Enantioselective Copper-Catalyzed Oxy-Alkynylation of Diazo Compounds

Durga Prasad Hari and Jerome Waser

Laboratory of Catalysis and Organic Synthesis, Ecole Polytechnique Fédérale de Lausanne, EPFL SB ISIC LCSO, BCH 4306, 1015 Lausanne, Switzerland.

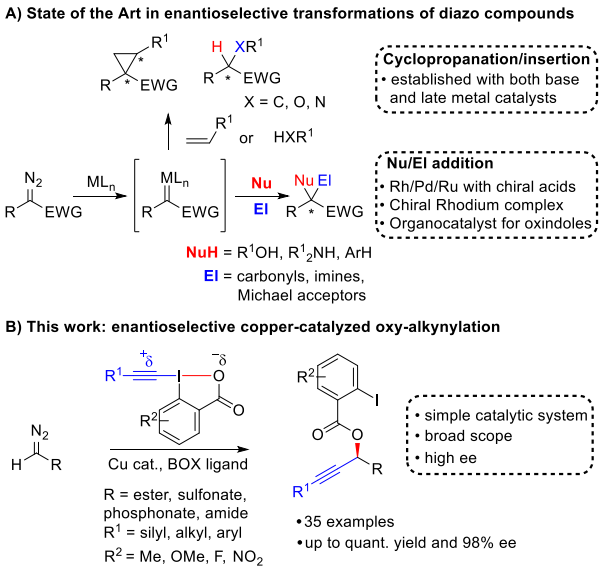
Supporting Information Placeholder

ABSTRACT: Enantioselective catalytic methods allowing the addition of both a nucleophile and an electrophile onto diazo compounds give a fast access into important building blocks. Herein, we report the highly enantioselective oxyalkynylation of diazo compounds using ethynylbenziodoxol-(on)e (EBX) reagents and a simple copper bisoxazoline (BOX) catalyst. The obtained α-benzoyloxy propargylic esters are useful building blocks, which are difficult to synthesize in enantiopure form using other methods. The obtained products could be efficiently transformed into vicinal diols and α-hydroxy propargylic esters without loss in enantiopurity.

Due to the different biological and optical properties of enantiomers, the synthesis of enantiopure compounds is an important field of research in organic chemistry. In this respect, enantioselective metal-catalyzed reactions of diazo compounds proceeding via carbenoid intermediates have been highly successful.[1] Asymmetric cyclopropanation and insertion into carbon or heteroatom- hydrogen bonds are now broadly used for the asymmetric synthesis of important building blocks. The generation of ylides by reaction of electrophilic carbenes with nucleophiles opened the way for [2,3] sigmatropic rearrangements and cycloaddition reactions.[2] Recently, researchers have focused on direct reactions of ylides generated from diazo compounds with electrophiles, allowing the introduction of more diverse functionalities on the carbon center.[3] The development of enantioselective variations of such processes is highly challenging. Recent breakthroughs have been realized based on elegant cooperative catalytic systems involving late metal catalysts such as rhodium/iridium,[4] palladium[5] and ruthenium,[6] and either a chiral phosphoric or Lewis acid (Scheme 1A). Nevertheless, this approach is limited to electrophilic partners that can be activated by Brønsted or Lewis acids, and it is based on a relative complex dual catalyst system. Transformations relying on a single chiral catalyst remain extremely rare in this new type of carbene transformations, including two examples of rhodium catalysts[7] and an organocatalytic system specific to diazo compounds derived from oxindoles.[8]

Surprisingly, despite their success in enantioselective cyclopropanation and X-H insertion reactions,[9] copper catalysts have been used so far only in racemic multi-component reactions involving diazo compounds.[10] Recently, our group developed a copper-catalyzed oxyalkynylation of diazo compounds[11] based on the use of EthynylBenziodoXolones (EBX) reagents.[12] Herein, we report the successful development of an enantioselective variation of this transformation, which constitutes the first asymmetric simultaneous introduction of an alkyne and an ester onto a diazo compound (Scheme 1B). Importantly, the reaction required a single copper catalyst bearing a broadly available BOX ligand, and gave products in high yield with up to 98% *ee*. The obtained propargylic benzoyloxy esters are useful building blocks, which are difficult to access using traditional methods, such as alkyne addition to aldehydes,[13] due to the sensitivity of the products and required starting materials to basic conditions.[14] Furthermore, they could be easily transformed into other important building blocks, such as propargylic alcohols.

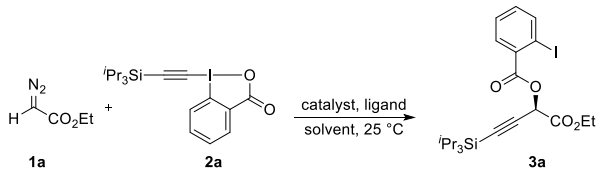
Scheme 1. Enantioselective transformations of diazo compounds.



We started our investigations by screening various ligands,[15] using ethyl diazoacetate (**1a**) with 1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)- one (TIPS-EBX, **2a**) and $Cu(OTf)_2$ as the copper source (Table 1).[16] Several classes of ligands, such as diimines, Salen, Phox or biphos-

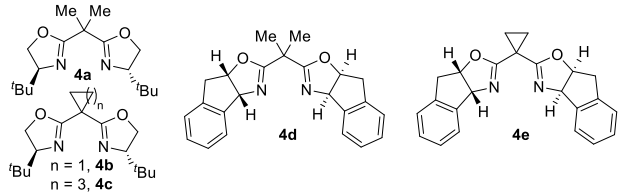
phines gave either low selectivity or low conversion.[15] ^{t}Bu-BOX ligand **4a** gave the desired propargylic ester **3a** in excellent yield with a promising 56% ee (entry 1). The use of cyclopropyl and cyclopentyl derived BOX ligands (**4b** and **4c**) didn't improve the enantioselectivity (entries 2 and 3). Indane-BOX ligand **4d** gave results identical to the ones obtained with ligand **4a**, whereas a slightly better enantioselectivity was observed with cyclopropyl substituted ligand **4e** (entries 4 and 5). Among the solvents tested[15] (entries 6-8), chlorobenzene emerged as the best solvent (84% yield with 70% *ee*, entry 7). Generating a cationic complex in situ from $AgSbF_6$ and CuCl provided a slight improvement (entry 9). No reaction was observed when using $AgClO_4$ or NaBARF(entries 10 and 11). $AgNTf_2$ gave the desired product in 91% yield and 84% ee (entry 12). Without $AgNTf_2$, no product was obtained (entry 13). Finally, the enantioselectivity could be improved to 90% by lowering the concentration of the reaction (entry 14).

Table 1. Optimization of the reaction conditions.[a]



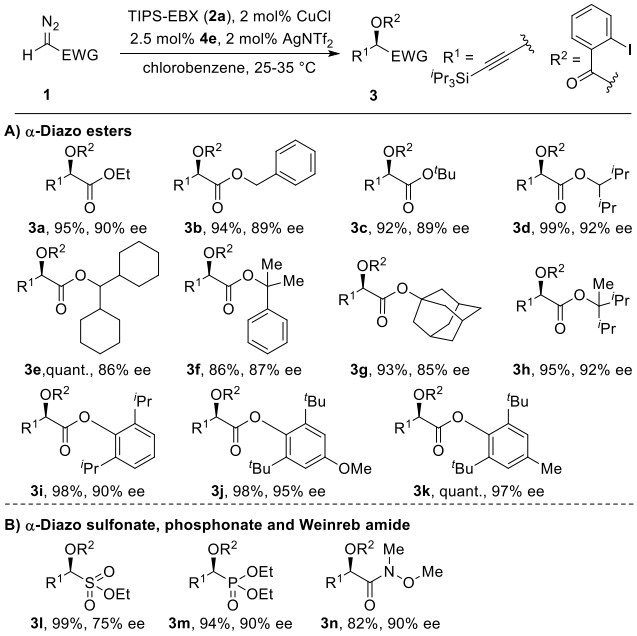
Entry	Catalyst	Ligand	Solvent	Time (h)	Yield[b] (%)	ee[c] (%)
1	$Cu(OTf)_2$	**4a**	DCE	0.5	97	56[e]
2	$Cu(OTf)_2$	**4b**	DCE	0.5	98	55[e]
3	$Cu(OTf)_2$	**4c**	DCE	0.5	98	54[e]
4	$Cu(OTf)_2$	**4d**	DCE	2	98	54
5	$Cu(OTf)_2$	**4e**	DCE	0.5	97	62
6	$Cu(OTf)_2$	**4e**	DCM	0.5	98	40
7	$Cu(OTf)_2$	**4e**	PhCl	2	84	70
8	$Cu(OTf)_2$	**4e**	xylene	2	79	69
9	$CuCl/AgSbF_6$	**4e**	PhCl	1	89	72
10	$CuCl/AgClO_4$	**4e**	PhCl	24	<5	nd[f]
11	CuCl/NaBARF	**4e**	PhCl	24	<5	nd
12	$CuCl/AgNTf_2$	**4e**	PhCl	18	91	84
13	CuCl	**4e**	PhCl	24	<5	nd
14[d]	$CuCl/AgNTf_2$	**4e**	PhCl	18	95	90

[a]Reaction conditions: 0.30 mmol ethyldiazoacetate (**1a**), 0.15 mmol TIPS-EBX (**2a**), copper catalyst (2.0 mol%), ligand (2.5 mol%), solvent (0.05 M), for entries 9-12 and 14: AgX or NaBARF (2.0 mol%). [b]Yield after purification by column chromatography. [c]Obtained by chiral HPLC. [d]0.025 M instead of 0.05 M. [e] The opposite enantiomer of the product was obtained. [f]nd = not determined.



To further improve the enantioselectivity, we investigated the influence of the structure of the *α*-diazo ester (Scheme 2A). Aliphatic diazoesters of different steric bulk afforded products **3a-h** in 85-92% *ee*. Hindered aryl diazo esters[18] provided higher enantioselectivities (up to 97%) (products **3i-k**). The reaction was not limited to *α*-diazo esters. Both ethyl diazomethanesulfonate and diethyl (diazomethyl)phosphonate gave the desired product **3l** and **3m** in high yield and moderate to high selectivity (Scheme 2B). Finally, diazo Weinreb amide also delivered the product **3n**, which open up possibilities for further derivatization.[19]

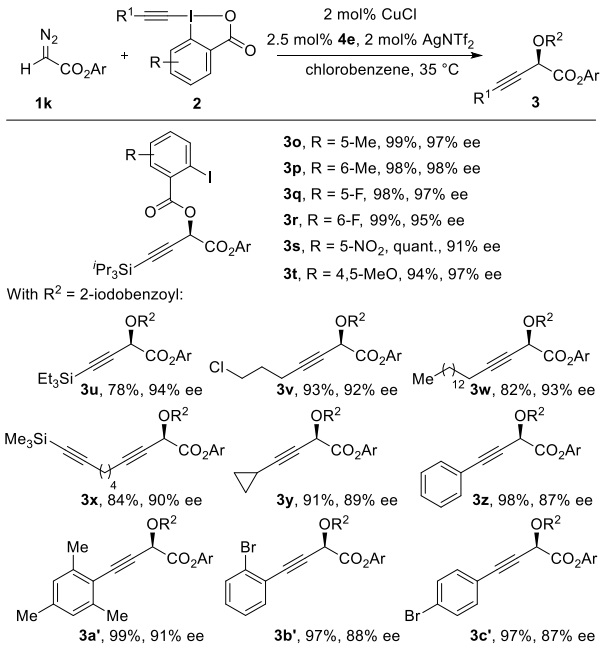
Scheme 2. Scope of diazo compounds with TIPS-EBX (2a).



We next examined the scope of R-EBX reagents using 2,6-di-*tert*-butyl-4-methylphenyl 2- diazoacetate (**1k**) (Scheme 3). Electron-donating and -withdrawing groups were well tolerated on the aryl ring of TIPS-EBX (**2a**) (products **30-t**). The reaction was successful with a triethyl silyl group (product **3u**), whereas no product could be isolated with a trimethylsilyl group. Aliphatic EBX reagents bearing substituents such as long alkyl chain, chloro, TMS-alkyne and a cyclopropyl group worked efficiently in this transformation, giving products **3v-y**. Finally, EBX reagents bearing aryl substituents on the alkyne led to the desired products **3z-c'** in excellent yields and good enantioselectivities.

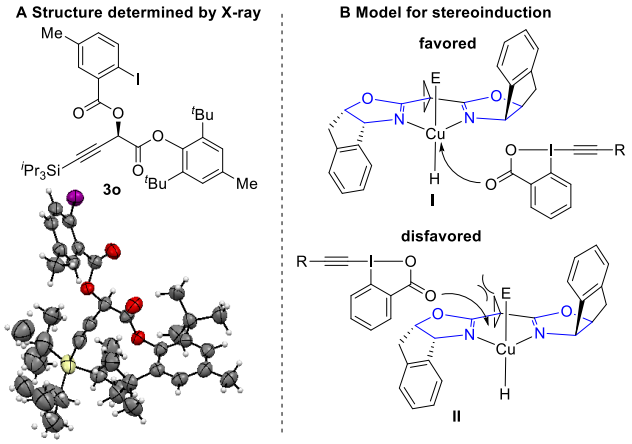
The absolute configuration of **30** could be determined by X-ray analysis (Figure 1A).[20] The observed stereochemistry would be in agreement with an attack of the carboxylate of the reagent in the free quadrant opposite to the ester group on a three coordinate copper carbene complex with a 90° angle between the ligand and the carbene plan,[9g] followed by stereospecific alkynylation with retention of configuration (**I**, Figure 1B). Further studies will be needed to support the proposed stereoinduction model.

Scheme 3. Scope of R-EBX reagents. Ar = 2,6-di-*tert*-butyl-4-methylphenyl.



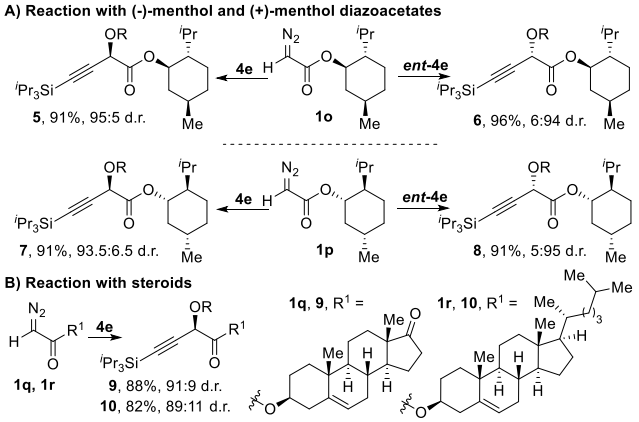
When (-) menthol diazoacetate **10** was subjected to the standard conditions, the desired product **5** was obtained in good yield with 95:5 d.r. (Scheme 4A).[21] The use of the *S*-enantiomer ***ent*-4i** of ligand **4i** afforded the other diastereomer **6** in good yield with 6:94 d.r, demonstrating that the configuration at the new stereocenter could be controlled by the chiral catalyst. Similar results were obtained with (+) menthol diazoacetate **1p**. All four diastereomers can therefore be obtained in good yield and selectivity. Good ligand control over the stereoselectivity could also be achieved with more complex diazo compounds **1q** and **1r** derived from steroids (Scheme 4B).

Figure 1. Absolute configuration and stereoinduction model.



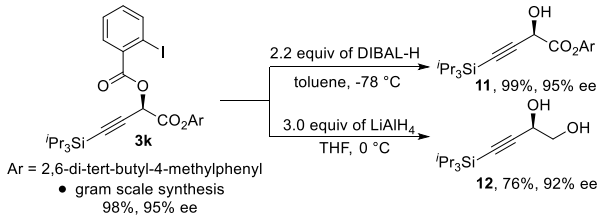
The obtained products were then further transformed into useful building blocks for organic synthesis (Scheme 5). Compound **3k** was synthesized on gram scale in 98% yield with 95% *ee*. The benzoyl group could be readily removed using DIBAL-H, thus affording the α-hydroxy propargylic ester **11** in 99% yield with retention of enantiopurity. Furthermore, vicinal diol **12**[22] could be synthesized by reduction of **3k** using $LiAlH_4$. Such alkynyl diol building blocks are useful in synthetic chemistry, but are usually accessed via longer multi step procedures.[23]

Scheme 4. Reactions with menthol and steroids esters.



Reaction conditions: 0.30 mmol diazoacetate (**1**), 0.15 mmol TIPS-EBX (**2a**), CuCl (2.0 mol%), ligand (2.5 mol%), $AgNTf_2$ (2 mol%), PhCl (0.025 M), 25 °C. R = 2-iodobenzoyl.

Scheme 5. Scale up and product modifications.



In summary, we have developed a highly enantioselective oxyalkynylation of diazo compounds. This transformation is the first example of copper-catalyzed addition of both a nucleophile and an electrophile onto a carbenoid intermediate. A broad range of EBX reagents and diazo compounds were well tolerated. The reaction proceeds under mild conditions, giving highly functionalized products with excellent yields and selectivities. The obtained products were efficiently transformed into useful building blocks, such as α-hydroxy propargylic esters and vicinal diols, in a single step without loss of enantioselectivity. Further extending this methodology to other diazo compounds and hypervalent iodine reagents is currently under investigation in our laboratory.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures and analytical data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

jerome.waser@epfl.ch

Notes

The authors declare no competing financial interests.

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(15) See Supporting Information for a full list of reaction conditions and ligands.

(16) $Cu(CH_3CN)_4\ BF_4$ was used for the racemic reaction. See ref. 11.

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(19) No reaction with alkyl-, aryl- and vinyl-substituted diazo compounds was observed, due to the lower reactivity of the copper bisoxazoline complexes compared to $Cu(CH_3CN)_4\ BF_4$.

(20) CCDC 1534166, see the Supporting Information, the configuration of the other substrates was assigned by analogy.

(21) The use of achiral ligand resulted in low selectivity (d.r. = 54:46).

(22) The enantioselectivity of **12** was determined after derivatization (see the Supporting Information).

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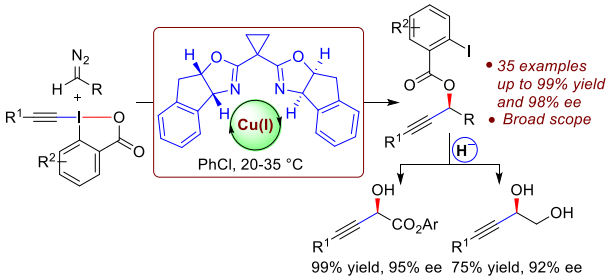
Cu(I)
PhCl, 20-35 °C
• 35 examples
up to 99% yield
and 98% ee
• Broad scope
99% yield, 95% ee
75% yield, 92% ee

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Durga Prasad Hari and Jerome Waser

Laboratory of Catalysis and Organic Synthesis, Ecole Polytechnique Fédérale de Lausanne, EPFL SB ISIC LCSO, BCH 4306, 1015 Lausanne, Switzerland.

Supporting Information

(200 pages)

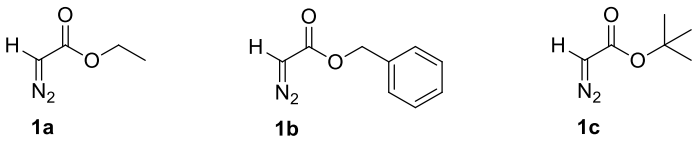
Table of Contents

1. General Methods

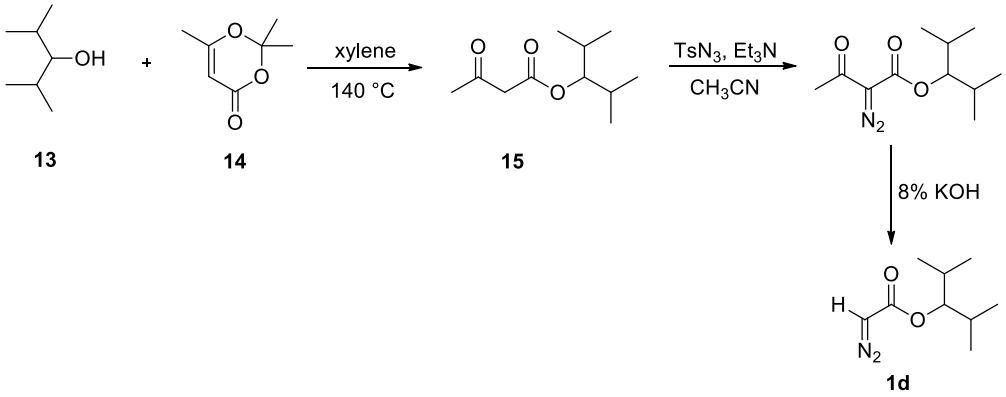
All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et_2O, CH_3CN, toluene, hexane and CH_2Cl_2 were dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 10 ppm, *Karl-Fischer* titration). The solvents were degassed by Freeze-Pump-Thaw method when mentioned. All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Aplichem or Merck and used as such unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F_{254} TLC glass plates or aluminium plates and visualized with UV light, permanganate stain, CAN stain or Anisaldehyde stain. Melting points were measured on a Büchi B-540 melting point apparatus using open glass capillaries, the data is uncorrected. ^{1}H-NMR spectra were recorded on a Brucker DPX-400 400 MHz spectrometer in chloroform-d, DMSO-d_6 or CD_3OD, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal DMSO signal at 2.50 ppm or the internal methanol signal at 3.30 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation).^{13}C-NMR spectra were recorded with ^{1}H-decoupling on a Brucker DPX-400 100 MHz spectrometer in chloroform-d, DMSO-d_6 or CD_3OD, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm, the internal DMSO signal at 39.5 ppm or the internal methanol signal at 49.0 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm^{-1} (w = weak, m = medium, s = strong, br = broad). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. HPLC measurements were done on a Agilent 1260 Infinity autosampler using a CHIRALPAK IA, IB, IC or ID column from DAICEL Chemical. Optical rotations were measured on a polarimeter using a 10 cm cell with a Na 589 nm filter. The specific solvents and concentrations (in g/100 mL) are indicated.

2. Synthesis of Diazo-compounds

Ethyl 2-diazoacetate (**1a**), benzyl 2-diazoacetate (**1b)**, and *tert*-butyl 2-diazoacetate (**1c**) were directly purchased from Sigma Aldrich.



2,4-Dimethylpentan-3-yl 2-diazoacetate (1d)

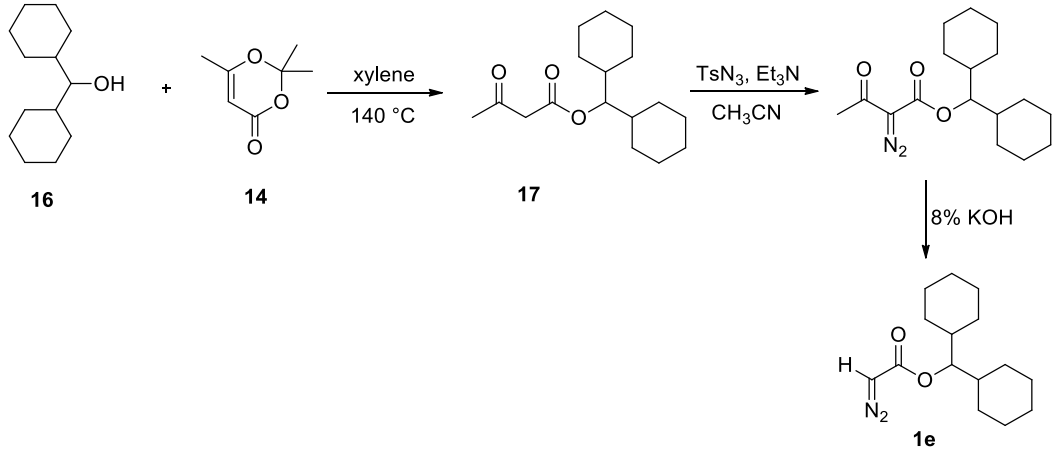


Following a slightly modified procedure,[1] a mixture of 2,4-dimethylpentan-3-ol (**13**) (3.50 mL, 25.0 mmol, 1.00 equiv), 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (**14**) (3.55 g, 25.0 mmol, 1.00 equiv), and xylene (5 mL) was stirred at 140 °C for 2 h. After cooling to room temperature, the xylene was evaporated and the residue was purified by flash column chromatography using 1:50 EtOAc:pentane as mobile phase to afford 2,4-dimethylpentan-3-yl 3-oxobutanoate (**15)** as a colorless oil (4.2 g, 21 mmol, 84%). TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.36, $KMnO_4$;^{1}H NMR (400 MHz, $CDCl_3$): δ 12.17 (s, 0.08H, O*H* of enol form), 4.97 (s, 0.08H, vinyl *H* of enol form), 4.60 (t, *J* = 6.1 Hz, 1H, OC*H*), 3.46 (s, 1.84H, CH_3COCH_2 of keto form), 2.26 (s, 2.76H, CH_3COCH_2 of keto form), 1.92 (s, 0.24H, CH_3 of enol form), 1.87 (dq, *J* = 13.3, 6.8 Hz, 2H, 2 X C*H*$(CH_3)_2$), 0.86 (d, *J* = 6.8 Hz, 6H, CH$(CH_3)_2$), 0.83 (d, *J* = 6.7 Hz, 6H, CH$(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.7, 167.0, 84.0, 50.1, 30.3, 29.2, 19.4, 17.1. Enol form, ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 172.7, 89.6, 81.9. Some carbons of enol form were not resolved at 100 MHz. The characterization data of keto form corresponded to the reported values.[1]

Following a slightly modified procedure,[1] to a solution of 2,4-dimethylpentan-3-yl 3-oxobutanoate (**15**) (1.0 g, 5.0 mmol, 1.0 equiv) in acetonitrile (6 mL was added triethylamine (660 mg, 6.50 mmol, 1.30 equiv). The reaction mixture was cooled in an ice bath and a solution of tosyl azide

(1.1 g, 5.5 mmol, 1.1 equiv) in acetonitrile (6 mL) was added slowly. The reaction mixture was allowed to warm to r.t. After stirring for 20 h, the solvent was removed under reduced pressure. The residue was dissolved in ether (30 mL) and washed with 8% aqueous KOH solution. The organic layer was separated, dried over $MgSO_4$, and evaporated. The crude product was re-dissolved in acetonitrile (15 mL) and 8% aqueous KOH (25 mL) solution was added at r.t. After vigorous stirring for 4 h, water (15 mL) was added and the reaction mixture was extracted with diethyl ether (2 X 30 mL). The combined organic layers were dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography using 1:20 Et_2O:pentane as mobile phase to afford 2,4-dimethylpentan-3-yl 2-diazoacetate (**1d)** as a yellow oil (800 mg, 4.35 mmol, 87%). TLC (Et_2O:pentane, 1:9 v/v): R_f = 0.55, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.73 (br s, 1H, C*H*N_2), 4.62 (t, *J* = 6.2 Hz, 1H, OC*H*), 1.88 (dq, *J* = 13.4, 6.7 Hz, 2H, 2 X C*H*$(CH_3)_2$), 0.88 (d, *J* = 6.8 Hz, 6H, CH(C*H*$_3)_2$), 0.85 (d, *J* = 6.7 Hz, 6H, CH(C*H*$_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 83.1, 45.8, 29.4, 19.5, 17.1. The characterization data corresponded to the reported values.[1]

Dicyclohexylmethyl 2-diazoacetate (1e)



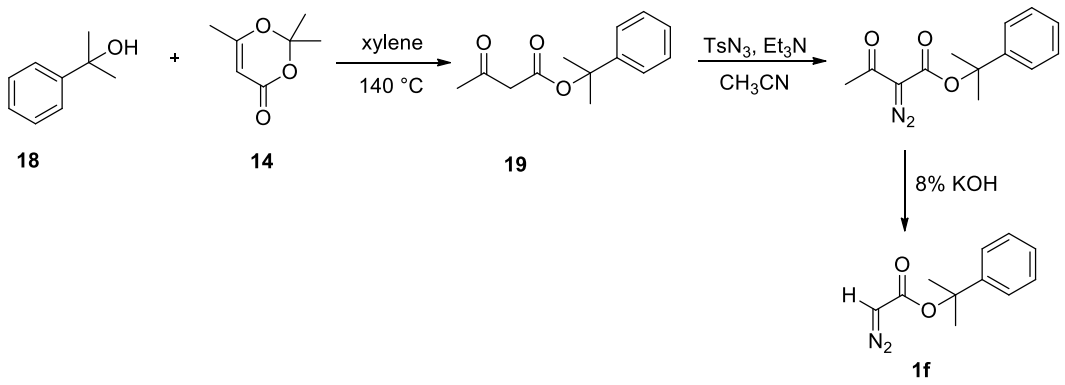
16 14 17 1e

Following a slightly modified procedure,[1] a mixture of dicyclohexylmethanol (**16**) (2.45 g, 12.5 mmol, 1.00 equiv), 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (**14**) (1.78 g, 12.5 mmol, 1.00 equiv), and xylene (2.5 mL) was stirred at 140 °C for 2 h. After cooling to room temperature, the xylene was evaporated and the residue was purified by flash column chromatography using 1:50 EtOAc:pentane as mobile phase to afford dicyclohexylmethyl 3-oxobutanoate (**17)** as a white solid (3.00 g, 10.7 mmol, 86%). Mp: 64.5–66.8 °C; TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.36, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.20 (s, 0.09H, O*H* of enol form), 4.99 (s, 0.09H, vinyl *H* of enol

form), 4.67 (t, *J* = 5.8 Hz, 1H, OC*H*), 3.47 (s, 1.8H, CH_3COCH_2 of keto form), 2.29 (s, 2.7H, CH_3COCH_2 of keto form), 1.95 (s, 0.27H, CH_3 of enol form), 1.81–1.42 (m, 12H, 2 X Cy–C*H* and 5 X Cy–CH_2), 1.34–0.83 (m, 10H, 5 X Cy–CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.9, 167.0, 82.8, 50.2, 38.2, 30.4, 29.8, 27.4, 26.3, 26.2, 26.0. Enol form, ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 172.8, 89.8, 80.8, 38.3, 21.2, some carbons of enol form were not resolved at 100 MHz; IR ν 2976 (s), 2928 (s), 2862 (m), 2109 (w), 1725 (m), 1646 (w), 1447 (m), 1403 (m), 1313 (m), 1246 (m), 1188 (m), 1152 (m), 1056 (s), 891 (w); HRMS (ESI) calcd. for $C_{17}H_{28}NaO_3^+$ $[M+Na]^+$ 303.1931; found 303.1928.

Following a slightly modified procedure,[1] to a solution of dicyclohexylmethyl 3-oxobutanoate (**17**) (1.4 g, 5.0 mmol, 1.0 equiv) in acetonitrile (6 mL) was added triethylamine (660 mg, 6.50 mmol, 1.30 equiv). The reaction mixture was cooled in an ice bath and a solution of tosyl azide (1.1 g, 5.5 mmol, 1.1 equiv) in acetonitrile (6 mL) was added slowly. The reaction mixture was allowed to warm to r.t. After stirring for 20 h, the solvent was removed under reduced pressure. The residue was dissolved in ether (30 mL) and washed with 8% aqueous KOH solution. The organic layer was separated, dried over $MgSO_4$, and evaporated. The crude product was re-dissolved in acetonitrile (15 mL) and 8% aqueous KOH (25 mL) solution was added at r.t. After vigorous stirring for 4 h, water (15 mL) was added and the reaction mixture was extracted with diethyl ether (2 X 30 mL). The combined organic layers were dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography using 1:40 Et_2O:pentane as mobile phase to afford dicyclohexylmethyl 2-diazoacetate (**1e)** as a yellow solid (1.10 g, 4.16 mmol, 83%). Mp (Dec.): 81.2–83.2 °C; TLC (Et_2O:pentane, 1:25 v/v): R_f = 0.52, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$):δ 4.73 (bs, 1H, C*H*N_2), 4.67 (t, *J* = 5.9 Hz, 1H, OC*H*), 1.84–1.45 (m, 12H, 2 X Cy–C*H* and 5 X Cy–CH_2), 1.31–0.88 (m, 10H, 5 X Cy–CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 82.0, 45.9, 38.4, 29.8, 27.4, 26.3, 26.2, 26.0; IR ν 2929 (s), 2855 (m), 2110 (s), 1692 (s), 1451 (w), 1377 (m), 1242 (m), 1191 (s), 1099 (w), 991 (w), 931 (w); HRMS (ESI) calcd. for $C_{15}H_{24}N_2O_2$ [M+] 264.1832; found 264.1836.

2-Phenylpropan-2-yl 2-diazoacetate (1f)

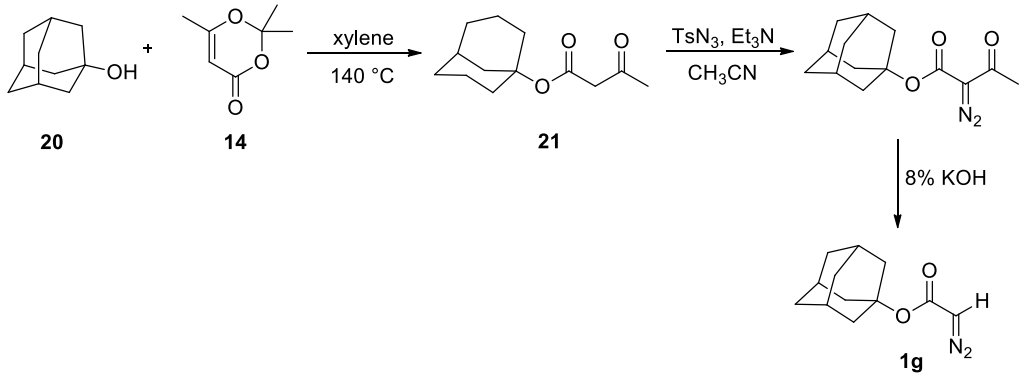


Following a slightly modified procedure,[1] a mixture of 2-phenylpropan-2-ol (**18**) (3.4 g, 25 mmol, 1.0 equiv), 2,2,6-trimethyl-4H-1,3-dioxin-4-one (**14**) (3.55 g, 25.0 mmol, 1.00 equiv), and xylene (5 mL) was stirred at 140 °C for 2 h. After cooling to room temperature, the xylene was evaporated and the residue was purified by flash column chromatography using 1:5 EtOAc:pentane as mobile phase to afford 2-phenylpropan-2-yl 3-oxobutanoate (**19)** as a colorless oil (2.60 g, 11.8 mmol, 48%). TLC (EtOAc:pentane, 1:4 v/v): R_f = 0.4, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.98 (s, 0.1H, O*H* of enol form), 7.41–7.31 (m, 4H, Ar*H*), 7.30–7.22 (m, 1H, Ar*H*), 5.06 (s, 0.1H, vinyl *H* of enol form), 3.43 (s, 1.8H, CH_3COCH_2 of keto form), 2.24 (s, 2.7H, CH_3COCH_2 of keto form), 1.93 (s, 0.3H, CH_3 of enol form), 1.80 (s, 5.4H, $OC(CH_3)_2Ar$ of keto form), 1.79 (s, 0.6H, $OC(CH_3)_2Ar$ of enol form); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.9, 165.5, 145.0, 128.2, 127.1, 124.2, 82.9, 51.1, 30.1, 28.3; Enol form, ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 171.7, 145.7, 128.1, 126.8, 123.9, 90.6, 81.5, 28.9, 21.1. The characterization data corresponded to the reported values.[2]

Following a slightly modified procedure,1 to a solution of 2-phenylpropan-2-yl 3-oxobutanoate (**19**) (1.1 g, 5.0 mmol, 1.0 equiv) in acetonitrile (6 mL) was added triethylamine (660 mg, 6.50 mmol, 1.30 equiv). The reaction mixture was cooled in an ice bath and a solution of tosyl azide (1.1 g, 5.5 mmol, 1.1 equiv) in acetonitrile (6 mL) was added slowly. The reaction mixture was allowed to warm to r.t. After stirring for 20 h, the solvent was removed under reduced pressure. The residue was dissolved in ether (30 mL) and washed with 8% aqueous KOH solution. The organic layer was separated, dried over $MgSO_4$, and evaporated. The crude product was re-dissolved in acetonitrile (15 mL) and 8% aqueous KOH (25 mL) solution was added at r.t. After vigorous stirring for 4 h, water (15 mL) was added and the reaction mixture was extracted with diethyl ether (2 X 30 mL). The combined organic layers were dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography using 1:10

Et_2O:pentane as mobile phase to afford 2-phenylpropan-2-yl 2-diazoacetate (**1f)** as a yellow oil (820 mg, 4.02 mmol, 80%). TLC (Et_2O:pentane, 1:10 v/v): R_f = 0.17, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.32 (m, 4H, Ar*H*), 7.28-7.24 (m, 1H, Ar*H*), 4.72 (br s, 1H, C*H*N_2), 1.81 (s, 6H, OC(C*H*$_3$)$_2$Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 145.6, 128.2, 127.0, 124.1, 82.4, 46.9, 28.9. The ^{1}H NMR data corresponded to the reported values.[2]

Adamantan-1-yl 2-diazoacetate (1g)

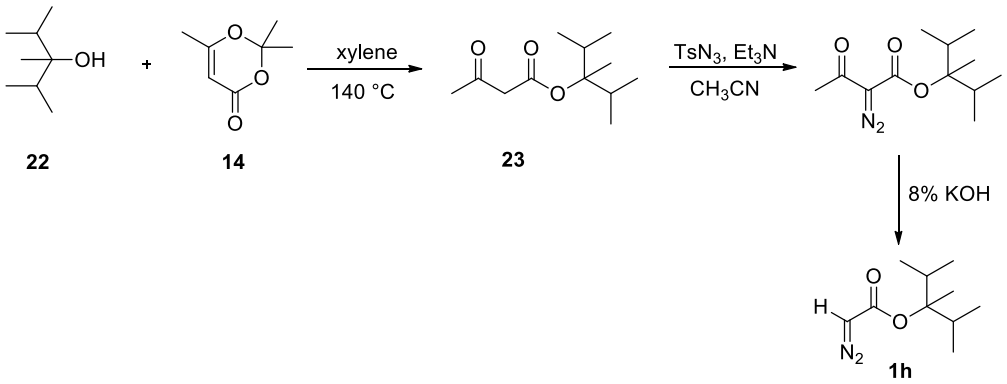


Following a slightly modified procedure,[1] a mixture of adamantan-1-ol (**20**) (3.81 g, 25.0 mmol, 1.00 equiv), 2,2,6-trimethyl-4H-1,3-dioxin-4-one (**14**) (3.55 g, 25.0 mmol, 1.00 equiv), and xylene (5 mL) was stirred at 140 °C for 2 h. After cooling to room temperature, the xylene was evaporated and the residue was purified by flash column chromatography using 1:50 EtOAc:pentane as mobile phase to afford adamantan-1-yl 3-oxobutanoate (**21)** as a colorless oil (5.2 g, 22 mmol, 88%). TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.35, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.20 (s, 0.07H, O*H* of enol form), 4.85 (s, 0.07H, vinyl *H* of enol form), 3.32 (s, 1.85H, CH_3COCH_2 of keto form), 2.22 (s, 2.8H, CH_3COCH_2 of keto form), 2.17-2.04 (m, 9H, 3 X C*H* and 3 X C*H*$_2$ of adamantly group), 1.87 (s, 0.2H, C*H*$_3$ of enol form), 1.69-1.55 (m, 6H, 3 X C*H*$_2$ of adamantly group); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.2, 166.0, 81.9, 51.6, 41.0, 35.9, 30.7, 29.9. Enol form,^{13}C NMR (100 MHz, $CDCl_3$): δ 174.6, 172.3, 91.1, 80.7, 41.4, 36.0, 21.1, One carbon of enol form was not resolved at 100 MHz. The characterization data corresponded to the reported values.[3]

Following a slightly modified procedure, to a solution of adamantan-1-yl 3-oxobutanoate (**21**) (1.18 g, 5.00 mmol, 1.00 equiv) in acetonitrile (6 mL) was added triethylamine (660 mg, 6.50 mmol, 1.30 equiv). The reaction mixture was cooled in an ice bath and a solution of tosyl azide (1.1 g, 5.5 mmol, 1.1 equi) in acetonitrile (6 mL) was added slowly. The reaction mixture was allowed to warm to r.t. After stirring for 20 h, the solvent was removed under reduced pressure. The residue

was dissolved in ether (30 mL) and washed with 8% aqueous KOH solution. The organic layer was separated, dried over $MgSO_4$, and evaporated. The crude product was re-dissolved in acetonitrile (15 mL) and 8% aqueous KOH (25 mL) solution was added at r.t. After vigorous stirring for 4 h, water (15 mL) was added and the reaction mixture was extracted with diethyl ether (2 X 30 mL). The combined organic layers were dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography using 1:20 Et_2O:pentane as mobile phase to afford adamantan-1-yl 2-diazoacetate (**1g)** as a yellow solid (960 mg, 4.36 mmol, 87%). TLC (Et_2O:pentane, 1:10 v/v): R_f = 0.54, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.60 (s, 1H, C*H*N_2), 2.22-2.06 (m, 9H, 3 X C*H* and 3 X C*H*$_2$), 1.69-1.61 (m, 6H, 3 X C*H*$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.9, 81.5, 46.7, 41.6, 36.1, 30.8. The characterization data corresponded to the reported values.[3]

