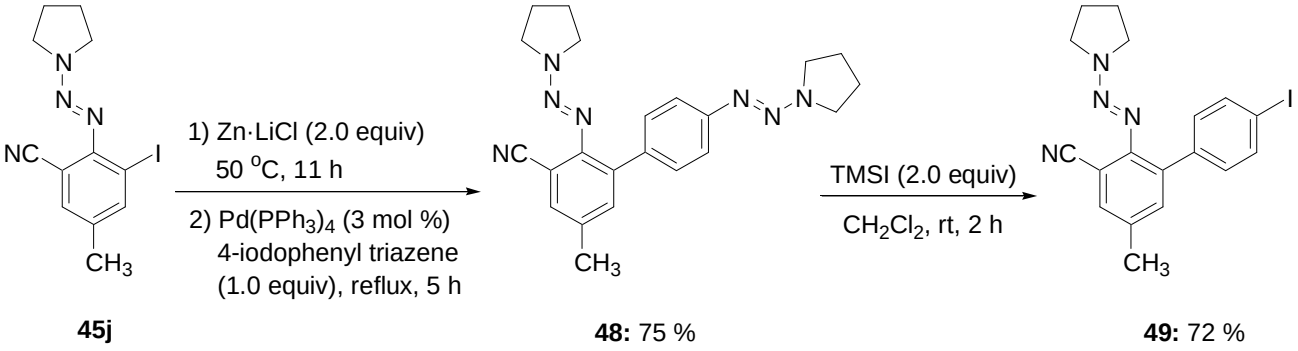
### 4.3 Two successive zinc insertions into diiodoaryl triazenes

Starting from the diiodoaryl triazene **44e**, a selective formation of the aryl zinc reagent **43e** is observed. Cyanation of **43e** with TsCN led to the product **45j** (see entry 10 of Table 4), which can be further employed in a zinc insertion/acylation reaction sequence to generate the polyfunctional triazene **46** in 64 % overall yield. Furthermore, by using our method,[52] triazene **46** can be readily converted to the aryl iodide **47** (35 °C, 24 h) in 66 % isolated yield (Scheme 31).




**Scheme 31.** Two successive zinc insertions into diiodophenyl triazene **44e** and iodolysis of **46**.

Alternatively, the arylzinc reagent derived from **45j** undergoes a Negishi cross-coupling reaction with 4-iodophenyl triazene to form a *bis*-triazene **48** (75 %), which can perform a selective iodination by using trimethylsilyl iodide in $CH_2Cl_2$ (room temperature, 2 h) to afford compound **49** in 72 % yield (Scheme 32).




**Scheme 32.** Preparation and a selective iodination of *bis*-triazene **48**.

## 4.4 A direct zinc insertion into bromophenyl triazenes

We have found that the insertion of zinc into a C–Br bond is also possible when employing the activated phenyl triazenes **44f**-**h**. Therefore, the functionalized arylzinc bromide **43f** was prepared in 84 % yield (50 °C, 24 h) starting from the corresponding triazene **44f**. Reaction of the resulting zinc reagent with ethyl 2-bromomethyl acrylate (0.4 mol% of CuCN·2LiCl) gives the desired triazene **45k** (70 %; entry 1, Table 5). Moreover, acylation of the copper derivative of **43f** with acyl or heteroaryl acid chlorides furnishes the expected ketones **45l** (52 %; entry 2) or **45m** (70 %; entry 3). The reaction of cyano-substituted dibromoaryl triazene (**44g**) with Zn·LiCl generates the corresponding arylzinc reagent **43g** in 83 % yield after 22 h at 50 °C. This species undergoes an addition-elimination reaction with 3-iodo-2-cyclohexen-1-one in the presence of CuCN·2LiCl leading to the triazene **45n** in 62 % yield (entry 4). A copper(I)-catalyzed acylation with pivaloyl acid chloride affords the ketone **45o** (70 %; entry 5). Interestingly, the zinc insertion reaction also shows an excellent regioselectivity in the case of tribromophenyl triazene (**44h**) and produces the corresponding arylzinc reagent **43h** in 80 % yield. Acylation with benzoyl chloride in the presence of CuCN·2LiCl gives the expected ketone **45p** in 79 % yield (entry 6). A palladium-catalyzed cross-coupling of **43h** with methyl 2-iodobenzoate is also efficiently performed leading to the biphenyl triazene **45q** (76 %; entry 7).

**Table 5.** Preparation and reaction of functionalized arylzinc bromides bearing a triazene moiety.

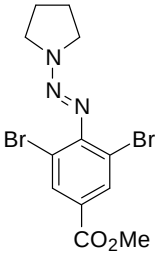
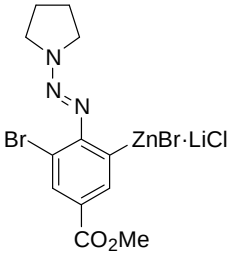
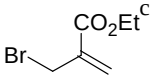
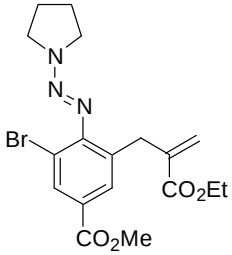
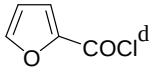
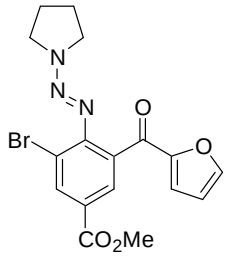
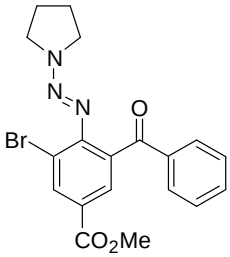
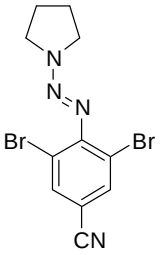
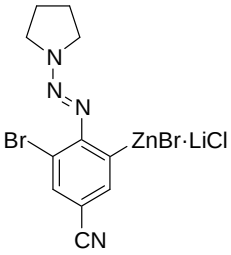
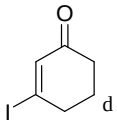
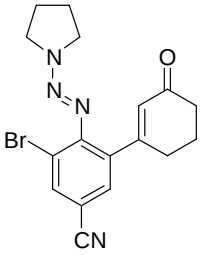
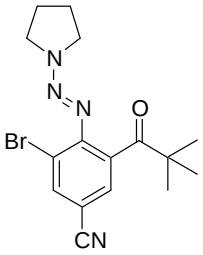
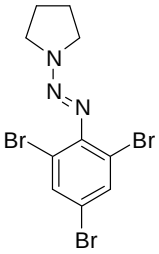
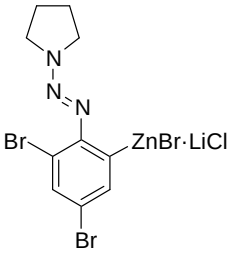
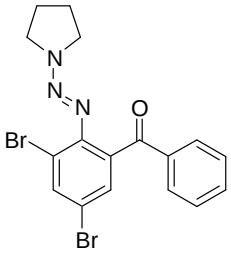
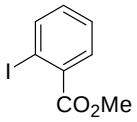
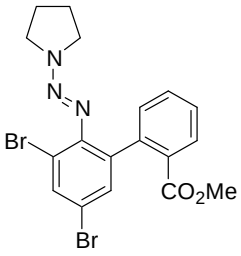
| entry | bromophenyl triazene of type **44** | T, t [°C, h] | zinc reagent of type **43** yield [%][a] | electrophile | product of type **45**, yield [%][b] |
|---|---|---|---|---|---|
| 1 |  **44f** | 50, 24 |  **43f:** 84 |  |  **45k:** 70 |
| 2 | **44f** | 50, 24 | **43f:** 84 |  |  **45l:** 52 |
| 3 | **44f** | 50, 24 | **43f:** 84 | PhCOCl[d] |  **45m:** 70 |
| 4 |  **44g** | 50, 22 |  **43g:** 83 |  |  **45n:** 62 |
| 5 | **44g** | 50, 22 | **43g:** 83 | *t*BuCOCl[d] |  **45o:** 70 |

**Table 5.** (continued)

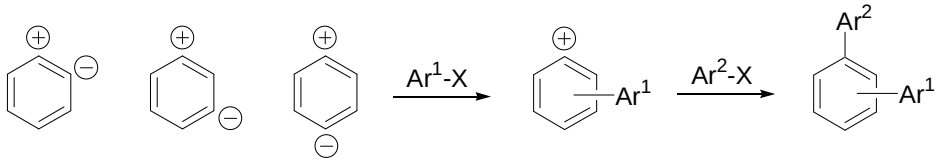
| | | | | | |
|---|---|---|---|---|---|
| |  | |  | PhCOCl[d] |  |
| 6 | **44h** | 50, 20 | **43h:** 80 | | **45p:** 79 |
| | | | |  |  |
| 7[e] | **44h** | 50, 20 | **43h:** 80 | | **45q:** 76 |

[a] Yield estimated after titration with $I_2$. [b] Isolated yield of analytically pure product based on the molarity of the zinc reagent. [c] 3 mol% of CuCN·2LiCl was added. [d] 1 equivalent of CuCN·2LiCl was added. [e] 3 mol% of $[Pd(PPh_3)_4]$ was added**.**

# 5. Synthesis of Functionalized *o*-, *m*-, or *p*-Terphenyls *via* Consecutive Cross-Coupling Reactions of Arylboronic Esters Bearing a Triazene Moiety

## 5.1 Introduction

The preparation and selective reaction of bimetallic[61] aromatic and heteroaromatic reagents have become an interesting task in organic synthesis.[62] It is noteworthy that the resulting polyfunctional oligoaryls are known to exhibit essential pharmaceutical or optoelectronical properties.[63] In the case of terphenyls, they have also attracted much interest of organic chemists due to their potential applications in optical,[64] electrical,[65] and liquid crystal[66] properties. Therefore, we envisioned that the aromatic derivatives of type **50**, which bear a donor and an acceptor substituents with different reactivity, would serve as versatile and efficient reagents to prepare compounds of type **51** and **52** *via* two successive cross-coupling reactions with $Ar^1$–X and $Ar^2$–X (Scheme 33). Herein, we wish to develop new synthetic methods for the preparation of functionalized terphenyls, which have been reported to show potent hepatoprotective activities.[67]




reagents of type **50** **51** **52**: terphenys

**Scheme 33.** Consecutive cross-couplings of reagents of type **50**.

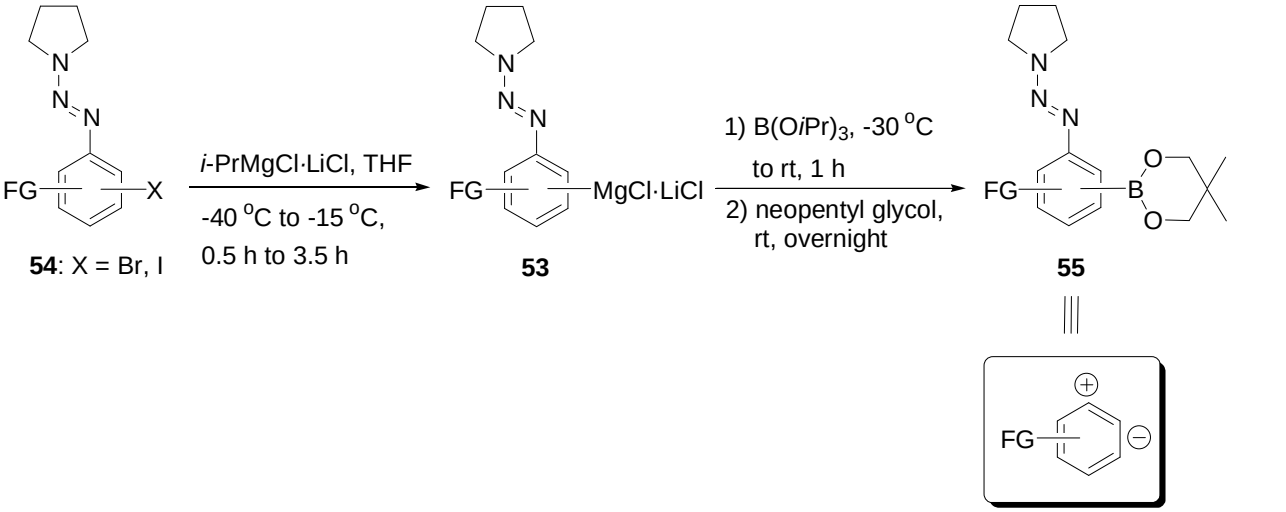
## 5.2 Preparation of arylboronic esters bearing a triazene functionality

Recently, Knochel and co-workers have developed a general halogen-magnesium exchange reaction employing the mixed Mg/Li reagent *i*-PrMgCl·LiCl.[51] Aryl bromides and iodides can undergo an efficient halogen-magnesium exchange under very mild conditions. Since this

34

[61] a) I. Marek, *Chem. Rev.* **2000**, *100*, 2887; b) I. Marek, *Tetrahedron* **2002**, *58*, 9463.
[62] O. Baron, P. Knochel, *Angew. Chem. Int. Ed.* **2005**, *44*, 3133.
[63] C. H. Cho, H. Park, M. A. Park, T. Y. Ryoo, Y. S. Lee, K. Park. *Eur. J. Org. Chem.* **2005**, 3177.
[64] a) P. Bordat, R. Brown, *Chem. Phys. Lett.* **2000**, *331*, 439; b) W. M. F. Fabian, J. M. Kauffman, *J. Lumin.* **1999**, *85*, 137.
[65] a) G. Schiavon, S. Zecchin, G. Zotti, S. Cattarin, *J. Electroanal. Chem.* **1986**, *213*, 53; b) I. B. Berlman, H. O. Wirth, O. J. Steingraber, *J. Phys. Chem.* **1971**, *75*, 318.
[66] a) R. S. Wright, T. K. Vinod, *Tetrahedron Lett.* **2003**, *44*, 7129; b) B. S. Udayakumar, G. B. Schuster, *J. Org. Chem.* **1992**, *57*, 348.
[67] V. J. Ram, A. Goel, G. K. Patnaik, *Bioorg. Med. Chem. Lett.* **1998**, *8*, 469.

exchange reaction proceeds well and tolerates many functional groups, we have prepared a variety of arylmagnesium reagents of type **53** starting from the corresponding bromo- or iodophenyl triazenes of type **54** and leading to arylboronic esters bearing a triazene moiety of type **55**. Compounds of type **55** can be useful reagents for the selective functionalization of aromatic derivatives *via* successive cross-coupling reactions (Scheme 34).




**Scheme 34.** Preparation of boronic esters bearing a triazene functionality of type **55**.

Thus, the Grignard reagents **57a-f** prepared from the readily available bromo- or iodoaryl triazenes (**56a-f**) reacted with triisopropyl borate (1.2 equiv, -30 °C to rt, 1 h), followed by the addition of neopentyl glycol (1.25 equiv, rt, overnight) leading to the desired triazene-substituted arylboronic esters **58a-f** (55-86 %; entries 1-6, Table 6).

**Table 6.** Arylboronic esters bearing a triazene moiety of type **58** obtained by the reaction of Grignard reagents **57** with triisopropyl borate and neopentyl glycol.

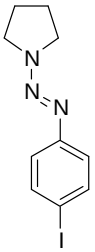
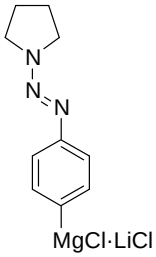
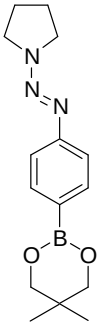
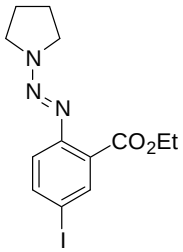
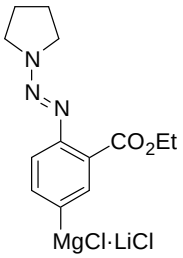
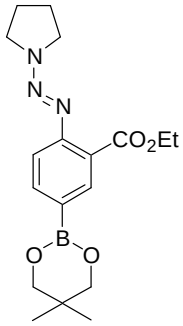
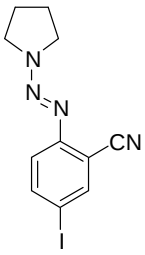
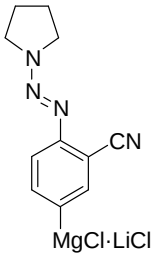
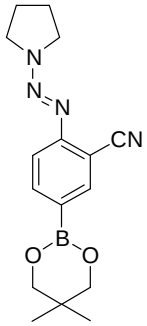
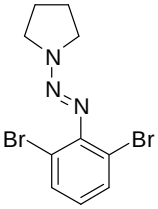
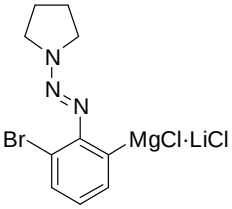
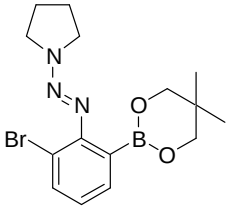
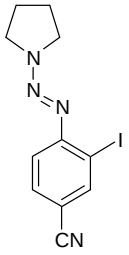
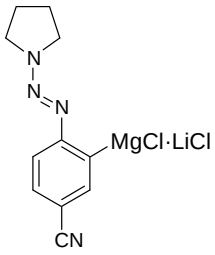
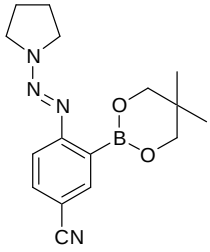
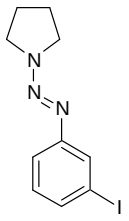
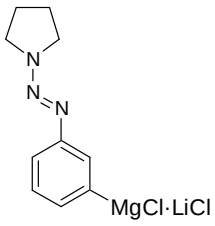
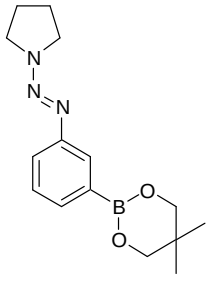
| entry | bromo-/iodoaryl triazene of type **56** | T, t [°C, h] | Grignard reagent of type **57** | electrophile[a] | product of type **58** yield [%][b] |
|---|---|---|---|---|---|
| 1 |  **56a** | -30, 1 |  **57a** | 1) $B(OiPr)_3$<br>2) neopentyl glycol |  **58a:** 86 |

**Table 6.** (continued)

| | | | | | |
|---|---|---|---|---|---|
| 2 |  **56b** | -40, 0.5 |  **57b** | 1) B(O*i*Pr)$_3$<br>2) neopentyl glycol |  **58b:** 78 |
| 3 |  **56c** | -40, 0.5 |  **57c** | 1) B(O*i*Pr)$_3$<br>2) neopentyl glycol |  **58c:** 83 |
| 4 |  **56d** | -15, 5 |  **57d** | 1) B(O*i*Pr)$_3$<br>2) neopentyl glycol |  **58d:** 55 |
| 5 |  **56e** | -40, 0.7 |  **57e** | 1) B(O*i*Pr)$_3$<br>2) neopentyl glycol |  **58e:** 65 |
| 6 |  **56f** | -30, 1 |  **57f** | 1) B(O*i*Pr)$_3$<br>2) neopentyl glycol |  **58f:** 86 |

[a] B(O*i*Pr)$_3$ was added at -30 $^{o}$C, then the reaction mixture was warmed to rt and stirred for 1 h; neopentyl glycol was added at rt and then the reaction mixture was stirred overnight. [b] Isolated yield of analytically pure product.

## 5.3 Preparation of polyfunctional aryl triazenes *via* Suzuki cross-coupling reactions of triazene-substituted arylboronic esters with aryl halides

All new triazene-substituted arylboronic esters of type **58** underwent Suzuki cross-coupling reactions smoothly. In the absence of Lewis acids, the triazene moiety, in general, is fairly compatible with the reaction conditions of Suzuki couplings. Accordingly, reaction of boronic ester **58a** with aryl bromides or aryl iodides in the presence of $[Pd(PPh_3)_4]$ (3 mol%) and $K_3PO_4$ (2 equiv) in dioxane/water (10 : 1) at 100 °C for 4-6 h furnishes the expected polyfunctional aryl triazenes **59a-e** in 61-89 % yield (entries 1-5, Table 7). Arylboronic esters bearing functional groups such as **58b** and **58c** also perform cross-coupling reactions efficiently with a variety of aryl halides, providing the triazenes **59f-h** (72-85 %; entries 6-8) and **59i-k** (52-72 %; entries 9-11), respectively. Starting from the functionalized boronic esters bearing a triazene in *ortho*-position, **58d** and **58e**, the coupling reactions proceed to completion at 100 °C after 2-6 h to give the triazenes **59l-p** in 46-86 % yield (entries 12-16, Table 7). Finally, not only boronic esters bearing a triazene in the *para*- or *ortho*-position undergo the Suzuki coupling reactions successfully, but also **58f** reacts with bromomesitylene or 5-bromopyrimidine affording the desired triazenes **59q** (62 %; entry 17) or **59r** (80 %; entry 18).

**Table 7.** Polyfunctional aryl triazenes of type **59** obtained by Suzuki cross-coupling reactions of arylboronic esters of type **58** with aryl halides.

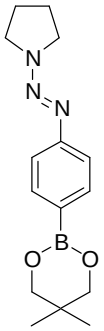
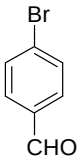
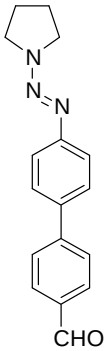
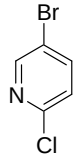
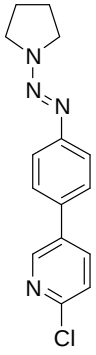
| entry[a] | arylboronic ester of type **58** | T, t [°C, h] | aryl halide | product of type **59** yield [%][b] |
|---|---|---|---|---|
| 1 |  **58a** | 100, 5 |  |  **59a:** 80 |
| 2 | **58a** | 100, 6 |  |  **59b:** 70 |

**Table 7.** (continued)

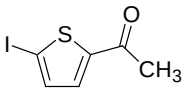
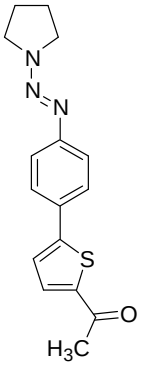
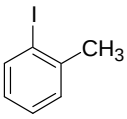
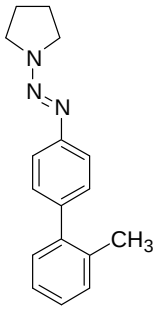
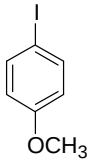
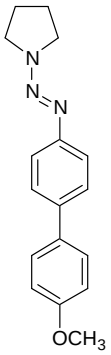
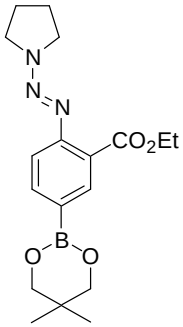
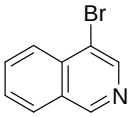
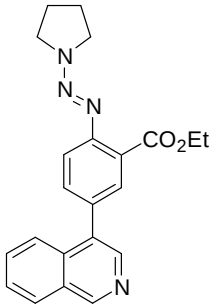
| | | | | |
|---|---|---|---|---|
| | | |  |  |
| 3 | **58a** | 100, 3 | | **59c:** 89 |
| | | |  |  |
| 4 | **58a** | 100, 5 | | **59d:** 75 |
| | | |  |  |
| 5 | **58a** | 100, 6 | | **59e:** 61 |
| |  | |  |  |
| 6 | **58b** | 100, 6 | | **59f:** 89 |

**Table 7.** (continued)

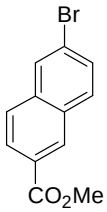
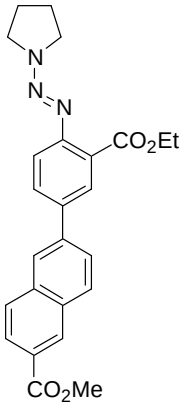
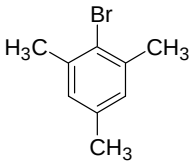
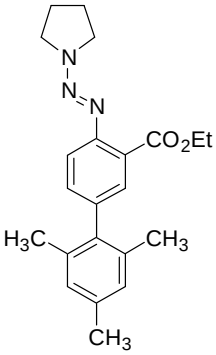
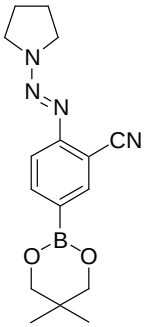
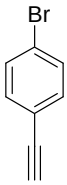
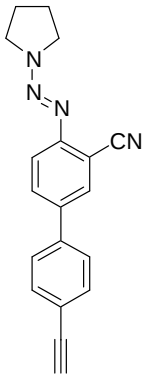
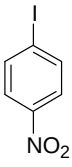
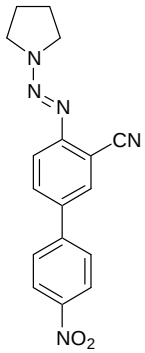
| | | | | |
|---|---|---|---|---|
| 7 | **58b** | 100, 6 |  |  **59g:** 70 |
| 8 | **58b** | 100, 7 |  |  **59h:** 89 |
| 9 |  **58c** | 100, 5 |  |  **59i:** 55 |
| 10 | **58c** | 100, 3 |  |  **59j:** 72 |

**Table 7.** (continued)

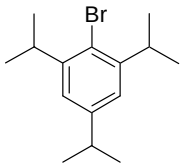
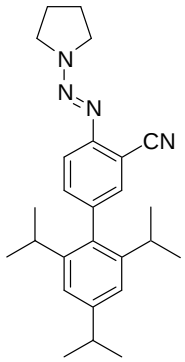
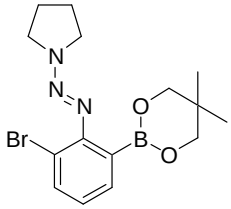
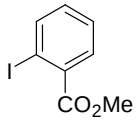
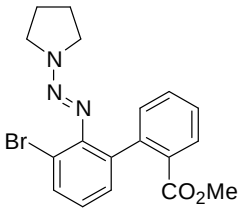
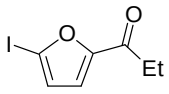
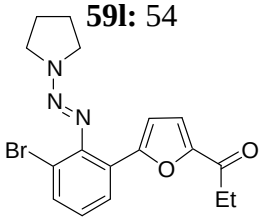
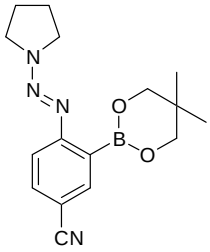
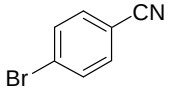
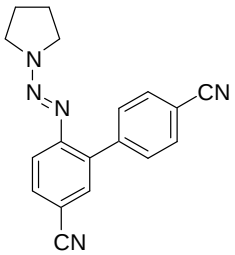
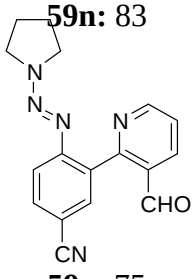
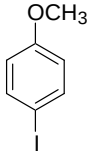
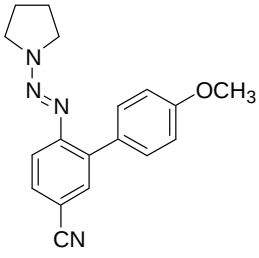
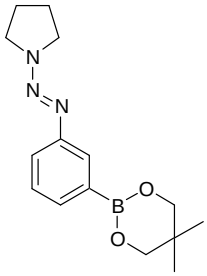
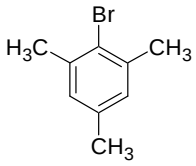
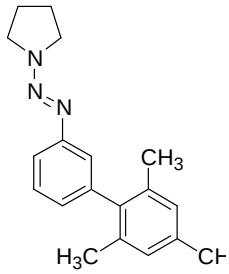
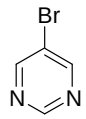
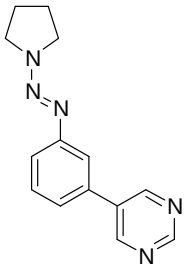
| | | | | |
|---|---|---|---|---|
| | | |  |  |
| 11 | **58c** | 100, 8 | | **59k:** 52 |
| |  | |  |  |
| 12 | **58d** | 100, 2 | | **59l:** 54 |
| | | |  |  |
| 13 | **58d** | 100, 3 | | **59m:** 46 |
| |  | |  |  |
| 14 | **58e** | 100, 6 | | **59n:** 83 |
| | | |  |  |
| 15 | **58e** | 100, 5 | | **59o:** 75 |
| | | |  |  |
| 16 | **58e** | 100, 6 | | **59p:** 86 |

**Table 7.** (continued)

| | | | | |
|---|---|---|---|---|
| 17 |  **58f** | 100, 7 |  |  **59q:** 62 |
| 18 | **58f** | 100, 5 |  |  **59r:** 80 |

[a] The Suzuki cross-coupling reactions were carried out under the following conditions: arylboronic ester (1 equiv), aryl halide (1.2 equiv), $Pd(PPh_3)_4$ (3 mol%), $K_3PO_4$ (2.0 equiv), and dioxane/water (v/v = 10 : 1), 100 $^oC$, 2-8 h. [b] Isolated yield of analytically pure product.

## 5.4 Synthesis of polyfunctional *o*-, *m*-, or *p*-terphenyls *via* palladium-catalyzed cross-coupling reactions of aryl triazenes with phenylboronic acids in the presence of $BF_3{\cdot}OEt_2$

Using our method, we have developed a new terphenyl synthesis. Starting from the functionalized aryl triazenes of type **59**, we performed a palladium catalyzed cross-coupling reaction with areneboronic acids by a $BF_3{\cdot}OEt_2$ induced triazene decomposition[68] leading to the terphenyls derivatives of type **60**. Therefore, reaction of aryl triazenes such as **59a, 59e, 59h,** or **59k** with 3-methoxybenzeneboronic acid (2 equiv) in the presence of $[Pd(OAc)_2]$ (10 mol%) and $BF_3{\cdot}OEt_2$ (1.5 equiv) in methanol/ether (2 : 1) at 0 $^oC$ for 3-5 h produces the polyfunctional *p*-terphenyls **60a** (65 %; entry 1, Table 8), **60b** (63 %; entry 2), **60c** (78 %; entry 3), or **60d** (72 %, entry 4). Furthermore, starting from **59p**, the cross-coupling with 3-methoxybenzeneboronic acid or 4-formylbenzeneboronic acid is complete after 5 or 11 h at 0 $^oC$ affording the polyfinctional *o*-terphenyls **60e** (72 %; entry 5) and **60f** (65 %; entry 6). A similar coupling reaction is also readily achieved for aryl triazene **59q** and 3-methoxybenzeneboronic acid or 4-formylbenzeneboronic acid, providing the *m*-terphenyls

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[68] T. Saeki, E. C. Son, K. Tamao, *Org. Lett.* **2004**, *6*, 617.

**60g** (73 %; entry 7) and **60h** (80 %; entry 8). It is worth noting that sensitive functional groups such as aldehyde, ester, and nitrile are also tolerated under the Lewis acid conditions (entries 1, 3, and 4-6, Table 8).

**Table 8.** Polyfunctional *o*-, *m*-, *p*-terphenyls of type **60** obtained by palladium-catalyzed cross-coupling reactions with aryl triazenes of type **59** and phenylboronic acids in the presence of $BF_3 \cdot OEt_2$

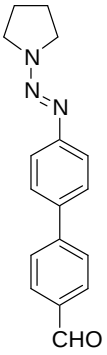
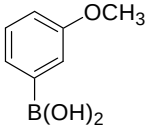
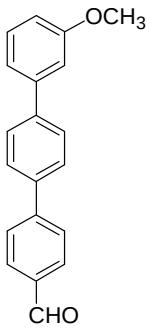
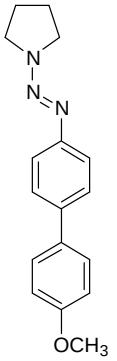
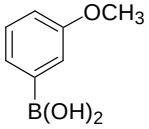
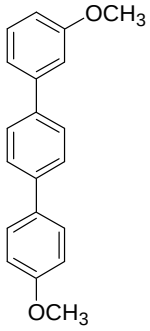
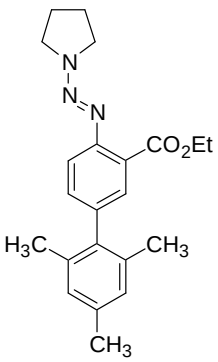
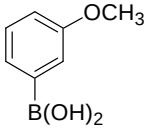
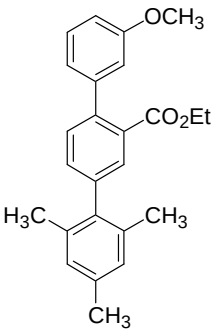
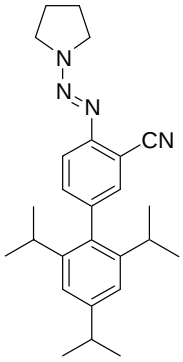
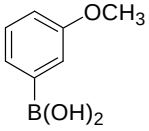
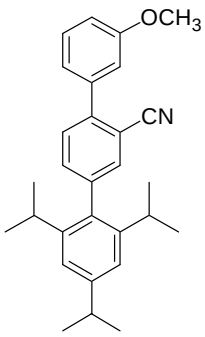
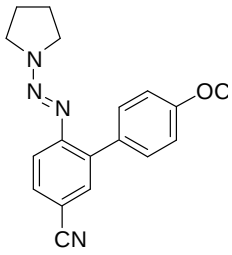
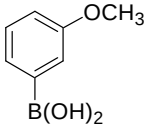
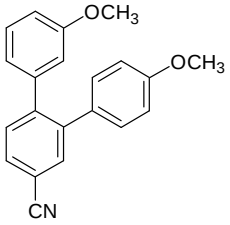
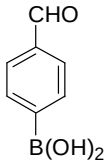
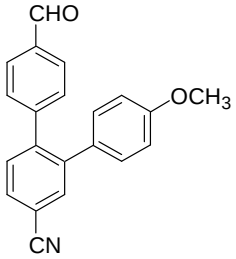
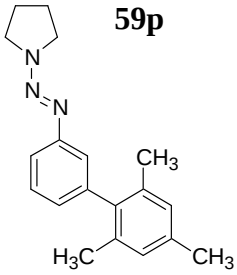
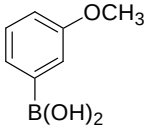
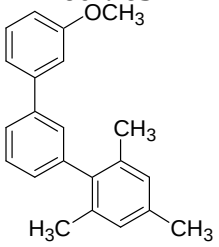
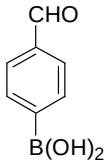
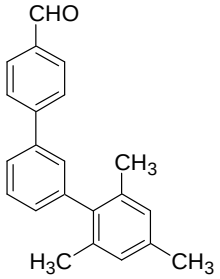
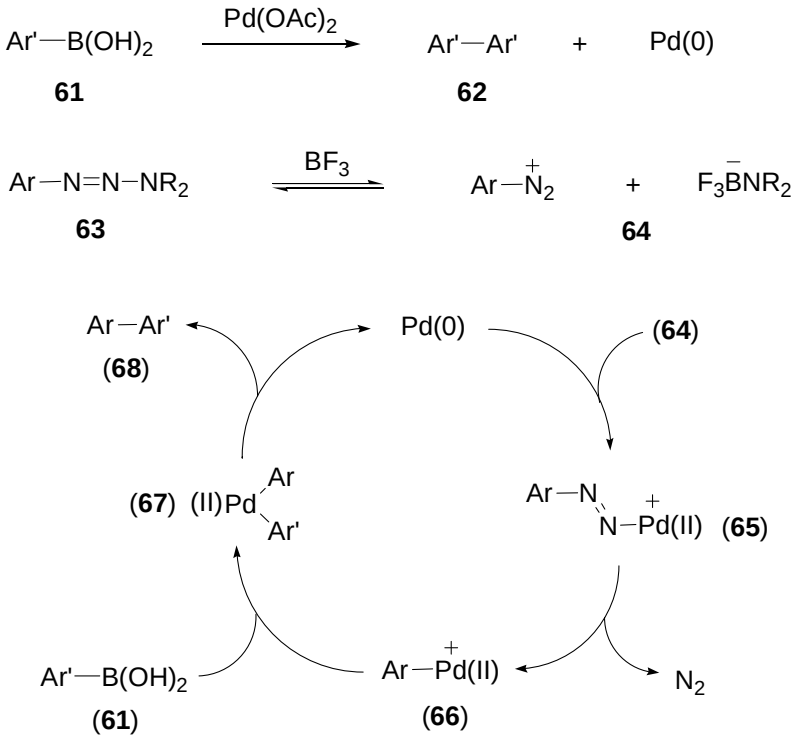
| entry[a] | aryl triazene of type **59** | T, t [°C, h] | phenylboronic acid | product of type **60** yield [%][b] |
|---|---|---|---|---|
| 1 |  **59a** | 0, 4 |  |  **60a:** 65 |
| 2 |  **59e** | 0, 3 |  |  **60b:** 63 |
| 3 |  **59h** | 0, 5 |  |  **60c:** 78 |

**Table 8.** (continued)

| | | | | |
|---|---|---|---|---|
| 4 |  **59k** | 0, 4.5 |  |  **60d:** 72 |
| 5 |  **59p** | 0, 5 |  |  **60e:** 72 |
| 6 | **59p** | 0, 11 |  |  **60f:** 65 |
| 7 |  **59q** | 0, 4.5 |  |  **60g:** 73 |
| 8 | **59q** | 0, 12 |  |  **60h:** 80 |

[a] The reactions were carried out under the following conditions: aryl triazene (1 equiv), phenylboronic acid (2 equiv), $Pd(OAc)_2$ (10 mol%), $BF_3{\cdot}OEt_2$ (1.5 equiv), and methanol/ether (v/v = 2 : 1), 0 $^oC$, 3-12 h. [b] Isolated yield of analytically pure product.

A tentative mechanism for the $BF_3 \cdot OEt_2$-induced cross-coupling reaction involving the formation of the diazonium salt (**64**) is described in Scheme 35.



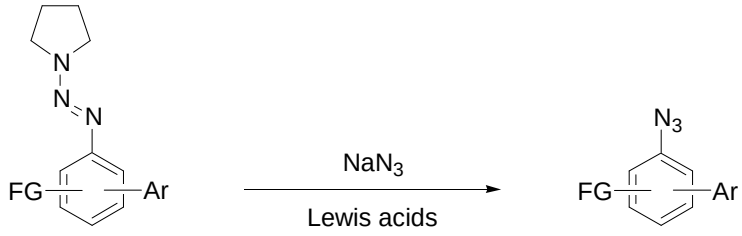

**Scheme 35.** A plausible mechanism for the palladium-catalyzed cross-coupling reaction of aryl triazenes with areneboronic acids in the presence of $BF_3 \cdot OEt_2$.

Reaction of $Pd(OAc)_2$ with the excess areneboronic acid **61** gives Pd(0) and biphenyl **62** as a byproduct. Boron trifluoride induced decomposition of aryl triazene **63** generates the diazonium salt **64**, which reacts with Pd(0) to form the aryldiazo-palladium (II) species **65**. After loss of nitrogen, the aryl-palladium (II) **66** proceeds a transmetalation with the areneboronic acid **61** leading to the diaryl-palladium (II) species **67**, which undergoes a reductive elimination affording the product **68** and regenerating Pd(0).

# 6. Synthesis of Ellipticine and Related Derivatives *via* a Key Transformation from Aryl Triazenes to Aryl Azides

## 6.1 Introduction

The use of aryl azides as synthetic intermediates has attracted much research interest due to their potential applications in organic synthesis.[69] They have been used for the synthesis of anilines,[70] cycloaddition reactions,[71] and the generation of nitrenes.[72] Recently, Bräse has prepared aryl azides starting from polymer-bound triazenes.[73] A variety of triazene resins have proved to be useful intermediates for the solid-phase synthesis of aryl azides. More recently, we also reported a novel halogen-magnesium exchange reaction on halogenated aryl triazenes (X = Br or I) by using the mixed Mg/Li-reagent *i*-PrMgCl·LiCl,[51] which allowed the preparation of polyfunctional aryl triazenes of type **69** (Scheme 36).[52] Using a triazene functionality (ArN=N-$NR_2$) can be considered as being the best way to protect a diazonium salt and to carry this reactive functionality through several synthetic steps. Of special synthetic interest is the conversion of a triazene moiety to an azide under mild reaction conditions, which could tolerate a number of functional groups. In spite of the importance and usefulness of azides, a practical synthesis of natural products using a strategy involving a triazene to azide conversion as a key step has not been reported yet. Therefore, we wish to develop an efficient method for the conversion of triazenes of type **69** to the polyfunctional aryl azides of type **70** (Scheme 36).




**69** **70**

**Scheme 36.** Preparation of aryl azides from aryl triazenes.

45

[69] a) S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem.* **2005**, *117*, 5320; *Angew. Chem. Int. Ed.* **2005**, *44*, 5188; b) S. Patai, *The Chemistry of Diazonium and Diazo Groups*, In *The Chemistry of Functional Groups*; S. Patai, Ed.; John Wiley: Chichester, **1978**.

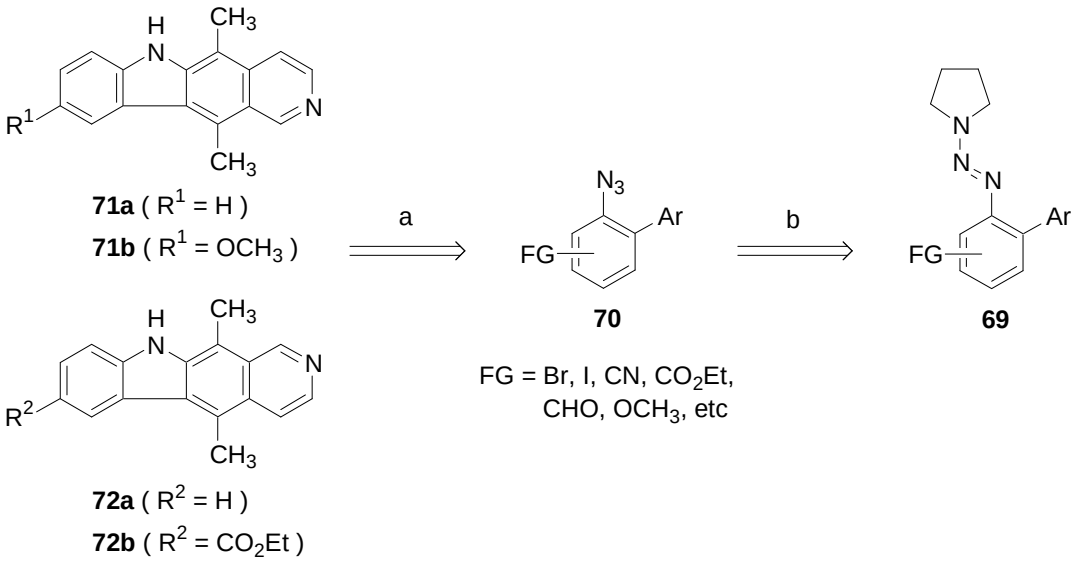
[70] H. M. S. Kumar, B. V. S. Reddy, S. Anjaneyulu, J. S. Jadav, *Tetrahedron Lett.* **1999**, *40*, 8305.

[71] a) R. Huisgen, *Angew. Chem.* **1963**, *75*, 604; *Angew. Chem. Int. Ed.* **1963**, *2*, 565; b) R. Huisgen, R. Knorr, L. Möbius, G. Szeimies, *Chem. Ber.* **1965**, *98*, 4014.

[72] a) F. Tiemann, *Ber. Dtsch. Chem. Ges.* **1891**, *24*, 4162; b) N. P. Gritsan, E. A. Pritchina, *Russ. Chem. Rev.* **1992**, *61*, 500; c) M. F. Budyka, M. M. Kantor, M. V. Alfimov, *Russ. Chem. Rev.* **1992**, *61*, 25; G. Bucher in *CRC Handbook of Organic Photochemistry and Photobiology* (Hrsg.: W. Horspool, F. Lenci), 2. Aufl., CRC, Boca Raton, **2004**, S. 44/1-44/31.

[73] S. Bräse, C. Gil, K. knepper, V. Zimmermann, *Synlett* **2004**, 1163.

By using this approach, we have envisioned that the biologically active compounds, ellipticine (**71a**) and 9-methoxyellipticine (**71b**), would be readily prepared in two steps starting from the corresponding aryl triazenes of type **69**. Similarly, the synthesis of isoellipticine (**72a**) and 7-carbethoxyisoellipticine (**72b**) might also be envisaged using the same approach (Scheme 37).

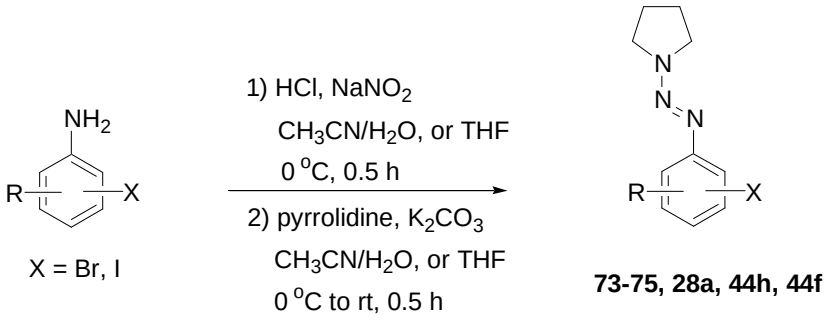



**Scheme 37.** Retrosynthetic analysis of compounds **71a**, **71b**, **72a**, and **72b**. a) Thermal decomposition of azides; b) Conversion of the triazene group to an azide.

## 6.2 Preparation of polyfunctional aryl triazenes

Aryl triazenes **73-79, 28a, 44h, 44f, 30j, 30g, 30l, 41a, 58a-b, and 58d** were easily synthesized and isolated mostly in good yields as shown in Schemes 38 and 39 (see also Figure 1). Thus, 1-(2-iodophenylazo)pyrrolidine **73** was obtained from 2-iodoaniline in 92 % yield *via* a diazotation and trapping with pyrrolidine. Triazenes **74** and **75** were also readily prepared from the corresponding anilines under the same reaction conditions.[52] 1-(4-Cyano-2-iodophenylazo)pyrrolidine (**29d**) was prepared from 2-iodo-4-cyanoaniline reacted with *i*PrMgCl·LiCl affording the expected arylmagnesium derivative, which was transmetalated with CuCN·2LiCl to the corresponding organocopper derivative.[53] This copper reagent readily underwent an addition-elimination reaction with 3-iodo-2-cyclohexen-1-one giving the triazene **76** in 81 % yield. Reaction of the arylmagnesium derivative of 1-(2-carbethoxy-4-iodophenylazo)pyrrolidine with *N*,*N*-dimethylformamide furnished the expected triazene **77**

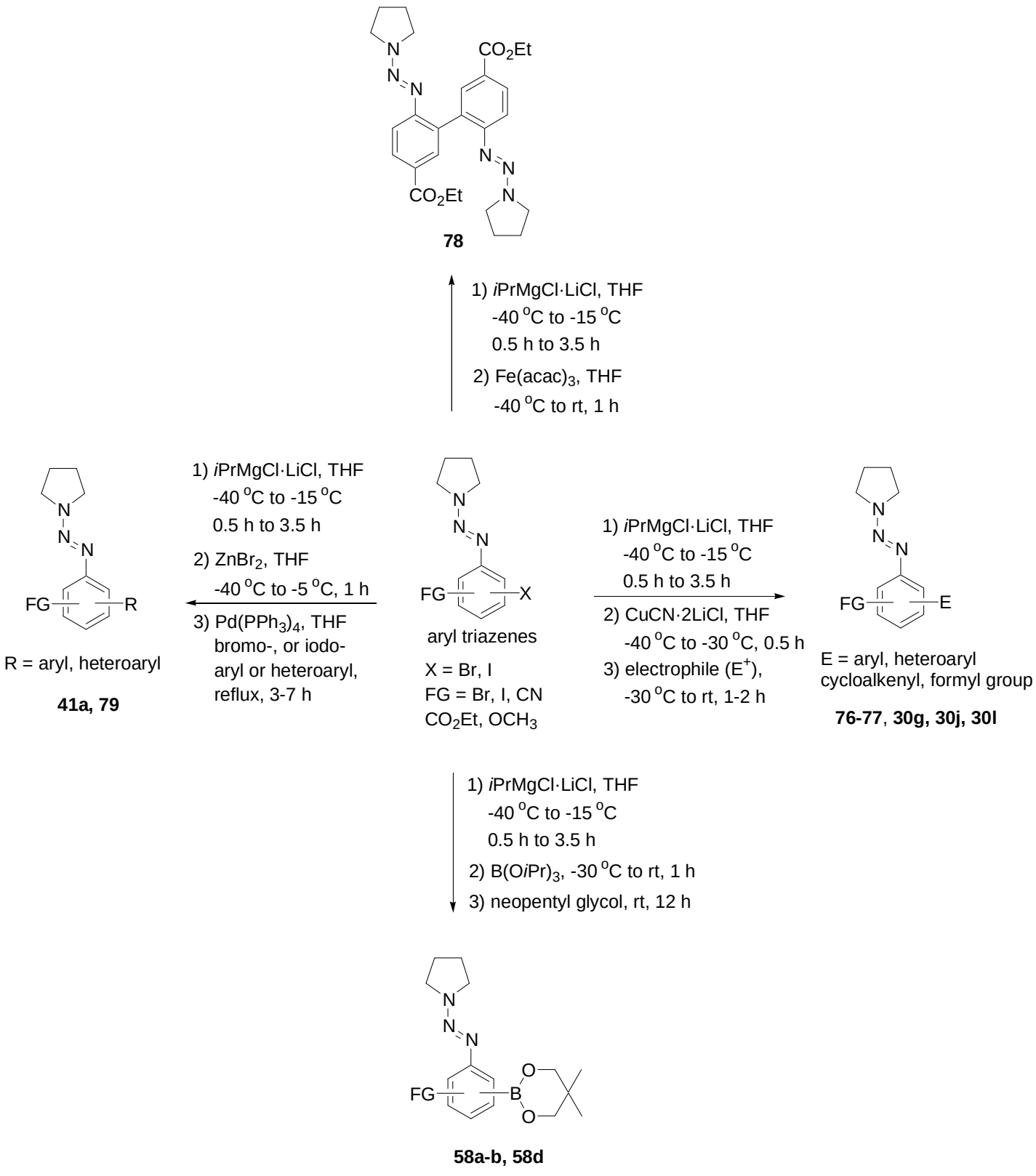
in 85 % yield. Iron(III)–catalyzed homo-coupling reaction[74] of the arylmagnesium derivative of 1-(4-carbethoxy-2-iodophenylazo)pyrrolidine afforded the *bis*-triazene **78** in 52 % yield. Starting from the arylmagnesium derivative of 1-(4-methoxy-2-iodophenylazo)pyrrolidine, we performed a Negishi cross-coupling[60] with 3-iodopyridine after a transmetalation to the corresponding zinc reagent leading to the triazene **79** in 76 % yield. Triazenes **28a, 44h,**[15] **44f,**[15] **30j, 30g, 30l, and 41a** were prepared in 85-93 % yield according to typical procedures (**TP1**, **TP3**, and **TP8**) in the experimental part or in the literatures. As described in chapter 5, treatment of the arylmagnesium derivative of 1-(4-iodophenylazo)pyrrolidine (**28e**), 1-(2-carbethoxy-4-iodophenylazo)pyrrolidine (**44a**), or 1-(2,6-dibromophenylazo)pyrrolidine (**28a**) with triisopropyl borate followed by the addition of neopentyl glycol produced the expected triazenes **58a** (86 %), **58b** (78 %), or **58d** (55 %) (Figure 1).