2,3,4-Trimethylpentan-3-yl 2-diazoacetate (1h)



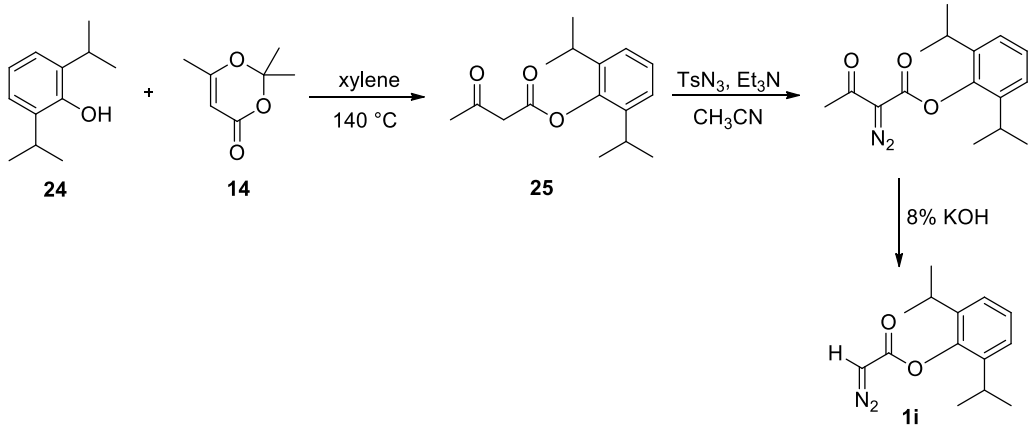
22 14 23 1h

Following a slightly modified procedure,[1] a mixture of 2,3,4-trimethylpentan-3-ol (**22**) (1.63 g, 12.5 mmol, 1.00 equiv), 2,2,6-trimethyl-4H-1,3-dioxin-4-one (**14**) (1.78 g, 12.5 mmol, 1.00 equiv), and xylene (2.5 mL) was stirred at 140 °C for 2 h. After cooling to room temperature, the xylene was evaporated and the residue was purified by flash column chromatography using 1:50 EtOAc:pentane as mobile phase to afford 2,3,4-trimethylpentan-3-yl 3-oxobutanoate (**23)** as a colorless oil (1.5 g, 7.0 mmol, 56%). TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.36, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): 12.28 (s, 0.05H, O*H* of enol form), 4.94 (s, 0.05H, vinyl *H* of enol form), δ 3.40 (s, 1.9H, CH_3COCH_2 of keto form), 2.33–2.21 (m, 4.85H, CH_3COCH_2 of keto form and 2 X C*H*$(CH_3)_2$), 1.44 (s, 2.85H, OCC*H*$_3$ of keto form), 1.42 (s, 0.15H, OCC*H*$_3$ of enol form) 0.95 (m, 12H, 2 X CH(C*H*$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.2, 166.3, 92.8, 51.5, 34.3, 30.2, 18.0,

17.8; Enol form, ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5, 172.8, 91.2, 76.0, some carbons of enol form were not resolved at 100 MHz. The characterization data corresponded to the reported values.[4]

Following a slightly modified procedure,[1] to a solution of 2,3,4-trimethylpentan-3-yl 3-oxobutanoate (**23**) (1.07 g, 5.00 mmol, 1.00 equiv) in acetonitrile (6 mL) was added triethylamine (660 mg, 6.50 mmol, 1.30 equiv). The reaction mixture was cooled in an ice bath and a solution of tosyl azide (1.1 g, 5.5 mmol, 1.1 equiv) in acetonitrile (6 mL) was added slowly. The reaction mixture was allowed to warm to r.t. After stirring for 20 h, the solvent was removed under reduced pressure. The residue was dissolved in ether (30 mL) and washed with 8% aqueous KOH solution. The organic layer was separated, dried over $MgSO_4$, and evaporated. The crude product was re-dissolved in acetonitrile (15 mL) and 8% aqueous KOH (25 mL) solution was added at r.t. After vigorous stirring for 4 h, water (15 mL) was added and the reaction mixture was extracted with diethyl ether (2 X 30 mL). The combined organic layers were dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography using 1:35 Et_2O:pentane as mobile phase to afford 2,3,4-trimethylpentan-3-yl 2-diazoacetate (**1h)** as a yellow oil (800 mg, 4.05 mmol, 81%). TLC (Et_2O:pentane, 1:25 v/v): R_f = 0.5, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.60 (br s, 1H, C*H*N_2), 2.26 (hept, *J* = 6.9 Hz, 2H, 2 X C*H*$(CH_3)_2$), 1.41 (s, 3H, OCC*H*$_3$), 0.93 (m, 12H, 2 X CH(C*H*$_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 91.9, 46.5, 34.5, 18.1, 18.0, 17.8. The ^{1}H NMR data corresponded to the reported values.[4]

2,6-Di*iso*propylphenyl 2-diazoacetate (1i)

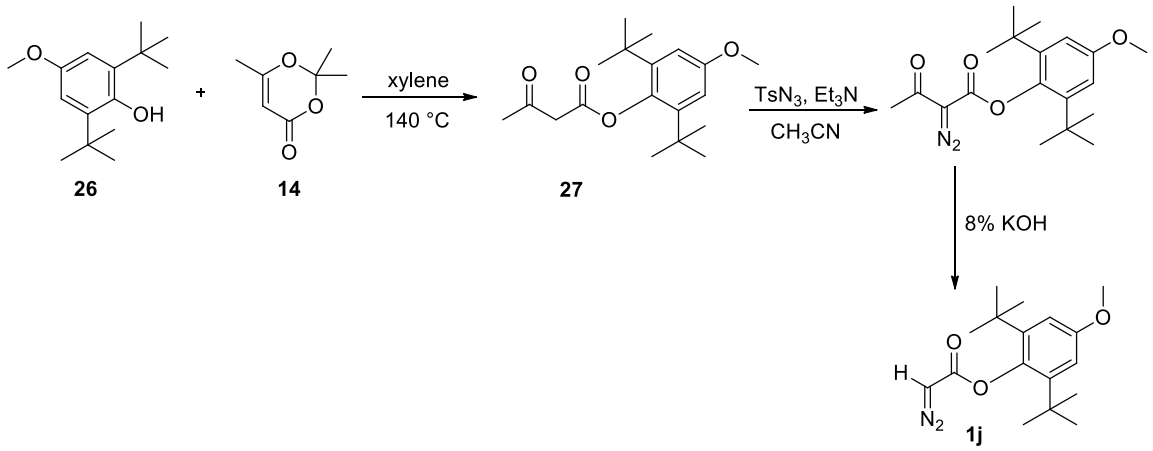


Following a slightly modified procedure,[1] a mixture of 2,6-di*iso*propylphenol (**24**) (4.46 g, 25.0 mmol, 1.00 equiv), 2,2,6-trimethyl-4H-1,3-dioxin-4-one (**14**) (3.55 g, 25.0 mmol, 1.00 equiv), and

xylene (5 mL) was stirred at 140 °C for 2 h. After cooling to room temperature, the xylene was evaporated and the residue was purified by flash column chromatography using 1:50 EtOAc:pentane as mobile phase to afford 2,6-di*iso*propylphenyl 3-oxobutanoate (**25)** as a colorless oil (5.00 g, 19.1 mmol, 76%). TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.35, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.08 (s, 0.22H, O*H* of enol form), 7.31–7.24 (m, 1H, Ar*H*), 7.24–7.18 (m, 2H, Ar*H*), 3.81 (s, 1.56H, CH_3COCH_2 of keto form), 3.03 (m, 2H, 2 X C*H*$(CH_3)_2$), 2.41 (s, 2.32H, CH_3COCH_2 of keto form), 1.28-1.21 (m, 12H, 2 X CH(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.9, 165.7, 145.1, 140.2, 126.8, 124.0, 49.6, 30.4, 27.4, 27.3; Enol form, ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.7, 171.5, 144.5, 140.5, 126.5, 123.9, 88.7, 23.7, 22.7, 21.4; IR ν 2966 (m), 2876 (w), 1760 (m), 1723 (m), 1634 (w), 1447 (m), 1410 (w), 1360 (m), 1315 (m), 1222 (s), 1140 (s), 1102 (m), 1053 (w), 976 (w); HRMS (ESI) calcd. for $C_{16}H_{22}NaO_3^+$ $[M+Na]^+$ 285.1461; found 285.1467.

Following a slightly modified procedure,[1] to a solution of 2,6-di*iso*propylphenyl 3-oxobutanoate (**25**) (1.31 g, 5.00 mmol, 1.00 equiv) in acetonitrile (6 mL) was added triethylamine (660 mg, 6.50 mmol, 1.30 equiv). The reaction mixture was cooled in an ice bath and a solution of tosyl azide (1.1 g, 5.5 mmol, 1.1 equiv) in acetonitrile (6 mL) was added slowly. The reaction mixture was allowed to warm to r.t. After stirring for 20 h, the solvent was removed under reduced pressure. The residue was dissolved in ether (30 mL) and washed with 8% aqueous KOH solution. The organic layer was separated, dried over $MgSO_4$, and evaporated. The crude product was re-dissolved in acetonitrile (15 mL) and 8% aqueous KOH (25 mL) solution was added at r.t. After vigorous stirring for 4 h, water (15 mL) was added and the reaction mixture was extracted with diethyl ether (2 X 30 mL). The combined organic layers were dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography using 1:30 Et_2O:pentane as mobile phase to afford 2,6-di*iso*propylphenyl 2-diazoacetate (**1i)** as a yellow oil (620 mg, 2.52 mmol, 50%). TLC (Et_2O:pentane, 1:30 v/v): R_f = 0.36, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.25 (m, 1H, Ar*H*), 7.23-7.20 (m, 2H, Ar*H*), 5.09 (br s, 1H, C*H*N_2), 3.05 (sept, *J* = 6.9 Hz, 2H, 2 X C*H*$(CH_3)_2$), 1.27 (d, *J* = 6.9 Hz, 12H, 2 X CH(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 145.1, 140.8, 126.7, 123.9, 46.3, 27.5, 23.4. The characterization data slightly differ from the reported values.[5]

2,6-Di-*tert*-butyl-4-methoxyphenyl 2-diazoacetate (1j)

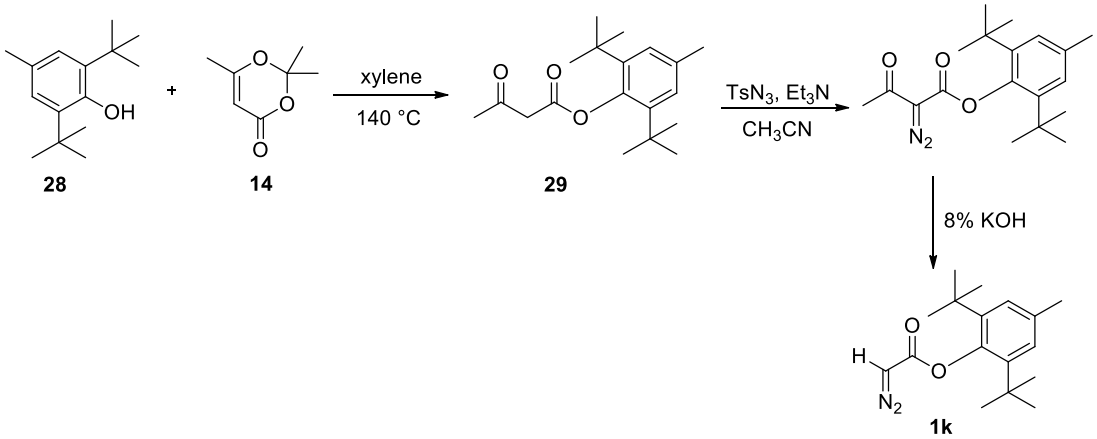


Following a slightly modified procedure,[1] a mixture of 2,6-di-*tert*-butyl-4-methoxyphenol (**26**) (5.91 g, 25.0 mmol, 1.00 equiv), 2,2,6-trimethyl-4H-1,3-dioxin-4-one (**14**) (3.55 g, 25.0 mmol, 1.00 equiv), and xylene (5 mL) was stirred at 140 °C for 2 h. After cooling to room temperature, the xylene was evaporated and the residue was purified by flash column chromatography using 1:30 EtOAc:pentane as mobile phase to afford 2,6-di-*tert*-butyl-4-methoxyphenyl 3-oxobutanoate (**27)** as a colorless thick oil (6.64 g, 20.0 mmol, 80%). Mp: 67.0–70.5 °C; TLC (EtOAc:pentane, 1:15 v/v): R_f = 0.46, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.15 (s, 0.55H, O*H* of enol form), 6.87 (s, 2H, Ar*H*), 5.32 (s, 0.55H, vinyl *H* of enol form), 3.80 (s, 3H, ArOC*H*$_3$), 3.73 (s, 0.9H, CH_3COCH_2 of keto form), 2.40 (s, 1.35H, CH_3COCH_2 of keto form), 2.07 (s, 1.65H, C*H*$_3$ of enol form), 1.33 (s, 8.1H, C(C*H*$_3$)$_3$ of keto form), 1.32 (s, 9.9H, C(C*H*$_3$)$_3$ of enol form); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.1, 167.9, 156.5, 143.3, 141.1, 111.7, 55.2, 50.6, 35.5, 31.3, 30.8; Enol form, ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.4, 173.5, 156.2, 143.6, 140.7, 111.5, 90.4, 55.2, 35.6, 31.2, 21.5; IR ν 2966 (s), 2913 (s), 2118 (w), 1758 (m), 1724 (m), 1634 (s), 1596 (m), 1408 (s), 1310 (m), 1223 (s), 1181 (s), 1143 (s), 1064 (s), 979 (w), 922 (w), 861 (w); HRMS (ESI) calcd. for $C_{19}H_{28}NaO_4^+$ $[M+Na]^+$ 343.1880; found 343.1884.

Following a slightly modified procedure,[1] to a solution of 2,6-di-*tert*-butyl-4-methoxyphenyl 3-oxobutanoate (**27**) (1.6 g, 5.0 mmol, 1.0 equiv) in acetonitrile (6 mL) was added triethylamine (660 mg, 6.50 mmol, 1.30 equiv). The reaction mixture was cooled in an ice bath and a solution of tosyl azide (1.1 g, 5.5 mmol, 1.1 equiv) in acetonitrile (6 mL) was added slowly. The reaction mixture was allowed to warm to r.t. After stirring for 20 h, the solvent was removed under reduced pressure. The residue was dissolved in ether (30 mL) and washed with 8% aqueous KOH solution. The organic layer was separated, dried over $MgSO_4$, and evaporated. The crude product was re-

dissolved in acetonitrile (15 mL) and 8% aqueous KOH (25 mL) solution was added at r.t. After vigorous stirring for 4 h, water (15 mL) was added and the reaction mixture was extracted with diethyl ether (2 X 30 mL). The combined organic layers were dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography using 1:20 EtOAc:pentane as mobile phase to afford 2,6-di-*tert*-butyl-4-methoxyphenyl 2-diazoacetate (**1j)** as a yellow solid (600 mg, 1.97 mmol, 40%). Mp (Dec.): 125.3–130.0 °C; TLC (EtOAc:pentane, 1:15 v/v): R_f = 0.31, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.86 (s, 2H, Ar*H*), 5.01 (s, 1H, C*H*N_2), 3.80 (s, 3H, ArOC*H*$_3$), 1.36 (s, 18H, 2 X C(C*H*$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8, 156.4, 143.9, 141.0, 111.6, 55.2, 47.4, 35.6, 31.4; IR ν 3105 (w), 2961 (m), 2114 (s), 1712 (s), 1593 (m), 1427 (w), 1365 (s), 1180 (s), 1149 (s), 1103 (w), 1064 (m), 919 (w), 862 (w); HRMS (ESI) calcd. for $C_{17}H_{24}N_2NaO_3^+$ $[M+Na]^+$ 327.1679; found 327.1679.

2,6-Di-*tert*-butyl-4-methylphenyl 2-diazoacetate (1k)



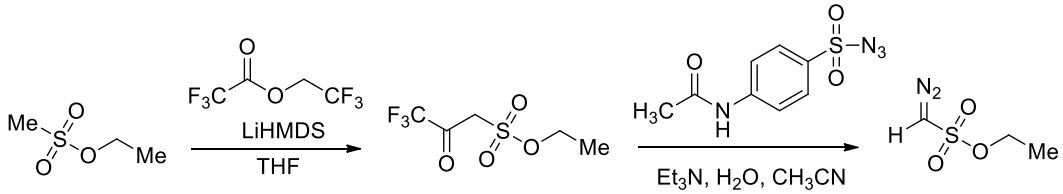
28 14 29 1k

Following a slightly modified procedure,[1] a mixture of 2,6-di-*tert*-butyl-4-methylphenol (**28**) (5.91 g, 25.0 mmol, 1.00 equiv), 2,2,6-trimethyl-4H-1,3-dioxin-4-one (**14**) (3.55 g, 25.0 mmol, 1.00 equiv), and xylene (5 mL) was stirred at 140 °C for 2 h. After cooling to room temperature, the xylene was evaporated and the residue was purified by flash column chromatography using 1:50 EtOAc:pentane as mobile phase to afford 2,6-di-*tert*-butyl-4-methylphenyl 3-oxobutanoate (**29)** as a white solid (6.40 g, 21.0 mmol, 84%). Mp: 96.5–99.6 °C; TLC (EtOAc:pentane, 1:50 v/v): R_f = 0.34, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): 12.16 (s, 0.55H, O*H* of enol form), δ 7.13 (s, 2H, Ar*H*), 5.39–5.24 (m, 0.55H, vinyl *H* of enol form), 3.73 (s, 1H, 0.9H, CH_3COCH_2 of keto form), 2.40 (s, 1H, 1.35H, CH_3COCH_2 of keto form), 2.33 (s, 3H, ArC*H*$_3$), 2.07 (s, 1.65H, C*H*$_3$ of enol form), 1.33 (s, 8.1H, C(C*H*$_3$)$_3$ of keto form), 1.32 (s, 9.9H, C(C*H*$_3$)$_3$ of enol form); ^{13}C NMR (100

MHz, $CDCl_3$): δ 200.2, 167.7, 145.3, 141.8, 135.0, 127.2, 50.7, 35.2, 31.4, 30.8, 21.5; Enol form, ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.4, 173.3, 144.9, 142.2, 134.6, 126.9, 90.4, 35.2, 31.4, 21.5, 21.5; IR ν 2964 (m), 2919 (m), 2880 (w), 2110 (w), 1757 (m), 1726 (m), 1633 (s), 1408 (m), 1369 (m), 1318 (m), 1219 (s), 1199 (s), 1143 (s), 1113 (m), 1030 (w), 978 (w), 924 (w); HRMS (ESI) calcd. for $C_{19}H_{28}NaO_3^+$ $[M+Na]^+$ 327.1931; found 327.1933.

Following a slightly modified procedure,[1] to a solution of 2,6-di-*tert*-butyl-4-methylphenyl 3-oxobutanoate (**29**) (1.52 g, 5.00 mmol, 1.00 equiv) in acetonitrile (6 mL) was added triethylamine (660 mg, 6.50 mmol, 1.30 equiv). The reaction mixture was cooled in an ice bath and a solution of tosyl azide (1.1 g, 5.5 mmol, 1.1 equiv) in acetonitrile (6 mL) was added slowly. The reaction mixture was allowed to warm to r.t. After stirring for 20 h, the solvent was removed under reduced pressure. The residue was dissolved in ether (30 mL) and washed with 8% aqueous KOH solution. The organic layer was separated, dried over $MgSO_4$, and evaporated. The crude product was re-dissolved in acetonitrile (15 mL) and 8% aqueous KOH (25 mL) solution was added at r.t. After vigorous stirring for 4 h, water (15 mL) was added and the reaction mixture was extracted with diethyl ether (2 X 30 mL). The combined organic layers were dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography using 1:30 Et_2O:pentane as mobile phase to afford 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k)** as a yellow solid (1.20 g, 4.16 mmol, 83%). TLC (Et_2O:pentane, 1:30 v/v): R_f = 0.36, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.12 (s, 2H, Ar*H*), 5.00 (s, 1H, C*H*N_2), 2.32 (s, 3H, ArC*H*$_3$), 1.36 (s, 18H, 2 X C(C*H*$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 145.1, 142.4, 134.8, 127.0, 47.3, 35.3, 31.5, 21.5. The ^1H NMR data corresponded to the reported values.[4]

Ethyl diazomethanesulfonate (1l)

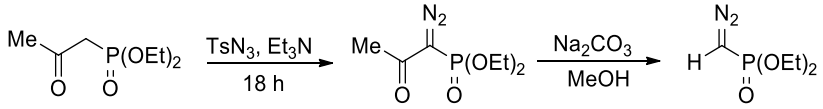


30 **31** **1l**

Following a reported procedure,[6] to a solution of ethyl methanesulfonate (**30)** (1.86 g, 15.0 mmol, 1.00 equiv) in dry THF (50 mL) was added a 1 M LiHMDS solution in hexane (18 mL, 18 mmol, 1.2 equiv) at -78 °C. After stirring the reaction mixture for 30 min at this temperature, 2,2,2-

trifluoroethyl trifluoroacetate (2.4 mL, 18 mmol, 1.2 equiv) was added rapidly in one portion *via* syringe. After 10 min, the reaction mixture was poured into a solution of diethyl ether (20 mL) and 5% HCl (50 mL). The mixture was extracted with diethyl ether (3 x 50 mL), washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to give a yellow oil **31**. This yellow oil was immediately dissolved in dry CH_3CN (30 mL). To this solution was added *p*-acetamidobenzenesulfonyl azide (4.32 g, 18.0 mmol, 1.20 equiv), Et_3N (2.5 mL, 18 mmol, 1.2 equiv), and water (0.27 mL, 15 mmol, 1.0 equiv). After stirring the reaction mixture overnight at room temperature, the solvent was removed under reduced pressure and the residue was filtered on short silica gel and washed with a mixture of ethyl acetate (100 mL) and hexane (100 mL). The filtrate was concentrated under vacuum and the residue was purified by flash column chromatography using 1:10 EtOAc:pentane as mobile phase to afford ethyl diazomethanesulfonate (**1l)** as a yellow oil (0.9 g, 6 mmol, 40%). TLC (EtOAc:pentane, 1:10 v/v): R_f = 0.25, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.25 (s, 1H, C*H*N_2), 4.26 (q, *J* = 7.1 Hz, 2H, C*H*$_2$$CH_3$), 1.41 (t, *J* = 7.1 Hz, 3H, CH_2C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 67.4, 52.4, 14.6. The characterization data corresponded to the reported values.[6]

Diethyl (diazomethyl)phosphonate (1m)

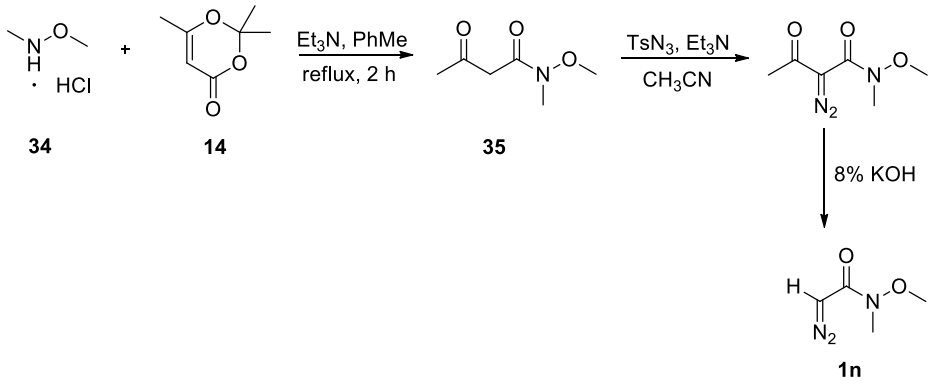


32 **33** **1m**

Following a reported procedure,[7] a mixture of diethyl (2-oxopropyl)phosphonate (**32**) (1.15 mL, 6.00 mmol, 1.00 equiv), tosyl azide (1.3 g, 6.6 mmol, 1.1 equiv) and triethylamine (6 mL) was stirred at room temperature for 18 h. After evaporation of triethylamine under reduced pressure, the residue was dissolved in diethyl ether (50 mL). The precipitate was filtered off, the filtrate was evaporated and the residue was purified by column chromatography using 1:1 EtOAc:pentane as mobile phase to afford diethyl (1-diazo-2-oxopropyl)phosphonate (**33**) as a yellow oil (810 mg, 3.68 mmol, 61%). TLC (EtOAc:pentane, 1:4 v/v): R_f = 0.49, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.04– 4.19 (m, 4H, 2 X C*H*$_2$$CH_3$) 2.19 (s, 3H, C*H*$_3$), 1.30 (t, *J* = 7.0 Hz, 6H, 2 X CH_2C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 190.1 (d, *J* = 13.2 Hz), 63.4 (d, *J* = 5.6 Hz), 27.1, 16.0 (d, *J* = 6.8 Hz). The values of the NMR spectra are in accordance with reported literature data.[8]

To a solution of diethyl (1-diazo-2-oxopropyl)phosphonate (**33**) (694 mg, 3.15 mmol, 1.00 equiv) in MeOH (9 mL) was added Na_2CO_3 (401 mg, 3.78 mmol, 1.20 equiv). The mixture was stirred at room temperature for 15 min. The precipitate was filtered off, the filtrate was evaporated and the residue was purified by column chromatography using 1:1 EtOAc:pentane as mobile phase to afford diethyl (diazomethyl)phosphonate (**1m)** as a yellow oil (533 mg, 2.99 mmol, 95%). TLC (EtOAc:pentane, 1:4 v/v): R_f = 0.41, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.17–4.08 (m, 4H, 2 X C*H*$_2$CH$_3$), 3.75 (d, *J* = 11.1 Hz, 1H, C*H*N$_2$), 1.34 (td, *J* = 7.1, 0.7 Hz, 6H, 2 X CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 62.6 (d, *J* = 5.3 Hz), 16.1 (d, *J* = 6.9 Hz). One carbon was not resolved at 100 MHz. The characterization data corresponded to the reported values.[8]

2-Diazo-*N*-methoxy-*N*-methylacetamide (1n)

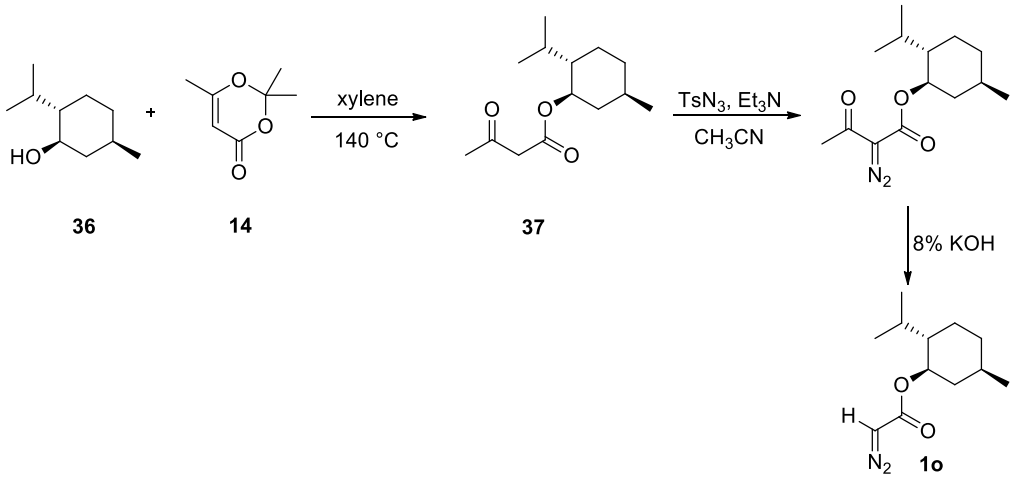


Following a reported procedure,[9] a mixture of *N*,*O*-dimethylhydroxylamine hydrochloride (**34**) (2.44 g, 25.0 mmol, 1.00 equiv), 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (**14**) (5.00 mL, 37.5 mmol, 1.50 equiv) and triethylamine (3.85 mL, 27.5 mmol, 1.10 equiv) was dissolved in toluene (75 mL) and refluxed for 2 h. The reaction mixture was cooled to room temperature and washed with aqueous hydrochloric acid (90 mL, 1.0 M) and the aqueous layer was extracted with ethyl acetate (3 x 100 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography using 1:1 EtOAc:pentane as mobile phase to afford *N*-methoxy-*N*-methyl-3-oxobutanamide (**35)** as a yellow oil (2.40 g, 16.5 mmol, 66%). TLC (EtOAc:pentane, 1:1 v/v): R_f = 0.26, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.65 (s, 0.13H, O*H* of enol form), 5.32 (s, 0.13H, vinyl *H* of enol form) 3.60 (s, 3H, OC*H*$_3$), 3.50 (s, 1.74H, CH$_3$COC*H*$_2$ of keto form), 3.13 (s, 2.6H, *N*-C*H*$_3$ of keto form), 3.11 (s, 0.4H, enol form of *N*-C*H*$_3$), 2.17 (s, 2.6H, C*H*$_3$COCH$_2$ of keto form), 1.89 (s, 0.4H, enol form of C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.7, 167.8, 61.1, 48.3, 31.8, 30.0; Enol form, ^{13}C

NMR (100 MHz, $CDCl_3$): δ 175.0, 172.2, 86.5, 21.6. Two carbons were not resolved at 100 MHz. The characterization data corresponded to the reported values.[9]

Following a slightly modified procedure,[1] to a solution of *N*-methoxy-*N*-methyl-3-oxobutanamide (**35**) (0.73 g, 5.0 mmol, 1.0 equiv) in acetonitrile (6 mL) was added triethylamine (660 mg, 6.50 mmol, 1.30 equiv). The reaction mixture was cooled in an ice bath and a solution of tosyl azide (1.1 g, 5.5 mmol, 1.1 equiv) in acetonitrile (6 mL) was added slowly. The reaction mixture was allowed to warm to r.t. After stirring for 20 h, the solvent was removed under reduced pressure. The residue was dissolved in ether (30 mL) and washed with 8% aqueous KOH solution. The organic layer was separated, dried over $MgSO_4$, and evaporated. The crude product was re-dissolved in acetonitrile (15 mL) and 8% aqueous KOH (25 mL) solution was added at r.t. After vigorous stirring for 4 h, water (15 mL) was added and the reaction mixture was extracted with diethyl ether (2 X 30 mL). The combined organic layers were dried over $MgSO_4$, and concentrated under reduced pressure. Purification by column chromatography using 1:1 EtOAc:pentane as mobile phase to afford 2-diazo-*N*-methoxy-*N*-methylacetamide (**1n)** as a yellow liquid (350 mg, 2.71 mmol, 54%). TLC (EtOAc:pentane, 1:1 v/v): R_f = 0.27, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.30 (s, 1H, C*H*N_2), 3.60 (s, 3H, OC*H*$_3$), 3.12 (s, 3H, C*H*$_3$);^{13}C NMR (100 MHz, $CDCl_3$): δ 168.1, 61.3, 46.1, 33.0. The values of the NMR spectra are in accordance with reported literature data.[10]

(1*R*,2*S*,5*R*)-2-*Iso*propyl-5-methylcyclohexyl 2-diazoacetate (1o)



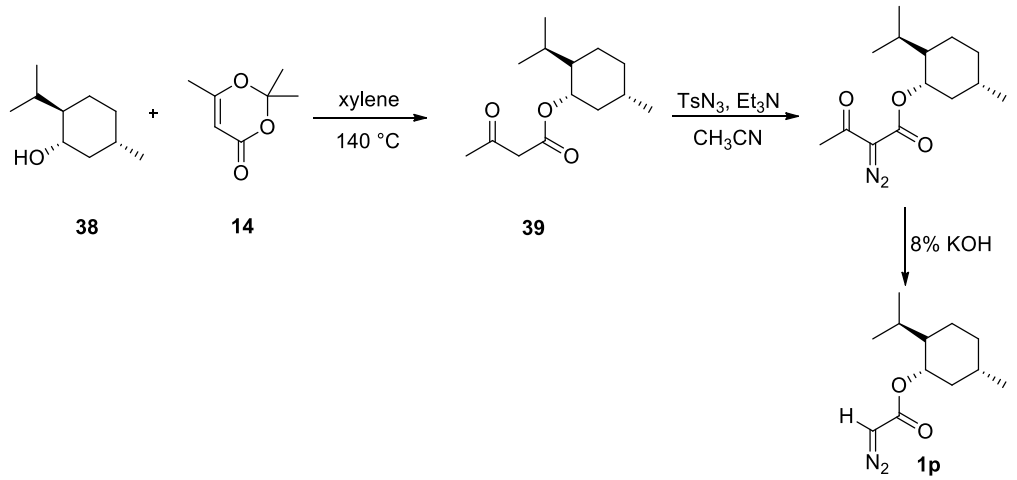
36 **14** **37** **1o**

Following a slightly modified procedure,[1] a mixture of (1*R*,2*S*,5*R*)-2-*iso*propyl-5-methylcyclohexanol (**36**) (1.95 g, 12.5 mmol, 1.00 equiv), 2,2,6-trimethyl-4H-1,3-dioxin-4-one

(**14**) (1.78 g, 12.5 mmol, 1.00 equiv), and xylene (2.5 mL) was stirred at 140 °C for 2 h. After cooling to room temperature, the xylene was evaporated and the residue was purified by flash column chromatography using 1:50 EtOAc:pentane as mobile phase to afford (1*R*,2*S*,5*R*)-2-*iso*propyl-5-methylcyclohexyl 3-oxobutanoate (**37)** as a colorless liquid (1.70 g, 7.07 mmol, 57%). TLC (EtOAc:pentane, 1:25 v/v): R_f = 0.3, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.18 (s, 0.08H, O*H* of enol form), 4.94 (s, 0.08H, vinyl *H* of enol form), 4.71 (td, *J* = 10.9, 4.4 Hz, 1H, OC*H*), 3.41 (s, 1.84H, CH_3COCH_2 of keto form), 2.24 (s, 2.75H, CH_3COCH_2 of keto form), 2.04-1.95 (m, 1H), 1.93 (s, 0.025H, C*H*$_3$ of enol form), 1.90-1.79 (m, 1H), 1.71–1.61 (m, 2H), 1.54-1.40 (m, 1H), 1.39-1.29 (m, 1H), 1.10–0.92 (m, 2H), 0.91-0.83 (m, 7H), 0.74 (d, *J* = 7.0 Hz, 3H, C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.7, 166.7, 75.4, 50.5, 46.7, 40.6, 34.0, 31.3, 30.0, 26.0, 23.1, 21.9, 20.7, 16.0; Enol form, ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 172.3, 90.0, 73.6, 46.9, 40.9, 34.1, 26.2, 23.4, 22.0, 21.2, 20.6, 16.3. One carbon of enol form was not resolved at 100 MHz. The ^{1}H NMR data corresponded to the reported values.[11]

Following a slightly modified procedure,[11] to a solution of (1*R*,2*S*,5*R*)-2-*iso*propyl-5-methylcyclohexyl 3-oxobutanoate (**37**) (0.72 g, 3.0 mmol, 1.0 equiv) in acetonitrile (3.0 mL) was added triethylamine (0.33 g, 3.3 mmol, 1.1 equiv). The reaction mixture was cooled in an ice bath and a solution of tosyl azide (0.77 g, 3.9 mmol, 1.3 equiv) in acetonitrile (3.0 mL) was added slowly. The reaction mixture was allowed to warm to r.t. After stirring for 6 h, the reaction mixture was treated with a solution of $LiOH{\cdot}H_2O$ (0.38 g, 9.0 mmol, 3.0 equiv) in water (3 mL) and stirred for another 6 h. The resulting mixture was extracted with diethyl ether (2 × 15 mL). The combined organic layers were washed with brine (15 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography using 1:30 Et_2O:pentane as mobile phase to afford (1R,2S,5R)-2-*iso*propyl-5-methylcyclohexyl 2-diazoacetate (**1o)** as a yellow solid (0.60 g, 2.7 mmol, 89%). TLC (Et_2O:pentane, 1:30 v/v): R_f = 0.2, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.80-4.67 (m, 2H, C*H*N_2 and OC*H*), 2.10–1.96 (m, 1H), 1.93-1.79 (m, 1H), 1.73–1.60 (m, 2H), 1.56-1.42 (m, 1H), 1.40-1.30 (m, 1H), 1.12–0.93 (m, 2H), 0.92-0.86 (m, 7H), 0.77 (d, *J* = 7.0 Hz, 3H, C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 74.7, 47.1, 46.2, 41.2, 34.1, 31.4, 26.3, 23.5, 22.0, 20.7, 16.4. The characterization data corresponded to the reported values (except one peak in ^{1}H NMR at 4.67 ppm).[12]

(1*S*,2*R*,5*S*)-2-*iso*propyl-5-methylcyclohexyl 2-diazoacetate (1p)

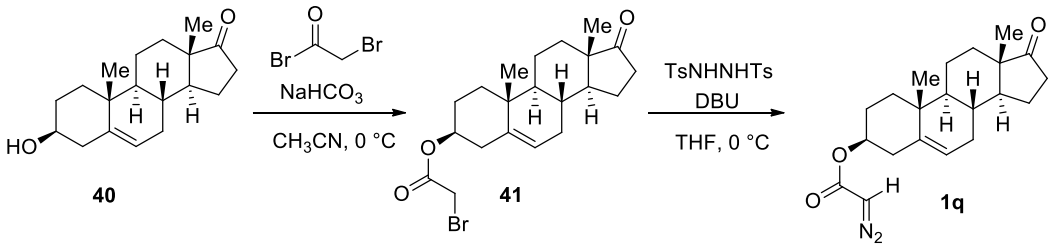


Following a slightly modified procedure,[1] a mixture of (1*S*,2*R*,5*S*)-2-*iso*propyl-5-methylcyclohexanol (**38**) (1.95 g, 12.5 mmol, 1.00 equiv), 2,2,6-trimethyl-4H-1,3-dioxin-4-one (**14**) (1.78 g, 12.5 mmol, 1.00 equiv), and xylene (2.5 mL) was stirred at 140 °C for 2 h. After cooling to room temperature, the xylene was evaporated and the residue was purified by flash column chromatography using 1:50 EtOAc:pentane as mobile phase to afford (1*S*,2*R*,5*S*)-2-*iso*propyl-5-methylcyclohexyl 3-oxobutanoate (**39)** as a white solid (1.90 g, 7.91 mmol, 63%). TLC (EtOAc:pentane, 1:25 v/v): R_f = 0.3, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.18 (s, 0.08H, O*H* of enol form), 4.94 (s, 0.08H, vinyl *H* of enol form), 4.72 (td, *J* = 10.9, 4.4 Hz, 1H, OC*H*), 3.42 (s, 1.84H, CH_3COCH_2 of keto form), 2.25 (s, 2.76H, CH_3COCH_2 of keto form), 2.05-1.95 (m, 1H), 1.93 (s, 0.025H, CH_3 of enol form), 1.90-1.79 (m, 1H), 1.72–1.60 (m, 2H), 1.54-1.41 (m, 1H), 1.40-1.31 (m, 1H), 1.13–0.91 (m, 2H), 0.92-0.84 (m, 7H), 0.75 (d, *J* = 7.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.7, 166.7, 75.4, 50.5, 46.8, 40.6, 34.1, 31.3, 30.0, 26.0, 23.1, 21.9, 20.7, 16.0; Enol form, ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 172.3, 90.0, 73.6, 46.9, 40.9, 34.1, 26.2, 23.4, 22.0, 21.2, 20.6, 16.3. One carbon of enol form was not resolved at 100 MHz. The characterization data corresponded to the reported values.[13]