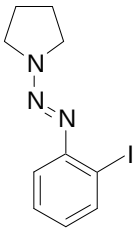

**Scheme 38.** Synthesis of aryl triazenes **73-75**, **28a**, **44h** and **44f**.

47

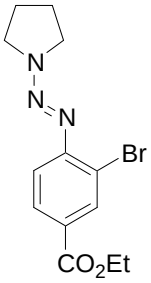
[74] T. Nagono, T. Hayashi, *Org. Lett.* **2005**, *7*, 491.



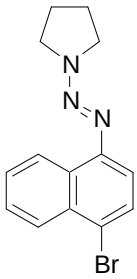

**Scheme 39.** Synthesis of aryl triazenes **78**; **76-77, 30g, 30j, 30l**; **58a-b, 58d**; **41a, 79**.



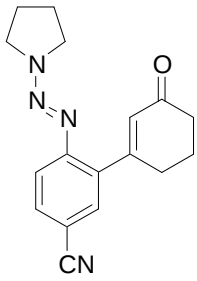
**73**: 92 %



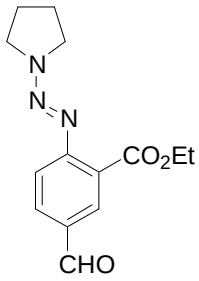
**74**: 94 %



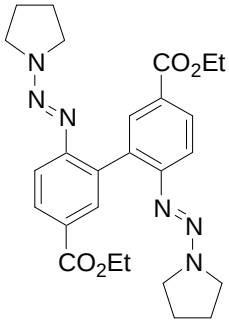
**75**: 96 %



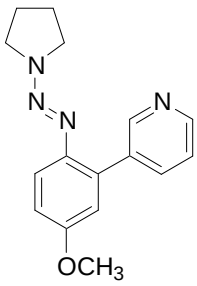
**76**: 81 %



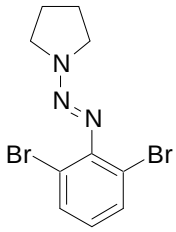
**77**: 85 %



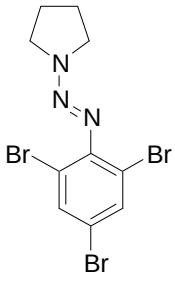
**78**: 52 %



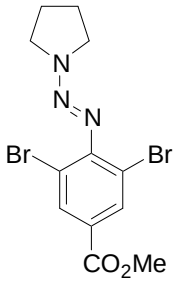
**79**: 76 %



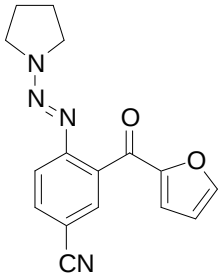
**28a**: 88 %



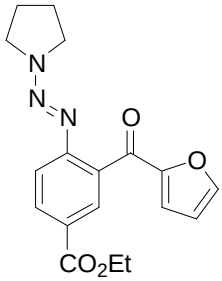
**44h**: 85 %



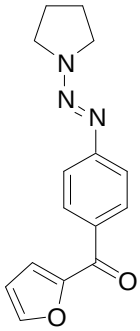
**44f**: 81 %



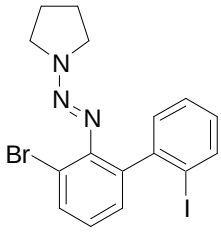
**30j**: 85 %



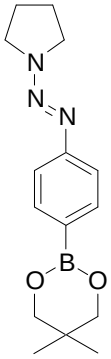
**30g**: 86 %



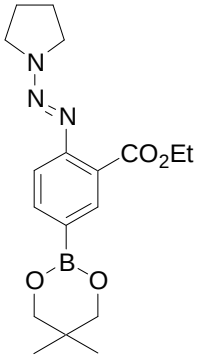
**30l**: 88 %



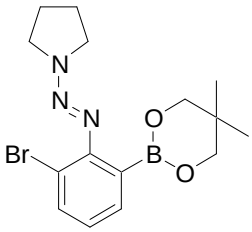
**41a**: 88 %



**58a**: 86 %



**58b**: 78 %



**58d**: 55 %

**Figure 1.** Polyfunctional aryl triazenes prepared.[a]

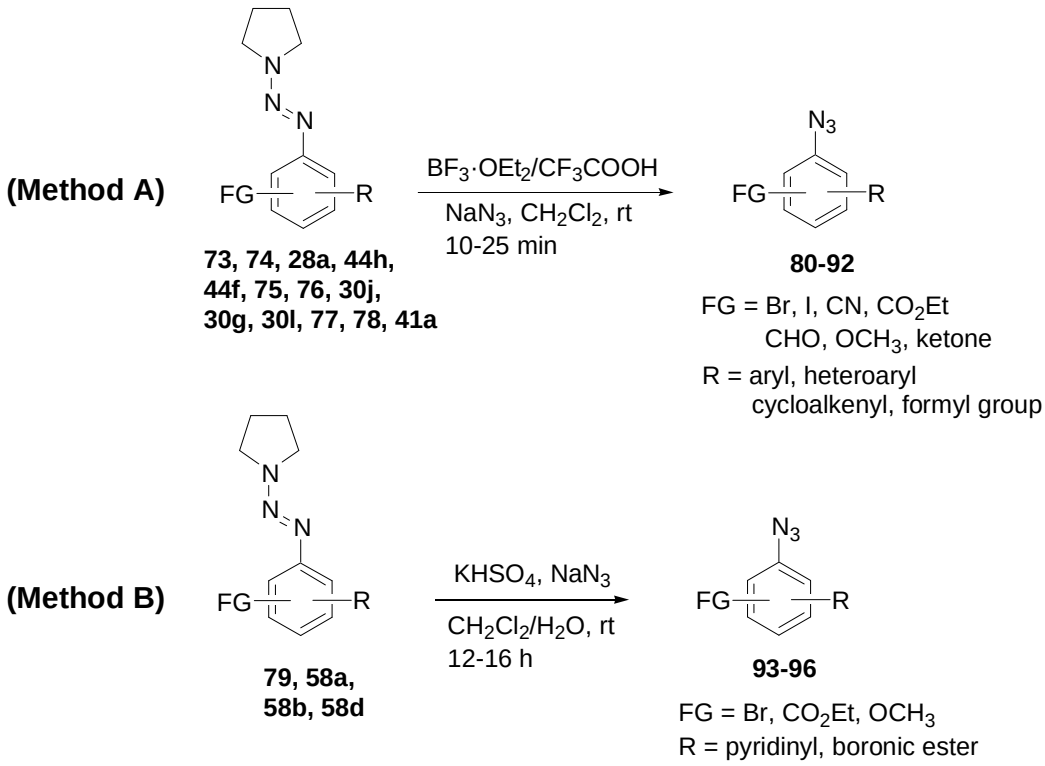
[a] Isolated yield of analytically pure product.

## 6.3 Preparation of polyfunctional aryl azides

The triazene moieties can be readily converted the corresponding azides in moderate to excellent yields.[73] However, we have found that the azidation reactions were best performed either by using $BF_3 \cdot OEt_2$/TFA (trifluoroacetic acid) in dichloromethane (Method A) or by using $KHSO_4$ in dichloromethane/water (Method B) at room temperature in the presence of sodium azide (Scheme 40). Thus, the azidation of 1-(2-iodophenylazo)pyrrolidine **73** was accomplished by using a mixture of $BF_3 \cdot OEt_2$ and TFA (1/1, 2 equiv to the triazene) and sodium azide (2 equiv to the triazene) in dichloromethane at room temperature (Method A) affording the expected 1-azido-2–iodo-benzene (**80**) in 80 % yield (entry 1 of Table 9). Azidation of the aryl triazenes **74, 28a, 44h, 44f, 75-76, 30j, 30g, 30l, 77-78,** and **41a** with the same reaction conditions as described in Scheme 40 furnished the aryl azides **81-92** in 63-94 % yield (entries 2-13, Table 9).

It is worth noting that the combination of $BF_3 \cdot OEt_2$ and TFA seems to be a more efficient reagent than either reagent alone, $BF_3 \cdot OEt_2$ or TFA, respectively, in these azidation reactions. For instance, the reaction of **74-78**; **28a, 44h, 44f, 30j, 30g, 30l,** and **41a** with either $BF_3 \cdot OEt_2$ (2.0 equiv) or TFA (2.0 equiv) in the presence of sodium azide (2.0 equiv) hardly proceeded to completion, and 30-40 % of the starting material was recovered even when the reaction mixture was stirred at room temperature for 1 h. The mixture of $BF_3 \cdot OEt_2$ and TFA can be regarded as a super-Brønsted acid, a more powerful and convenient reagent for the conversion of triazenes to azides. A range of functional groups are also tolerated under our mild reaction conditions giving a practical access to a variety of functionalized aryl azides.

The triazenes **79**, **58a-b**, and **58d** were readily converted to the corresponding aryl azides **93-96** in 78-96 % yield (entries 14-17, Table 9) using $KHSO_4$ (10 equiv) in dichloromethane at room temperature in the presence of sodium azide (5 equiv). It is interesting to note that some heterocycles or reactive functional groups, such as a pyridine ring (compound **93**) or boronic esters (compound **94-96**) are tolerated. Thus, using $KHSO_4$ as reagent, a smooth conversion of an aryl triazene to an aryl azide is achieved. However, the reaction time is usually longer (12-16 h; Method B).




**Scheme 40.** Synthesis of polyfunctional aryl azides **80-92** (Method A); **93-96** (Method B).

**Table 9.** Polyfunctional aryl azides (**80-96**) obtained from the corresponding aryl triazenes by using either Method A or Method B.

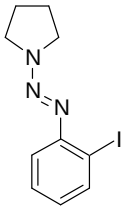
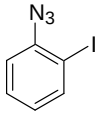
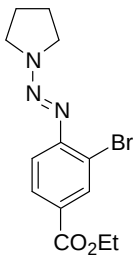
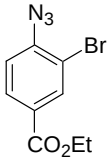
| entry | aryl triazenes | method[a] | aryl azides yield [%][b] |
|---|---|---|---|
| 1 |  **73** | A |  **80:** 80 |
| 2 |  **74** | A |  **81:** 78 |

**Table 9.** (continued)

| | | | |
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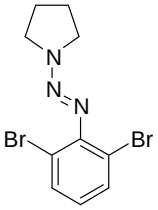
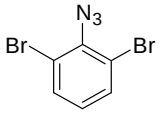
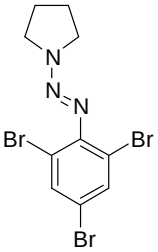
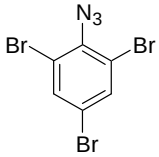
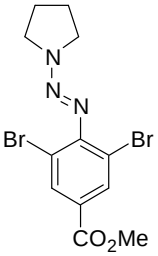
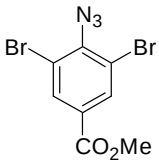
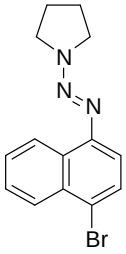
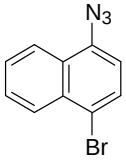
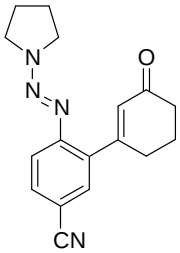
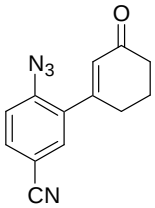
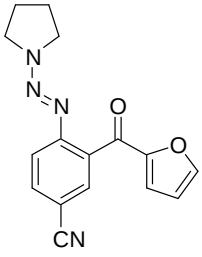
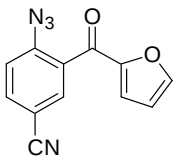
| 3 |  **28a** | A |  **82:** 88 |
| 4 |  **44h** | A |  **83:** 82 |
| 5 |  **44f** | A |  **84:** 84 |
| 6 |  **75** | A |  **85:** 81 |
| 7 |  **76** | A |  **86:** 76 |
| 8 |  **30j** | A |  **87:** 63 |

**Table 9.** (continued)

| | | | |
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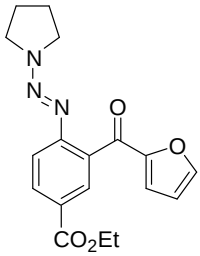
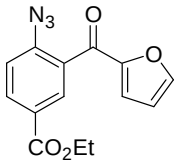
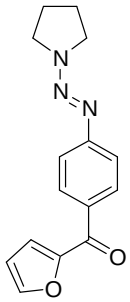
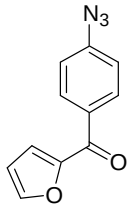
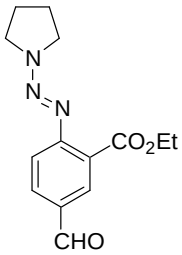
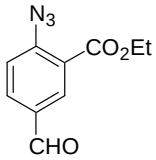
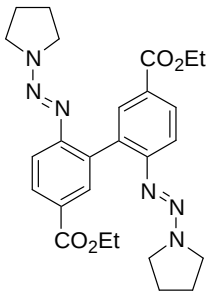
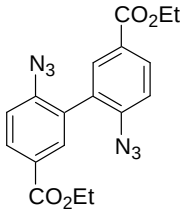
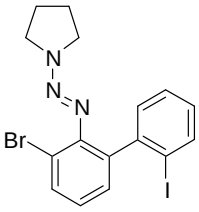
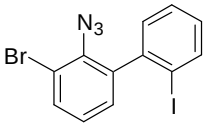
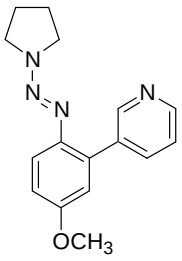
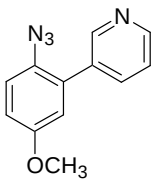
| 9 |  **30g** | A |  **88:** 86 |
| 10 |  **30l** | A |  **89:** 93 |
| 11 |  **77** | A |  **90:** 94 |
| 12 |  **78** | A |  **91:** 72 |
| 13 |  **41a** | A |  **92:** 78 |
| 14 |  **79** | B |  **93:** 78 |

**Table 9.** (continued)

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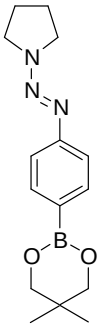
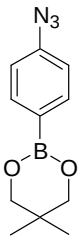
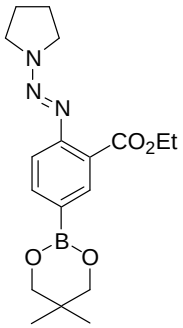
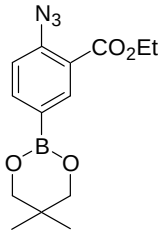
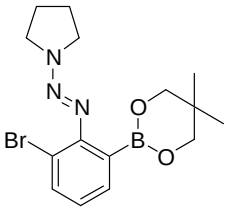
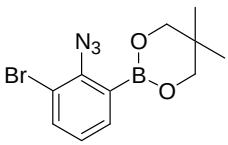
| 15 |  **58a** | B |  **94:** 96 |
| 16 |  **58b** | B |  **95:** 88 |
| 17 |  **58d** | B |  **96:** 92 |

[a] Method A: $BF_3{\cdot}OEt_2$/TFA, $NaN_3$, $CH_2Cl_2$, rt, 10-25 min; Method B: $KHSO_4$, $NaN_3$, $CH_2Cl_2/H_2O$, rt, 12-16 h. TFA = trifluoroacetic acid. [b] Isolated yield of analytically pure product.

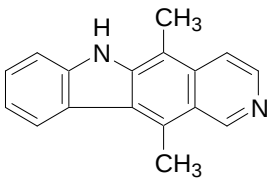
## 6.4 Synthesis of ellipticine and 9-methoxyellipticine by the thermal decomposition of azides

The Ochrosia and Aspidosperma plant alkaloids ellipticine (**71a**)[75] and its 9-oxygenated derivatives have been shown to exhibit potential anticancer activities.[76] Particularly, 9-methoxyellipticine (**71b**) was used to treat patients with acute myeloblastic leukemia[77] (Figure 2). Therefore, the preparation of **71a** or **71b** has attracted the interest of synthetic organic chemists for the past half century and numerous procedures have been reported.[78]

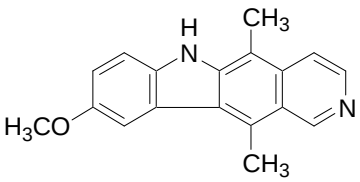
54

[75] a) S. Goodwin, A. F. Smith, E. C. Horning, *J. Am. Chem. Soc.* **1959**, *81*, 1903; b) R. B. Woodward, G. A. Iacobucci, F. A. Hochstein, *Ibid.* **1959**, *81*, 4434.
[76] N. Van-Bac, C. Moisand, A. Gouyette, G. Muzard, N. Dat-Xuong, J. B. Le Pecq, C. Paoletti, *Cancer Treat. Rep.* **1980**, *64*, 879 and references cited therein.
[77] G. Mathé, M. Hayat, F. De Vassal, L. Schwarzenberg, M. Schneider, J. R. Schlumberger, C. Jasmin, C. Rosenfeld, *Rev. Eur. Etud. Clin. Biol.* **1970**, *15*, 541.
[78] a) M. Sainsbury, *Ellipticines*, in: *Chemistry of Antitumour Agents* (Ed.: D. E. V. Wilman), Blackie, Glasgow and London, **1990**; b) G. W. Gribble, *Synthesis and Antitumour Activity of Ellipticine Alkaloids and Related Compounds*, in: *The*

Because of our interest in triazenes and azides chemistry, we have focused our attention on the synthesis of polyfunctional aryl azides, which can undergo a thermal decomposition to give ellipticine derivatives such as ellipticine (**71a**) and 9-methoxyellipticine (**71b**).[79]



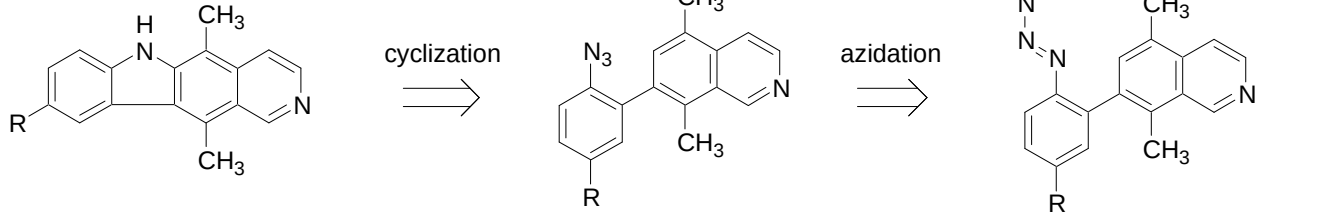

**71a**, ellipticine




**71b**, 9-methoxyellipticine

**Figure 2.** Potent antitumor agents: ellipticine **71a** and 9-methoxyellipticine **71b**.

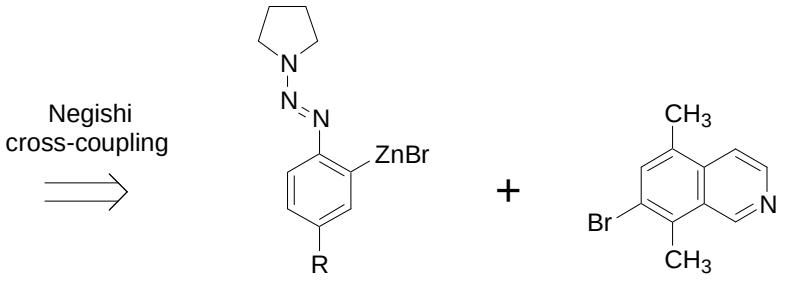
Herein, we describe a short and practical synthesis of these potent anticancer agents in three steps. The precursors were prepared by using a Negishi cross-coupling reaction of 1-(2-iodophenylazo)pyrrolidine (**73**) or 1-(4-methoxy-2-iodophenylazo)pyrrolidine (**97**) with 7-bromo-5,8-dimethyl-isoquinoline (**98**) to give the aryl triazene **99a** or **99b** which was then converted to the aryl azide **100a** or **100b** followed by a thermal cyclization (Scheme 41).




R = H, ellipticine, **71a**
R = $OCH_3$, 9-methoxyellipticine, **71b**

R = H, aryl azide, **100a**
R = $OCH_3$, aryl azide, **100b**

R = H, aryl triazene, **99a**
R = $OCH_3$, aryl triazene, **99b**




R = H, zinc derivative of **73**
R = $OCH_3$, zinc derivative of **97**

**98**

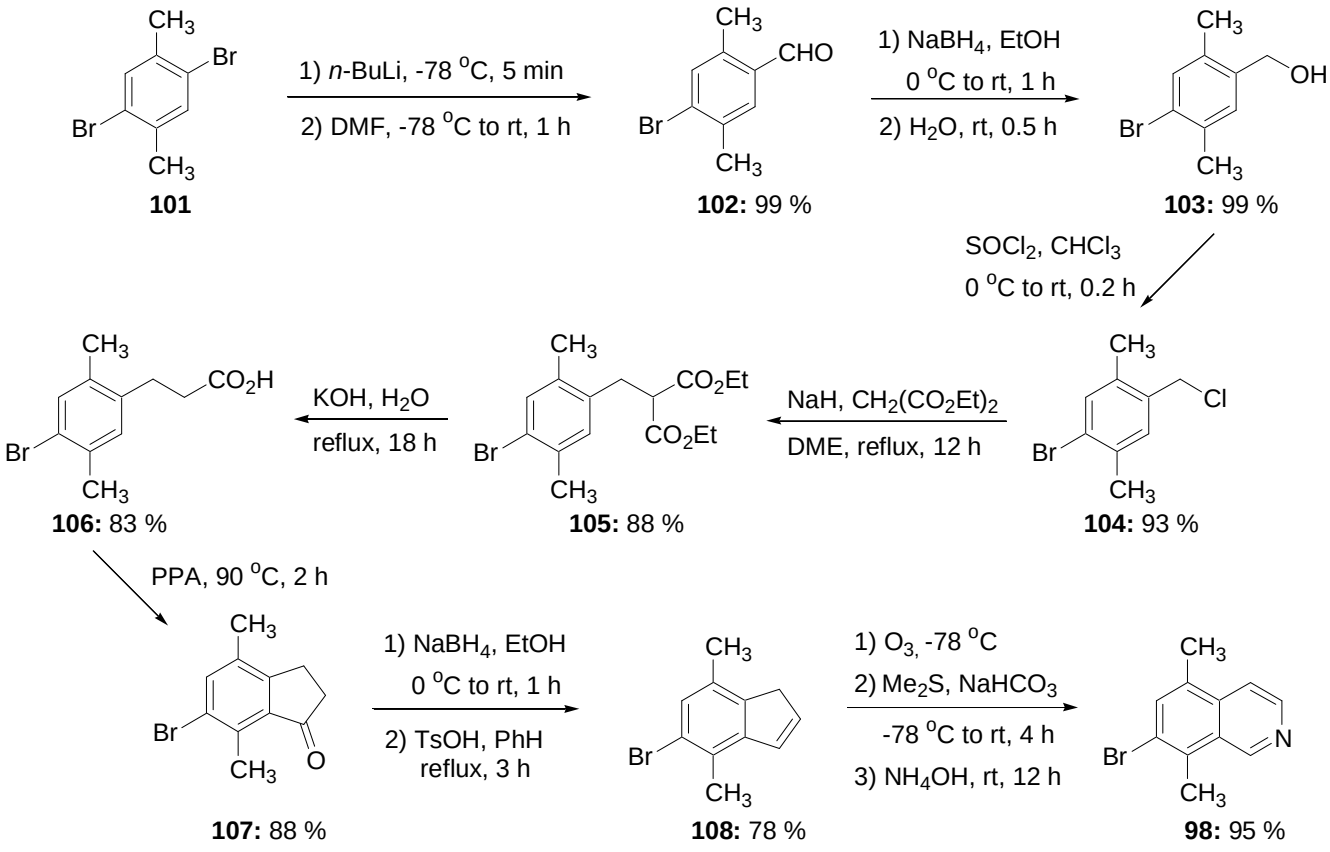
**Scheme 41.** Retrosynthetic analysis of **71a** and **71b**.

---

*Alkaloids*, vol. 39 (Ed.: A. Brossi), Academic Press, San Diego, **1990**, p. 239; c) G. W. Gribble, M. G. Saulnier, *Heterocycles* **1985**, *23*, 1277; d) G. W. Gribble, *Synthetic Approaches to the Ellipticine Alkaloids via Metalation and Cycloaddition Chemistry*, in: *Advances in Heterocyclic Natural Product Synthesis*, vol. 1 (Ed.: W. H. Pearson), Jai Press, Greenwich, **1990**; e) G. W. Gribble, *Synlett* **1991**, 289; f) G. W. Gribble, M. G. Saulnier, M. P. Sibi, J. A. Obaza-Nutaitis, *J. Org. Chem.* **1984**, *49*, 4518; g) C. May, C. J. Moody, *J. Chem. Soc., Chem. Commun.* **1984**, 926; h) C. May, C. J. Moody, *J. Chem. Soc., Perkin Trans. 1* **1988**, 247.

[79] a) P. A. S. Smith, B. B. Brown, *J. Am. Chem. Soc.* **1951**, *73*, 2435; b) H. Jian, J. M. Tour, *J. Org. Chem.* **2003**, *68*, 5091.

The preparation of 7-bromo-5,8-dimethyl-isoquinoline **98** was achieved starting from the 1,4-dibromo-2,5-dimethyl-benzene **101**. First, we have performed a Br/Li-exchange with *n*-BuLi leading to the lithium derivative of **101** which reacted with *N*,*N*-dimethylformamide to afford the aldehyde **102** in 99 % yield. The reaction of **102** with $NaBH_4$ provided the benzyl alcohol **103** (99 %), which was then converted to the benzyl chloride **104** (93 %) by the addition of $SOCl_2$. The malonate **105** was prepared by the reaction of **104** with diethyl malonate[80] in 88 % yield. Hydrolysis and decarboxylation gave the corresponding carboxylic acid **106** in 83 % overall yield. Polyphosphoric acid (PPA) catalyzed ring closure[81] furnished the indanone **107** (88 %), which was then reduced to the corresponding indanol, followed by a dehydration with catalytic amount of *p*-TsOH in refluxing benzene which gave the indene **108** in 78 % overall yield. Ozonolysis of **108** in a mixture of $MeOH/CH_2Cl_2$, followed by a reduction workup with $Me_2S$ and treatment with conc. $NH_4OH$ provided 7-bromo-5,8-dimethyl-isoquinoline **98** in 95 % yield (Scheme 42).[82]

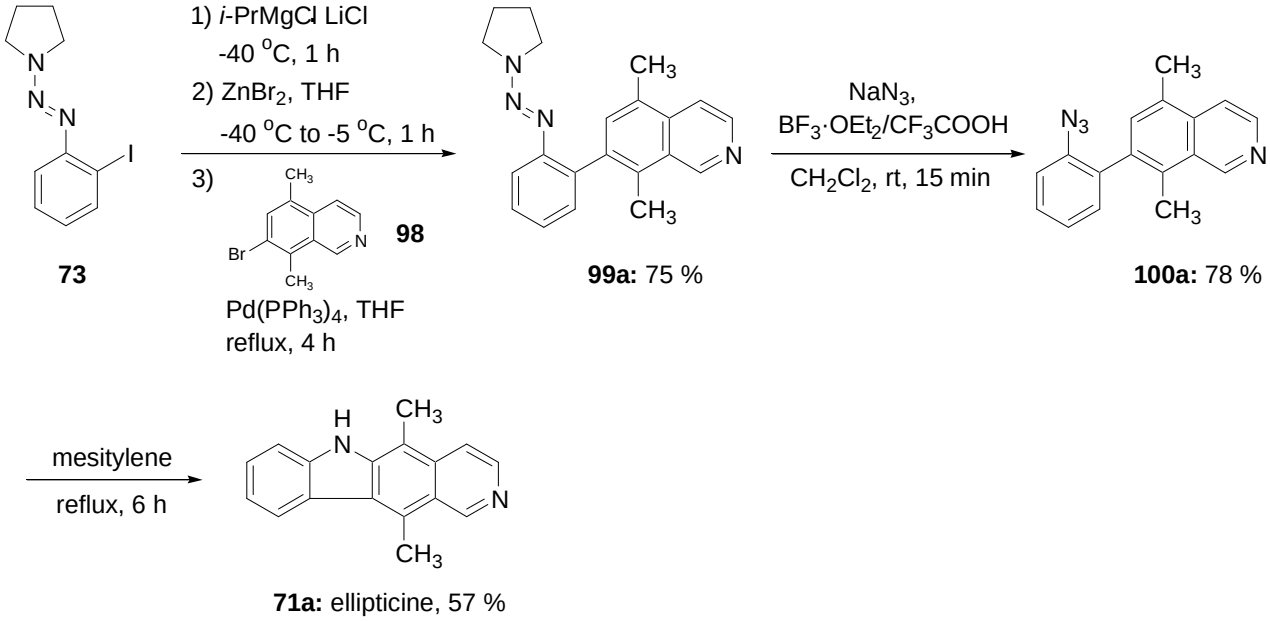



**Scheme 42.** Synthesis of the isoquinoline **98**.

56

[80] D. L. Musso, F. R. Cochran, J. L. Kelley, E. W. McLean, J. L. Selph, G. C. Rigdon, G. F. Orr, R. G. Davis, B. R. Cooper, V. L. Styles, J. B. Thompson, W. R. Hall, *J. Med. Chem.* **2003**, *46*, 399.
[81] M. L. Lewis, A. de Meijere, *Synlett* **1997**, 261.
[82] R. B. Miller, J. G. Stowell, S. Dugar, T. E. Moock, C. W. Jenks, S. C. Farmer, B. Phan, C. E. Wujcik, M. M. Olmstead, *Tetrahedron* **2002**, *58*, 6061.

A new ellipticine synthesis[83] was accomplished by starting with the arylmagnesium derivative of **73**. We have performed after a transmetalation to the zinc derivative a Negishi cross-coupling with 7-bromo-5,8-dimethyl-isoquinoline **98** leading to the polyfunctional aryl triazene **99a** (75 %), which was readily converted to the corresponding aryl azide **100a** (78 %) by the addition of $BF_3 \cdot OEt_2$/TFA in dichloromethane in the presence of $NaN_3$ (Method A). Thermal decomposition of azide **100a** in refluxing mesitylene (6 h) gave ellipticine (**71a**) in 57 % yield (Scheme 43).

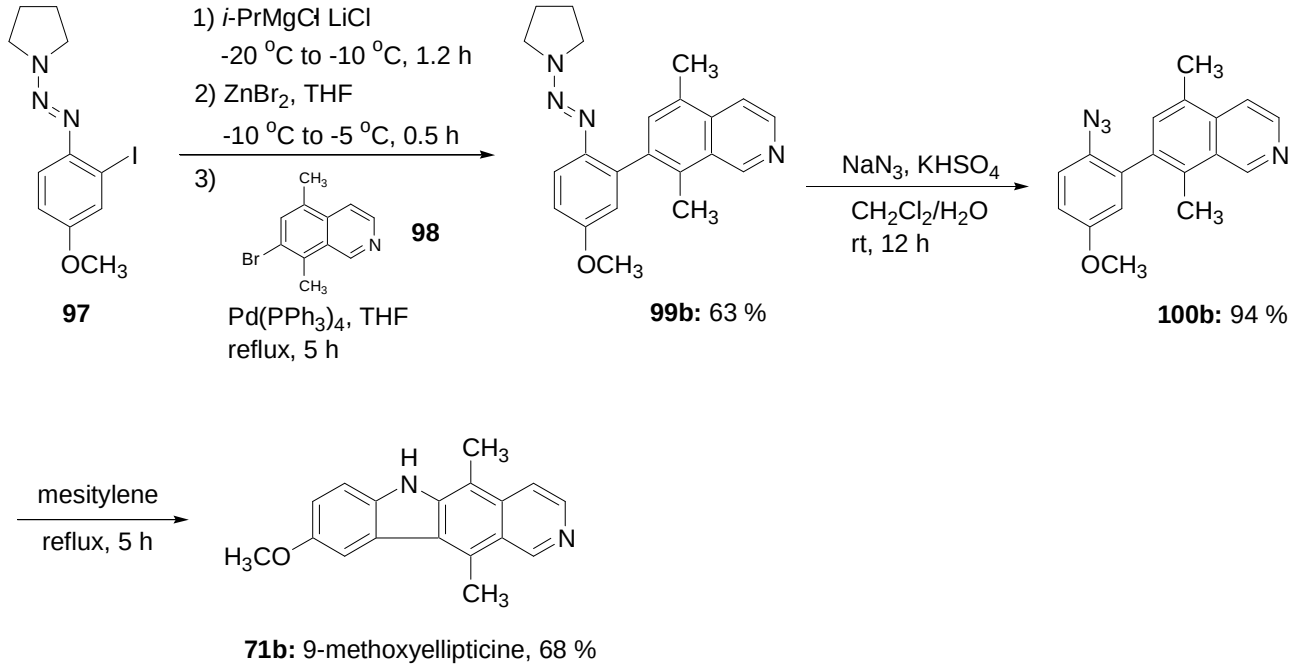



**Scheme 43.** Synthesis of ellipticine **71a**.

The same approach can be used to prepare 9-methoxyellipticine (**71b**). Indeed, the polyfunctional aryl triazene **99b** obtained from the arylzinc derivative of 1-(4-methoxy-2-iodophenylazo)pyrrolidine **97** and the isoquinoline **98** in 63 % yield was readily converted to the aryl azide **100b** (94 %) by using $KHSO_4$ in dichloromethane/water in the presence of $NaN_3$ (Method B). A solution of **100b** in mesitylene was heated at reflux for 5 h to give 9-methoxyellipticine (**71b**) in 68 % yield (Scheme 44).

57

[83] H. S. Knölker, K. R. Reddy, *Chem. Rev.* **2002**, *102*, 4303.



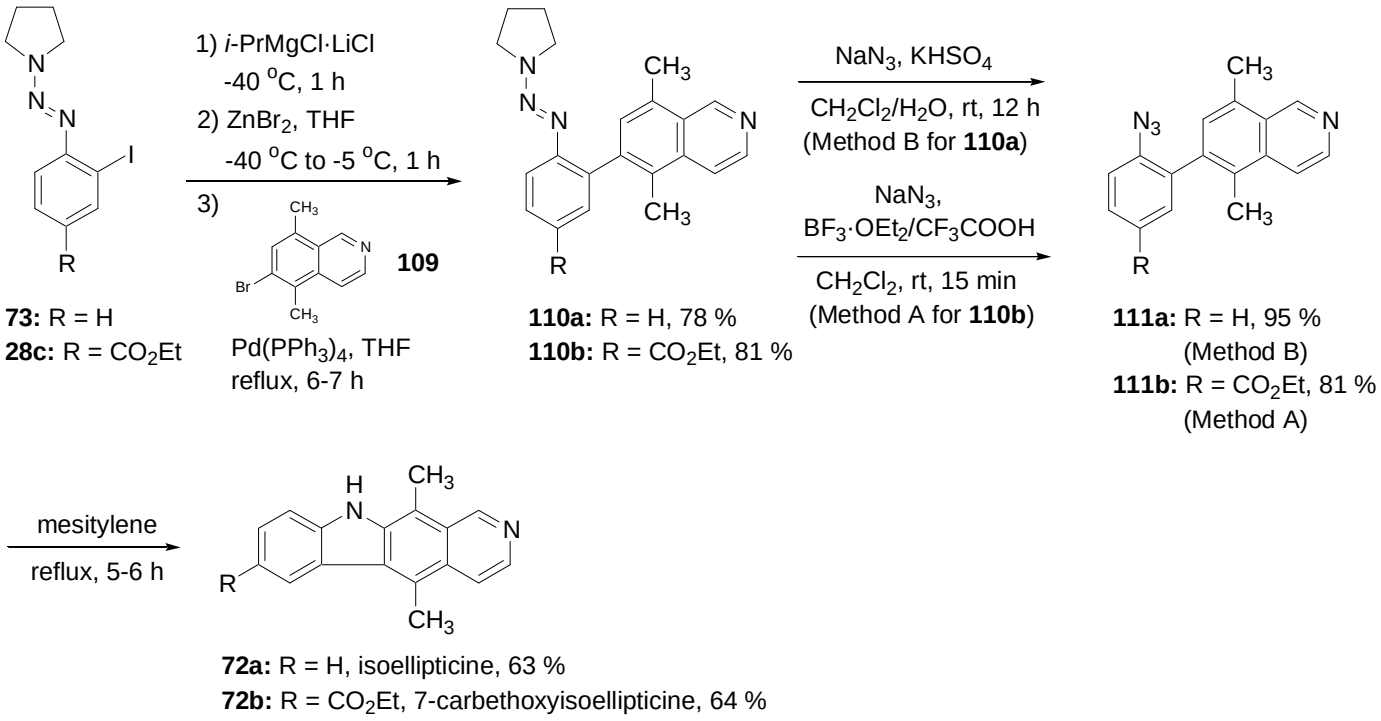

**Scheme 44.** Synthesis of 9-methoxyellipticine **71b**.

## 6.5 Synthesis of isoellipticine and 7-carbethoxyisoellipticine by the thermal decomposition of azides

Interestingly, we found that our method could also successfully be applied to the preparation of isoellipticine (**72a**) and a related derivative, 7-carbethoxyisoellipticine (**72b**). Thus, starting from the arylzinc derivatives of **73** and **28c**, a Negishi cross-coupling with 6-bromo-5,8-dimethyl-isoquinoline **109**[84] was carried out to give the derived polyfunctional aryl triazenes **110a** (78 %) and **110b** (81 %). The triazenes **110a-b** were readily converted to the aryl azides **111a** (95 %) and **111b** (81 %) by using Method B and Method A, respectively. Thermal decomposition of the aryl azides **111a-b** in refluxing mesitylene (5-6 h) furnished the isoellipticines (**72a**) (63 %) or 7-carbethoxyisoellipticine (**72b**) (64 %); (Scheme 45).

58

[84] a) R. B. Miller, T. Moock, *Tetrahedron Lett*. **1980**, *21*, 3319; b) R. B. Miller, J. G. Stowell, S. Dugar, T. E. Moock, C. W. Jenks, S. C. Farmer, B. Phan, C. E. Wujcik, M. M. Olmstead, *Tetrahedron* **2002**, *58*, 6061.




**73:** R = H
**28c:** R = $CO_2Et$

**109**

**110a:** R = H, 78 %
**110b:** R = $CO_2Et$, 81 %

**111a:** R = H, 95 %
(Method B)
**111b:** R = $CO_2Et$, 81 %
(Method A)

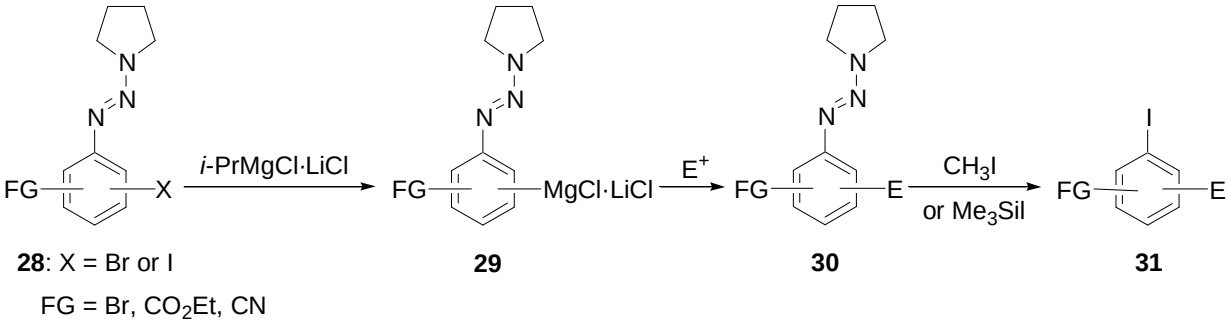
**72a:** R = H, isoellipticine, 63 %
**72b:** R = $CO_2Et$, 7-carbethoxyisoellipticine, 64 %

**Scheme 45.** Synthesis of isoellipticine **72a** and 7-carbethoxyisoellipticine **72b**.

## 7. Summary

### 7.1 Preparation of polyfunctional arylmagnesium reagents bearing a triazene moiety

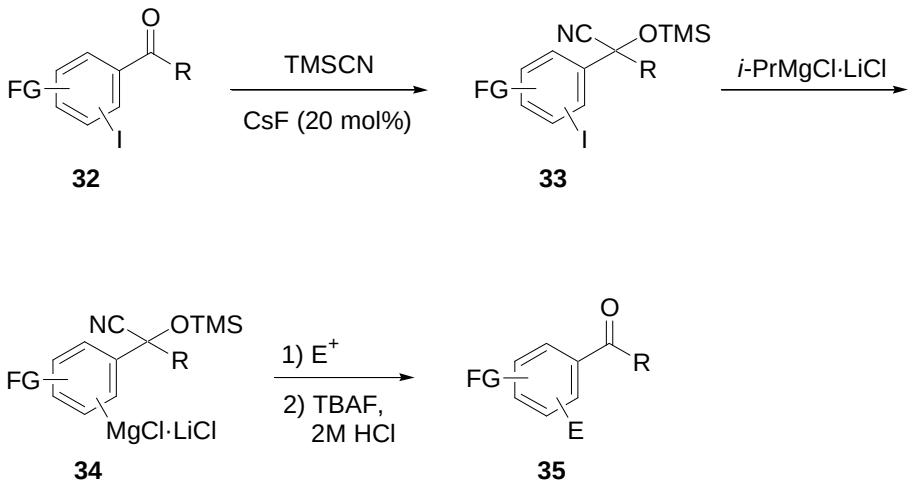
We have shown that the reaction of iodo- or bromo- substituted aryltriazenes (**28**) with *i*-PrMgCl·LiCl generates magnesiated derivatives (**29**) which react with various electrophiles (acid chlorides, 3-iodoenones, allylic halides, aldehydes) to afford polyfunctional triazenes (**30**) which can be readily converted to the corresponding polyfunctional aryl iodides (**31**) (Scheme 46).




**Scheme 46.** Preparation of polyfunctional triazenes (**30**) and aryl iodides (**31**).

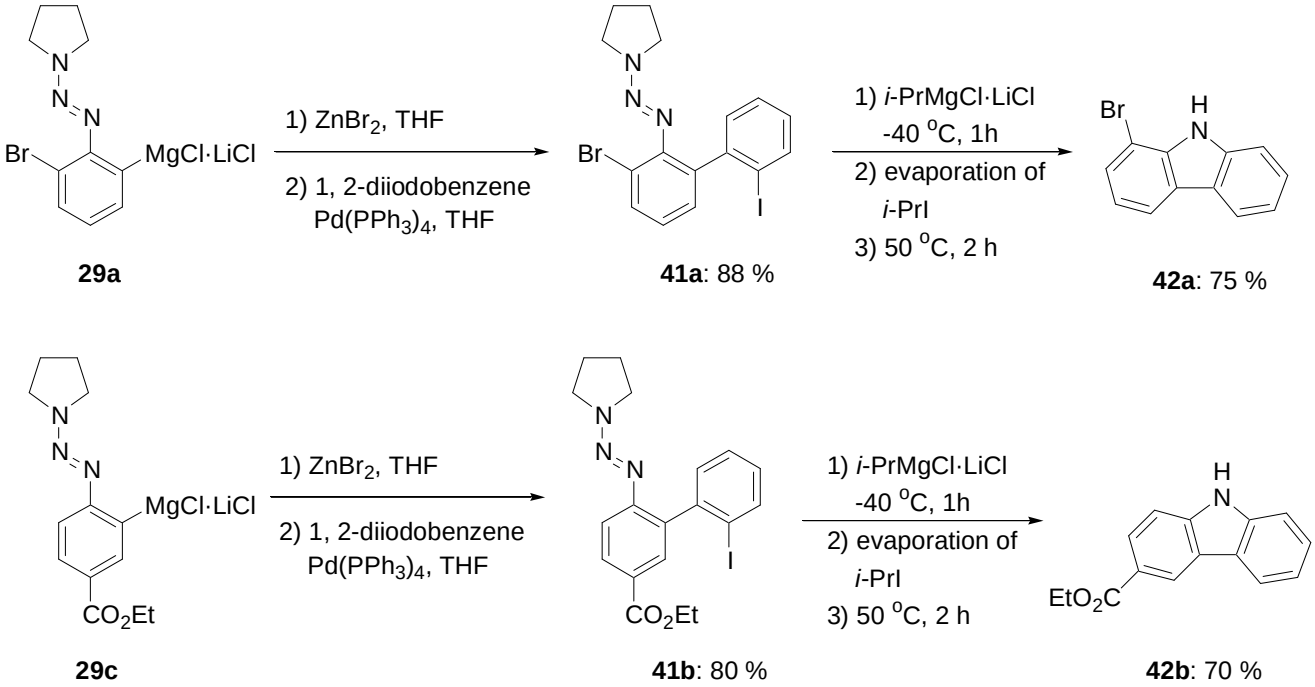
As an application of the versatility of these aryl iodides (**31**), we have prepared polyfunctionalized arylmagnesium derivatives bearing silylated cyanohydrins (**34**) as masked ketones *via* a smooth magnesiation of the silylated cyanohydrins (**33**), which are readily available by a CsF-catalyzed silylcyanation of iodoketones (**32**) with trimethylsilyl cyanide (TMSCN) (Scheme 47).

These functionalized Grignard reagents (**34**) react with electrophiles in satisfactory yields leading to polyfunctional ketones (**35**) after simple deprotection procedures. The use of the powerful I/Mg-exchange reagent *i*-PrMgCl·LiCl allows generation of the intermediate Grignard reagents bearing silylated cyanohydrins under very mild conditions (Scheme 47).




**Scheme 47.** Application of the iodoketones (**32**).

Additionally, we have also developed a new synthesis of functionalized carbazoles (**42a-b**). Biphenyls (**41a-b**) prepared from the corresponding Grignard reagents (**29a** and **29c**) undergo a cyclization to give carbazoles after the reaction with *i*-PrMgCl·LiCl (Scheme 48).

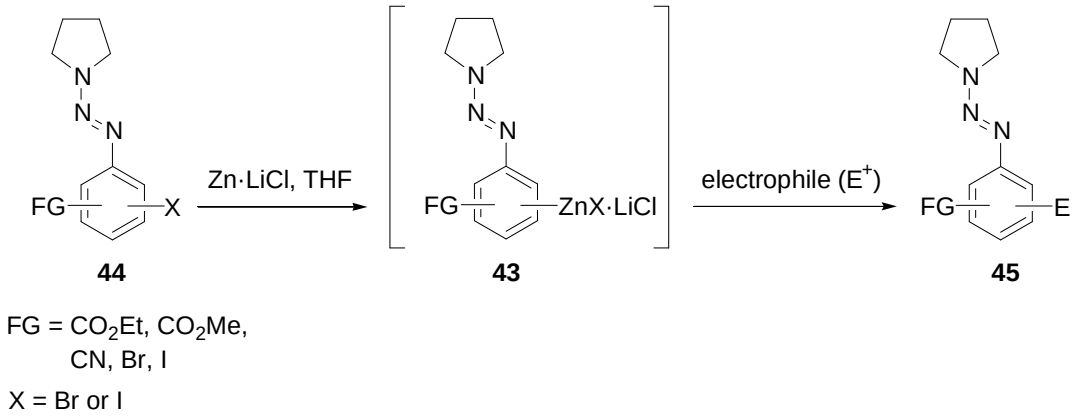



**Scheme 48.** A new carbazole synthesis.

## 7.2 Preparation of polyfunctional arylzinc reagents bearing a triazene moiety

The preparation of arylzinc reagents bearing a triazene moiety by a direct zinc insertion has been achieved. Starting from the bromo- or iodophenyl triazenes (**44**), we have demonstrated

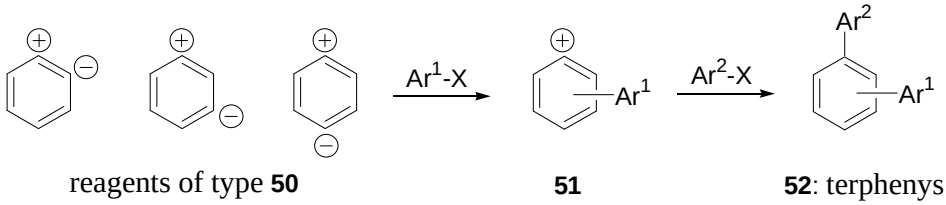
that the use of Zn powder in the presence of LiCl in THF allows a simple preparation of a range of polyfunctional arylzinc reagents bearing a triazene of type **43**, which react with electrophiles to provide polyfunctional triazenes (**45**) (Scheme 49).




**Scheme 49.** Preparation and reaction of polyfunctional arylzinc reagents bearing a triazene moiety of type **43**.

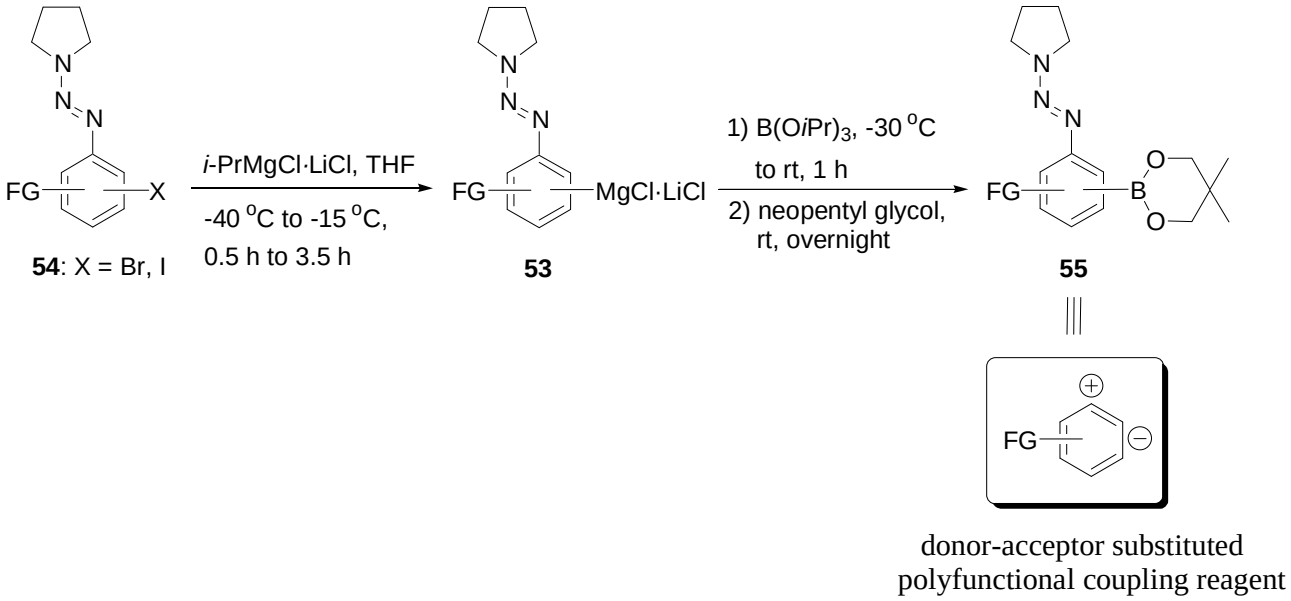
## 7.3 Synthesis of functionalized *o*-, *m*-, or *p*-terphenyls *via* consecutive cross-coupling reactions of arylboronic esters bearing a triazene moiety

A facile method for the preparation of functionalized *o*-, *m*-, or *p*-terphenyls (**52**) has been developed. We have designed a number of useful coupling reagents of type **50**, which undergo two successive cross-coupling reactions smoothly leading to the biphenyls (**51**) and terphenyls (**52**) (Scheme 50).




**Scheme 50.** Synthesis of *o*-, *m*-, or *p*-terphenyls (**52**) *via* two successive cross-coupling reactions.

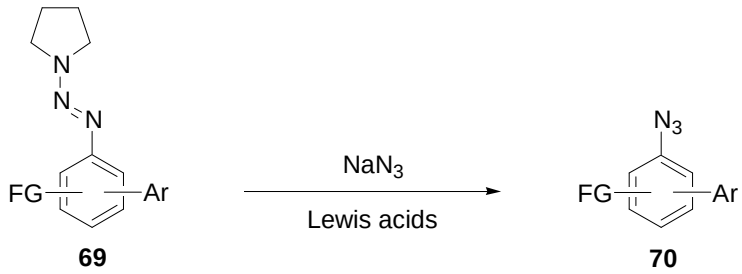
Reagents of type **50** can be readily prepared from the bromo- or iodophenyl triazenes (**54**), which perform a general Br-, or I/Mg exchange reaction producing the arylmagnesium species (**53**). The Gignard reagents react with triisopropyl borate and neopentyl glycol to afford the triazene-substituted arylboronic esters (**55**) as the useful coupling reagents (Scheme 51).



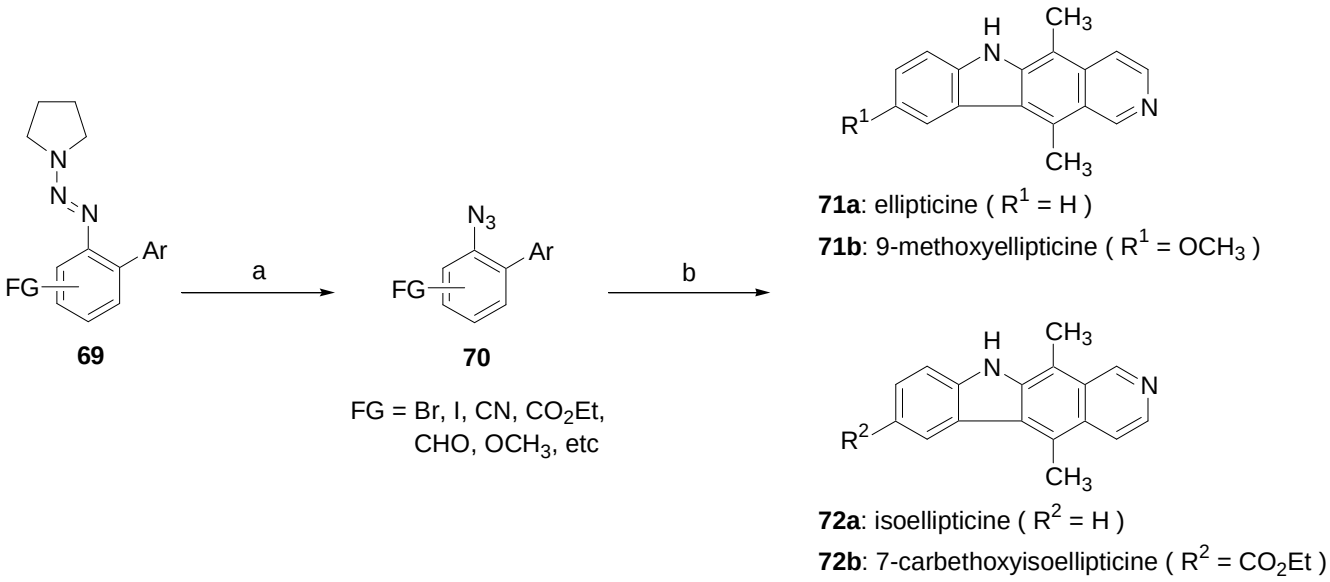

**Scheme 51.** Preparation of arylboronic esters bearing a triazene of type **55**.

## 7.4 Synthesis of ellipticine and related derivatives *via* a key-transformation from aryl triazenes to aryl azides

We have developed a novel and efficient synthetic method for the preparation of polyfunctional aryl azides (**70**) from the corresponding polyfunctional aryl triazenes (**69**), which are readily obtained from the anilines or the iodo- or bromo-substituted aryl triazenes by using Knochel's exchange protocol (Scheme 52). Furthermore, as an application of the versatility of these polyfunctional aryl azides (**70**), we have used them for a new synthesis of ellipticine (**71a**), 9-methoxyellipticine (**71b**), isoellipticine (**72a**), and 7-carbethoxyisoellipticine (**72b**) (Scheme 53).




**Scheme 52.** Preparation of aryl azides (**70**) from aryl triazenes (**69**).




**69**

**70**

FG = Br, I, CN, $CO_2Et$, CHO, $OCH_3$, etc

**71a**: ellipticine ( $R^1$ = H )

**71b**: 9-methoxyellipticine ( $R^1$ = $OCH_3$ )

**72a**: isoellipticine ( $R^2$ = H )

**72b**: 7-carbethoxyisoellipticine ( $R^2$ = $CO_2Et$ )

**Scheme 53.** Synthesis of ellipticine (**71a**), 9-methoxyellipticine (**71b**), isoellipticine (**72a**), and 7-carbethoxyisoellipticine (**72b**). a) Conversion of the triazene group to an azide; b) Thermal decomposition of azides.

# EXPERIMENTAL PART

## 8. General Conditions

All reactions were carried out with magnetic stirring and, if air or moisture sensitive, in flame-dried glassware under argon. Syringes were used to transfer reagents, and solvents were purged with argon prior to use.

### Solvents

Solvents were dried according to standard methods by distillation from drying agents as stated below and were stored under argon.

**$CH_2Cl_2$** and **toluene** were predried over $CaCl_{2(s)}$ and distilled from $CaH_{2(s)}$.

**Diethyl ether** and **THF** were continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen.

**1,2-dimethoxyethane (DME)** was predried over $CaCl_{2(s)}$ and freshly distilled from sodium benzophenone ketyl under nitrogen.

**Dimethylformamide (DMF)** was heated to reflux for 14 h over $CaH_{2(s)}$ and distilled from $CaH_{2(s)}$.

**Ethanol** was treated with phthalic anhydride (25g/L) and sodium, heated to reflux for 6 h and distilled.

**Methanol** was treated with magnesium turnings (20g/L) and sodium, heated to reflux for 6 h and distilled.

**Pyridine** and **triethylamine** were dried over $KOH_{(s)}$ and distilled from $KOH_{(s)}$.

### Reagents

Reagents of >98% purity were used as obtained.

***n*-Butyllithium** was used as a 1.5 M solution in hexane purchased by Chemetall.

**CuCN·2LiCl** solution (1.0 M/THF) was prepared by drying CuCN (869 mg, 10 mmol) and LiCl (848 mg, 20 mmol) in a Schlenk flask under vacuum for 5 h at 140 °C. After cooling to room temperature, dry THF (10 mL) was added and stirred continuously until the salts were dissolved.

***i*-PrMgCl:** A dry three-necked flask equipped with an argon inlet, a dropping funnel and a thermometer was charged with magnesium turnings (110 mmol). A small amount of THF was added to cover the magnesium, and a solution of isopropyl chloride (100 mmol) in THF (50 mL) was added dropwise, keeping the temperature of the mixture below 30 °C (water bath). After the addition was complete, the reaction mixture was stirred for 12 h at room temperature. The grey solution of *i*-PrMgCl was cannulated to another flask under argon and removed in this way from excess of magnesium. A yield of ca. 95-98 % of *i*-PrMgCl was obtained and the *i*-PrMgCl solution was titrated prior to use according to reported literature.[85]

***i*-PrMgCl·LiCl:** A dry three-necked flask equipped with an argon inlet, a dropping funnel and a thermometer was charged with magnesium turnings (110 mmol) and anhydrous LiCl (100 mmol). A small amount of THF was added to cover the magnesium, and a solution of isopropyl chloride (100 mmol) in THF (50 mL) was added dropwise, keeping the temperature of the mixture below 30 °C (water bath). After the addition was complete, the reaction mixture was stirred for 12 h at room temperature. The grey solution of *i*-PrMgCl·LiCl was cannulated to another flask under argon and removed in this way from excess of magnesium. A yield of ca. 95-98 % of *i*-PrMgCl·LiCl was obtained and the *i*-PrMgCl·LiCl-solution was titrated prior to use according to reported literature.[85]

**$ZnBr_2$** solution (1.0 M/THF) was prepared by drying $ZnBr_2$ (33.78 g, 150 mmol) under vacuum for 5 h at 150 °C. After cooling to room temperature, dry THF (150 mmol) was added and stirred continuously until the salts were dissolved.

## Chromatography

Thin layer chromatography (TLC) was performed using aluminium plates coated with $SiO_2$ (Merck 60, F-254). The spots were visualized by UV light and/or by staining of the TLC plate with the solution bellow followed by heating with a heat gun:

- $KMnO_4$ (0.3 g), $K_2CO_3$ (20 g), KOH (0.3 g) in water (300 mL)

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[85] a) H. S. Lin, L. Paquette, *Synth. Commun.* **1994**, *24*, 2503; b) A. Krasovskiy, P. Knochel, *Synthesis* **2006**, *5*, 890.

Flash column chromatography was performed using $SiO_2$ 60 (0.04-0.063 mm, 230-400 mesh ASTM) from Merck. The diameters of the columns and the amount of silicagel were calculated according to the recommendation of W. C. Still.[86]

## Analysis

Analytical data collection was done as follows:

- **Melting points** were uncorrected and measured on a Büchi B-540 apparatus.
- **NMR** spectra were recorded on a Bruker ARX 200, AC 300, WH 400, or AMX 600 instruments. Chemical shifts were given relative to $CDCl_3$ (7.26 ppm for $^1H$ NMR, 77.0 ppm for $^{13}C$ NMR), DMSO-$d_6$ (2.50 ppm for $^1H$ NMR, 39.4 ppm for $^{13}C$ NMR), acetone-$d_6$ (2.04 ppm for $^1H$ NMR, 29.3 ppm for $^{13}C$ NMR). For the characterization of the observed signal multiplicities the following abbreviations were applied: s (single), d (doublet), dd (double doublet), dt (double triplet), t (triplet), td (triple doublet), q (quartet), quint (quintet), m (multiplet), as well as br (broad).
- **IR** spectra were recorded from 4000-400 $cm^{-1}$ on a Nicolet 510 FT-IR, a Perkin-Elmer 281 IR spectrometer, or a Perkin Elmer Spectrometer BX FT-IR-System with a Smith Dura sampl IR II ATR-unit. Samples were measured either as neat materials (neat) or as a film between potassium bromide plates (film) or as potassium bromide tablets (KBr). The absorption bands are reported in wave numbers ($cm^{-1}$). For the band characterization the following abbreviations were applied: br (broad), s (strong), m (medium), vs (very strong), w (weak).
- **Gas chromatography (GC)** was performed using a Hewlett-Packard 5890 Series II (Column A: 2.5 % phenylmethylpolysiloxane (HP Ultra 2) 12 m × 0.2 mm × 0.33 μm). The compounds were detected with a flame ionization detector.
- **Mass spectroscopy:** Mass spectra were recorded on a Varian MAT CH 7A for electron impact ionization (EI) and high resolution mass spectra (HRMS) on a Varian MAT 711 spectrometers. Fast atom bombardment (FAB) samples were recorded in either a 2-nitrobenzyl alcohol- or glycerine-matrix. Additionally, for the combination of gas chromatography with mass spectroscopic detection, a GC/MS from Hewlett-Packard HP 6890/MSD 5973 was used (Column B: 5 % phenylmethylpolysiloxane (HP 5) 30 m × 0.25 mm × 0.25 μm; Column C: 5 % phenylmethylpolysiloxane (HP 5) 15 m × 0.25 mm × 0.25 μm).

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[86] W. C. Still, M. Khan, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923.

- **Elemental analysis** was carried out on a Heraeus CHN-Rapid-Elementanalyzer in the microanalytical laboratories of the Department Chemie und Biochemie, Ludwig-Maximilians Universität, Munich.

## 9. Typical Procedures (TP)

### 9.1 Typical procedure for the preparation of functionalized bromo- or iodophenyl triazenes *via* the reaction of pyrrolidine with diazonium salts generated from the corresponding anilines (TP1)

A solution of the corresponding aniline (18.1 mmol) in conc. HCl (7.2 mL) was cooled in an ice bath while a solution of $NaNO_2$ (1.3 g, 19 mmol) in cold water (40 mL) was added dropwise. The resulting solution of the diazonium salt was stirred at 0 $^oC$ for 30 min and then added at once to a solution of pyrrolidine (2.6 g, 36.2 mmol) and $K_2CO_3$ (12.5 g, 90.5 mmol) in 1:2 acetonitrile/water (25 mL). The reaction mixture was stirred for 30 min at 0 $^oC$ and was extracted with $CH_2Cl_2$ (3 × 50 mL). The organic layer was washed twice with brine, dried ($MgSO_4$), filtered, and concentrated by evaporation. Purification by flash chromatography furnished the product **28a-e, 44a, 44c, 44g, 56f, 73-75.**

### 9.2 Typical procedure for the preparation of polyfunctional aryl triazenes *via* the reaction of electrophiles with the arylmagnesium reagents bearing a triazene moiety generated from the corresponding bromophenyl triazenes (TP2)

To a solution of the corresponding bromophenyl triazene (1 mmol) in THF (0.25 mL) was slowly added *i*-PrMgCl·LiCl (0.55 mL, 1.1 mmol, 2.0 M in THF) at -40 °C. The reaction temperature was gradually increased to -15 °C. After 5 h, a complete conversion to the Grignard reagent was observed as indicated by GC-analysis of hydrolyzed reaction aliquots. CuCN·2LiCl (1 mmol, 1.0 M in THF) was added dropwise at -30 °C and the reaction mixture was stirred at -30 °C for 0.5 h. Electrophile (1.5-2 mmol) in THF (1 mL) was added. The mixture was stirred at -30 $^oC$ for 1 h, then slowly warmed to rt and quenched with aqueous $NH_4Cl$ (10 mL). The aqueous phase was extracted with ether (3 × 10 mL). The organic layers were washed with brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography furnished the product **30a-e**.

### 9.3 Typical procedure for the preparation of polyfunctional aryl triazenes *via* the reaction of electrophiles with the arylmagnesium reagents bearing a triazene moiety generated from the corresponding iodophenyl triazenes (TP3)

To a solution of the corresponding iodophenyl triazene (0.5 mmol) in THF (0.5 mL) was slowly added *i*-PrMgCl·LiCl (0.53 mmol, 2.05 M in THF) at -40 °C. The reaction mixture was continuously stirred at -40 °C for 0.7-1 h. A complete conversion to the Grignard reagent was

observed as indicated by GC-analysis of hydrolyzed reaction aliquots. CuCN·2LiCl (0.5 mmol, 1.0 M in THF) was added dropwise at -40 °C and then the reaction mixture was slowly warmed to -30 °C over 0.5 h. Electrophile (0.75 mmol) in THF (0.1 mL) was added and the mixture was stirred at -30 °C for 1 h and then slowly warmed to rt and stirred again for 1 h before the addition of aqueous $NH_4Cl$ (2 mL). The aqueous phase was extracted with diethyl ether (2 × 10 mL). The organic fractions were washed with brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography furnished the product **30f-l, 76-77**.

### 9.4 Typical procedure for the preparation of functionalized aryl iodides *via* the reaction of aryl triazenes with methyl iodide (TP4)

The corresponding triazene (0.55 mmol) was dissolved in freshly distilled iodomethane (3 mL) and heated in a sealed tube at 120 °C for 24 h. The reaction mixture was cooled, diluted with dichloromethane, and filtered through a pad of Celite and silica gel. The solvent was removed under reduced pressure. Purification by flash chromatography furnished the product **31a, 31d, 31g, 31j-k**.

### 9.5 Typical procedure for the preparation of functionalized aryl iodides *via* the reaction of aryl triazenes with trimethylsilyl iodide (TP5)

To a solution containing the corresponding triazene (0.28 mmol) in $CH_2Cl_2$ (0.3 mL) was added trimethylsilyl iodide (112 mg, 0.56 mmol). The mixture was stirred at 40 °C for 20 min. The progress of the reaction was monitored by TLC. After the reaction mixture was cooled to rt, 5 % sodium bicarbonate solution (7 mL) was added. The reaction mixture was extracted with $CH_2Cl_2$ (2 × 10 mL). The organic layers were combined, washed with water, and dried ($MgSO_4$). The solvent was removed under reduced pressure. Purification by flash chromatography furnished the product **31b-c, 31e-f, 31h-i, 47, 49**.

### 9.6 Typical procedure for the preparation of silylated cyanohydrins *via* CsF-catalyzed silylcyanations of the corresponding iodoketones with trimethylsilyl cyanide (TP6)

To a stirred solution of 4-iodo-3-(3-oxo-cyclohex-1-enyl)-benzoic acid ethyl ester (**32a**) (370 mg, 1 mmol) or 4-iodo-3-(3-oxo-cyclohex-1-enyl)-benzonitrile (**32b**) (323 mg, 1 mmol) and CsF (30.4 mg, 0.2 mmol) in dry $CH_3CN$ (1.5 mL) was added trimethylsilyl cyanide (150 mg, 1.5 mmol) dropwise at room temperature. The resulting reaction mixture was continuously

stirred at room temperature and the reaction progress was followed by TLC. After 2 h, the reaction mixture was diluted with water (10 mL) and extracted with ether (2 × 15 mL). The organic layer was washed twice with brine, dried ($MgSO_4$), filtered, and concentrated by evaporation. The crude product **33a** or **33b** was obtained as colorless oil and used directly in the next step.

### 9.7 Typical procedure for the preparation of polyfunctional ketones *via* the reaction of magnesiated silylated cyanohydrins with an electrophile followed by a deprotection (TP7)

To a solution of **33a** (235 mg, 0.5 mmol) or **33b** (211 mg, 0.5 mmol) in THF (0.35 mL) was slowly added *i*-PrMgCl·LiCl (0.28 mL, 0.55 mmol, 2.0 M in THF) at -40 °C. The reaction mixture was continuously stirred at -40 °C for 1 h. A complete conversion to the Grignard reagent was observed as indicated by GC-analysis of hydrolyzed reaction aliquots. CuCN·2LiCl (0.5 mL, 0.5 mmol 1.0 M in THF) was added dropwise at -40 °C and then the reaction mixture was slowly warmed to -30 $^{o}$C over 40 min. Furoyl chloride (98 mg, 0.75 mmol) in THF (0.1 mL) was added and the mixture was stirred at -30 $^{o}$C for 1 h and then warmed to rt and stirred again for 1 h. TBAF (0.75 mL, 1.0 M in THF) was added. After 30 min, HCl (0.38 mL, 2.0 M) was added and the reaction mixture was stirred for another 2 h before the addition of aqueous $NH_4Cl$ (2 mL). The aqueous phase was extracted with diethyl ether (2 × 10 mL). The combined organic layers were washed with brine (10 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. Purification by flash chromatography furnished the product **35a-b**.

### 9.8 Typical procedure for the preparation of polyfunctional aryl triazenes *via* Negishi cross-coupling reactions of aryl halides with the arylzincs derived from arylmagnesium reagents (TP8)

To a solution of the corresponding triazene (3 mmol) in THF (0.75 mL) was slowly added *i*-PrMgCl·LiCl (3.3 mmol, 2.0 M in THF) at -40 °C. The reaction temperature was gradually increased to -15 °C. After 1-4 h, a complete conversion to the Grignard reagent was observed as indicated by GC-analysis of hydrolyzed reaction aliquots. $ZnBr_2$ (3 mmol, 1.0 M in THF) was added at -20 °C and the reaction mixture was slowly warmed to -5 $^{o}$C. After 1 h, the zinc reagent was transferred to a solution of tetrakis(triphenylphosphine)palladium (3 mol%) and aryl halide (3 mmol) in THF (3.5 mL). The reaction mixture was heated at reflux for 3-7 h. The mixture was cooled and quenched with aqueous $NH_4Cl$. The aqueous phase was extracted with ether (2 × 30 mL). The organic fractions were washed with brine (50 mL), dried

($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography furnished the product **41a-b, 79, 99a-b, 110a-b**.

### 9.9 Typical procedure for the preparation of functionalized carbazoles (TP9)

To a solution of the corresponding triazene **41a** or **41b** (0.5 mmol) in THF (0.25 mL) was slowly added *i*-PrMgCl·LiCl (0.27 mL, 0.55 mmol, 2.0 M in THF) at -40 °C. The reaction mixture was continuously stirred at -40 $^{o}$C. After 1 h, isopropyl iodide resulting from the I/Mg exchange was evaporated *in vacuo* (evaporation was done twice, 1 h for each time). Then the mixture was heated to 55 $^{o}$C for 2 h after the addition of fresh THF (1.5 mL). The mixture was cooled to rt and quenched as usual. The aqueous phase was extracted with ether (2 × 5 mL). The organic fractions were washed with brine (5 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography furnished the product **42a-b**.

### 9.10 Typical procedure for the preparation of functionalized aryl triazenes *via* the reactions of arylzinc iodides or brimides with electrophiles in the presence of CuCN·2LiCl (TP10)

Anhydrous LiCl (8 mmol) was placed in an Ar-flushed flask and dried for 5 min at 200 $^{o}$C under vacuum (1 mbar). Zinc dust (8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich) was added under Ar and the mixture was dried again for 10 min at 200 $^{o}$C under vacuum (1 mbar). The reaction flask was evacuated and refilled with Ar twice. THF (4 mL) was added and the zinc was activated with $BrCH_2CH_2Br$ (5 mol%) and $Me_3SiCl$ (2 mol%). The corresponding iodo- or bromophenyl triazene (4 mmol) was added neat at room temperature and then the reaction mixture was gradually increased to 50 °C. The insertion reaction was complete after 7-30 h (checked by GC analysis of reaction aliquots, the conversion was 80-97 %). Titration of an aliquot (1 mL) of the organozinc reagent with iodine indicated that the concentration of the arylzinc reagent was 0.87-0.90 M. The solution of the corresponding arylzinc iodide or arylzinc bromide (3 mmol) was carefully separated from the remaining zinc dust by using a syringe and transferred to another Ar-flushed flask. Allyl bromide (4.5 mmol), acid chloride (4.5 mmol) or 3-iodo-cyclohex-2-enone (3 mmol) was added at -20 $^{o}$C or -30 $^{o}$C, followed by CuCN·2LiCl (0.02 mmol or 3 mmol, 1.0 M in THF). After 1-5 h at low temperature, the reaction mixture was gradually warmed to rt and stirred for 1 h and then quenched with saturated aqueous $NH_4Cl$ solution (5 mL). The aqueous phase was extracted with ether (3 × 5 mL) and concentrated in vacuo. Purification by flash chromatography furnished the product **45a-b, 45d-e, 45g, 45i, 45k-p, 46**.

## 9.11 Typical procedure for the preparation of functionalized aryl triazenes *via* the reactions of arylzinc iodides or brimides with electrophiles in the absence of CuCN·2LiCl (TP11)

Anhydrous LiCl (8 mmol) was placed in an Ar-flushed flask and dried for 5 min at 200 $^{o}$C under vacuum (1 mbar). Zinc dust (8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich) was added under Ar and the mixture was dried again for 10 min at 200 $^{o}$C under vacuum (1 mbar). The reaction flask was evacuated and refilled with Ar twice. THF (4 mL) was added and the zinc was activated with $BrCH_2CH_2Br$ (5 mol%) and $Me_3SiCl$ (2 mol%). The corresponding iodophenyl triazene **44b** or **44e** (4 mmol) was added neat at room temperature and then the reaction mixture was gradually increased to 50 °C. The insertion reaction was complete after 15-30 h (checked by GC analysis of reaction aliquots, the conversion was about 85-97 %). Titration of an aliquot (1 mL) of the organozinc reagent with iodine indicated that the concentration of **43b** or **43e** was 0.87-0.88 M. The solution of the corresponding arylzinc iodide (3 mmol) was carefully separated from the remaining zinc dust by using a syringe and transferred to another Ar-flushed flask. To a solution of 4-iododiazobenzene tetrafluoroborate (3 mmol) in THF/NMP (3 mL, v/v = 1 : 1) or *p*-toluenesulfonyl cynide (4.5 mmol) was slowly added the freshly prepared organozinc reagent at -20 $^{o}$C or -10 $^{o}$C. The reaction mixture was gradually warmed to rt and stirred for 2 or 24 h and then quenched with saturated aqueous $NH_4Cl$ solution (5 mL). The aqueous phase was extracted with ether (3 × 5 mL) and concentrated in vacuo. Purification by flash chromatography furnished the product **45c, 45j**.

## 9.12 Typical procedure for the preparation of functionalized aryl triazenes *via* Negishi cross-coupling reactions of arylzinc iodides or brimides with aryl halides (TP12)

Anhydrous LiCl (8 mmol) was placed in an Ar-flushed flask and dried for 5 min at 200 $^{o}$C under vacuum (1 mbar). Zinc dust (8 mmol, 2 equiv, <10 micron, 98+%, Aldrich) was added under Ar and the mixture was dried again for 10 min at 200 $^{o}$C under vacuum (1 mbar). The reaction flask was evacuated and refilled with Ar twice. THF (4 mL) was added and the zinc was activated with $BrCH_2CH_2Br$ (5 mol%) and $Me_3SiCl$ (2 mol%). The corresponding iodo- or bromophenyl triazene (4 mmol) was added neat at room temperature and then the reaction mixture was gradually increased to 50 °C. The insertion reaction was complete after 8-24 h (checked by GC analysis of reaction aliquots, the conversion was 80-93 %). Titration of an aliquot (1 mL) of the organozinc reagent with iodine indicated that the concentration of the arylzinc reagent was 0.87-0.90 M. The solution the corresponding arylzinc iodide or arylzinc

bromide (3 mmol) was carefully separated from the remaining zinc dust and then transferred to a solution of tetrakis(triphenylphosphine)palladium (0.09 mmol) and the aryl halides (3 mmol) in THF (3 mL). The reaction mixture was heated under reflux for 2-6 h. The mixture was cooled and quenched with saturated aqueous $NH_4Cl$ solution (5 mL). The aqueous phase was extracted with ether (3 × 5 mL) and concentrated in vacuo. Purification by flash chromatography furnished the product **45f, 45h, 45q, 48**.

### 9.13 Typical procedure for the preparation of functionalized arylboronic esters bearing a triazene moiety (TP13)

To a solution of the corresponding bromo- or iodophenyl triazene (5 mmol) in THF (3.3 mL) was slowly added *i*-PrMgCl·LiCl (5.5 mmol, 2.0 M in THF) at -40 °C or -15 $^oC$. The reaction mixture was continuously stirred at low temperarure for 0.5-5 h. A complete conversion to the corresponding Grignard reagent was observed as indicated by GC-analysis of hydrolyzed reaction aliquots. $B(OiPr)_3$ (6 mmol) in THF (1 mL) was added and the mixture was stirred at low temperature for 1 h and then warmed to rt and continuously stirred for 2 h before the addition of neopentyglycol (6.25 mmol). The reaction mixture was stirred at rt for 12 h and then aqueous $NH_4Cl$ (10 mL) was added. The aqueous phase was extracted with $CH_2Cl_2$ (2 × 30 mL). The organic fractions were washed with brine (50 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. Purification by flash chromatography furnished the product **58a-f**.

### 9.14 Typical procedure for the preparation of functionalized aryl triazenes *via* Suzuki cross-coupling reactions of arylboronic esters with aryl halides (TP14)

In a nitrogen flushed sealed tube the corresponding arylboronic ester (1 mmol) and aryl halide (1.2 mmol) were dissolved in dioxane/water (10 mL/1 mL) and then $K_3PO_4$ (2 mmol) and $Pd(PPh_3)_4$ (3 mol%) were added. The reaction mixture was stirred at 100 °C for 2-8 h, and then cooled to room temperature. Aqueous $NH_4Cl$ (25 mL) was added. The aqueous phase was extracted with ether (3 × 20 mL). The organic fractions were washed with brine (50 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography furnished the product **59a-r**.

### 9.15 Typical procedure for the preparation of polyfunctional *o*-, *m*-, or *p*-terphenyls *via* palladium-catalyzed cross-coupling reactions of aryl triazenes with phenylboronic acids in the presence of $BF_3{\cdot}OEt_2$ (TP15)

To a solution of the corresponding aryl triazene (0.5 mmol), phenylboronic acid (1 mmol), $Pd(OAc)_2$ (10 mol%) in methanol/ether (4 mL / 2 mL) was added $BF_3 \cdot OEt_2$ (0.75 mmol) dropwise at 0 °C. A complete consumption of the aryl triazene was followed by thin layer chromatography. After 3-12 h, water (5 mL) was added and the aqueous phase was extracted with ethyl acetate (2 × 10 mL). The organic fractions were washed with brine (20 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. Purification by flash chromatography furnished the product **60a-h**.

### 9.16 Typical procedure for the preparation of functionalized aryl azides from aryl triazenes *via* the addition of $BF_3 \cdot OEt_2$ and $CF_3COOH$ in the presence of $NaN_3$ (TP16)

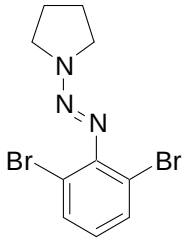
To a solution of the corresponding aryl triazene (0.5 mmol) and $NaN_3$ (65 mg, 1 mmol) in $CH_2Cl_2$ (0.5 mL) was slowly added $BF_3 \cdot OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol) at rt. The reaction mixture was stirred at rt for 10-25 min before the addition of $H_2O$ (2 mL). The aqueous phase was extracted with diethyl ether (2 × 5 mL). The organic fractions were washed with brine (10 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. Purification by flash chromatography furnished the product **80-92, 100a, 111b**.

### 9.17 Typical procedure for the preparation of functionalized aryl azides from aryl triazenes *via* the addition of $KHSO_4$ in the presence of $NaN_3$ (TP17)

To a solution of the corresponding aryl triazene (0.45 mmol) and $KHSO_4$ (612 mg, 4.5 mmol) in $CH_2Cl_2/H_2O$ (3 mL/2 mL) was added $NaN_3$ (146 mg, 2.25 mmol) at rt. The reaction mixture was stirred vigorously at rt for 12-16 h. Then the aqueous phase was extracted with diethyl ether (2 × 10 mL). The organic fractions were washed with brine (20 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. Purification by flash chromatography furnished the product **93-96, 100b, 111a**.

## 10. Preparation of Polyfunctional Arylmagnesium Reagents Bearing a Triazene Moiety

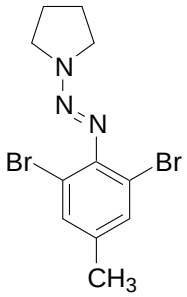
**Synthesis of 1-(2,6-dibromophenylazo)pyrrolidine (28a):**




Prepared according to **TP1** from 2,6-dibromoaniline (4.6 g, 18.1 mmol), concentrated HCl (7.2 mL), $NaNO_2$ (1.3 g, 19 mmol), pyrrolidine (2.6 g, 36.2 mmol), and $K_2CO_3$ (12.5 g, 90.5 mmol). Reaction condition: 0 °C, 0.5 h; 25 °C, 0.5 h. Purification by flash chromatography (*n*-pentane/ether = 9 : 1) yielded **28a** (5.7 g, 95 %) as a yellow liquid.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.50 (d, $J$ = 8.0 Hz, 2H), 6.82 (t, $J$ = 8.0 Hz, 1H), 3.93 (br s, 2H), 3.71 (br s, 2H), 2.05 (br s, 4H).
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 148.1, 132.3, 126.5, 117.9, 51.2, 46.6, 24.0, 23.6;
**MS** (70 eV, EI) *m/z* (%): 333 (14) [$M^+$], 263 (69), 235 (100), 168 (6), 154 (12), 75 (16).
**IR** (neat): 3065 (w), 2950 (w), 2974 (w), 2873 (w), 1922 (w), 1865 (m), 1666 (m), 1548 (m), 1416 (m), 1339 (w), 1260 (m), 970 (w).
**HRMS** (EI) for **$C_{10}H_{11}BrN_3$** (330.9320): found: 330.9318.

**Synthesis of 1-(2,6-dibromo-3-methylphenylazo)pyrrolidine[87] (28b):**




Prepared according to **TP1** from 2,6-dibromotoluidine (4.8 g, 18.1 mmol), concentrated HCl (7.2 mL), $NaNO_2$ (1.3 g, 19 mmol), pyrrolidine (2.6 g, 36.2 mmol), and $K_2CO_3$ (12.5 g, 90.5

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[87] a) K. C. Nicolaou, H. Li, C. N. C. Boddy, J. M. Ramanjulu, T. Y. Yue, S. Natarajan, X. J. Chu, S. Bräse, F. Rübsam, *Chem. Eur. J.* **1999**, *5*, 2584; b) K. C. Nicolaou, C. N. C. Boddy, S. Natarajan, T. Y. Yue, H. Li, S. Bräse, J. M. Ramanjulu, *J. Am. Chem. Soc.* **1997**, *119*, 3421.

mmol). Reaction condition: 0 °C, 0.5 h; 25 °C, 0.5 h. Purification by flash chromatography (*n*-pentane/ether = 9 : 1) yielded **28b** (5.7 g, 90 %) as a brown solid.

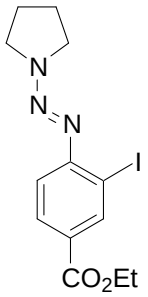
**mp**.: 52.5-53.0 °C (lit.[87] 53 °C).

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.33 (s, 2H), 3.91 (br s, 2H), 3.70 (br s, 2H), 2.26 (s, 3H), 2.04 (br s, 4H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 145.6, 136.7, 132.8, 117.3, 51.1, 46.4, 23.7, 20.2.

**MS** (70 eV, EI) *m/z* (%): 347 (20) [$M^+$], 277 (76), 249 (100), 170 (34), 168 (34), 89 (36).

**Synthesis of 1-(4-carbethoxy-2-iodophenylazo)pyrrolidine (28c):**




Prepared according to **TP1** from ethyl 4-amino-3-iodobenzoate[88] (5.3 g, 18.1 mmol), concentrated HCl (7.2 mL), $NaNO_2$ (1.3 g, 19 mmol), pyrrolidine (2.6 g, 36.2 mmol), and $K_2CO_3$ (12.5 g, 90.5 mmol). Reaction condition: 0 °C, 0.5 h; 25 °C, 0.5 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 2) yielded **28c** (5.9 g, 88 %) as a brown powder.

**mp**.: 128.5-130.0 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.48 (d, $J$ = 1.8 Hz, 1 H), 7.90 (dd, $J$ = 8.4, 1.8 Hz, 1H), 7.37 (d, $J$ = 8.4 Hz, 1H), 4.32 (q, $J$ = 7.1 Hz, 2H), 3.93 (br s, 2H), 3.73 (br s, 2H), 2.02 (br s, 4H), 1.35 (t, $J$ = 7.1 Hz, 3H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 165.3, 153.8, 140.6, 130.0, 127.8, 116.5, 95.5, 60.9, 51.2, 47.5, 23.9, 23.4, 14.3.

**MS** (70 eV, EI) *m/z* (%): 373 (31) [$M^+$], 303 (50), 275 (100), 247 (50), 229 (38).

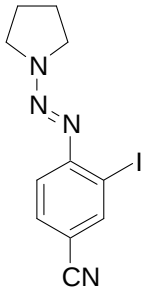
**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2967 (w), 2875 (w), 1694 (vs), 1588 (s), 1552 (s), 1374 (m), 1305 (m), 1267 (s), 1244 (m), 1108 (s), 1029 (m), 905 (w).

**HRMS** (EI) for **$C_{13}H_{16}IN_3O_2$** (373.0287): found: 373.0249.

**Synthesis of 1-(4-cyano-2-iodophenylazo)pyrrolidine (28d):**

78

[88] C. Koradin, W. Dohle, A. L. Rodriguez, B. Schmid, P. Knochel, *Tetrahedron.* **2003**, *59*, 1571



Prepared according to **TP1** from 4-amino-3-iodobenzonitrile [89] (4.4 g, 18.1 mmol), concentrated HCl (7.2 mL), $NaNO_2$ (1.3 g, 19 mmol), pyrrolidine (2.6 g, 36.2 mmol), and $K_2CO_3$ (12.5 g, 90.5 mmol). Reaction condition: 0 °C, 0.5 h; 25 °C, 0.5 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 2) yielded **28d** (5.5 g, 90 %) as a brown powder.

**mp**.: 159.0-159.8 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.07 (d, $J$ = 1.8 Hz, 1H), 7.50 (dd, $J$ = 8.4, 1.8 Hz, 1H), 7.40 (d, $J$ = 8.4 Hz, 1H), 3.97 (t, $J$ = 6.5 Hz, 2H), 3.75 (t, $J$ = 6.5 Hz, 2H), 1.96-2.18 (m, 4H).

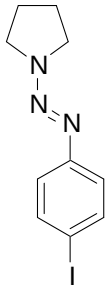
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 154.0, 142.7, 132.3, 118.0, 117.0, 108.9, 95.6, 51.5, 47.8, 23.9, 23.4.

**MS** (70 eV, EI) *m/z* (%): 326 (24) [$M^+$], 256 (48), 228 (100), 101 (24).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2974 (w), 2954 (w), 2865 (w), 2219 (s), 1585 (s), 1375 (m), 1307 (m), 1273 (m).

**HRMS** (EI) for **$C_{11}H_{11}IN_4$** (326.0028): found: 326.0005.

**Synthesis of 1-(4-iodophenylazo)pyrrolidine[90] (28e):**



Prepared according to **TP1** from 4-iodoaniline (4 g, 18.1 mmol), concentrated HCl (7.2 mL), $NaNO_2$ (1.3 g, 19 mmol), pyrrolidine (2.6 g, 36.2 mmol), and $K_2CO_3$ (12.5 g, 90.5 mmol). Reaction condition: 0 °C, 0.5 h; 25 °C, 0.5 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 2) yielded **28e** (5.0 g, 92 %) as a brown crystals.

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[89] G. Vaidyanathan, D. J. Affleck, M. R. Zalutsky, *J. Med. Chem.* **1994**, *37*, 3655.
[90] A. Godt, *J. Org. Chem.* **1997**, *62*, 7471.

**mp**.: 111.5-111.9 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.57-7.62 (m, 2H), 7.13-7.18 (m, 2H), 3.75 (br s, 4H), 1.99 (br s, 4H).

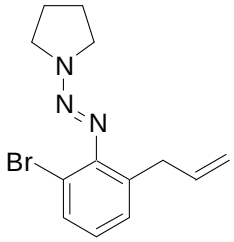
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 151.0, 137.7, 122.3, 89.0, 23.7.

**MS** (70 eV, EI) *m/z* (%): 301 (33) [$M^+$], 231 (67), 203 (100), 76 (28).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2978 (w), 2936 (w), 2868 (w), 1637 (m), 1477 (m), 1417 (m), 1389 (m), 1339 (m), 1313 (w), 1259 (w), 1219 (m), 828 (w).

**HRMS** (EI) for **$C_{10}H_{12}IN_3$** (301.0076): found: 301.0088.

**Synthesis of (2-allyl-6-bromo-phenyl)-pyrrolidin-1-yl-diazene (30a):**




Prepared according to **TP2** from 1-(2,6-dibromophenylazo)pyrrolidine (**28a**) (333 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), CuCN·2LiCl (one drop of 1.0 M solution in THF, ca. 0.02 mmol, ca. 0.4 mol%), and allyl bromide (183 mg, 1.5 mmol). Reaction condition: -40 °C to -15 °C, 5 h; -15 °C to 25 °C, 1 h. Purification by flash chromatography (*n*-pentane/ether = 19 : 1) yielded **30a** (229 mg, 78 %) as a pale yellow oil.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.43 (dd, $J$ = 8.0, 1.3, Hz, 1H), 7.11 (dd, $J$ = 7.5, 1.3 Hz, 1H), 6.91 (t, $J$ = 7.7 Hz, 1H), 5.79-5.92 (m, 1H), 4.94-5.04 (m, 2H), 3.79 (br s, 4H), 2.03 (br s, 4H).

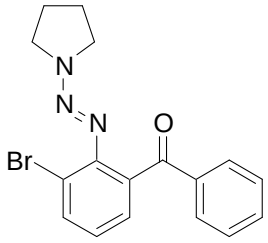
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 193.6, 148.3, 137.0, 134.5, 131.1, 129.0, 125.8, 117.3, 115.6, 36.4, 23.8.

**MS** (70 eV, EI) *m/z* (%): 293 (2) [$M^+$], 279 (2), 264 (2), 250 (2), 223 (11), 208 (4), 186 (4), 130 (5), 116 (100), 102 (4), 83 (9), 63 (5).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3058 (w), 2975 (w), 2872 (w), 1736 (m), 1637 (m), 1560 (m), 1421 (m), 1336 (w), 1210 (w), 1160 (m), 1107 (w), 1027 (w), 995 (w) $cm^{-1}$.

**HRMS** (EI) for **$C_{13}H_{16}BrN_3$** (293.0528): found: 293.0545.

**Synthesis of [3-bromo-2-(pyrrolidin-1-ylazo)-phenyl]-phenyl-methanone (30b):**



Prepared according to **TP2** from 1-(2,6-dibromophenylazo)pyrrolidine (**28a**) (333 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), CuCN·2LiCl (1 mL, 1 mmol, 1.0 M in THF), and benzoyl chloride (210 mg, 1.5 mmol). Reaction condition: -40 °C to -15 °C, 5 h; -30 °C, 0.5 h; -30 °C to 25 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 1) yielded **30b** (293 mg, 82 %) as a white solid.

**mp**.: 113.5-114.0 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.74 (dd, $J$ = 8.0, 1.3 Hz, 1H), 7.58-7.66 (m, 2H), 7.28-7.46 (m, 4H), 7.09 (t, $J$ = 8.0 Hz, 1H), 3.47 (br s, 2H), 3.22 (br s, 2H), 1.60-1.80 (m, 4H).

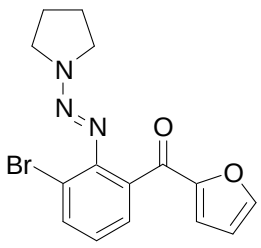
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 196.4, 147.8, 137.5, 134.9, 132.6, 132.1, 128.9, 128.8, 128.2, 125.6, 119.2, 50.5, 46.9, 23.6, 23.2.

**MS** (70 eV, EI) *m/z* (%): 357 (3) [$M^+$], 287 (19), 180 (100), 166 (3), 152 (39), 139 (1), 126 (1), 105 (21), 77 (26), 51 (5).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2974 (w), 2950 (w), 2863 (w), 1664 (vs), 1596 (s), 1581 (s), 1450 (m), 1395 (m), 1364 (m), 1303 (m), 1273 (m), 1259 (m), 1225 (s), 1156 (s), 1129 (m), 1071 (m), 949 (w).

**HRMS** (EI) for **$C_{17}H_{16}BrN_3O$** (357.0477): found: 357.0445.

**Synthesis of [3-bromo-2-(pyrrolidin-1-ylazo)-phenyl]-furan-2-yl-methanone (30c):**



Prepared according to **TP2** from 1-(2,6-dibromophenylazo)pyrrolidine (**28a**) (333 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), CuCN·2LiCl (1 mL, 1 mmol, 1.0 M in THF), and furoyl chloride (195 mg, 1.5 mmol). Reaction condition: -40 °C to -15 °C, 5 h; -30 °C, 0.5 h; -30 °C to 25 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **30c** (295 mg, 85 %) as a yellow solid.

**mp**.: 101.5-102.0 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.69 (dd, $J$ = 8.0, 1.3 Hz, 1H), 7.44-7.50 (m, 1H), 7.32 (dd, $J$ = 7.5, 1.3 Hz, 1H), 7.03 (t, $J$ = 7.8 Hz, 1H), 6.84 (d, $J$ = 3.5 Hz, 1H), 6.40 (dd, $J$ = 3.5, 1.8, Hz, 1H), 3.56 (br s, 2H), 3.46 (br s, 2H), 1.85 (br s, 2H), 1.79 (br s, 2H).

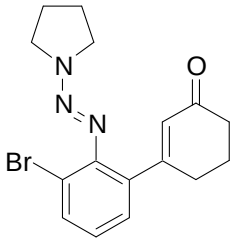
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 184.1, 152.6, 147.8, 145.7, 135.1, 131.6, 128.4, 125.3, 119.3, 117.4, 111.9, 50.7, 46.8, 23.7, 23.4.

**MS** (70 eV, EI) *m/z* (%): 347 (11) [$M^+$], 277 (57), 249 (100), 170 (23).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3132 (w), 2972 (w), 2875 (w), 1647 (s), 1566 (s), 1466 (m), 1399 (m), 1366 (m), 1312 (m), 1224 (m), 1130 (m), 1012 (w), 973 (w).

**HRMS** (EI) for **$C_{15}H_{14}BrN_3O$** (347.0269): found: 347.0274.

**Synthesis of 3-[3-bromo-2-(pyrrolidin-1-ylazo)-phenyl]-cyclohex-2-enone (30d):**




Prepared according to **TP2** from 1-(2,6-dibromophenylazo)pyrrolidine (**28a**) (333 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), CuCN·2LiCl (1 mL, 1 mmol, 1.0 M in THF), and 3-iodo-cyclohex-2-enone (222 mg, 1 mmol). Reaction condition: -40 °C to -15 °C, 5 h; -30 °C, 0.5 h; -30 °C, 3 h; 25 °C, 1 h. Purification by flash chromatography (*n*-pentane/ether = 2 : 3) yielded **30d** (278 mg, 80 %) as a white solid.

**mp**.: 101.5-102.0 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.56 (dd, $J$ = 8.0, 1.5 Hz, 1H), 7.06 (dd, $J$ = 7.5, 1.5, Hz, 1H), 6.96 (t, $J$ = 7.7 Hz, 1H), 6.00 (s, 1H), 3.81 (br s, 2H), 3.66 (br s, 2H), 2.34-2.42 (m, 3H), 1.90-2.10 (m, 7H).

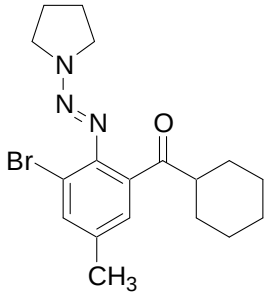
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 199.4, 164.0, 146.7, 134.8, 133.4, 128.6, 127.9, 125.7, 118.9, 51.1, 46.7, 37.5, 30.6, 23.9, 23.5, 23.2.

**MS** (70 eV, EI) *m/z* (%): 347 (4) [$M^+$], 277 (8), 249 (12), 142 (100), 128 (27), 114 (27).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2975 (w), 2948 (w), 2873 (w), 1663 (s), 1408 (m), 1346 (m), 1317 (m), 1244 (s), 1210 (s), 1188 (m), 962 (w).

**HRMS** (EI) for **$C_{16}H_{18}BrN_3O$** (347.0633): found: 347.0662.

**Synthesis of [3-bromo-5-methyl-2-(pyrrolidin-1-ylazo)-phenyl]-cyclohexyl-methanone (30e):**




Prepared according to **TP2** from 1-(2,6-dibromo-4-methylphenylazo)pyrrolidine (**28b**) (367 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), CuCN·2LiCl (1 mL, 1 mmol, 1.0 M in THF), and cyclohexoyl chloride (221 mg, 1.5 mmol). Reaction condition: -40 °C to -15 °C, 5 h; -30 °C, 0.5 h; -30 °C to 25 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 4 : 1) yielded **30e** (309 mg, 82 %) as an orange solid.

**mp**.: 124.0-124.6 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.44 (s, 1H), 6.93 (s, 1H), 3.82 (br s, 2H), 3.71 (br s, 2H), 2.32-2.48 (m, 1H), 2.28 (s, 3H), 2.00 (br s, 4H), 1.04-2.12 (m, 10H).

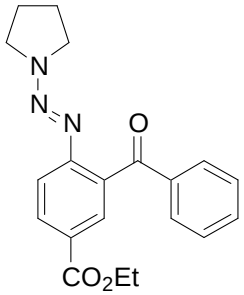
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 193.8, 144.6, 135.7, 134.8, 134.2, 128.2, 119.0, 51.2, 50.4, 47.2, 29.2, 25.9, 25.8, 24.0, 23.6, 20.4.