Following a slightly modified procedure,[11] to a solution of (1*S*,2*R*,5*S*)-2-*iso*propyl-5-methylcyclohexyl 3-oxobutanoate (**39**) (0.72 g, 3.0 mmol, 1.0 equiv) in acetonitrile (3.0 mL) was added triethylamine (0.33 g, 3.3 mmol, 1.1 equiv). The reaction mixture was cooled in an ice bath and a solution of tosyl azide (0.77 g, 3.9 mmol, 1.3 equiv) in acetonitrile (3.0 mL) was added slowly. The reaction mixture was allowed to warm to r.t. After stirring for 6 h, the reaction mixture

was treated with a solution of $LiOH \cdot H_2O$ (0.38 g, 9.0 mmol, 3.0 equiv) in water (3 mL) and stirred for another 6 h. The resulting mixture was extracted with diethyl ether (2 × 15 mL). The combined organic layers were washed with brine (15 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography using 1:30 Et_2O:pentane as mobile phase to afford (1*S*,2*R*,5*S*)-2-*iso*propyl-5-methylcyclohexyl 2-diazoacetate (**1p)** as a yellow solid (500 mg, 2.23 mmol, 74%). TLC (Et_2O:pentane, 1:30 v/v): R_f = 0.2, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 4.74 (m, 2H, C*H*N_2 and OC*H*), 2.06-1.98 (m, 1H), 1.92-1.81 (m, 1H), 1.73–1.61 (m, 2H), 1.56-1.41 (m, 1H), 1.40-1.30 (m, 1H), 1.13–0.92 (m, 2H), 0.92-0.86 (m, 7H), 0.77 (d, *J* = 6.9 Hz, 3H, C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 74.7, 47.1, 46.2, 41.2, 34.1, 31.4, 26.3, 23.5, 22.0, 20.7, 16.4. The characterization data corresponded to the reported values.[14]

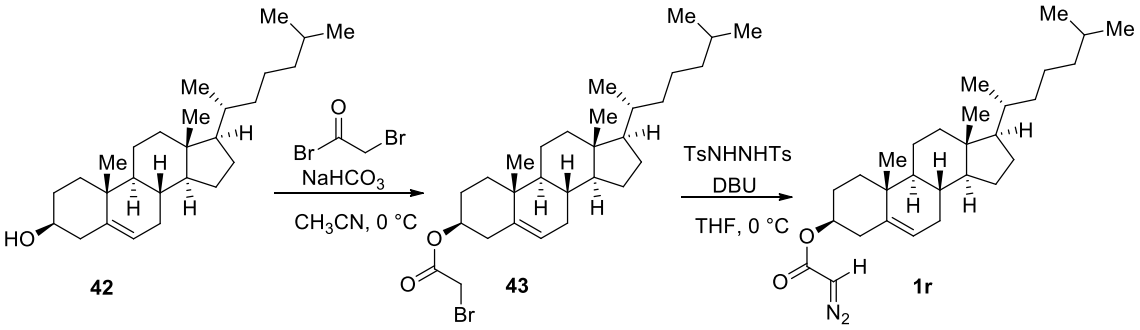
(3*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-10,13-Dimethyl-17-oxo-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-diazoacetate (1q)



Following reported procedure,[15] dehydroepiandrosterone **40** (1.16 g, 4.00 mmol. 1.00 equiv) and $NaHCO_3$ (1.6 g, 20 mmol, 5.0 equiv) were dissolved in dry CH_2Cl_2 (20 mL) and bromoacetyl bromide (0.7 mL, 8 mmol, 2 equiv) was added slowly at 0 °C and the reaction mixture was stirred for 6 h at room temperature. The reaction was then quenched with water (50 mL) and the solution was extracted with CH_2Cl_2 (3 x 100 mL). After washing with water (100 mL) and drying over $MgSO_4$, the solvent was evaporated and the residue was used in the next step without further purification. The resulting crude bromoacetamide **41** and *N,N'*-ditosylhydrazine (2.72 g, 8.00 mmol, 2.00 equiv) were dissolved in dry THF (20 mL) and cooled down to 0 ˚C, then DBU (3.0 mL, 20 mmol, 5.0 equiv) was added dropwise and stirred at room temperature for 1 h. After quenching with saturated solution of $NaHCO_3$ (40 mL) and extracting with diethyl ether (3 X 100 mL), the organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting crude product was purified by flash chromatography using EtOAc:pentane 1:5 as mobile phase to

afford **1q** (1.1 g, 3.1 mmol, 77%) as a pale yellow solid. Mp (Dec.): 192.3–196.8 °C; TLC (EtOAc:pentane, 1:5 v/v): R_f = 0.42, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 5.41 (d, *J* = 5.0 Hz, 1H, olefinic *H*), 4.84–4.54 (m, 2H, N_2C*H* and O*CH*), 2.56–2.24 (m, 3H), 2.17–2.02 (m, 2H), 2.00–1.78 (m, 4H), 1.74–1.41 (m, 6H), 1.34–1.22 (m, 2H), 1.16 (td, *J* = 13.9, 13.2, 4.2 Hz, 1H), 1.08–0.97 (m, 4H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 221.0, 166.3, 139.8, 122.0, 75.0, 51.6, 50.1, 47.5, 46.3, 38.2, 36.9, 36.7, 35.8, 31.4, 31.4, 30.7, 27.9, 21.8, 20.3, 19.3, 13.5. The characterization data corresponded to the reported values.[15]

3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-diazoacetate (1r)



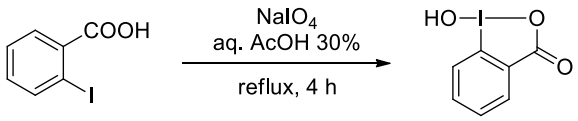
Following a reported procedure,[15] cholesterol **42** (773 mg, 2.00 mmol, 1.00 equiv) and $NaHCO_3$ (840 mg, 10.0 mmol, 5.00 equiv) were dissolved in dry CH_2Cl_2 (10 mL) and bromoacetyl bromide (0.53 mL, 6.0 mmol, 3.0 equiv) was added slowly at 0 °C and stirred for 6 h at room temperature, the reaction was quenched with H_2O (25 mL) and the solution was extracted with CH_2Cl_2 (3 x 50 mL). After washing with water (50 mL) and drying over $MgSO_4$, the solvent was evaporated and the residue was used in the next step without further purification. The resulting crude bromoacetamide **43** and *N,N′*-ditosylhydrazine (1.36 g, 4.00 mmol, 2.00 equiv) were dissolved in dry THF (10 mL) and cooled down to 0 ˚C, then DBU (1.5 mL, 10 mmol, 5.0 equiv) was added dropwise and stirred at room temperature for 1 h. After quenching with saturated solution of $NaHCO_3$ (20 mL) and extracting with diethyl ether (3 x 50 mL), the organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting crude product was purified by flash chromatography using Et_2O:pentane 1:20 as mobile phase to afford **1r** (750 mg, 1.65 mmol, 82%) as a pale yellow solid. TLC (Et_2O:pentane, 1:20 v/v): R_f = 0.4, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 5.38 (d, *J* = 5.1 Hz, 1H, olefinic *H*), 4.75–4.65 (m, 2H, N_2C*H* and O*CH*), 2.45–2.23 (m,

2H), 2.08–1.76 (m, 5H), 1.64–0.80 (m, 33H), 0.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 139.5, 122.8, 74.6, 56.7, 56.1, 50.0, 46.3, 42.3, 39.7, 39.5, 38.3, 36.9, 36.5, 36.2, 35.8, 31.9, 31.8, 28.2, 28.0, 28.0, 24.3, 23.8, 22.8, 22.5, 21.0, 19.3, 18.7, 11.8. The characterization data corresponded to the reported values.[15]

3. Preparation of EBX reagents

The synthesis of R-EBX reagents **2a-2p** except **2e** had been already described before. The procedures are taken here from the indicated publications to facilitate reproduction of the results by having all the data in the same file.

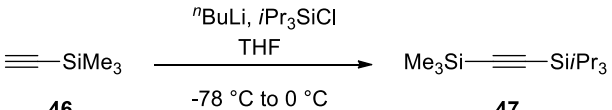
1-Hydroxy-1,2-benziodoxol-3-(1H)-one (45)



44 **45**

Following a reported procedure,[16] $NaIO_4$ (7.24 g, 33.8 mmol, 1.05 equiv) and 2-iodobenzoic acid (**44**) (8.00 g, 32.2 mmol, 1.00 equiv) were suspended in 30% (v/v) aq. AcOH (48 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (180 mL) and allowed to cool to room temperature, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 20 mL) and acetone (3 x 20 mL), and air-dried in the dark to give the pure product **45** (8.3 g, 31 mmol, 98%) as a white solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 8.02 (dd, *J* = 7.7, 1.4 Hz, 1H, Ar*H*), 7.97 (m, 1H, Ar*H*), 7.85 (dd, *J* = 8.2, 0.7 Hz, 1H, Ar*H*), 7.71 (td, *J* = 7.6, 1.2 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $(CD_3)_2SO$): δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4; IR ν 3083 (w), 3060 (w), 2867 (w), 2402 (w), 1601 (m), 1585 (m), 1564 (m), 1440 (m), 1338 (s), 1302 (m), 1148 (m), 1018 (w), 834 (m), 798 (w), 740 (s), 694 (s), 674 (m), 649 (m). The values of the NMR spectra are in accordance with reported literature data.[16]

Tri*iso*propylsilyl trimethylsilylacetylene (47)

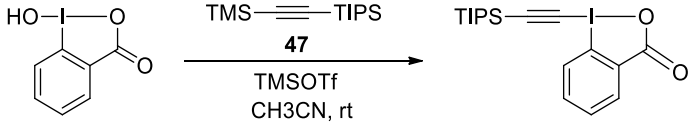


46 **47**

Following a reported procedure,[17] BuLi (2.5 M in hexanes, 12.0 mL, 29.9 mmol, 0.98 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (**46**) (3.0 g, 30 mmol, 1.0 equiv) in THF (48 mL) at -78 °C. The mixture was then warmed to 0 °C and stirred for 5 min. The mixture was then cooled back to -78 °C and chlorotri*iso*propylsilane (6.4 mL, 30 mmol, 1.0 equiv) was added dropwise. The mixture was then allowed to warm to room temperature and stirred overnight.

A saturated solution of ammonium chloride (40 mL) was added, and the reaction mixture was extracted with diethyl ether (2 x 60 mL). The organic layer was washed with water and brine, then dried over $MgSO_4$, filtered and concentrated under reduced pressure to obtain a colorless liquid which was further purified by Kugelrohr distillation (56-57 °C/0.25 mm of Hg) to yield **47** (7.16 g, 28.0 mmol, 92% yield) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.08 (m, 21H, TIPS), 0.18 (s, 9H, TMS); IR ν 2959 (m), 2944 (m), 2896 (w), 2867 (m), 1464 (w), 1385 (w), 1250 (m), 996 (w), 842 (s), 764 (s), 675 (m), 660 (m). The values of the NMR spectra are in accordance with reported literature data.[17]

1-[(Tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (2a)

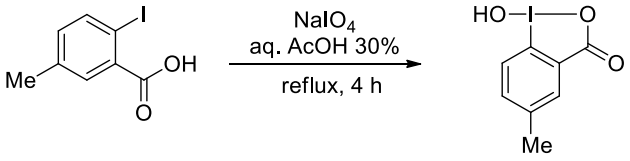


45 **2a**

Following a reported procedure,[18] 2-iodosylbenzoic acid (**45**) (21.7 g, 82.0 mmol, 1.00 equiv) was charged in oven-dried three-neck 1L flask equipped with a magnetic stirrer. After 3 vacuum/nitrogen cycles, anhydrous acetonitrile (500 mL) was added *via* canula and cooled to 0 °C. Trimethylsilyltriflate (16.4 mL, 90.0 mmol, 1.10 equiv) was added dropwise *via* a dropping funnel over 30 min (no temperature increase was observed). After 15 min, (trimethylsilyl)(tri*iso*propylsilyl)acetylene (**47**) (23.0 g, 90.0 mmol, 1.10 equiv) was added *via* canula over 15 min (no temperature increase was observed). After 30 min, the suspension became an orange solution. After 10 min, pyridine (7.0 mL, 90 mmol, 1.1 equiv) was added *via* syringe. After 15 min, the reaction mixture was transferred in a one-neck 1L flask and reduced under vacuum until a solid was obtained. The solid was dissolved in CH_2Cl_2 (200 mL) and transferred in a 1L separatory funnel. The organic layer was added and washed with 1 M HCl (200 mL) and the aqueous layer was extracted with CH_2Cl_2 (200 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (2 x 200 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 120 mL) afforded **2a** (30.1 g, 70.2 mmol, 86%) as colorless crystals. Mp (Dec.): 170.0-176.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (m, 1H, Ar*H*), 8.29 (m, 1H, Ar*H*), 7.77 (m, 2H, Ar*H*), 1.16 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 134.6, 132.3, 131.4, 131.4, 126.1, 115.6, 114.1, 64.6, 18.4, 11.1;

IR ν 2943 (m), 2865 (m), 1716 (m), 1618 (m), 1604 (s), 1584 (m), 1557 (m), 1465 (m), 1439 (w), 1349 (m), 1291 (m), 1270 (w), 1244 (m), 1140 (m), 1016 (m), 999 (m), 883 (m), 833 (m), 742 (m), 702 (s), 636 (m). The characterization data corresponded to the reported values.[18]

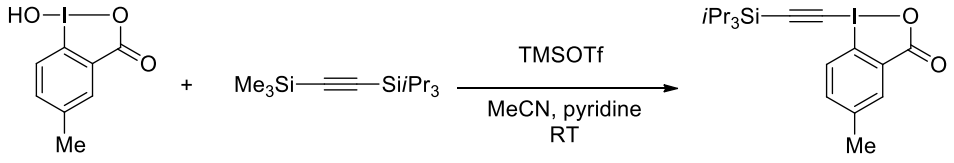
5-Methyl-2-iodosylbenzoic acid (49)



48 **49**

Following a reported procedure,[19] $NaIO_4$ (1.25 g, 5.84 mmol, 1.05 equiv) and 2-iodo-5-methylbenzoic acid (**48**) (1.46 g, 5.56 mmol, 1.00 equiv) were suspended in 30% (v/v) aq. AcOH (15 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (40 mL) and allowed to cool to room temperature, protecting it from light. The crude product was collected by filtration, washed on the filter with ice water (3 x 4 mL) and acetone (3 x 4 mL), and air-dried in the dark to give the pure product **49** (1.39 g, 5.00 mmol, 90%) as a colorless solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 7.84 (s, 1H, Ar*H*), 7.78 (m, 1H, Ar*H*), 7.69 (m, 1H, Ar*H*), 2.47 (s, 3H, CH_3). The characterization data corresponded to the reported values.[19]

5-Methyl-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (2b)

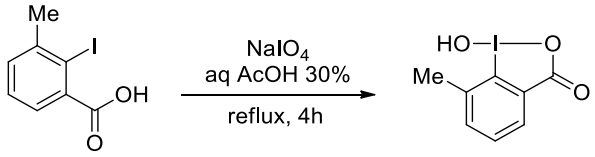


49 **47** **2b**

Following a reported procedure,[19] trimethylsilyltriflate (400 µL, 2.20 mmol, 1.10 equiv) was added dropwise to a stirred solution of **49** (556 mg, 2.00 mmol, 1.00 equiv) in acetonitrile (10 mL). After 20 min, (trimethylsilyl)(tri*iso*-propylsilyl)acetylene (**47**) (560 mg, 2.20 mmol, 1.10 equiv) was then added dropwise, followed, after 20 min, by the addition of pyridine (180 µL, 2.20 mmol, 1.10 equiv). The mixture was stirred for 20 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in CH_2Cl_2 (20 mL). The organic layer was washed with 1 M HCl (20 mL) and the aqueous layer was extracted with CH_2Cl_2 (20 mL). The organic layers

were combined, washed with a saturated solution of $NaHCO_3$ (40 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 25 mL) and wash with hexanes afforded **2b** (559 mg, 1.26 mmol, 63%) as colorless crystals. Mp (Dec.): 192.0-197.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (d, *J* = 1.5 Hz, 1H, Ar*H*), 8.12 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.57 (dd, *J* = 8.5, 1.8 Hz, 1H, Ar*H*), 2.51 (s, 3H, ArC*H*$_3$), 1.16 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 142.5, 135.6, 133.0, 131.2, 125.8, 113.8, 111.8, 64.6, 20.7, 18.5, 11.2. The characterization data corresponded to the reported values.[19]

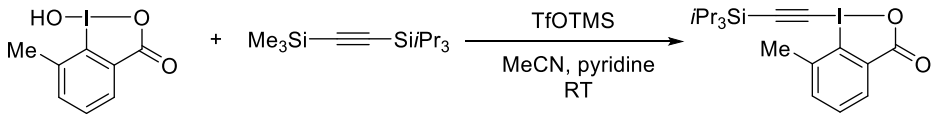
3-Methyl-2-iodosylbenzoic acid (51)



50 **51**

Following a reported procedure,[19] $NaIO_4$ (1.25 g, 5.84 mmol, 1.05 equiv) and 2-iodo-3-methylbenzoic acid (**50**) (1.46 g, 5.56 mmol, 1.00 equiv) were suspended in 30% (v:v) aq. AcOH (15 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (40 mL) and allowed to cool to RT, protecting it from light. The crude product was collected by filtration, washed on the filter with ice water (3 x 4 mL) and acetone (3 x 4 mL), and air-dried in the dark to give the pure product **51** (1.24 g, 4.46 mmol, 80%) as a white solid. ^{1}H NMR (400 MHz, DMSO) δ 8.30 (br s, 1 H, OH), 7.85 (m, 1 H, ArH), 7.57 (m, 2 H, ArH), 2.64 (s, 3 H, ArH). The characterization data corresponded to the reported values.[19]

3-Methyl-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (2c)

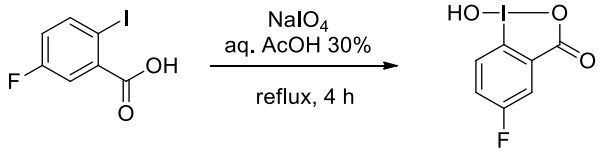


51 **47** **2c**

Following a reported procedure,[19] trimethylsilyltriflate (2.10 mL, 11.6 mmol, 1.1 equiv) was added dropwise to a stirred solution of **51** (2.93 g, 10.5 mmol, 1.0 equiv) in acetonitrile (45 mL). After 20 min, (trimethylsilyl)(tri*iso*-propylsilyl)acetylene (**47**) (2.94 g, 11.6 mmol, 1.1 equiv) was then added dropwise, followed, after 30 min, by the addition of pyridine (934 µL, 11.6 mmol, 1.1 equiv). The mixture was stirred 20 min. The solvent was then removed under reduced pressure and the

yellow crude oil was dissolved in dichloromethane (30 mL). The organic layer was washed with 1 M HCl (20 mL) and the aqueous layer was extracted with CH_2Cl_2 (30 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (40 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 10 mL) and wash with pentane afforded **2c** (2.79 g, 6.31 mmol, 60 %) as colorless cristals. Mp (Dec.): 138.0–145.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$); δ 8.21 (dd, 1H, *J* = 6.8, 2.5 Hz, Ar*H*), 7.50 (m, 2H, Ar*H*), 2.87 (s, 3H, C*H*$_3$), 1.10 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 140.3, 138.0, 133.3, 131.7, 130.8, 119.1, 112.5, 66.9, 24.0, 18.5, 11.2; IR 2946 (w), 2867 (w), 2244 (w), 1649 (m), 1562 (w), 1464 (w), 1326 (w), 1281 (w), 998 (w), 907 (s), 884 (w), 763 (w), 728 (s), 687 (s), 647 (m). The characterization data corresponded to the reported values.[19]

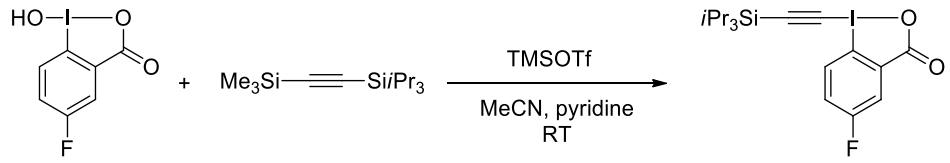
5-Fluoro-2-iodosylbenzoic acid (53)



52 **53**

Following a reported procedure,[19] $NaIO_4$ (656 mg, 3.07 mmol, 1.05 equiv) and 2-iodo-4-fluorobenzoic acid (**52**) (778 mg, 2.92 mmol, 1.00 equiv) were suspended in 30% (v/v) aq. AcOH (7 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (20 mL) and allowed to cool to room temperature, protecting it from light. The crude product was collected by filtration, washed on the filter with ice water (3 x 4 mL) and acetone (3 x 4 mL), and air-dried in the dark to give the pure product **53** (738 mg, 2.62 mmol, 90%) as a white solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 7.88-7.79 (m, 3H, Ar*H* and O*H*), 7.75 (m, 1H, Ar*H*). The characterization data corresponded to the reported values.[19]

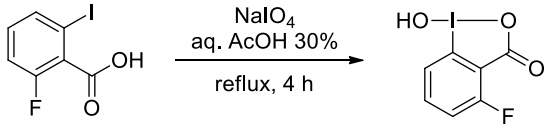
5-Fluoro-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (2d)



53 **47** **2d**

Following a reported procedure,[19] trimethylsilyltriflate (247 μL, 1.36 mmol, 1.10 equiv, freshly distilled) was added dropwise to a stirred solution of **53** (350 mg, 1.24 mmol, 1.00 equiv) in acetonitrile (5 mL). (Trimethylsilyl)(tri*iso*-propylsilyl)acetylene (**47**) (349 mg, 1.36 mmol, 1.10 equiv) was then added dropwise, followed, after 15 min, by the addition of pyridine (110 μL, 1.36 mmol, 1.10 equiv). The mixture was stirred for 10 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in CH_2Cl_2 (50 mL). The organic layer was washed with 1 M HCl (50 mL) and the aqueous layer was extracted with CH_2Cl_2 (50 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (2 x 50 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 5 mL) afforded **2d** (381 mg, 0.854 mmol, 69%) as a white solid. Mp (Dec.); 185.0-189.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (dd, *J* = 9.0, 4.2 Hz, 1H, Ar*H*), 8.10 (dd, *J* = 7.9, 2.9 Hz, 1H, Ar*H*), 7.48 (m, 1H, Ar*H*), 1.16 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6 (d, *J* = 254 Hz), 165.2 (d, *J* = 7 Hz), 134.2 (d, *J* = 7 Hz), 127.8 (d, *J* = 8 Hz), 122.2 (d, *J* = 24 Hz), 119.4 (d, *J* = 24 Hz), 115.0, 108.0 (d, *J* = 1 Hz), 64.0, 18.5, 11.2. The characterization data corresponded to the reported values.[19]

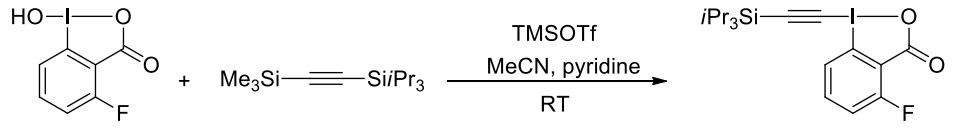
6-Fluoro-2-iodosylbenzoic acid (55)



54 **55**

Following a slightly modified procedure,[19] $NaIO_4$ (656 mg, 3.07 mmol, 1.05 equiv) and 2-iodo-6-fluorobenzoic acid (**54**) (778 mg, 2.92 mmol, 1.00 equiv) were suspended in 30% (v/v) aq. AcOH (7 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (20 mL) and allowed to cool to room temperature, protecting it from light. The crude product was collected by filtration, washed on the filter with ice water (3 x 4 mL) and acetone (3 x 4 mL), and air-dried in the dark to give the pure product **55** (738 mg, 2.62 mmol, 90%) as a white solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 8.21 (s, 1H, O*H*), 7.89 (td, *J* = 8.1, 4.6 Hz, 1H, Ar*H*), 7.70 (d, *J* = 8.1 Hz, 1H, Ar*H*), 7.53 (dd, *J* = 10.3, 8.1 Hz, 1H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9 (d, *J* = 263.9 Hz), 163.9 (d, *J* = 4.4 Hz), 135.3 (d, *J* = 8.6 Hz), 123.3, 122.6 (d, *J* = 3.9 Hz), 119.3 (d, *J* = 12.0 Hz), 118.7 (d, *J* = 21.8 Hz). The characterization data corresponded to the reported values.[20]

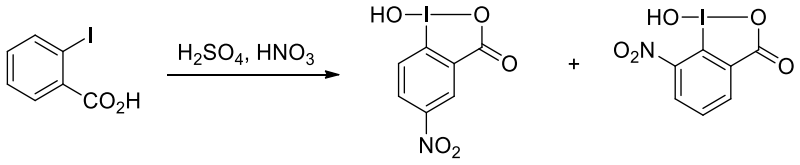
6-Fluoro-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (2e)



55 **47** **2e**

Trimethylsilyltriflate (247 µL, 1.36 mmol, 1.10 equiv, freshly distilled) was added dropwise to a stirred solution of **55** (350 mg, 1.24 mmol, 1.00 equiv) in acetonitrile (5 mL). (Trimethylsilyl)(tri*iso*-propylsilyl)acetylene (**47**) (349 mg, 1.36 mmol, 1.10 equiv) was then added dropwise, followed, after 15 min, by the addition of pyridine (110 µL, 1.36 mmol, 1.10 equiv). The mixture was stirred for 10 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in CH_2Cl_2 (50 mL). The organic layer was washed with 1 M HCl (50 mL) and the aqueous layer was extracted with CH_2Cl_2 (50 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (2 x 50 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 5 mL) afforded **2e** (414 mg, 0.854 mmol, 75%) as a white solid. Mp (Dec.); 165.0-170.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, *J* = 8.3 Hz, 1H, Ar*H*), 7.65 (td, *J* = 8.2, 4.3 Hz, 1H, Ar*H*), 7.45 (t, *J* = 8.7 Hz, 1H, Ar*H*), 1.19-1.13 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0 (d, *J* = 269.3 Hz), 162.7 (d, *J* = 4.5 Hz), 134.8 (d, *J* = 8.6 Hz), 122.1 (d, *J* = 4.0 Hz), 120.5 (d, *J* = 22.8 Hz), 119.7 (d, *J* = 12.8 Hz), 118.5, 114.9, 66.2, 18.5, 11.1; IR ν 2951 (m), 2869 (m), 2247 (w), 2138 (w), 1638 (s), 1569 (w), 1460 (m), 1322 (m), 1252 (m), 1069 (m), 1007 (w), 914 (m), 866 (m); HRMS (ESI) calcd. for $C_{18}H_{25}FIO_2Si^+$ $[M+H]^+$ 447.0647; found 447.0647.

2-Iodosyl-5-nitrobenzoic acid (57) and 2-iodosyl-3-nitrobenzoic acid (58)

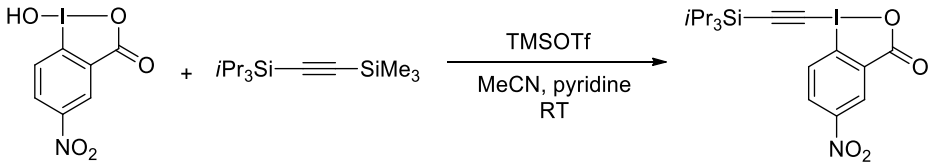


56 **57** **58**

Following a reported procedure,[19] fuming nitric acid (3.3 mL) was added to 2-iodobenzoic acid (**56**) (5.0 g, 20 mmol, 1.0 equiv) in concentrated H_2SO_4 (6.7 mL). The reaction was equipped with a cooler and a nitrous vapor trap and was heated at 100 °C for 1 h. The reaction mixture was then poured in ice-water and filtered. The resulting solid was refluxed in water (50 mL) and filtered. A second crop of precipitate was filtered from the mother liquors. Both solids were combined, washed

with acetone (10 mL) and dried under vacuum to afford **57** (2.19 g, 7.10 mmol, 36 %). The mother liquors were reduced to one third and then kept at 4 °C, the resulting precipitate was filtered, washed with acetone (10 mL) and dried under vacuum to afford **58** (630 mg, 2.04 mmol, 10 %). **57**: ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 8.73 (dd, *J* = 8.8, 2.6 Hz, 1H, Ar*H*), 8.58 (d, *J* = 2.4 Hz, 1H, Ar*H*), 8.54 (br s, 1H, O*H*), 8.11 (d, *J* = 8.8 Hz, 1H, Ar*H*). **58**: ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 7.92 (dd, *J* = 7.9, 1.5 Hz, 1H, Ar*H*), 7.79 (m, 1H, Ar*H*), 7.67 (m, 1H, Ar*H*). The characterization data corresponded to the reported values.[19]

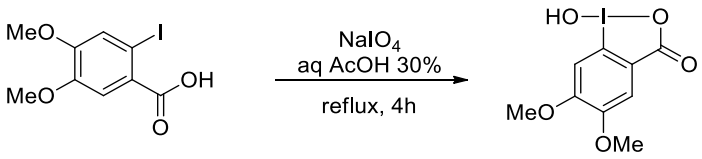
5-Nitro-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (2f)



57 **47** **2f**

Following a reported procedure,[19] trimethylsilyltriflate (646 µL, 3.56 mmol, 1.10 equiv, freshly distilled over CaH_2) was added dropwise to a stirred solution of 2-iodosylbenzoic acid **57** (1.00 g, 3.23 mmol, 1.00 equiv) in acetonitrile (15 mL) at 0 °C. After 15 min at room temperature, (trimethylsilyl)(tri*iso*-propylsilyl)acetylene (**47**) (906 mg, 3.56 mmol, 1.10 equiv) was then added dropwise, followed, after 30 min, by the addition of pyridine (290 µL, 3.56 mmol, 1.10 equiv). The mixture was stirred for 20 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in CH_2Cl_2 (25 mL). The organic layer was washed with 1 M HCl (25 mL) and the aqueous layer was extracted with CH_2Cl_2 (25 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 20 mL) afforded **2f** (960 mg, 2.02 mmol, 63%) as a white solid. Mp (Dec.); 198.0-206.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.20 (d, *J* = 2.6 Hz, 1H, Ar*H*), 8.60 (ddd, *J* = 9.0, 2.5, 0.4 Hz, 1H, Ar*H*), 8.53 (d, *J* = 8.9 Hz, 1H, Ar*H*), 1.30-1.14 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 150.7, 134.4, 129.0, 128.2, 126.5, 122.7, 115.2, 63.1, 18.5, 11.3. The characterization data corresponded to the reported values.[19]

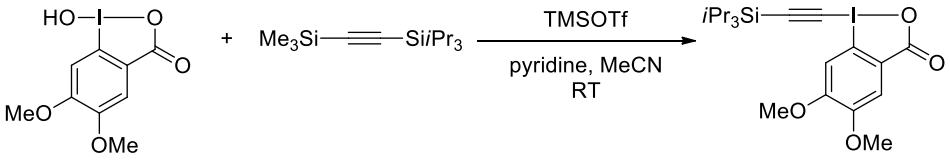
4,5-Dimethoxy-2-iodosylbenzoic acid (60)



59 **60**

Following a reported procedure,[19] $NaIO_4$ (1.25 g, 5.84 mmol, 1.05 equiv) and 2-iodo-4,5-dimethoxybenzoic acid (**59**) (1.71 g, 5.56 mmol, 1.00 equiv) were suspended in 30% (v:v) aq. AcOH (15 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (40 mL) and allowed to cool to RT, protecting it from light. The crude product was collected by filtration, washed on the filter with ice water (3 x 4 mL) and acetone (3 x 4 mL), and air-dried in the dark to give the pure product **60** (1.64 g, 5.06 mmol, 91%) as a colorless solid. ^{1}H NMR (400 MHz, DMSO); δ 7.45 (s, 1H, ArH), 7.23 (s, 1H, ArH), 3.88 (d, 6H, *J* = 0.9 Hz, Me). The characterization data corresponded to the reported values.[19]

4,5-Dimethoxy-1-[(tr*iiso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (2g)

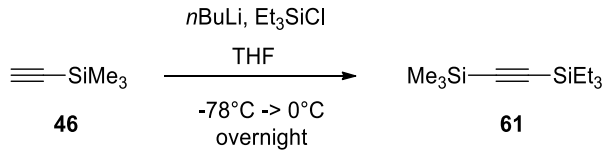


60 **47** **2g**

Following a reported procedure,[19] trimethylsilyltriflate (400 µL, 2.20 mmol, 1.1 equiv, freshly distilled) was added dropwise to a stirred solution of **60** (648 mg, 2.00 mmol, 1.0 equiv) in acetonitrile (10 mL). After 2 min, (trimethylsilyl)(tri*iso*-propylsilyl)acetylene (**47**) (560 mg, 2.20 mmol, 1.1 equiv) was added dropwise, followed, after 20 min, by the addition of pyridine (180 µL, 2.20 mmol, 1.1 equiv). The mixture was stirred 20 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in dichloromethane (20 mL). The organic layer was washed with 1 M HCl (20 mL) and the aqueous layer was extracted with CH_2Cl_2 (20 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (40 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 8 mL) and wash with hexanes afforded **2g** (575 mg, 1.18 mmol, 59%) as colorless cristals. Mp (Dec.) 180.0–183.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.83 (s, 1H, Ar*H*), 7.61 (s, 1H, Ar*H*), 3.99 (s, 3H, OMe), 3.97 (s, 3H, OMe), 1.14 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$); δ 166.7, 154.9, 152.2, 124.5, 113.8, 113.2, 107.8, 104.7, 66.0, 56.7, 56.5,

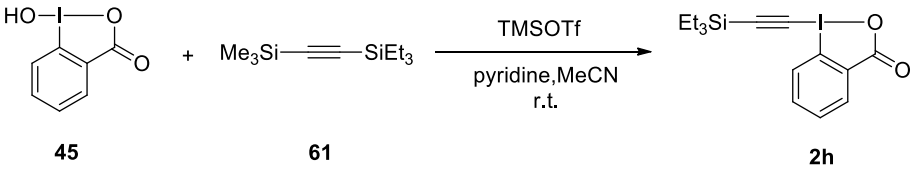
18.5, 11.2; IR 2945 (w), 1616 (m), 1569 (w), 1497 (m), 1464 (w), 1396 (m), 1317 (w), 1269 (m), 1215 (m), 1181 (w), 1129 (w), 1026 (w), 921 (w), 884 (w), 778 (w), 734 (m), 708 (m), 639 (s). The characterization data corresponded to the reported values.[19]

Triethyl trimethylsilylacetylene (61)



Following a reported procedure,[19] *n*-butyllithium (2.5 M in hexanes, 5.4 mL, 14 mmol, 1.0 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (**46**) (1.36 g, 13.8 mmol, 1.00 equiv) in THF (21 mL) at -78 °C. The mixture was then warmed to 0 °C and stirred for 5 min. The mixture was then cooled back to -78 °C and chlorotriethylsilane (2.3 mL, 14 mmol, 0.98 equiv) was added dropwise. The mixture was then allowed to warm to room temperature and stirred overnight. A saturated solution of ammonium chloride (20 mL) was added, and the reaction mixture was extracted with diethyl ether (2 x 20 mL). The organic layer was washed with water and brine, then dried over $MgSO_4$, filtered and concentrated under reduced pressure to obtain a colorless liquid which was further purified by Kugelrohr distillation to yield **61** (3.4 g, 11 mmol, 83% yield) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): 0.99 (t, J = 7.9 Hz, 9H, $SiCH_2\mathit{CH}_3$), 0.59 (q, J = 7.9 Hz, 6H, $Si\mathit{CH}_2CH_3$), 0.17 (s, 9H, TMS); ^{13}C NMR (100 MHz, $CDCl_3$): 115.4, 111.2, 7.4, 4.4, 0.0; IR ν 2958 (m), 2913 (m), 2879 (m), 1462 (w), 1414 (w), 1381 (w), 1250 (m), 1015 (m), 973 (w), 908 (w), 844 (s), 773 (s), 731 (s), 702 (sh), 679 (sh). The characterization data corresponded to the reported values.[19]

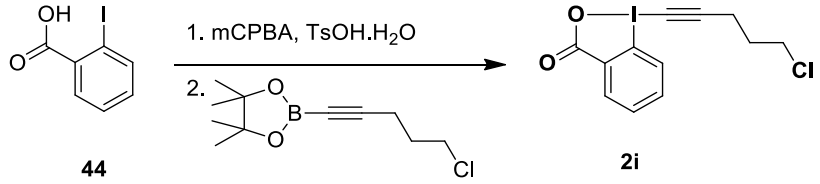
1-[(Triethylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (2h)



Following a reported procedure,[19] trimethylsilyltriflate (2.78 mL, 15.4 mmol, 1.1 equiv, freshly distilled over CaH_2) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (**45**) (3.71 g, 14.0 mmol, 1.0 equiv) in acetonitrile (50 mL). After 15 min, (trimethylsilyl)(triethylsilyl)acetylene (**61**) (3.26 g, 15.4 mmol, 1.1 equiv) was then added

dropwise. After 30 min pyridine (1.25 mL, 15.4 mmol, 1.1 equiv) was added and the mixture was stirred for an additional 15 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in dichloromethane (50 mL). The organic layer was washed with 1 M HCl (50 mL), and the aqueous layer was extracted with CH_2Cl_2 (50 mL). The organic layers were washed twice with saturated $NaHCO_3$ (75 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The resulting solid was recristalized twice in CH_3CN. The solid was washed with cold acetonitirile, hexanes and dried under high vacuum to afford **2h** (2.95 g, 7.64 mmol, 55% yield) as a slightly brown solid. Mp (Dec.) 155.0–158.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (m, 1H, Ar*H*), 8.24 (m, 1H, Ar*H*), 7.75 (m, 2H, Ar*H*), 1.06 (t, *J* = 8.0 Hz, 9H, $SiCH_2\mathit{CH_3}$), 0.73 (q, *J* = 8.0 Hz; 6H, $Si\mathit{CH_2}CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 134.8, 132.5, 131.6, 131.3, 126.1, 115.5, 115.1, 64.6, 7.4, 4.1; IR ν 3064 (w), 3062 (m), 2957 (m), 2911 (m), 2877 (m), 1621 (s), 1587 (m), 1561 (m), 1460 (m), 1440 (m), 1415 (w), 1378 (w), 1336 (m), 1297 (m), 1237 (w), 1149 (w), 1113 (w), 1010 (m), 976 (w), 912 (w), 912 (w), 834 (m), 804 (w), 739 (s), 693 (m), 675 (m), 647 (w). The characterization data corresponded to the reported values.[19]

(5-Chloropent-1-ynyl)-1,2-benziodoxol-3(1H)-one (2i)

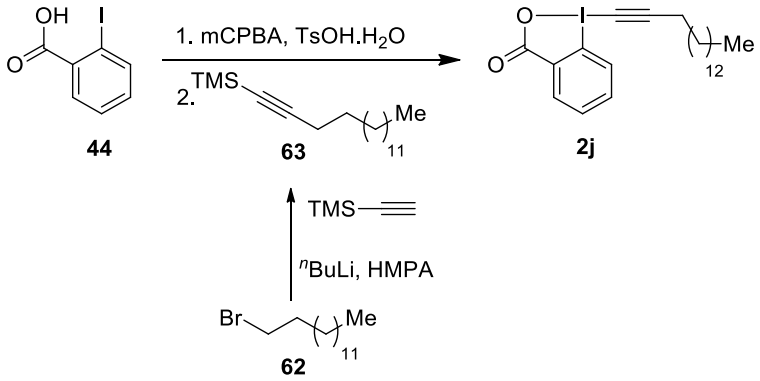


44 **2i**

Following a reported procedure,[21] 2-iodobenzoic acid (**44**) (3.76 g, 15.2 mmol, 1.00 equiv), *para*-toluenesulfonic acid monohydrate ($TsOH.H_2O$, 2.88 g, 15.2 mmol, 1.00 equiv) and *meta*-chloroperoxybenzoic acid (mCPBA-70%, 4.11 g, 16.7 mmol, 1.10 equiv) were dissolved in CH_2Cl_2 (30 mL) and 2,2,2-trifluoroethanol (30 mL). The mixture was stirred at room temperature under nitrogen for 1 h, after which 5-chloro-1-pentynyl-1-boronic acid pinacol ester (4.85 g, 21.2 mmol, 1.40 equiv) was added in one portion. The reaction mixture was stirred for 90 minutes at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in CH_2Cl_2 (15 mL) and under vigorous stirring, saturated solution of $NaHCO_3$ (15 mL) was added. The mixture was stirred for 10 minutes, the two layers were separated and the aqueous layer was extracted with additional portions of CH_2Cl_2 (3 x 15 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash column

chromatography using ethyl acetate to afford **2i** (3.76 g, 10.8 mmol, 71%) as a white solid. TLC (EtOAc): R_f = 0.15, $KMnO_4$; Mp: 138.5-141.7 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.41-8.34 (m, 1H, Ar*H*), 8.22-8.13 (m, 1H, Ar*H*), 7.82-7.68 (m, 2H, Ar*H*), 3.71 (t, *J* = 6.1 Hz, 2H, ClC*H*$_2$CH$_2$), 2.82 (t, *J* = 6.9 Hz, 2H, CCC*H*$_2$CH$_2$), 2.18-2.05 (m, 2H, ClCH$_2$C*H*$_2$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.8, 134.9, 132.5, 131.6, 131.6, 126.4, 115.8, 107.1, 43.4, 41.2, 30.7, 18.0; IR ν 2942 (w), 2866 (w), 2171 (w), 2091 (w), 1727 (w), 1617 (s), 1556 (w), 1441 (w), 1339 (m), 1213 (w), 1023 (w), 846 (w), 742 (s). The characterization data corresponded to the reported values.[21]

Hexadecynyl-1,2-benziodoxol-3(1*H*)-one (2j)

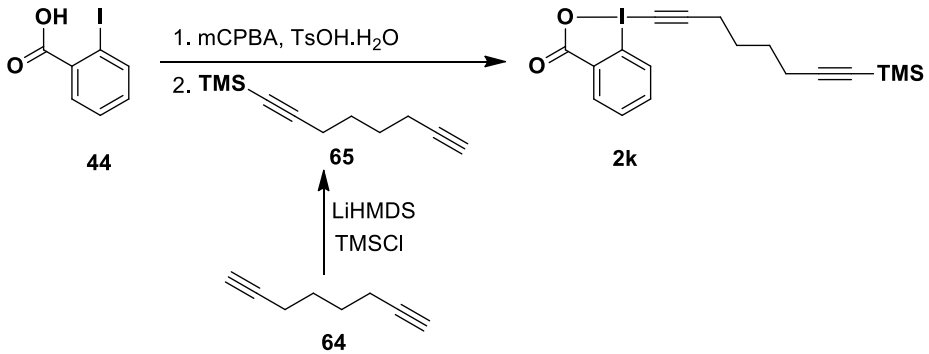


Following a reported procedure,[21] to a mixture of trimethylsilylacetylene (8.33 g, 85.0 mmol, 1.20 equiv) and dry THF (46 mL) was added at -78 °C under nitrogen 2.5 M ^{n}BuLi in hexanes (33.9 mL, 85.0 mmol, 1.20 equiv) over a 10 minute time period. The resulting light yellow solution was stirred at -78 °C for 1 h, after which a mixture consisting of 1-bromotetradecane (**62**) (19.6 g, 70.7 mmol, 1.00 equiv), hexamethylphosphoramide (HMPA, 14.2 mL, 78.0 mmol, 1.10 equiv) and dry THF (23 mL) was slowly added *via* cannula over a 20 minutes time period. The reaction mixture was stirred for 1 h at -78 °C, followed by 24 h of stirring at room temperature. The reaction was quenched at 0 °C with saturated aq. NH_4Cl (50 mL) and diluted with water (10 mL) and EtOAc (50 mL). The two layers were separated and the aq. layer was extracted with additional portions of EtOAc (3 x 50 mL). The combined organic layers were washed with water (2 x 100 mL), brine (100 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The light brown crude liquid was finally pushed through a small plug of silica gel with pentane as eluent to afford pure hexadec-1-yn-1-yltrimethylsilane (**63**) (19.3 g, 65.5 mmol, 92.7% yield) as a colorless liquid. TLC (pentane): R_f = 0.78, $KMnO_4$; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.19 (t, *J* = 7.1 Hz, 2H, CCC*H*$_2$), 1.54-1.44 (m, 2H, C*H*$_2$), 1.42-1.18 (m, 22H, C*H*$_2$), 0.87 (t, *J* = 6.7 Hz, 3H, CH$_2$C*H*$_3$), 0.13 (s, 9H, TMS); ^{13}C

NMR ($CDCl_3$, 100 MHz): δ 107.7, 84.3, 32.2, 29.9, 29.8, 29.7, 29.6, 29.3, 29.0, 28.9, 22.9, 20.0, 14.3, 0.3; IR ν 2924 (m), 2854 (m), 2175 (w), 1461 (w), 1249 (w), 910 (w), 841 (s), 761 (w), 736 (m). The characterization data corresponded to the reported values.[21]

Following a reported procedure,[21] 2-iodobenzoic acid (**44**) (8.00 g, 32.2 mmol, 1.00 equiv), *para*-toluenesulfonic acid monohydrate ($TsOH.H_2O$, 6.13 g, 32.2 mmol, 1.00 equiv) and *meta*-chloroperoxybenzoic acid (mCPBA-70%, 8.74 g, 35.5 mmol, 1.10 equiv) were dissolved in CH_2Cl_2 (60 mL) and 2,2,2-trifluoroethanol (60 mL). The mixture was stirred at room temperature under nitrogen for 1 h, after which hexadec-1-yn-1-yltrimethylsilane (**63**) (13.3 g, 45.1 mmol, 1.40 equiv) was added in one portion. The reaction mixture was stirred for 14 h at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in CH_2Cl_2 (400 mL) and under vigorous stirring, saturated solution of $NaHCO_3$ (400 mL) was added. The mixture was stirred for 1 h, the two layers were separated and the aqueous layer was extracted with additional portions of CH_2Cl_2 (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography using EtOAc to afford **2j** (6.02 g, 12.9 mmol, 40%) as a white solid. TLC (EtOAc): R_f = 0.36, $KMnO_4$; Mp: 102.6-105.3 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.44-8.37 (m, 1H, Ar*H*), 8.21-8.14 (m, 1H, Ar*H*), 7.80-7.70 (m, 2H, Ar*H*), 2.59 (t, *J* = 7.1 Hz, 2H, CCC*H*$_2$), 1.65 (p, *J* = 7.1 Hz, 2H, CCCH$_2$C*H*$_2$), 1.52-1.40 (m, 2H), 1.39-1.19 (m, 20H, C*H*$_2$), 0.86 (t, *J* = 6.7 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.6, 134.7, 132.5, 131.7, 131.6, 126.2, 115.7, 109.9, 39.5, 32.1, 29.8, 29.7, 29.6, 29.5, 29.2, 29.1, 28.3, 22.8, 20.6, 14.3; IR ν 2924 (s), 2853 (m), 2166 (w), 1649 (m), 1623 (m), 1439 (w), 908 (m), 736 (s). The characterization data corresponded to the reported values.[21]

8-(Trimethylsilyl)octa-1,7-diyn-1-yl-1,2-benziodoxol-3(1*H*)-one (2k)

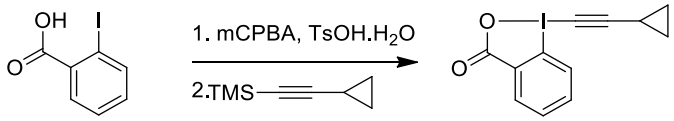


Following a reported procedure,[15] to a solution of 1,7-octadiyne **64** (10.6 g, 100 mmol, 1.00 equiv) in dry THF (150 mL) was added at -78 °C under nitrogen 1 M lithium bis(trimethylsilyl)amide in THF (LiHMDS, 100 mL, 100 mmol, 1.00 equiv). The solution was stirred at -78 °C for 30 minutes, after which trimethylsilyl chloride (TMSCl, 13.0 mL, 100 mmol, 1.00 equiv) was added dropwise. The reaction was warmed to room temperature and stirred for 2 h. The reaction was cooled to 0 °C and quenched by adding water (10 mL). The mixture was diluted with 1 M HCl (200 mL) and extracted with diethyl ether (100 mL and 2 x 75 mL). The combined organic layers were washed with brine (200 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by vacuum distillation using a 20 cm Vigreux column (oil bath set to 98 °C at 0.3 mbar) furnishing pure trimethyl(octa-1,7-diyn-1-yl)silane (**65**) (8.37 g, 46.9 mmol, 47%) as a colorless liquid. TLC (pentane): R_f = 0.2, $KMnO_4$; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.28-2.17 (m, 4H), 1.93 (t, *J* = 2.7 Hz, 1H, CC*H*), 1.68-1.57 (m, 4H), 0.13 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 107.0, 84.9, 84.2, 68.6, 27.7, 27.6, 19.5, 18.1, 0.3; IR ν 3309 (w), 2951 (w), 2175 (w), 1250 (m), 912 (w), 841 (s), 761 (m), 734 (m). The characterization data corresponded to the reported values.[15]

Following a reported procedure,[15] 2-iodobenzoic acid (**44**) (8.43 g, 33.3 mmol, 1.00 equiv), *para*-toluenesulfonic acid monohydrate ($TsOH.H_2O$, 6.40 g, 33.3 mmol, 1.00 equiv) and *meta*-chloroperoxybenzoic acid (mCPBA-70%, 9.04 g, 36.7 mmol, 1.10 equiv) were dissolved in CH_2Cl_2 (60 mL) and 2,2,2-trifluoroethanol (60 mL). The mixture was stirred at room temperature under nitrogen for 1 h, after which trimethyl(octa-1,7-diyn-1-yl)silane (**65**) (8.32 g, 46.7 mmol, 1.40 equiv) was added. The reaction mixture was stirred for 15 h at room temperature and then filtered and concentrated in vacuo. The resulting light being solid was dissolved in CH_2Cl_2 (500 mL) and under vigorous stirring, saturated solution of $NaHCO_3$ (500 mL) was added. The mixture was stirred for 1 h, the two layers were separated and the aqueous layer was extracted with additional portions of CH_2Cl_2 (3 x 150 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography using ethyl acetate to afford **2k** (4.2 g, 9.9 mmol, 30%) as a white solid. Mp: 152.3–155.6 °C; TLC (EtOAc:MeOH, 9:1 v/v): R_f = 0.59, $KMnO_4$; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.37 (dd, *J* = 6.7, 2.3 Hz, 1H, Ar*H*), 8.17 (dd, *J* = 7.8, 1.5 Hz, 1H, Ar*H*), 7.82-7.66 (m, 2H, Ar*H*), 2.63 (t, *J* = 6.8 Hz, 2H,), 2.29 (t, *J* = 6.7 Hz, 2H), 1.83-1.62 (m, 4H), 0.13 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.7, 134.8, 132.4, 131.7, 131.5, 126.3, 115.7, 109.1, 106.4, 85.4, 40.0, 27.7, 27.3, 20.2, 19.4,

0.3; IR ν 2955 (w), 2170 (w), 1647 (m), 1621 (s), 1439 (w), 1329 (m), 1296 (w), 1249 (m), 840 (s), 746 (s). The characterization data corresponded to the reported values.[15]

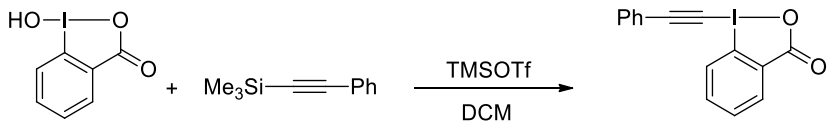
2-Cyclopropylethynyl-1,2-benziodoxol-3(1*H*)-one (2l)



44 **2l**

Following a reported procedure,[15] 2-iodobenzoic acid (**44**) (6.41 g, 25.8 mmol, 1.00 equiv), *para*-toluenesulfonic acid monohydrate ($TsOH{\cdot}H_2O$, 4.91 g, 25.8 mmol, 1.00 equiv) and *meta*-chloroperoxybenzoic acid (*m*CPBA-70%, 7.00 g, 28.4 mmol, 1.10 equiv) were dissolved in dichloromethane (48 mL) and 2,2,2-trifluoroethanol (48 mL). The mixture was stirred at room temperature under nitrogen for 1 h, after which (cyclopropylethynyl)trimethylsilane (5.00 g, 36.2 mmol, 1.40 equiv) was added in one portion. The reaction mixture was stirred for 12 h at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in CH_2Cl_2 (400 mL) and under vigorous stirring, a saturated solution of $NaHCO_3$ (400 mL) was added. The mixture was stirred for 1 h, the two layers were separated and the aqueous layer was extracted with additional portions of CH_2Cl_2 (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography using ethyl acetate to afford **2l** (2.11 g, 6.76 mmol, 26 %) as a white solid. Mp (Dec.): 174.2–177.6 °C; TLC (EtOAc:MeOH, 9:1 v/v): R_f = 0.46, $KMnO_4$; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.34 (dd, *J* = 7.0, 2.1 Hz, 1H, Ar*H*), 8.18-8.09 (m, 1H, Ar*H*), 7.81-7.63 (m, 2H, Ar*H*), 1.59 (tt, *J* = 8.2, 5.0 Hz, 1H, C*H*), 1.07-0.85 (m, 4H, CH_2CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.7, 134.7, 132.3, 131.7, 131.4, 126.2, 115.9, 113.3, 35.0, 9.8, 1.1; IR ν 3464 (w), 3077 (w), 3012 (w), 2238 (w), 2159 (m), 1607 (s), 1559 (m), 1438 (m), 1338 (m), 1298 (m), 833 (m), 744 (s), 691 (m). The characterization data corresponded to the reported values.[15]

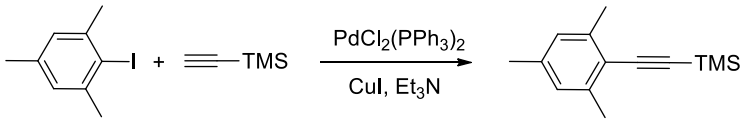
1-[Phenylethynyl]-1,2-benziodoxol-3(1*H*)-one (2m)



45 **66** **2m**

Following a reported procedure,[19] trimethylsilyl triflate (7.50 mL, 41.5 mmol, 1.10 equiv) was added to a suspension of 2-iodosylbenzoic acid (**45**) (10.0 g, 37.7 mmol, 1.00 equiv) in CH_2Cl_2 (100 mL) at room temperature. The resulting yellow mixture was stirred for 1 h, followed by the dropwise addition of trimethyl(phenylethynyl)silane (**66**) (8.10 mL, 41.5 mmol, 1.10 equiv) (slightly exothermic). The resulting suspension was stirred for 6 h at room temperature, during this time a white solid was formed. A saturated solution of $NaHCO_3$ (100 mL) was then added and the mixture was stirred vigorously. The resulting suspension was filtered on a glass filter of porosity 4. The two layers of the mother liquors were separated and the organic layer was washed with saturated solution of $NaHCO_3$ (100 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting mixture was combined with the solid obtained by filtration and boiled in CH_3CN (*ca* 300 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **2m** (6.08 g, 17.4 mmol, 46 %) as a white solid. Mp (Dec.); 155.0–160.0 °C (lit 153-155°C); ^{1}H NMR (400 MHz, $CDCl_3$); δ 8.46 (m, 1H, Ar*H*), 8.28 (m, 1H, Ar*H*), 7.80 (m, 2H, Ar*H*), 7.63 (m, 2H, Ar*H*), 7.48 (m, 3H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9, 134.9, 132.9, 132.5, 131.6, 131.3. 130.8, 128.8, 126.2, 120.5, 116.2, 106.6, 50.2. The characterization data corresponded to the reported values.[19]

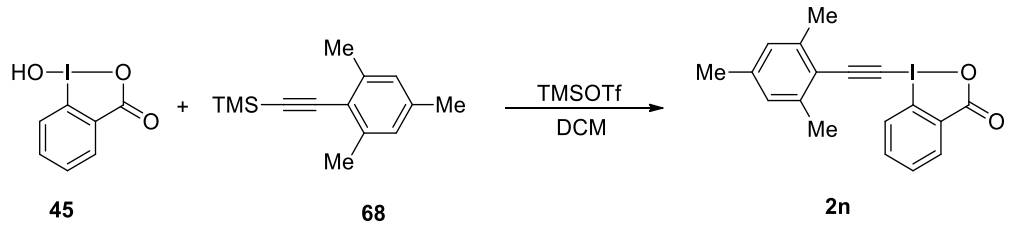
(Mesitylethynyl)trimethylsilane (68)



67 **46** **68**

Following a reported procedure,[19] iodo-mestylene (**67**) (1.05 g, 4.27 mmol, 1 equiv) was dissolved in Et_3N (10 mL) (without prior drying). After three freeze-thraw-pump cycle, $PdCl_2(PPh_3)_2$ (30 mg, 0.42 mmol, 0.1 equiv) and CuI (16 mg, 0.84 mmol, 0.2 equiv) were added under N_2. After the addition of trimethylsilylacetylene (**46**) (1.2 mL, 8.5 mmol, 2 equiv), the green suspension was stirred at RT for 1 h. The reaction mixture was reduced under vacuum, dissolved in CH_2Cl_2 (30 mL), washed with 5% EDTA solution (30 mL) and water (30 mL). The organic layers were them dried over $MgSO_4$, filtered and reduced under vacuum. The resulting oil was purified by column chromatography (PET) to afford **68** (526 mg, 2.43 mmol, 66%) along with 15% of starting material. TLC (pentane): R_f = 0.5, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.87 (s, 2H, Ar*H*), 2.41 (s, 6H, C*H*$_3$), 2.29 (s, 3H, C*H*$_3$), 0.28 (s, 9H, TMS).

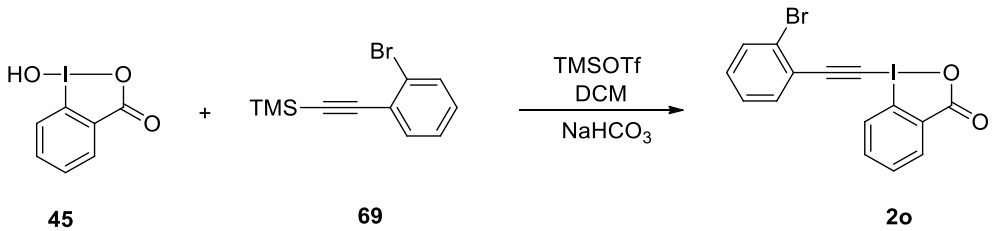
1-[2,4,6-Trimethylphenylethynyl]-1,2-benziodoxol-3(1*H*)-one (2n)



45 **68** **2n**

Following a reported procedure,[19] trimethylsilyl triflate (212 μL, 1.15 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**45**) (1.00 g, 1.05 mmol, 1 equiv) in CH_2Cl_2 (4 mL) at RT. The resulting yellow mixture was stirred for 1 h, followed by the dropwise addition of (mesitylethynyl)trimethylsilane (**68**) (250 mg, 1.15 mmol, 1.1 equiv) dissolved in CH_2Cl_2 (1 mL). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (5 mL) was then added and the mixture was stirred vigorously. The layers were separated and the organic layer was washed with sat. $NaHCO_3$ (10 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was recrystallized in CH_3CN (ca 20 mL). The mother liquors were concentrated and and the obtained solid recrystallized in CH_3CN (4 mL). Both solids were combined, washed with pentane and dried under high vacuum to afford **2n** (120 mg, 0.307 mmol, 30%) as a tan solid. Mp (Dec.) 171.0–175.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (m, 1H, Ar*H*), 8.28 (m, 1H, Ar*H*), 7.72 (m, 2H, Ar*H*), 6.92 (s, 2H, MesH), 2.45 (s, 6H, 2 X C*H*$_3$), 2.31 (s, 3H, C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.7, 142.1, 140.5, 134.5, 132.2, 131.5, 131.3, 128.0, 126.2, 117.5, 116.5, 105.1, 55.6, 21.4, 21.0; IR 2979 (w), 2916 (w), 2247 (w), 2131 (w), 1650 (m), 1623 (m), 1562 (w), 1439 (w), 1333 (w), 1292 (w), 1212 (w), 1146 (w), 1008 (w), 906 (s), 855 (w), 833 (w), 729 (s), 647 (m). The characterization data corresponded to the reported values.[19]

1-[2-Bromophenylethynyl]-1,2-benziodoxol-3(1H)-one (2o)

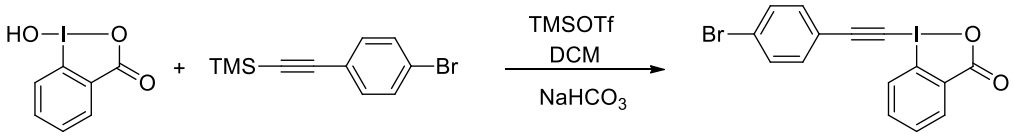


45 **69** **2o**

Following a reported procedure,[22] trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**45**) (1.32 g, 5.00 mmol, 1.00 equiv) in CH_2Cl_2 (15 mL)

at room temperature. The resulting suspension was stirred for 3 h, followed by the drop wise addition of ((2-bromophenyl)ethynyl)trimethylsilane (**69**) (1.17 g, 5.50 mmol, 1.10 equiv). The resulting suspension was stirred for 6 h at room temperature. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with saturated solution of $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was boiled in CH_3CN (*ca* 20 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **2o** (1.50 g, 3.51 mmol, 70%) as a white solid. Mp (Dec.): 174.0-177.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (td, *J* = 7.3, 2.1 Hz, 2H, Ar*H*), 7.84–7.74 (m, 2H, Ar*H*), 7.68 (d, *J* = 1.1 Hz, 1H, Ar*H*), 7.61 (dd, *J* = 7.6, 1.7 Hz, 1H, Ar*H*), 7.36 (dtd, *J* = 22.4, 7.5, 1.5 Hz, 2H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 135.2, 134.7, 133.0, 132.7 , 131.8, 131.3, 127.6, 126.8, 126.4, 123.2, 116.5, 104.3, 55.4; IR ν 2358 (w), 2155 (w), 1638 (s), 1616 (m), 1585 (w), 1466 (w), 1316 (m), 1147 (w). The characterization data corresponded to the reported values.[22]

1-[4-Bromophenylethynyl]-1,2-benziodoxol-3(1H)-one (2p)



45 **70** **2p**

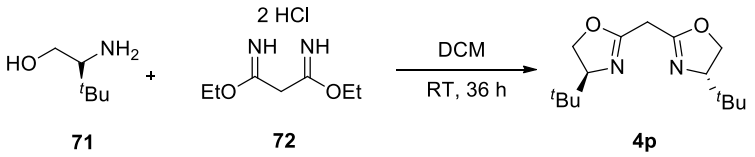
Following a reported procedure,[22] trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**45**) (1.32 g, 5.00 mmol, 1 equiv) in CH_2Cl_2 (15 mL) at RT. The resulting suspension was stirred for 3 h, followed by the drop wise addition of ((4-bromophenyl)ethynyl)trimethylsilane (**70**) (1.17 g, 5.50 mmol, 1.1 equiv), which was dissolved in CH_2Cl_2 (1 mL). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with sat. $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was boiled in CH_3CN (20 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **2p** (1.00 g, 2.34 mmol, 47%) as a pale yellow solid. Mp (Dec.):158.0-163.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51–8.30 (m, 1 H, Ar*H*), 8.30–8.13 (m, 1 H, Ar*H*), 7.84–7.72 (m, 2 H, Ar*H*), 7.58 (d, 2 H, *J* = 8.5 Hz, Ar*H*), 7.46 (d, 2 H, *J* = 8.5 Hz, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 135.1, 134.3, 132.7, 132.3,

131.9, 131.4, 126.3, 125.7, 119.6, 116.3, 105.4, 52.1; IR ν 2155 (w), 1612 (s), 1559 (w), 1479 (w), 1445 (w), 1328 (m), 1297 (w), 1007 (w), 906 (w). The characterization data corresponded to the reported values.[22]

4. Synthesis of ligands

Ligands **4a, 4g-i** and **4k-n** were purchased from Aldrich and TCI, and used as such unless stated otherwise. Ligand **4f** was synthesized using a reported procedure.[23]

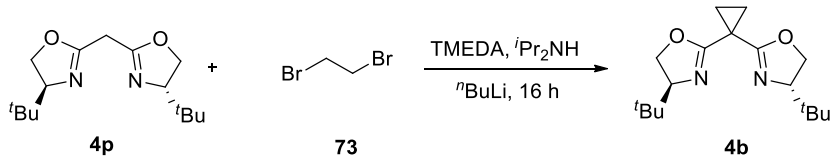
Bis((*S*)-4-(*tert*-butyl)-4,5-dihydrooxazol-2-yl)methane (4p)



71 72 4p

Following a reported procedure,[24] to a solution of (*S*)-*tert*-leucinol (**71)** (0.94 g, 8.0 mmol, 2.0 equiv) in CH_2Cl_2 (40 mL) was added imidate **72** (0.93 g, 4.0 mmol, 1.0 equiv). The resulting cloudy solution was stirred at room temperature for 36 h. The reaction mixture was diluted with water (8 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine (40 mL), dried over $MgSO_4$, and concentrated. The resulting oily residue was distilled bulb-to-bulb (Kugelrohr distillation, 150 °C at 0.2 mbar) to afford bis((*S*)-4-(*tert*-butyl)-4,5-dihydrooxazol-2-yl)methane (**4p**) (0.600 g, 2.84 mmol, 71%) as a white solid: TLC (EtOAc:pentane, 1:1 v/v): R_f = 0.16, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.13 (dd, *J* = 10.1, 8.7 Hz, 2H, 2 X OCH_a), 4.02 (dd, *J* = 8.7, 7.7 Hz, 2H, 2 X C(CH_3)$_3$C*H*), 3.81 (ddt, *J* = 10.1, 7.8, 1.1 Hz, 2H, 2 X OCH_b), 3.27 (t, *J* = 1.2 Hz, 2H, O(C=N)CH_2), 0.82 (s, 18H, 2 X C(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5, 76.0, 69.1, 34.0, 28.4, 26.0. The characterization data corresponded to the reported values.[24]

(4*S*,4'*S*)-2,2'-(Cyclopropane-1,1-diyl)bis(4-(tert-butyl)-4,5-dihydrooxazole) (4b)

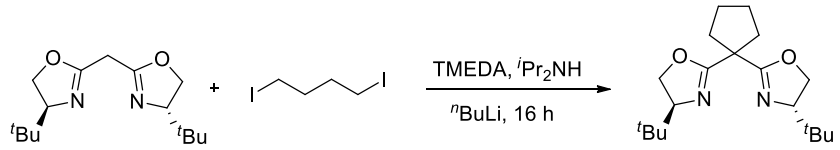


4p 73 4b

Following a reported procedure,[24] to a solution of bis((*S*)-4-(*tert*-butyl)-4,5-dihydrooxazol-2-yl)methane (**4p**) (75 mg, 0.28 mmol, 1.0 equiv) in THF (5 mL) in a 20 mL microwave vial, was added TMEDA (85 µL, 0.56 mmol, 2.0 equiv) and *i*-Pr_2NH (40 mL, 0.28 mmol, 1.0 equiv). The solution was cooled to -78 °C and *n*-BuLi (0.38 mL, 1.5 M in hexane, 0.56 mmol, 2.0 equiv) was added. The reaction mixture was warmed to -20 °C and stirred at that temperature for 30 minutes. The solution was cooled back to -78 °C and 1,2 dibromoethane (**73**) (25 µL, 0.28 mmol, 2.0 equiv) was added in 10 minutes. After the addition, the cold bath was removed and the reaction mixture

was allowed to stir at room temperature for an additional 16 h. The reaction mixture was quenched by the addition of sat. aq. NH_4Cl (2.5 mL) and diluted with water (2 mL) to dissolve the resulting salts. The mixture was extracted with diethylether (3 X 10 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, and concentrated. The resulting oily residue was purified by column chromatography using 1:2 to 1:1 EtOAc:pentane as mobile phase to afford (4*S*,4'*S*)-2,2'-(cyclopropane-1,1-diyl)bis(4-(*tert*-butyl)-4,5-dihydrooxazole) (**4b**) as a white solid. TLC (EtOAc:pentane, 1:2 v/v): R_f = 0.15, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.18 (dd, *J* = 10.0, 8.6 Hz, 2H, 2 X OCH_a), 4.10 (dd, *J* = 8.7, 7.3 Hz, 2H, 2 X C$(CH_3)_3$C*H*), 3.82 (dd, *J* = 10.0, 7.2 Hz, 2H, 2 X OCH_b), 1.52–1.47 (m, 2H, 2 X CH_a of CyP), 1.30–1.24 (m, 2H, 2 X CH_b of CyP), 0.86 (s, 18H, 2 X C(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 75.2, 69.1, 33.8, 25.7, 18.2, 15.1. The characterization data corresponded to the reported values.[24]

(4*S*,4'*S*)-2,2'-(Cyclopentane-1,1-diyl)bis(4-(*tert*-butyl)-4,5-dihydrooxazole) (4c)

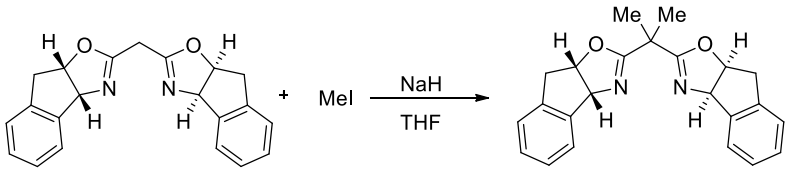


4p **74** **4c**

Following a reported procedure,[24] to a solution of bis((*S*)-4-(*tert*-butyl)-4,5-dihydrooxazol-2-yl)methane (**4p**) (75 mg, 0.28 mmol, 1.0 equiv) in THF (5 mL) in a 20 mL microwave vial was added TMEDA (85 μL, 0.56 mmol, 2.0 equiv) and *i*-Pr_2NH (40 mL, 0.28 mmol, 1.0 equiv). The solution was cooled to -78 °C and *n*-BuLi (0.38 mL, 1.5 M in hexane, 0.56 mmol, 2.0 equiv) was added. The reaction mixture was warmed to -20 °C and stirred at that temperature for 30 minutes. The solution was cooled back to -78 °C and 1,4 diiodobutane (37 μL, 0.28 mmol, 2.0 equiv) was added in 10 minutes. After the addition. the cold bath was removed and the reaction mixture was allowed to stir at room temperature for an additional 16 h. The reaction mixture was quenched by the addition of sat. aq. NH_4Cl (2.5 mL) and diluted with water (2 mL) to dissolve the resulting salts. The mixture was extracted with diethylether (3 X 10 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, and concentrated. The resulting oily residue was purified by column chromatography using 1:4 EtOAc:pentane as mobile phase to afford (4*S*,4'*S*)-2,2'-(cyclopentane-1,1-diyl)bis(4-(*ter*t-butyl)-4,5-dihydrooxazole) (**4c**) as a white solid. TLC (EtOAc:pentane, 1:2 v/v): R_f = 0.6, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.15 (dd, *J* = 10.1, 8.6 Hz, 2H, 2 X OCH_a), 4.07 (dd, *J* = 8.7, 7.1 Hz, 2H, 2 X C$(CH_3)_3$C*H*), 3.84 (dd, *J* = 10.0, 7.1 Hz,

2H, 2 X OCH_b), 2.43-2.33 (m, 2H, 2 X CCH_aCH$_2$), 2.20–2.05 (m, 2H, 2 X CCH_bCH$_2$), 1.81–1.62 (m, 4H, 2 X CCH$_2$CH_2), 0.86 (s, 18H, 2 X C(CH_3)$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ 168.0, 75.3, 69.1, 49.1, 35.4, 33.9, 25.7, 25.0. The characterization data corresponded to the reported values.[24]

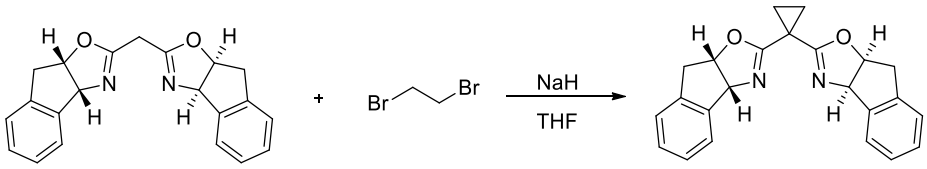
(3a*R*,3a'*R*,8a*S*,8a'*S*)-2,2'-(Propane-2,2-diyl)bis(8,8a-dihydro-3a*H*-indeno[1,2-d]oxazole) (4d)



75 **4d**

Following a reported procedure,[25] a Schlenk tube was charged with dry THF (2 mL), TMEDA (46 µL, 0.30 mmol, 2.0 equiv) and *i*-Pr$_2$NH (43 µL, 0.30 mmol, 2.0 equiv). The solution was cooled to -20 °C and *n*-BuLi (0.20 mL, 1.5 M in hexane, 0.30 mmol, 2.0 equiv) was added. The reaction mixture was stirred for 1 h at that temperature and **75** (50 mg, 0.15 mmol, 1.0 equiv) in THF (2mL) was added. The mixture was stirred for 3 h. Then, MeI (38 µL, 0.6 mmol, 4.0 equiv) was added at -20 °C. After the addition, the cold bath was removed and the reaction mixture was heated to 60 °C for an additional 24 h. The solution was cooled, washed with sat. NH$_4$Cl (20 mL) and extracted with EtOAc (3 x 30 mL). The combined organic layers were dried over MgSO$_4$, and removed under reduced pressure, to afford (3a*R*,3a'*R*,8a*S*,8a'*S*)-2,2'-(propane-2,2-diyl)bis(8,8a-dihydro-3a*H*-indeno[1,2-d]oxazole) (**4d**) (53.5 mg, 0.15 mmol, quant.) as a white solid. No purification was needed. TLC (EtOAc:MeOH, 9:1 v/v): R$_f$ = 0.53, KMnO$_4$; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.54–7.45 (m, 2H, Ar*H*), 7.30–7.18 (m, 6H, Ar*H*), 5.52 (d, *J* = 7.9 Hz, 2H, 2 X N-C*H*), 5.28-5.25 (m, 2H, 2 X O-C*H*), 3.30 (dd, *J* = 17.9, 7.1 Hz, 2H, 2 X ArCH_a), 2.95 (dd, *J* = 17.9, 1.9 Hz, 2H, 2 X ArCH_b), 1.42 (s, 6H, 2 X CH_3); ^{13}C NMR (100 MHz, CDCl$_3$): δ 169.1, 141.8, 139.7, 128.3, 127.3, 125.6, 125.0, 83.2, 76.5, 39.6, 38.4, 23.9. The characterization data corresponded to the reported values.[25]

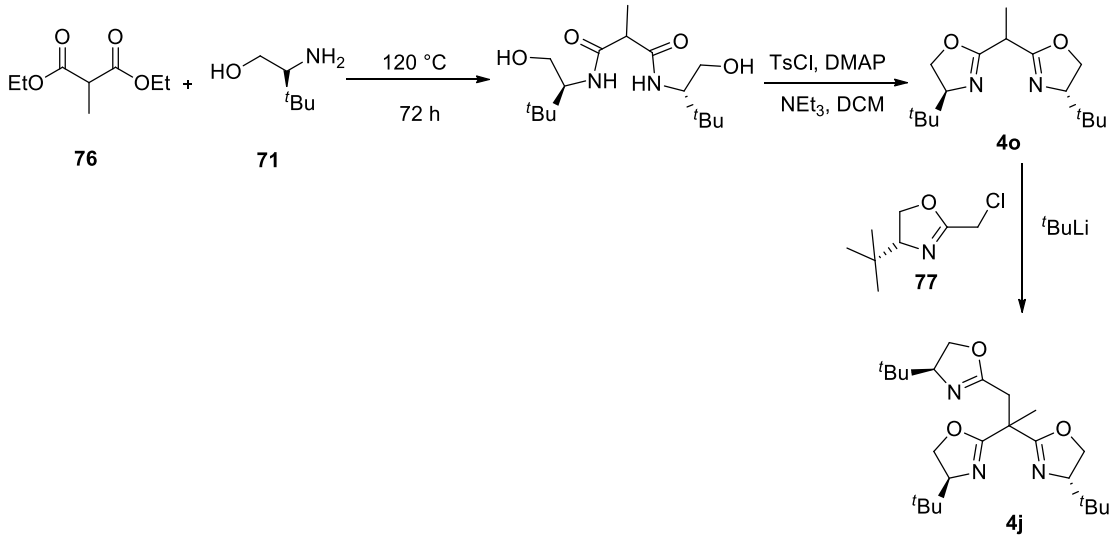
(3a*R*,3a'*R*,8a*S*,8a'*S*)-2,2'-(Cyclopropane-1,1-diyl)bis(8,8a-dihydro-3a*H*-indeno[1,2-d]oxazole) (4e)



75 **73** **4e**

Following a reported procedure,[26] to a solution of dihydrobisoxazoline **75** (330 mg, 1.00 mmol, 1.00 equiv) in THF (4 mL), was added NaH (120 mg, 60% dispersion in paraffin liquid, 3.00 mmol, 3.00 equiv) in portions at 0 °C. After complete addition, the mixture was stirred for 30 min. at that temperature. A solution of dibromoethane (**73**) (130 μL, 1.50 mmol, 1.50 equiv) in THF (1 mL) was then added dropwise at 0 °C over 10 minutes. After the addition, the ice bath was removed and the reaction mixture was heated to 50 °C for an additional 2 h. The reaction was quenched with sat. NH_4Cl (10 mL) and extracted with CH_2Cl_2 (3 X 20 mL). The combined organic layers were dried over $MgSO_4$, and removed under reduced pressure. The crude product was purified by chromatography on silica gel using 2% MeOH/EtOAc followed by recrystallization (EtOAc/hexane, 1:4, 15 mL) to afford (3a*R*,3a'*R*,8a*S*,8a'*S*)-2,2'-(cyclopropane-1,1-diyl)bis(8,8a-dihydro-3a*H*-indeno[1,2-d]oxazole) (**4e**) (220 mg, 0.617 mmol, 62%) as a white solid. TLC (EtOAc:MeOH, 9:1 v/v): R_f = 0.50, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.41 (m, 2H, Ar*H*), 7.25–7.17 (m, 6H, Ar*H*), 5.52 (d, *J* = 7.9 Hz, 2H, 2 x N-C*H*), 5.41–5.23 (m, 2H, 2 X O-C*H*), 3.38 (dd, *J* = 17.9, 7.0 Hz, 2H, 2 X ArCH_a), 3.19 (dd, *J* = 17.9, 1.9 Hz, 2H, 2 X ArCH_b), 1.44–1.15 (m, 4H, CH_2CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.0, 141.9, 139.8, 128.5, 127.5, 125.7, 125.3, 83.5, 76.5, 39.8, 18.5, 16.0. The characterization data corresponded to the reported values.[27]

(4*S*,4'*S*,4''*S*)-2,2',2''-(Propane-1,2,2-triyl)tris(4-(*tert*-butyl)-4,5-dihydrooxazole) (4j)



Following a reported procedure,[28] diethyl methylmalonate (**76)** (0.850 mL, 5.00 mmol, 1.00 equiv) and (*S*)-*tert*-leucinol (**71**) (1.23 g, 10.5 mmol, 2.10 equiv) were added to a Schlenk tube. The mixture was stirred for 3 days at 120 °C. The reaction mixture was cooled down to room

temperature to obtain the product, which was used in the following step without further purification.