**MS** (70 eV, EI) *m/z* (%): 377 (6) [$M^+$], 307 (28), 201 (100), 185 (22), 173 (19).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2934 (w), 2848 (w), 1688 (s), 1597 (m), 1446 (m), 1409 (s), 1340 (m), 1313 (m), 1260 (m), 1210 (w), 1150 (w), 1117 (w), 997 (w).

**HRMS** (EI) for **$C_{18}H_{24}BrN_3O$** (377.1103): found: 377.1080.

**Synthesis of 3-benzoyl-4-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (30f):**



Prepared according to **TP3** from 1-(4-carbethoxy-2-iodophenylazo)pyrrolidine (**28c**) (373 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), CuCN·2LiCl (1 mL, 1 mmol, 1.0 M in THF), and benzoyl chloride (210 mg, 1.5 mmol). Reaction condition: -40 °C, 0.7 h; -30 °C, 0.5 h; -30 °C to 25 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 2 : 1) yielded **30f** (274 mg, 78 %) as yellow crystals.

**mp**.: 102.3-103.5 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.06-8.16 (m, 2H), 7.64-7.74 (m, 2H), 7.40-7.56 (m, 2H), 7.28-7.38 (m, 2H), 4.34 (q, $J$ = 7.1 Hz, 2H), 3.68 (br s, 2H), 3.05 (br s, 2H), 1.72-1.84 (m, 4H), 1.36 (t, $J$ = 7.1 Hz, 3H).

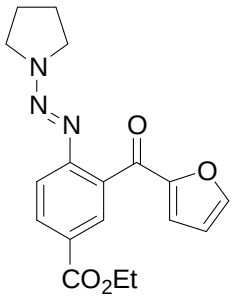
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 197.5, 166.1, 152.9, 138.3, 132.9, 132.2, 132.0, 130.5, 129.3, 128.1, 126.6, 119.0, 60.9, 50.9, 46.5, 23.7, 23.2, 14.3.

**MS** (70 eV, EI) *m/z* (%): 351 (13) [$M^+$], 281 (43), 253 (33), 225 (30), 181 (100), 152 (63), 105 (47), 77 (37).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3064 (w), 2983 (w), 2889 (w), 1709 (vs), 1662 (s), 1601 (s), 1394 (m), 1312 (m), 1241 (m), 1126 (s), 1026 (w).

**HRMS** (EI) for **$C_{20}H_{21}N_3O_3$** (351.1583): found: 351.1571.

**Synthesis of 3-(furan-2-carbonyl)-4-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (30g):**



Prepared according to **TP3** from 1-(4-carbethoxy-2-iodophenylazo)pyrrolidine (**28c**) (373 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), CuCN·2LiCl (1 mL, 1 mmol, 1.0 M in THF), and furoyl chloride (195 mg, 1.5 mmol). Reaction condition: -40 °C, 0.7 h; -30 °C,

0.5 h; -30 °C to 25 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **30g** (293 mg, 86 %) as a pale brown powder.

**mp**.: 113.8-115.0 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.02-8.12 (m, 2H), 7.50-7.58 (m, 2H), 6.92 (d, $J$ = 3.5 Hz, 1H), 6.45 (dd, $J$ = 3.5, 1.8 Hz, 1H), 4.33 (q, $J$ = 7.1 Hz, 2H), 3.77 (br s, 2H), 3.30 (br s, 2H), 1.82-1.94 (m, 4H), 1.34 (t, $J$ = 7.1 Hz, 3H).

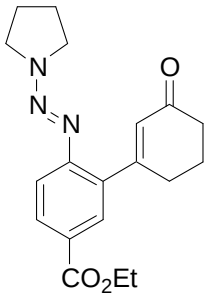
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 193.6, 184.7, 165.9, 153.4, 153.0, 146.2, 132.3, 132.2, 130.1, 126.3, 118.8, 118.5, 112.0, 60.9, 51.1, 46.6, 23.8, 23.3, 14.3.

**MS** (70 eV, EI) *m/z* (%): 341 (16) [$M^+$], 296 (13), 271 (63), 243 (100), 215 (91), 187 (31), 159 (44), 95 (69).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3118 (w), 2982 (w), 2878 (w), 1709 (vs), 1643 (vs), 1604 (s), 1567 (m), 1467 (m), 1405 (m), 1266 (m), 1243 (w), 1178 (s), 1030 (s), 979 (w).

**HRMS** (EI) for **$C_{19}H_{23}N_3O_3$** (341.1376): found: 341.1348.

**Synthesis of 3-(3-oxo-cyclohex-1-enyl)-4-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (30h):**




Prepared according to **TP3** from 1-(4-carbethoxy-2-iodophenylazo)pyrrolidine (**28c**) (373 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), CuCN·2LiCl (1 mL, 1 mmol, 1.0 M in THF), and 3-iodo-cyclohex-2-enone (222 mg, 1 mmol). Reaction condition: -40 °C, 0.7 h; -30 °C, 0.5 h; -30 °C, 3 h; 25 °C, 1 h. Purification by flash chromatography (*n*-pentane/ether = 2 : 3) yielded **30h** (273 mg, 80 %) as yellow crystals.

**mp**.: 118.5-119.0 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.94 (dd, $J$ = 8.4, 1.8 Hz, 1H), 7.85 (d, $J$ = 1.8 Hz, 1H), 7.49 (d, $J$ = 8.4 Hz, 1H), 6.12 (s, 1H), 4.34 (q, $J$ = 7.1 Hz, 2H), 3.94 (br s, 2H), 3.61 (br s, 2H), 2.76 (t, $J$ = 6.0 Hz, 2H), 2.47 (t, $J$ = 6.0 Hz, 2H), 1.94-2.16 (m, 6H), 1.3337 (t, $J$ = 7.1 Hz, 3H).

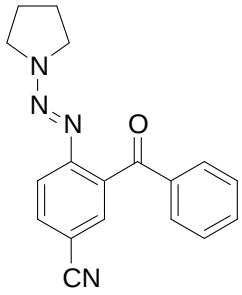
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 200.0, 166.3, 163.8, 151.7, 135.1, 130.6, 129.8, 128.6, 126.6, 116.7, 60.9, 51.2, 46.9, 38.6, 31.2, 23.9, 23.5, 23.4, 14.3.

**MS** (70 eV, EI) *m/z* (%): 341 (4) [$M^+$], 296 (17), 257 (100), 215 (48), 197 (43), 143 (43), 128 (85), 56 (43).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2948 (w), 2879 (w), 1704 (s), 1668 (s), 1596 (m), 1397 (m), 1311 (w), 1242 (w), 1133 (s), 1028 (m), 965 (w).

**HRMS** (EI) for **$C_{19}H_{23}N_3O_3$** (341.1739): found: 341.1702.

**Synthesis of 3-benzoyl-4-(pyrrolidin-1-ylazo)-benzonitrile (30i):**




Prepared according to **TP3** from 1-(4-cyano-2-iodophenylazo)pyrrolidine (**29d**) (326 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), CuCN·2LiCl (1 mL, 1 mmol, 1.0 M in THF), and benzoyl chloride (210 mg, 1.5 mmol). Reaction condition: -40 °C, 0.7 h; -30 °C, 0.5 h; -30 °C to 25 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **30i** (261 mg, 86 %) as a yellow powder.

**mp**.: 157.8-159.0 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.62-7.72 (m, 4H), 7.53-7.59 (m, 1H), 7.44-7.52 (m, 1H), 7.31-7.40 (m, 2H), 3.69 (t, *J* = 6.2 Hz, 2H), 3.04 (t, *J* = 6.2 Hz, 2H), 1.74-1.85 (m, 4H).

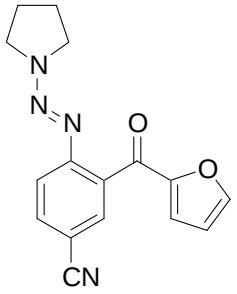
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 196.1, 152.6, 137.7, 134.1, 133.8, 132.8, 132.6, 129.2, 128.2, 119.5, 118.8, 107.6, 51.5, 46.7, 23.6, 23.1.

**MS** (70 eV, EI) *m/z* (%): 304 (20) [$M^+$], 234 (65), 206 (100), 178 (85), 151 (50), 105 (55), 77 (50).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2947 (w), 2874 (w), 2222 (s), 1665 (vs), 1594 (m), 1393 (m), 1310 (w), 1267 (w), 1120 (m), 966 (m).

**HRMS** (EI) for **$C_{18}H_{16}N_4O$** (304.1324): found: 304.1321.

**Synthesis of 3-(furan-2-carbonyl)-4-(pyrrolidin-1-ylazo)-benzonitrile (30j):**



Prepared according to **TP3** from 1-(4-cyano-2-iodophenylazo)pyrrolidine (**29d**) (326 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), CuCN·2LiCl (1 mL, 1 mmol, 1.0 M in THF), and furoyl chloride (195 mg, 1.5 mmol). Reaction condition: -40 °C, 0.7 h; -30 °C, 0.5 h; -30 °C to 25 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **30j** (250 mg, 85 %) as a brown powder.

**mp**.: 161.0-161.6 °C.

**$^{1}$H-NMR** (400 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.52-7.66 (m, 4H), 6.96 (d, $J$ = 3.4 Hz, 1H), 6.48 (dd, $J$ = 3.4, 1.8 Hz, 1H), 3.79 (br s, 2H), 3.29 (br s, 2H), 1.86-1.94 (m, 4H).

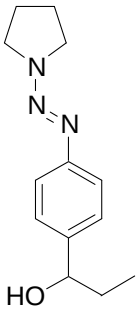
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 183.2, 153.0, 152.8, 146.5, 134.3, 133.2, 132.5, 119.2, 119.0, 118.7, 112.2, 107.3, 51.3, 46.8, 23.7, 23.2.

**MS** (70 eV, EI) *m/z* (%): 294 (8) [$M^+$], 224 (38), 196 (100), 168 (13), 140 (46), 95 (33).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3126 (w), 2991 (w), 2953 (w), 2876 (w), 2216 (s), 1653 (s), 1598 (s), 1567 (m), 1465 (m), 1392 (w), 1311 (w), 1269 9 (w), 1230 (w), 1102 (w), 1018 (w).

**HRMS** (EI) for **$C_{16}H_{14}N_4O_2$** (294.1117): found: 294.1125.

**Synthesis of 1-[4-(pyrrolidin-1-ylazo)-phenyl]-propan-1-ol (30k):**



Prepared according to **TP3** from 1-(4-iodophenylazo)pyrrolidine (**28e**) (301 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), and propionaldehyde (70 mg, 1.2 mmol). Reaction condition: -30 °C, 1 h; -30 °C to 25 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 2 : 3) yielded **30k** (210 mg, 90 %) as an off-white powder.

**mp**.: 52.5-53.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.34 (d, $J$ = 8.4 Hz, 2H), 7.24 (d, $J$ = 8.4 Hz, 2H), 4.52 (t, $J$ = 6.7 Hz, 1H), 3.75 (br s, 4 H), 2.12 (s, 1H), 1.93-2.04 (m, 4H), 1.63-1.86 (m, 2H), 0.87 (t, $J$ = 7.3 Hz, 3H).

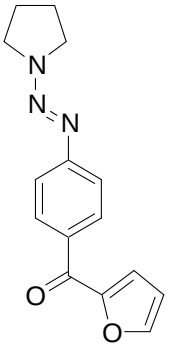
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 150.8, 141.3, 126.5, 120.2, 75.7, 31.7, 23.7, 10.1.

**MS** (70 eV, EI) *m/z* (%): 233 (28) [$M^+$], 163 (40), 135 (100), 117 (47), 91 (24).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3143 (broad), 2972 (w), 2930 (w), 2873 (w), 1636 (m), 1408 (m), 1342 (w), 1318 (w), 1262 (m), 1222 (m), 1156 (w), 1097 (m), 844 (m).

**HRMS** (EI) for **$C_{13}H_{19}N_3O$** (233.1528): found: 233.1527.

**Synthesis of furan-2-yl-[4-(pyrrolidin-1-ylazo)-phenyl]-methanone (30l):**




Prepared according to **TP3** from 1-(4-iodophenylazo)pyrrolidine (**28e**) (301 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), CuCN·2LiCl (1 mL, 1 mmol, 1.0 M in THF), and furoyl chloride (195 mg, 1.5 mmol). Reaction condition: -30 °C, 1 h; -30 °C, 0.5 h; -30 °C to 25 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **30l** (237 mg, 88 %) as yellow crystals.

**mp**.: 136.0-137.0 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.98 (d, $J$ = 8.8 Hz, 2H), 7.66 (d, $J$ = 1.8 Hz, 1H), 7.47 (d, $J$ = 8.8 Hz, 2H), 7.20 (d, $J$ = 3.5 Hz, 1H), 6.55 (dd, $J$ = 3.5, 1.8 Hz, 1H), 3.92 (br s, 2H), 3.70 (br s, 2H), 2.02 (br s, 4H).

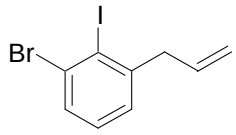
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 181.7, 155.0, 152.6, 146.6, 133.4, 130.6, 120.1, 119.8, 112.0, 23.7.

**MS** (70 eV, EI) *m/z* (%): 269 (13) [$M^+$], 199 (35), 171 (100), 115 (47), 95 (47).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3136 (w), 2978 (w), 2953 (w), 2924 (w), 2874 (w), 1626 (vs), 1597 (s), 1561 (m), 1466 (m), 1421 (w), 1394 (w), 1310 (w), 1143 (w), 951 (w).

**HRMS** (EI) for **$C_{15}H_{15}N_3O_2$** (269.1164): found: 269.1153.

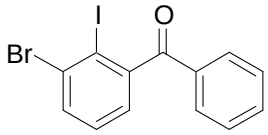
**Synthesis of 1-allyl-3-bromo-2-iodo-benzene (31a):**




Prepared according to **TP4** from (2-allyl-6-bromo-phenyl)-pyrrolidin-1-yl-diazene (**30a**) (293 mg, 1 mmol), methyl iodide (6 mL). Reaction condition: 120 °C, 24 h. Purification by flash chromatography (*n*-pentane/ether = 19 : 1) yielded **31a** (267 mg, 83 %) as a colourless oil.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.48 (dd, $J$ = 7.1, 2.2 Hz, 1H), 7.06-7.18 (m, 2H), 5.84-6.02 (m, 1H), 5.02-5.20 (m, 2H), 3.56-3.64 (m, 2H).
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 146.4, 135.3, 131.2, 130.6, 129.2, 127.6, 117.1, 107.9, 47.4.
**MS** (70 eV, EI) *m/z* (%): 322 (46) [$M^+$], 243 (8), 116 (100), 89 (19).
**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3078 (w), 2978 (w), 2917 (w), 1639 (m), 1573 (m), 1552 (m), 1434 (w), 1402 (w), 1009 (w), 918 (w).
**HRMS** (EI) for **$C_{15}H_{15}N_3O_2$** (269.1164): found: 269.1153.

**Synthesis of (3-bromo-2-iodo-phenyl)-phenyl-methanone (31b):**

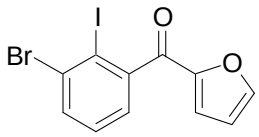



Prepared according to **TP5** from [3-bromo-2-(pyrrolidin-1-ylazo)-phenyl]-phenyl-methanone (**30b**) (357 mg, 1 mmol), trimethylsilyl iodide (400 mg, 2 mmol). Reaction condition: 40 °C, 5 h. Purification by flash chromatography (*n*-pentane/ether = 4 : 1) yielded **31b** (339 mg, 88 %) as a yellow oil.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.75-7.81 (m, 2H), 7.72 (dd, $J$ = 7.8, 1.6 Hz, 1H), 7.55-7.64 (m, 1H), 7.40-7.44 (m, 2H), 7.30 (t, $J$ = 7.8 Hz, 1H), 7.13 (dd, $J$ = 7.8, 1.6 Hz, 1H).
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 16.4, 148.0, 134.8, 133.9, 133.4, 131.7, 130.4, 129.3, 128.8, 126.0, 99.2.
**MS** (70 eV, EI) *m/z* (%): 386 (45) [$M^+$], 309 (16), 281 (8), 180 (18), 105 (100), 77 (45).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3060 (w), 1673 (vs), 1595 (s), 1580 (m), 1450 (m), 1392 (m), 1314 (m), 1297 (w), 1198 (w), 1178 (m), 1015 (w), 944 (w).
**HRMS** (EI) for **$C_{13}H_8BrIO$** (385.8803): found: 385.8787.

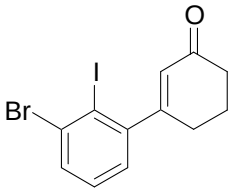
**Synthesis of (3-bromo-2-iodo-phenyl)-furan-2-yl-methanone (31c):**




Prepared according to **TP5** from [3-bromo-2-(pyrrolidin-1-ylazo)-phenyl]-furan-2-yl-methanone (**30c**) (347 mg, 1 mmol), trimethylsilyl iodide (400 mg, 2 mmol). Reaction condition: 40 °C, 5 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **31c** (256 mg, 68 %) as a brown oil.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.72 (dd, $J$ = 7.5, 1.3 Hz, 1H), 7.68 (d, $J$ = 1.5 Hz, 1H), 7.29 (t, $J$ = 7.5 Hz, 1H), 7.21 (dd, $J$ = 7.5, 1.3 Hz, 1H), 7.01 (d, $J$ = 3.5 Hz, 1H), 6.55 (dd, $J$ = 3.5, 1.5 Hz, 1H).
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 183.7, 150.6, 148.3, 146.7, 133.9, 131.8, 129.2, 126.1, 121.9, 112.8, 99.6.
**MS** (70 eV, EI) *m/z* (%): 376 (100) [$M^+$], 249 (20), 114 (16), 95 (68).
**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3130 (w), 2919 (w), 2850 (w), 1658 (vs), 1560 (m), 1461 (m), 1393 (w), 1307 (w), 1177 (m), 1026 (w), 962 (w).
**HRMS** (EI) for **$C_{11}H_6BrIO_2$** (375.8596): found: 375.8589.

**Synthesis of 3-(3-bromo-2-iodo-phenyl)-cyclohex-2-enone (31d):**




Prepared according to **TP4** from 3-[3-bromo-2-(pyrrolidin-1-ylazo)-phenyl]-cyclohex-2-enon (**30d**) (347 mg, 1 mmol), methyl iodide (6 mL). Reaction condition: 120 °C, 48 h. Purification by flash chromatography (*n*-pentane/ether = 7 : 3) yielded **31d** (327 mg, 87 %) as an off-white powder.

**mp**.: 107.0-107.7 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.58 (dd, $J$ = 7.7, 1.5 Hz, 1 H), 7.21 (t, $J$ = 7.7 Hz, 1 H), 6.98 (dd, $J$ = 7.7, 1.5 Hz, 1 H), 5.88 (t, $J$ = 1.8 Hz, 1 H), 2.44-2.60 (m, 4 H), 2.14-2.28 (m, 2 H).

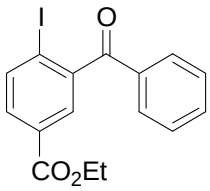
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 199.2, 165.3, 149.0, 132.1, 131.3, 129.5, 128.8, 125.6, 102.6, 37.2, 20.9, 23.0.

**MS** (70 eV, EI) *m/z* (%): 376 (100) [$M^+$], 249 (11), 221 (36), 193 (61).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3054 (w), 2941 (w), 2864 (w), 1660 (s), 1435 (m), 1391 (m), 1344 (w), 1302 (w), 1248 (m), 1187 (m), 1130 (m), 962 (w).

**HRMS** (EI) for **$C_{12}H_{10}BrIO$** (375.8960): found: 375.8931.

**Synthesis of 3-benzoyl-4-iodo-benzoic acid ethyl ester (31e):**




Prepared according to **TP5** from 3-benzoyl-4-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (**30f**) (351 mg, 1 mmol), trimethylsilyl iodide (400 mg, 2 mmol). Reaction condition: 40 °C, 6 h. Purification by flash chromatography (*n*-pentane/ether = 7 : 3) yielded **31e** (274 mg, 72 %) as a brown oil.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.00 (d, $J$ = 8.0 Hz, 1H), 7.90 (d, $J$ = 2.0 Hz, 1H), 7.75-7.82 (m, 3H), 7.54-7.64 (m, 1H), 7.45 (t, $J$ = 8.0 Hz, 2H), 4.35 (q, $J$ = 7.1 Hz, 2H), 1.34 (t, $J$ = 7.1 Hz, 3H).

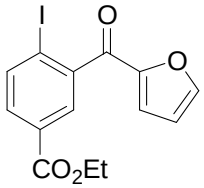
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 196.4, 165.4, 144.7, 140.0, 135.2, 134.0, 131.5, 130.4, 130.0, 128.9, 128.7, 98.2, 61.5, 14.2.

**MS** (70 eV, EI) *m/z* (%): 380 (59) [$M^+$], 335 (11), 303 (24), 275 (8), 253 (7), 105 (100), 77 (34).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3063 (w), 2981 (w), 1716 (vs), 1674 (vs), 1590 (s), 1450 (m), 1367 (m), 1241 (m), 1107 (s), 1016 (m), 963 (w).

**HRMS** (EI) for **$C_{16}H_{13}IO_3$** (379.9909): found: 379.9905.

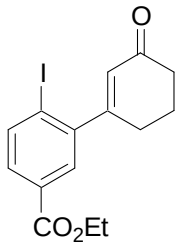
**Synthesis of 3-(furan-2-carbonyl)-4-iodo-benzoic acid ethyl ester (31f):**




Prepared according to **TP5** from 3-(furan-2-carbonyl)-4-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (**30g**) (341 mg, 1 mmol), trimethylsilyl iodide (400 mg, 2 mmol). Reaction condition: 40 °C, 6 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **31f** (289 mg, 78 %) as a brown oil.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.97-8.03 (m, 2H), 7.79 (dd, $J$ = 8.2, 2.0 Hz, 1H), 7.69 (s, 1H), 7.05 (d, $J$ = 3.5 Hz, 1H), 6.58 (dd, $J$ = 3.5, 1.8 Hz, 1H), 4.35 (q, $J$ = 7.1 Hz, 2H), 1.36 (t, $J$ = 7.1 Hz, 3H).
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 183.3, 165.3, 151.0, 148.3, 143.4, 140.3, 132.0, 130.4, 129.2, 122.0, 112.8, 98.5, 61.6, 14.2.
**MS** (70 eV, EI) *m/z* (%): 370 (100) [$M^+$], 342 (10), 325 (56), 303 (17), 275 (11), 243 (8), 95 (83).
**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3130 (w), 2982 (w), 2930 (w), 1722 (vs), 1659 (vs), 1590 (s), 1563 (m), 1462 (m), 1387 (w), 1284 (w), 1248 (m), 1187 (s), 1109 (m), 1016 (w).
**HRMS** (EI) for **$C_{14}H_{11}IO_4$** (369.9702): found: 369.9694.

**Synthesis of 4-iodo-3-(3-oxo-cyclohex-1-enyl)-benzoic acid ethyl ester (31g):**




Prepared according to **TP4** from 3-(3-oxo-cyclohex-1-enyl)-4-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (**30h**) (341 mg, 1 mmol), methyl iodide (6 mL). Reaction condition: 120 °C, 48 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **31g** (281 mg, 76 %) as a brown oil.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.94 (d, $J$ = 8.2 Hz, 1H), 7.74 (d, $J$ = 2.0 Hz, 1H), 7.65 (dd, $J$ = 8.2, 2.0 Hz, 1H), 5.95 (t, $J$ = 1.8 Hz, 1H), 4.36 (q, $J$ = 7.1 Hz, 2H), 2.46-2.64 (m, 4H), 2.16-2.28 (m, 2H), 1.38 (t, $J$ = 7.1 Hz, 3H).

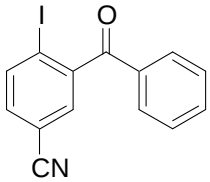
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 199.1, 165.6, 163.8, 146.0, 139.8, 130.8, 130.2, 129.5, 128.3, 101.3, 61.5, 37.2, 30.8, 23.0, 14.3.

**MS** (70 eV, EI) *m/z* (%): 370 (100) [$M^+$], 342 (16), 325 (18), 215 (55), 187 (95).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2980 (w), 2940 (w), 1722 (vs), 1681 (s), 1587 (s), 1454 (m), 1291 (m), 1239 (w), 1107 (s), 1015 (s), 962 (w).

**HRMS** (EI) for **$C_{15}H_{15}IO_3$** (370.0066): found: 370.0079.

**Synthesis of 3-benzoyl-4-iodo-benzonitrile (31h):**




Prepared according to **TP5** from 3-benzoyl-4-(pyrrolidin-1-ylazo)-benzonitrile (**30i**) (304 mg, 1 mmol), trimethylsilyl iodide (400 mg, 2 mmol). Reaction condition: 40 °C, 6 h. Purification by flash chromatography (*n*-pentane/ether = 4 : 1) yielded **31h** (233 mg, 70 %) as a yellow powder.

**mp**.: 127.0-128.0 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.06 (d, $J$ = 8.0 Hz, 1H), 7.75 (d, $J$ = 8.0 Hz, 2H), 7.60-7.68 (m, 1H), 7.38-7.53 (m, 4H).

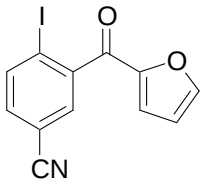
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 195.0, 145.8, 140.9, 134.6, 134.4, 133.5, 131.0, 130.4, 129.0, 117.4, 112.4, 98.4.

**MS** (70 eV, EI) *m/z* (%): 333 (63) [$M^+$], 256 (15), 228 (10), 206 (6), 105 (100), 77 (38).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3056 (w), 2228 (s), 1670 (vs), 1592 (m), 1450 (m), 1294 (m), 1255 (w), 1180 (m), 1020 (w).

**HRMS** (EI) for **$C_{14}H_8INO$** (332.9651): found: 332.9673.

**Synthesis of 3-(furan-2-carbonyl)-4-iodo-benzonitrile (31i):**




Prepared according to **TP5** from 3-(furan-2-carbonyl)-4-(pyrrolidin-1-ylazo)-benzonitrile (**30j**) (294 mg, 1 mmol), trimethylsilyl iodide (400 mg, 2 mmol). Reaction condition: 40 °C, 6 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **31i** (265 mg, 82 %) as a brown powder.

**mp**.: 105.0-105.5 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.02 (d, $J$ = 8.4 Hz, 1H), 7.66 (s, 1H), 7.57 (d, $J$ = 2.0 Hz, 1H), 7.37 (dd, $J$ = 8.4, 2.0 Hz, 1H), 7.08 (d, $J$ = 3.7 Hz, 1H), 6.57 (dd, $J$ = 3.7, 2.0 Hz, 1H).

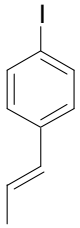
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 193.7, 181.8, 148.7, 144.3, 141.1, 133.9, 131.3, 122.2, 117.3, 113.1, 112.3, 98.7.

**MS** (70 eV, EI) *m/z* (%): 323 (98) [$M^+$], 256 (18), 228 (12), 196 (18), 140 (12), 95 (100).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3143 (w), 3129 (w), 2232 (s), 1646 (vs), 1563 (m), 1461 (m), 1400 (w), 1303 (m), 1082 (w), 1033 (w).

**HRMS** (EI) for **$C_{12}H_6INO_2$** (322.9443): found: 322.9414.

**Synthesis of 1-iodo-4-propenyl-benzene (31j):**




Prepared according to **TP4** from 1-[4-(pyrrolidin-1-ylazo)-phenyl]-propan-1-ol (**30k**) (233 mg, 1 mmol), methyl iodide (6 mL). Reaction condition: 120 °C, 48 h. Purification by flash chromatography (*n*-pentane) yielded **31j** (207 mg, 85 %) as white crystals.

**mp**.: 69.5-69.8 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.58 (d, $J$ = 8.4 Hz, 2H), 7.05 (d, $J$ = 8.4 Hz, 2H), 6.14-6.36 (m, 2H), 1.86 (d, $J$ = 5.3 Hz, 3H).

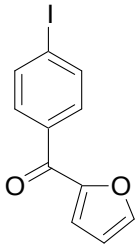
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 137.5, 130.0, 127.6, 126.8, 91.6, 18.5.

**MS** (70 eV, EI) *m/z* (%): 244 (100) [$M^+$], 117 (44), 91 (14).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3020 (w), 2956 (w), 2926 (w), 2905 (w), 1655 (m), 1580 (m), 1482 (m), 1441 (m), 1395 (w), 1001 (w), 966 (w).

**HRMS** (EI) for **$C_9H_9I$** (243.9749): found: 243.9756.

**Synthesis of furan-2-yl-(4-iodo-phenyl)-methanone (31k):**




Prepared according to **TP4** from furan-2-yl-[4-(pyrrolidin-1-ylazo)-phenyl]-methanone (**30l**) (269 mg, 1 mmol), methyl iodide (6 mL). Reaction condition: 120 °C, 48 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **31k** (268 mg, 90 %) as a brown solid.

**mp**.: 63.4-64.0 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.80-7.86 (m, 2H), 7.65-7.71 (m, 3H), 7.22 (d, *J* = 3.5 Hz, 2H), 6.57 (dd, *J* = 3.5, 1.8 Hz, 1H).

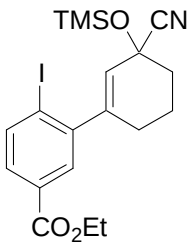
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 193.6, 152.1, 147.2, 137.7, 136.4, 130.7, 120.5, 112.3, 100.3.

**MS** (70 eV, EI) *m/z* (%): 298 (100) [$M^+$], 270 (13), 231 (63), 203 (21), 115 (17), 95 (33).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3129 (w), 1636 (vs), 1582 (s), 1464 (m), 1392 (m), 1312 (m), 1176 (w), 1006 (m), 950 (w).

**HRMS** (EI) for **$C_{11}H_7IO_2$** (297.9491): found: 297.9505.

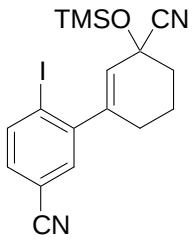
**Synthesis of 3-(3-cyano-3-trimethylsilanyloxy-cyclohex-1-enyl)-4-iodo-benzoic acid ethyl ester (33a):**



Prepared according to **TP6** from 4-iodo-3-(3-oxo-cyclohex-1-enyl)-benzoic acid ethyl ester (**32a**) (370 mg, 1 mmol), CsF (30.4 mg, 0.2 mmol), and trimethylsilyl cyanide (150 mg, 1.5 mmol). Reaction condition: 25 °C, 2 h. **33a** (436 mg, 93 %) was obtained as a colourless oil.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.90 (d, $J$ = 8.4 Hz, 1H), 7.73 (s, 1H), 7.60 (d, $J$ = 8.4 Hz, 1H), 5.62 (s, 1H), 4.35 (q, $J$ = 7.1 Hz, 2H), 1.90-2.36 (m, 6H), 1.38 (t, $J$ = 7.1 Hz, 3H), 0.25 (s, 9H).
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 165.8, 146.5, 146.2, 139.6, 130.7, 129.7, 128.7, 127.5, 121.3, 103.4, 67.1, 61.3, 36.6, 29.4, 18.9, 14.2, 1.6.
**MS** (70 eV, EI) *m/z* (%): 469 (69) [$M^+$], 454 (100), 441 (39), 427 (67), 408 (40), 379 (40), 334 (38), 296 (14), 215 (17), 187 (22), 152 (17), 75 (28).
**IR** (neat): 2958 (w), 2870 (w), 2231 (s), 1722 (s), 1589 (s), 1454 (m), 1367 (m), 1296 (w), 1252 (s), 1109 (s), 1015 (m), 906 (w).
**HRMS** (EI) for **$C_{19}H_{24}INO_3Si$** (469.0570): found: 469.0595.

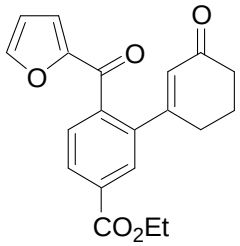
**Synthesis of 3-(3-cyano-3-trimethylsilanyloxy-cyclohex-1-enyl)-4-iodo-benzonitrile (33b):**




Prepared according to **TP6** from 4-iodo-3-(3-oxo-cyclohex-1-enyl)-benzonitrile (**32b**) (323 mg, 1 mmol), CsF (30.4 mg, 0.2 mmol), and trimethylsilyl cyanide (150 mg, 1.5 mmol). Reaction condition: 25 °C, 2 h. **33b** (405 mg, 96 %) was obtained as a colorless oil.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.96 (d, $J$ = 8.2 Hz, 1H), 7.37 (s, 1H), 7.22 (d, $J$ = 8.2 Hz, 1H), 5.62 (s, 1H), 1.90-2.30 (m, 6H), 0.25 (s, 9H).
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 147.3, 145.5, 140.4, 131.8, 130.9, 128.4, 120.9, 117.8, 112.5, 103.6, 66.9, 36.5, 29.2, 18.9, 1.5.
**MS** (70 eV, EI) *m/z* (%): 422 (22) [$M^+$], 407 (72), 380 (100), 366 (8), 332 (14), 280 (11), 168 (11), 140 (19), 75 (31).
**IR** (neat): 3060 (w), 2958 (w), 2232 (s), 1658 (m), 1585 (m), 1456 (m), 1254 (m), 1188 (w), 1112 (w), 1032 (w), 958 (w).
**HRMS** (EI) for **$C_{17}H_{19}IN_2OSi$** (422.0311): found: 422.0316.

**Synthesis of 4-(furan-2-carbonyl)-3-(3-oxo-cyclohex-1-enyl)-benzoic acid ethyl ester (35a):**




Prepared according to **TP7** from 3-(3-cyano-3-trimethylsilanyloxy-cyclohex-1-enyl)-4-iodo-benzoic acid ethyl ester (**33a**) (235 mg, 0.5 mmol), *i*-PrMgCl (0.28 mL, 1.1 equiv., 2.0 M in THF), CuCN·2LiCl (0.5 mL, 0.5 mmol, 1.0 M in THF), furoyl chloride (98 mg, 0.75 mmol), TBAF (0.75 mL, 1.0 M in THF), and HCl (0.38 mL, 2.0 M) Reaction condition: -40 °C, 1 h; -40 °C to -30 °C, 1 h; -30 °C to 25 °C, 2 h; 25 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 2 : 3) yielded **35a** (294 mg, 87 %) as a pale yellow solid.

**mp**.: 79.8-80.4 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.08 (dd, $J$ = 8.0, 1.3 Hz, 1H), 7.98 (d, $J$ = 1.8 Hz, 1H), 7.61-7.66 (m, 2H), 7.06 (d, $J$ = 3.5 Hz, 1H), 6.55 (dd, $J$ = 3.5, 1.8 Hz, 1H), 5.92 (s, 1H), 4.39 (q, $J$ = 7.0 Hz, 2H), 2.55-2.62 (m, 2H), 2.31-2.38 (m, 2H), 1.94-2.04 (m, 2H), 1.39 (t, $J$ = 7.0 Hz, 3H).

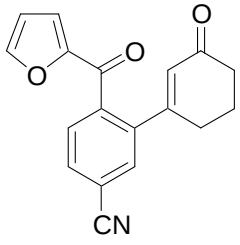
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 198.7, 183.2, 165.2, 160.9, 152.1, 147.9, 140.9, 140.0, 132.7, 129.3, 129.2, 129.0, 128.9, 121.0, 112.7, 61.6, 37.0, 31.1, 22.9, 14.2.

**MS** (70 eV, EI) *m/z* (%): 338 (13) [$M^+$], 309 (50), 293 (28), 282 (100), 253 (25), 237 (98), 225 (30), 209 (28), 181 (50), 152 (50), 95 (43).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3133 (w), 3177 (w), 2939 (w), 1721 (vs), 1662 (vs), 1646 (s), 1563 (m), 1464 (m), 1394 (w), 1296 (w), 1255 (m), 1222 (w), 1188 (s), 1103 (s).

**HRMS** (EI) for **$C_{20}H_{18}O_5$** (338.1154): found: 338.1164.

**Synthesis of 4-(Furan-2-carbonyl)-3-(3-oxo-cyclohex-1-enyl)-benzonitrile (35b):**



Prepared according to **TP7** from 3-(3-cyano-3-trimethylsilanyloxy-cyclohex-1-enyl)-4-iodo-benzonitrile (**33b**) (211 mg, 0.5 mmol), *i*-PrMgCl (0.28 mL, 1.1 equiv., 2.0 M in THF), CuCN·2LiCl (0.5 mL, 0.5 mmol, 1.0 M in THF), furoyl chloride (98 mg, 0.75 mmol), TBAF (0.75 mL, 1.0 M in THF), and HCl (0.38 mL, 2.0 M) Reaction condition: -40 °C, 1 h; -40 °C to -30 °C, 1 h; -30 °C to 25 °C, 2 h; 25 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 7) yielded **35b** (118 mg, 81 %) as a yellow solid.

**mp**.: 134.2-136.0 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.60-7.76 (m, 4H), 7.12 (d, $J$ = 1.8 Hz, 1H), 6.58 (dd, $J$ = 3.5, 1.8 Hz, 1H), 5.88 (s, 1H), 2.52-2.62 (m, 2H), 2.30-2.40 (m, 2H), 1.94-2.06 (m, 2H).

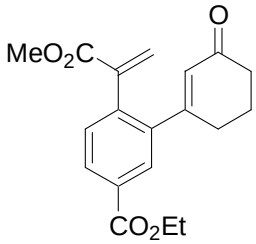
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 198.2, 182.1, 159.0, 151.8, 148.1, 141.7, 140.1, 131.7, 131.3, 129.7, 129.5, 121.2, 117.4, 114.9, 113.0, 37.0, 30.9, 22.9.

**MS** (70 eV, EI) *m/z* (%): 291 (8) [$M^+$], 262 (94), 235 (100), 206 (83), 190 (17), 178 (39).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3131 (w), 3036 (w), 2946 (w), 2236 (s), 1670 (vs), 1646 (vs), 1563 (s), 1464 (m), 1390 (m), 1309 (m), 1190 (m), 1031 (w), 953 (w).

**HRMS** (EI) for **$C_{18}H_{13}NO_3$** (291.0895): found: 291.0900.

**Synthesis of 4-(1-methoxycarbonyl-vinyl)-3-(3-oxo-cyclohex-1-enyl)-benzoic acid ethyl ester (36):**




To a solution of 3-(3-cyano-3-trimethylsilanyloxy-cyclohex-1-enyl)-4-iodo-benzoic acid ethyl ester (**33a**) (600 mg, 1.28 mmol) in THF (0.85 mL) was slowly added *i*-PrMgCl·LiCl (0.9 mL, 1.41 mmol, 1.55 M in THF) at -40 °C. The reaction mixture was continuously stirred at -40 °C for 1 h. A complete conversion to the Grignard reagent **34a** was observed as indicated by GC-analysis of hydrolyzed reaction aliquots. $ZnBr_2$ (1.3 mL, 1.28 mmol, 1.0 M in THF) was added at -20 °C and the reaction mixture was slowly warmed to -5 °C. After 1 h, the zinc reagent was transferred to a solution of tetrakis(triphenylphosphine)palladium (74 mg, 0.06 mmol) and 2-iodo-acrylic acid methyl ester[91] (300 mg, 1.41 mmol) in THF (2 mL). The

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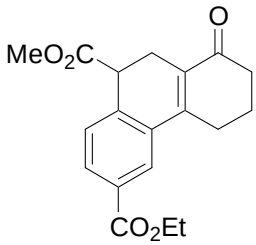
[91] E. Piers, P. L. Gladstone, J. G. K. Yee, E. J. McEachern, *Tetrahedron* **1998**, *54*, 10609.

reaction mixture was heated under reflux for 2 h. The mixture was cooled and then TBAF (2 mL, 1.0 M in THF) was added. After 30 min, HCl (1.3 mL, 2.0 M) was added and the reaction mixture was stirred for 2 h before the addition of aqueous $NH_4Cl$ (5 mL). The aqueous phase was extracted with diethyl ether (2 × 15 mL). The combined organic layers were washed with brine (15 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. Purification by flash chromatography (pentane/ether = 2 : 3) yielded the pure product **36** (340 mg, 81 %) as a colorless liquid.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.99 (d, $J$ = 8.0 Hz, 1H), 7.90 (s, 1H), 7.34 (d, $J$ = 8.0 Hz, 1H), 6.43 (s, 1H), 5.93 (d, $J$ = 1.0 Hz, 1H), 5.88 (d, $J$ = 1.0 Hz, 1H), 4.37 (q, $J$ = 7.2 Hz, 2H), 3.68 (s, 1H), 2.56-2.66 (m, 2H), 2.36-2.45 (m, 2H), 2.00-2.12 (m, 2H), 1.38 (t, $J$ = 7.2 Hz, 3H).
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 199.0, 166.3, 165.7, 161.5, 140.7, 140.0, 139.2, 130.7, 130.6, 129.6, 129.5, 128.0, 65.8, 61.3, 52.3, 37.1, 30.4, 23.0, 14.3.
**MS** (70 eV, EI) *m/z* (%): 328 (9) [$M^+$], 310 (13), 300 (35), 283 (18), 272 (45), 240 (47), 227 (25), 213 (100), 195 (45), 185 (35), 168 (27), 152 (24), 139 (44), 128 (16), 115 (20).
**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2952 (w), 1722 (vs), 1668 (vs), 1616 (s), 1437 (m), 1409 (m), 1294 (m), 1243 (m), 1218 (s), 1111 (s), 1023 (m), 962 (w).
**HRMS** (EI) for **$C_{19}H_{20}O_5$** (328.1311): found: 328.1293.

**Synthesis of 8-oxo-5,6,7,8,9,10-hexahydro-phenanthrene-3,10-dicarboxylic acid 3-ethyl ester 10-methyl ester (37):**




Dienic ketone (**36**) (115 mg, 0.35 mmol) was dissolved in mesitylene (5 mL) and heated in a sealed tube at 220 °C for 72 h. The reaction mixture was cooled and then the mesitylene was evaporated. Purification of the crude product by column chromatography (pentane/ether = 2 : 3) provided **37** (98 mg, 85 %) as an orange solid.

**mp**.: 109.8-112.2 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.10 (s, 1H), 7.98 (d, $J$ = 8.0 Hz, 1H), 7.30 (d, $J$ = 8.0 Hz, 1H), 4.36 (q, $J$ = 7.2 Hz, 2H), 3.62 (s, 3H), 3.12-3.26 (m, 1H), 2.74-2.86 (m, 2H), 2.44-2.66 (m, 3H), 2.02-2.20 (m, 2H), 1.37 (t, $J$ = 7.2 Hz, 3H).

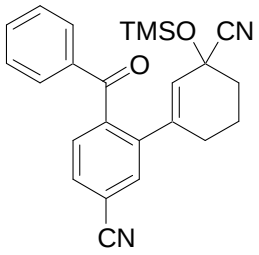
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 198.0, 172.6, 165.9, 148.1, 139.0, 134.2, 131.0, 130.6, 130.2, 128.6, 125.9, 61.1, 52.2, 43.4, 37.3, 25.9, 22.7, 22.0, 14.3.

**MS** (70 eV, EI) *m/z* (%): 328 (6) [$M^+$], 283 (6), 269 (100), 241 (5), 223 (6), 213 (8), 167 (8), 153 (7), 139 (8).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2958 (w), 2930 (w), 2869 (w), 1728 (vs), 1709 (vs), 1657 (s), 1616 (s), 1385 (m), 1332 (m), 1280 (m), 1104 (s), 1019 (s), 957 (m).

**HRMS** (EI) for **$C_{19}H_{20}O_5$** (328.1311): found: 328.1323.

**Synthesis of 4-benzoyl-3-(3-cyano-3-trimethylsilanyloxy-cyclohex-1-enyl)-benzonitrile (38):**




To a solution of 3-(3-cyano-3-trimethylsilanyloxy-cyclohex-1-enyl)-4-iodo-benzonitrile (**33b**) (1.27 g, 3 mmol) in THF (2 mL) was slowly added *i*-PrMgCl·LiCl (2.2 mL, 3.3 mmol, 1.5 M in THF) at -40 °C. The reaction mixture was continuously stirred at -40 °C for 1 h. A complete conversion to the Grignard reagent **34b** was observed as indicated by GC-analysis of hydrolyzed reaction aliquots. CuCN·2LiCl (3 mL, 3 mmol, 1.0 M in THF) was added dropwise at -40 °C and then the reaction mixture was slowly warmed to -30 °C over 40 min. Benzoyl chloride (635 mg, 4.5 mmol) in THF (0.7 mL) was added and the mixture was stirred at -30 °C for 1 h and then warmed to rt and stirred for another 1 h before the addition of aqueous $NH_4Cl$ (5 mL). The aqueous phase was extracted with diethyl ether (2 × 30 mL). The combined organic layers were washed with brine (30 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. Purification by flash chromatography (pentane/ether = 7 : 3) yielded the pure product **38** (973 mg, 81 %) as a white powder.

**mp**.: 122.5-123.6 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.70 (d, $J$ = 8.0 Hz, 1H), 7.54-7.66 (m, 5H), 7.38-7.48 (m, 2H), 5.53 (s, 1H), 2.00-2.60 (m, 2H), 1.50-1.84 (m, 4H), 0.14 (s, 9H).

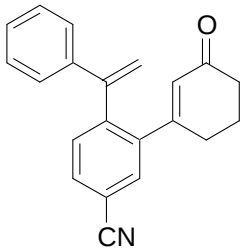
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 196.4, 142.4, 141.3, 140.7, 136.7, 133.8, 131.5, 131.2, 129.7, 129.6, 129.4, 128.7, 120.5, 117.7, 114.2, 66.6, 36.0, 29.1, 18.5, 1.3.

**MS** (70 eV, EI) *m/z* (%): 400 (9) [$M^+$], 385 (7), 371 (98), 258 (100), 245 (31), 232 (13), 215 (18), 105 (18), 75 (49).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2967 (w), 2233 (s), 1673 (s), 1598 (m), 1449 (m), 1280 (m), 1254 (m), 1100 (m), 1032 (m), 848 (m).

**HRMS** (EI) for **$C_{24}H_{24}N_2O_2Si$** (400.1607): found: 400.1591.

**Synthesis of 3-(3-oxo-cyclohex-1-enyl)-4-(1-phenyl-vinyl)-benzonitrile (39):**




To a solution of triphenylmethylphosphonium bromide (393 mg, 1.1 mmol) in THF (1.5 mL) was slowly added *n*-BuLi (0.77 mL, 1.2 mmol, 1.55 M in hexane) at -78 °C. The reaction mixture was continuously stirred at -78 °C for 15 min and then warmed to rt and stirred for 1 h. 4-Benzoyl-3-(3-cyano-3-trimethylsilanyloxy-cyclohex-1-enyl)-benzonitrile (**38**) (400 mg, 1 mmol) in THF (1.5 mL) was added dropwise at -78 °C and the reaction mixture was stirred at the same temperature for 30 min and then warmed to rt and stirred again for 3 h. TBAF (1.5 mL, 1.0 M in THF) was added. After 30 min, HCl (1 mL, 2.0 M) was added and the reaction mixture was stirred for 1 h before the addition of aqueous $NH_4Cl$ (2 mL). The aqueous phase was extracted with diethyl ether (2 × 15 mL). The combined organic layers were washed with brine (15 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. Purification by flash chromatography (pentane/ether = 1 : 1) yielded the pure product **39** (248 mg, 83 %) as a colorless liquid.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.62 (d, $J$ = 8.0 Hz, 1H), 7.40-7.50 (m, 2H), 7.18-7.24 (m, 3H), 7.00-7.08 (m, 2H), 5.87 (s, 1H), 5.66 (d, $J$ = 1.0 Hz, 1H), 5.34 (d, $J$ = 1.0 Hz, 1H), 2.15-2.23 (m, 2H), 2.05-2.13 (m, 2H), 1.55-1.67 (m, 2H).

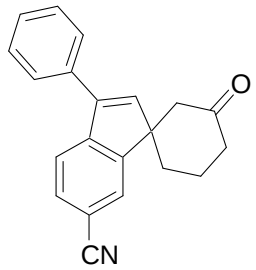
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 193.7, 159.7, 148.2, 144.7, 141.0, 140.1, 131.95, 131.91, 131.2, 130.4, 128.5, 128.3, 127.3, 118.1, 118.0, 112.1, 36.8, 30.0, 22.5.

**MS** (70 eV, EI) *m/z* (%): 299 (33) [$M^+$], 281 (53), 271 (40), 255 (33), 242 (100), 228 (53), 215 (18), 166 (15), 120 (18), 91 (15).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2946 (w), 2229 (s), 1669 (s), 1493 (m), 1447 (m), 1346 (m), 1325 (w), 1252 (w), 1189 (w), 1133 (w), 963 (w).

**HRMS** (EI) for **$C_{21}H_{17}NO$** (299.1310): found: 299.1304.

**Synthesis of 6-cyano-3'-oxo-3-phenyl-spiro[cyclohexane-1, 1'-[H]-indene] (40):**




3-(3-Oxo-cyclohex-1-enyl)-4-(1-phenyl-vinyl)-benzonitrile (**39**) (67 mg, 0.22 mmol) was dissolved in $CHCl_3$ (3 mL) at 0 °C. $BF_3{\cdot}Et_2O$ (190 mg, 1.34 mmol) was slowly added and the resulting solution was stirred at 40 °C for 7 h. The reaction mixture was then quenched with $H_2O$ (2 mL) and $CH_2Cl_2$ (5 mL), and the aqueous phase was extracted with $CH_2Cl_2$ (5 mL). Combined organic phases were dried ($MgSO_4$) and evaporated to yield a crude product. Purification by flash chromatography (pentane/ether = 2 : 3) yielded **40** (57 mg, 86 %) as a white powder.

**mp**.: 156.8-158.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.30-7.70 (m, 8H), 6.67 (s, 1H), 2.48-2.92 (m, 3H), 1.88-2.40 (m, 4H), 1.56-1.84 (m, 1H).

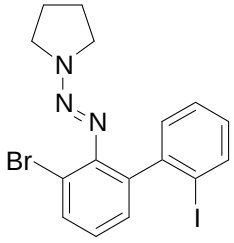
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 209.7, 151.4, 146.1, 142.8, 141.0, 133.9, 132.0, 128.8, 128.5, 127.6, 125.4, 121.7, 119.4, 109.1, 55.9, 48.0, 33.0, 24.9.