Following a reported procedure,[29] a 50 mL Schlenk flask was charged with bis((*S*)-1-hydroxy-3,3-dimethylbutan-2-yl)-2-methylmalonamide (1.44 g, 4.54 mmol, 1.00 equiv), 4-(dimethylamino)-pyridine (0.06 g, 0.05 mmol, 0.100 equiv), and CH_2Cl_2 (40 mL). Triethylamine (3.00 mL, 21.5 mmol, 4.75 equiv) was then added. A solution of *p*-toluenesulfonyl chloride (1.88 g, 9.90 mmol, 2.10 equiv) in CH_2Cl_2 (10 mL) was added slowly. The resulting bright yellow solution was stirred at room temperature for 24 h. It was diluted with CH_2Cl_2 (10 mL) and washed with sat. NH_4Cl (15 mL). The aq. layer was back-extracted with CH_2Cl_2 (3 X 15 mL). The combined organic extracts were washed with sat.$NaHCO_3$ (30 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude product was purified by column chromatography using 98:2 CH_2Cl_2:MeOH to afford (4*S*,4'*S*)-2,2'-(ethane-1,1-diyl)bis(4-(*tert*-butyl)-4,5-dihydrooxazole) (**4o**) (1.00 g, 3.57 mmol, 79%) as a colorless thick liquid. TLC (EtOAc:MeOH, 9:1 v/v): R_f = 0.53, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.21–4.13 (m, 2H, 2 X OCH_a), 4.12–4.01 (m, 2H, 2 X C$(CH_3)_3$C*H*), 3.97–3.76 (m, 2H, 2 X OCH_b), 3.61–3.45 (m, 1H, CH_3C*H*), 1.46 (d, *J* = 7.3 Hz, 3H, CH_3CH), 0.88 (s, 9H, C(CH_3)$_3$), 0.87 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 165.3, 75.4, 68.9, 34.0, 33.8, 25.7, 25.6, 15.3. The characterization data corresponded to the reported values.[29]

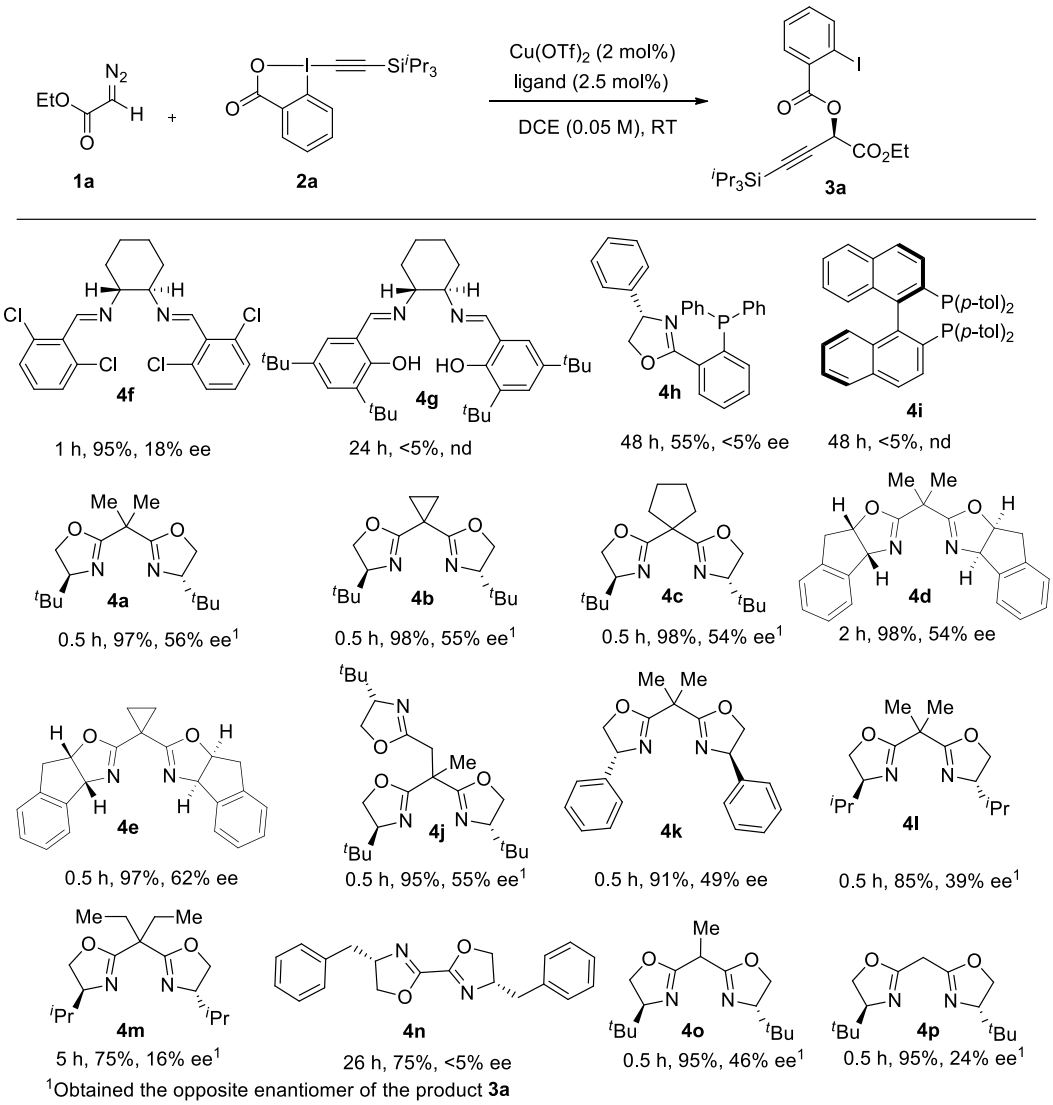
Following a reported procedure,[30] to a solution of bisoxazoline **4o** (70 mg, 0.25 mmol, 1.0 equiv) in dry THF (5 mL) was added dropwise *t*-BuLi (0.23 mL, 1.6 M in heptane, 0.36 mmol, 1.44 equiv) over 15~20 minutes. at -78 ℃ under nitrogen. The resulting yellow solution was stirred for an additional 1 h at this temperature. Then a solution of 2-chloromethyl oxazoline (**77**) (66 mg, 0.38 mmol, 1.5 equiv) in THF (2.5 mL) was added dropwise at -78 ℃ over 10 minutes. The solution was slowly warmed to room temperature and was stirred for further 10 h. The mixture was diluted with CH_2Cl_2 (5 mL) and was washed with H_2O (5 mL). The aqueous layer was extracted with CH_2Cl_2 (5 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography using 10:1 pentane/acetone to afford (4*S*,4'*S*,4"*S*)-2,2',2"-(propane-1,2,2-triyl)tris(4-(t*ert*-butyl)-4,5-dihydrooxazole) (**4j**) (48.0 mg, 0.114 mmol, 46%) as a white solid. TLC (acetone:pentane, 1:10 v/v): R_f = 0.37, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.19–3.77 (m, 9H, 3 X OCH_2 and 3 X C$(CH_3)_3$C*H*), 3.14 (d, *J* = 15.1 Hz, 1H, CH_aCCH_3), 2.91 (d, *J* = 15.1 Hz, 1H, CH_bCCH_3), 1.60 (s, 3H, CH_2CCH_3), 0.89–0.77 (m, 27H,

3 X C(C*H*$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 166.7, 163.7, 75.7, 75.6, 75.4, 69.1, 69.0, 68.3, 40.8, 34.8, 33.9, 33.8, 33.4, 25.9, 25.8, 25.7, 21.2. The characterization data corresponded to the reported values.[30]

5. Optimization of the reaction conditions

a) Screening of ligands

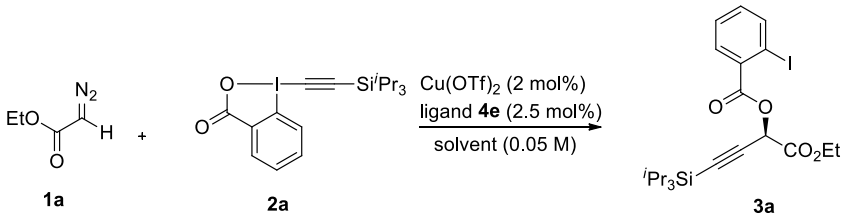
A flame dried 5 mL microwave vial was charged under nitrogen with catalyst (3.00 µmol, 0.02 equiv), ligand (3.75 µmol, 0.025 equiv) and dry DCE (1 mL). The resulting solution was stirred at room temperature for 30 minutes. To this solution was added a mixture of 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (**2a**) (0.15 mmol, 1.0 equiv) and ethyl 2-diazoacetate (**1a**) (0.30 mmol, 2.0 equiv) in dry DCE (2 mL) in 2 min and the resulting reaction mixture was stirred until the reaction was completed (monitored by TLC, EtOAc:pentane, 1:40 v/v), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane, 1:40 v/v) directly without any further work-up.



[1]Obtained the opposite enantiomer of the product **3a**

b) Screening of solvents

A flame dried 5 mL microwave vial was charged under nitrogen with $Cu(OTf)_2$(3.00 µmol, 0.02 equiv), ligand **4e** (3.75 µmol, 0.025 equiv) and solvent (1 mL). The resulting solution was stirred at room temperature for 30 minutes. To this solution was added a mixture of 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (**2a**) (0.15 mmol, 1.0 equiv) and ethyl 2-diazoacetate (**1a**) (0.30 mmol, 2.0 equiv) in solvent (2 mL) in 2 min and the resulting reaction mixture was stirred until the reaction was completed (monitored by TLC, EtOAc:pentane, 1:40 v/v), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane, 1:40 v/v) directly without any further work-up.

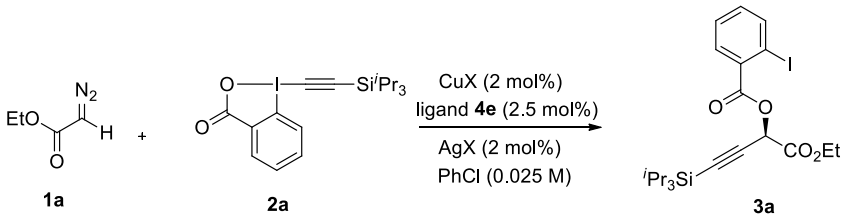


Entry	solvent	Time	Yield (%)	ee
1	xylenes	2 h	79	69
2	PhCl	2 h	84	70
3	toluene	2 h	80	59
4	PhCl/$PhCH_3$	2 h	68	55
5	PhCl/*p*-xylene	2 h	78	65
6	*o*-dichlorobenzene	3 h	78	71

c) Screening of copper catalysts

A flame dried 5 mL microwave vial was charged under nitrogen with catalyst (3.00 µmol, 0.02 equiv), AgX (3.00 µmol, 0.02 equiv), ligand **4e** (3.75 µmol, 0.025 equiv) and dry PhCl (1 mL). The resulting solution was stirred at room temperature for 30 minutes. To this solution was added a mixture of 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (**2a**) (0.15 mmol, 1.0 equiv) and ethyl 2-diazoacetate (**1a**) (0.30 mmol, 2.0 equiv) in dry PhCl (2 mL) in 2 min and the

resulting reaction mixture was stirred until the reaction was completed (monitored by TLC, EtOAc:pentane, 1:40 v/v), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane, 1:40 v/v) directly without any further work-up.



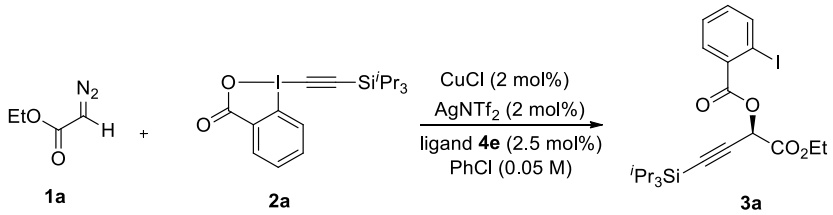
1a 2a 3a

Entry	CuX/AgX	Time	Yield (%)	ee
1	CuCl/$AgSbF_6$	1 h	95	83
2	CuCl/$AgClO_4$	24 h	<5	nd
3	CuCl/AgOTf	2 h	88	80
4	CuCl/AgOTs	24 h	<5	nd
5	CuCl/$AgNTf_2$	2 h	91	84
6	CuCl/$AgBF_4$	3 h	93	80
7	CuCl/$AgPF_6$	2 h	82	57
8	CuBr/$AgNTf_2$	2 h	90	83
9	CuBr/ $AgSbF_6$	20 h	91	83
10	CuCl/ NaBARF	20 h	<5	nd

d) Screening of equivalents of diazo and TIPS-EBX

A flame dried 5 mL microwave vial was charged under nitrogen with CuCl (3 µmol, 0.02 equiv), $AgNTf_2$ (3.00 µmol, 0.02 equiv), ligand **4e** (3.75 µmol, 0.025 equiv) and dry PhCl (1 mL). The resulting solution was stirred at room temperature for 30 minutes. To this solution was added a mixture of 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (**2a**) and ethyl 2-diazoacetate (**1a**) in dry PhCl (2 mL) in 2 min and the resulting reaction mixture was stirred until the reaction was completed (monitored by TLC, EtOAc:pentane, 1:40 v/v), the solvent was

evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane, 1:40 v/v) directly without any further work-up.

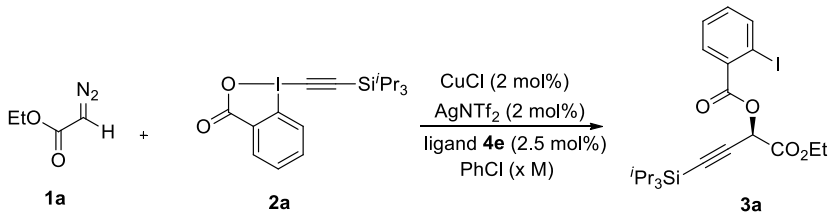


1a 2a 3a

Entry	1a (equiv)	2a (equiv)	Time	Yield (%)	ee
1	1.2	1	24 h	60	84
2	2	1	2 h	91	84
3	1	1.2	24 h	61	84

e) Screening of concentration

A flame dried 5 mL microwave vial was charged under nitrogen with CuCl (3.00 µmol, 0.02 equiv), $AgNTf_2$ (3.00 µmol, 0.02 equiv), ligand **4e** (3.75 µmol, 0.025 equiv) and dry PhCl. The resulting solution was stirred at room temperature for 30 minutes. To this solution was added a mixture of 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (**2a**) (0.15 mmol, 1.0 equiv) and ethyl 2-diazoacetate (**1a**) (0.30 mmol, 2.0 equiv) in dry PhCl in 2 min and the resulting reaction mixture was stirred until the reaction was completed (monitored by TLC, EtOAc:pentane, 1:40 v/v), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane, 1:40 v/v) directly without any further work-up.

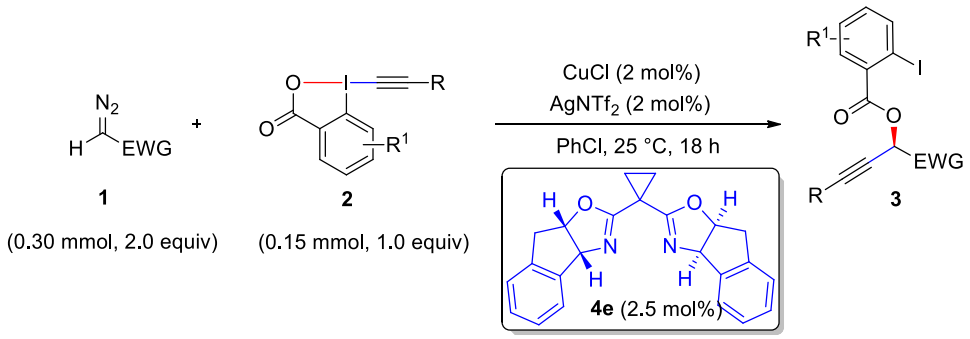


1a 2a 3a

Entry	Concentration (x M)	Time	Yield (%)	ee
1	0.05 M	2 h	91	84
2	0.025 M	18 h	95	90

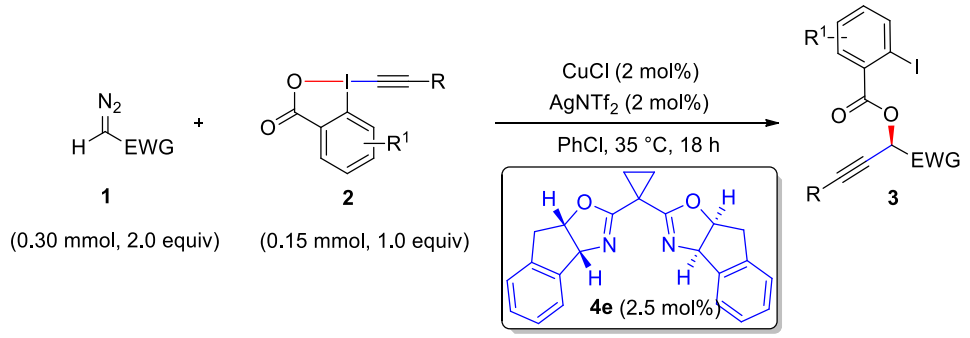
6. Copper catalyzed synthesis of chiral propargylic esters

General procedure A:



A flame dried 20 mL microwave vial was charged under nitrogen with CuCl (0.3 mg, 3 µmol, 0.02 equiv), $AgNTf_2$ (1.2 mg, 3.0 µmol, 0.02 equiv), ligand **4e** (1.4 mg, 3.8 µmol, 0.025 equiv) and dry PhCl (1 mL). The resulting solution was stirred at room temperature for 1 h and then added to a mixture of R-EBX **2** (0.15 mmol, 1.0 equiv) and diazo compound **1** (0.30 mmol, 2.0 equiv) in dry PhCl (5 mL) in 2 min and the resulting reaction mixture was stirred at 25 ℃ for 18 h. After the reaction was completed (monitored by TLC, EtOAc;pentane or Et_2O:pentane), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane or Et_2O:pentane) directly without any further work-up.

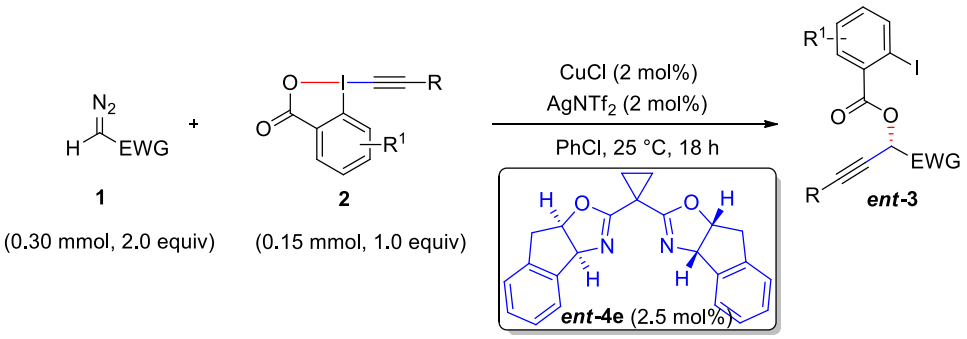
General procedure B:



A flame dried 20 mL microwave vial was charged under nitrogen with CuCl (0.3 mg, 3 µmol, 0.02 equiv), $AgNTf_2$ (1.2 mg, 3.0 µmol, 0.02 equiv), ligand **4e** (1.4 mg, 3.8 µmol, 0.025 equiv) and dry PhCl (1 mL). The resulting solution was stirred at room temperature for 1 h and then added to a mixture of R-EBX **2** (0.15 mmol, 1.0 equiv) and diazo compound **1** (0.30 mmol, 2.0 equiv) in dry PhCl (5 mL) in 2 min and the resulting reaction mixture was stirred at 35 ℃ for 18 h. After the

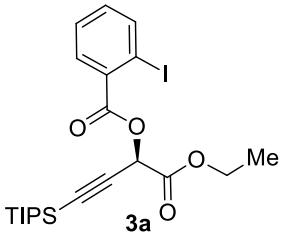
reaction was completed (monitored by TLC, EtOAc;pentane or Et_2O:pentane, or toluene:pentane), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (Et_2O:pentane or toluene:pentane) directly without any further work-up.

General procedure C:



A flame dried 20 mL microwave vial was charged under nitrogen with CuCl (0.3 mg, 3 µmol, 0.02 equiv), $AgNTf_2$ (1.2 mg, 2.0 µmol, 0.02 equiv), ligand ***ent*-4e** (1.4 mg, 3.8 µmol, 0.025 equiv) and dry PhCl (1 mL). The resulting solution was stirred at room temperature for 1 h and then added to a mixture of R-EBX **2** (0.15 mmol, 1.0 equiv) and diazo compound **1** (0.30 mmol, 2.0 equiv) in dry PhCl (5 mL) in 2 min and the resulting reaction mixture was stirred at 25℃ for 18 h. After the reaction was completed (monitored by TLC, EtOAc;pentane or Et_2O:pentane), the solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (EtOAc:pentane or Et_2O:pentane) directly without any further work-up.

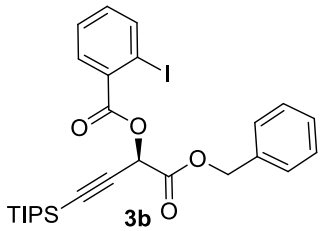
(*R*)-1-Ethoxy-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3a)



Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and ethyl 2-diazoacetate (**1a**) (36 µL, 0.30 mmol, 13 wt. % dichloromethane, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in

vacuo and purified by flash chromatography using EtOAc:pentane 1:40 as mobile phase to afford **3a** (73.0 mg, 0.142 mmol, 95%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.14, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.02 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.99 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.44 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 5.98 (s, 1H, OC*H*CC), 4.44–4.17 (m, 2H, C*H*$_2$CH$_3$), 1.32 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 1.11–1.03 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 164.9, 141.5, 133.3, 133.2, 131.8, 128.0, 97.6, 94.5, 90.6, 63.9, 62.6, 18.5, 14.0, 11.0; IR ν 2945 (m), 2866 (m), 2188 (w), 1745 (s), 1583 (w), 1464 (m), 1241 (s), 1203 (s), 1092 (s), 1020 (s), 883 (m); HRMS (ESI) calcd. for $C_{22}H_{32}IO_4Si^+$ $[M+H]^+$ 515.1109; found 515.1095; Chiral HPLC conditions: *ee* = 90%, Chiralpak IB 99.75:0.25 Hexane/*i*PrOH, 1 mL/min, 30 min. t_r (minor) = 18.7 min. and t_r (major) = 22.8 min. λ = 250 cm^{-1}; $[\alpha]_D^{25.0}$ = -28.9 (c = 0.5, $CHCl_3$).

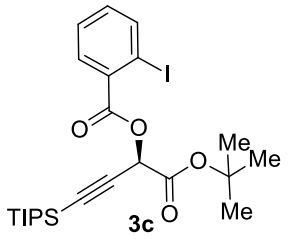
(*R*)-1-(Benzyloxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3b)



Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and benzyl 2-diazoacetate (**1b**) (59.0 mg, 0.300 mmol, 10 wt % dichloromethane, 2.00 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:60 as mobile phase to afford **3b** (81.0 mg, 0.140 mmol, 94%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.29, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.02 (dd, *J* = 7.9, 1.1 Hz, 1H, Ar*H*), 7.97 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.43 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.39–7.32 (m, 5H, Ar*H*), 7.19 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 6.05 (s, 1H, OC*H*CC), 5.35 (d, *J* = 12.2 Hz, 1H, ArC*H*$_2$), 5.20 (d, *J* = 12.2 Hz, 1H, ArC*H*$_2$), 1.07–1.00 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.3, 164.9, 141.5, 134.8, 133.3, 133.2, 131.9, 128.6, 128.5, 128.3, 128.0, 97.2, 94.6, 90.9, 68.0, 63.9, 18.5, 11.0; IR ν 2943 (m), 2865 (m), 2189 (w), 1763 (s), 1741 (s), 1584 (w), 1463 (m), 1381 (w), 1324 (m), 1242 (s), 1192 (s), 1094 (s), 1016 (s), 883 (m); HRMS (ESI) calcd. for $C_{27}H_{33}INaO_4Si^+$ $[M+Na]^+$ 599.1085;

found 599.1092; Chiral HPLC conditions: *ee* = 89%, Chiralpak IB 95:5 Hexane/*i*PrOH, 1 mL/min, 30 min. t_r (major) = 5.6 min. and t_r (minor) = 7.0 min. $\lambda = 250$ cm^{-1}; $[\alpha]_D^{25.0} = -9.3$ (c = 0.5, $CHCl_3$).

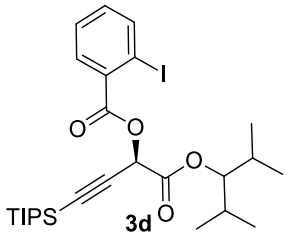
(*R*)-1-(*T*ert-butoxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3c)



3c

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and *tert*-butyl 2-diazoacetate (**1c**) (49 µL, 0.30 mmol, 15 wt. % dichloromethane, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:60 as mobile phase to afford **3c** (75.0 mg, 0.138 mmol, 92%) as a colorless oil. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.25, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04–7.97 (m, 2H, Ar*H*), 7.43 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 5.87 (s, 1H, OC*H*CC), 1.51 (s, 9H, C(C*H*$_3$)$_3$), 1.09 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 164.2, 141.5, 133.6, 133.2, 131.9, 128.0, 98.2, 94.5, 89.8, 83.6, 64.4, 27.8, 18.5, 11.1; IR ν 2944 (m), 2867 (m), 2188 (w), 1744 (s), 1584 (w), 1465 (m), 1371 (m), 1245 (s), 1158 (s), 1097 (s), 1017 (m), 881 (w), 846 (w); HRMS (ESI) calcd. for $C_{24}H_{35}INaO_4Si^+$ $[M+Na]^+$ 565.1242; found 565.1245; Chiral HPLC conditions: *ee* = 89%; Chiralpak IB 99.75:0.25 Hexane/*i*PrOH, 0.5 mL/min, 31 min. t_r (minor) = 14.1 min. and t_r (major) = 15.2 min. $\lambda = 250$ cm^{-1}; $[\alpha]_D^{25.0} = -23.0$ (c = 0.5, $CHCl_3$).

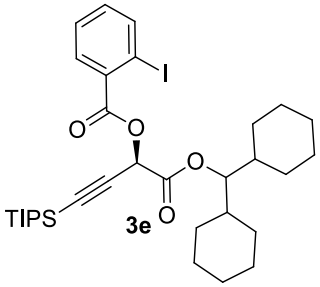
(*R*)-1-((2,4-Dimethylpentan-3-yl)oxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3d)



3d

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and 2,4-dimethylpentan-3-yl 2-diazoacetate (**1d**) (56 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:60 as mobile phase to afford **3d** (87.0 mg, 0.149 mmol, 99%.) as a colorless thick liquid. TLC (Et_2O:pentane, 1:40 v/v): R_f = 0.24, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (t, *J* = 7.9 Hz, 2H, Ar*H*), 7.43 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.18 (t, *J* = 7.1 Hz, 1H, Ar*H*), 6.02 (s, 1H, OC*H*CC), 4.70 (t, *J* = 6.1 Hz, 1H, *i*Pr$_2$C*H*), 1.97 (dp, *J* = 13.3, 6.6 Hz, 2H, 2 X C*H*(CH_3)$_2$), 1.08 (s, 21H, TIPS), 0.94 (s, 6H, CH(C*H*$_3$)$_2$), 0.92 (s, 6H, CH(C*H*$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 165.0, 141.4, 133.7, 133.1, 131.8, 127.9, 97.7, 94.4, 90.4, 85.7, 64.0, 29.6, 29.5, 19.5, 19.4, 18.5, 17.3, 16.9, 11.0; IR ν 2962 (s), 2871 (m), 2727 (w), 2188 (w), 1732 (s), 1578 (w), 1465 (m), 1380 (m), 1246 (s), 1126 (m), 1094 (s), 1010 (s), 890 (m); HRMS (ESI) calcd. for $C_{27}H_{41}INaO_4Si^+$ $[M+Na]^+$ 607.1711; found 607.1706; Chiral HPLC conditions: *ee* = 92%; Chiralpak IB 99.75:0.25 Hexane/*i*PrOH, 0.3 mL/min, 31 min. t_r (minor) = 21.3 min. and t_r (major) = 22.6 min. λ = 250 cm^{-1}; $[\alpha]_D^{25.0}$ = -16.9 (c = 0.5, $CHCl_3$).

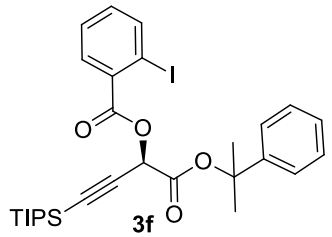
(*R*)-1-(Dicyclohexylmethoxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3e)



Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and 2,2'-(cyclopropane-1,1-diyl)bis(8,8a-dihydro-3aH-indeno[1,2-d]oxazole) (**1e**) (79 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:60 as mobile phase to afford **3e** (100 mg, 0.150 mmol, quant.) as a colorless thick liquid. TLC (Et_2O:pentane, 1:40 v/v): R_f = 0.26, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.02–7.98 (m, *J* = 7.3 Hz, 2H, Ar*H*), 7.43 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.18 (t, *J* = 7.7 Hz, 1H, Ar*H*), 6.02 (s, 1H, OC*H*CC), 4.74 (t, *J* = 5.9 Hz, 1H, (Cy)$_2$C*H*), 1.91–1.52 (m, 12H, 2 X Cy–C*H* and 5 X Cy–C*H*$_2$), 1.39–0.93 (m, 31H, TIPS and 5 X Cy–C*H*$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 164.9, 141.5, 133.6,

133.1, 131.9, 127.9, 97.8, 94.5, 90.3, 84.4, 63.9, 38.4, 29.7, 29.6, 27.2, 27.2, 26.3, 26.2, 26.2, 26.0, 26.0, 18.5, 11.1; IR ν 2928 (s), 2855 (s), 2189 (w), 1743 (s), 1578 (w), 1453 (m), 1244 (s), 1091 (s), 1015 (m), 989 (m), 929 (w), 888 (m); HRMS (ESI) calcd. for $C_{33}H_{49}INaO_4Si^+$ $[M+Na]^+$ 687.2337; found 687.2337; Chiral HPLC conditions: *ee* = 86%; Chiralpak IB 99.75:0.25 Hexane/*i*PrOH, 0.3 mL/min, 31 min. t_r (major) = 21.2 min. and t_r (minor) = 25.7 min. λ = 280 cm^{-1}; $[\alpha]_D^{25.0}$ = -14.2 (c = 0.5, $CHCl_3$). Two carbons were not resolved at 100 MHz.

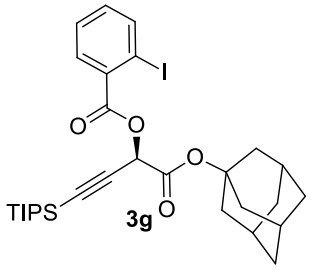
(*R*)-1-Oxo-1-((2-phenylpropan-2-yl)oxy)-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3f)



3f

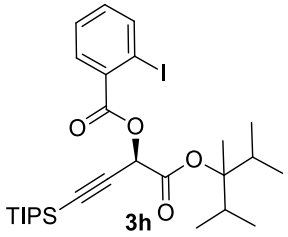
Following general procedure **B**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and 2-phenylpropan-2-yl 2-diazoacetate (**1f**) (62 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:60 as mobile phase to afford **3f** (78.0 mg, 0.129 mmol, 86%) as a colorless thick liquid. TLC (EtOAc:pentane, 1:25 v/v): R_f = 0.4, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.84 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.30 (t, *J* = 7.7 Hz, 3H, Ar*H*), 7.21 (t, *J* = 7.5 Hz, 2H, Ar*H*), 7.15 (t, *J* = 3.6 Hz, 1H, Ar*H*), 7.05 (t, *J* = 7.6 Hz, 1H, Ar*H*), 5.89 (s, 1H, OC*H*CC), 1.74 (s, 3H, CH_3), 1.70 (s, 3H, CH_3), 1.01 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 163.4, 144.8, 141.4, 133.4, 133.1, 131.9, 128.3, 127.9, 127.2, 124.1, 97.7, 94.5, 90.2, 84.6, 64.2, 28.9, 28.0, 18.6, 11.1; IR ν 2951 (m), 2866 (m), 2189 (w), 1744 (s), 1579 (w), 1461 (m), 1240 (s), 1133 (s), 1095 (s), 1014 (m), 884 (w); HRMS (ESI) calcd. for $C_{29}H_{37}INaO_4Si^+$ $[M+Na]^+$ 627.1398; found 627.1399; Chiral HPLC conditions: *ee* = 87%; Chiralpak IB 99.75:0.25 Hexane/*i*PrOH, 1 mL/min, 30 min. t_r (major) = 11.6 min. and t_r (minor) = 13.1 min. λ = 250 cm^{-1}; $[\alpha]_D^{25.0}$ = -29.1 (c = 0.5, $CHCl_3$).

((*R*)-1-(Adamantan-1-yloxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3g)



Following general procedure **B**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and adamantan-1-yl 2-diazoacetate (**1g**) (66 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:60 as mobile phase to afford **3g** (87.0 mg, 0.140 mmol, 93%) as a white foam. Mp: 85.0–86.5 °C; TLC (Et_2O:pentane, 1:40 v/v): R_f = 0.13, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 3.6 Hz, 1H, Ar*H*), 7.99 (d, *J* = 3.4 Hz, 1H, Ar*H*), 7.43 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.18 (t, *J* = 7.6 Hz, 1H, Ar*H*), 5.87 (s, 1H, OC*H*CC), 2.22–2.12 (m, 9H, 3 X C*H* and 3 X CH_2), 1.72–1.62 (m, 6H, 3 X CH_2), 1.09 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 163.8, 141.4, 133.6, 133.1, 131.9, 128.0, 98.3, 94.5, 89.7, 83.7, 64.4, 41.0, 36.0, 30.9, 18.6, 11.1; IR ν 2918 (s), 2864 (s), 2189 (w), 1743 (s), 1582 (w), 1461 (m), 1323 (m), 1244 (s), 1210 (s), 1090 (s), 1053 (s), 881 (w); HRMS (ESI) calcd. for $C_{30}H_{41}INaO_4Si^+$ $[M+Na]^+$ 643.1711; found 643.1707; Chiral HPLC conditions: *ee* = 85%; Chiralpak IB 99:1 Hexane/*i*PrOH, 0.5 mL/min, 20 min. t_r (major) = 9.8 min. and t_r (minor) = 10.7 min. λ = 250 $cm^{-1;}$ $[\alpha]_D^{25.0}$ = -10.2 (c = 0.5, $CHCl_3$).

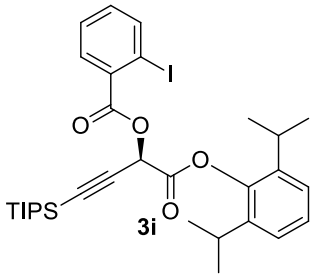
(*R*)-1-Oxo-4-(tri*iso*propylsilyl)-1-((2,3,4-trimethylpentan-3-yl)oxy)but-3-yn-2-yl 2-iodobenzoate (3h)



Following general procedure **B**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and 2,3,4-trimethylpentan-3-yl 2-diazoacetate (**1h**) (60 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:60 as mobile phase to afford **3h** (85.0

mg, 0.142 mmol, 95%) as a colorless thick liquid. TLC (Et_2O:pentane, 1:40 v/v): R_f = 0.36, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 7.9 Hz, 2H, Ar*H*), 7.42 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.17 (t, *J* = 7.6 Hz, 1H, Ar*H*), 5.89 (s, 1H, OC*H*CC), 2.37–2.24 (m, 2H, 2 X C*H*(CH_3)$_2$), 1.47 (s, 3H, OCC*H*$_3$), 1.08 (s, 21H, TIPS), 1.03–0.95 (m, 12H, 2 X CH(C*H*$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 164.1, 141.4, 133.6, 133.1, 131.9, 127.9, 98.1, 94.6, 94.5, 89.7, 64.4, 34.5, 34.4, 18.5, 18.1, 18.1, 17.8, 17.7, 11.0; IR ν 2950 (s), 2870 (m), 2188 (w), 1746 (s), 1579 (w), 1465 (m), 1384 (w), 1240 (s), 1095 (s), 1015 (m), 887 (w); HRMS (ESI) calcd. for $C_{28}H_{43}INaO_4Si^+$ $[M+Na]^+$ 621.1868; found 621.1869; Chiral HPLC conditions: *ee* = 92%; Chiralpak IC 99.75:0.25 Hexane/*i*PrOH, 0.4 mL/min, 60 min. t_r (major) = 34.6 min. and t_r (minor) = 46.4 min. λ = 254 cm^{-1}; $[\alpha]_D^{25.0}$ = -14.1 (c = 0.5, $CHCl_3$). One carbon was not resolved at 100 MHz.

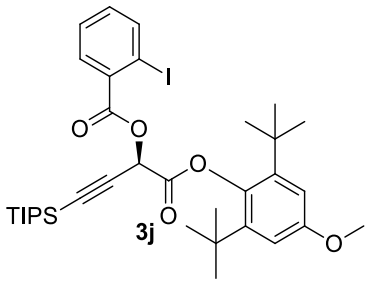
(*R*)-1-(2,6-Di*iso*propylphenoxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3i)



Following general procedure **B**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and 2,6-di*iso*propylphenyl 2-diazoacetate (**1i**) (74 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:70 as mobile phase to afford **3i** (95.0 mg, 0.147 mmol, 98%) as a colorless thick liquid. TLC (Et_2O:pentane, 1:40 v/v): R_f = 0.39, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 8.0 Hz, 1H, Ar*H*), 8.02 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.47 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.28 (d, *J* = 5.5 Hz, 1H, Ar*H*), 7.24–7.20 (m, 3H, Ar*H*), 6.34 (s, 1H, OC*H*CC), 3.18–3.11 (m, 2H, 2 X C*H*(CH_3)$_2$), 1.31–1.21 (m, 12H, 2 X CH(C*H*$_3$)$_2$), 1.17 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 164.2, 144.8, 141.5, 140.5, 133.3, 133.2, 131.8, 128.0, 127.0, 124.1, 96.6, 94.5, 91.5, 63.8, 27.0, 23.8, 23.1, 18.5, 11.1; IR ν 2960 (s), 2871 (m), 2189 (w), 1779 (m), 1741 (m), 1579 (w), 1463 (m), 1323 (m), 1240 (s), 1171 (s), 1087 (s), 1013 (m), 884 (w); HRMS (ESI) calcd. for $C_{32}H_{44}IO_4Si^+$ $[M+H]^+$ 647.2048; found 647.2043; Chiral

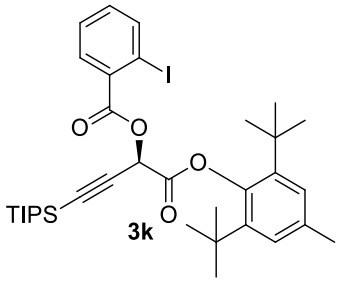
HPLC conditions: *ee* = 90%; Chiralpak IB 99.75:0.25 Hexane/*i*PrOH, 0.5 mL/min, 31 min. t_r (major) = 11.1 min. and t_r (minor) = 13.2 min. λ = 250 cm^{-1}; $[\alpha]_D^{25.0}$ = -21.4 (c = 0.5, $CHCl_3$).

(*R*)-1-(2,6-Di-*tert*-butyl-4-methoxyphenoxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3j)



Following general procedure **B**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methoxyphenyl 2-diazoacetate (**1j**) (91 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:25 as mobile phase to afford **3j** (104 mg, 0.148 mmol, 98%) as a colorless thick liquid. TLC (Et_2O:pentane, 1:25 v/v): R_f = 0.16, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.93 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.42 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.19 (t, *J* = 7.6 Hz, 1H, Ar*H*), 6.87 (s, 2H, Ar*H*), 6.59 (s, 1H, OC*H*CC), 3.79 (s, 3H, OCH_3), 1.37 (s, 18H, 2 X C(CH_3)$_3$), 1.10 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.7, 164.5, 156.6, 143.7, 143.3, 141.5, 141.4, 133.7, 133.2, 131.5, 127.9, 111.7, 97.1, 94.5, 91.9, 64.0, 55.2, 35.7, 35.6, 31.6, 31.4, 18.5, 11.1; IR ν 2954 (s), 2870 (m), 2188 (w), 1774 (s), 1747 (s), 1592 (m), 1463 (m), 1425 (m), 1309 (m), 1239 (s), 1179 (s), 1094 (s), 1012 (m), 879 (w); HRMS (ESI) calcd. for $C_{35}H_{49}INaO_5Si^+$ $[M+Na]^+$ 727.2286; found 727.2294; Chiral HPLC conditions: *ee* = 95%; Chiralpak IA 99:1 Hexane/*i*PrOH, 0.2 mL/min, 60 min. t_r (major) = 32.1 min. and t_r (minor) = 48.4 min. λ = 254 cm^{-1}; $[\alpha]_D^{25.0}$ = -28.0 (c = 0.5, $CHCl_3$). One carbon was not resolved at 100 MHz.

(*R*)-1-(2,6-Di-*tert*-butyl-4-methylphenoxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3k)

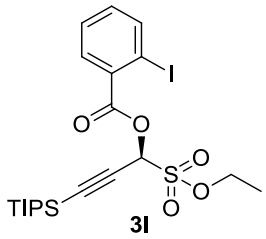


Following general procedure **B**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:60 as mobile phase to afford **3k** (103 mg, 0.150 mmol, quant.) as a colorless thick liquid. TLC (Et_2O:pentane, 1:40 v/v): R_f = 0.3, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (dd, *J* = 8.0, 1.1 Hz, 1H, Ar*H*)), 7.92 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*)), 7.41 (td, *J* = 7.7, 0.9 Hz, 1H, Ar*H*)), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*)), 7.13 (s, 2H, Ar*H*)), 6.59 (s, 1H, OC*H*CC), 2.32 (s, 3H, ArC*H*$_3$), 1.36 (s, 18H, 2 X C(C*H*$_3$)$_3$), 1.10 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 164.5, 145.7, 142.1, 141.8, 141.4, 135.2, 133.7, 133.1, 131.5, 127.9, 127.2, 97.1, 94.4, 91.9, 64.0, 35.4, 35.3, 31.7, 31.6, 21.5, 18.5, 11.1; IR ν 2945 (m), 2866 (m), 1773 (s), 1746 (s), 1584 (w), 1465 (m), 1366 (w), 1271 (m), 1239 (s), 1183 (s), 1130 (m), 1094 (s), 1017 (s), 998 (w), 921 (w), 885 (m); HRMS (ESI) calcd. for $C_{35}H_{49}INaO_4Si^+$ $[M+Na]^+$ 711.2337; found 711.2341; Chiral HPLC conditions: *ee* = 97%; Chiralpak IA 99.75:0.25 Hexane/*i*PrOH, 0.5 mL/min, 30 min. t_r (major) = 11.6 min. and t_r (minor) = 15.0 min. λ=250 cm^{-1}; $[\alpha]_D^{25.0}$ = -26.4 (c = 0.5, $CHCl_3$). One carbon was not resolved at 100 MHz.

Large scale procedure:

1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (643 mg, 1.50 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (865 mg, 3.00 mmol, 2.00 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:60 as mobile phase to afford **3k** (1.01 g, 0.147 mmol, 98%) as a colorless thick liquid. Chiral HPLC conditions: *ee* = 95%; Chiralpak IA 99.75:0.25 Hexane/*i*PrOH, 0.5 mL/min, 30 min. t_r (major) = 11.6 min. and t_r (minor) = 15.0 min. λ = 250 cm^{-1}; $[\alpha]_D^{25.0}$ = –26.4 (c = 0.5, $CHCl_3$).

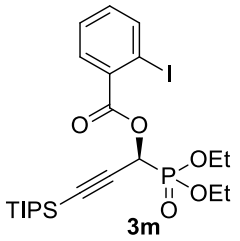
(*S*)-1-(Ethoxysulfonyl)-3-(tri*iso*propylsilyl)prop-2-yn-1-yl 2-iodobenzoate (3l)



3l

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and ethyl diazomethanesulfonate (**1l**) (45 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:20 as mobile phase to afford **3l** (82.0 mg, 0.149 mmol, 99%) as a colorless oil. TLC (EtOAc:pentane, 1:20 v/v): R_f = 0.3, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.94 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.46 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.23 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 6.71 (s, 1H, OC*H*CC), 4.51 (q, *J* = 7.1 Hz, 2H, CH_2CH$_3$), 1.43 (t, *J* = 7.1 Hz, 3H, CH$_2$CH_3), 1.13–1.07 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1, 141.8, 133.8, 132.2, 131.9, 128.2, 95.6, 94.9, 93.6, 73.9, 70.8, 18.5, 15.3, 11.0; IR ν 2947 (m), 2868 (m), 1755 (s), 1584 (w), 1466 (m), 1383 (s), 1238 (s), 1180 (m), 1078 (s), 1009 (m), 924 (s), 887 (w); HRMS (ESI) calcd. for $C_{21}H_{31}INaO_5SSi^+$ $[M+Na]^+$ 573.0598; found 573.0599; Chiral HPLC conditions: *ee* = 75%; Chiralpak IB 99:1 Hexane/*i*PrOH, 1 mL/min, 20 min. t_r (minor) = 8.0 min. and t_r (major) = 9.0 min. λ = 254 cm^{-1}; $[\alpha]_D^{25.0}$ = -14.3 (c = 0.5, $CHCl_3$).

(*S*)-1-(Diethoxyphosphoryl)-3-(tri*iso*propylsilyl)prop-2-yn-1-yl 2-iodobenzoate (3m)

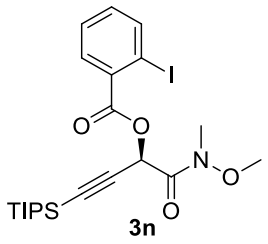


3m

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and diethyl (diazomethyl)phosphonate (**1m**) (54 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and

purified by flash chromatography using EtOAc:pentane 1:4 as mobile phase to afford **3m** (82.0 mg, 0.142 mmol, 94%) as a colorless oil. TLC (EtOAc:pentane, 1:4 v/v): R_f = 0.35, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (dd, *J* = 8.0, 1.1 Hz, 1H, Ar*H*), 7.84 (dd, *J* = 7.9, 1.7 Hz, 1H, Ar*H*), 7.42 (td, *J* = 7.6, 1.1 Hz, 1H, Ar*H*), 7.18 (td, *J* = 7.7, 1.6 Hz, 1H, Ar*H*), 6.05 (d, *J* = 17.0 Hz, 1H, OC*H*P), 4.35–4.18 (m, 4H, 2 X C*H*$_2$CH$_3$), 1.35 (td, *J* = 7.1, 3.5 Hz, 6H, 2 X CH$_2$C*H*$_3$), 1.08 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.4 (d, *J* = 8.0 Hz), 141.4, 133.8, 133.1, 131.4, 127.9, 97.4 (d, *J* = 5.8 Hz), 94.4, 91.8 (d, *J* = 8.2 Hz), 64.1 (d, *J* = 6.9 Hz), 64.0 (d, *J* = 6.5 Hz), 60.2 (d, *J* = 174.4 Hz), 18.5, 16.4 (m, 2 X C), 11.1; IR ν 2944 (w), 2866 (w), 2181 (w), 1744 (m), 1464 (w), 1270 (m), 1241 (m), 1020 (s), 977 (m), 884 (w); HRMS (ESI) calcd. for $C_{23}H_{37}IO_5PSi^+$ $[M+H]^+$ 579.1187; found 579.1195; Chiral HPLC conditions: *ee* = 90%; Chiralpak IB 99:1 Hexane/*i*PrOH, 1 mL/min, 40 min. t_r (major) = 28.9 min. and t_r (minor) = 34.6 min. λ = 230 cm^{-1}; $[\alpha]_D^{25.0}$ = -14.0 (c = 0.5, $CHCl_3$).

(*R*)-1-(Methoxy(methyl)amino)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (3n)

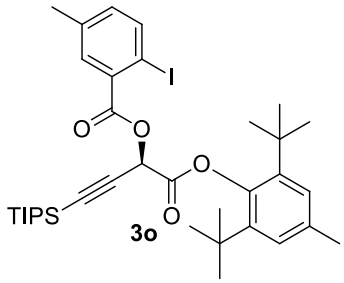


3n

Following general procedure **B**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and 2-diazo-*N*-methoxy-*N*-methylacetamide (**1n**) (39 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:10 as mobile phase to afford **3n** (65.0 mg, 0.123 mmol, 82%) as a white foam. Mp: 44.2–46.5 °C; TLC (Et_2O:pentane, 1:10 v/v): R_f = 0.34, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 7.8 Hz, 1H, Ar*H*), 8.00 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.43 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.17 (t, *J* = 7.7 Hz, 1H, Ar*H*), 6.36 (s, 1H, OC*H*CC), 3.87 (s, 3H, NOC*H*$_3$), 3.26 (s, 3H, NC*H*$_3$), 1.08 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 165.2, 141.3, 133.4, 133.1, 132.1, 128.0, 98.2, 94.5, 90.3, 63.2, 61.5, 32.7, 18.5, 11.0; IR ν 2962 (s), 2876 (m), 2185 (w), 1738 (m), 1698 (m), 1578 (w), 1463 (m), 1387 (m), 1246 (s), 1067 (s), 987 (w), 887 (w); HRMS (ESI) calcd. for $C_{22}H_{33}INO_4Si^+$ $[M+H]^+$ 530.1218; found 530.1226;

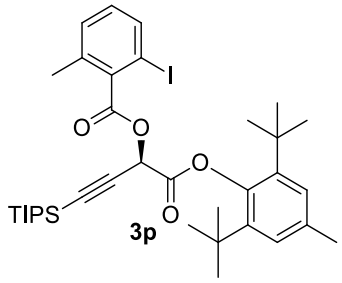
Chiral HPLC conditions: *ee* = 90%; Chiralpak IB 97:3 Hexane/*i*PrOH, 1 mL/min, 30 min. t_r (minor) = 23.2 min. and t_r (major) = 25.3 min. λ = 250 cm^{-1}; $[\alpha]_D^{25.0}$ = -8.2 (c = 0.5, $CHCl_3$).

(*R*)-1-(2,6-Di-*tert*-butyl-4-methylphenoxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodo-5-methylbenzoate (3o)



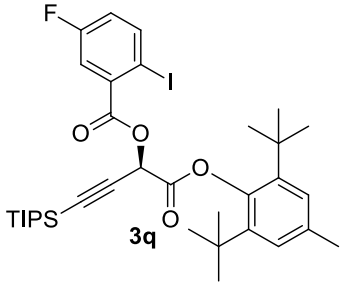
Following general procedure **B**, 5-methyl-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2b**) (67.0 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:60 as mobile phase to afford **3o** (104 mg, 0.148 mmol, 99%) as a white solid. Mp: 75.0–77.5 °C; TLC (Et_2O:pentane, 1:60 v/v): R_f = 0.25, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.1 Hz, 1H, Ar*H*), 7.73 (d, *J* = 2.0 Hz, 1H, Ar*H*), 7.13 (s, 2H, Ar*H*), 7.00 (dd, *J* = 8.1, 2.1 Hz, 1H, Ar*H*), 6.58 (s, 1H, OC*H*CC), 2.32 (s, 3H, ArCH_3), 2.31 (s, 3H, ArCH_3), 1.37 (s, 18H, 2 X C(CH_3)$_3$), 1.10 (s, 21H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 164.6, 145.8, 142.1, 141.8, 141.1, 138.1, 135.2, 134.2, 133.5, 132.3, 127.1, 97.2, 91.9, 90.3, 64.0, 35.4, 35.3, 31.7, 31.6, 21.5, 20.8, 18.5, 11.1; IR ν 2955 (m), 2869 (m), 2239 (w), 2188 (w), 1744 (s), 1464 (m), 1187 (s), 1096 (s), 1011 (m), 886 (m); HRMS (ESI) calcd. for $C_{36}H_{51}INaO_4Si^+$ $[M+Na]^+$ 725.2494; found 725.2491; Chiral HPLC conditions: *ee* = 97%; Chiralpak IA 99.75:0.25 Hexane/*i*PrOH, 0.3 mL/min, 30 min. t_r (major) = 19.3 min. and t_r (minor) = 24.8 min. λ = 254 cm^{-1}; $[\alpha]_D^{25.0}$ = -20.1 (c = 0.5, $CHCl_3$). One carbon was not resolved at 100 MHz.

(*R*)-1-(2,6-Di-*tert*-butyl-4-methylphenoxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodo-6-methylbenzoate (3p)



Following general procedure **B**, 6-methyl-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2c**) (67.0 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:60 as mobile phase to afford **3p** (103 mg, 0.147 mmol, 98%) as a white foam. Mp: 49.2–52.5 °C; TLC (Et_2O:pentane, 1:40 v/v): R_f = 0.22, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.17 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.13 (s, 2H, Ar*H*), 7.01 (t, *J* = 7.8 Hz, 1H, Ar*H*), 6.63 (s, 1H, OC*H*CC), 2.39 (s, 3H, ArCH_3), 2.32 (s, 3H, ArCH_3), 1.38 (s, 9H, C(CH_3)$_3$), 1.37 (s, 9H, C(CH_3)$_3$), 1.11 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1, 165.2, 145.7, 142.3, 141.8, 138.4, 137.6, 136.4, 135.2, 131.0, 129.8, 127.2, 127.2, 96.5, 92.3, 91.7, 64.0, 35.4, 35.2, 31.8, 31.5, 21.5, 20.0, 18.6, 11.1; IR ν 2952 (m), 2866 (m), 1775 (m), 1749 (s), 1464 (w), 1237 (m), 1184 (m), 1092 (s), 1063 (s), 997 (w), 885 (w); HRMS (ESI) calcd. for $C_{36}H_{51}INaO_4Si^+$ $[M+Na]^+$ 725.2494; found 725.2491; Chiral HPLC conditions: *ee* = 98%; Chiralpak IA 99.75:0.25 Hexane/*i*PrOH, 0.2 mL/min, 40 min. t_r (major) = 25.4 min. and t_r (minor) = 27.3 min. λ = 273 cm^{-1}; $[\alpha]_D^{25.0}$ = -55.8 (c = 0.5, $CHCl_3$). Enantoselctivity determination is not precise due to peak overlap.

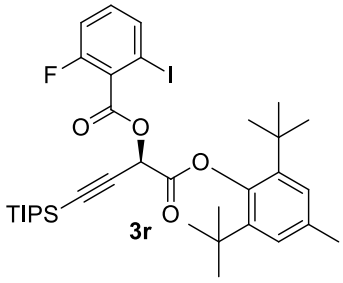
(*R*)-1-(2,6-Di-*tert*-butyl-4-methylphenoxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 5-fluoro-2-iodobenzoate (3q)



Following general procedure **B**, 5-fluoro-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2c**) (67.0 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate

(**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:70 as mobile phase to afford **3q** (104 mg, 0.147 mmol, 98%) as a colorless thick liquid. TLC (Et_2O:pentane, 1:60 v/v): R_f = 0.1, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (dd, *J* = 8.7, 5.3 Hz, 1H, Ar*H*), 7.65 (dd, *J* = 8.9, 2.9 Hz, 1H, Ar*H*), 7.13 (s, 2H, Ar*H*), 6.96 (td, *J* = 8.3, 3.0 Hz, 1H, Ar*H*), 6.56 (s, 1H, OC*H*CC), 2.32 (s, 3H, ArCH_3), 1.36 (s, 18H, 2 X C(CH_3)$_3$), 1.10 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.3, 163.4 (d, *J* = 2.0 Hz), 162.3 (d, *J* = 249.7 Hz), 145.7, 142.8 (d, *J* = 7.2 Hz), 142.1, 141.7, 135.3, 135.2 (d, *J* = 7.0 Hz), 127.2, 120.9 (d, *J* = 21.6 Hz), 119.0 (d, *J* = 24.4 Hz), 96.7, 92.4, 87.5 (d, *J* = 3.5 Hz), 64.3, 35.4, 35.3, 31.7, 31.6, 21.5, 18.5, 11.1; IR ν 2949 (m), 2866 (m), 2189 (w), 1751 (m), 1597 (w), 1581 (w), 1465 (m), 1426 (w), 1271 (m), 1237 (m), 1183 (s), 1077 (m), 1014 (m), 920 (w), 886 (m); HRMS (ESI) calcd. for $C_{35}H_{48}FINaO_4Si^+$ $[M+Na]^+$ 729.2243; found 729.2251; Chiral HPLC conditions: *ee* = 97%; Chiralpak IB 99.75:0.25 Hexane/*i*PrOH, 0.4 mL/min, 31 min. t_r (major) = 15.1 min. and t_r (minor) = 16.3 min. λ=254 cm^{-1}; $[\alpha]_D^{25.0}$ = -23.0 (c = 0.5, $CHCl_3$). One carbon was not resolved at 100 MHz.

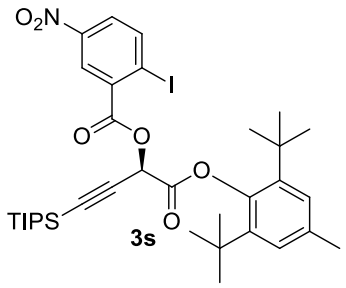
(*R*)-1-(2,6-Di-*tert*-butyl-4-methylphenoxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-fluoro-6-iodobenzoate (3r)



Following general procedure **B**, 6-fluoro-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2d**) (67.0 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:70 as mobile phase to afford **3r** (105 mg, 0.149 mmol, 99%) as a white foam. Mp: 41.5–43.3 °C; TLC (Et_2O:pentane, 1:60 v/v): R_f = 0.1, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72–7.58 (m, 1H, Ar*H*), 7.20–7.05 (m, 4H, Ar*H*), 6.56 (s, 1H, OC*H*CC), 2.32 (s, 3H, ArCH_3), 1.37 (s, 9H, C(CH_3)$_3$), 1.36 (s, 9H, C(CH_3)$_3$), 1.11 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.8, 163.2, 159.4 (d,

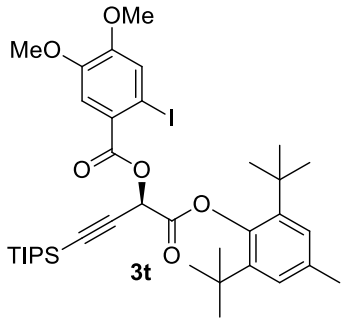
J = 257.5 Hz), 145.7, 142.2, 141.8, 135.2 (d, *J* = 3.7 Hz), 135.2, 132.8 (d, *J* = 8.4 Hz), 127.2, 127.1, 126.9 (d, *J* = 18.5 Hz), 115.8 (d, *J* = 21.2 Hz), 96.5, 92.5, 64.6, 35.4, 35.2, 31.7, 31.5, 21.5, 18.5, 11.1; IR ν 2955 (s), 2868 (m), 2189 (w), 1755 (s), 1599 (m), 1569 (w), 1451 (s), 1256 (s), 1183 (s), 1096 (s), 1058 (m), 996 (m), 864 (m); HRMS (ESI) calcd. for $C_{35}H_{48}FINaO_4Si^+$ $[M+Na]^+$ 729.2243; found 729.2251; Chiral HPLC conditions: *ee* = 95%; Chiralpak IA 99.75:0.25 Hexane/*i*PrOH, 0.3 mL/min, 30 min. t_r (major) = 22.0 min. and t_r (minor) = 24.4 min. λ=280 cm^{-1}; $[\alpha]_D^{25.0}$ = -40.8 (c = 0.5, $CHCl_3$). One carbon was not resolved at 100 MHz.

(*R*)-1-(2,6-Di-*tert*-butyl-4-methylphenoxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodo-5-nitrobenzoate (3s)



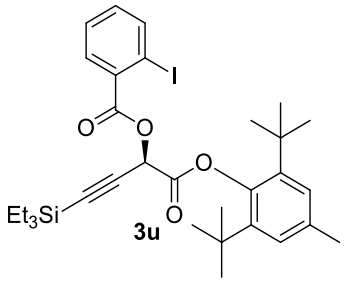
Following general procedure **B**, 5-nitro-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2e**) (71.0 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:30 as mobile phase to afford **3s** (110 mg, 0.150 mmol, quant.) as a pale yellow foam. Mp: 39.5–42.5 °C; TLC (Et_2O:pentane, 1:25 v/v): R_f = 0.15, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.71 (d, *J* = 2.7 Hz, 1H, Ar*H*), 8.23 (d, *J* = 8.6 Hz, 1H, Ar*H*), 8.01 (dd, *J* = 8.6, 2.7 Hz, 1H, Ar*H*), 7.13 (s, 2H, Ar*H*), 6.57 (s, 1H, OC*H*CC), 2.32 (s, 3H, ArCH_3), 1.38 (s, 9H, C(CH_3)$_3$), 1.37 (s, 9H, C(CH_3)$_3$), 1.13–1.09 (m, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 162.9, 147.7, 145.7, 142.9, 142.1, 141.7, 135.3, 135.2, 127.2, 127.2, 126.8, 126.0, 102.8, 96.4, 93.0, 64.8, 35.4, 35.3, 31.7, 31.6, 21.5, 18.5, 11.1; IR ν 2952 (s), 2867 (m), 2354 (w), 1756 (s), 1603 (m), 1531 (s), 1465 (m), 1348 (s), 1233 (s), 1099 (s), 1016 (m), 916 (m); HRMS (ESI) calcd. for $C_{35}H_{48}INNaO_6Si^+$ $[M+Na]^+$ 756.2188; found 756.2193; Chiral HPLC conditions: *ee* = 91%; Chiralpak IC 99:1 Hexane/*i*PrOH, 0.25 mL/min, 60 min. t_r (minor) = 37.8 min. and t_r (major) = 42.4 min. λ = 280 cm^{-1}; $[\alpha]_D^{25.0}$ = -15.2 (c = 0.5, $CHCl_3$).

(*R*)-1-(2,6-Di-*tert*-butyl-4-methylphenoxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodo-4,5-dimethoxybenzoate (3t)



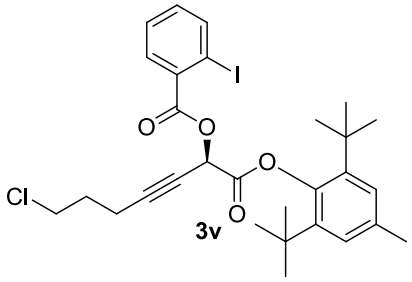
Following general procedure **B**, 4,5-dimethoxy-1-[(tri*iso*propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2f**) (73.5 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:60 as mobile phase to afford **3t** (106 mg, 0.142 mmol, 94%) as a white foam. Mp: 49.3–52.5 °C; TLC (Et_2O:pentane, 1:40 v/v): R_f = 0.25, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.56 (s, 1H, Ar*H*), 7.41 (s, 1H, Ar*H*), 7.12 (s, 2H, Ar*H*), 6.56 (s, 1H, OC*H*CC), 3.92 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 2.32 (s, 3H, ArCH_3), 1.37 (s, 9H, C(CH_3)$_3$), 1.36 (s, 9H, C(CH_3)$_3$), 1.09 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.7, 163.3, 152.4, 148.6, 145.7, 142.1, 141.7, 135.2, 127.2, 127.1 124.7, 123.8, 114.2, 97.5, 91.5, 85.4, 63.8, 56.3, 55.8, 35.3, 35.3, 31.6, 31.6, 21.5, 18.5, 11.1; IR ν 2952 (m), 2867 (w), 1773 (w), 1741 (m), 1592 (w), 1509 (m), 1464 (w), 1371 (w), 1340 (w), 1266 (s), 1206 (s), 1176 (s), 1100 (s), 1009 (w), 883 (w); HRMS (ESI) calcd. for $C_{37}H_{53}INaO_6Si^+$ $[M+Na]^+$ 771.2548; found 771.2557; Chiral HPLC conditions: *ee* = 97%; Chiralpak IA 99:1 Hexane/*i*PrOH, 0.5 mL/min, 25 min. t_r (major) = 14.7 min. and t_r (minor) = 18.3 min. λ=254 cm^{-1}; $[\alpha]_D^{25.0}$ = -8.2 (c = 0.5, $CHCl_3$).

(*R*)-1-(2,6-Di-*tert*-butyl-4-methylphenoxy)-1-oxo-4-(triethylsilyl)but-3-yn-2-yl 2-iodobenzoate (3u)



Following general procedure **B**, 1-[(triethylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2g**) (58.0 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:60 as mobile phase to afford **3u** (74.0 mg, 0.114 mmol, 78%) as a white solid. Mp: 98.5–102.0 °C; TLC (Et_2O:pentane, 1:40 v/v): R_f = 0.28, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.95 (d, *J* = 7.3 Hz, 1H, Ar*H*), 7.41 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.18 (t, *J* = 7.9 Hz, 1H, Ar*H*), 7.13 (s, 2H, Ar*H*), 6.56 (s, 1H, OC*H*CC), 2.32 (s, 3H, ArCH_3), 1.37 (s, 9H, C(CH_3)$_3$), 1.37 (s, 9H, C(CH_3)$_3$), 1.01 (t, *J* = 7.9 Hz, 9H, 3 X CH_2CH_3), 0.66 (q, *J* = 7.9 Hz, 6H, 3 X CH_2CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.3, 164.5, 145.8, 142.1, 141.8, 141.4, 135.2, 133.7, 133.2, 131.7, 127.9, 127.2, 127.0, 96.2, 94.5, 93.0, 64.0, 35.3, 35.3, 31.6, 31.6, 21.5, 7.3, 4.0; IR ν 2958 (m), 2879 (m), 2190 (w), 1938 (w), 1775 (m), 1745 (s), 1589 (w), 1464 (m), 1424 (m), 1238 (s), 1184 (s), 1094 (s), 1013 (s), 864 (w); HRMS (ESI) calcd. for $C_{32}H_{44}IO_4Si^+$ $[M+H]^+$ 647.2048; found 647.2054; Chiral HPLC conditions: *ee* = 94%; Chiralpak IA 99.75:0.25 Hexane/*i*PrOH, 0.5 mL/min, 30 min. t_r (major) = 12.0 min. and t_r (minor) = 16.4 min. λ = 254 cm^{-1}; $[\alpha]_D^{25.0}$ = -27.6 (c = 0.5, $CHCl_3$).

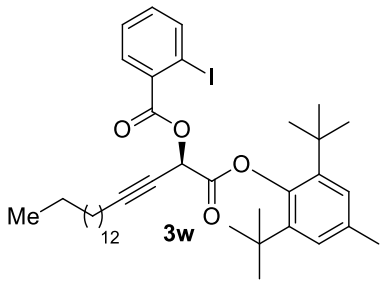
(*R*)-7-Chloro-1-(2,6-di-*tert*-butyl-4-methylphenoxy)-1-oxohept-3-yn-2-yl 2-iodobenzoate (3v)



Following general procedure **B**, (5-chloropent-1-ynyl)-1,2-benziodoxol-3(1H)-one (**2h**) (52.5 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and

purified by flash chromatography using EtOAc:pentane 1:50 as mobile phase to afford **3v** (85 mg, 0.14 mmol, 93%) as a colorless thick liquid. TLC (EtOAc:pentane, 1:40 v/v): R_f = 0.18, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.97 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.41 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.18 (t, *J* = 7.7 Hz, 1H, Ar*H*), 7.14 (s, 1H, Ar*H*), 7.13 (s, 1H, Ar*H*), 6.51 (s, 1H, OC*H*CC), 3.67 (t, *J* = 6.3 Hz, 2H, ClCH_2CH_2), 2.57–2.50 (m, 2H, CCCH_2CH_2), 2.32 (s, 3H, ArCH_3), 2.03 (p, *J* = 6.5 Hz, 2H, ClCH$_2$CH_2), 1.37 (s, 9H, C(CH_3)$_3$), 1.36 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 164.6, 145.7, 142.0, 141.9, 141.4, 135.2, 133.6, 133.2, 131.7, 127.9, 127.3, 127.0, 94.5, 88.5, 72.5, 63.8, 43.4, 35.3, 35.3, 31.6, 31.3, 30.8, 21.5, 16.3; IR ν 2961 (m), 2870 (w), 2250 (w), 1778 (s), 1745 (s), 1466 (w), 1428 (m), 1241 (s), 1185 (s), 1097 (s), 1042 (w), 1013 (m), 862 (w); HRMS (ESI) calcd. for $C_{29}H_{34}ClINaO_4^+$ $[M+Na]^+$ 631.1083; found 631.1088; Chiral HPLC conditions: *ee* = 92%; Chiralpak IA 99.75:0.25 Hexane/*i*PrOH, 1 mL/min, 30 min. t_r (major) = 12.8 min. and t_r (minor) = 16.4 min. λ = 250 cm^{-1}; $[\alpha]_D^{25.0}$ = -23.8 (c = 0.5, $CHCl_3$).

(*R*)-1-(2,6-Di-*tert*-butyl-4-methylphenoxy)-1-oxooctadec-3-yn-2-yl 2-iodobenzoate (3w)

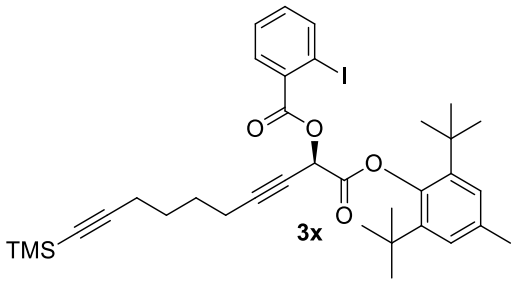


3w

Following general procedure **B**, hexadecynyl-1,2-benziodoxol-3(1H)-one (**2i**) (70.5 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:40 as mobile phase to afford **3w** (90.0 mg, 0.123 mmol, 82%) as a colorless thick liquid. TLC (Et_2O:pentane, 1:40 v/v): R_f = 0.1, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (dd, *J* = 7.9, 0.9 Hz, 1H, Ar*H*), 7.97 (dd, *J* = 7.8, 1.6 Hz, 1H, Ar*H*), 7.40 (td, *J* = 7.7, 1.1 Hz, 1H, Ar*H*), 7.17 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 7.14–7.11 (m, 2H, Ar*H*), 6.51 (t, *J* = 2.2 Hz, 1H, OC*H*CC), 2.38–2.26 (m, 5H, ArCH_3 and CCCH_2), 1.62–1.52 (m, 2H, CH_2), 1.38 (s, 9H, C(CH_3)$_3$), 1.36 (s, 9H, C(CH_3)$_3$), 1.33–1.19 (m, 22H), 0.88 (t, *J* = 6.8 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 164.6, 145.8, 142.1, 142.0, 141.4, 135.1, 133.7, 133.1,

131.7, 127.9, 127.3, 126.9, 94.5, 90.7, 71.3, 64.0, 35.3, 35.3, 31.9, 31.6, 31.3, 29.7, 29.7, 29.6, 29.5, 29.4, 29.1, 28.9, 28.0, 22.7, 21.5, 18.9, 14.1; IR ν 2925 (s), 2856 (m), 2247 (w), 1777 (m), 1744 (s), 1465 (m), 1428 (w), 1368 (w), 1242 (s), 1184 (s), 1097 (s), 1044 (w), 1015 (m), 863 (w); HRMS (ESI) calcd. for $C_{40}H_{57}INaO_4^+$ $[M+Na]^+$ 751.3194; found 751.3175; Chiral HPLC conditions: *ee* = 93%; Chiralpak IA 99.75:0.25 Hexane/*i*PrOH, 0.5 mL/min, 30 min. t_r (major) = 16.6 min. and t_r (minor) = 21.0 min. λ = 250 cm^{-1}; $[\alpha]_D^{25.0}$ = -20.3 (c = 0.5, $CHCl_3$). Two carbons were not resolved at 100 MHz.

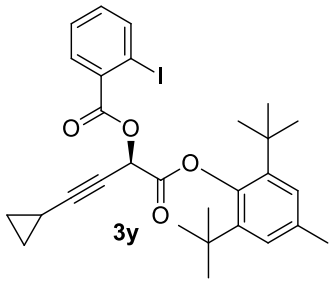
(*R*)-1-(2,6-Di-*tert*-butyl-4-methylphenoxy)-1-oxo-10-(trimethylsilyl)deca-3,9-diyn-2-yl 2-iodobenzoate (3x)



Following general procedure **B**, 8-(trimethylsilyl)octa-1,7-diyn-1-yl-1,2-benziodoxol-3(1H)-one (**2j**) (64.0 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:30 as mobile phase to afford **3x** (86.0 mg, 0.126 mmol, 84%) as a colorless thick liquid. TLC (Et_2O:pentane, 1:20 v/v): R_f = 0.25, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (dd, *J* = 7.9, 0.9 Hz, 1H, Ar*H*), 7.97 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.40 (td, *J* = 7.7, 1.1 Hz, 1H, Ar*H*), 7.17 (td, *J* = 7.6, 1.7 Hz, 1H, Ar*H*), 7.15–7.10 (m, 2H, Ar*H*), 6.50 (t, *J* = 2.2 Hz, 1H, OC*H*CC), 2.38–2.36 (m, 2H, TMSCCCH_2), 2.32 (s, 3H, ArCH_3), 2.25 (t, *J* = 6.7 Hz, 2H, CHCCCH_2), 1.69–1.64 (m, 4H,$CH_2CH_2CH_2CH_2$), 1.37 (s, 9H, C(CH_3)$_3$), 1.36 (s, 9H, C(CH_3)$_3$), 0.14 (s, 9H, TMS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.7, 164.6, 145.8, 142.0, 141.9, 141.4, 135.1, 133.7, 133.1, 131.7, 127.9, 127.3, 127.0, 106.7, 94.5, 90.0, 84.9, 71.7, 63.9, 35.3, 35.3, 31.6, 31.3, 27.6, 27.0, 21.5, 19.4, 18.5, 0.2; IR ν 2959 (m), 2867 (w), 2248 (w), 2174 (w), 1776 (s), 1744 (s), 1590 (w), 1465 (w), 1427 (m), 1368 (w), 1245 (s), 1184 (s), 1098 (s), 1016 (m); HRMS (ESI) calcd. for $C_{35}H_{45}INaO_4Si^+$ $[M+Na]^+$ 707.2024; found 707.2022; Chiral HPLC conditions: *ee* = 90%; Chiralpak IA 99.75:0.25 Hexane/*i*PrOH, 1 mL/min,

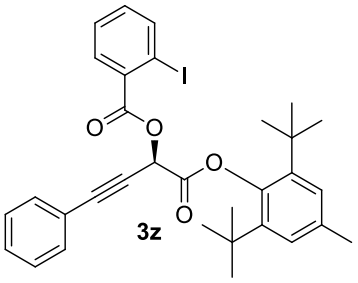
30 min. t_r (major) = 8.7 min. and t_r (minor) = 11.0 min. λ = 250 cm^{-1}; $[\alpha]_D^{25.0}$ = -16.4 (c = 0.5, $CHCl_3$).

(*R*)-4-Cyclopropyl-1-(2,6-di-*tert*-butyl-4-methylphenoxy)-1-oxobut-3-yn-2-yl 2-iodobenzoate (3y)



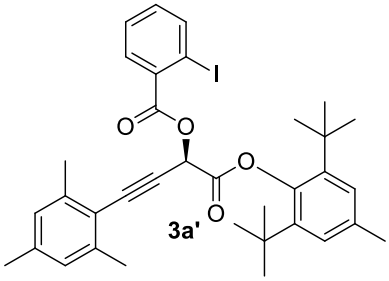
Following general procedure **B**, 2-cyclopropylethynyl-1,2-benziodoxol-3(1H)-one (**2k**) (47.0 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:30 as mobile phase to afford **3y** (78.0 mg, 0.136 mmol, 91%) as a white foam. Mp: 44.5–47.3 °C; TLC (Et_2O:pentane, 1:30 v/v): R_f = 0.15, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (t, *J* = 8.4 Hz, 2H, Ar*H*), 7.40 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.17 (t, *J* = 7.7 Hz, 1H, Ar*H*), 7.13 (d, *J* = 4.8 Hz, 2H, Ar*H*), 6.49–6.47 (m, 1H, OC*H*CC), 2.32 (s, 3H, ArCH_3), 1.38 (s, 9H, C(CH_3)$_3$), 1.36 (s, 10H, C(CH_3)$_3$ and cy-C*H*), 0.90–0.78 (m, 4H, cy-CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.7, 164.6, 145.8, 142.1, 142.0, 141.3, 135.1, 133.7, 133.1, 131.7, 127.9, 127.3, 126.9, 94.5, 93.5, 66.6, 64.0, 35.3, 35.3, 31.6, 31.3, 21.5, 8.2, 8.2, -0.4; IR ν 2961 (w), 2251 (w), 1774 (m), 1744 (s), 1590 (w), 1472 (w), 1427 (w), 1366 (w), 1242 (s), 1187 (s), 1098 (s), 1011 (m), 918 (w), 863 (w); HRMS (ESI) calcd. for $C_{29}H_{33}INaO_4^+$ $[M+Na]^+$ 595.1316; found 595.1320; Chiral HPLC conditions: *ee* = 89%; Chiralpak IA 99.75:0.25 Hexane/*i*PrOH, 0.3 mL/min, 60 min. t_r (major) = 34.7 min. and t_r (minor) = 47.1 min. λ = 250 cm^{-1}; $[\alpha]_D^{25.0}$ = -27.3 (c = 0.5, $CHCl_3$).

(*R*)-1-(2,6-Di-*tert*-butyl-4-methylphenoxy)-1-oxo-4-phenylbut-3-yn-2-yl 2-iodobenzoate (3z)



Following general procedure **B**, 1-[phenylethynyl]-1,2-benziodoxol-3(1H)-one (**2l**) (52.5 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using toluene:pentane 1:1 as mobile phase to afford **3z** (89.0 mg, 0.146 mmol, 98%) as a white foam. Mp: 50.0–52.5 °C;TLC (toluene:pentane, 1:1 v/v): R_f = 0.36, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (dd, *J* = 7.6, 1.4 Hz, 2H, Ar*H*), 7.57–7.50 (m, 2H, Ar*H*), 7.46–7.31 (m, 4H, Ar*H*), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 7.16–7.11 (m, 2H, Ar*H*), 6.76 (s, 1H, OC*H*CC), 2.33 (s, 3H, ArCH_3), 1.39 (s, 9H, C(CH_3)$_3$), 1.39 (s, 9H, C(CH_3)$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 164.6, 145.8, 142.1, 142.0, 141.4, 135.2, 133.5, 133.2, 132.1, 131.8, 129.3, 128.4, 128.0, 127.4, 127.0, 121.4, 94.6, 88.9, 80.1, 64.1, 35.3, 35.3, 31.7, 31.3, 21.5; IR ν 2961 (m), 2872 (w), 2240 (w), 1777 (s), 1746 (s), 1589 (w), 1466 (w), 1428 (w), 1242 (s), 1184 (s), 1097 (s), 1046 (w), 1014 (m), 914 (w), 865 (w); HRMS (ESI) calcd. for $C_{32}H_{33}INaO_4^+$ $[M+Na]^+$ 631.1316; found 631.1321; Chiral HPLC conditions: ee = 87%; Chiralpak IA 99.75:0.25 Hexane/*i*PrOH, 0.5 mL/min, 40 min. t_r (major) = 23.7 min and t_r (minor) = 30.7 min. λ=250 cm^{-1}; $[\alpha]_D^{25.0}$ = -43.5 (c = 0.5, $CHCl_3$).

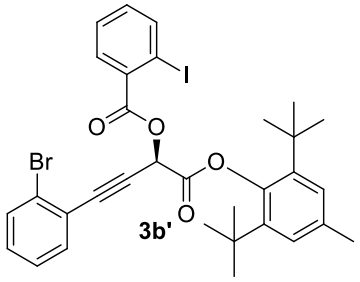
(*R*)-1-(2,6-Di-*tert*-butyl-4-methylphenoxy)-4-mesityl-1-oxobut-3-yn-2-yl 2-iodobenzoate (3a')



Following general procedure **B**, 1-[2,4,6-trimethylphenylethynyl]-1,2-benziodoxol-3(1H)-one (**2k**) (58.5 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated

in vacuo and purified by flash chromatography using Et_2O:pentane 1:35 as mobile phase to afford **3a'** (97.0 mg, 0.149 mmol, 99%) as a white foam. Mp: 46.5–49.0 °C;TLC (Et_2O:pentane, 1:35 v/v): R_f = 0.1, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (dd, *J* = 12.6, 7.8 Hz, 2H, Ar*H*), 7.43 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.19 (t, *J* = 7.7 Hz, 1H, Ar*H*), 7.14 (s, 1H, Ar*H*), 7.13 (s, 1H, Ar*H*), 6.87 (s, 2H, Ar*H*), 6.85 (s, 1H, OC*H*CC), 2.42 (s, 6H, 2 X ArCH_3), 2.32 (s, 3H, ArCH_3), 2.28 (s, 3H, ArCH_3), 1.38 (s, 9H, C(CH_3)$_3$), 1.34 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 164.6, 145.7, 142.1, 141.8, 141.5, 141.0, 138.8, 135.2, 133.7, 133.2, 131.6, 128.0, 127.6, 127.2, 127.1, 118.2, 94.6, 87.2, 87.1, 64.5, 35.3, 35.3, 31.6, 31.5, 21.5, 21.4, 21.0; IR ν 2966 (s), 2919 (m), 2230 (w), 2105 (w), 1773 (m), 1746 (s), 1605 (w), 1592 (w), 1473 (m), 1428 (m), 1372 (w), 1241 (s), 1190 (s), 1097 (s), 1047 (m), 1024 (m), 913 (w); HRMS (ESI) calcd. for $C_{35}H_{39}INaO_4^+$ $[M+Na]^+$ 673.1785; found 673.1799; Chiral HPLC conditions: ee = 91%; Chiralpak IA 99.75:0.25 Hexane/*i*PrOH, 0.5 mL/min, 40 min. t_r (major) = 19.6 min and t_r (minor) = 22.7 min. λ = 254 cm^{-1}; $[\alpha]_D^{25.0}$ = -37.2 (c = 0.5, $CHCl_3$).