**MS** (70 eV, EI) *m/z* (%): 299 (90) [$M^+$], 281 (80), 271 (10), 256 (15), 243(100), 227 (69), 215 (15), 201 (19), 193 (19), 120 (13), 100 (13), 91 (10).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3062 (w), 2956 (w), 2222 (s), 1706 (vs), 1606 (s), 1492 (m), 1470 (m), 1445 (m), 1414 (w), 1350 (w), 1229 (w), 1073 (w), 950 (w).

**HRMS** (EI) for **$C_{21}H_{17}NO$** (299.1310): found: 299.1287.

**Synthesis of (3-bromo-2'-iodo-biphenyl-2-yl)-pyrrolidin-1-yl-diazene (41a):**



Prepared according to **TP8** from 1-(2,6-dibromophenylazo)pyrrolidine (**28a**) (999 mg, 3 mmol), *i*-PrMgCl (1.6 mL, 1.1 equiv., 2.0 M in THF), $ZnBr_2$ (3 mL, 3 mmol, 1.0 M solution in THF), tetrakis(triphenylphosphine)palladium (116 mg, 0.1 mmol), and 1, 2-diiodobenzene (1.2 g, 3.3 mmol). Reaction condition: -40 °C to -15 °C, 5 h; -20 °C to -5 °C, 1 h; reflux, 3 h. Purification by flash chromatography (*n*-pentane/ether = 9 : 1) yielded **41a** (1.2 g, 88 %) as a yellow solid.

**mp.**: 64.4-65.0 °C..

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.80 (d, $J$ = 7.7 Hz, 1H), 7.62 (dd, $J$ = 7.7, 1.8 Hz, 1H), 7.25 (t, $J$ = 7.7 Hz, 1H), 7.14 (dd, $J$ = 7.7, 1.8 Hz, 1H), 7.06 (dd, $J$ = 7.7, 1.8 Hz, 1H), 7.01 (t, $J$ = 7.7 Hz, 1H), 6.91 (t, $J$ = 7.7 Hz, 1H), 5.30-3.50 (m, 4H), 1.81 (br s, 4H).

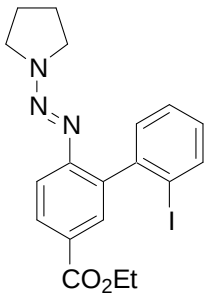
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 147.2, 145.7, 138.2, 138.1, 132.7, 131.1, 129.9, 127.8, 127.1, 125.1, 118.5, 100.3, 23.7.

**MS** (70 eV, EI) *m/z* (%): 455 (9) [$M^+$], 385 (31), 357 (81), 278 (39), 230 (61), 151 (100).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3055 (w), 2972 (w), 2871 (w), 1557 (m), 1415 (m), 1316 (m), 1220 (m), 1010 (m).

**HRMS** (EI) for **$C_{16}H_{15}BrIN_3$** (454.9494): found: 454.9533.

**Synthesis of 2'-iodo-6-(pyrrolidin-1-ylazo)-biphenyl-3-carboxylic acid ethyl ester (41b):**



Prepared according to **TP8** from 1-(4-carbethoxy-2-iodophenylazo)pyrrolidine (**28c**) (1.12 g, 3 mmol), *i*-PrMgCl (1.6 mL, 1.1 equiv., 2.0 M in THF), $ZnBr_2$ (3 mL, 3 mmol, 1.0 M solution in THF), tetrakis(triphenylphosphine)palladium (116 mg, 0.1 mmol), and 1, 2-diiodobenzene (1.2 g, 3.3 mmol). Reaction condition: -40 °C, 0.7 h; -20 °C to -5 °C, 1 h; reflux, 3 h.

Purification by flash chromatography (*n*-pentane/ether = 4 : 1) yielded **41b** (1.08 g, 80 %) as a yellow solid.

**mp.**: 89.0-89.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.02 (dd, $J$ = 8.0, 2.0 Hz, 1H), 7.82-7.89 (m, 2H), 7.54 (d, $J$ = 8.0 Hz, 1H), 7.34 (t, $J$ = 8.0 Hz, 1H), 7.27 (d, $J$ = 2.0 Hz, 1H), 6.98 (t, $J$ = 8.0 Hz, 1H), 4.34 (q, $J$ = 7.1 Hz, 2H), 3.85 (br s, 2H), 3.31 (br s, 2H), 1.91 (br s, 4H), 1.36 (t, $J$ = 7.1 Hz, 3H).

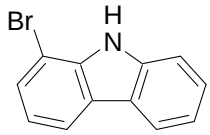
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 166.5, 151.8, 145.3, 138.5, 138.3, 131.8, 130.6, 130.1, 128.2, 127.4, 126.2, 116.4, 100.6, 60.7, 50.9, 46.5, 23.9, 23.4, 14.3.

**MS** (70 eV, EI) *m/z* (%): 449 (10) [$M^+$], 404 (7), 379 (12), 351 (100), 323 (38), 307 (37), 196 (21), 152 (38).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2974 (w), 2921 (w), 2874 (w), 1698 (vs), 1601 (s), 1310 (m), 1264 (m), 1231 (m), 1106 (s), 1011 (s).

**HRMS** (EI) for **$C_{19}H_{20}IN_3O_2$** (449.0600): found: 449.0561.

**Synthesis of 1-bromo-9*H*-carbazole (42a):**




Prepared according to **TP9** from (3-bromo-2'-iodo-biphenyl-2-yl)-pyrrolidin-1-yl-diazene (**41a**) (228 mg, 0.5 mmol), *i*-PrMgCl (0.27 mL, 1.1 equiv., 2.0 M in THF). Reaction condition: -40 °C, 1 h; 55 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 32 : 1) yielded **42a** (92 mg, 75 %) as a white solid.

**mp.**: 121.5-122.0 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.18 (br s, 1H, N-H), 7.99 (q, $J$ = 8.0 Hz, 2H), 7.53 (d, $J$ = 8.0 Hz, 1H), 7.40-7.46 (m, 2H), 7.19-7.28 (m, 1H), 7.09 (t, $J$ = 8.0 Hz, 1H).

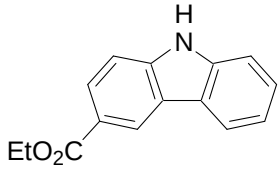
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 139.1, 138.1, 127.9, 126.5, 124.6, 123.6, 120.8, 120.5, 120.1, 119.3, 111.0, 104.1.

**MS** (70 eV, EI) *m/z* (%): 245 (100) [$M^+$], 166 (45), 139 (23).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3409 (vs), 3051 (w), 2962 (w), 2919 (w), 1603 (m), 1496 (w), 1454 (w), 1424 (m), 1320 (w), 1136 (m), 754 (w).

**HRMS** (EI) for **$C_{12}H_8BrN$** (244.9840): found: 244.9836.

**Synthesis of 3-carbethoxy-9*H*-carbazole (42b):**




Prepared according to **TP9** from 2'-iodo-6-(pyrrolidin-1-ylazo)-biphenyl-3-carboxylic acid ethyl ester (**41b**) (225 mg, 0.5 mmol), *i*-PrMgCl (0.27 mL, 1.1 equiv., 2.0 M in THF). Reaction condition: -40 °C, 1 h; 55 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 7 : 3) yielded **42b** (84 mg, 70 %) as a yellow solid.

**mp.**: 161.8-163.0 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.78 (s, 1H), 8.40 (br s, 1H, N-H), 8.05-8.13 (m, 2H), 7.33-7.42 (m, 3H), 7.20-7.27 (m, 1H), 4.41 (q, $J$ = 7.1 Hz, 2H), 1.41 (t, $J$ = 7.1 Hz, 3H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 194.2, 167.5, 142.3, 139.9, 127.4, 126.5, 123.3, 122.8, 121.7, 120.6, 120.2, 110.9, 110.1, 60.7, 14.5.

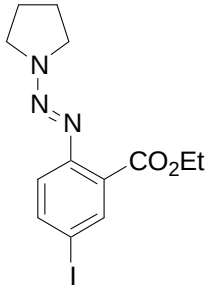
**MS** (70 eV, EI) *m/z* (%): 239 (86) [$M^+$], 224 (11), 211 (31), 194 (100), 166 (46), 139 (31).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3297 (s), 2980 (w), 2902 (w), 1686 (vs), 1603 (s), 1336 (m), 1266 (s), 1101 (m), 1034 (m), 911 (w).

**HRMS** (EI) for **$C_{15}H_{13}NO_2$** (239.0946): found: 239.0926.

## 11. Preparation of Polyfunctional Arylzinc Reagents Bearing a Triazene Moiety

**Synthesis of 1-(2-carbethoxy-4-iodophenylazo)pyrrolidine (44a):**



Prepared according to **TP1** from 2-carbethoxy-4-iodoaniline [92] (5.3 g, 18.1 mmol), concentrated HCl (7.2 mL), $NaNO_2$ (1.3 g, 19 mmol), pyrrolidine (2.6 g, 36.2 mmol), and $K_2CO_3$ (12.5 g, 90.5 mmol). Reaction condition: 0 °C, 0.5 h; 25 °C, 0.5 h. Purification by flash chromatography (*n*-pentane/ether = 2 : 1) yielded **44a** (5.9 g, 87 %) as a yellow solid.

**mp**.: 95.1-96.1 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.87 (d, $J$ = 2.0 Hz, 1H), 7.63 (dd, $J$ = 8.8, 2.0 Hz, 1H), 7.14 (d, $J$ = 8.8 Hz, 1H), 4.29 (q, $J$ = 7.1 Hz, 2H), 3.85 (br s, 2H), 3.63 (br s, 2H), 1.98 (br s, 4H), 1.32 (t, $J$ = 7.1 Hz, 3H).

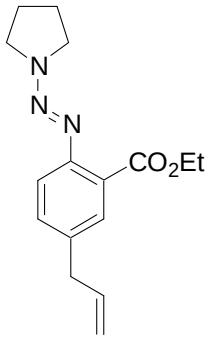
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 166.9, 149.7, 140.0, 137.7, 128.2, 121.0, 87.7, 61.0, 50.9, 46.6, 23.8, 23.4, 14.2.

**MS** (70 eV, EI) *m/z* (%): 373 (17) [$M^+$], 303 (87), 247 (100), 203 (5), 148 (10), 120 (14), 75 (10).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2976 (w), 2876 (w), 1718 (s), 1573 (w), 1467 (m), 1416 (m), 1362 (m), 1312 (w), 1225 (m), 1072 (s).

**HRMS** (EI) for **$C_{13}H_{16}IN_3O_2$** (373.0287): found: 373.0245.

**Synthesis of 5-allyl-2-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (45a):**




Prepared according to **TP10** from 1-(2-carbethoxy-4-iodophenylazo)pyrrolidine (**44a**) (1.5 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), CuCN·2LiCl (one drop of 1.0 M solution in THF, ca. 0.02 mmol, ca. 0.4 mol%), and allyl bromide (549 mg, 4.5 mmol). Reaction condition: 50 °C, 7 h; -20 °C to rt, 1 h. Purification by flash chromatography (*n*-pentane/ether = 4 : 1) yielded **45a** (654 mg, 76 %) as a pale yellow liquid.

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[92] N. V. Harris, C. Smith, K. Bowden, *Synlett* **1990**, 577.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.78-7.88 (m, 2H), 7.41 (d, $J$ = 8.4 Hz, 1H), 5.92-6.09 (m, 1H), 4.94-5.12 (m, 2H), 4.33 (q, $J$ = 7.1 Hz, 2H), 3.56-4.04 (m, 6H), 2.02 (br s, 4H), 1.37 (t, $J$ = 7.1 Hz, 3H).

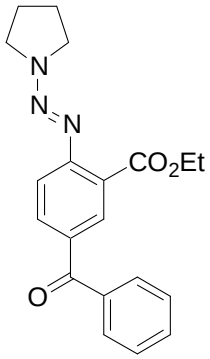
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 193.5, 166.8, 152.2, 137.4, 134.1, 131.3, 128.4, 126.6, 116.0, 115.2, 60.6, 51.4, 46.9, 35.7, 23.8, 14.4.

**MS** (70 eV, EI) *m/z* (%): 287 (5) [$M^+$], 242 (15), 217 (10), 190 (10), 145 (20), 117 (100);

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3077 (w), 2977 (m), 2874 (m), 1711 (vs), 1637 (w), 1602 (m), 1398 (s), 1264 (s), 1107 (s), 1026 (m), 908 (m)

**HRMS** (EI) for **$C_{16}H_{21}N_3O_2$** (287.1634): found: 286.1550 ([M−H]$^+$).

**Synthesis of 5-benzoyl-2-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (45b)**




Prepared according to **TP10** from 1-(2-carbethoxy-4-iodophenylazo)pyrrolidine (**44a**) (1.5 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), CuCN·2LiCl (3 mL of 1.0 M solution in THF, 3 mmol), and benzoyl chloride (635 mg, 4.5 mmol). Reaction condition: 50 °C, 7 h; -20 $^o$C to rt, 2 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **45b** (853 mg, 81 %) as a pale red liquid.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.06 (s, 1H), 7.85 (d, $J$ = 8.6 Hz, 1H), 7.76 (d, $J$ = 8.4 Hz, 2H), 7.57 (t, $J$ = 7.5 Hz, 1H), 7.52 (d, $J$ = 8.6 Hz, 1H), 7.44-7.49 (m, 2H), 4.34 (q, $J$ = 7.1 Hz, 2H), 3.95 (br s, 2H), 3.71 (br s, 2H), 1.98-2.12 (m, 4H), 1.35 (t, $J$ = 7.1 Hz, 3H).

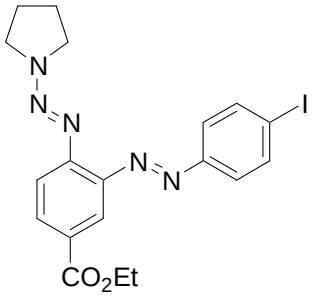
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 195.3, 168.0, 153.2, 137.8, 133.1, 132.2, 131.9, 129.8, 128.4, 128.3, 126.4, 118.8, 61.1, 51.3, 46.9, 23.9, 23.5, 14.3.

**MS** (70 eV, EI) *m/z* (%): 351 (5) [$M^+$], 281 (28), 254 (9), 225 (100), 209 (9), 177 (8), 141 (14), 105 (75), 77 (30).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3061 (w), 2977 (w), 2874 (w), 1719 (s), 1651 (vs), 1595 (vs), 1394 (vs), 1302 (s), 1239 (s), 1071 (m), 959 (m).

**HRMS** (EI) for **$C_{20}H_{21}N_3O_3$** (351.1583): found: 352.1651 ([M+H]$^+$).

**Synthesis of 3-(4-iodo-phenylazo)-4-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (45c):**



Prepared according to **TP11** from 1-(4-carbethoxy-2-iodophenylazo)pyrrolidine (**44b**) (see also **28c**) (1.5 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), and 4-iodo-diazobenzene tetrafluoroborate (954 mg, 3 mmol). Reaction condition: 50 °C, 30 h; -20 $^oC$ to rt, 2 h. Purification by flash chromatography (*n*-pentane/ether = 7 : 3) yielded **45c** (944 mg, 66 %) as a red powder.

**mp.**: 146.2-148.5.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.22 (s, 1H), 8.06 (d, $J$ = 8.4 Hz, 1H), 7.83 (d, $J$ = 8.4 Hz, 2H), 7.66 (d, $J$ = 8.4 Hz, 2H), 7.57 (d, $J$ = 8.4 Hz, 1H), 4.37 (q, $J$ = 7.1 Hz, 2H), 3.96 (br s, 2H), 3.78 (br s, 2H), 1.97-2.12 (m, 4H), 1.39 (t, $J$ = 7.1 Hz, 3H).

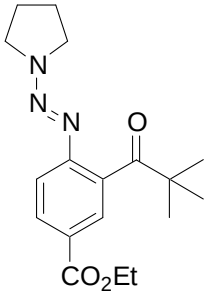
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 166.3, 152.3, 151.4, 145.0, 138.2, 132.1, 126.9, 124.7, 119.6, 118.3, 97.5, 61.0, 51.5, 47.0, 23.9, 23.5, 14.4.

**MS** (70 eV, EI) *m/z* (%): 477 (1) [$M^+$], 432 (5), 404 (8), 393 (100), 380 (22), 365 (15), 348 (28), 267 (18), 247 (17), 231 (17), 203 (73), 177 (24), 149 (72), 121 (15), 103 (26), 76 (22).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2953 (w), 2874 (w), 1695 (vs), 1596 (s), 1579 (w), 1458 (w), 1382 (m), 1240 (m), 1112 (s), 1002 (m), 822 (s).

**HRMS** (EI) for **$C_{19}H_{20}IN_5O_2$** (477.0662): found: 477.0630.

**Synthesis of 3-(2,2-dimethyl-propionyl)-4-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (45d):**



Prepared according to **TP10** from 1-(4-carbethoxy-2-iodophenylazo)pyrrolidine (**44b**) (see also **28c**) (1.5 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), $CuCN{\cdot}2LiCl$ (3 mL of 1.0 M solution in THF, 3 mmol), and *t*-butoyl chloride (545 mg, 4.5 mmol). Reaction condition: 50 °C, 30 h; -20 °C to rt, 12 h. Purification by flash chromatography (*n*-pentane/ether = 7 : 3) yielded **45d** (725 mg, 73 %) as a yellow solid.

**mp.**: 76.1-78.8.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.94 (d, $J$ = 8.4 Hz, 1H), 7.72 (s, 1H), 7.51 (d, $J$ = 8.4 Hz, 1H), 4.34 (q, $J$ = 7.1 Hz, 2H), 3.91 (t, $J$ = 6.2 Hz, 2H), 3.91 (t, $J$ = 6.2 Hz, 2H), 3.58 (t, $J$ = 6.2 Hz, 2H), 1.92-2.08 (m, 4H), 1.36 (t, $J$ = 7.1 Hz, 3H), 1.22 (s, 9H).

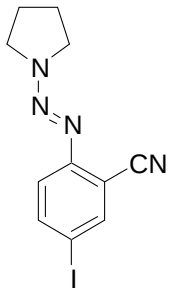
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 214.9, 166.2, 151.1, 136.3, 130.4, 126.9, 126.1, 116.6, 60.8, 51.3, 47.0, 44.9, 27.2, 23.9, 23.5, 14.4.

**MS** (70 eV, EI) *m/z* (%): 331 (27) [$M^+$], 286 (12), 274 (61), 261 (23), 177 (100), 163 (20), 149 (27), 121 (10), 103 (7).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2976 (w), 2930 (w), 2882 (w), 1690 (vs), 1595 (s), 1476 (m), 1388 (vs), 1292 (s), 1245 (s), 1094 (vs), 986 (m).

**HRMS** (EI) for **$C_{18}H_{25}N_3O_3$** (331.1896): found: 331.1878.

**Synthesis of 1-(2-cyano-4-iodophenylazo)pyrrolidine (44c):**




Prepared according to **TP1** from 2-cyano-4 iodoaniline[92] (4.4 g, 18.1 mmol), concentrated HCl (7.2 mL), $NaNO_2$ (1.3 g, 19 mmol), pyrrolidine (2.6 g, 36.2 mmol), and $K_2CO_3$ (12.5 g, 90.5 mmol). Reaction condition: 0 °C, 0.5 h; 25 °C, 0.5 h. Purification by flash chromatography (*n*-pentane/ether = 2 : 1) yielded **44c** (5.5 g, 93 %) as a pale brown solid.

**mp**.: 143.7-144.9 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.84 (s, 1H), 7.70 (d, $J$ = 8.4 Hz, 1H), 7.27 (d, $J$ = 8.4 Hz, 1H), 3.60-4.04 (m, 4H), 1.90-2.03 (m, 4H).

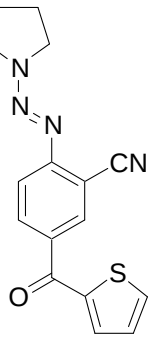
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 153.5, 141.8, 140.9, 118.9, 116.4, 109.0, 86.6, 51.4, 47.3, 23.9, 23.3.

**MS** (70 eV, EI) *m/z* (%): 326 (17) [$M^+$], 256 (84), 228 (100), 207 (9), 126 (10), 101 (61), 70 (21).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3064 (w), 2970 (w), 2871 (w), 2222 (m), 1410 (s), 1380 (s), 1312 (s), 1274 (s).

**HRMS** (EI) for **$C_{11}H_{11}IN_4$** (326.0028): found: 326.0055.

**Synthesis of 2-(pyrrolidin-1-ylazo)-5-(thiophene-2-carbonyl)-benzonitrile (45e):**




Prepared according to **TP10** from 1-(2-cyano-4-iodophenylazo)pyrrolidine (**44c**) (1.3 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), CuCN·2LiCl (3 mL of 1.0 M solution in THF, 3 mmol), and *t*-butoyl chloride (657 mg, 4.5 mmol). Reaction condition: 50 °C, 8 h; -20 $^o$C to rt, 12 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **45e** (400 mg, 43 %) as a pale yellow solid.

**mp.**: 152.3-154.5.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.12 (s, 1H), 7.98 (d, $J$ = 8.8 Hz, 1H), 7.72 (d, $J$ = 4.9 Hz, 1H), 7.61-7.67 (m, 2H), 7.17 (dd, $J$ = 4.9, 4.0 Hz, 1H), 3.98-4.03 (m, 2H), 3.77-3.83 (m, 2H), 2.02-2.14 (m, 4H).

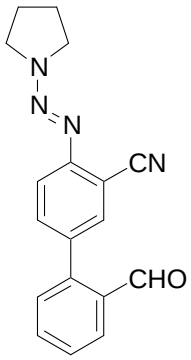
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 185.5, 156.6, 143.0, 134.7, 134.4, 134.3, 133.9, 133.7, 128.1, 117.3, 117.1, 107.0, 51.8, 47.7, 23.9, 23.3.

**MS** (70 eV, EI) *m/z* (%): 310 (14) [$M^+$], 240 (37), 212 (100), 184 (8), 140 (14), 111 (74).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2971 (w), 2879 (w), 2226 (w), 1625 (s), 1589 (s), 1392 (s), 1309 (s), 1264 (vs), 1094 (m), 944 (m).

**HRMS** (EI) for **$C_{16}H_{14}N_4OS$** (310.0888): found: 311.0954 ([M+H]$^+$).

**Synthesis of 2'-formyl-4-(pyrrolidin-1-ylazo)-biphenyl-3-carbonitrile (45f):**




Prepared according to **TP12** from 1-(2-cyano-4-iodophenylazo)pyrrolidine (**44c**) (1.3 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), tetrakis(triphenylphosphine)palladium (104 mg, 0.09 mmol), and 2-iodobenzaldehyde (696 mg, 3 mmol). Reaction condition: 50 °C, 8 h; reflux, 2 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **45f** (648 mg, 71 %) as a pale yellow solid.

**mp.**: 73.8-76.7.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.97 (s, 1H), 8.01 (d, $J$ = 7.9 Hz, 1H), 7.61-7.66 (m, 2H), 7.60 (s, 1H), 7.44 (d, $J$ = 8.2 Hz, 1H), 7.40 (d, $J$ = 7.9 Hz, 1H), 7.21 (t, $J$ = 8.2 Hz, 1H), 3.95-4.01 (m, 2H), 3.75-3.82 (m, 2H), 2.00-2.12 (m, 4H).

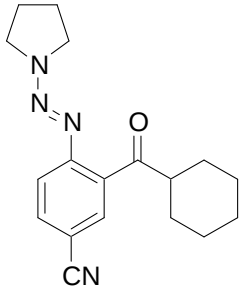
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 191.6, 153.6, 143.6, 134.8, 134.1, 133.9, 133.8, 133.6, 130.6, 128.3, 128.1, 117.6, 117.3, 107.4, 51.5, 47.3, 23.9, 23.4.

**MS** (70 eV, EI) *m/z* (%): 304 (43) [$M^+$], 234 (72), 206 (100), 177 (42), 151 (41).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3057 (w), 2973 (w), 2873 (w), 2748 (w), 2223 (m), 1689 (s), 1596 (m), 1470 (m), 1384 (s), 1307 (s), 1267 (s), 1098 (m), 903 (w).

**HRMS** (EI) for **$C_{18}H_{16}N_4O$** (304.1324): found: 304.1328.

**Synthesis of 3-cyclohexanecarbonyl-4-(pyrrolidin-1-ylazo)-benzonitrile (45g):**



Prepared according to **TP10** from 1-(4-cyano-2-iodophenylazo)pyrrolidine (**44d**) (see also **28d**) (1.3 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), CuCN·2LiCl (3 mL of 1.0 M solution in THF, 3 mmol), and cyclohexoyl chloride (662 mg, 4.5 mmol). Reaction condition: 50 °C, 24 h; -20 °C to rt, 12 h. Purification by flash chromatography (*n*-pentane/ether = 7 : 3) yielded **45g** (539 mg, 58 %) as a pale yellow solid.

**mp.**: 117.0-119.1.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.51-7.58 (m, 3H), 3.92-3.98 (m, 2H), 3.58-3.64 (m, 2H), 3.14 (tt, $J$ = 11.5, 3.1 Hz, 1H), 1.98-2.12 (m, 4H), 1.80-1.90 (m, 2H), 1.70-1.79 (m, 2H), 1.60-1.67 (m, 1H), 1.32-1.43 (m, 2H), 1.13-1.25 (m, 3H).

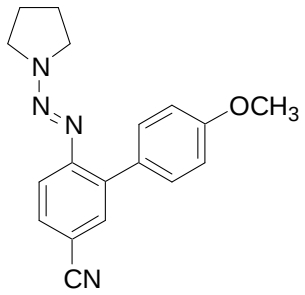
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 208.8, 151.6, 135.8, 133.8, 132.3, 118.8, 117.9, 107.5, 51.6, 50.6, 47.2, 28.5, 25.9, 25.8, 23.8, 23.4.

**MS** (70 eV, EI) *m/z* (%): 310 (13) [$M^+$], 240 (12), 130 (100), 102 (16), 83 (14).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2943 (w), 2855 (w), 2218 (s), 1683 (vs), 1596 (s), 1390 (vs), 1156 (m), 992 (m).

**HRMS** (EI) for **$C_{18}H_{22}N_4O$** (310.1794): found: 310.1771.

**Synthesis of 4'-methoxy-6-(pyrrolidin-1-ylazo)-biphenyl-3-carbonitrile (45h):**




Prepared according to **TP12** from 1-(4-cyano-2-iodophenylazo)pyrrolidine (**44d**) (see also **28d**) (1.3 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), tetrakis(triphenylphosphine)palladium (104 mg, 0.09 mmol), and 4-iodoanisole (702 mg, 3 mmol). Reaction condition: 50 °C, 24 h; reflux, 6 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 2) yielded **45h** (689 mg, 75 %) as a yellow solid.

**mp.**: 120.3-122.2.

**$^{1}$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.60 (s, 1H), 7.51 (d, $J$ = 8.4 Hz, 1H), 7.48 (d, $J$ = 8.4 Hz, 1H), 7.43 (d, $J$ = 8.6 Hz, 2H), 6.90 (d, $J$ = 8.6 Hz, 2H), 3.92 (br s, 2H), 3.83 (s, 3H), 3.49 (br s, 2H), 1.95-2.00 (m, 4H).

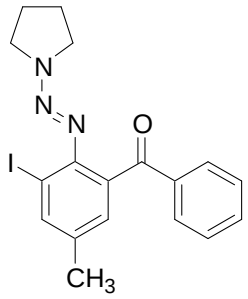
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 158.9, 151.5, 136.3, 134.2, 131.3, 131.0, 130.5, 119.6, 117.9, 113.0, 107.7, 55.2, 51.1, 46.9, 23.9, 23.3.

**MS** (70 eV, EI) *m/z* (%): 306 (22) [$M^+$], 236 (11), 208 (100), 193 (32), 177 (6), 165 (19).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2948 (w), 2879 (w), 2830 (w), 2215 (s), 1595 (m), 1513 (m), 1479 (m), 1383 (s), 1243 (s), 1173 (s), 1030 (m).

**HRMS** (EI) for **$C_{18}H_{18}N_4O$** (306.1481): found: 306.1483.

**Synthesis of [3-iodo-5-methyl-2-(pyrrolidin-1-ylazo)-phenyl]-phenyl-methanone (45i):**




Prepared according to **TP10** from 1-(2,6-diiodo-4-methylphenylazo)pyrrolidine[87b] (**44e**) (1.76 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), $CuCN{\cdot}2LiCl$ (3 mL of 1.0 M solution in THF, 3 mmol), and benzoyl chloride (635 mg, 4.5 mmol). Reaction condition: 50 °C, 15 h; -20 °C to rt, 2 h. Purification by flash chromatography (*n*-pentane/ether = 4 : 1) yielded **45i** (1.04 g, 83 %) as a pale brown solid.

**mp.**: 122.5-124.0.

**$^{1}$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.82 (s, 1H), 7.62 (d, $J$ = 7.3 Hz, 2H), 7.41 (t, $J$ = 7.3 Hz, 1H), 7.31 (t, $J$ = 7.3 Hz, 2H), 7.18 (s, 1H), 3.43 (br s, 2H), 3.24 (br s, 2H), 2.32 (s, 3H), 1.58-1.80 (m, 4H).

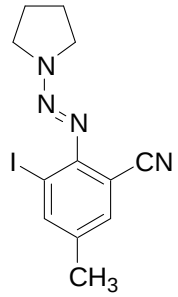
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 196.5, 147.1, 141.4, 137.6, 136.0, 132.0, 130.9, 130.3, 128.8, 128.1, 95.7, 50.3, 47.0, 23.6, 23.2, 20.2.

**MS** (70 eV, EI) *m/z* (%): 419 (20) [$M^+$], 349 (23), 194 (100), 165 (59), 105 (15), 77 (27).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3026 (w), 2971 (w), 2871 (w), 1663 (vs), 1592 (m), 1447 (m), 1404 (s), 1361 (s), 1308 (s), 1258 (s), 1109 (m), 977 (w).

**HRMS** (EI) for **$C_{18}H_{18}IN_3O$** (419.0495): found: 419.0509.

**Synthesis of 3-iodo-5-methyl-2-(pyrrolidin-1-ylazo)-benzonitrile (45j):**



Prepared according to **TP11** from 1-(2,6-diiodo-4-methylphenylazo)pyrrolidine[87b] (**44e**) (1.76 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), and *p*-toluenesulfonyl cynide (815 mg, 4.5 mmol). Reaction condition: 50 °C, 15 h; -10 °C to rt, 24 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 1) yielded **45j** (714 mg, 70 %) as a pale yellow solid.

**mp.**: 76.0-78.2.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.84 (s, 1H), 7.36 (s, 1H), 4.00 (t, $J$ = 6.4 Hz, 2H), 3.73 (t, $J$ = 6.4 Hz, 2H), 2.27 (s, 3H), 1.94-2.16 (m, 4H).

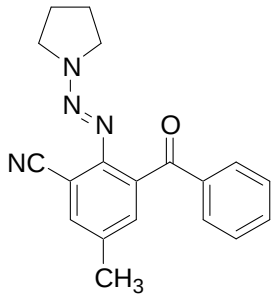
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 144.0, 135.6, 134.9, 118.2, 117.2, 102.4, 95.7, 51.1, 47.2, 24.0, 23.5, 19.9.

**MS** (70 eV, EI) *m/z* (%): 340 (28) [$M^+$], 270 (80), 242 (100), 144 (9), 115 (80), 70 (11).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2976 (w), 2221 (m), 1634 (m), 1404 (s), 1309 (s), 1228 (m), 1106 (w).

**HRMS** (EI) for **$C_{12}H_{13}IN_4$** (340.0185): found: 340.0180.

**Synthesis of 3-benzoyl-5-methyl-2-(pyrrolidin-1-ylazo)-benzonitrile (46):**



Prepared according to **TP10** from 1-(5-cyano-2-iodo-4-methylphenylazo)pyrrolidine (**45j**) (1.36 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), CuCN·2LiCl (3 mL of 1.0 M solution in THF, 3 mmol), and benzoyl chloride (635 mg, 4.5 mmol). Reaction condition: 50

°C, 11 h; -20 °C to rt, 2 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 2) yielded **46** (878 mg, 92 %) as a pale yellow solid.

**mp.**: 120.0-121.1.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.63 (d, $J$ = 7.1 Hz, 2H), 7.54 (s, 1H), 7.45 (t, $J$ = 7.1 Hz, 1H), 7.28-7.40 (m, 3H), 3.47 (t, $J$ = 6.6 Hz, 2H), ), 3.28 (t, $J$ = 6.6 Hz, 2H), 2.38 (s, 3 H), 1.60-1.86 (m, 4H).

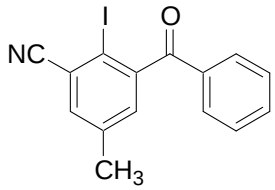
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 196.0, 150.2, 137.3, 135.2, 134.5, 134.3, 132.4, 131.5, 128.9, 128.3, 117.7, 106.5, 50.7, 47.1, 23.7, 23.2, 20.5.

**MS** (70 eV, EI) *m/z* (%): 318 (34) [$M^+$], 248 (60), 220 (100), 192 (36), 177 (20), 165 (43), 105 (30), 77 (24).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3035 (w), 2962 (w), 2217 (m), 1668 (vs), 1578 (m), 1450 (m), 1396 (s), 1365 (s), 1306 (s), 1211 (s), 992 (w).

**HRMS** (EI) for **$C_{19}H_{18}N_4O$** (318.1481): found: 318.1462.

**Synthesis of 3-benzoyl-2-iodo-5-methyl-benzonitrile (47):**




Prepared according to **TP5** from 3-benzoyl-5-methyl-2-(pyrrolidin-1-ylazo)-benzonitrile (**46**) (161 mg, 0.51 mmol), trimethylsilyl iodide (202 mg, 1.02 mmol). Reaction condition: 35 °C, 24 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 1) yielded **47** (113 mg, 64 %) as a pale yellow solid.

**mp.**: 133.5-135.0.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.76 (d, $J$ = 7.1 Hz, 2H), 7.63 (t, $J$ = 7.1 Hz, 1H), 7.49-7.53 (m, 2H), 7.46 (d, $J$ = 7.1 Hz, 2H), 2.38 (s, 3H).

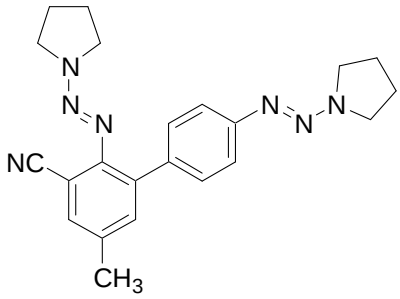
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 195.8, 146.8, 139.3, 135.6, 134.7, 134.3, 132.3, 130.4, 128.9, 122.3, 119.1, 92.3, 20.7.

**MS** (70 eV, EI) *m/z* (%): 347 (100) [$M^+$], 270 (22), 220 (34), 190 (11), 165 (6), 115 (15), 105 (98), 77 (40).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3041 (w), 2922 (w), 2852 (w), 2230 (m), 1667 (vs), 1594 (m), 1578 (m), 1448 (m), 1412 (m), 1318 (s), 1212 (m), 1020 (m), 878 (m).

**HRMS** (EI) for **$C_{15}H_{10}INO$** (346.9807): found: 346.9789.

**Synthesis of 5-methyl-2,4'-bis-(pyrrolidin-1-ylazo)-biphenyl-3-carbonitrile (48):**



Prepared according to **TP12** from 1-(5-cyano-2-iodo-4-methylphenylazo)pyrrolidine (**45j**) (1.36 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), tetrakis(triphenylphosphine)palladium (104 mg, 0.09 mmol), and 4-iodophenyl triazene (903 mg, 3.0 mmol). Reaction condition: 50 °C, 11 h; reflux, 5 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **48** (871 mg, 75 %) as a yellow solid.

**mp.**: 151.4-152.6.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.38 (d, $J$ = 8.4 Hz, 2H), 7.32-7.36 (m, 4H), 3.88 (br s, 2H), 3.78 (br s, 4H), 3.48 (br s, 2H), 2.34 (s, 3H), 1.98-2.03 (m, 4H), 1.92-1.97 (m, 4H).

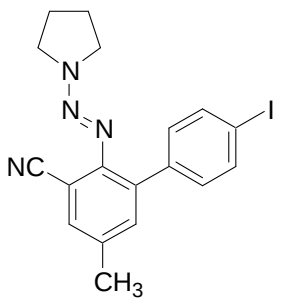
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 150.3, 149.3, 136.5, 135.5, 135.4, 134.4, 133.0, 130.6, 119.5, 119.3, 103.7, 50.8, 46.6, 23.9, 23.8, 23.4, 20.6.

**MS** (70 eV, EI) *m/z* (%): 387 (100) [$M^+$], 348 (11), 289 (59), 277 (53), 262 (49), 219 (65), 205 (12), 191 (72), 165 (13), 152 (25), 116 (10), 70 (19).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3051 (w), 2974 (w), 2874 (w), 2210 (w) 1596 (w), 1397 (s), 1340 (s), 1312 (m), 1218 (m), 1148 (m), 970 (w).

**HRMS** (EI) for **$C_{22}H_{25}N_7$** (387.2171): found: 387.2174.

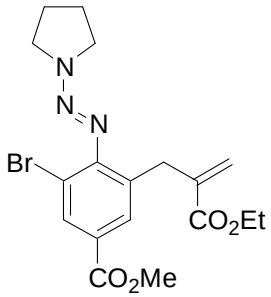
**Synthesis of 4'-iodo-5-methyl-2-(pyrrolidin-1-ylazo)-biphenyl-3-carbonitrile (49):**



Prepared according to **TP5** from 5-methyl-2,4'-bis-(pyrrolidin-1-ylazo)-biphenyl-3-carbonitrile (**48**) (194 mg, 0.5 mmol), trimethylsilyl iodide (202 mg, 1 mmol). Reaction condition: 25 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 1) yielded **49** (150 mg, 72 %) as a yellow liquid.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.67 (d, $J$ = 8.4 Hz, 2H), 7.40 (s, 1H), 7.27 (s, 1H), 7.15 (d, $J$ = 8.4 Hz, 2H), 3.91 (br s, 2H), 3.48 (br s, 2H), 2.36 (s, 3H), 1.93-2.04 (m, 4H).
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 149.0, 138.4, 136.6, 135.2, 133.8, 131.9, 130.0, 127.5, 119.1, 103.8, 92.8, 50.9, 46.7, 23.9, 23.4, 20.5.
**MS** (70 eV, EI) *m/z* (%): 416 (14) [$M^+$], 346 (21), 319 (39), 191 (100), 177 (8), 165 (9), 70 (4).
**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3051 (w), 2949 (w), 2871 (w), 2220 (m), 1598 (w), 1399 (s), 1340 (s), 1308 (s), 1259 (m), 1221 (m), 1153 (m), 1004 (m).
**HRMS** (EI) for **$C_{18}H_{17}IN_4$** (416.0498): found: 416.0504.

**Synthesis of 3-bromo-5-(2-ethoxycarbonyl-allyl)-4-(pyrrolidin-1-ylazo)-benzoic acid methyl ester (45k):**




Prepared according to **TP10** from 1-(2,6-dibromo-4-carbmethoxyphenylazo)pyrrolidine[87a] (**44f**) (1.56 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), $CuCN{\cdot}2LiCl$ (one drop of 1.0 M solution in THF, ca. 0.02 mmol, ca. 0.4 mol%), and ethyl 2-bromomethyl acrylate (579 mg, 3 mmol). Reaction condition: 50 °C, 24 h; -20 °C to rt, 1 h. Purification by flash chromatography (*n*-pentane/ether = 7 : 3) yielded **45k** (890 mg, 70 %) as a yellow liquid.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.14 (s, 1H), 7.77 (s, 1H), 6.18 (d, $J$ = 1.2 Hz, 1H), 5.20 (d, $J$ = 1.2 Hz, 1H), 4.17 (q, $J$ = 7.1 Hz, 2H), 3.50-4.00 (m, 9H), 2.02 (br s, 4H), 1.25 (t, $J$ = 7.1 Hz, 3H).

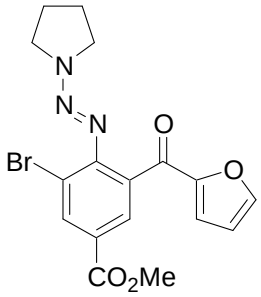
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 166.9, 165.9, 152.2, 139.0, 133.0, 132.9, 131.4, 127.1, 126.4, 117.5, 60.7, 52.1, 51.0, 46.4, 33.9, 24.0, 23.6, 14.2.

**MS** (70 eV, EI) *m/z* (%): 423 (8) [$M^+$], 353 (18), 297 (100), 267 (16), 195 (9), 146 (18), 131 (27), 115 (25).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2977 (w), 2951 (w), 1713 (vs), 1630 (w), 1598 (w), 1552 (w), 1416 (s), 1263 (vs), 1192 (m), 1131 (vs), 1026 (m).

**HRMS** (EI) for **$C_{18}H_{22}BrN_3O_4$** (423.0794): found: 423.0777.

**Synthesis of 3-bromo-5-(furan-2-carbonyl)-4-(pyrrolidin-1-ylazo)-benzoic acid methyl ester (45l):**




Prepared according to **TP10** from 1-(2,6-dibromo-4-carbmethoxyphenylazo)pyrrolidine[87a] (**44f**) (1.56 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), CuCN·2LiCl (3 mL of 1.0 M solution in THF, 3 mmol), and furoyl chloride (590 mg, 4.5 mmol). Reaction condition: 50 °C, 24 h; -20 °C to rt, 12 h. Purification by flash chromatography (*n*-pentane/ether = 2 : 3) yielded **45l** (633 mg, 52 %) as a yellow solid.

**mp.**: 132.8-134.9.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.35 (s, 1H), 7.98 (d, $J$ = 1.8 Hz, 1H), 7.47 (s, 1H), 6.87 (d, $J$ = 3.5 Hz, 1H), 6.42 (dd, $J$ = 3.5, 1.8 Hz, 1H), 3.87 (s, 3H), 3.57 (t, $J$ = 7.1 Hz, 2H), 3.51 (t, $J$ = 7.1 Hz, 2H), 1.91 (quint, $J$ = 7.1 Hz, 2H), 1.81 (quint, $J$ = 7.1 Hz, 2H).

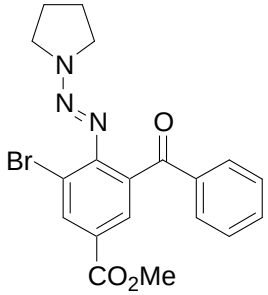
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 183.3, 165.2, 152.3, 151.1, 145.9, 136.1, 130.9, 129.8, 126.6, 119.2, 117.6, 112.0, 52.3, 51.0, 47.2, 23.7, 23.3.

**MS** (70 eV, EI) *m/z* (%): 405 (18) [$M^+$], 335 (43), 307 (100), 279 (15), 251 (10), 222 (7), 113 (10), 95 (35).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3132 (w), 2957 (w), 2875 (w), 1717 (vs), 1655 (vs), 1593 (m), 1565 (m), 1463 (s), 1377 (vs), 1254 (vs), 1164 (m), 1002 (m).

**HRMS** (EI) for **$C_{17}H_{16}BrN_3O_4$** (405.0324): found: 405.0329.

**Synthesis of 3-benzoyl-5-bromo-4-(pyrrolidin-1-ylazo)-benzoic acid methyl ester (45m):**




Prepared according to **TP10** from 1-(2,6-dibromo-4-carbmethoxyphenylazo)pyrrolidine[87a] (**44f**) (1.56 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), $CuCN{\cdot}2LiCl$ (3 mL of 1.0 M solution in THF, 3 mmol), and benzoyl chloride (635 mg, 4.5 mmol). Reaction condition: 50 °C, 24 h; -20 °C to rt, 2 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **45m** (874 mg, 70 %) as a yellow solid.

**mp.**: 131.5-133.6.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.39 (d, $J$ = 2.2 Hz, 1H), 8.01 (d, $J$ = 2.2 Hz, 1H), 7.63 (d, $J$ = 7.5 Hz, 2H), 7.45 (t, $J$ = 7.5 Hz, 1H), 7.33 (t, $J$ = 7.5 Hz, 2H), 3.89 (s, 3H), 3.47 (t, $J$ = 6.6 Hz, 2H), 3.30 (t, $J$ = 6.6 Hz, 2H), 1.60-1.85 (m, 4H).

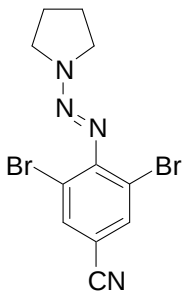
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 195.4, 165.4, 151.0, 137.0, 135.9, 132.4, 131.9, 130.2, 128.8, 128.3, 126.9, 119.1, 52.3, 50.7, 47.3, 23.6, 23.2.

**MS** (70 eV, EI) *m/z* (%): 415 (39) [$M^+$], 345 (100), 317 (22), 273 (31), 258 (53), 207 (67), 194 (78), 179 (43), 165 (33), 151 (57), 105 (95), 77 (75).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3000 (w), 2952 (w), 2874 (w), 1718 (vs), 1663 (vs), 1593 (s), 1448 (m), 1378 (vs), 1296 (s), 1242 (s), 1144 (s), 1001 (m).

**HRMS** (EI) for **$C_{19}H_{18}BrN_3O_3$** (415.0532): found: 415.0523.

**Synthesis of 3,5-dibromo-4-(pyrrolidin-1-ylazo)-benzonitrile (44g):**



Prepared according to **TP1** from 2,6-dibromo-4-cyanoaniline [93] (5.0 g, 18.1 mmol), concentrated HCl (7.2 mL), $NaNO_2$ (1.3 g, 19 mmol), pyrrolidine (2.6 g, 36.2 mmol), and $K_2CO_3$ (12.5 g, 90.5 mmol). Reaction condition: 0 °C, 0.5 h; 25 °C, 0.5 h. Purification by flash chromatography (*n*-pentane/ether = 4 : 1) yielded **44g** (5.2 g, 80 %) as a colorless solid.

**mp.**: 125.9-127.5.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.78 (s, 2H), 3.96 (t, $J$ = 7.1 Hz, 2H), 3.71 (t, $J$ = 7.1 Hz, 1H), 2.00-2.16 (m, 4H).

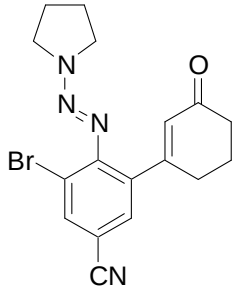
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 152.1, 135.6, 118.2, 116.5, 109.7, 51.4, 46.9, 23.9, 23.5.

**MS** (70 eV, EI) *m/z* (%): 358 (16) [$M^+$], 288 (67), 260 (100), 216 (13), 179 (15).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3066 (w), 2972 (w), 2879 (w), 2230 (m), 1526 (m), 1406 (s), 1307 (s), 1222 (m), 903 (w).

**HRMS** (EI) for **$C_{11}H_{10}Br_2N_4$** (355.9272): found: 355.9283.

**Synthesis of 3-bromo-5-(3-oxo-cyclohex-1-enyl)-4-(pyrrolidin-1-ylazo)-benzonitrile (45n):**




Prepared according to **TP10** from 3,5-dibromo-4-(pyrrolidin-1-ylazo)-benzonitrile (**44g**) (1.43 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), $CuCN{\cdot}2LiCl$ (3 mL of 1.0 M solution in THF, 3 mmol), and 3-iodo-cyclohex-2-enone (666 mg, 3 mmol). Reaction condition: 50 °C, 22 h; -30 °C to -20 °C, 5 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 4) yielded **45n** (694 mg, 62 %) as a yellow solid.

**mp.**: 143.9-145.8.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.83 (d, $J$ = 1.8 Hz, 1H), 7.32 (d, $J$ = 1.8 Hz, 1H), 5.95 (s, 1H), 3.85 (t, $J$ = 6.2 Hz, 2H), 3.66 (t, $J$ = 6.2 Hz, 2H), 2.32-2.46 (m, 4H), 1.92-2.16 (m, 6H).

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[93] Y. Miura, M. Momoki, M. Nakatsuji, *J. Org. Chem.* 1998, *63*, 1555.

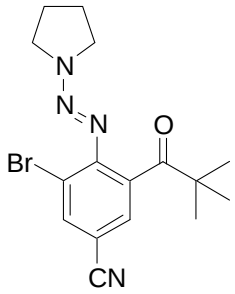
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 198.7, 161.7, 150.2, 136.4, 134.9, 131.5, 128.9, 119.5, 117.3, 108.7, 51.5, 47.3, 37.4, 30.3, 23.9, 23.4, 23.1.

**MS** (70 eV, EI) *m/z* (%): 372 (3) [$M^+$], 355 (3), 344 (4), 316 (5), 289 (13), 260 (12), 234 (16), 220 (20), 167 (100), 153 (20), 139 (34).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3038 (w), 2953 (w), 2865 (w), 2222 (m), 1664 (vs), 1613 (s), 1384 (vs), 1300 (vs), 1188 (m), 964 (m).

**HRMS** (EI) for **$C_{17}H_{17}BrN_4O$** (372.0586): found: 372.0600.

**Synthesis of 3-bromo-5-(2,2-dimethyl-propionyl)-4-(pyrrolidin-1-ylazo)-benzonitrile (45o):**




Prepared according to **TP10** from 3,5-dibromo-4-(pyrrolidin-1-ylazo)-benzonitrile (**44g**) (1.43 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), $CuCN{\cdot}2LiCl$ (3 mL of 1.0 M solution in THF, 3 mmol), and *t*-butoyl chloride (545 mg, 4.5 mmol). Reaction condition: 50 °C, 22 h; -20 °C to rt, 12 h. Purification by flash chromatography (*n*-pentane/ether = 7 : 3) yielded **45o** (762 mg, 70 %) as a yellow solid.

**mp.**: 108.7-110.5.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.84 (d, $J$ = 1.8 Hz, 1H), 7.21 (d, $J$ = 1.8 Hz, 1H), 3.89 (t, $J$ = 6.2 Hz, 2H), 3.70 (t, $J$ = 6.2 Hz, 2H), 1.94-2.14 (m, 4H), 1.12 (s, 9H).

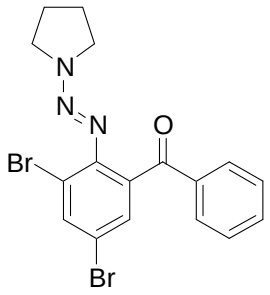
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 211.5, 148.7, 136.7, 133.4, 129.3, 119.9, 117.5, 108.1, 51.5, 48.1, 44.9, 27.4, 24.0, 23.2.

**MS** (70 eV, EI) *m/z* (%): 362 (16) [$M^+$], 292 (23), 237 (13), 208 (100), 194 (54), 180 (21), 100 (37), 70 (32).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2956 (w), 2870 (w), 2223 (s), 1689 (vs), 1587 (m), 1477 (m), 1381 (vs), 1299 (vs), 1122 (s), 1003 (m), 916 (w).

**HRMS** (EI) for **$C_{16}H_{19}BrN_4O$** (362.0742): found: 362.0753.

**Synthesis of [3,5-dibromo-2-(pyrrolidin-1-ylazo)-phenyl]-phenyl-methanone (45p):**



Prepared according to **TP10** from 1-(2,4,6-tribromophenylazo)pyrrolidine[87a] (**44h**) (1.65 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%, Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), CuCN·2LiCl (3 mL of 1.0 M solution in THF, 3 mmol), and benzoyl chloride (635 mg, 4.5 mmol). Reaction condition: 50 °C, 20 h; -20 °C to rt, 2 h. Purification by flash chromatography (*n*-pentane/ether = 4 : 1) yielded **45p** (1.04 g, 79 %) as a yellow solid.

**mp.**: 148.3-150.1.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.85 (d, $J$ = 1.8 Hz, 1H), 7.59-7.65 (m, 2H), 7.40-7.48 (m, 2H), 7.28-7.37 (m, 2H), 3.43 (t, $J$ = 6.5 Hz, 2H), 3.22 (t, $J$ = 6.5 Hz, 2H), 1.58-1.82 (m, 4H).

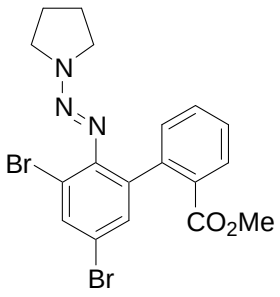
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 194.7, 146.9, 136.9, 136.8, 133.3, 132.4, 131.5, 128.8, 128.3, 120.0, 117.6, 50.5, 47.0, 23.6, 23.2.

**MS** (70 eV, EI) *m/z* (%): 437 (10) [$M^+$], 367 (29), 258 (100), 230 (14), 151 (21), 105 (49), 77 (53).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3070 (w), 2920 (w), 2872 (w), 1658 (vs), 1572 (m), 1448 (m), 1400 (m), 1245 (m), 1156 (w), 960 (w).

**HRMS** (EI) for **$C_{17}H_{15}Br_2N_3O$** (434.9582): found: 434.9599.

**Synthesis of 3',5'-dibromo-2'-(pyrrolidin-1-ylazo)-biphenyl-2-carboxylic acid methyl ester (45q):**



Prepared according to **TP12** from 1-(2,4,6-tribromophenylazo)pyrrolidine[87a] (**44h**) (1.65 g, 4 mmol), LiCl (344 mg, 8 mmol), zinc dust (520 mg, 8 mmol, 2.0 equiv, <10 micron, 98+%,

Aldrich), $BrCH_2CH_2Br$ (5 mol%), $Me_3SiCl$ (2 mol%), tetrakis(triphenylphosphine)palladium (104 mg, 0.09 mmol), and methyl-2-iodobenzoate (903 mg, 3 mmol). Reaction condition: 50 °C, 20 h; reflux, 2 h. Purification by flash chromatography (*n*-pentane/ether = 7 : 3) yielded **45q** (1.06 g, 76 %) as a pale yellow solid.

**mp.**: 90.5-92.7.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.80 (d, $J$ = 8.4 Hz, 1H), 7.70 (d, $J$ = 2.3 Hz, 1H), 7.45 (dd, $J$ = 8.4, 7.1 Hz, 1H), 7.28-7.36 (m, 2H), 7.21 (dd, $J$ = 8.4, 7.1 Hz, 1H), 3.60 (s, 3H), 3.36 (br s, 4H), 1.84 (br s, 4H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 167.7, 150.2, 146.4, 139.7, 137.6, 134.3, 131.7, 131.4, 131.2, 129.4, 127.1, 117.8, 117.0, 51.9, 50.7, 46.1, 23.6, 23.5.

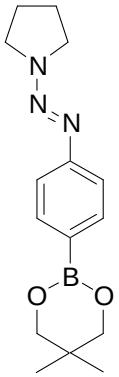
**MS** (70 eV, EI) *m/z* (%): 467 (12) [$M^+$], 397 (30), 369 (100), 354 (63), 290 (20), 245 (22), 219 (15), 164 (20), 150 (44).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2965 (w), 2874 (w), 1710 (vs), 1598 (m), 1539 (m), 1403 (s), 1341 (s), 1213 (m), 1122 (m), 1051 (m), 968 (w).

**HRMS** (EI) for **$C_{18}H_{17}Br_2N_3O_2$** (464.9687): found: 464.9668.

## 12. Synthesis of Functionalized *o*-, *m*-, or *p*-Terphenyls *via* Consecutive Cross-Coupling Reactions of Arylboronic Esters Bearing a Triazene Moiety

**Synthesis of [4-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)-phenyl]-pyrrolidin-1-yl-diazene (58a):**




Prepared according to **TP13** from 1-(4-iodophenylazo)pyrrolidine (**56a**) (see also **28e**) (1.51 g, 5 mmol), *i*-PrMgCl (2.8 mL, 1.1 equiv., 2.0 M in THF), $B(OiPr)_3$ (1.4 mL, 6 mmol), and neopentyglycol (650 mg, 6.25 mmol). Reaction condition: -30 °C, 1 h; 25 °C, 2 h; 25 °C, 12

h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **58a** (1.23 g, 86 %) as a white powder.

**mp**.: 209.0-210.5 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.75 (d, $J$ = 8.4 Hz, 2H), 7.37 (d, $J$ = 8.4 Hz, 2H), 3.76 (br s, 4H), 3.74 (s, 4H), 2.00 (br s, 4H), 1.00 (s, 6H).

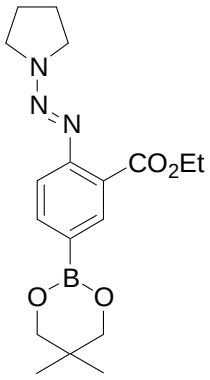
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 153.3, 134.6, 119.5, 72.3, 31.9, 23.8, 21.9.

**MS** (70 eV, EI) *m/z* (%): 287 (13) [$M^+$], 217 (10), 189 (100), 147 (6), 121 (15), 103 (6), 69 (17).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2959 (w), 2930 (w), 2876 (w), 1699 (w), 1596 (m), 1476 (m), 1412 (m), 1391 (m), 1338 (m), 1293 (s), 1245 (s), 1154 (m), 1128 (s), 844 (s).

**HRMS** (EI) for **$C_{15}H_{22}BN_3O_2$** (287.1805): found: 287.1810.

**Synthesis of 5-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)-2-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (58b):**




Prepared according to **TP13** from 1-(2-carbethoxy-4-iodophenylazo)pyrrolidine (**56b**) (see also **44a**) (373 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), B(O*i*Pr)$_3$ (0.28 mL, 1.2 mmol), and neopentyglycol (130 mg, 1.25 mmol). Reaction condition: -40 °C, 0.5 h; 25 °C, 2 h; 25 °C, 12 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 2) yielded **58b** (280 mg, 78 %) as a brown solid.

**mp**.: 142.6-143.7 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.02 (s, 1H), 7.78 (d, $J$ = 8.0 Hz, 1H), 7.35 (d, $J$ = 8.0 Hz, 1H), 4.30 (q, $J$ = 7.5 Hz, 2H), 3.40-4.00 (br s, 4H), 3.73 (s, 4H), 1.98 (br s, 4H), 1.33 (t, $J$ = 7.5 Hz, 3H).

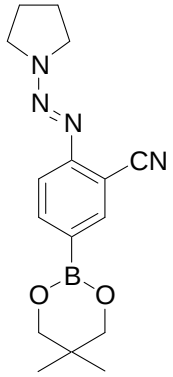
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 168.8, 151.9, 136.8, 135.1, 125.8, 118.3, 72.2, 60.6, 48.2, 46.3, 31.8, 23.72, 23.70, 21.9, 14.3.

**MS** (70 eV, EI) *m/z* (%): 359 (4) [$M^+$], 314 (3), 289 (14), 261 (49), 233 (100), 217 (8), 147 (9), 131 (19), 69 (12).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2959 (m), 1716 (s), 1599 (m), 1483 (m), 1469 (s), 1310 (s), 1263 (s), 1125 (m).

**HRMS** (EI) for **$C_{18}H_{26}BN_3O_4$** (359.2016): found: 359.2022.

**Synthesis of 5-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)-2-(pyrrolidin-1-ylazo)-benzonitrile (58c**):




Prepared according to **TP13** from 1-(2-cyano-4-iodophenylazo)pyrrolidine (**56c**) (see also **44c**) (326 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), $B(OiPr)_3$ (0.28 mL, 1.2 mmol), and neopentyglycol (130 mg, 1.25 mmol). Reaction condition: -40 °C, 0.5 h; 25 °C, 2 h; 25 °C, 12 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 2) yielded **58c** (259 mg, 83 %) as a yellow solid.

**mp**.: 139.7-141.3 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.01 (s, 1H), 7.84 (d, $J$ = 8.4 Hz, 1H), 7.48 (d, $J$ = 8.4 Hz, 1H), 3.66-4.04 (m, 4H), 3.73 (s, 4H), 1.92-2.12 (m, 4H), 1.00 (s, 6H).

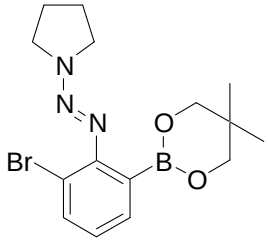
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 155.3, 139.1, 138.3, 118.3, 116.2, 106.7, 72.3, 51.3, 47.1, 31.9, 23.9, 23.4, 21.8.

**MS** (70 eV, EI) *m/z* (%): 312 (15) [$M^+$], 242 (42), 214 (99), 172 (45), 158 (9), 146 (30), 128 (20), 102 (12), 69 (100), 56 (13).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2964 (m), 2877 (w), 2222 (m), 1597 (m), 1558 (w), 1480 (m), 1406 (s), 1376 (m), 1312 (s), 1270 (s), 1127 (s).

**HRMS** (EI) for **$C_{16}H_{21}BN_4O_2$** (312.1758): found: 312.1745.

**Synthesis of [2-bromo-6-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)-phenyl]-pyrrolidin-1-yl-diazene (58d):**



Prepared according to **TP13** from 1-(2,6-dibromophenylazo)pyrrolidine (**56d**) (see also **28a**) (333 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), B(O*i*Pr)$_3$ (0.28 mL, 1.2 mmol), and neopentyglycol (130 mg, 1.25 mmol). Reaction condition: -40 °C to -15 °C, 5 h; 25 °C, 2 h; 25 °C, 12 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **58d** (201 mg, 55 %) as a brown solid.

**mp**.: 103.5-104.2 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.53 (d, $J$ = 7.6 Hz, 1H), 7.34 (d, $J$ = 7.6 Hz, 1H), 6.95 (t, $J$ = 7.6 Hz, 1H), 3.80 (br s, 4H), 3.66 (s, 4H), 2.01 (br s, 4H), 1.03 (s, 6H).

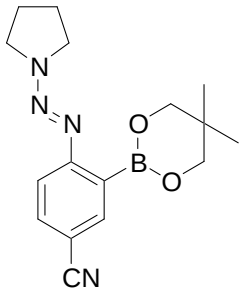
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 151.4, 133.5, 131.4, 125.8, 119.0, 72.5, 51.3, 47.1, 31.7, 23.8, 22.0.

**MS** (70 eV, EI) *m/z* (%): 365 (5) [$M^+$], 295 (26), 267 (22), 225 (22), 199 (19), 183 (17), 146 (15), 69 (100), 41 (27).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3048 (w), 2962 (w), 2931 (w), 2872 (w), 1476 (m), 1424 (m), 1396 (s), 1359 (m), 1314 (s), 1244 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_{15}H_{21}BBrN_3O_2$** (365.0910): found: 365.0899.

**Synthesis of 3-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)-4-(pyrrolidin-1-ylazo)-benzonitrile (58e):**



Prepared according to **TP13** from 1-(4-cyano-2-iodophenylazo)pyrrolidine (**56e**) (see also **28d**) (326 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), B(O*i*Pr)$_3$ (0.28 mL, 1.2 mmol), and neopentyglycol (130 mg, 1.25 mmol). Reaction condition: -40 °C, 0.7 h; 25 °C, 2 h; 25 °C, 12 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 3) yielded **58e** (203 mg, 65 %) as a brown solid.

**mp**.: 146.2-148.1 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.67 (s, 1H), 7.46 (d, $J$ = 8.4 Hz, 1H), 7.36 (d, $J$ = 8.4 Hz, 1H), 3.55-4.10 (m, 8H), 1.97 (br s, 4H), 0.99 (s, 6H).

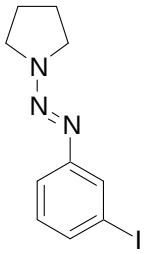
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 158.1, 137.1, 133.8, 133.4, 120.2, 107.7, 73.0, 51.9, 47.3, 32.2, 24.3, 24.0, 22.3.

**MS** (70 eV, EI) *m/z* (%): 312 (17) [$M^+$], 242 (40), 214 (96), 172 (43), 146 (30), 128 (25), 102 (11), 69 (100).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2950 (m), 2833 (w), 2225 (m), 1600 (m), 1550 (w), 1425 (s), 1366 (m), 1305 (s), 1115 (s).

**HRMS** (EI) for **$C_{16}H_{21}BN_4O_2$** (312.1758): found: 312.1750.

**Synthesis of 1-(3-iodophenylazo)pyrrolidine (56f):**




Prepared according to **TP1** from 3-iodoaniline (3.9 g, 18.1 mmol), concentrated HCl (7.2 mL), $NaNO_2$ (1.3 g, 19 mmol), pyrrolidine (2.6 g, 36.2 mmol), and $K_2CO_3$ (12.5 g, 90.5 mmol). Reaction condition: 0 °C, 0.5 h; 25 °C, 0.5 h. Purification by flash chromatography (*n*-pentane/ether = 2 : 1) yielded **56f** (5.2 g, 95 %) as a brown solid.

**mp**.: 45.8-46.9 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.77 (s, 1H), 7.41 (d, $J$ = 7.4 Hz, 1H), 7.33 (d, $J$ = 7.4 Hz, 1H), 7.01 (t, $J$ = 7.4 Hz, 1H), 3.76 (br s, 4H), 1.94-2.06 (m, 4H).

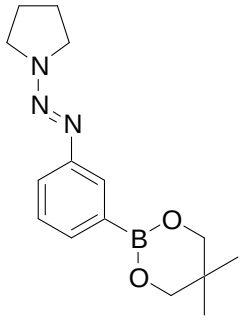
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 152.7, 133.7, 130.3, 128.8, 120.3, 94.5, 51.2, 46.5, 23.8.

**MS** (70 eV, EI) *m/z* (%): 301 (15) [$M^+$], 231 (65), 203 (100), 76 (12).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3058 (w), 2961 (w), 2874 (w), 1580 (m), 1554 (m), 1393 (s), 1309 (s), 1152 (w), 986 (w).

**HRMS** (EI) for **$C_{10}H_{12}IN_3$** (301.0076): found: 301.0093.

**Synthesis of [3-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)-phenyl]-pyrrolidin-1-yl-diazene (58f):**



Prepared according to **TP13** from 1-(3-iodophenylazo)pyrrolidine (**56f**) (1.51 g, 5 mmol), *i*-PrMgCl (2.8 mL, 1.1 equiv., 2.0 M in THF), B(O*i*Pr)$_3$ (1.4 mL, 6 mmol), and neopentyglycol (650 mg, 6.25 mmol). Reaction condition: -30 °C, 1 h; 25 °C, 2 h; 25 °C, 12 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **58f** (1.23 g, 86 %) as a brown solid.

**mp**.: 145.9-147.6 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.83 (s, 1H), 7.75 (d, $J$ = 7.5 Hz, 1H), 7.45 (d, $J$ = 7.5 Hz, 1H), 7.30 (t, $J$ = 7.5 Hz, 1H), 3.60-3.90 (m, 4H), 3.75 (s, 4H), 1.95-2.01 (m, 4H), 1.00 (s, 6H).

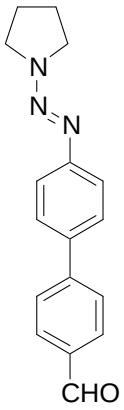
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 150.7, 130.6, 128.1, 125.6, 122.9, 72.2, 50.1, 47.0, 31.8, 23.8, 21.9.

**MS** (70 eV, EI) *m/z* (%): 287 (14) [$M^+$], 258 (11), 217 (11), 203 (7), 189 (100), 147 (21), 133 (13), 121 (46), 103 (27).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2953 (w), 2874 (w), 1479 (m), 1396 (m), 1293 (s), 1121 (s), 918 (w).

**HRMS** (EI) for **$C_{15}H_{22}BN_3O_2$** (287.1805): found: 287.1813.

**Synthesis of 4'-(Pyrrolidin-1-ylazo)-biphenyl-4-carbaldehyde (59a):**



Prepared according to **TP14** from arylboronic ester (**58a**) (287 mg, 1 mmol), 4-bromobenzaldehyde (222 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3

mol%). Reaction condition: 100 °C, 5 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 2) yielded **59a** (223 mg, 80 %) as a yellow solid.

**mp**.: 144.5-145.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 10.01 (s, 1H), 7.90 (d, $J$ = 8.5 Hz, 2H), 7.74 (d, $J$ = 8.3 Hz, 2H), 7.60 (d, $J$ = 8.3 Hz, 2H), 7.49 (d, $J$ = 8.5 Hz, 2H), 3.80 (br s, 4H), 1.96-2.08 (m, 4H).

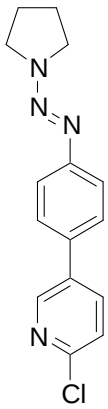
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 191.9, 151.7, 147.0, 135.9, 134.7, 130.2, 127.8, 127.1, 120.9, 71.7, 23.8.

**MS** (70 eV, EI) *m/z* (%): 279 (18) [$M^+$], 209 (30), 181 (95), 152 (100), 127 (10).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2958 (w), 2881 (w), 2808 (w), 2728 (w), 1694 (vs), 1592 (vs), 1487 (m), 1386 (s), 1153 (m), 818 (s).

**HRMS** (EI) for **$C_{17}H_{17}N_3O$** (279.1372): found: 279.1381.

**Synthesis of [4-(6-chloro-pyridin-3-yl)-phenyl]-pyrrolidin-1-yl-diazene (59b):**




Prepared according to **TP14** from arylboronic ester (**58a**) (287 mg, 1 mmol), 5-bromo-2-chloro-pyridine (230 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 6 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 2) yielded **59b** (201 mg, 70 %) as a yellow solid.

**mp**.: 157.0-159.5 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.59 (d, $J$ = 2.6 Hz, 1H), 7.81 (dd, $J$ = 8.4, 2.6 Hz, 1H), 7.49 (s, 4H), 7.34 (d, $J$ = 8.4 Hz, 1H), 3.80 (br s, 4H), 2.02 (br s, 4H).

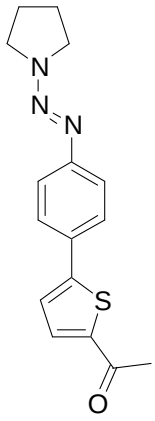
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 151.7, 149.7, 147.6, 136.7, 135.5, 132.8, 127.4, 124.1, 121.1, 51.0, 46.3, 23.8.

**MS** (70 eV, EI) *m/z* (%): 286 (23) [$M^+$], 216 (31), 188 (100), 153 (40), 126 (11).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3032 (w), 2972 (w), 2866 (w), 1601 (w), 1447 (m), 1399 (s), 1316 (s), 1222 (m), 1101 (s), 998 (m).

**HRMS** (EI) for **$C_{15}H_{15}ClN_4$** (286.0985): found: 286.0987.

**Synthesis of 1-{5-[4-(pyrrolidin-1-ylazo)-phenyl]-thiophen-2-yl}-ethanone (59c):**




Prepared according to **TP14** from arylboronic ester (**58a**) (287 mg, 1 mmol), 5-acetyl-2-iodothiophene (302 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 3 h. Purification by flash chromatography (*n*-pentane/ether = 2 : 3) yielded **59c** (201 mg, 70 %) as a yellow solid.

**mp**.: 171.8-173.8 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.62 (d, $J$ = 4.0 Hz, 1H), 7.59 (d, $J$ = 8.4 Hz, 2H), 7.43 (d, $J$ = 8.4 Hz, 2H), 7.26 (d, $J$ = 4.0 Hz, 1H), 3.79 (br s, 4H), 2.53 (s, 3H), 2.02 (br s, 4H).

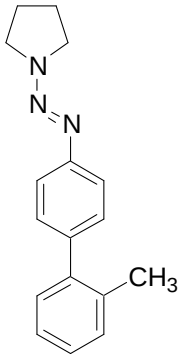
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 190.4, 153.2, 142.3, 134.7, 133.5, 129.9, 126.8, 123.1, 120.9, 51.0, 47.1, 26.5, 23.7.

**MS** (70 eV, EI) *m/z* (%): 299 (40) [$M^+$], 229 (27), 201 (100), 186 (8), 158 (16), 115 (7).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3002 (w), 2920 (w), 2844 (w), 1698 (vs), 1582 (s), 1478 (m), 1436 (m), 1398 (m), 1296 (s), 1216 (s), 1034 (m).

**HRMS** (EI) for **$C_{16}H_{17}N_3OS$** (299.1092): found: 299.1089.

**Synthesis of (2'-methyl-biphenyl-4-yl)-pyrrolidin-1-yl-diazene (59d):**



Prepared according to **TP14** from arylboronic ester (**58a**) (287 mg, 1 mmol), 2-iodotoluene (262 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 4 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **59d** (199 mg, 75 %) as a brown solid.

**mp**.: 60.0-61.8 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.46 (d, $J$ = 8.4 Hz, 2H), 7.29 (d, $J$ = 8.4 Hz, 2H), 7.21-7.27 (m, 4H), 3.82 (br s, 4H), 2.30 (s, 3H), 2.04 (br s, 4H).

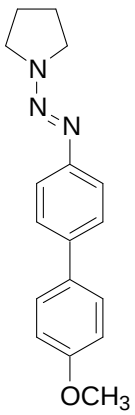
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 150.2, 141.8, 138.7, 135.4, 130.3, 129.8, 129.7, 128.5, 128.4, 127.0, 125.7, 120.0, 71.7, 67.1, 23.8, 21.3, 20.5.

**MS** (70 eV, EI) *m/z* (%): 265 (27) [$M^+$], 195 (33), 167 (100), 152 (44), 115 (5).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2962 (m), 2864 (m), 1600 (w), 1478 (m), 1392 (m), 1316 (m), 1155 (m), 1032 (m), 943 (w).

**HRMS** (EI) for **$C_{17}H_{19}N_3$** (265.1579): found: 265.1575.

**Synthesis of (4'-methoxy-biphenyl-4-yl)-pyrrolidin-1-yl-diazene (59e):**



Prepared according to **TP14** from arylboronic ester (**58a**) (287 mg, 1 mmol), 4-iodoanisole (281 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction

condition: 100 °C, 6 h. Purification by flash chromatography (*n*-pentane/ether = 4 : 1) yielded **59e** (171 mg, 61 %) as a pale yellow solid.

**mp**.: 121.8-124.0 °C.

**$^{1}$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.49-7.55 (m, 4H), 7.45 (d, $J$ = 8.4 Hz, 2H), 6.95 (d, $J$ = 8.8 Hz, 2H), 3.83 (s, 3H), 3.79 (br s, 4H), 2.01 (br s, 4H).

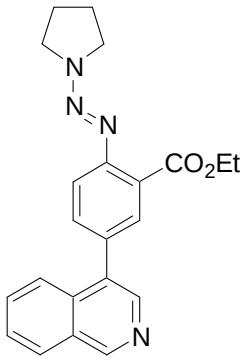
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 158.8, 150.2, 137.5, 133.6, 127.8, 127.0, 120.6, 114.1, 67.0, 55.3, 23.8.

**MS** (70 eV, EI) *m/z* (%): 281 (38) [$M^+$], 211 (14), 183 (100), 168 (22), 152 (10), 140 (12).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3032 (w), 2968 (w), 2871 (w), 1605 (m), 1490 (s), 1396 (s), 1319 (s), 1184 (m), 1030 (m), 905 (w).

**HRMS** (EI) for **$C_{17}H_{19}N_3O$** (281.1582): found: 281.1503.

**Synthesis of 5-isoquinolin-4-yl-2-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (59f):**




Prepared according to **TP14** from arylboronic ester (**58b**) (359 mg, 1 mmol), 4-bromoisoquinolin (250 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 6 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 4) yielded **59f** (318 mg, 85 %) as a yellow liquid.

**$^{1}$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.22 (s, 1H), 8.47 (s, 1H), 8.01 (d, $J$ = 8.4 Hz, 1H), 7.90 (d, $J$ = 8.4 Hz, 1H), 7.74 (s, 1H), 7.66 (t, $J$ = 8.0 Hz, 1H), 7.61 (t, $J$ = 8.0 Hz, 1H), 7.50-7.57 (m, 2H), 4.34 (q, $J$ = 7.1 Hz, 2H), 3.94 (br s, 2H), 3.72 (br s, 2H), 2.04 (br s, 4H), 1.34 (t, $J$ = 7.1 Hz, 3H).

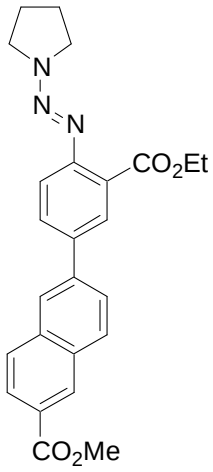
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 168.3, 152.0, 149.9, 142.7, 134.2, 133.1, 133.0, 132.4, 130.8, 130.7, 128.4, 127.9, 127.2, 126.6, 124.7, 119.6, 61.0, 51.2, 46.6, 23.3, 20.9, 14.3.

**MS** (70 eV, EI) *m/z* (%): 374 (15) [$M^+$], 304 (30), 277 (68), 248 (100), 232 (38), 220 (13), 204 (32), 177 (12).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2973 (m), 2870 (m), 1718 (vs), 1620 (m), 1568 (m), 1406 (s), 1312 (m), 1238 (m), 1073 (m), 895 (m).

**HRMS** (EI) for **$C_{22}H_{22}N_4O_2$** (374.1743): found: 374.1759.

**Synthesis of 6-[3-ethoxycarbonyl-4-(pyrrolidin-1-ylazo)-phenyl]-naphthalene-2-carboxylic acid methyl ester (59g):**




Prepared according to **TP14** from arylboronic ester (**58b**) (359 mg, 1 mmol), 4-bromoisoquinolin (250 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 6 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 4) yielded **59g** (318 mg, 85 %) as a yellow liquid.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.59 (s, 1H), 8.05 (d, $J$ = 7.2 Hz, 2H), 7.98 (d, $J$ = 7.2 Hz, 2H), 7.90 (d, $J$ = 8.6 Hz, 1H), 7.79 (d, $J$ = 8.6 Hz, 1H), 7.74 (d, $J$ = 8.6 Hz, 1H), 7.53 (d, $J$ = 8.6 Hz, 1H), 4.37 (q, $J$ = 7.2 Hz, 2H), 3.96 (s, 3H), 3.92 (br s, 2H), 3.70 (br s, 2H), 2.02 (br s, 4H), 1.38 (t, $J$ = 7.2 Hz, 3H).

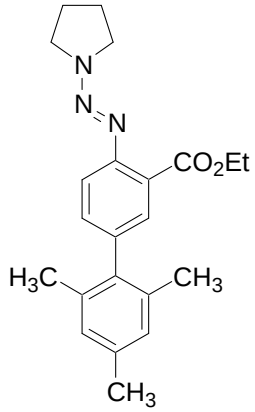
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 168.6, 167.2, 149.7, 139.8, 136.5, 135.8, 131.5, 130.7, 130.1, 129.8, 128.3, 128.2, 127.2, 126.9, 126.0, 125.7, 125.1, 119.9, 61.0, 52.2, 51.0, 46.5, 23.9, 23.6, 14.4.

**MS** (70 eV, EI) *m/z* (%): 431 (15) [$M^+$], 361 (19), 334 (65), 305 (100), 289 (22), 202 (25), 189 (11), 137 (13).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2955 (w), 2875 (w), 1706 (vs), 1627 (m), 1406 (m), 1311 (m), 1270 (m), 1240 (m), 1209 (s), 1136 (m), 1085 (s).

**HRMS** (EI) for **$C_{25}H_{25}N_3O_4$** (431.1845): found: 431.1829.

**Synthesis of 2',4',6'-trimethyl-4-(pyrrolidin-1-ylazo)-biphenyl-3-carboxylic acid ethyl ester (59h):**




Prepared according to **TP14** from arylboronic ester (**58b**) (359 mg, 1 mmol), 1-bromomesitylene (239 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 7 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 2) yielded **59h** (263 mg, 72 %) as a pale yellow solid.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.45-7.53 (m, 2H), 7.23 (d, $J$ = 8.8 Hz, 1H), 6.98 (s, 2H), 4.38 (q, $J$ = 7.1 Hz, 2H), 3.86 (br s, 4H), 2.37 (s, 3H), 2.00-2.12 (m, 10H), 1.39 (t, $J$ = 7.1 Hz, 3H).

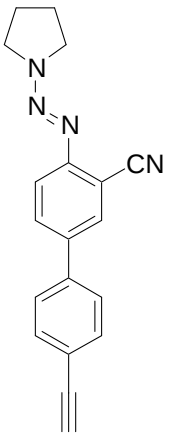
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 168.3, 149.0, 137.3, 136.6, 136.1, 132.5, 130.3, 128.0, 126.6, 124.5, 119.5, 60.7, 50.8, 46.6, 23.7, 20.9, 20.7, 14.3.

**MS** (70 eV, EI) *m/z* (%): 365 (36) [$M^+$], 295 (20), 267 (64), 239 (100), 164 (8).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2977 (w), 2919 (w), 2873 (w), 1692 (vs), 1603 (m), 1472 (m), 1399 (s), 1235 (s), 1089 (s), 1017 (m).

**HRMS** (EI) for **$C_{22}H_{27}N_3O_2$** (365.2103): found: 365.2130.

**Synthesis of 4'-ethynyl-4-(pyrrolidin-1-ylazo)-biphenyl-3-carbonitrile (59i):**



Prepared according to **TP14** from arylboronic ester (**58c**) (312 mg, 1 mmol), 1-bromo-4-ethynylbenzene (217 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 5 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **59i** (165 mg, 55 %) as a yellow solid.

**mp**.: 145.9-148.0 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.78 (s, 1H), 7.66 (d, $J$ = 8.8 Hz, 1H), 7.59 (d, $J$ = 8.8 Hz, 1H), 7.54 (d, $J$ = 8.4 Hz, 2H), 7.49 (d, $J$ = 8.4 Hz, 2H), 3.92-4.02 (m, 2H), 3.70-3.82 (m, 2H), 3.13 (s, 1H), 1.98-2.12 (m, 4H).

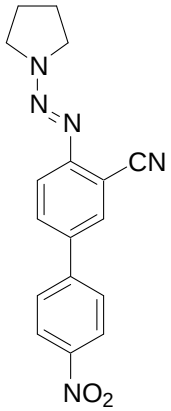
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 153.1, 139.2, 136.4, 132.7, 131.6, 131.2, 126.5, 121.4, 117.9, 117.7, 107.7, 83.3, 78.2, 51.4, 47.2, 23.9, 23.4.

**MS** (70 eV, EI) *m/z* (%): 300 (19) [$M^+$], 230 (23), 202 (100), 175 (32), 150 (8).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3258 (m), 3038 (w), 2969 (w), 2876 (w), 2214 (m), 1601 (w), 1479 (m), 1383 (s), 1309 (m), 1256 (m), 1162 (m), 1102 (m), 907 (w).

**HRMS** (EI) for **$C_{13}H_{12}N_4$** (300.1375): found: 301.1445 ([M+H]$^+$).

**Synthesis of 4'-nitro-4-(pyrrolidin-1-ylazo)-biphenyl-3-carbonitrile (59j):**




Prepared according to **TP14** from arylboronic ester (**58c**) (312 mg, 1 mmol), 4-iodo-nitrobenzene (299 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 3 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **59j** (231 mg, 72 %) as a orange solid.

**mp**.: 149.1-151.4 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.28 (d, $J$ = 8.8 Hz, 2H), 7.83 (s, 1H), 7.67-7.72 (m, 3H), 7.64 (d, $J$ = 8.8 Hz, 1H), 3.96-4.02 (m, 2H), 3.75-3.81 (m, 2H), 2.01-2.13 (m, 4H).

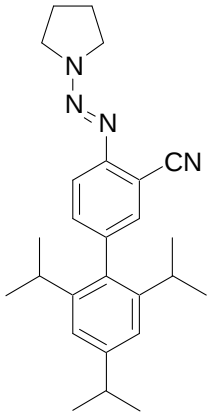
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 154.1, 141.1, 145.3, 134.7, 131.8, 131.7, 127.3, 124.3, 118.0, 117.6, 107.6, 51.6, 47.4, 23.9, 23.4.

**MS** (70 eV, EI) *m/z* (%): 321 (17) [$M^+$], 251 (41), 223 (63), 206 (27), 193 (15), 177 (100), 164 (10), 150 (20).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3096 (w), 2978 (w), 2872 (w), 2224 (m), 1593 (s), 1511 (s), 1478 (m), 1383 (m), 1338 (m), 1268 (m), 1106 (m), 1030 (w).

**HRMS** (EI) for **$C_{17}H_{15}N_5O_2$** (321.1226): found: 321.1231.

**Synthesis of 2',4',6'-triisopropyl-4-(pyrrolidin-1-ylazo)-biphenyl-3-carbonitrile (59k):**




Prepared according to **TP14** from arylboronic ester (**58c**) (312 mg, 1 mmol), 2-bromo-1,3,5-triisopropylbenzene (340 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 8 h. Purification by flash chromatography (*n*-pentane/ether = 7 : 3) yielded **59k** (210 mg, 52 %) as a pale yellow solid.

**mp**.: 75.0-77.0 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.56 (d, $J$ = 8.4 Hz, 1H), 7.39 (s, 1H), 7.28 (d, $J$ = 8.4 Hz, 1H), 7.03 (s, 2H), 3.94-4.00 (m, 2H), 3.75-3.81 (m, 2H), 2.91 (sept, $J$ = 7.1 Hz, 1H), 2.56 (sept, $J$ = 7.1 Hz, 2H), 2.00-2.12 (m, 4H), 1.28 (d, $J$ = 7.1 Hz, 6H), 1.07 (d, $J$ = 7.1 Hz, 6H), 1.04 (d, $J$ = 7.1 Hz, 6H).

**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 152.4, 148.5, 146.6, 137.6, 134.9, 134.8, 133.8, 120.7, 118.2, 117.0, 106.9, 51.4, 47.1, 34.3, 30.3, 24.1, 24.0, 23.9, 23.5.

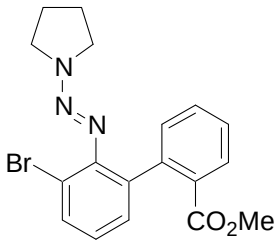
**MS** (70 eV, EI) *m/z* (%): 402 (34) [$M^+$], 232 (18), 304 (100), 289 (11), 274 (8), 262 (16), 246 (21), 227 (79), 204 (20), 190 (11).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2958 (s), 2868 (m), 2224 (m), 1606 (w), 1569 (w), 1410 (s), 1312 (s), 1271 (m), 1105 (m), 970 (w).

**HRMS** (EI) for **$C_{26}H_{34}N_4$** (402.2783): found: 403.2850 ([M+H]$^+$).

**Synthesis of 3'-bromo-2'-(pyrrolidin-1-ylazo)-biphenyl-2-carboxylic acid methyl ester (59l):**

**0,**




Prepared according to **TP14** from arylboronic ester (**58d**) (366 mg, 1 mmol), methyl-2-iodobenzoate (314 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 2 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 1) yielded **59l** (210 mg, 54 %) as a yellow solid.

**mp**.: 75.6-77.4 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.80 (d, $J$ = 7.9 Hz, 1H), 7.56 (d, $J$ = 7.9 Hz, 1H), 7.44 (t, $J$ = 7.5 Hz, 1H), 7.31 (t, $J$ = 7.5 Hz, 1H), 7.22 (d, $J$ = 7.5 Hz, 1H), 7.18 (d, $J$ = 7.5 Hz, 1H), 7.02 (t, $J$ = 7.9 Hz, 1H), 3.58 (s, 3H), 3.38 (br s, 4H), 1.84 (br s, 4H).

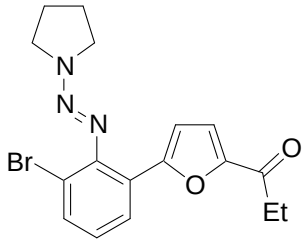
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 168.0, 147.2, 141.0, 136.4, 132.2, 131.5, 131.4, 131.2, 129.3, 129.0, 126.6, 125.3, 117.1, 51.8, 50.7, 45.9, 23.6.

**MS** (70 eV, EI) *m/z* (%): 387 (10) [$M^+$], 317 (35), 289 (100), 274 (53), 210 (67), 167 (21), 139 (36).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3064 (w), 2950 (w), 2864 (w), 1708 (vs), 1599 (m), 1406 (s), 1286 (s), 1122 (s), 1048 (m), 966 (w) $cm^{-1}$.

**HRMS** (EI) for **$C_{18}H_{18}BrN_3O_2$** (387.0582): found: 387.0568.

**Synthesis of 1-{5-[3-bromo-2-(pyrrolidin-1-ylazo)-phenyl]-thiophen-2-yl}-propan-1-one (59m):**




Prepared according to **TP14** from arylboronic ester (**58d**) (366 mg, 1 mmol), 1-(5-iodo-furan-2-yl)-propan-1-one (300 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 3 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **59m** (173 mg, 46 %) as a pale yellow solid.

**mp**.: 65.6-67.9 °C.

**$^{1}$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.81 (d, $J$ = 7.9 Hz, 1H), 7.58 (d, $J$ = 7.9 Hz, 1H), 7.15 (d, $J$ = 3.7 Hz, 1H), 7.07 (t, $J$ = 7.9 Hz, 1H), 6.51 (d, $J$ = 3.7 Hz, 1H), 3.65-3.95 (m, 4H), 2.85 (q, $J$ = 7.5 Hz, 2H), 1.95-2.15 (m, 4H), 1.20 (t, $J$ = 7.5 Hz, 3H).

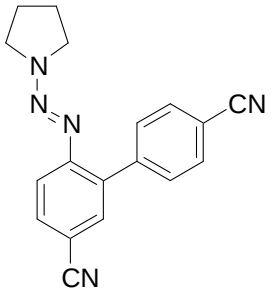
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 190.0, 154.7, 151.2, 147.8, 233.7, 126.8, 126.0, 124.7, 118.1, 117.8, 112.6, 51.2, 46.7, 31.6, 24.1, 23.8, 8.2.

**MS** (70 eV, EI) *m/z* (%): 375 (5) [$M^+$], 307 (42), 279 (37), 250 (11), 221 (22), 170 (100), 142 (34), 113 (26), 70 (21).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3110 (w), 2932 (w), 2871 (w), 1675 (vs), 1550 (m), 1506 (m), 1411 (s), 1311 (m), 1244 (m), 1018 (m), 984 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_{17}H_{18}BrN_3O_2$** (375.0582): found: 375.0597.

**Synthesis of 6-(pyrrolidin-1-ylazo)-biphenyl-3,4'-dicarbonitrile (59n):**




Prepared according to **TP14** from arylboronic ester (**58e**) (312 mg, 1 mmol), 4-bromobenzonitrile (218 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 6 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **59n** (250 mg, 83 %) as a pale yellow solid.

**mp**.: 174.4-176.6 °C.

**$^{1}$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.65 (d, $J$ = 8.4 Hz, 2H), 7.54-7.62 (m, 5H), 3.93 (br s, 2H), 3.43 (br s, 2H), 1.97-2.03 (m, 4H).

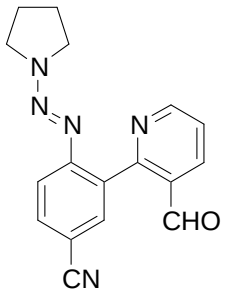
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 151.5, 143.3, 134.7, 134.1, 132.6, 131.4, 130.8, 119.1, 118.9, 117.9, 110.9, 108.0, 51.4, 47.1, 23.9, 23.3.

**MS** (70 eV, EI) *m/z* (%): 301 (10) [$M^+$], 231 (22), 203 (100), 176 (21).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3069 (w), 2970 (w), 2874 (w), 2218 (s), 1667 (w), 1605 (m), 1480 (m), 1378 (s), 1315 (s), 1127 (m), 970 (w).

**HRMS** (EI) for **$C_{18}H_{15}N_5$** (301.1327): found: 301.1341.

**Synthesis of 3-(3-formyl-pyridin-2-yl)-4-(pyrrolidin-1-ylazo)-benzonitrile (59o):**



Prepared according to **TP14** from arylboronic ester (**58e**) (312 mg, 1 mmol), 2-bromo-3-pyridine-carbaldehyde (223 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 5 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 4) yielded **59o** (229 mg, 75 %) as a brown solid.

**mp**.: 164.3-166.0 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.72 (s, 1H), 8.84 (d, $J$ = 4.9 Hz, 1H), 8.21 (d, $J$ = 7.5 Hz, 1H), 7.99 (s, 1H), 7.60-7.67 (m, 2H), 7.41 (dd, $J$ = 7.5, 4.9 Hz, 1H), 3.88 (br s, 2H), 3.21 (br s, 2H), 1.95 (br s, 4H).

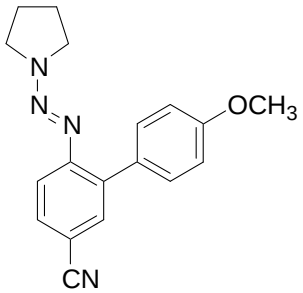
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 190.7, 157.8, 153.2, 151.6, 135.4, 133.8, 133.6, 132.1, 130.8, 122.8, 119.0, 117.0, 108.4, 51.6, 47.5, 23.8, 23.3.

**MS** (70 eV, EI) *m/z* (%): 306 (2) $[M+H]^+$, 248 (4), 235 (6), 222 (11), 207 (100), 179 (5), 152 (18).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3051 (w), 2973 (w), 2879 (w), 2769 (w), 2220 (s), 1693 (vs), 1577 (s), 1399 (s), 1363 (m), 1311 (m), 1130 (m), 977 (w).

**HRMS** (EI) for **$C_{17}H_{15}N_5O$** (305.1277): found: 306.1350 ($[M+H]^+$).

**Synthesis of 4'-methoxy-6-(pyrrolidin-1-ylazo)-biphenyl-3-carbonitrile (59p):**



Prepared according to **TP14** from arylboronic ester (**58e**) (312 mg, 1 mmol), 4-iodoanisole (281 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 6 h. Purification by flash chromatography (*n*-pentane/ether = 3 : 2) yielded **59p** (263 mg, 86 %) as a yellow solid.

**mp.**: 120.3-122.2.

**$^{1}$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.60 (s, 1H), 7.51 (d, $J$ = 8.4 Hz, 1H), 7.48 (d, $J$ = 8.4 Hz, 1H), 7.43 (d, $J$ = 8.6 Hz, 2H), 6.90 (d, $J$ = 8.6 Hz, 2H), 3.92 (br s, 2H), 3.83 (s, 3H), 3.49 (br s, 2H), 1.95-2.00 (m, 4H).

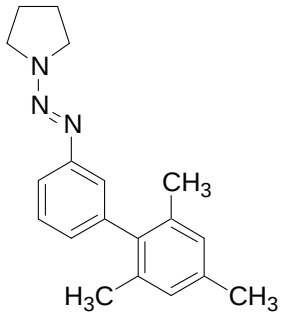
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 158.9, 151.5, 136.3, 134.2, 131.3, 131.0, 130.5, 119.6, 117.9, 113.0, 107.7, 55.2, 51.1, 46.9, 23.9, 23.3.

**MS** (70 eV, EI) *m/z* (%): 306 (22) [$M^+$], 236 (11), 208 (100), 193 (32), 177 (6), 165 (19).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2948 (w), 2879 (w), 2830 (w), 2215 (s), 1595 (m), 1513 (m), 1479 (m), 1383 (s), 1243 (s), 1173 (s), 1030 (m).

**HRMS** (EI) for **$C_{18}H_{18}N_4O$** (306.1481): found: 306.1483.

**Synthesis of pyrrolidin-1-yl-(2',4',6'-trimethyl-biphenyl-3-yl)-diazene (59q):**




Prepared according to **TP14** from arylboronic ester (**58f**) (287 mg, 1 mmol), 1-bromomesitylene (239 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 7 h. Purification by flash chromatography (*n*-pentane/ether = 4 : 1) yielded **59q** (182 mg, 62 %) as a white solid.

**mp**.: 113.4-115.0 °C.

**$^{1}$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.35-7.41 (m, 2H), 7.25 (s, 1H), 6.94 (s, 2H), 6.92 (d, $J$ = 7.1 Hz, 1H), 3.79 (br s, 4H), 2.34 (s, 3H), 2.05 (s, 6H), 2.01 (br s, 4H).

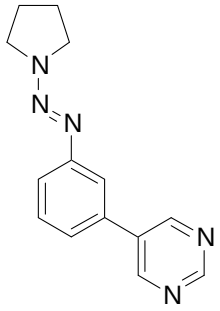
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 151.5, 141.6, 139.1, 136.3, 135.9, 128.8, 127.9, 126.1, 121.2, 118.6, 51.3, 47.0, 23.8, 21.0, 20.7.

**MS** (70 eV, EI) *m/z* (%): 293 (22) [$M^+$], 223 (11), 195 (100), 180 (67), 165 (64), 152 (9).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2948 (w), 2918 (w), 2871 (w), 1600 (w), 1570 (w), 1404 (s), 1314 (m), 1278 (m), 1208 (w), 1142 (w), 1031 (w), 972 (w).

**HRMS** (EI) for **$C_{19}H_{23}N_3$** (293.1892): found: 293.1885.

**Synthesis of (3-pyrimidin-5-yl-phenyl)-pyrrolidin-1-yl-diazene (59r):**



Prepared according to **TP14** from arylboronic ester (**58f**) (287 mg, 1 mmol), 4-bromopyrimidine (191 mg, 1.2 mmol), $K_3PO_4$ (424 mg, 2 mmol), and $Pd(PPh_3)_4$ (35 mg, 3 mol%). Reaction condition: 100 °C, 5 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 4) yielded **59r** (202 mg, 80 %) as a pale yellow solid.

**mp**.: 84.9-86.5 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.16 (s, 1H), 8.95 (s, 2H), 7.60 (s, 1H), 7.47 (d, $J$ = 7.7 Hz, 1H), 7.42 (t, $J$ = 7.7 Hz, 1H), 7.29 (d, $J$ = 7.7 Hz, 1H), 3.90 (br s, 2H), 3.68 (br s, 2H), 2.01 (br s, 4H).

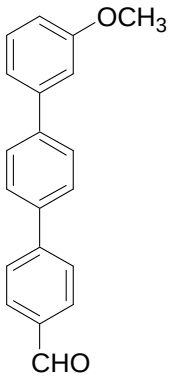
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 157.3, 154.9, 152.3, 134.7, 134.4, 129.8, 123.3, 120.9, 118.9, 51.0, 46.3, 23.7.

**MS** (70 eV, EI) *m/z* (%): 253 (18) [$M^+$], 183 (28), 155 (100), 128 (54), 102 (68), 75 (17).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3051 (w), 2951 (w), 2864 (w), 1606 (w), 1575 (w), 1397 (s), 1333 (s), 1304 (s), 1210 (m), 1110 (w), 898 (m).

**HRMS** (EI) for **$C_{14}H_{15}N_5$** (253.1327): found: 253.1317.

**Synthesis of 3''-methoxy-[1,1';4',1'']terphenyl-4-carbaldehyde (60a):**




Prepared according to **TP15** from aryl triazene (**59a**) (140 mg, 0.5 mmol), 3-methoxybenzeneboronic acid (152 mg, 1 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), and

$BF_3 \cdot OEt_2$ (0.2 mL, 0.75 mmol). Reaction condition: 0 °C, 4 h. Purification by flash chromatography (*n*-pentane/ethyl acetate = 1 : 9) yielded **60a** (94 mg, 65 %) as a white solid.

**mp**.: 140.5-142.1 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 10.05 (s, 1H), 7.96 (d, $J$ = 7.9 Hz, 2H), 7.79 (d, $J$ = 7.9 Hz, 2H), 7.70 (s, 4H), 7.37 (t, $J$ = 7.9 Hz, 1H), 7.14-7.25 (m, 2H), 6.92 (d, $J$ = 7.9 Hz, 1H), 3.87 (s, 3H).

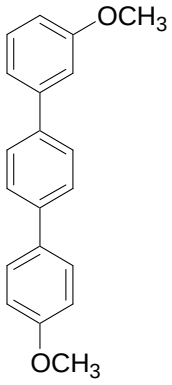
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 191.8, 160.0, 146.6, 141.8, 141.2, 138.6, 135.2, 130.3, 129.9, 127.7, 127.6, 127.5, 119.6, 113.0, 112.9, 55.3.

**MS** (70 eV, EI) *m/z* (%): 288 (100) [$M^+$], 215 (6), 143 (4).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3045 (w), 2917 (w), 2844 (w), 2740 (w), 1688 (vs), 1599 (s), 1446 (m), 1307 (m), 1235 (m), 1033 (m).

**HRMS** (EI) for **$C_{20}H_{16}O_2$** (288.1150): found: 288.1132.

**Synthesis of 4,3''-dimethoxy-[1,1';4',1'']terphenyl (60b):**




Prepared according to **TP15** from aryl triazene (**59e**) (141 mg, 0.5 mmol), 3-methoxybenzeneboronic acid (152 mg, mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), and $BF_3 \cdot OEt_2$ (0.2 mL, 0.75 mmol). Reaction condition: 0 °C, 3 h. Purification by flash chromatography (*n*-pentane/ethyl acetate = 1 : 9) yielded **60b** (91 mg, 63 %) as a brown solid.