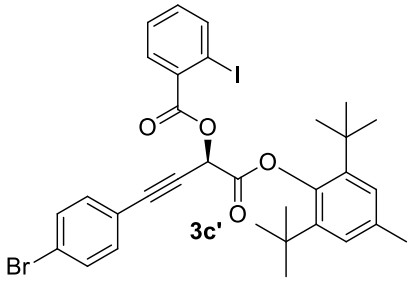
(*R*)-4-(2-Bromophenyl)-1-(2,6-di-*tert*-butyl-4-methylphenoxy)-1-oxobut-3-yn-2-yl 2-iodobenzoate (3b')



Following general procedure **B**, 1-[2-bromophenylethynyl]-1,2-benziodoxol-3(1H)-one (**2l**) (64.5 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using toluene:pentane 1:1 as mobile phase to afford **3b'** (100 mg, 0.145 mmol, 97%) as a white foam. Mp: 47.3–50.6 °C;TLC (toluene:pentane, 1:1 v/v): R_f = 0.35, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.61 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.55 (dd, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 7.43 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.30 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.26–7.16 (m, 2H, Ar*H*), 7.13 (d, *J* = 6.9 Hz, 2H, Ar*H*), 6.81 (s, 1H, OC*H*CC), 2.32 (s, 3H, ArCH_3), 1.40 (s, 9H, C(CH_3)$_3$), 1.37 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.2, 164.5, 145.7, 142.1, 141.9, 141.5, 135.2, 133.8, 133.5, 133.3, 132.6, 131.8, 130.4, 128.0, 127.3,

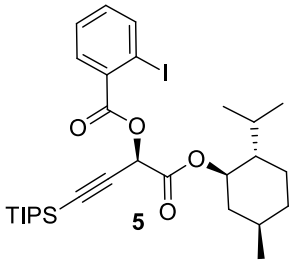
127.1, 127.0, 125.9, 123.7, 94.6, 87.2, 84.4, 64.0, 35.3, 31.7, 31.4, 21.5; IR ν 2961 (m), 2922 (m), 2242 (w), 2113 (w), 1776 (m), 1745 (m), 1588 (w), 1467 (m), 1427 (m), 1370 (w), 1238 (s), 1183 (s), 1091 (s), 1042 (m), 1021 (m), 864 (w); HRMS (ESI) calcd. for $C_{32}H_{32}BrINaO_4^+$ $[M+Na]^+$ 709.0421; found 709.0432; Chiral HPLC conditions: *ee* = 88%; Chiralpak IA 99.75:0.25 Hexane/*i*PrOH, 1 mL/min, 30 min. t_r (major) = 15.7 min and t_r (minor) = 20.2 min. λ = 254 cm^{-1}. $[\alpha]_D^{25.0}$ = -32.5 (c = 0.5, $CHCl_3$). One carbon was not resolved at 100 MHz.

(*R*)-4-(4-Bromophenyl)-1-(2,6-di-*tert*-butyl-4-methylphenoxy)-1-oxobut-3-yn-2-yl 2-iodobenzoate (3c')



Following general procedure **B**, 1-[4-bromophenylethynyl]-1,2-benziodoxol-3(1H)-one (**2m**) (64.5 mg, 0.150 mmol, 1.00 equiv) and 2,6-di-*tert*-butyl-4-methylphenyl 2-diazoacetate (**1k**) (87 mg, 0.30 mmol, 2.0 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using toluene:pentane 1:1 as mobile phase to afford **3c'** (100 mg, 0.145 mmol, 97%) as a white foam. Mp: 59.0–61.5 °C;TLC (toluene:pentane, 1:1 v/v): R_f = 0.35, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 7.9 Hz, 2H, Ar*H*), 7.50 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.44–7.38 (m, 3H, Ar*H*), 7.19 (t, *J* = 7.7 Hz, 1H, Ar*H*), 7.14 (d, *J* = 9.1 Hz, 2H, Ar*H*), 6.73 (s, 1H, OC*H*CC), 2.33 (s, 3H, ArCH_3), 1.39 (s, 9H, C(CH_3)$_3$), 1.37 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.2, 164.5, 145.7, 142.0, 141.9, 141.5, 135.3, 133.4, 133.3, 131.8, 131.7, 128.0, 127.4, 127.0, 123.8, 120.3, 94.6, 87.8, 81.3, 64.0, 35.3, 35.3, 31.7, 31.3, 21.5; IR ν 2964 (m), 2917 (w), 2243 (w), 2105 (w), 1775 (s), 1746 (s), 1590 (w), 1480 (m), 1427 (w), 1242 (s), 1189 (s), 1096 (s), 1046 (m), 1018 (m), 914 (w), 865 (w); HRMS (ESI) calcd. for $C_{32}H_{32}BrINaO_4^+$ $[M+Na]^+$ 709.0421; found 709.0427; Chiral HPLC conditions: *ee* = 87%; Chiralpak IA 99.75:0.25 Hexane/*i*PrOH, 1 mL/min, 30 min. t_r (major) = 12.1 min and t_r (minor) = 17.1 min. λ = 254 cm^{-1}. $[\alpha]_D^{25.0}$ = -47.3 (c = 0.5, $CHCl_3$). One carbon was not resolved at 100 MHz.

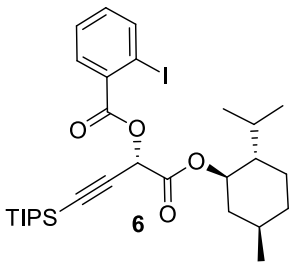
(*R*)-1-(((1*R*,2*S*,5*R*)-2-*Iso*propyl-5-methylcyclohexyl)oxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (5)



5

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and (1*R*,2*S*,5*R*)-2-*iso*propyl-5-methylcyclohexyl 2-diazoacetate (**1o**) (68.0 mg, 0.300 mmol, 2.00 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:70 as mobile phase to afford **5** (85.0 mg, 0.136 mmol, 91%) as a white foam. Mp: 67.2–69.0 °C; TLC (Et_2O:pentane, 1:40 v/v): R_f = 0.2, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (t, *J* = 7.6 Hz, 2H, Ar*H*), 7.44 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.18 (t, *J* = 7.7 Hz, 1H, Ar*H*), 5.93 (s, 1H, OC*H*CC), 4.88–4.73 (m, 1H, OC*H*), 2.15–1.92 (m, 2H), 1.69 (d, *J* = 11.7 Hz, 2H), 1.62–1.40 (m, 2H), 1.16–1.04 (m, 24H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 7.0 Hz, 3H), 0.80–0.74 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 164.9, 141.5, 133.5, 133.2, 131.9, 128.0, 97.5, 94.5, 90.3, 76.9, 64.2, 46.9, 40.5, 34.1, 31.4, 25.7, 23.0, 21.9, 20.8, 18.5, 15.8, 11.0; IR ν 2956 (s), 2872 (s), 1748 (s), 1584 (w), 1463 (m), 1383 (w), 1323 (w), 1241 (s), 1213 (m), 1075 (s), 1026 (m), 886 (w); HRMS (ESI) calcd. for $C_{30}H_{45}INaO_4Si^+$ $[M+Na]^+$ 647.2024; found 647.2016; Chiral HPLC conditions: *dr* = 95:5; Chiralpak IB 99.75:0.25 Hexane/*i*PrOH, 0.3 mL/min, 31 min. t_r (major) = 23.1 min. and t_r (minor) = 25.2 min. λ = 214 cm^{-1}; $[\alpha]_D^{25.0}$ = -34.2 (c = 0.5, $CHCl_3$).

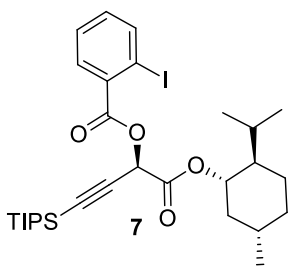
(*S*)-1-(((1*R*,2*S*,5*R*)-2-*Iso*propyl-5-methylcyclohexyl)oxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (6)



6

Following general procedure **C**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and (1*R*,2*S*,5*R*)-2-*iso*propyl-5-methylcyclohexyl 2-diazoacetate (**1o**) (68.0 mg, 0.300 mmol, 2.00 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:70 as mobile phase to afford **6** (90.0 mg, 0.144 mmol, 96%) as a colorless thick liquid. TLC (Et_2O:pentane, 1:40 v/v): R_f = 0.2, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.97 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.44 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.18 (t, *J* = 7.6 Hz, 1H, Ar*H*), 5.93 (s, 1H, OC*H*CC), 4.82 (td, *J* = 10.9, 4.2 Hz, 1H, OC*H*), 2.09–1.95 (m, 2H), 1.69 (d, *J* = 11.7 Hz, 2H), 1.56–1.39 (m, 2H), 1.15–0.98 (m, 24H), 0.96–0.84 (m, 6H), 0.80–0.74 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 165.0, 141.4, 133.5, 133.2, 131.8, 127.9, 97.6, 94.5, 90.3, 76.7, 64.2, 46.8, 40.4, 34.1, 31.3, 26.1, 23.3, 21.9, 20.7, 18.5, 16.3, 11.0; IR ν 2949 (s), 2866 (s), 2189 (w), 2117 (w), 1745 (s), 1578 (w), 1462 (m), 1377 (w), 1322 (m), 1241 (s), 1206 (s), 1092 (s), 1016 (s), 915 (w), 885 (m); HRMS (ESI) calcd. for $C_{30}H_{45}INaO_4Si^+$ $[M+Na]^+$ 647.2024; found 647.2016; Chiral HPLC conditions: *dr* = 6:94; Chiralpak IB 99.75:0.25 Hexane/*i*PrOH, 0.3 mL/min, 50 min. t_r (minor) = 21.6 min. and t_r (major) = 22.6 min. λ = 214 cm^{-1}; $[\alpha]_D^{25.0}$ = -6.0 (c = 0.5, $CHCl_3$).

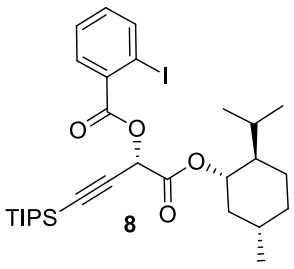
(*R*)-1-(((1*S*,2*R*,5*S*)-2-*Iso*propyl-5-methylcyclohexyl)oxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (7)



7

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and (1*S*,2*R*,5*S*)-2-*iso*propyl-5-methylcyclohexyl 2-diazoacetate (**1p**) (68.0 mg, 0.300 mmol, 2.00 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:70 as mobile phase to afford **7** (85.0 mg, 0.136 mmol, 91%) as a colorless thick liquid. TLC (Et_2O:pentane, 1:40 v/v): R_f = 0.2, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.97 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.44 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.18 (t, *J* = 7.6 Hz, 1H, Ar*H*), 5.93 (s, 1H, OC*H*CC), 4.82 (td, *J* = 10.9, 4.2 Hz, 1H, OC*H*), 2.09–1.95 (m, 2H), 1.69 (d, *J* = 11.7 Hz, 2H), 1.55–1.37 (m, 2H), 1.15–0.98 (m, 24H), 0.95–0.83 (m, 6H), 0.80–0.74 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 165.0, 141.4, 133.5, 133.2, 131.8, 128.0, 97.6, 94.5, 90.3, 76.7, 64.2, 46.9, 40.4, 34.1, 31.3, 26.1, 23.3, 21.9, 20.7, 18.5, 16.3, 11.0; IR ν 2952 (s), 2868 (s), 2188 (w), 2106 (w), 1746 (s), 1589 (w), 1460 (m), 1376 (w), 1322 (m), 1242 (s), 1210 (s), 1090 (s), 1021 (m), 958 (w), 897 (w), 886 (w); HRMS (ESI) calcd. for $C_{30}H_{45}INaO_4Si^+$ $[M+Na]^+$ 647.2024; found 647.2016; Chiral HPLC conditions: *dr* = 93.5:6.5; Chiralpak IB 99.75:0.25 Hexane/*i*PrOH, 0.3 mL/min, 50 min. t_r (major) = 19.1 min. and t_r (minor) = 32.0 min. λ = 250 cm^{-1}; $[\alpha]_D^{25.0}$ = +4.7 (c = 0.5, $CHCl_3$).

(*S*)-1-(((1*S*,2*R*,5*S*)-2-*Iso*propyl-5-methylcyclohexyl)oxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (8)

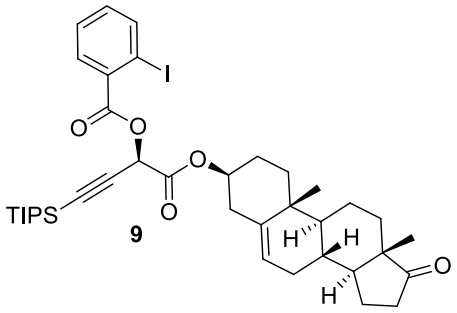


8

Following general procedure **C**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and (1*S*,2*R*,5*S*)-2-*iso*propyl-5-methylcyclohexyl 2-diazoacetate (**1p**) (68.0 mg, 0.300 mmol, 2.00 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:70 as mobile phase to afford **8** (85.0 mg, 0.136 mmol, 91%) as a white foam. Mp: 67.2–69.0 °C; TLC (Et_2O:pentane, 1:40 v/v): R_f = 0.2, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (t, *J* = 7.5 Hz, 2H,

Ar*H*), 7.44 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.18 (t, *J* = 7.6 Hz, 1H, Ar*H*), 5.93 (s, 1H, OC*H*CC), 4.81 (td, *J* = 10.9, 4.3 Hz, 1H, OC*H*), 2.14–1.91 (m, 2H), 1.69 (d, *J* = 11.7 Hz, 2H), 1.47 (t, *J* = 10.2 Hz, 2H), 1.13–0.99 (m, 24H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 7.0 Hz, 3H), 0.80–0.74 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 164.9, 141.5, 133.4, 133.2, 131.9, 128.0, 97.4, 94.5, 90.3, 76.9, 64.1, 46.8, 40.5, 34.0, 31.4, 25.7, 22.9, 21.9, 20.8, 18.5, 15.8, 11.0; IR ν 2952 (s), 2868 (s), 2116 (w), 1746 (s), 1588 (w), 1462 (m), 1376 (w), 1322 (m), 1242 (s), 1210 (s), 1090 (s), 1021 (m), 914 (w), 886 (w); HRMS (ESI) calcd. for $C_{30}H_{45}INaO_4Si^+$ $[M+Na]^+$ 647.2024; found 647.2016; Chiral HPLC conditions: *dr* = 5:95; Chiralpak IB 99.75:0.25 Hexane/*i*PrOH, 0.3 mL/min, 50 min. t_r (minor) = 19.3 min. and t_r (major) = 30.9 min. λ = 254 cm^{-1}; $[\alpha]_D^{25.0}$ = +39.1 (c = 0.5, $CHCl_3$).

(*R*)-1-(((3*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-10,13-Dimethyl-17-oxo-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (9)

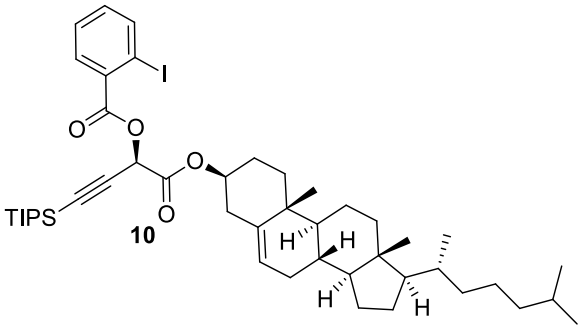


9

Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and (3*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-10,13-dimethyl-17-oxo-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-diazoacetate (**1q**) (107 mg, 0.300 mmol, 2.00 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:10 as mobile phase to afford **9** (100 mg, 0.132 mmol, 88%) as colorless thick liquid. TLC (EtOAc:pentane, 1:10 v/v): R_f = 0.24, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (t, *J* = 8.9 Hz, 2H, Ar*H*), 7.44 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.19 (t, *J* = 7.7 Hz, 1H, Ar*H*), 5.95 (s, 1H, OC*H*CC), 5.42 (d, *J* = 5.1 Hz, 1H, olefinic *H*), 4.78–4.70 (m, 1H, OC*H*), 2.57–2.33 (m, 3H), 2.13–2.04 (m, 2H), 2.00–1.79 (m, 4H), 1.76–1.59 (m, 4H), 1.58–1.40 (m, 2H), 1.38–1.21 (m, 2H), 1.22–1.13 (m, 2H),

1.09 (s, 21H), 1.04 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 221.0, 164.9, 164.8, 141.5, 139.4, 133.4, 133.2, 131.8, 128.0, 122.3, 97.6, 94.5, 90.5, 76.2, 64.0, 51.6, 50.0, 47.5, 37.7, 36.8, 36.7, 35.8, 31.4, 31.4, 30.7, 27.2, 21.8, 20.3, 19.2, 18.5, 13.5, 11.0; IR ν 3056 (w), 2948 (m), 2867 (m), 2190 (w), 1739 (s), 1464 (w), 1265 (s), 1212 (m), 1095 (m), 1018 (m), 885 (w); HRMS (ESI) calcd. for $C_{39}H_{53}INaO_5Si^+$ $[M+Na]^+$ 779.2599; found 779.2598; Chiral HPLC conditions: *dr* = 91:9; Chiralpak IB 95:5 Hexane/*i*PrOH, 1 mL/min, 31 min. t_r (minor) = 15.9 min. and t_r (major) = 18.1 min. λ = 230 cm^{-1}; $[\alpha]_D^{25.0}$ = -10.2 (c = 0.5, $CHCl_3$).

(2*R*)-1-(((3*S*,8*S*,9*S*,10*R*,13*R*,14*S*)-10,13-Dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl 2-iodobenzoate (10)

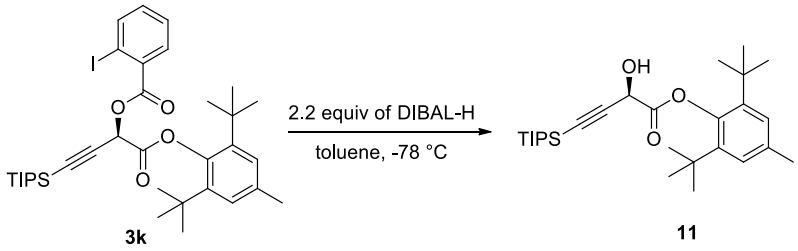


Following general procedure **A**, 1-[(tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**2a**) (65.0 mg, 0.150 mmol, 1.00 equiv) and 3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H cyclopenta[a]phenanthren-3-yl 2-diazoacetate (**1r**) (136 mg, 0.300 mmol, 2.00 equiv) were stirred for 18 h. The crude reaction mixture was concentrated in vacuo and purified by flash chromatography using Et_2O:pentane 1:70 as mobile phase to afford **10** (118 mg, 0.138 mmol, 92%) as a white foam. Mp: 43.0–46.5 °C; TLC (Et_2O:pentane, 1:50 v/v): R_f = 0.2, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (t, *J* = 8.8 Hz, 2H, Ar*H*), 7.44 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.19 (t, *J* = 7.6 Hz, 1H, Ar*H*), 5.96 (s, 1H, OC*H*CC), 5.39 (d, *J* = 4.7 Hz, 1H, olefinic *H*), 4.74 (tt, *J* = 11.8, 4.6 Hz, 1H, OC*H*), 2.45–2.33 (m, 2H), 2.09–1.75 (m, 5H), 1.74–0.94 (m, 45H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 6H), 0.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 164.8, 141.5, 139.2, 133.4, 133.2, 131.8, 128.0, 123.1, 97.7, 94.5, 90.4, 76.5, 64.1, 56.6, 56.1, 49.9, 42.3, 39.7, 39.5, 37.8, 36.8, 36.5, 36.2, 35.8, 31.9, 31.8, 28.2, 28.0, 27.3, 24.3, 23.8, 22.8, 22.6, 21.0, 19.2,

18.7, 18.5, 11.8, 11.1; IR ν 2945 (s), 2866 (s), 2256 (w), 2188 (w), 1747 (s), 1579 (w), 1463 (m), 1376 (m), 1323 (m), 1240 (s), 1208 (s), 1088 (s), 1017 (s), 914 (m); HRMS (ESI) calcd. for $C_{47}H_{71}INaO_4Si^+$ $[M+Na]^+$ 877.4059; found 877.4069; Chiral HPLC conditions: *dr* = 89:11; Chiralpak IB 99:1 Hexane/*i*PrOH, 0.25 mL/min, 40 min. t_r (minor) = 30.8 min. and t_r (major) = 34.9 min. $\lambda = 250$ cm^{-1}; $[\alpha]_D^{25.0} = -27.5$ (c = 0.5, $CHCl_3$).

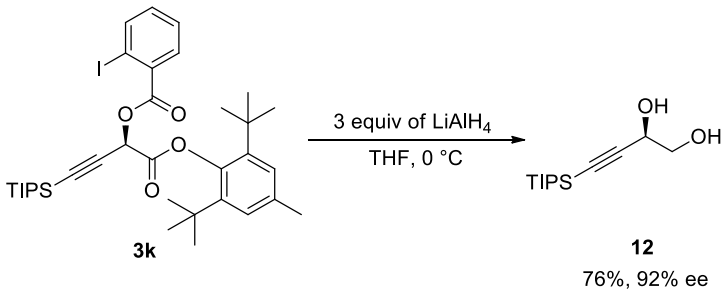
7. Product modifications

(*R*)-2,6-Di-*tert*-butyl-4-methylphenyl 2-hydroxy-4-(tri*iso*propylsilyl)but-3-ynoate (11)



(*R*)-1-(2,6-Di-*tert*-butyl-4-methylphenoxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl-2-iodo benzoate (**3k**) (83 mg, 0.12 mmol, 1.0 equiv) was dissolved in anhydrous toluene (1 mL) under N_2 in a 5 mL microwave vial. Then DIBAL-H (1.2 M in toluene, 0.220 mL, 0.264 mmol, 2.20 equiv) was added under N_2 at -78 °C and stirred for 1h. The resulting clear solution was quenched by the addition of sat. aq. potassium sodium tartrate (2 mL) and the mixture was stirred for 1 h at room temperature. Then the reaction mixture was diluted with water (5 mL) and extracted with EtOAc (3 X 10 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed in vacuo. The crude product was purified by column chromatography using 1:20 EtOAc:pentane to afford (*R*)-2,6-di-*tert*-butyl-4-methylphenyl 2-hydroxy-4-(tri*iso*propylsilyl)but-3-ynoate **(11)** (54.5 mg, 0.119 mmol, 99%) as a thick liquid. TLC (EtOAc:pentane, 1:15 v/v): R_f = 0.44, $KMnO_4$; ^1H NMR (400 MHz, $CDCl_3$): δ 7.14 (s, 2H, Ar*H*), 5.21 (s, 1H, OC*H*CC), 3.06 (s, 1H, O*H*), 2.33 (s, 3H, ArCH_3), 1.37 (s, 9H, C(CH_3)$_3$), 1.33 (s, 9H, C(CH_3)$_3$), 1.11 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 145.9, 142.2, 141.6, 135.3, 127.2, 127.1, 100.5, 90.5, 63.6, 35.4, 35.2, 31.6, 31.5, 21.5, 18.5, 11.1; IR ν 3470 (w), 2953 (s), 2870 (s), 2724 (w), 2178 (w), 1762 (s), 1599 (w), 1465 (m), 1426 (m), 1373 (m), 1191 (s), 1100 (s), 1019 (m), 889 (m); HRMS (ESI) calcd. for $C_{28}H_{46}NaO_3Si^+$ $[M+Na]^+$ 481.3108; found 481.3114; Chiral HPLC conditions: ee = 95%; Chiralpak IA 99:1 Hexane/*i*PrOH, 1 mL/min, 20 min. t_r (major) = 10.1 min. and t_r (minor) = 12.2 min. λ = 214 cm^{-1}; $[\alpha]_D^{25.0}$ = -34.2 (c = 0.5, $CHCl_3$).

(*R*)-4-(Tri*iso*propylsilyl)but-3-yne-1,2-diol (12)

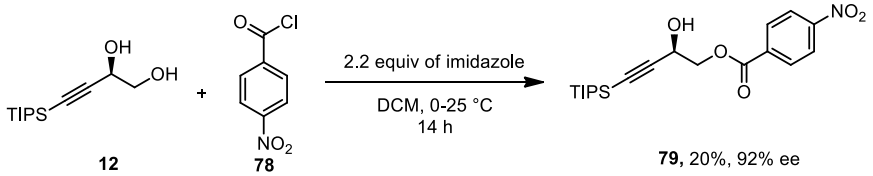


3k **12**
76%, 92% ee

(*R*)-1-(2,6-Di-*tert*-butyl-4-methylphenoxy)-1-oxo-4-(tri*iso*propylsilyl)but-3-yn-2-yl-2-iodo benzoate (**3k**) (207 mg, 0.300 mmol, 1.00 equiv) was dissolved in anhydrous THF (3 mL) under N_2 in a 5 mL microwave vial. Then $LiAlH_4$ (2.4 M in THF, 0.375 mL, 0.900 mmol, 3.00 equiv) was added under N_2 at 0 °C and stirred for 1 h. The resulting solution was quenched by the addition of sat. aq. potassium sodium tartrate (5 mL) and the biphasic mixture was stirred for 1 h at room temperature. Then the reaction mixture was diluted with water (5 mL) and extracted with EtOAc (3 X 20 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed in vacuo. The crude product was purified by column chromatography using 1:3 EtOAc:pentane to afford (*R*)-4-(tri*iso*propylsilyl)but-3-yne-1,2-diol **(12)** (55.0 mg, 0.227 mmol, 76%) as a white solid. Mp: 75.1–77.0 °C; TLC (EtOAc:pentane, 1:3 v/v): R_f = 0.24, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.48 (dd, *J* = 6.7, 3.8 Hz, 1H, OC*H*CC), 3.79–3.61 (m, 2H, C*H*$_2$OH), 2.27 (s, 2H, 2 X O*H*), 1.06 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 104.9, 87.7, 66.8, 63.8, 18.5, 11.0; IR ν 3300 (m), 2941 (s), 2867 (s), 2174 (w), 1463 (m), 1223 (w), 1089 (s), 1038 (s), 1009 (s), 882 (m); HRMS (ESI) calcd. for $C_{13}H_{26}NaO_2Si^+$ $[M+Na]^+$ 265.1594; found 265.1601; $[\alpha]_D^{25.0}$ = -17.9 (c = 0.5, $CHCl_3$).

Determination of the *ee* of 12:

(*R*)-2-Hydroxy-4-(tri*iso*propylsilyl)but-3-yn-1-yl 4-nitrobenzoate (79)



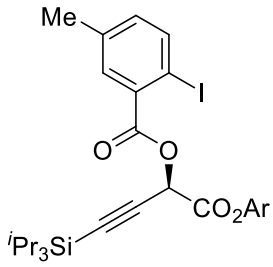
12 **78** **79,** 20%, 92% ee

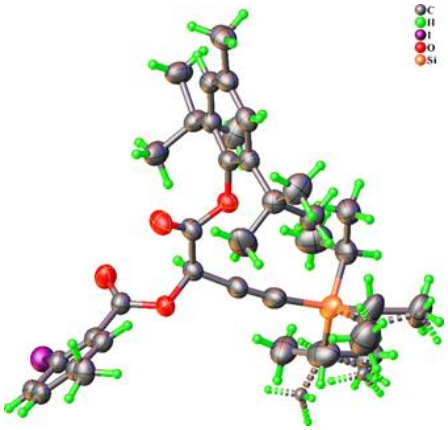
(*R*)-4-(Tri*iso*propylsilyl)but-3-yne-1,2-diol **(12)** (11.0 mg, 0.045 mmol, 1.00 equiv) and imidazole (6.8 mg, 0.10 mmol, 2.2 equiv) were dissolved in anhydrous DCM (0.45 mL) under N_2 in a 5 mL

microwave vial. Then *p*-nitrobenzoyl chloride (**78**) (9.3 mg, 0.05 mmol, 1.1 equiv), which was dissolved in DCM (0.25 mL), was added under N_2 at 0 °C. The reaction mixture was warmed-up to room temperature and stirred for 14 h. A sat. solution of $NaHCO_3$ (2.5 mL) was added, and the reaction mixture was extracted with DCM (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed in vacuo. The crude product was purified by column chromatography using 1:7 EtOAc:pentane as mobile phase to afford (*R*)-2-hydroxy-4-(tri*iso*propylsilyl)but-3-yn-1-yl 4-nitrobenzoate (**79**) (3.5 mg, 8.9 μmmol, 20%) as a thick yellow liquid. TLC (EtOAc:pentane, 1:7 v/v): R_f = 0.32, $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32–8.24 (m, 4H, Ar*H*), 4.78 (t, *J* = 5.0 Hz, 1H, OC*H*CC), 4.59–4.46 (m, 2H, OC*H*$_2$), 2.22 (bs, 1H, O*H*), 1.05 (s, 21H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.5, 150.7, 135.1, 130.9, 123.5, 103.8, 88.4, 68.5, 61.4, 18.5, 11.0; IR ν 3414 (w), 3114 (w), 2947 (m), 2867 (m), 1736 (s), 1608 (w), 1531 (s), 1465 (w), 1349 (m), 1276 (s), 1259 (s), 1097 (s), 1053 (m), 1017 (m); HRMS (ESI) calcd. for $C_{20}H_{29}AgNO_5Si^+$ $[M+Ag]^+$ 498.0860; found 498.0864; Chiral HPLC conditions: ee = 92%; Chiralpak IA 95:5 Hexane/*i*PrOH, 1 mL/min, 31 min. t_r (major) = 10.0 min. and t_r (minor) = 14.8 min. λ = 254 cm^{-1}.

8. Absolute configuration and stereochemical model for the reaction

CCDC 1534166





Empirical formula	C_{36} H_{51} I O_4 Si
Formula weight	702.76
Temperature	140.00(10) K
Wavelength	1.54184 Å
Crystal system	Orthorhombic
Space group	*P* 2_1 2_1 2_1
Unit cell dimensions	a = 9.3812(2) Å □= 90°.
b = 12.8730(2) Å	□= 90°.
c = 29.8093(7) Å	□ = 90°.
Volume	3599.90(13) Å^3
Z	4
Density (calculated)	1.297 Mg/m^3
Absorption coefficient	7.573 mm^{-1}
F(000)	1464
Crystal size	0.486 x 0.253 x 0.180 mm^3
Theta range for data collection	3.740 to 73.880°.
Index ranges	$-8 \le h \le 11$, $-15 \le k \le 14$, $-36 \le l \le 37$
Reflections collected	25820
Independent reflections	7160 [$R_{(int)}$ = 0.0451]
Completeness to theta = 67.684°	100.0 %
Absorption correction	Sphere
Max. and min. transmission	0.14825 and 0.05124

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7160 / 111 / 444
Goodness-of-fit on F^2	1.073
Final R indices [I>2sigma(I)]	R_1 = 0.0491, wR_2 = 0.1364
R indices (all data)	R_1 = 0.0494, wR_2 = 0.1368
Absolute structure parameter	0.003(5)
Largest diff. peak and hole	2.291 and -0.622 e.Å^{-3}

Stereochemical model for the reaction

A highly speculative model for rationalizing the observed absolute configuration is proposed in Figure S1 based on the following assumption:

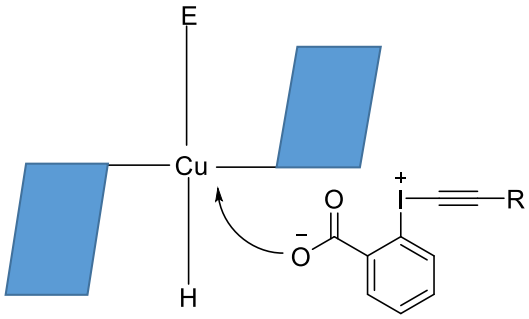
1) A tricoordinate copper carbene complex with a 90° angle between the carbene and the ligand plane, based on the proposed structure of this type of complexes. [31]

2) First and enantiodeterminating step if the attack of the carboxylate group of the reagent onto the copper.

3) The attack of the carboxylate occurs in the free quadrant on the opposite side of the ester group.

4) The following alkyne transfer occurs under retention of configuration.

This model allows rationalizing the observed absolute configuration. However, as the mechanism of the reaction is not yet established, it remains highly speculative.



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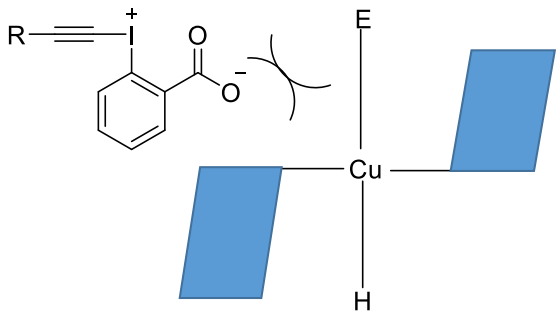

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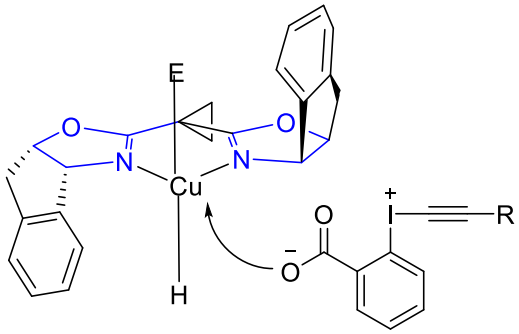

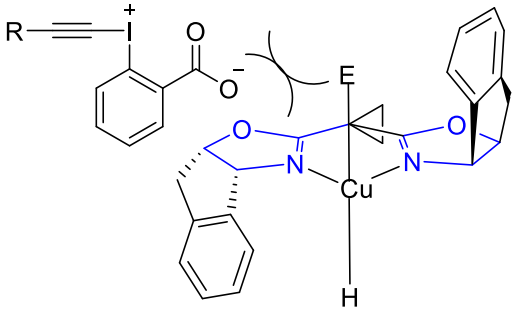

Figure S1. Spculative model for asymmetric induction.

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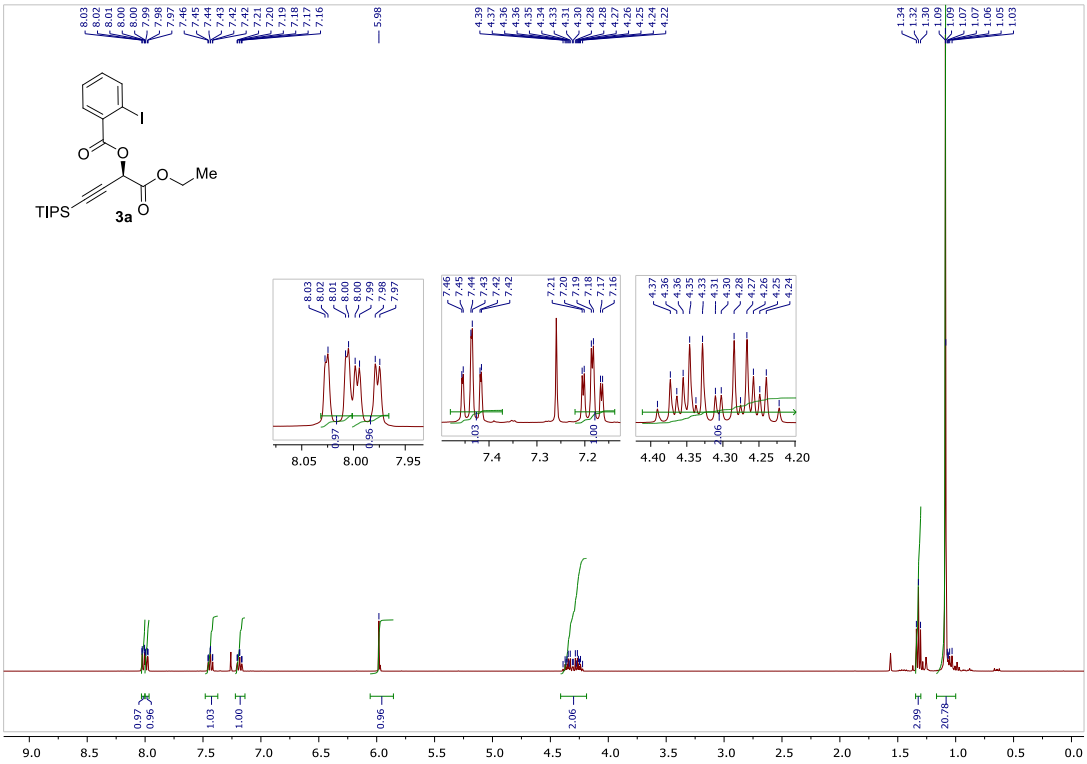
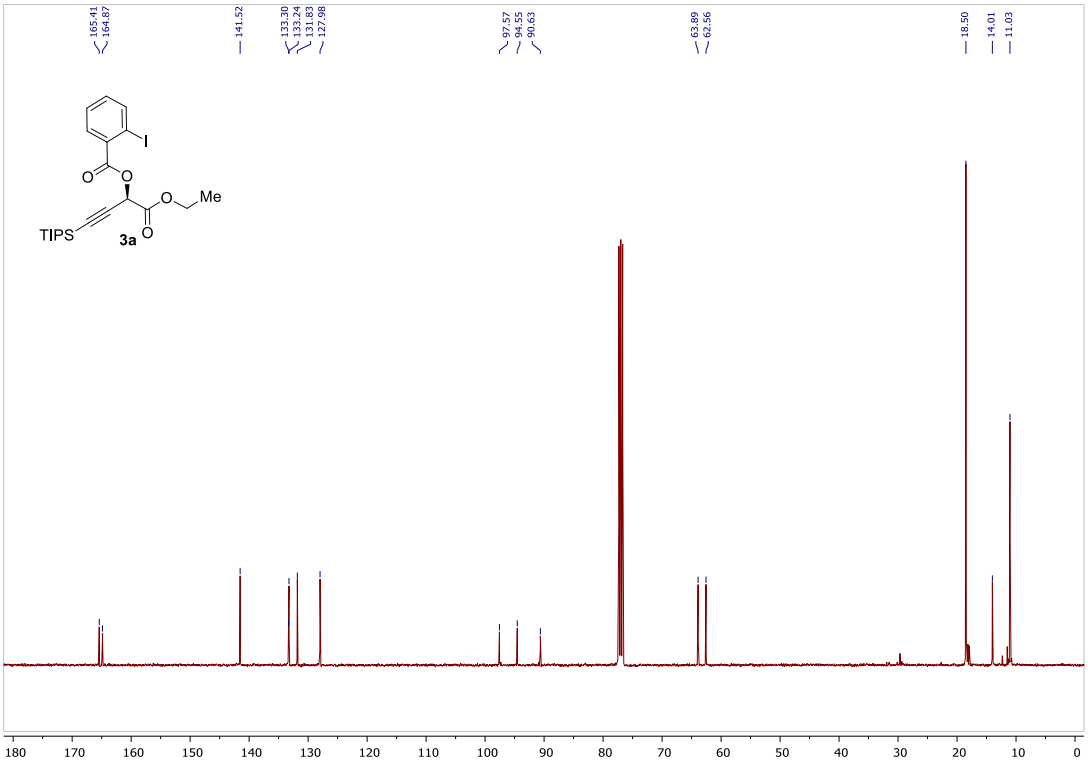
10. Spectra of new compounds

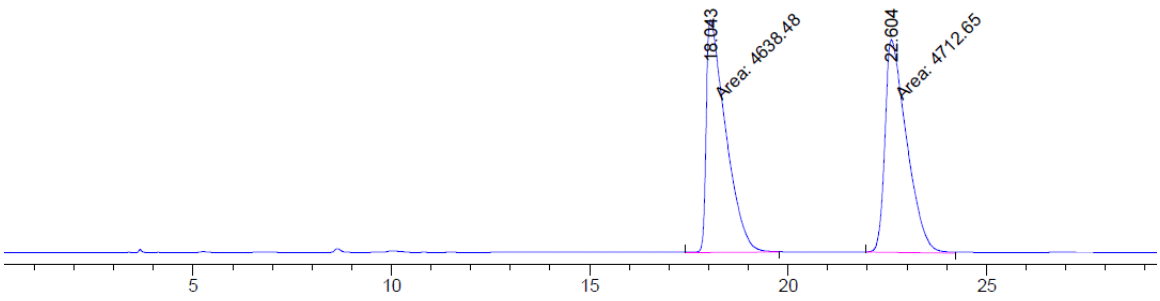
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3a**



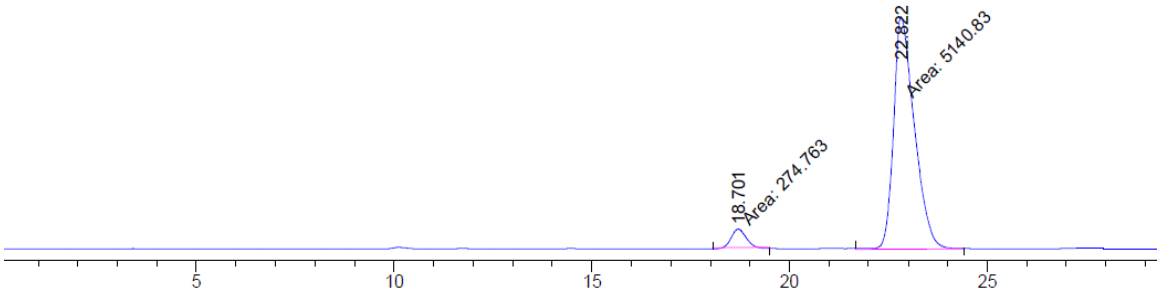
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3a**