**mp**.: 136.8-137.3 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.66 (s, 4H), 7.61 (d, $J$ = 8.8 Hz, 2H), 7.40 (t, $J$ = 7.9 Hz, 1H), 7.18-7.26 (m, 2H), 7.03 (d, $J$ = 8.8 Hz, 2H), 6.93 (d, $J$ = 7.9 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H).

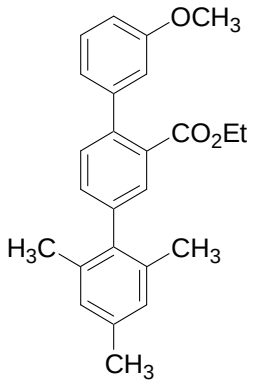
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 159.9, 159.2, 142.3, 139.9, 139.3, 133.2, 129.7, 128.0, 127.5, 127.0, 119.5, 114.2, 112.7, 112.6, 55.3, 55.2.

**MS** (70 eV, EI) *m/z* (%): 290 (100) [$M^+$], 275 (26), 247 (11), 204 (8), 145 (7).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3002 (w), 2941 (w), 2838 (w), 1602 (m), 1584 (m), 1479 (m), 1282 (m), 1249 (s), 1172 (m), 1028 (s), 872 (m).

**HRMS** (EI) for **$C_{20}H_{18}O_2$** (290.1307): found: 290.1297.

**Synthesis of 3-methoxy-2'',4'',6''-trimethyl-[1,1';4',1'']terphenyl-2'-carboxylic acid ethyl ester (60c):**




Prepared according to **TP15** from aryl triazene (**59h**) (183 mg, 0.5 mmol), 3-methoxybenzeneboronic acid (152 mg, 1 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), and $BF_3{\cdot}OEt_2$ (0.2 mL, 0.75 mmol). Reaction condition: 0 °C, 5 h. Purification by flash chromatography (*n*-pentane/ether = 7 : 3) yielded **60c** (146 mg, 78 %) as a pale yellow liquid.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.59 (s, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.25-7.34 (m, 2H), 6.84-6.97 (m, 5H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 3H), 2.33 (s, 3H), 2.04 (s, 6H), 1.03 (t, *J* = 7.1 Hz, 3H).

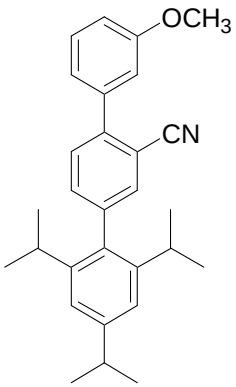
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 168.8, 159.3, 142.7, 140.2, 137.0, 136.0, 132.1, 131.4, 131.0, 130.6, 129.6, 129.0, 128.2, 127.2, 121.1, 113.9, 113.0, 61.0, 55.3, 21.0, 20.9, 13.7.

**MS** (70 eV, EI) *m/z* (%): 374 (100) [$M^+$], 345 (5), 329 (18), 302 (8), 286 (10), 271 (6), 256 (4), 241 (3), 172 (5).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2978 (w), 2834 (w), 1714 (vs), 1600 (m), 1473 (s), 1291 (s), 1232 (vs), 1169 (m), 1138 (m), 1092 (s), 1020 (s), 840 (s).

**HRMS** (EI) for **$C_{25}H_{26}O_3$** (374.1882): found: 374.1866.

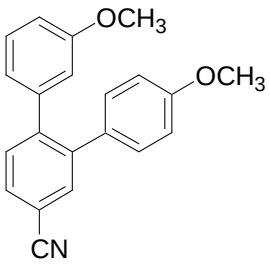
**Synthesis of 2'',4'',6''-triisopropyl-3-methoxy-[1,1';4',1'']terphenyl-2'-carbonitrile (60d):**




Prepared according to **TP15** from aryl triazene (**59k**) (201 mg, 0.5 mmol), 3-methoxybenzeneboronic acid (152 mg, 1 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), and $BF_3{\cdot}OEt_2$ (0.2 mL, 0.75 mmol). Reaction condition: 0 °C, 4.5 h. Purification by flash chromatography (*n*-pentane/ether = 9 : 1) yielded **60d** (148 mg, 72 %) as a pale yellow liquid.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.55 (d, $J$ = 8.0 Hz, 1H), 7.37-7.47 (m, 2H), 7.33 (t, $J$ = 8.0 Hz, 1H), 7.09-7.20 (m, 2H), 7.07 (s, 2H), 7.00 (d, $J$ = 8.0 Hz, 1H), 3.88 (s, 3H), 2.94 (sept, $J$ = 7.1 Hz, 1H), 2.54 (sept, $J$ = 7.1 Hz, 2H), 1.30 (d, $J$ = 7.1 Hz, 6H), 1.11 (d, $J$ = 7.1 Hz, 6H), 1.09 (d, $J$ = 7.1 Hz, 6H).
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 159.7, 148.9, 146.5, 143.4, 142.6, 140.9, 139.2, 134.7, 134.4, 129.7, 121.2, 120.8, 119.7, 114.7, 114.2, 112.8, 110.9, 55.4, 34.3, 30.4, 24.2, 24.1, 24.0.
**MS** (70 eV, EI) *m/z* (%): 411 (100) [$M^+$], 396 (48), 368 (24), 354 (52), 338 (10), 326 (16), 312 (60), 297 (16), 198 (24).
**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3057 (w), 2960 (s), 2869 (w), 2224 (m), 1599 (s), 1467 (s), 1224 (s), 1168 (m), 1032 (s), 842 (s).
**HRMS** (EI) for **$C_{29}H_{33}NO$** (411.2562): found: 411.2543.

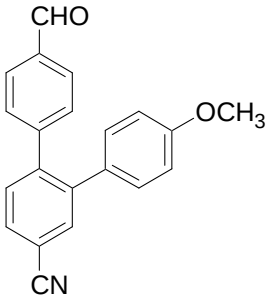
**Synthesis of 3,4''-dimethoxy-[1,1';2',1'']terphenyl-4'-carbonitrile (60e):**



Prepared according to **TP15** from aryl triazene (**59p**) (153 mg, 0.5 mmol), 3-methoxybenzeneboronic acid (152 mg, 1 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), and $BF_3 \cdot OEt_2$ (0.2 mL, 0.75 mmol). Reaction condition: 0 °C, 5 h. Purification by flash chromatography (*n*-pentane/ether = 4 : 1) yielded **60e** (113 mg, 72 %) as a colourless liquid.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.72 (s, 1H), 7.68 (d, $J$ = 7.9 Hz, 1H), 7.54 (d, $J$ = 7.9 Hz, 1H), 7.20 (d, $J$ = 8.4 Hz, 1H), 7.08 (d, $J$ = 8.8 Hz, 2H), 6.80-6.88 (m, 3H), 6.76 (d, $J$ = 8.4 Hz, 1H), 6.70 (s, 1H), 3.83 (s, 3H), 3.69 (s, 3H).
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 159.2, 159.0, 144.8, 141.3, 141.2, 133.9, 131.6, 131.2, 130.6, 130.3, 129.2, 121.9, 118.8, 114.9, 113.7, 113.3, 111.3, 55.2, 55.1.
**MS** (70 eV, EI) *m/z* (%): 315 (100) [$M^+$], 300 (4), 284 (20), 252 (5), 240 (15), 227 (10).
**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2917 (m), 2227 (m), 1736 (m), 1598 (m), 1514 (m), 1474 (m), 1291 (m), 1216 (s), 1176 (m), 1019 (m), 832 (m).
**HRMS** (EI) for **$C_{21}H_{17}NO_2$** (315.1259): found: 315.1244.

**Synthesis of 4-formyl-4''-methoxy-[1,1';2',1'']terphenyl-4'-carbonitrile (60f):**

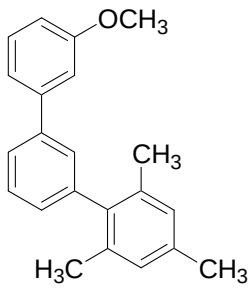



Prepared according to **TP15** from aryl triazene (**59p**) (153 mg, 0.5 mmol), 4-formylphenylboronic acid (150 mg, 1 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), and $BF_3 \cdot OEt_2$ (0.2 mL, 0.75 mmol). Reaction condition: 0 °C, 11 h. Purification by flash chromatography (*n*-pentane/ethyl acetate = 1 : 9) yielded **60f** (102 mg, 65 %) as a pale yellow solid.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 10.01 (s, 1H), 7.80 (d, $J$ = 8.4 Hz, 2H), 7.74 (s, 1H), 7.71 (d, $J$ = 7.9 Hz, 1H), 7.53 (d, $J$ = 7.9 Hz, 1H), 7.33 (d, $J$ = 8.4 Hz, 2H), 7.02 (d, $J$ = 8.8 Hz, 2H), 6.80 (d, $J$ = 8.8 Hz, 2H), 3.81 (s, 3H).
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 191.7, 159.2, 146.2, 143.5, 141.5, 135.2, 134.1, 131.1, 130.8, 130.7, 130.5, 130.2, 129.5, 118.5, 113.9, 112.2, 55.2.
**MS** (70 eV, EI) *m/z* (%): 313 (100) [$M^+$], 284 (8), 269 (6), 254 (10), 240 (13), 227 (7), 214 (4), 120 (4).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3054 (w), 2976 (w), 2840 (w), 2742 (w), 2228 (m), 1695 (vs), 1605 (s), 1513 (m), 1480 (m), 1300 (m), 1252 (m), 1207 (m), 1169 (m), 1026 (m), 923 (w).
**HRMS** (EI) for **$C_{21}H_{15}NO_2$** (313.1103): found: 313.1083.

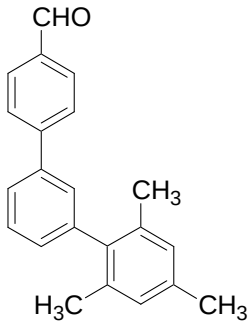
**Synthesis of 3''-methoxy-2,4,6-trimethyl-[1,1';3',1'']terphenyl (60g):**




Prepared according to **TP15** from aryl triazene (**59q**) (147 mg, 0.5 mmol), 3-methoxybenzeneboronic acid (152 mg, 1 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), and $BF_3{\cdot}OEt_2$ (0.2 mL, 0.75 mmol). Reaction condition: 0 °C, 4.5 h. Purification by flash chromatography (*n*-pentane/ethyl acetate = 19 : 1) yielded **60g** (110 mg, 73 %) as a white solid.

**mp**.: 62.6-64.2 °C.
**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.53-7.59 (m, 1H), 7.46 (t, $J$ = 7.9 Hz, 1H), 7.39 (s, 1H), 7.34 (t, $J$ = 7.9 Hz, 1H), 7.20 (d, $J$ = 7.9 Hz, 1H), 7.09-7.16 (m, 2H), 6.95 (s, 2H), 6.85-6.91 (m, 1H), 3.84 (s, 3H), 2.33 (s, 3H), 2.04 (s, 6H).
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 160.0, 142.6, 141.5, 141.0, 138.9, 136.7, 136.0, 129.7, 128.8, 128.4, 128.1, 128.0, 125.3, 119.6, 112.9, 112.7, 55.3, 21.0, 20.8.
**MS** (70 eV, EI) *m/z* (%): 302 (100) [$M^+$], 287 (13), 272 (7), 257 (4), 194 (3).
**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2948 (w), 2917 (w), 1594 (s), 1466 (s), 1326 (m), 1211 (s), 1040 (s).
**HRMS** (EI) for **$C_{22}H_{22}O$** (302.1671): found: 302.1670.

**Synthesis of 2,4,6-trimethyl-[1,1';3',1'']terphenyl-4''-carbaldehyde (60h):**

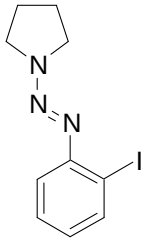


Prepared according to **TP15** from aryl triazene (**59q**) (147 mg, 0.5 mmol), 4-formylphenylboronic acid (150 mg, 1 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), and $BF_3 \cdot OEt_2$ (0.2 mL, 0.75 mmol). Reaction condition: 0 °C, 12 h. Purification by flash chromatography (*n*-pentane/ether = 9 : 1) yielded **60h** (120 mg, 80 %) as a colourless liquid.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 10.04 (s, 1H), 7.94 (d, $J$ = 8.4 Hz, 2H), 7.76 (d, $J$ = 8.4 Hz, 2H), 7.60 (d, $J$ = 8.0 Hz, 1H), 7.51 (t, $J$ = 8.0 Hz, 1H), 7.43 (s, 1H), 7.19 (d, $J$ = 8.0 Hz, 1H), 6.96 (s, 2H), 2.33 (s, 3H), 2.04 (s, 6H).
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 191.9, 147.1, 141.9, 139.7, 138.5, 136.9, 135.9, 135.2, 130.3, 129.5, 129.1, 128.3, 128.2, 127.6, 125.5, 21.0, 20.8.
**MS** (70 eV, EI) *m/z* (%): 300 (100) [$M^+$], 285 (14), 271 (6), 257 (12), 242 (13), 195 (8), 179 (7), 165 (10), 149 (9).
**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2947 (w), 2916 (w), 2854 (w), 2731 (w), 1699 (vs), 1602 (vs), 1566 (m), 1472 (m), 1377 (m), 1303 (m), 1211 (s), 1167 (s), 1008 (m), 834 (s).
**HRMS** (EI) for **$C_{22}H_{20}O$** (300.1514): found: 300.1491.

## 13. Synthesis of Ellipticine and Related Derivatives *via* a Key Transformation from Aryl Triazenes to Aryl Azides

**Synthesis of 1-(2-iodophenylazo)pyrrolidine (73):**




Prepared according to **TP1** from 2-iodoaniline (5.4 g, 18.1 mmol), concentrated HCl (7.2 mL), $NaNO_2$ (1.3 g, 19 mmol), pyrrolidine (2.6 g, 36.2 mmol), and $K_2CO_3$ (12.5 g, 90.5 mmol). Reaction condition: 0 °C, 0.5 h; 25 °C, 0.5 h. Purification by flash chromatography (*n*-pentane/ether = 2 : 1) yielded **73** (5.0 g, 92 %) as a yellow solid.

**mp**.: 61.5-62.3 °C.
**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.81 (d, $J$ = 8.0 Hz, 1H), 7.34 (d, $J$ = 8.0 Hz, 1H), 7.24 (t, $J$ = 8.0 Hz, 1H), 6.80 (t, $J$ = 8.0 Hz, 1H), 3.90 (br s, 2H), 3.71 (br s, 2H), 2.00 (br s, 4H).

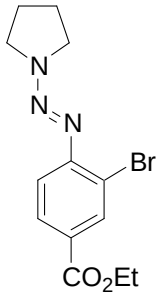
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 150.5, 139.0, 128.6, 126.5, 117.4, 96.3, 50.9, 47.0, 24.0, 23.5.

**MS** (70 eV, EI) *m/z* (%): 301 (14) [$M^+$], 231 (52), 203 (100), 76 (25).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3048 (w), 2960 (w), 2871 (w), 1558 (w), 1458 (m), 1394 (s), 1339 (m), 1304 (m), 1264 (m), 1150 (w), 1014 (s).

**HRMS** (EI) for **$C_{10}H_{12}IN_3$** (301.0076): found: 301.0076.

**Synthesis of 3-bromo-4-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (74):**




Prepared according to **TP1** from ethyl 4-amino-3-bromobenzoate[94] (4.4 g, 18.1 mmol), concentrated HCl (7.2 mL), $NaNO_2$ (1.3 g, 19 mmol), pyrrolidine (2.6 g, 36.2 mmol), and $K_2CO_3$ (12.5 g, 90.5 mmol). Reaction condition: 0 °C, 0.5 h; 25 °C, 0.5 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **74** (5.5 g, 94 %) as a yellow solid.

**mp**.: 103.6-104.8 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.23 (d, $J$ = 1.9 Hz, 1 H), 7.87 (dd, $J$ = 8.3, 1.9 Hz, 1H), 7.43 (d, $J$ = 8.3 Hz, 1H), 4.34 (q, $J$ = 7.2 Hz, 2H), 3.94 (br s, 2H), 3.73 (br s, 2H), 2.04 (br s, 4H), 1.36 (t, $J$ = 7.2 Hz, 3H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 165.5, 152.1, 134.5, 129.1, 127.5, 118.9, 117.4, 60.9, 51.3, 47.2, 23.9, 23.4, 14.3.

**MS** (70 eV, EI) *m/z* (%): 325 (26) [$M^+$], 280 (50), 255 (73), 227 (100), 199 (84), 183 (42), 171 (11), 156 (13), 143 (32), 103 (26), 92 (11).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2970 (w), 2876 (w), 1698 (s), 1592 (m), 1471 (w), 1374 (s), 1298 (s), 1265 (s), 1240 (s), 1105 (m), 1028 (m), 901 (w).

**HRMS** (EI) for **$C_{13}H_{16}BrN_3O_2$** (325.0426): found: 325.0433.

**Synthesis of (4-bromo-naphthalen-1-yl)-pyrrolidin-1-yl-diazene (75):**

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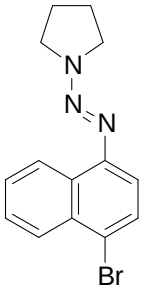
[94] Y. Tobe, N. Utsumi, K. Kawabata, A. Nagono, K, Adachi, S. Araki, M. Sonoda, K. Hirose, K. Naemura, *J. Am. Chem. Soc.* **2002**, *124*, 5350-5364.



Prepared according to **TP1** from 1-amino-4-bromonaphthalene (4 g, 18.1 mmol), concentrated HCl (7.2 mL), $NaNO_2$ (1.3 g, 19 mmol), pyrrolidine (2.6 g, 36.2 mmol), and $K_2CO_3$ (12.5 g, 90.5 mmol). Reaction condition: 0 °C, 0.5 h; 25 °C, 0.5 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **75** (5.3 g, 96 %) as a brown solid.

**mp**.: 80.5-81.7 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.67 (d, $J$ = 8.4 Hz, 1H), 8.20 (d, $J$ = 8.4 Hz, 1H), 7.72 (d, $J$ = 8.1 Hz, 1H), 7.56-7.61 (m, 1H), 7.50-7.55 (m, 1H), 7.34 (d, $J$ = 8.1 Hz, 1H), 3.95 (br s, 2H), 3.81 (br s, 2H), 2.03 (br s, 4H).

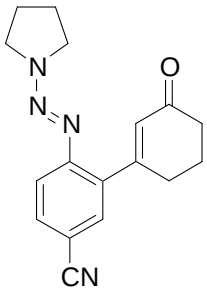
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 146.5, 132.3, 130.4, 130.0, 127.1, 126.7, 125.7, 124.1, 118.5, 51.0, 46.7, 23.6.

**MS** (70 eV, EI) *m/z* (%): 303 (19) [$M^+$], 33 (18), 205 (100), 140 (14), 126 (89).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3049 (w), 2970 (w), 2871 (w), 1575 (m), 1497 (w), 1397 (s), 1296 (m), 1147 (m), 1022 (m), 829 (s).

**HRMS** (EI) for **$C_{13}H_{14}BrN_3$** (303.0371): found: 304.0422 ([M+H]$^+$).

**Synthesis of 3-(3-oxo-cyclohex-1-enyl)-4-(pyrrolidin-1-ylazo)-benzonitrile (76):**



Prepared according to **TP3** from1-(4-cyano-2-iodophenylazo)pyrrolidine (**28d**) (326 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), CuCN·2LiCl (1 mL of 1.0 M solution in THF, 1 mmol), 3-iodo-cyclohex-2-enone (222 mg, 1 mmol). Reaction condition: -40 °C,

0.7 h; -30 °C, 0.5 h; -30 °C 3 h. Purification by flash chromatography (*n*-pentane/ether = 2 : 3) yielded **76** (238 mg, 81 %) as a yellow solid.

**mp**.: 116.7-117.3 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) *δ*/ppm: 7.47-7.57 (m, 2H), 7.42 (d, *J* = 1.8 Hz, 1H), 6.05 (s, 1H), 3.94 (t, *J* = 6.2 Hz, 2H), 3.60 (t, *J* = 6.2 Hz, 2H), 2.71 (t, *J* = 6.2 Hz, 2H), 2.46 (t, *J* = 6.2 Hz, 2H), 1.96-2.16 (m, 6H).

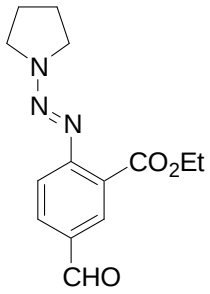
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) *δ*/ppm: 199.5, 162.2, 151.5, 135.9, 132.8, 132.0, 128.9, 119.0, 117.4, 107.6, 51.4, 47.0, 37.5, 30.9, 23.8, 23.4, 23.3.

**MS** (70 eV, EI) *m/z* (%): 294 (4) [$M^+$], 265 (8), 238 (13), 224 (8), 211 (46), 196 (17), 182 (33), 168 (50), 153 (88), 140 (100), 127 (25).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3066 (w), 3034 (w), 2979 (w), 2945 (w), 2859 (w), 2221 (s), 1668 (s), 1595 (m), 1450 (m), 1391 (s), 1309 (m), 1268 (m), 1238 (m), 1185 (m), 968 (m).

**HRMS** (EI) for **$C_{17}H_{18}N_4O$** (294.1481): found: 294.1475.

**Synthesis of 5-formyl-2-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (77):**




Prepared according to **TP3** from1-(2-carbethoxy-4-iodophenylazo)pyrrolidine (**44a**) (373 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), *N*,*N*-dimethylformamide (0.16 mL, 2 mmol). Reaction condition: -40 °C, 0.5 h; -40 °C to rt, 2 h. Purification by flash chromatography (*n*-pentane/ether = 2 : 3) yielded **77** (234 mg, 85 %) as a yellow liquid.

**$^{1}$H-NMR** (600 MHz, $CDCl_3$, 25 °C) *δ*/ppm: 9.92 (s, 1H), 8.09 (d, *J* = 1.9 Hz, 1H), 7.87 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.56 (d, *J* = 8.5 Hz, 1H), 4.35 (q, *J* = 7.0 Hz, 2H), 3.90-4.00 (m, 2H), 3.66-3.74 (m, 2H), 1.98-2.10 (m, 4H), 1.36 (t, *J* = 7.0 Hz, 3H).

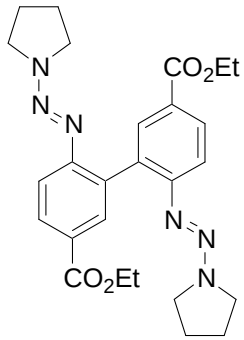
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) *δ*/ppm: 190.7, 167.5, 154.7, 132.4, 132.2, 131.8, 127.0, 119.4, 61.1, 51.4, 47.1, 23.9, 23.4, 14.3.

**MS** (70 eV, EI) *m/z* (%): 275 (9) [$M^+$], 230 (6), 205 (42), 149 (100), 133 (9), 121 (25), 103 (8).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2977 (w), 2874 (w), 2728 (w), 1717 (s), 1686 (s), 1594 (s), 1394 (s), 1306 (s), 1222 (m), 1182 (s), 1068 (m).

**HRMS** (EI) for $\mathbf{C_{14}H_{17}N_3O_3}$ (275.1270): found: 275.1273.

**Synthesis of 6,6'-bis-(pyrrolidin-1-ylazo)-biphenyl-3,3'-dicarboxylic acid diethyl ester (78):**




To a solution of 1-(4-carbethoxy-2-iodophenylazo)pyrrolidine (**28c**) (373 mg, 1 mmol) in THF (0.6 mL) was slowly added *i*-PrMgCl·LiCl (0.51 mL, 1.05 equiv., 2.05 M in THF) at -40 °C. The reaction mixture was continuously stirred at -40 °C for 40 min. A complete conversion to the corresponding Grignard reagent was observed as indicated by GC-analysis of hydrolyzed reaction aliquots. $Fe(acac)_3$ (177 mg, 0.5 mmol) in THF (1 mL) was added dropwise at -40 °C and then the reaction mixture was slowly warmed to rt and stirred for 1 h before the addition of aqueous $NH_4Cl$ (4 mL). The aqueous phase was extracted with diethyl ether (2 × 20 mL). The organic fractions were washed with brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded the pure product **78** (128 mg, 52 %) as a yellow solid.

**mp**.: 139.7-141.3 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.10 (d, $J$ = 2.0 Hz, 2H), 7.96 (dd, $J$ = 8.4, 2.0 Hz, 2H), 7.45 (d, $J$ = 8.4 Hz, 2H), 4.35 (q, $J$ = 7.1 Hz, 4H), 3.79 (br s, 4H), 3.31 (br s, 4H), 1.90 (br s, 8H), 1.37 (t, $J$ = 7.1 Hz, 6H).

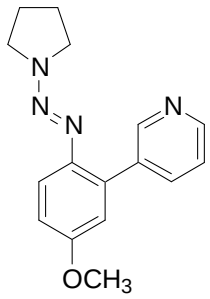
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 167.3, 153.0, 134.3, 133.6, 129.6, 126.3, 116.8, 61.0, 51.0, 46.8, 24.2, 14.8.

**MS** (70 eV, EI) *m/z* (%): 594 (100) ([M+triethylamine+H]$^+$), 493 (63) ([M+H]$^+$).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3068 (w), 2963 (w), 2873 (w), 1701 (s), 1596 (m), 1384 (m), 1308 (m), 1228 (s), 1098 (s), 1035 (m).

**HRMS** (EI) for $\mathbf{C_{26}H_{32}N_6O_4}$ (492.2485): found: 493.2555 ([M+H]$^+$).

**Synthesis of (4-methoxy-2-pyridin-3-yl-phenyl)-pyrrolidin-1-yl-diazene (79)**




Prepared according to **TP8** from1-(4-methoxy-2-iodophenylazo)pyrrolidine (**97**) (prepared from 2-iodo-4-methoxyaniline[95] according to **TP1**) (330 mg, 1 mmol), *i*-PrMgCl (0.55 mL, 1.1 equiv., 2.0 M in THF), $ZnBr_2$ (1 mL, 1 mmol, 1.0 M solution in THF,), tetrakis(triphenylphosphine)palladium (35 mg, 0.03 mmol), and 3-iodopyridine (206 mg, 1 mmol). Reaction condition: -20 °C to -10 °C, 1 h; -10 °C to -5 °C, 0.5 h; reflux, 3 h. Purification by flash chromatography (ether) yielded **79** (214 mg, 76 %) as a white solid.

**mp**.: 62.5-64.8 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.78 (d, $J$ = 2.0 Hz, 1H), 8.49 (dd, $J$ = 4.8, 2.0 Hz, 1H), 7.81-7.87 (m, 1H), 7.45 (d, $J$ = 8.4 Hz, 1H), 7.27 (dd, $J$ = 8.4, 4.8 Hz, 1H), 6.85-6.91 (m, 2H), 3.20-4.04 (br s, 4H), 3.83 (s, 3H), 1.89-1.96 (m, 4H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 157.4, 151.1, 147.5, 142.2, 137.3, 135.7, 133.4, 122.4, 118.3, 114.8, 114.6, 55.5, 23.7.

**MS** (70 eV, EI) *m/z* (%): 282 (26) [$M^+$], 212 (45), 184 (100), 169 (31), 154 (10), 141 (13), 127 (5), 114 (7).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2965 (w), 2900 (w), 1600 (m), 1483 (m), 1427 (m), 1395 (m), 1312 (s), 1270 (m), 1214 (s), 1174 (m), 1109 (m), 1028 (s), 852 (m) $cm^{-1}$

**HRMS** (EI) for **$C_{16}H_{18}N_4O$** (282.1481): found: 282.1464.

The analytical data for the starting material 1-(4-methoxy-2-iodophenylazo)pyrrolidin (**97**):

**mp**.: 47.8-49.3 $^oC$ (a brown solid)

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.35 (d, $J$ = 2.9 Hz, 1H), 7.28 (d, $J$ = 8.9 Hz, 1H), 6.85 (dd, $J$ = 8.9, 2.9 Hz, 1H), 3.40-4.00 (br s, 4H), 3.76 (s, 3H), 1.96-2.05 (m, 4H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 157.5, 144.5, 123.1, 117.5, 115.3, 96.4, 55.6, 23.8.

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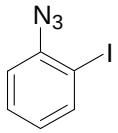
[95] a) Y. Kondo, S. Kojima, T. Sakamoto, *J. Org. Chem.* **1997**, *62*, 6507; b) D. Lizos, R. Tripoli, J. A. Murphy, *Chem. Commum*. **2001**, 2732.

**MS** (70 eV, EI) *m/z* (%): 331 (30) [$M^+$], 261 (61), 233 (100), 218 (28), 203 (13), 106 (20), 91 (4), 78 (20).
**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2959 (w), 2870 (w), 1587 (m), 1557 (w), 1475 (m), 1419 (m), 1393 (m), 1344 (m), 1313 (m), 1214 (m), 1175 (m), 1017 (m), 1034 (m) $cm^{-1}$
**HRMS** (EI) for **$C_{11}H_{14}IN_3O$** (331.0182): found: 331.0197.

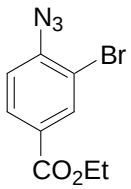
**Synthesis of 1-azido-2-iodo-benzene (80):**




Prepared according to **TP16** from 1-(2-iodophenylazo)pyrrolidine (**73**) (151 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3{\cdot}OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 15 min. Purification by flash chromatography (*n*-pentane) yielded **80** (98 mg, 80 %) as a pale yellow liquid.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.78 (d, $J$ = 7.9 Hz, 1H), 7.38 (t, $J$ = 8.0 Hz, 1H), 7.13 (d, $J$ = 8.0 Hz, 1H), 6.86 (t, $J$ = 7.9 Hz, 1H).
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 141.9, 140.2, 129.7, 126.5, 118.6, 88.0.
**MS** (70 eV, EI) *m/z* (%): 245 (16) [$M^+$], 217 (56), 127 (8), 90 (100), 63 (25).
**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3059 (w), 2127 (s), 2107 (s), 2088 (s), 1578 (m), 1464 (s), 1433 (m), 1303 (s), 1287 (s), 1146 (w), 1016 (s).
**HRMS** (EI) for **$C_6H_4IN_3$** (244.9450): found: 244.9462.

**Synthesis of 4-azido-3-bromo-benzoic acid ethyl ester (81):**




Prepared according to **TP16** from 3-bromo-4-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (**74**) (163 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3{\cdot}OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 15 min. Purification by

flash chromatography (*n*-pentane/ether = 19 : 1) yielded **81** (105 mg, 78 %) as a white powder.

**mp**.: 47.4-48.6 °C.

**$^{1}$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.19 (s, 1H), 7.98 (d, $J$ = 8.5 Hz, 1H), 7.17 (d, $J$ = 8.5 Hz, 1H), 4.34 (q, $J$ = 7.2 Hz, 2H), 1.37 (t, $J$ = 7.2 Hz, 3H).

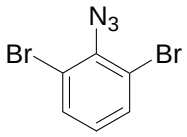
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 64.6, 143.0, 135.1, 129.8, 128.1, 118.9, 113.5, 61.4, 14.3.

**MS** (70 eV, EI) *m/z* (%): 269 (8) [$M^+$], 243 (59), 226 (8), 215 (48), 198 (100), 170 (23), 143 (8), 134 (16), 117 (8), 106 (11), 90 (38).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2980 (w), 2130 (s), 2091 (s), 1705 (s), 1595 (m), 1565 (w), 1483 (w), 1394 (w), 1368 (m), 1279 (s), 1247 (s), 1110 (s), 1029 (s).

**HRMS** (EI) for **$C_9H_8BrN_3O_2$** (268.9800): found: 268.9770.

**Synthesis of 2-azido-1,3-dibromo-benzene (82):**




Prepared according to **TP16** from 1-(2,6-dibromophenylazo)pyrrolidine (**28a**) (167 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3{\cdot}OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 20 min. Purification by flash chromatography (*n*-pentane) yielded **82** (121 mg, 88 %) as a colourless oil.

**$^{1}$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.50 (d, $J$ = 8.0 Hz, 2H), 6.91 (t, $J$ = 8.0 Hz, 1H).

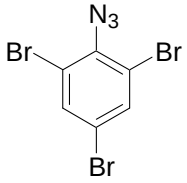
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 136.7, 132.9, 127.8, 118.9.

**MS** (70 eV, EI) *m/z* (%): 277 (8) [$M^+$], 249 (50), 168 (100), 143 (7), 117 (10), 88 (14).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2967 (w), 2140 (s), 2097 (s), 1552 (m), 1427 (s), 1299 (m), 1199 (m), 1141 (m).

**HRMS** (EI) for **$C_6H_3Br_2N_3$** (274.8694): found: 274.8692.

**Synthesis of 1-azido-2,4,6–tribromo-benzene (83):**



Prepared according to **TP16** from 1-(2,4,6-tribromophenylazo)pyrrolidine (**44h**) (206 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3 \cdot OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 30 min. Purification by flash chromatography (*n*-pentane) yielded **83** (146 mg, 82 %) as a pink solid.

**mp**.: 70.6-71.8 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.65 (s, 2H).

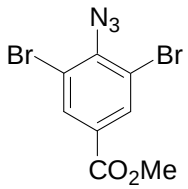
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 136.0, 135.2, 119.3, 119.1.

**MS** (70 eV, EI) *m/z* (%): 355 (8) [$M^+$], 343 (12), 329 (100), 250 (19), 223 (8), 168 (23), 143 (6), 90 (15).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3056 (w), 2141 (s), 2103 (s), 1556 (w), 1533 (m), 1428 (s), 1368 (m), 1296 (s), 1146 (m).

**HRMS** (EI) for **$C_6H_2Br_2N_3$** (352.7799): found: 352.7785.

**Synthesis of methyl 4-azido-3,5–dibromo-benzoate (84):**




Prepared according to **TP16** from 1-(2,6-dibromo-4-carbmethoxyphenylazo)pyrrolidine (**44f**) (196 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3 \cdot OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 20 min. Purification by flash chromatography (*n*-pentane/ether = 9 : 1) yielded **84** (141 mg, 84 %) as a pale yellow solid.

**mp**.: 80.4-81.9 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.14 (s, 2H); 3.90 (s, 3H).

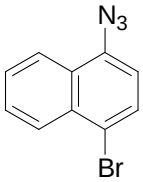
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 164.0, 140.4, 134.1, 129.2, 118.1, 52.7.

**MS** (70 eV, EI) *m/z* (%): 334 (8) [$M^+$], 306 (100), 278 (34), 264 (60), 248 (48), 198 (47), 88 (75).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3078 (w), 2953 (w), 2130 (s), 2098 (s), 1715 (s), 1584 (w), 1543 (w), 1425 (s), 1375 (s), 1306 (m), 1266 (s), 1193 (s), 1128 (s).

**HRMS** (EI) for **$C_8H_5Br_2N_3O_2$** (332.8748): found: 332.8761.

**Synthesis of 1-azido-4-bromo-naphthalene (85):**




Prepared according to **TP16** from (4-bromo-naphthalen-1-yl)-pyrrolidin-1-yl-diazene (**75**) (152 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3{\cdot}OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 10 min. Purification by flash chromatography (*n*-pentane/ether = 19 : 1) yielded **85** (100 mg, 81 %) as a pale yellow solid.

**mp**.: 41.8-43.2 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.18 (d, $J$ = 8.6 Hz, 1H), 8.09 (d, $J$ = 8.6 Hz, 1H), 7.72 (d, $J$ = 8.0 Hz, 1H), 7.62 (t, $J$ = 7.0 Hz, 1H), 7.53 (t, $J$ = 7.0 Hz, 1H), 7.08 (d, $J$ = 8.0 Hz, 1H).

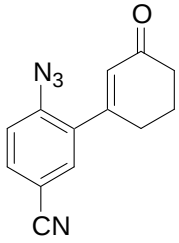
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 136.6, 129.4, 128.3, 127.9, 127.2, 127.1, 126.9, 123.0, 118.4, 114.2.

**MS** (70 eV, EI) *m/z* (%): 248 (5) [$M^+$], 220 (25), 140 (100), 113 (12).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3047 (w), 2110 (s), 1621 (w), 1585 (m), 1503 (m), 1455 (m), 1421 (m), 1375 (s), 1314 (m), 1283 (s), 1194 (m), 1115 (m), 1006 (m).

**HRMS** (EI) for **$C_{10}H_6BrN_3$** (246.9745): found: 246.9727.

**Synthesis of 4-azido-3-(3-oxo-cyclohex-1-enyl)-benzonitrile (86):**




Prepared according to **TP16** from 3-(3-oxo-cyclohex-1-enyl)-4-(pyrrolidin-1-ylazo)-benzonitrile (**76**) (147 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3{\cdot}OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 10 min. Purification by flash chromatography (*n*-pentane/ether = 3 : 7) yielded **86** (90 mg, 76 %) as a brown solid.

**mp**.: 122.9-124.2 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.65 (d, $J$ = 8.4 Hz, 1H), 7.47 (s, 1H), 7.27 (d, $J$ = 8.4 Hz, 1H), 6.05 (s, 1H), 2.61-2.66 (m, 2H), 2.45-2.50 (m, 2H), 2.09-2.16 (m, 2H).

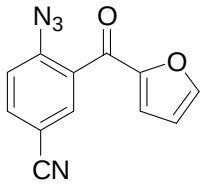
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 198.8, 157.4, 141.8, 133.4, 132.7, 132.6, 130.0, 119.5, 117.8, 108.6, 37.3, 30.0, 23.0.

**MS** (70 eV, EI) *m/z* (%): 238 (3) [$M^+$], 210 (84), 181 (72), 168 (33), 154 (100), 140 (12), 127 (29), 77 (8).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2924 (w), 2226 (m), 2139 (s), 2110 (s), 1666 (s), 1595 (m), 1482 (s), 1345 (m), 1318 (s), 1230 (m), 1158 (m), 961 (m) $cm^{-1}$; MS (EI, 70 ev), m/z (%): 238 ($M^+$, 3), 210 (84), 181 (72), 168 (33), 154 (100), 140 (12), 127 (29), 77 (8).

**HRMS** (EI) for **$C_{13}H_{10}N_4O$** (238.0855): found: 238.0870.

**Synthesis of 4-azido-3-(furan-2-carbonyl)-benzonitrile (87):**




Prepared according to **TP16** from 3-(furan-2-carbonyl)-4-(pyrrolidin-1-ylazo)-benzonitrile (**30j**) (147 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3{\cdot}OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 15 min. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **87** (75 mg, 63 %) as a white solid.

**mp**.: 119.9-121.3 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.78 (dd, $J$ = 8.2, 2.0 Hz, 1H), 7.74 (d, $J$ = 1.5 Hz, 1H), 7.68 (d, $J$ = 2.0 Hz, 1H), 7.34 (d, $J$ = 8.2 Hz, 1H), 7.14 (d, $J$ = 3.3 Hz, 1H), 6.60 (dd, $J$ = 3.3, 1.5 Hz, 1H).

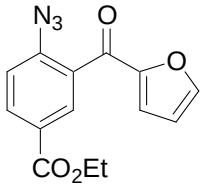
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 179.4, 151.8, 148.3, 143.1, 135.2, 133.4, 131.0, 121.3, 119.9, 117.5, 112.9, 108.2.

**MS** (70 eV, EI) *m/z* (%): 238 (2) [$M^+$], 210 (100), 194 (37), 182 (31), 154 (80), 127 (56), 95 (36).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3116 (w), 2230 (m), 2135 (s), 2115 (s), 1642 (s), 1601 (m), 1562 (m), 1484 (m), 1464 (s), 1411 (m), 1390 (m), 1290 (s), 1160 (m), 1090 (m), 1032 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_{12}H_6N_4O_2$** (238.0491): found: 238.0492.

**Synthesis of ethyl 4-azido-3-(furan-2-carbonyl)-benzoate (88):**



Prepared according to **TP16** from 3-(furan-2-carbonyl)-4-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (**30g**) (171 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3 \cdot OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 20 min. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **88** (123 mg, 86 %) as a white solid.

**mp**.: 97.6-99.0 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.18 (dd, $J$ = 8.6, 1.9 Hz, 1H), 8.13 (d, $J$ = 1.7 Hz, 1H), 7.67 (s, 1H), 7.29 (d, $J$ = 8.6 Hz, 1H), 7.08 (d, $J$ = 3.6 Hz, 1H), 6.57 (dd, $J$ = 3.6, 1.7 Hz, 1H), 4.36 (q, $J$ = 7.2 Hz, 2H), 1.36 (t, $J$ = 7.2 Hz, 3H).

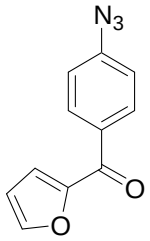
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 180.9, 165.0, 152.2, 148.0, 142.8, 133.0, 131.0, 130.1, 126.7, 121.2, 119.0, 112.7, 61.4, 14.3.

**MS** (70 eV, EI) *m/z* (%):285 (21) [$M^+$], 257 (100), 228 (9), 212 (34), 201 (29), 184 (58), 156 (50), 128 (17), 95 (45).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3127 (w), 2122 (s), 2087 (s), 1712 (s), 1650 (s), 1603 (m), 1560 (m), 1457 (s), 1392 (m), 1283 (s), 1256 (s), 1185 (m), 1136 (w), 1020 (s) $cm^{-1}$.

**HRMS** (EI) for **$C_{14}H_{11}N_3O_4$** (285.0750): found: 285.0741.

**Synthesis of 4-azido-1-(furan-2-carbonyl)-benzene (89):**




Prepared according to **TP16** from furan-2-yl-[4-(pyrrolidin-1-ylazo)-phenyl]-methanone (**30l**) (135 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3 \cdot OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 20 min. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **89** (99 mg, 93 %) as a white solid.

**mp**.: 79.0-80.2 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.03 (d, $J$ = 8.4 Hz, 2H), 7.68 (d, $J$ = 1.9 Hz, 1H), 7.24 (d, $J$ = 3.5 Hz, 1H), 7.11 (d, $J$ = 8.4 Hz, 2H), 6.59 (dd, $J$ = 3.5, 1.9 Hz, 1H).

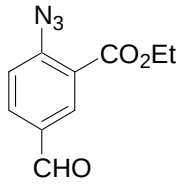
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 180.8, 152.4, 146.9, 144.6, 133.6, 131.4, 120.1, 118.9, 112.3.

**MS** (70 eV, EI) *m/z* (%):213 (17) [$M^+$], 185 (57), 172 (6), 158 (12), 146 (13), 120 (49), 95 (100).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3126 (w), 2120 (s), 2082 (s), 1640 (s), 1598 (s), 1501 (m), 1461 (s), 1389 (m), 1283 (s), 1174 (m), 1033 (m), 955 (m) $cm^{-1}$.

**HRMS** (EI) for $\mathbf{C_{11}H_7N_3O_2}$ (213.0538): found: 213.0522.

**Synthesis of ethyl 2-azido-5-formyl-benzoate (90):**




Prepared according to **TP16** from 5-formyl-2-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (**77**) (138 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3{\cdot}OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 15 min. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **90** (103 mg, 94 %) as a orange solid.

**mp**.: 38.6-39.9 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.94 (s, 1H), 8.31 (d, *J* = 2.3 Hz, 1H), 8.00 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 4.37 (q, *J* = 7.0 Hz, 2H), 1.38 (t, *J* = 7.0 Hz, 3H).

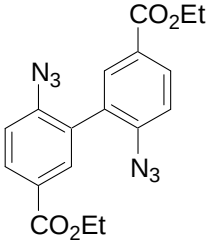
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 189.8, 164.2, 145.7, 134.0, 133.0, 132.4, 123.3, 120.4, 61.8, 14.2.

**MS** (70 eV, EI) *m/z* (%):219 (2) [$M^+$], 191 (14), 174 (21), 163 (100), 146 (18), 135 (10), 118 (12), 107 (73), 90 (15).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3065 (w), 2987 (w), 2841 (w), 2769 (w), 2119 (s), 1718 (s), 1691 (s), 1595 (s), 1572 (s), 1476 (m), 1367 (m), 1294 (m), 1255 (s), 1179 (m), 1133 (m), 1061 (m), 932 (m) $cm^{-1}$.

**HRMS** (EI) for $\mathbf{C_{10}H_9N_3O_3}$ (219.0644): found: 219.0622.

**Synthesis of 6,6'-diazido-biphenyl-3,3'-dicarboxylic acid diethyl ester (91):**



Prepared according to **TP16** from 6,6'-bis-(pyrrolidin-1-ylazo)-biphenyl-3,3'-dicarboxylic acid diethyl ester (**78**) (201 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3 \cdot OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 15 min. Purification by flash chromatography (*n*-pentane/ether = 3 : 2) yielded **91** (137 mg, 72 %) as a white solid.

**mp**.: 118.0-119.2 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.11 (dd, $J$ = 8.4, 1.9 Hz, 2H), 7.88 (d, $J$ = 1.9 Hz, 2H), 7.27 (d, $J$ = 8.4 Hz, 2H), 4.36 (q, $J$ = 6.9 Hz, 4H), 1.37 (t, $J$ = 6.9 Hz, 6H).

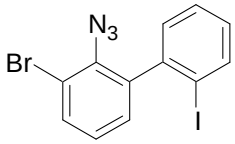
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 165.5, 142.9, 132.9, 131.0, 129.0, 126.9, 118.2, 61.2, 14.3.

**MS** (70 eV, EI) *m/z* (%):649 (20) $[2(M\text{-}56, 2N_2)+H]^+$, 325 (100) $[M\text{-}56+H]^+$**.**

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3066 (w), 2985 (w), 2128 (s), 2101 (s), 1715 (s), 1560 (m), 1576 (m), 1478 (m), 1386 (w), 1363 (m), 1306 (m), 1250 (m), 1216 (m), 1150 (m), 1120 S), 1023 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_{18}H_{16}N_6O_4$** (380.1233): found: 325.1171 $[M\text{-}2N_2+H]^+$.

**Synthesis of 2-azido-3-bromo-2'-iodo-biphenyl (92):**




Prepared according to **TP16** from (3-bromo-2'-iodo-biphenyl-2-yl)-pyrrolidin-1-yl-diazene (**41a**) (228 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3 \cdot OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 15 min. Purification by flash chromatography (*n*-pentane/ether = 99 : 1) yielded **92** (132 mg, 66 %) as a pale yellow oil.

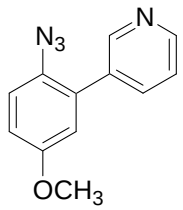
**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.93 (d, $J$ = 8.1 Hz, 1H), 7.48 (d, $J$ = 7.7 Hz, 1H), 7.36 (d, $J$ = 7.7 Hz, 1H), 7.23-7.30 (m, 3H), 7.03 (t, $J$ = 7.7 Hz, 1H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 146.0, 145.1, 139.6, 132.2, 130.7, 129.9, 129.5, 129.2, 128.2, 128.0, 127.8, 98.1.

**MS** (70 eV, EI) *m/z* (%):398 (7) $[M^+]$, 370 (14), 358 (51), 278 (6), 246 (20), 165 (18), 152 (100), 76 (15).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3052 (w), 2923 (w), 2138 (s), 2102 (s), 1593 (m), 1561 (s), 1454 (s), 1429 (m), 1244 (w), 1060 (m), 1008 (s) $cm^{-1}$.
**HRMS** (EI) for **$C_{12}H_7BrIN_3$** (398.8868): found: 398.8868.

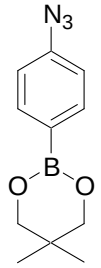
**Synthesis of 3-(2-azido-5-methoxy-phenyl)-pyridine (93):**




Prepared according to **TP17** from (4-methoxy-2-pyridin-3-yl-phenyl)-pyrrolidin-1-yl-diazene (**79**) (127 mg, 0.45 mmol), $KHSO_4$ (612 mg, 4.5 mmol), $NaN_3$ (146 mg, 2.25 mmol). Reaction condition: 25 °C, 12 h. Purification by flash chromatography (ether) yielded **93** (87 mg, 86 %) as a brown liquid.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.67 (d, $J$ = 2.0 Hz, 1H), 8.58 (dd, $J$ = 4.8, 2.0 Hz, 1H), 7.75-7.80 (m, 1H), 7.31-7.36 (m, 1H), 7.17 (d, $J$ = 8.8 Hz, 1H), 6.97 (dd, $J$ = 8.8, 2.9 Hz, 1H), 6.85 (d, $J$ = 2.9 Hz, 1H), 3.81 (s, 3H).
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 156.9, 149.8, 148.5, 136.8, 133.8, 129.8, 128.3, 122.9, 119.9, 116.3, 115.0, 55.6.
**MS** (70 eV, EI) *m/z* (%):226 (3) [$M^+$], 198 (24), 183 (100), 155 (41).
**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2965 (w), 2922 (m), 2853 (m), 2120 (s), 1605 (w), 1465 (w), 1400 (w), 1290 (w), 1261 (w), 1230 (m), 1032 (m) $cm^{-1}$.
**HRMS** (EI) for **$C_{12}H_{10}N_4O$** (226.0855): found: 226.0856.

**Synthesis of 2-(4-azido-phenyl)-5,5-dimethyl-[1,3,2]dioxaborinane (94):**




Prepared according to **TP17** from [4-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)-phenyl]-pyrrolidin-1-yl-diazene (**58a**) (129 mg, 0.45 mmol), $KHSO_4$ (612 mg, 4.5 mmol), $NaN_3$ (146

mg, 2.25 mmol). Reaction condition: 25 °C, 12 h. Purification by flash chromatography (ether) yielded **94** (100 mg, 96 %) as a white powder.

**mp**.: 74.7-75.6 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.77 (d, $J$ = 8.6 Hz, 2H), 6.99 (d, $J$ = 8.6 Hz, 2H), 3.74 (s, 4H), 1.00 (s, 6H).

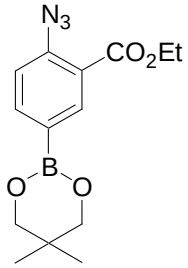
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 142.2, 135.5, 118.2, 72.3, 31.9, 21.9.

**MS** (70 eV, EI) *m/z* (%):231 (8) [$M^+$], 203 (100), 188 (13), 161 (9), 147 (12), 134 (19), 117 (36), 91 (20).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3074 (w), 2963 (m), 2906 (w), 2121 (s), 2084 (s), 1597 (s), 1567 (m), 1478 (m), 1421 (m), 1380 (m), 1304 (m), 1277 (m), 1182 (m), 1138 (m), 1016 (w) $cm^{-1}$.

**HRMS** (EI) for **$C_{11}H_{14}BN_3O_2$** (231.1179): found: 231.1162.

**Synthesis of 2-azido-5-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)-benzoic acid ethyl ester (95):**




Prepared according to **TP17** from 5-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)-2-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (**58b**) (162 mg, 0.45 mmol), $KHSO_4$ (612 mg, 4.5 mmol), $NaN_3$ (146 mg, 2.25 mmol). Reaction condition: 25 °C, 12 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **95** (85 mg, 62 %) as a brown liquid.

**$^{1}$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 8.21 (s, 1H), 7.89 (d, $J$ = 8.1 Hz, 1H), 7.17 (d, $J$ = 8.1 Hz, 1H), 4.34 (q, $J$ = 7.2 Hz, 2H), 3.74 (s, 4H), 1.37 (t, $J$ = 7.2 Hz, 3H), 0.99 (s, 6H).

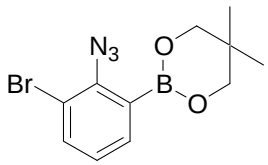
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 165.6, 141.9, 138.4, 138.2, 137.2, 122.2, 118.9, 72.3, 61.2, 31.9, 21.8, 14.3.

**MS** (70 eV, EI) *m/z* (%):275 (67) [M-28, $N_2$]$^+$, 229 (100), 204 (8), 145 (16), 118 (12).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2962 (m), 2904 (w), 2122 (m), 1715 (m), 1600 (m), 1478 (m), 1257 (s), 1074 (s), 1010 (s), 787 (s) $cm^{-1}$.

**HRMS** (EI) for **$C_{14}H_{18}BN_3O_4$** (231.1179): found: 276.1400 [M-$N_2$+H]$^+$.

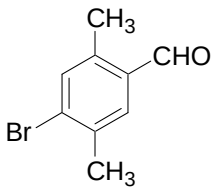
**Synthesis of 2-(2-azido-3-bromo-phenyl)-5,5-dimethyl-[1,3,2]dioxaborinane (96):**




Prepared according to **TP17** from [2-bromo-6-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)-phenyl]-pyrrolidin-1-yl-diazene (**58d**) (165 mg, 0.45 mmol), $KHSO_4$ (612 mg, 4.5 mmol), $NaN_3$ (146 mg, 2.25 mmol). Reaction condition: 25 °C, 12 h. Purification by flash chromatography (*n*-pentane/ether = 1 : 1) yielded **96** (128 mg, 92 %) as a brown solid.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.66 (d, $J$ = 7.4 Hz, 1H), 7.59 (d, $J$ = 7.4 Hz, 1H), 7.01 (t, $J$ = 7.4 Hz, 1H), 3.81 (s, 4H), 1.04 (s, 6H).
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 142.9, 135.5, 135.0, 134.4, 126.2, 117.8, 72.5, 31.8, 21.9.
**MS** (70 eV, EI) *m/z* (%):281 (100) $[M\text{-}28, N_2]^+$, 226 (10), 197 (69), 171 (4), 118 (21), 91 (21).
**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2962 (w), 2936 (w), 2134 (s), 2101 (s), 1586 (m), 1477 (s), 1426 (s), 1406 (s), 1376 (m), 1296 (s), 1248 (s), 1199 (m), 1146 (s), 1109 (m), 972 (m) $cm^{-1}$.
**HRMS** (EI) for **$C_{11}H_{13}BBrN_3O_2$** (309.0284): found: 282.0295 $[M\text{-}N_2+H]^+$.

**Synthesis of 4-bromo-2,5-dimethyl-benzaldehyde (102):**




To a solution of 1,4-dibromo-2,5-dimethyl-benzene (**101**) (2.64 g, 10 mmol) in THF (5 mL) was slowly added *n*-BuLi (4.4 mL, 10.5 mmol, 2.4 M in hexane) at -78 °C. The reaction mixture was continuously stirred at -78°C for 10 min. After 10 minutes, a complete conversion to the corresponding lithium reagent was observed as indicated by GC-analysis of hydrolyzed reaction aliquots. *N*,*N*-dimethylformamide (1.6 mL, 20 mmol) was added and the reaction mixture was warmed to rt and stirred again for 1 h before the addition of aq. $NH_3$ (20 mL). The aqueous phase was extracted with ether (2 × 50 mL). The organic layers were washed with brine (100 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give the pure product **102** (2.1 g, 99 %) as a white powder.

**mp**.: 58.2-59.8 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) *δ*/ppm: 10.15 (s, 1H), 7.58 (s, 1H), 7.41 (s, 1H), 2.56 (s, 3H), 2.38 (s, 3H).

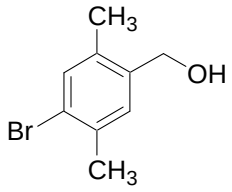
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) *δ*/ppm: 191.7, 139.2, 136.1, 135.4, 133.5, 133.0, 131.2.

**MS** (70 eV, EI) *m/z* (%):213 (100) [$M^+$], 183 (32), 104 (35), 77 (31).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2956 (w), 2923 (w), 2862 (w), 2836 (w), 2760 (w), 2724 (w), 1682 (s), 1595 (m), 1546 (m), 1443 (m), 1382 (m), 1235 (m), 1182 (m), 959 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_9H_9BrO$** (211.9837): found: 211.9836.

**Synthesis of 4-bromo-2,5-dimethyl-benzyl alcohol (103):**




A solution of **102** (1.02 g, 4.77 mmol) in EtOH (20 mL) was cooled in an ice bath and $NaBH_4$ (181 mg, 4.77 mmol) was added over 5 min with stirring. Then the reaction mixture was gradually warmed to rt. After 0.5 h the solvent was evaporated and $H_2O$ (20 mL) was added. The aqueous mixture was extracted with ether (2 × 20 mL) and the combined organic layers were washed with brine, dried ($Na_2SO_4$) and concentrated *in vacuo* to give the pure product **103** (1.01 g, 99 %) as a white powder.

**mp**.: 92.0-92.7 °C.

**$^{1}$H-NMR** (600 MHz, $CDCl_3$, 25 °C) *δ*/ppm: 7.32 (s, 1H), 7.19 (s, 1H), 4.58 (s, 2H), 2.34 (s, 3H), 2.25 (s, 3H).

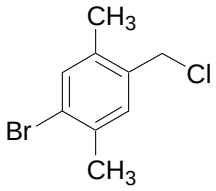
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) *δ*/ppm: 137.8, 135.20, 135.18, 133.7, 129.9, 123.7, 62.8, 22.3, 17.8.

**MS** (70 eV, EI) *m/z* (%):214 (60) [$M^+$], 196 (100), 185 (13), 171 (8), 135 (19), 117 (38), 107 (54), 91 (75), 77 (25).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3100-3400 (broad), 2981 (m), 2918 (m), 2858 (m), 1754 (w), 1557 (w), 1484 (s), 1452 (s), 1387 (m), 1282 (w), 1185 (w), 1134 (w), 1040 (s), 957 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_9H_{11}BrO$** (213.9993): found: 213.9991.

**Synthesis of 4-bromo-2,5-dimethyl-benzyl chloride (104):**




To a solution of **103** (930 mg, 4.35 mmol) in $CHCl_3$ (3 mL) in an ice bath was added slowly a solution of $SOCl_2$ (0.4 mL) in $CHCl_3$ (0.6 mL). After 10 min, the reaction mixture was warmed to rt and stirred for 0.5 h before the addition of $H_2O$ (5 mL). The aqueous phase was extracted with ether (2 × 5 mL). The organic layers were washed with brine (10 mL), dried ($Na_2SO_4$) and concentrated *in vacuo* to give the pure product **104** (945 mg, 93 %) as a pale yellow liquid.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.36 (s, 1H), 7.15 (s, 1H), 4.50 (s, 2H), 2.34 (s, 3H), 2.33 (s, 3H).

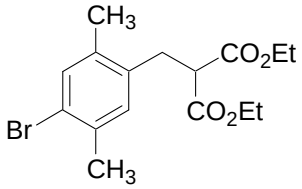
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 136.3, 135.7, 134.7, 134.2, 132.0, 125.1, 44.1, 22.2, 18.0.

**MS** (70 eV, EI) *m/z* (%):234 (33) [$M^+$], 197 (100), 115 (30), 103 (8), 91 (18), 77 (8).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2948 (m), 2921 (m), 2876 (w), 1488 (s), 1449 (s), 1263 (s), 962 (s).

**HRMS** (EI) for **$C_9H_{10}BrCl$** (231.9654): found: 231.9644.

**Synthesis of 2-(4-bromo-2,5-dimethyl-benzyl)-malonic acid diethyl ester (105):**




To a mixture of sodium hydride (720 mg, 18 mmol, 60% dispersion in mineral oil) in dimethoxyethane (4.5 mL) under a nitrogen atmosphere was added dropwise a solution of diethyl malonate (3.04 g, 19 mmol) in dimethoxyethane (9 mL). After the reaction mixture was stirred at rt for 2 h, a solution of **104** (840 mg, 3.6 mmol) in dimethoxyethane (1.8 mL) was added dropwiswe. The reaction mixture was refluxed for 12 h and then concentrated *in vacuo*, and the residue was treated with a mixture of water (6 mL) and methylene chloride (6 mL). The aqueous phase was extracted with methylene chloride (2 × 10 mL). The organic layers were washed with brine (30 mL), dried ($Na_2SO_4$) and concentrated *in vacuo* to give the crude product. Purification by flash chromatography (*n*-pentane/ether = 9 : 1) yielded the pure product **105** (1.13 g, 88 %) as a white powder

**mp**.: 47.8-48.7 °C.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.28 (s, 1H), 6.97 (s, 1H), 4.14 (q, $J$ = 7.2 Hz, 4H), 3.56 (t, $J$ = 7.8 Hz, 1H), 3.12 (d, $J$ = 7.8 Hz, 2H), 2.28 (s, 3H), 2.25 (s, 3H), 1.20 (t, $J$ = 7.2 Hz, 6H).

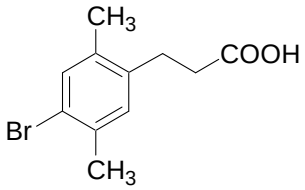
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 168.8, 135.6, 135.4, 135.3, 135.0, 133.8, 131.6, 61.5, 52.2, 31.3, 22.2, 18.5, 14.0.

**MS** (70 eV, EI) *m/z* (%):356 (30) [$M^+$], 338 (30), 312 (19), 284 (48), 265 (50), 239 (100), 210 (29), 197 (81), 185 (48), 158 (59), 145 (10), 129 (60), 115 (66), 103 (14), 91 (30), 77 (14).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3100-3400 (broad), 2981 (m), 2918 (m), 2858 (m), 1754 (w), 1557 (w), 1484 (s), 1452 (s), 1387 (m), 1282 (w), 1185 (w), 1134 (w), 1040 (s), 957 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_{16}H_{21}BrO_4$** (356.0623): found: 356.0619.

**Synthesis of 3-(4-bromo-2,5-dimethyl-phenyl)-propionic acid (106):**




A mixture of malonic ester (**105**) (927 mg, 2.6 mmol) and potassium hydroxide (296 mg, 5.2 mmol) in water (4.5 mL) was refluxed for 5 h. The reaction mixture was concentrated *in vacuo* to remove the ethanol, and then a solution of conc. sulfuric acid (0.5 mL) and water (1.5 mL) was added. The mixture was refluxed for 20 h. The reaction mixture was chilled in an ice bath and the resulting solid was filtered and washed with water to give the pure product **106** (555 mg, 83 %) as a white powder.

**mp**.: 93.2-94.5 °C.

**$^{1}$H-NMR** (400 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 12.0 (br s, 1H), 7.29 (s, 1H), 7.06 (s, 1H), 2.68 (t, $J$ = 7.8 Hz, 2H), 2.41 (t, $J$ = 7.8 Hz, 2H), 2.21 (s, 3H), 2.16 (s, 3H).

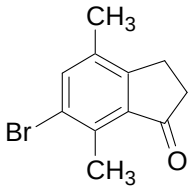
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 174.4, 139.3, 136.4, 134.9, 133.7, 131.8, 121.9, 34.5, 27.8, 22.5, 18.7.

**MS** (70 eV, EI) *m/z* (%): 256 (50) [$M^+$], 240 (3), 225 (2), 210 (8), 197 (100), 135 (23), 117 (32), 103 (9), 91 (21).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2900-3400 (broad), 2571 (w), 1692 (s), 1487 (m), 1453 (m), 1416 (m), 1304 (m), 1213 (w), 1166 (w), 1024 (m), 962 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_{11}H_{13}BrO_2$** (256.0099): found: 256.0087.

**Synthesis of 6-bromo-4,7-dimethyl-indan-1-one (107):**




The mixture of **106** (475 mg, 1.86 mmol) and polyphosphoric acid (2.2 mL) was heated at 100°C for 2.5 h. After the mixture was cooled, ice water (7.5 mL) was added and the reaction mixture was stirred for 0.5 h, and then the aqueous phase was extracted with ether (2 × 15 mL). The organic layers were washed with 10 % aqueous sodium bicarbonate (30 mL) and water (2 × 20 mL), dried ($Na_2SO_4$) and concentrated *in vacuo* to give the pure product **107** (391 mg, 88 %) as a pale yellow solid.

**mp**.: 127.8-128.6 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.51 (s, 1H), 2.80-2.90 (m, 2H), 2.60-2.72 (m, 5H), 2.27 (s, 3H).

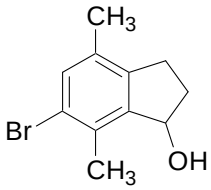
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 207.1, 154.1, 137.8, 135.6, 135.3, 134.4, 124.9, 36.8, 23.6, 17.1, 16.5.

**MS** (70 eV, EI) *m/z* (%): 238 (100) [$M^+$], 223 (6), 210 (12), 196 (6), 159 (41), 131 (35), 115 (32), 103 (6), 91 (16).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3076 (w), 3030 (w), 2920 (w), 2857 (w), 1697 (s), 1568 (w), 1469 (m), 1435 (m), 1367 (w), 1252 (m), 1220 (m), 1102 (w), 989 (w) $cm^{-1}$.

**HRMS** (EI) for **$C_{11}H_{11}BrO$** (237.9993): found: 237.9984.

**Synthesis of 6-bromo-4,7-dimethyl-indan-1-ol:**




A solution of **107** (180 mg, 0.76 mmol) in EtOH (3.2 mL) was cooled in an ice bath and $NaBH_4$ (29 mg, 0.76 mmol) was added over 5 min with stirring. Then the reaction mixture was gradually warmed to rt. After 0.5 h the solvent was evaporated and $H_2O$ (5 mL) was added. The aqueous mixture was extracted with ether (2 × 5 mL) and the combined organic

layers were washed with brine, dried ($Na_2SO_4$) and concentrated *in vacuo* to give 6-bromo-4,7-dimethyl-indan-1-ol (179 mg, 98 %) as a pale yellow solid.

**mp**.: 124.0-125.5 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.27 (s, 1H), 5.27 (d, $J$ = 6.0 Hz, 1H), 2.88-3.02 (m, 1H), 2.68 (ddd, $J$ = 17.0, 9.5, 2.6 Hz, 1H), 2.41 (s, 3H), 2.30-2.37 (m, 1H), 2.18 (s, 3H), 1.96-2.12 (m, 1H), 1.64 (br s, 1H).

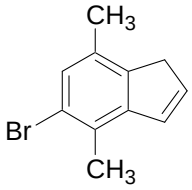
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 144.2, 142.1, 133.2, 133.1, 132.0, 123.2, 76.0, 34.8, 28.7, 18.4, 15.2.

**MS** (70 eV, EI) *m/z* (%): 240 (72) [$M^+$], 222 (100), 209 (4), 197 (8), 183 (10), 161 (30), 143 (86), 128 (48), 115 (40), 103 (8), 91 (16).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3000-3400 (broad), 2922 (m), 1467 (s), 1378 (m), 1308 (w), 1254 (w), 1180 (m), 1154 (m), 1044 (s), 958 (s) $cm^{-1}$.

**HRMS** (EI) for **$C_{11}H_{13}BrO$** (240.0150): found: 240.0143.

**Synthesis of 5-bromo-4,7-dimethyl-1H-indene (108):**




A solution of 6-Bromo-4,7-dimethyl-indan-1-ol (164 mg, 0.68 mmol) and *p*-TsOH (1.7 mg, 0.0068 mmol) in benzene (17 mL) was heated at reflux. After 2 h, the reaction mixture was allowed to cool and the solvent was evaporated *in vacuo* (30°C, 30 mmHg) to give the crude product. Purification by flash chromatography (pentane) yielded the pure product **108** (130 mg, 86 %) as a pale yellow liquid.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 7.53 (s, 1H), 7.27 (dt, $J$ = 5.7, 2.0 Hz, 1H), 6.89 (dt, $J$ = 5.7, 2.0 Hz, 1H), 3.56 (t, $J$ = 2.0 Hz, 2H), 2.78 (s, 3H), 2.61 (s, 3H).

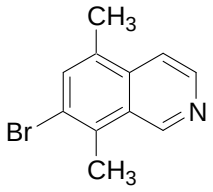
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 144.8, 141.3, 134.5, 131.7, 130.9, 129.3, 127.5, 123.0, 38.3, 18.6, 18.1.

**MS** (70 eV, EI) *m/z* (%): 222 (34) [$M^+$], 207 (4), 143 (100), 128 (52), 115 (20), 102 (8), 89 (8), 77 (8).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3061 (w), 2974 (w), 2919 (w), 2857 (w), 1666(w), 1583 (w), 1549 (w), 1461 (m), 1372 (m), 1247 (w), 1170 (w), 950 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_{11}H_{11}Br$** (222.0044): found: 222.0038.

**Synthesis of 7-bromo-5,8-dimethyl-isoquinoline (98):**




A solution of **108** (100 mg, 0.45 mmol) in MeOH (2.5 mL) and $CH_2Cl_2$ (2.5 mL) was cooled to -78°C and treated with ozone until the solution turned blue. Then the solution was purged with nitrogen until the blue color disappeared. $Me_2S$ (0.3 mL) and $NaHCO_3$ (52 mg) were added, and the reaction mixture was stirred for 4 h at rt. Conc. $NH_4OH$ (2.5 mL) was added and reaction mixture was stirred overnight. The solvent was mostly evaporated and the remaining aqueous suspension was extracted with $CHCl_3$ and the combined organic layers were washed with brine, dried ($Na_2SO_4$) and evaporated to afford the crude product. Recrystallization (EtOAc) gave **98** (101 mg, 95 %) as bright yellow crystals.

**mp**.: 102.5-103.5 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.39 (s, 1H), 8.54 (d, $J$ = 5.3, 1H), 7.63 (d, $J$ = 5.3 Hz, 1H), 7.56 (s, 1H), 2.75 (s, 3H), 2.53 (s, 3H).

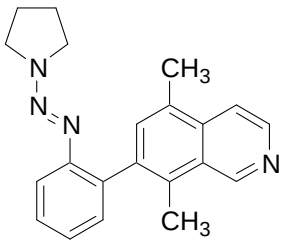
**$^{13}$C-NMR** (100 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 149.4, 142.8, 134.6, 134.5, 133.0, 132.0, 128.2, 123.2, 117.2, 18.0, 17.6.

**MS** (70 eV, EI) *m/z* (%): 235 (100) [$M^+$], 220 (3), 156 (86), 141 (11), 128 (23), 116 (6), 102 (6), 77 (11).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3050 (w), 2945 (w), 2920 (w), 2855 (w), 1588(m), 1564 (m), 1491 (m), 1433 (m), 1378 (m), 1274 (m), 1212 (w), 1072 (w) $cm^{-1}$.

**HRMS** (EI) for **$C_{11}H_{10}BrN$** (234.9997): found: 235.0007.

**Synthesis of [2-(5,8-dimethyl-isoquinolin-7-yl)-phenyl]-pyrrolidin-1-yl-diazene (99a):**




Prepared according to **TP8** from 1-(2-iodophenylazo)pyrrolidine (**73**) (903 mg, 3 mmol), *i*-PrMgCl·LiCl (2.4 mL, 3.3 mmol, 1.39 M in THF), $ZnBr_2$ (3 mL, 3 mmol, 1.0 M in THF),

tetrakis(triphenylphosphine)palladium (104 mg, 0.09 mmol), 7-bromo-5,8-dimethyl-isoquinoline (**98**) (705 mg, 3 mmol). Reaction condition: -40 °C to -30 °C, 1 h; -30 °C to -5 °C, 0.5 h; reflux, 6 h. Purification by flash chromatography (ether) yielded **99a** (743 mg, 75 %) as a pale yellow solid.

**mp**.: 121.3-123.6 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.53 (s, 1H), 8.57 (d, $J$ = 5.7 Hz, 1H), 7.49 (d, $J$ = 7.6 Hz, 1H), 7.44 (s, 1H), 7.32-7.37 (m, 1H), 7.17-7.23 (m, 2H), 2.80-4.10 (br s, 4H), 2.62 (s, 3H), 2.49 (s, 3H), 1.83 (br s, 4H).

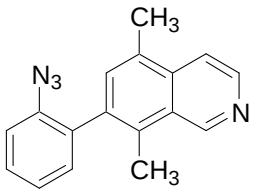
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 150.1, 148.9, 142.0, 138.8, 135.9, 134.7, 134.2, 130.8, 130.7, 129.7, 128.3, 127.9, 124.9, 117.3, 117.0, 23.6, 18.3, 15.5.

**MS** (70 eV, EI) *m/z* (%): 330 (6) [$M^+$], 260 (6), 245 (46), 232 (98), 217 (100), 202 (11), 189 (15), 108 (9).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2990 (w), 2868 (w), 1597 (w), 1406 (s), 1315 (m), 1268 (m), 1200 (w), 1095 (w) $cm^{-1}$.

**HRMS** (EI) for **$C_{21}H_{22}N_4$** (330.1844): found: 330.1844.

**Synthesis of 7-(2-azido-phenyl)-5,8-dimethyl-isoquinoline (100a):**




Prepared according to **TP16** from 2-(5,8-dimethyl-isoquinolin-7-yl)-phenyl]-pyrrolidin-1-yl-diazene (**99a**) (165 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3{\cdot}OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 10 min. Purification by flash chromatography (ether) yielded **100a** (107 mg, 78 %) as a yellow liquid.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.55 (s, 1H), 8.61 (d, $J$ = 5.7 Hz, 1H), 7.79 (d, $J$ = 5.7 Hz, 1H), 7.42-7.51 (m, 1H), 7.21-7.35 (m, 4H), 2.67 (s, 3H), 2.55 (s, 3H).

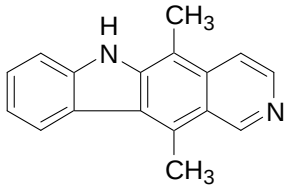
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 150.0, 142.7, 138.1, 136.0, 135.2, 133.1, 132.8, 131.4, 131.0, 130.9, 129.0, 127.7, 124.7, 118.4, 117.3, 18.3, 15.1.

**MS** (70 eV, EI) *m/z* (%): 274 (10) [$M^+$], 246 (100), 231 (80), 203 (10), 152 (5), 109 (6), 88 (4).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2923 (w), 2120 (s), 1599 (w), 1570 (w), 1487 (w), 1443 (w), 1386 (w), 1284 (m), 1095 (w), 961 (w) $cm^{-1}$.

**HRMS** (EI) for **$C_{17}H_{14}N_4$** (274.1218): found: 274.1232.

**Synthesis of ellipticine (71a):**




A solution of the aryl azide (**100a**) (101 mg, 0.37 mmol) in mesitylene (5 mL) was heated at reflux. After 6 h, the solvent was evaporated *in vacuo* to give the crude product. Purification by flash chromatography (methanol/ether = 1 : 9) yielded the pure product **71a** (52 mg, 57 %) as a yellow solid.

**mp**.: 247.3-249.1 °C. (lit.[96] m.p. 243-250 °C)

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.71 (s, 1H), 8.49 (d, $J$ = 5.8 Hz, 1H), 8.37 (d, $J$ = 7.8 Hz, 1H), 7.85 (d, $J$ = 5.8 Hz, 1H), 7.46-7.54 (m, 2H), 7.28-7.34 (m, 2H), 3.30 (s, 3H), 2.77 (s, 3H).

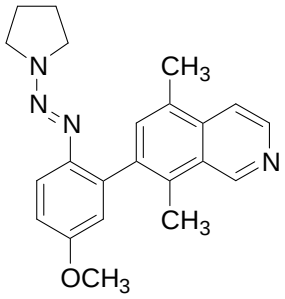
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 150.2, 144.6, 141.8, 141.2, 130.3, 129.5, 129.0, 127.4, 126.1, 124.3, 124.2, 120.2, 116.1, 115.1, 110.6, 14.9, 12.2.

**MS** (70 eV, EI) *m/z* (%): 246 (100) [$M^+$], 231 (97), 216 (6), 204 (12), 176 (6), 122 (6), 109 (5), 96 (6), 51 (3).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3480 (s), 1630 (m), 1605 (m), 1440 (w), 1400 (w), 1377 (w), 1303 (m), 1230 (m), 1010 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_{17}H_{14}N_2$** (246.1157): found: 246.1145.

**Synthesis of [2-(5,8-dimethyl-isoquinolin-7-yl)-4-methoxy-phenyl]-pyrrolidin-1-yl-diazene (99b):**

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[96] C. K. Sha, J. F. Yang, *Tetrahedron* **1992**, *48*, 10645.

Prepared according to **TP8** from 1-(4-methoxy-2-iodophenylazo)pyrrolidine (**97**) (993 mg, 3 mmol), *i*-PrMgCl·LiCl (2.4 mL, 3.3 mmol, 1.39 M in THF), $ZnBr_2$ (3 mL, 3 mmol, 1.0 M in THF), tetrakis(triphenylphosphine)palladium (104 mg, 0.09 mmol), 7-bromo-5,8-dimethyl-isoquinoline (**98**) (705 mg, 3 mmol). Reaction condition: -40 °C to -30 °C, 1 h; -30 °C to -5 °C, 0.5 h; reflux, 4.5 h. Purification by flash chromatography (ether) yielded **99b** (680 mg, 63 %) as a brown solid.

**mp**.: 62.1-64.5 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.52 (s, 1H), 8.57 (d, $J$ = 6.0 Hz, 1H), 7.76 (d, $J$ = 6.0 Hz, 1H), 7.45 (d, $J$ = 9.0 Hz, 1H), 7.43 (s, 1H), 6.91 (dd, $J$ = 9.0, 2.8 Hz, 1H), 6.76 (d, $J$ = 2.8 Hz, 1H), 3.82 (s, 3H), 2.90-3.75 (br s, 4H), 2.62 (s, 3H), 2.51 (s, 3H), 1.77-1.84 (m, 4H).

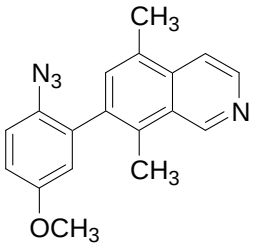
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 157.3, 150.3, 143.1, 142.4, 138.8, 137.2, 135.0, 134.1, 131.1, 130.0, 128.1, 118.2, 117.5, 115.5, 114.4, 55.8, 23.9, 18.5, 15.8.

**MS** (70 eV, EI) *m/z* (%): 360 (28) [$M^+$], 290 (22), 275 (15), 262 (100), 247 (56), 231 (22), 219 (18), 204 (15).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2962 (w), 2850 (w), 1596 (m), 1495 (m), 1407 (m), 1319 (m), 1269 (m), 1209 (m), 1109 (w), 1035 (m), 817 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_{22}H_{24}N_4O$** (360.1950): found: 360.1933.

**Synthesis of 7-(2-azido-5-methoxy-phenyl)-5,8-dimethyl-isoquinoline (100b):**




Prepared according to **TP17** from [2-(5,8-dimethyl-isoquinolin-7-yl)-4-methoxy-phenyl]-pyrrolidin-1-yl-diazene (**99b**) (162 mg, 0.45 mmol), $KHSO_4$ (612 mg, 4.5 mmol), $NaN_3$ (146 mg, 2.25 mmol). Reaction condition: 25 °C, 12 h. Purification by flash chromatography (ether) yielded **100b** (129 mg, 94 %) as a brown liquid.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.53 (s, 1H), 8.60 (d, $J$ = 5.8 Hz, 1H), 7.76 (d, $J$ = 5.8 Hz, 1H), 7.30 (s, 1H), 7.18 (d, $J$ = 8.8 Hz, 1H), 6.98 (dd, $J$ = 8.8, 3.1 Hz, 1H), 6.76 (d, $J$ = 3.1 Hz, 1H), 3.81 (s, 3H), 2.64 (s, 3H), 2.53 (s, 3H).

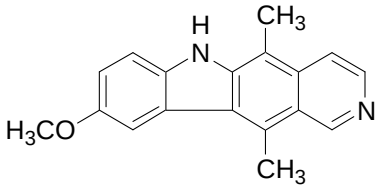
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 156.6, 150.2, 150.1, 143.0, 135.9, 134.3, 133.4, 132.5, 131.0, 130.6, 127.7, 119.5, 117.2, 116.7, 114.6, 55.6, 18.4, 15.1.

**MS** (70 eV, EI) *m/z* (%): 304 (6) [$M^+$], 276 (100), 261 (96), 246 (23), 233 (30), 218 (28), 204 (7), 117 (5), 102 (3).

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 2938 (w), 2110 (s), 1596 (m), 1488 (m), 1462 (m), 1420 (m), 1384 (m), 1285 (m), 1225 (m), 1177 (m), 1032 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_{18}H_{16}N_4O$** (304.1324): found: 304.1340.

**Synthesis of 9-methoxyellipticine (71b):**




A solution of the aryl azide (**100b**) (100 mg, 0.33 mmol) in mesitylene (3.3 mL) was heated at reflux. After 5 h, the solvent was evaporated *in vacuo* to give the crude product. Purification by flash chromatography (methanol/ether = 1 : 9) yielded the pure product **71b** (62 mg, 68 %) as a amber solid.

**mp**.: 276.3-278.5 °C. (lit.[97] m.p. 275-278 °C dec)

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.14 (s, 1H), 8.69 (d, $J$ = 5.2 Hz, 1H), 7.59 (d, $J$ = 8.4 Hz, 1H), 7.19 (d, $J$ = 5.2 Hz, 1H), 6.98 (d, $J$ = 2.6 Hz, 1H), 6.87 (dd, $J$ = 8.4, 2.6 Hz, 1H), 6.49 (s, 1H), 3.85 (s, 3H), 2.07 (s, 3H).

**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 158.6, 152.4, 148.2, 146.1, 144.1, 143.4, 135.0, 124.2, 122.2, 118.5, 116.5, 115.5, 114.6, 112.7, 108.6, 55.7, 27.6, 18.9.

**MS** (70 eV, EI) *m/z* (%): 276 (100) [$M^+$], 261 (60), 246 (27), 233 (27), 218 (33), 204 (5), 190 (10), 177 (5), 164 (7), 138 (7), 116 (7), 109 (7), 95 (5), 88 (5).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3310 (s), 2921 (m), 1722 (w), 1588 (s), 1468 (s), 1367 (w), 1348 (w), 1285 (s), 1207 (m), 1027 (s) $cm^{-1}$.

**HRMS** (EI) for **$C_{18}H_{16}N_2O$** (276.1263): found: 276.1268.

**Synthesis of [2-(5,8-dimethyl-isoquinolin-6-yl)-phenyl]-pyrrolidin-1-yl-diazene (110a):**

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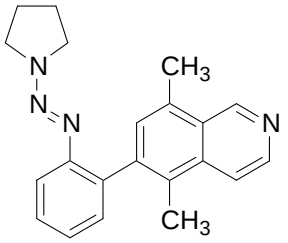
[97] G. W. Gribble, M. G. Saulnier, J. A. Obaza-Nutaitis, D. M. Ketcha, *J. Org. Chem*. **1992**, *57*, 5891



Prepared according to **TP8** from 1-(2-iodophenylazo)pyrrolidine (**73**) (903 mg, 3 mmol), *i*-PrMgCl·LiCl (2.4 mL, 3.3 mmol, 1.39 M in THF), $ZnBr_2$ (3 mL, 3 mmol, 1.0 M in THF), tetrakis(triphenylphosphine)palladium (104 mg, 0.09 mmol), 6-bromo-5,8-dimethyl-isoquinoline[84] (**109**) (705 mg, 3 mmol). Reaction condition: -40 °C to -30 °C, 1 h; -30 °C to -5 °C, 0.5 h; reflux, 6 h. Purification by flash chromatography (ether) yielded **110a** (772 mg, 78 %) as a pale yellow solid.

**mp**.: 55.5-56.5 °C.

**$^1$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.42 (s, 1H), 8.56 (d, $J$ = 6.2 Hz, 1H), 7.80 (d, $J$ = 6.2 Hz, 1H), 7.49 (d, $J$ = 8.0 Hz, 1H), 7.31-7.38 (m, 1H), 7.30 (s, 1H), 7.18-7.22 (m, 2H), 3.00-4.00 (br s, 4H), 2.73 (s, 3H), 2.36 (s, 3H), 1.77-1.87 (m, 4H).

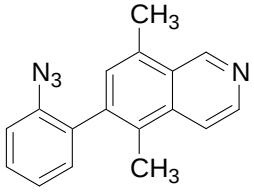
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 149.6, 148.7, 142.9, 141.8, 136.1, 135.7, 131.3, 130.4, 129.1, 128.3, 126.9, 124.9, 117.6, 117.1, 65.8, 23.7, 18.2, 15.6.

**MS** (70 eV, EI) *m/z* (%): 330 (5) [$M^+$], 260 (5), 245 (40), 232 (100), 217 (66), 202 (11), 189 (16), 108 (9).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2970 (w), 2867 (w), 1612 (w), 1443 (w), 1408 (m), 1314 (m), 1268 (w), 1209 (w), 1157 (w), 1102 (w) $cm^{-1}$.

**HRMS** (EI) for **$C_{21}H_{22}N_4$** (330.1844): found: 330.1837.

**Synthesis of 6-(2-azido-phenyl)-5,8-dimethyl-isoquinoline (111a):**



Prepared according to **TP17** from 2-(5,8-dimethyl-isoquinolin-6-yl)-phenyl]-pyrrolidin-1-yl-diazene (**110a**) (149 mg, 0.45 mmol), $KHSO_4$ (612 mg, 4.5 mmol), $NaN_3$ (146 mg, 2.25 mmol). Reaction condition: 25 °C, 12 h. Purification by flash chromatography (ether) yielded **111a** (117 mg, 95 %) as a pale yellow liquid.

**$^{1}$H-NMR** (300 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.46 (s, 1H), 8.60 (d, $J$ = 5.8 Hz, 1H), 7.83 (d, $J$ = 5.8 Hz, 1H), 7.40-7.50 (m, 1H), 7.15-7.30 (m, 4H), 2.77 (s, 3H), 2.39 (s, 3H).

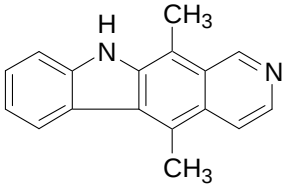
**$^{13}$C-NMR** (75 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 149.7, 143.4, 138.9, 138.0, 135.7, 133.3, 132.6, 131.2, 130.1, 129.5, 129.1, 124.8, 118.4, 117.9, 117.7, 18.3, 15.3.

**MS** (70 eV, EI) *m/z* (%): 274 (8) [$M^+$], 246 (100), 231 (74), 217 (10), 204 (12), 189 (8), 176 (8), 152 (6), 122 (8), 108 (14)

**IR** (neat) $\tilde{\nu}$ ($cm^{-1}$): 3057 (w), 2961 (w), 2923 (w), 2855 (w), 2123 (s), 2098 (s), 1612 (m), 1482 (m), 1382 (w), 1301 (m), 1277 (m), 1034 (w) $cm^{-1}$.

**HRMS** (EI) for **$C_{17}H_{14}N_4$** (274.1218): found: 274.1221.

**Synthesis of isoellipticine (72a):**




A solution of the aryl azide (**111a**) (22 mg, 0.08 mmol) in mesitylene (1 mL) was heated at reflux. After 5 h, the solvent was evaporated *in vacuo* to give the crude product. Purification by flash chromatography (methanol/ether = 1 : 9) yielded the pure product **72a** (12 mg, 63 %) as a yellow solid.

**mp**.: 309.0-310.0 °C. (lit.[96] m.p. 312-314 $^{o}$C )

**$^{1}$H-NMR** (400 MHz, DMSO-$d_6$, 25 °C) $\delta$/ppm: 11.4 (br s, 1H), 9.54 (s, 1H), 8.08 (d, $J$ = 6.0 Hz, 1H), 7.44-7.58 (m, 2H), 7.20 (t, $J$ = 8.0 Hz, 1H), 3.10 (s, 3H), 2.92 (s, 3H).

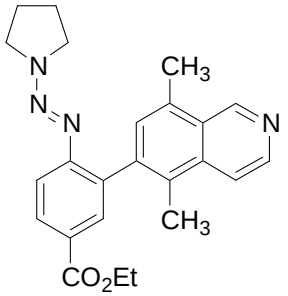
**$^{13}$C-NMR** (100 MHz, DMSO-$d_6$, 25 °C) $\delta$/ppm: 149.5, 143.8, 139.2, 139.1, 128.9, 128.3, 126.4, 125.9, 125.5, 124.9, 123.3, 119.6, 117.5, 111.4, 111.3, 15.2, 12.6.

**MS** (70 eV, EI) *m/z* (%): 246 (100) [$M^+$], 231 (29), 217 (9), 123 (12), 108 (9), 95 (6).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3420 (s), 3143 (m), 3076 (m), 2977 (w), 2921 (w), 2869 (w), 1613 (m), 1596 (m), 1497 (w), 1461 (w), 1406 (m), 1319 (m), 1273 (m), 1230 (m), 1012 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_{17}H_{14}N_2$** (246.1157): found: 246.1140.

**Synthesis of 3-(5,8-dimethyl-isoquinolin-6-yl)-4-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (110b):**



Prepared according to **TP8** from 1-(4-carbethoxy-2-iodophenylazo)pyrrolidine (**28c**) (1.2 g, 3 mmol), *i*-PrMgCl·LiCl (2.4 mL, 3.3 mmol, 1.39 M in THF), $ZnBr_2$ (3 mL, 3 mmol, 1 M in THF), tetrakis(triphenylphosphine)palladium (104 mg, 0.09 mmol), 6-bromo-5,8-dimethyl-isoquinoline[84] (**109**) (705 mg, 3 mmol). Reaction condition: -40 °C to -30 °C, 1 h; -30 °C to -5 °C, 0.5 h; reflux, 6 h. Purification by flash chromatography (ether) yielded **110b** (977 mg, 81 %) as a white solid.

**mp**.: 71.6-72.0 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.47 (s, 1H), 8.58 (d, $J$ = 5.9 Hz, 1H), 8.02 (d, $J$ = 8.8 Hz, 1H), 7.91 (s, 1H), 7.82 (d, $J$ = 5.9 Hz, 1H), 7.56 (d, $J$ = 8.8 Hz, 1H), 7.29 (s, 1H), 4.35 (q, $J$ = 7.3 Hz, 2H), 3.84 (br s, 2H), 3.14 (br s, 2H), 2.75 (s, 3H), 2.35 (s, 3H), 1.86 (br s, 4H), 1.36 (t, $J$ = 7.3 Hz, 3H).

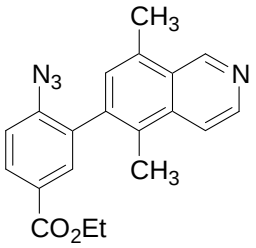
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 166.8, 152.4, 149.8, 142.9, 136.1, 136.0, 132.3, 132.0, 131.3, 130.0, 129.5, 127.2, 126.7, 118.0, 117.0, 116.8, 61.0, 51.2, 46.7, 24.1, 23.5, 18.4, 15.9, 14.6.

**MS** (70 eV, EI) *m/z* (%): 402 (7) [$M^+$], 357 (8), 317 (56), 260 (25), 232 (100), 216 (41), 202 (15), 189 (7), 115 (5), 86 (14).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2975 (w), 2870 (w), 1707 (s), 1600 (m), 1401 (m), 1362 (m), 1310 (m), 1283 (m), 1263 (m), 1240 (s), 1100 (s), 1026 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_{24}H_{26}N_4O_2$** (402.2056): found: 402.2042.

**Synthesis of 4-azido-3-(5,8-dimethyl-isoquinolin-6-yl)-benzoic acid ethyl ester (111b):**



Prepared according to **TP16** from 3-(5,8-dimethyl-isoquinolin-6-yl)-4-(pyrrolidin-1-ylazo)-benzoic acid ethyl ester (**110b**) (201 mg, 0.5 mmol), $NaN_3$ (65 mg, 1 mmol), $BF_3 \cdot OEt_2$ (0.25 mL, 1 mmol) and trifluoroacetic acid (0.08 mL, 1 mmol). Reaction condition: 25 °C, 20 min. Purification by flash chromatography (ether) yielded **111b** (131 mg, 76 %) as a pale yellow solid.

**mp**.: 122.5-123.9 °C.

**$^1$H-NMR** (600 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 9.46 (s, 1H), 8.62 (d, $J$ = 5.8 Hz, 1H), 8.12 (d, $J$ = 8.4 Hz, 1H), 7.91 (s, 1H), 7.83 (d, $J$ = 5.8 Hz, 1H), 7.30 (d, $J$ = 8.4 Hz, 1H), 7.16 (s, 1H), 4.36 (q, $J$ = 7.0 Hz, 2H), 2.77 (s, 3H), 2.38 (s, 3H), 1.37 (t, $J$ = 7.0 Hz, 3H).

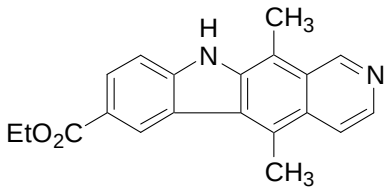
**$^{13}$C-NMR** (150 MHz, $CDCl_3$, 25 °C) $\delta$/ppm: 165.6, 149.7, 143.4, 142.5, 138.0, 135.7, 133.2, 132.9, 132.5, 130.5, 129.8, 129.6, 127.2, 127.0, 118.2, 117.6, 61.2, 18.3, 15.3, 14.3.

**MS** (70 eV, EI) *m/z* (%): 346 (18) [$M^+$], 318 (100), 303 (43), 289 (77), 275 (54), 245 (70), 230 (20), 216 (12), 189 (8), 145 (7), 108 (11).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 2970 (w), 2124 (s), 1712 (s), 1604 (m), 1586 (m), 1494 (w), 1466 (w), 1444 (w), 1385 (w), 1364 (w), 1285 (s), 1228 (s), 1126 (m), 1098 (m), 1026 (m) $cm^{-1}$.

**HRMS** (EI) for **$C_{20}H_{18}N_4O_2$** (346.1430): found: 346.1442.

**Synthesis of 7-carbethoxyisoellipticine (72b):**




A solution of the aryl azide (**111b**) (464 mg, 1.34 mmol) in the mixture of mesitylene (14 mL) and *N*,*N*-dimethylformamide (1 mL) was heated at reflux. After 6 h, the solvent was evaporated *in vacuo* to give the crude product. Purification by flash chromatography (methanol/ether = 1 : 9) yielded the pure product **72b** (273 mg, 64 %) as a bright yellow solid.

**mp**.: 250 °C dec.

**$^1$H-NMR** (300 MHz, DMSO-$d_6$, 25 °C) $\delta$/ppm: 11.73 (s, 1H), 9.55 (s, 1H), 8.88 (s, 1H), 8.40 (d, $J$ = 5.9 Hz, 1H), 8.05-8.15 (m, 2H), 7.56 (d, $J$ = 8.6 Hz, 1H), 4.33 (q, $J$ = 7.0 Hz, 2H), 3.09 (s, 3H), 2.90 (s, 3H), 1.34 (t, $J$ = 7.0 Hz, 3H)

**$^{13}$C-NMR** (75 MHz, DMSO-$d_6$, 25 °C) $\delta$/ppm: 166.9, 149.6, 146.8, 139.7, 139.3, 129.5, 129.4, 126.3, 126.2, 125.8, 123.1, 120.9, 117.5, 117.4, 112.3, 111.1, 61.1, 15.2, 15.0, 12.5.

**MS** (70 eV, EI) *m/z* (%): 318 (100) [$M^+$], 304 (33), 289 (40), 273 (21), 245 (33), 229 (19), 207 (35), 191 (6), 175 (6), 115 (10), 73 (10).

**IR** (KBr) $\tilde{\nu}$ ($cm^{-1}$): 3200 (s), 2925 (w), 1710 (s), 1612 (m), 1465 (w), 1364 (w), 1277 (m), 1244 (s), 1167 (m), 1098 (m), 1017 (m) $cm^{-1}$.

**HRMS** (EI) for $\mathbf{C_{20}H_{18}N_2O_2}$ (318.1368): found: 318.1349.

## 14. Curriculum Vitae

Name: Ching-Yuan, Liu
Date of birth: 12th March, 1978
Nationality: Taiwanese
Place of birth: Taipei, Taiwan, Republic of China
Gender: male
Marital status: single

**EDUCATION**

| | | |
|---|---|---|
| Oct./2003 - Mar./2007 | **Ludwig-Maximilians-Universität (University of Munich)**<br>**Department Chemie und Biochemie**<br>Ph.D. under the supervision of Prof. Dr. Paul Knochel | Germany |
| Sep./2000 - Jun./2002 | **National Taiwan University (NTU)**<br>**Department of Chemistry**<br>Master of Science Degree under the supervision of Prof. Dr. Tien-Yau, Luh<br><br>Thesis Title: "Combining Furan Annulation, Heck, and Sonogashira Cross-coupling Reactions Leading to Molecular Wires" | Taipei, Taiwan |
| Sep./1996 - Jun./2000 | **National Tsing-Hua University (NTHU)**<br>**Department of Nuclear Science**<br>**Department of Chemistry**<br>Bachelor of Science Degree in Nuclear Science (major) and Chemistry (minor). | Hsinchu, Taiwan |
| Sep./1993 - Jun./1996 | **Taipei Municipal Sungshen Senior High school**<br>Graduated with Honor.<br>Ranked 2nd in a class of fifty students. | Taipei, Taiwan |

**EXPERIENCE**

| | |
|---|---|
| Sep./2004 - Sep./2006 | *Teaching Assistant*, **Department Chemie und Biochemie, Ludwig-Maximilians-Universität (University of Munich)**<br><br>Employed by the University of Munich with the engagement in teaching and supervising *Organisch-Chemisches Praktikum* (organic chemistry practice) of the students of Biology. |
| Jul./2002 - Jul./2003 | *Teaching Assistant*, **Department of Chemistry, National Taiwan University (NTU)**<br><br>Employed by National Taiwan University with the engagement in teaching courses and experiments including *sophomore organic chemistry* and *organic chemistry laboratory*. |

**LANGUAGES**

*Chinese*: mother tongue
*English*: fluent in writing, reading, and speaking
*German*: fluent in reading and speaking
*Japanese*: basic level

## PUBLICATIONS

1. **C.-Y. Liu**, P. Knochel, "Preparation of Polyfunctional Aryl Azides from Aryl Triazenes. A New Synthesis of Ellipticine, 9-Methoxyellipticine, Isoellipticine, and 7-Carbethoxyisoellipticine", *J. Org. Chem.* **2007**, *submitted for publication.*

2. **C.-Y. Liu**, P. Knochel, "A Direct Insertion Reaction of Zn·LiCl into Functionalized Iodo- or Bromophenyl Triazenes", *manuscript in preparation.*

3. **C.-Y. Liu**, A. Gavryushin, P. Knochel, "Synthesis of Functionalized *o*-, *m*-, or *p*-Terphenyls *via* Consecutive Cross-Coupling Reactions of Arylboronic Esters Bearing a Triazene Moiety", *manuscript in preparation.*

4. **C.-Y. Liu**, H. Ren, P. Knochel, "Magnesiated Unsaturated Silylated Cyanohydrins as Synthetic Equivalents of Aromatic and Heterocyclic Grignard Reagents Bearing a Ketone or an Aldehyde", *Org. Lett.* **2006**, *8*, 617-619.

5. **C.-Y. Liu**, P. Knochel, "Preparation of Polyfunctional Arylmagnesium Reagents Bearing a Triazene Moiety. A New Carbazole Synthesis", *Org. Lett.* **2005**, *7*, 2543-2546.

6. **C.-Y. Liu**, T.-Y. Luh, "Combining Furan Annulation, Heck Reaction, and Sonogashira Coupling for the Synthesis of Oligoaryls", *Org. Lett.* **2002**, *4*, 4305-4307.

7. C. F. Lee, **C.-Y. Liu**, H. C. Song, S. J. Luo, J. C. Tseng, H. H. Tso, T. Y. Luh, "Bidirectional Iterative Synthesis of Alternating Benzene–Furan Oligomers Towards Molecular Wires ", *Chem. Commun.* **2002**, 2824.

## POSTERS AND SEMINARS

1. "*Preparation of Polyfunctional Arylmagnesium Reagents Bearing a Triazene Moiety. A New Approach to Ellipticine and Isoellipticine*"; im Rahmen des organisch-chemischen Doktorandenkolloquiums der **LMU** (Lecture, Ludwig-Maximilians-Universität München) (University of Munich), 26$^{th}$, June, 2006 in Munich, Germany

2. "*Preparation of Polyfunctional Arylmagnesium Reagents Bearing a Triazene Moiety. A New Carbazole Synthesis*"; Poster P-354, 13th IUPAC International Symposium on Organometallic Chemistry directed toward Organic Synthesis (OMCOS-13), Geneva, Switzerland, 17$^{th}$-21$^{th}$, July, 2005.

3. "*Preparation of Polyfunctional Arylmagnesium Reagents Bearing a Triazene Moiety. A New Carbazole Synthesis*"; Poster, Industrietag (Industry day), München, Germany, 15$^{th}$, October, 2004.

4. "Combining Furan Annulation, Heck Reaction, and Sonogashira Coupling for the Synthesis of Oligoaryls"; Poster, 12th IUPAC International Symposium on Organometallic Chemistry directed toward Organic Synthesis (OMCOS-12), Toronto, Canada, 6$^{th}$-10$^{th}$, July, 2003.

5. "Combination of Furan Annulation, Heck, and Sonogashira Cross-Coupling Reactions Leading to Molecular Wires"; Poster, International Chemical Conference Taipei (ICCT, Materials Chemistry), Taipei, Taiwan, 23$^{th}$-26$^{th}$, February, 2002.

München, den 07.02.2007