HPLC of compound **3a**

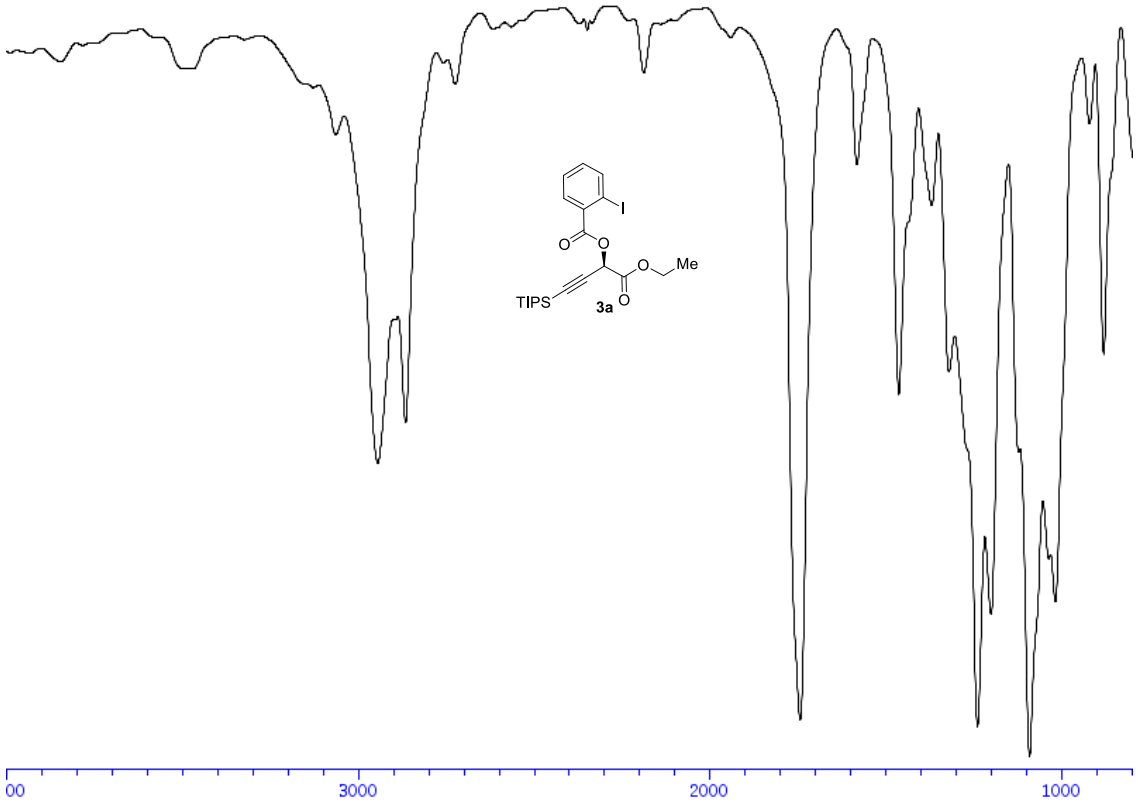


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.043	MM	0.5715	4638.47852	135.26520	49.6034
2	22.604	MM	0.6354	4712.64990	123.60860	50.3966

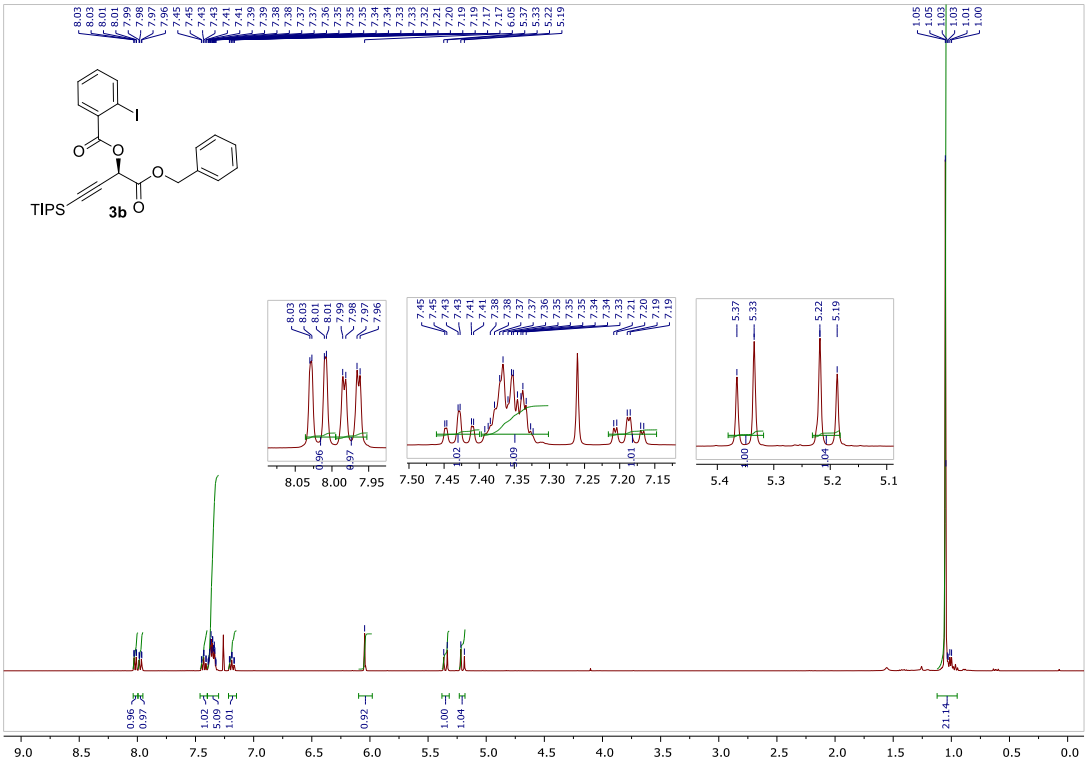


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.701	MM	0.4165	274.76254	10.99382	5.0735
2	22.822	MM	0.6116	5140.82861	140.10083	94.9265

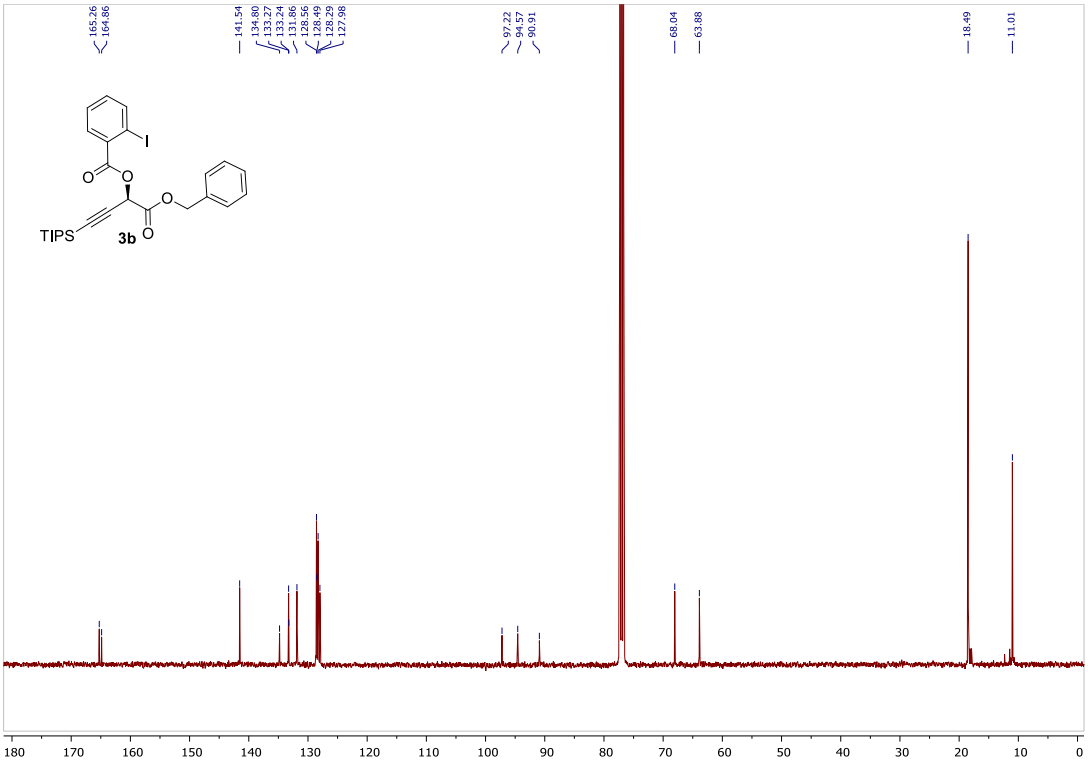
IR of compound **3a**



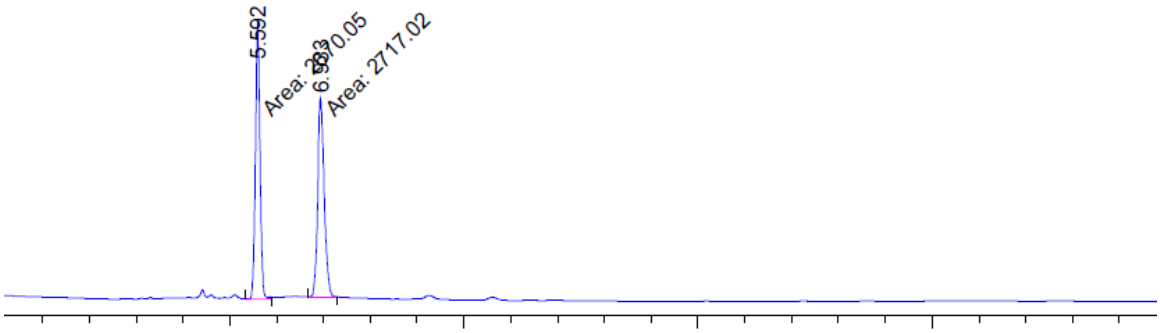
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3b**



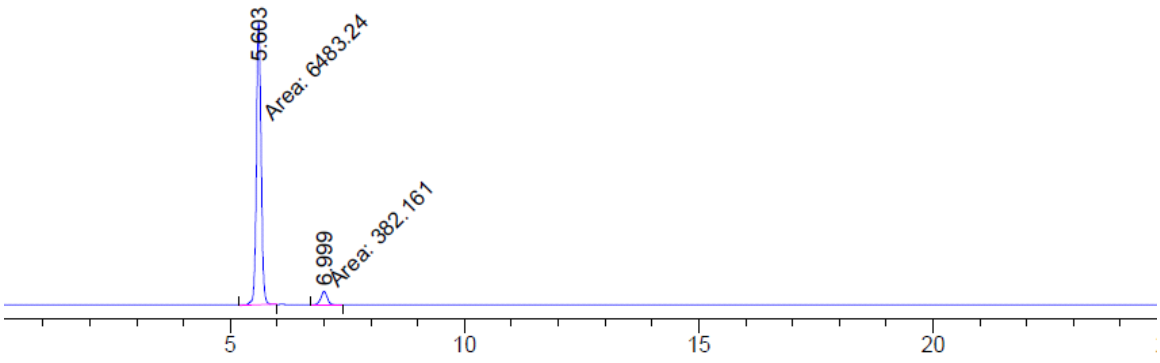
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3b**



HPLC of compound **3b**

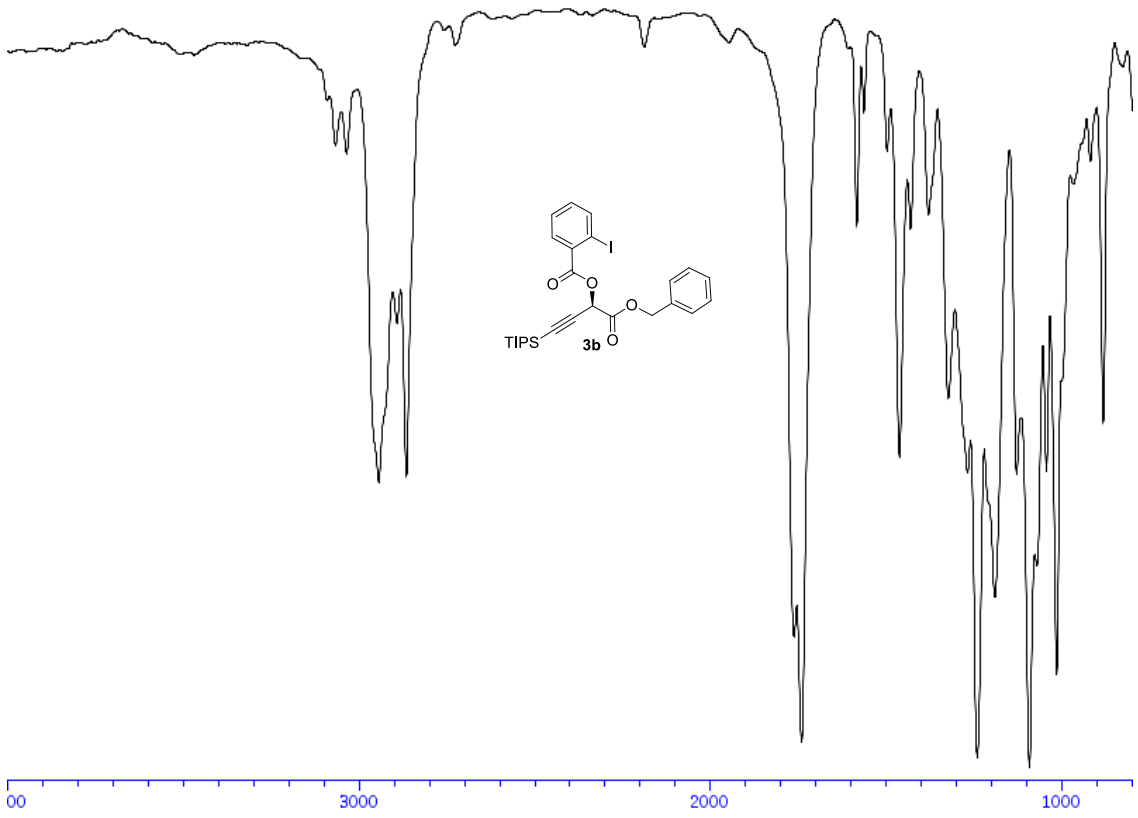


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.592	MM	0.1132	2670.05347	393.07788	49.5641
2	6.933	MM	0.1619	2717.01978	279.69778	50.4359

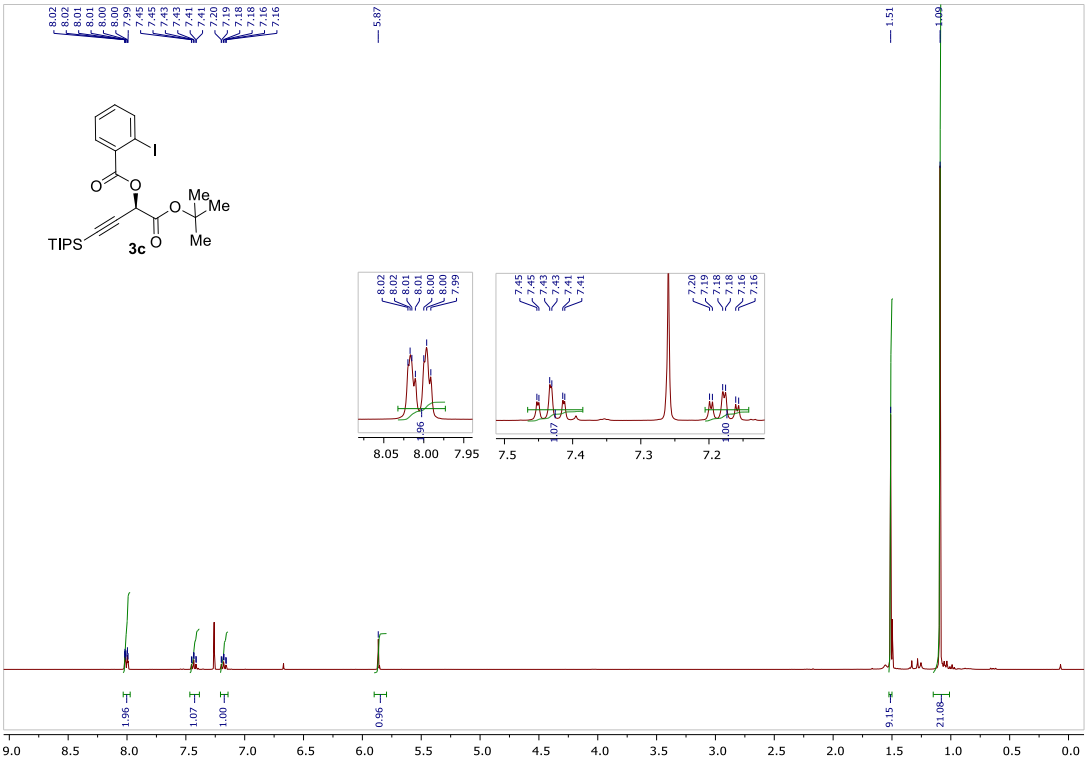


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.603	MM	0.1175	6483.24072	919.63336	94.4335
2	6.999	MM	0.1493	382.16150	42.67556	5.5665

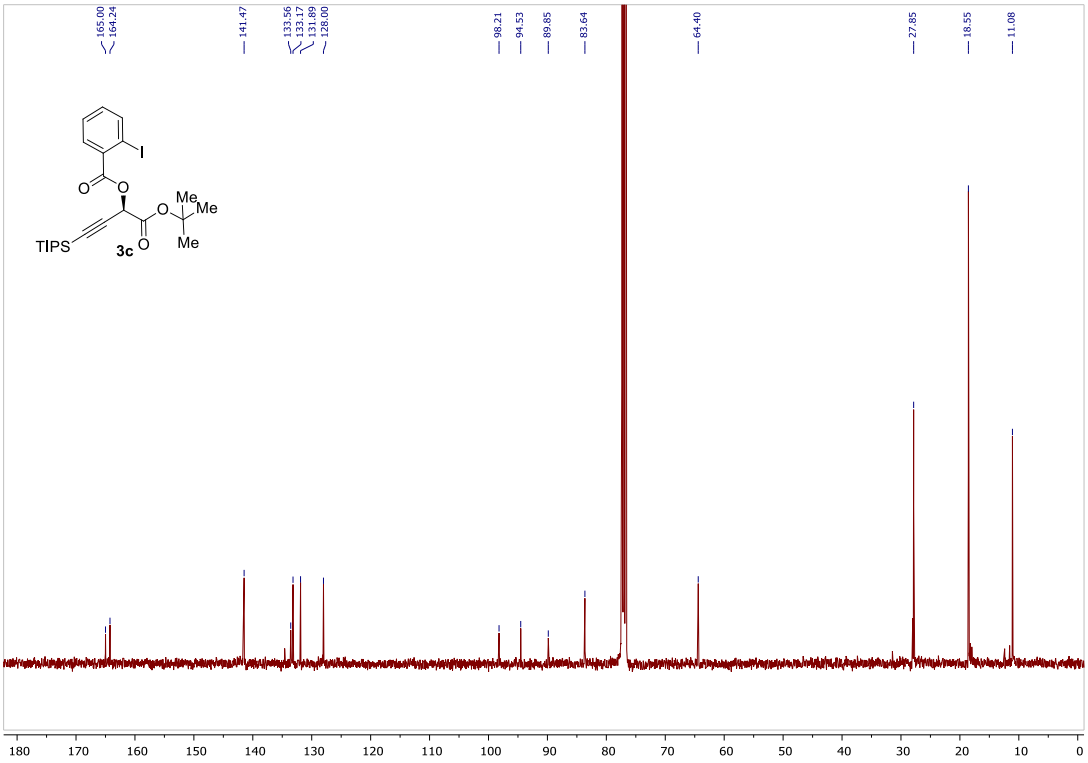
IR of compound **3b**



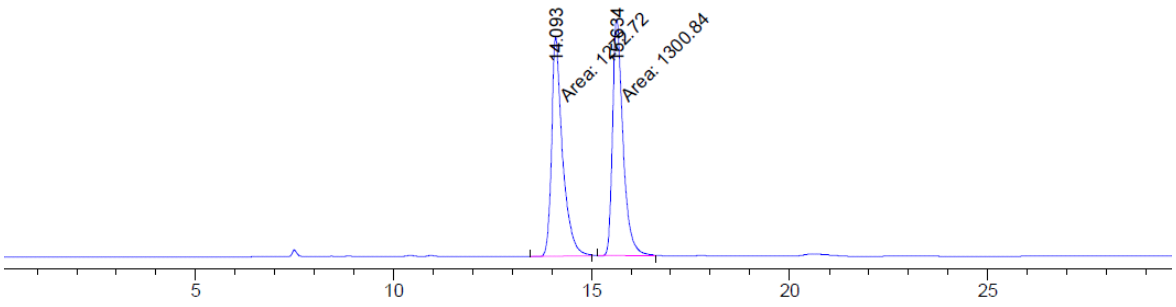
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3c**



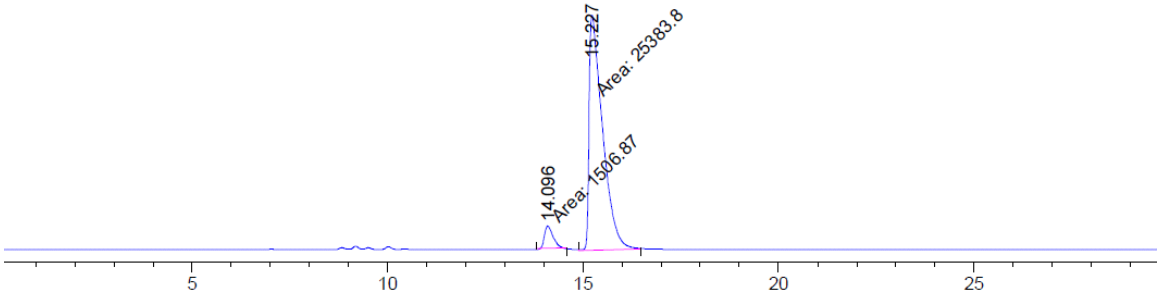
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3c**



HPLC of compound **3c**

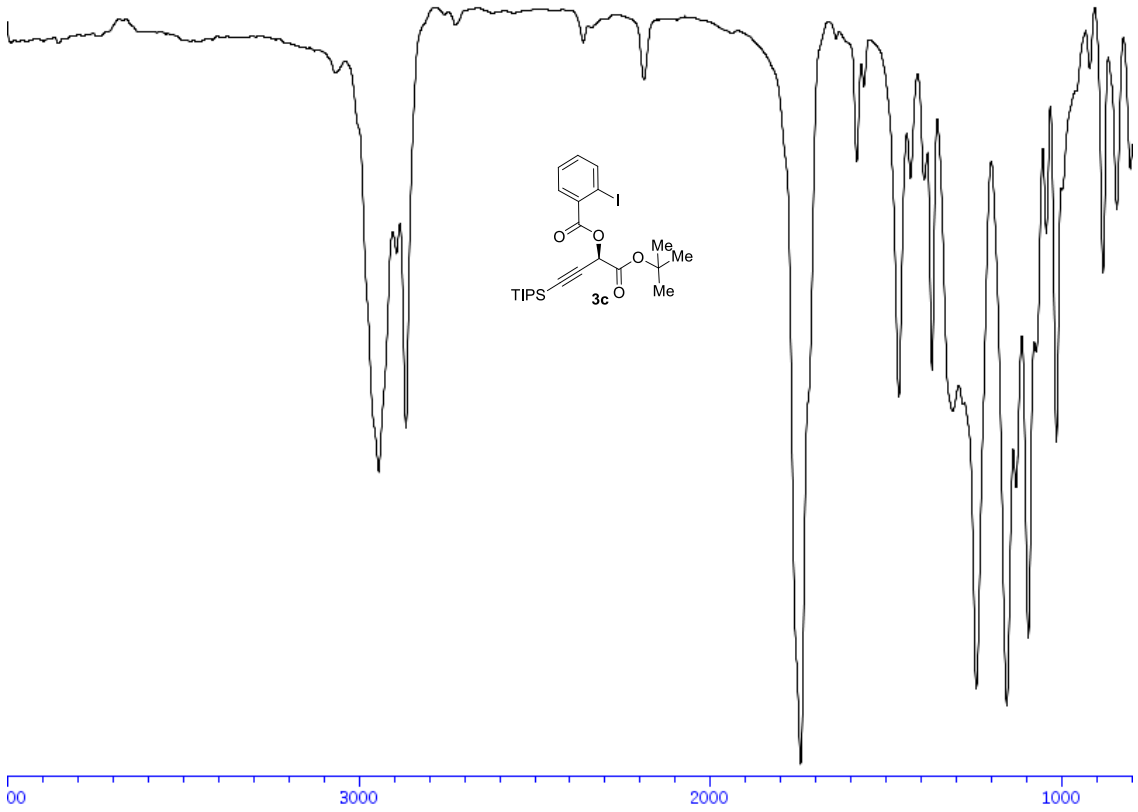


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.093	MM	0.3204	1272.72205	66.19562	49.4537
2	15.634	MM	0.3039	1300.84045	71.35202	50.5463

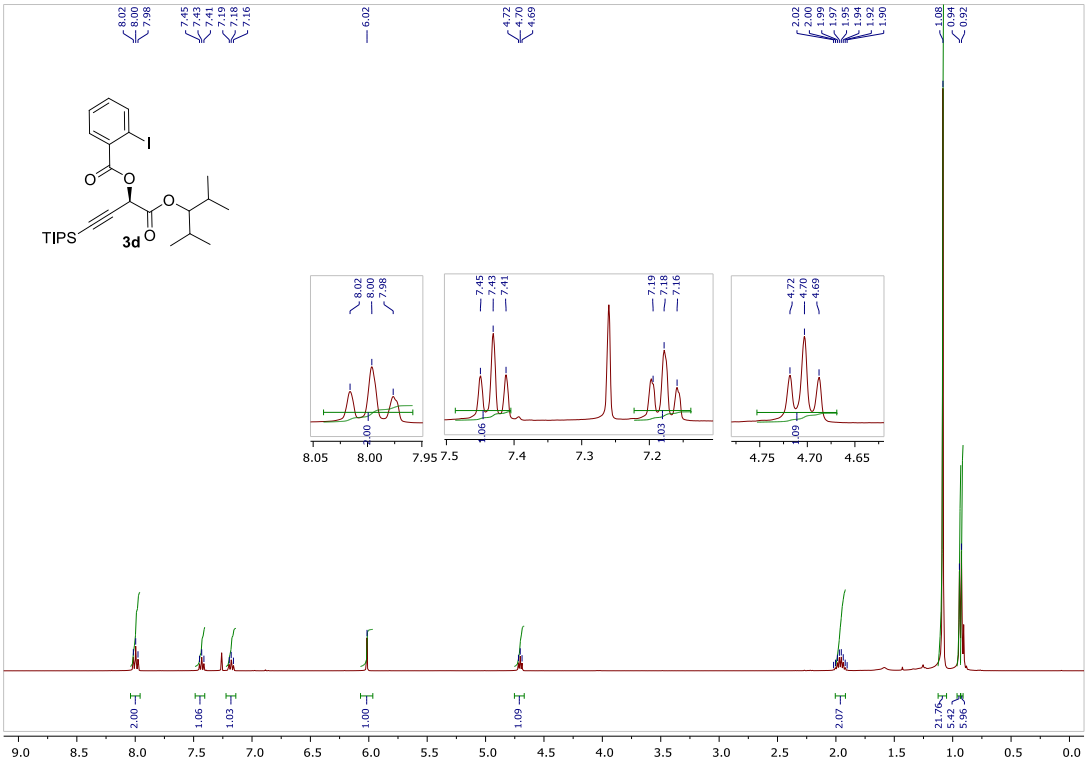


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.096	MM	0.2501	1506.86731	100.41984	5.6037
2	15.227	MM	0.3986	2.53838e4	1061.43518	94.3963

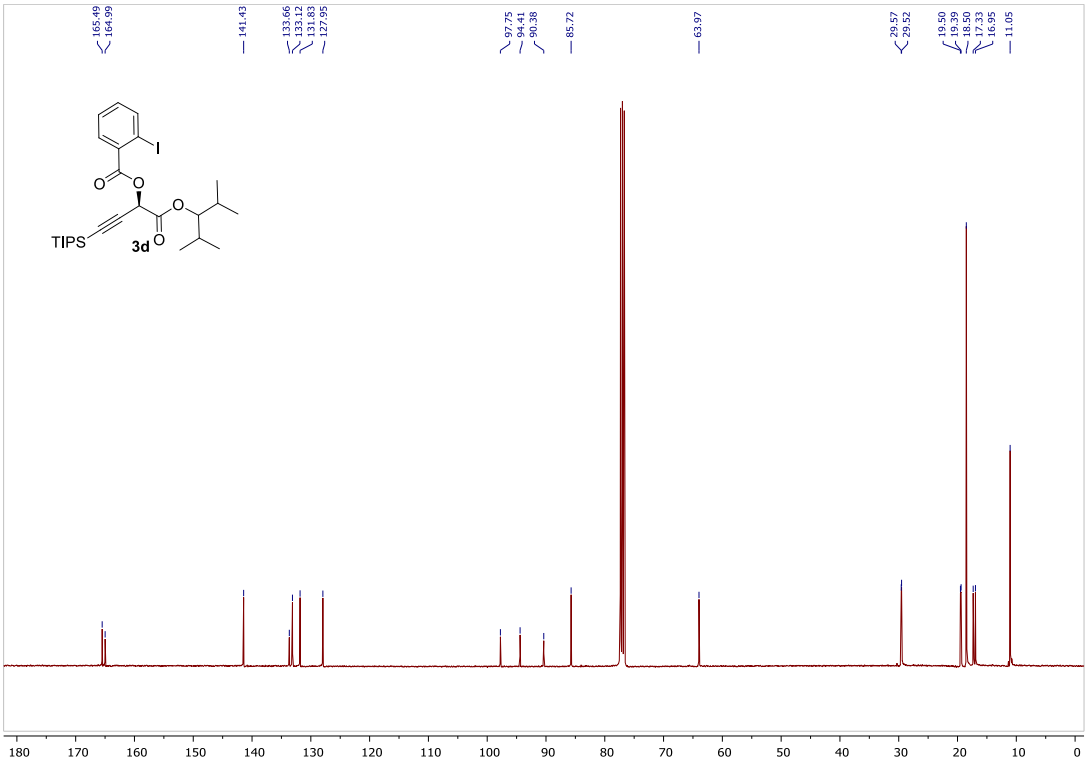
IR of compound **3c**



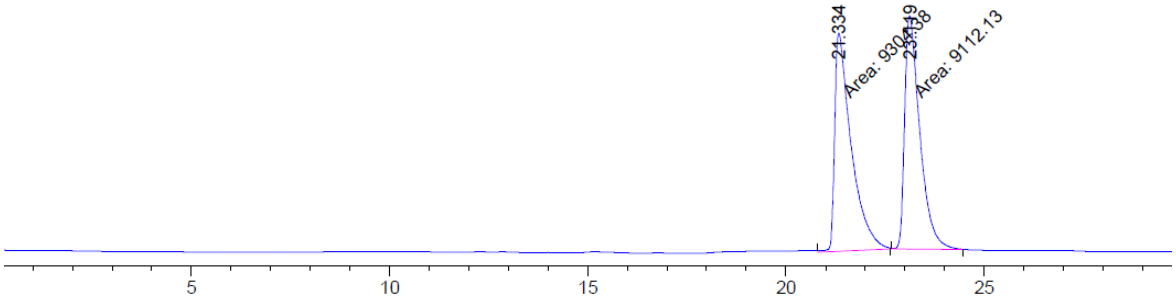
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3d**



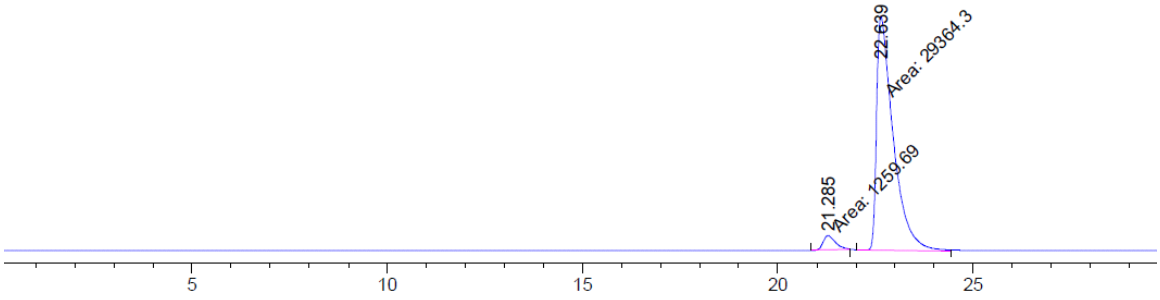
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3d**



HPLC of compound **3d**

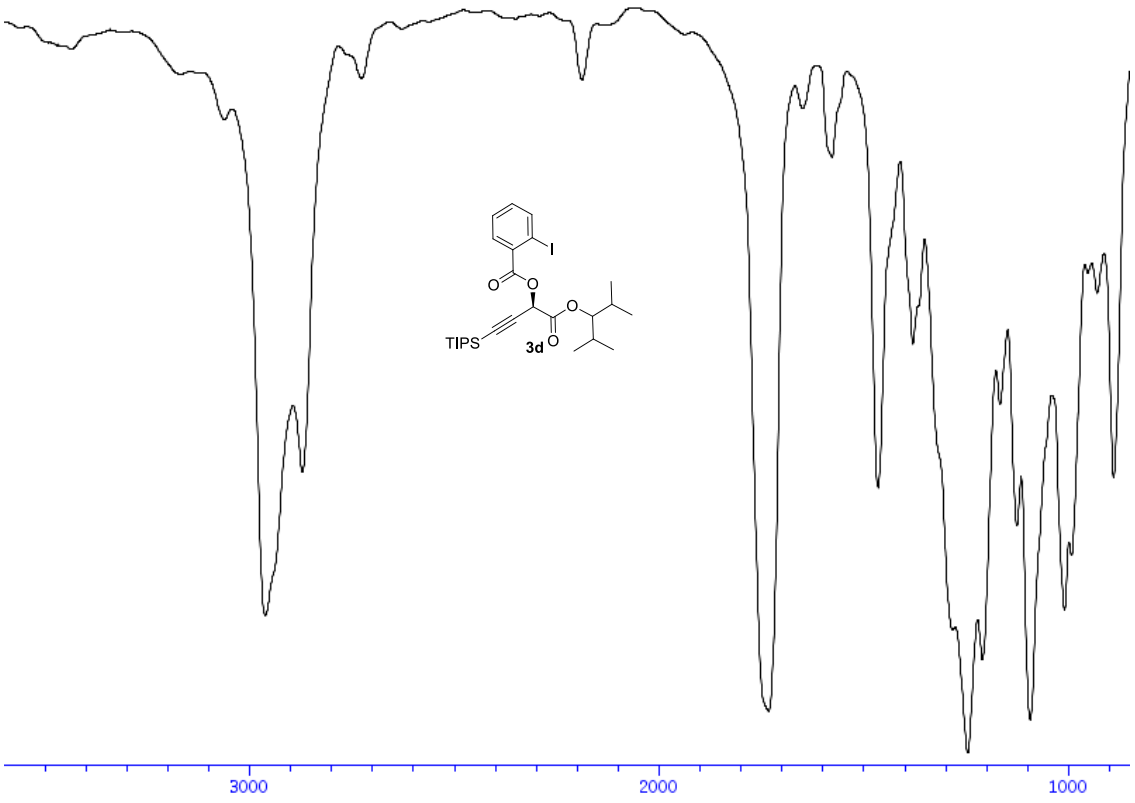


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.334	MM	0.4856	9304.37793	319.33688	50.5219
2	23.119	MM	0.4440	9112.12891	342.06113	49.4781

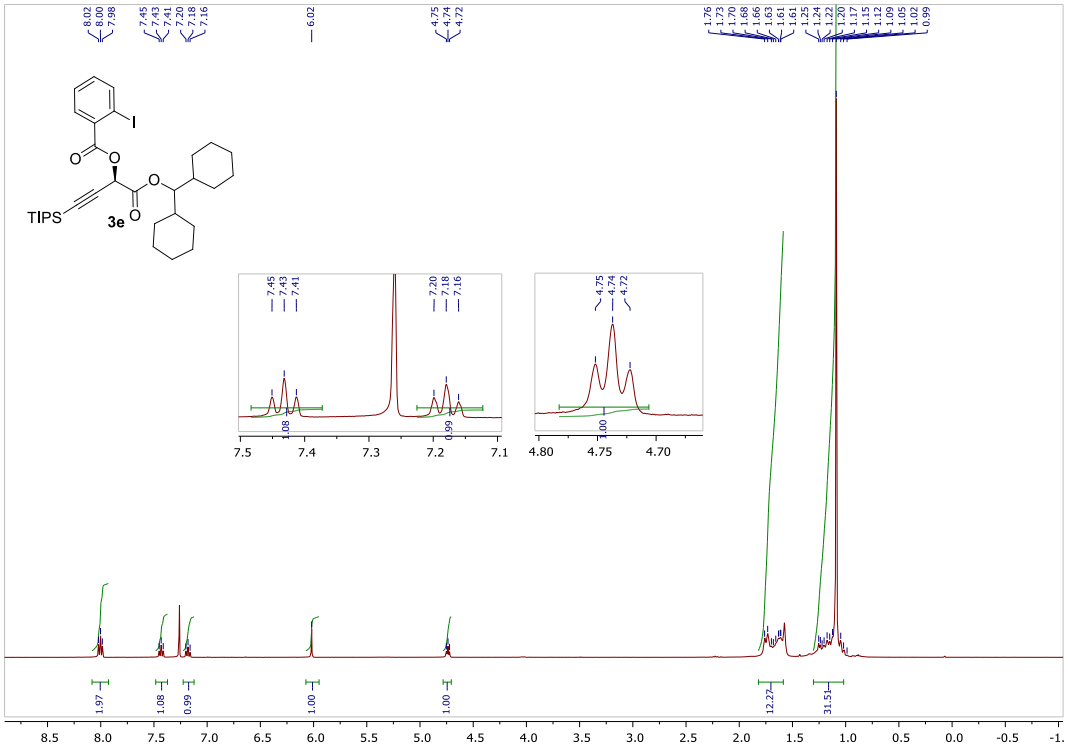


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.285	MM	0.3562	1259.69092	58.93820	4.1134
2	22.639	MM	0.4924	2.93643e4	993.90344	95.8866

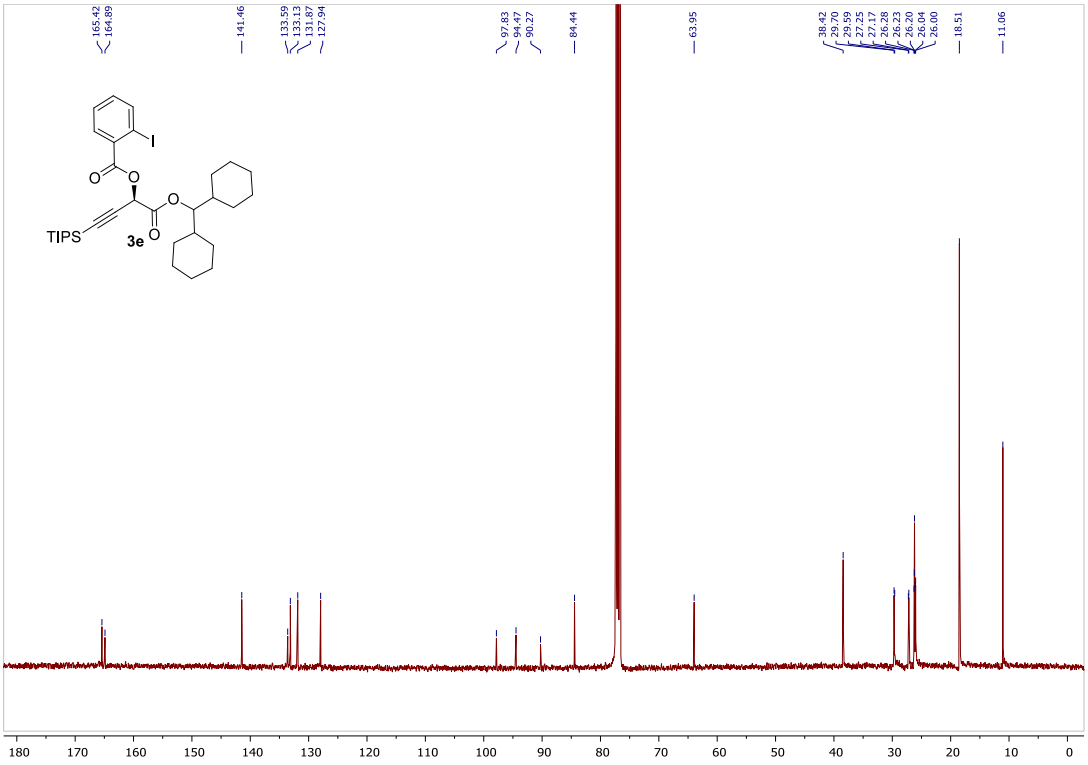
IR of compound **3d**



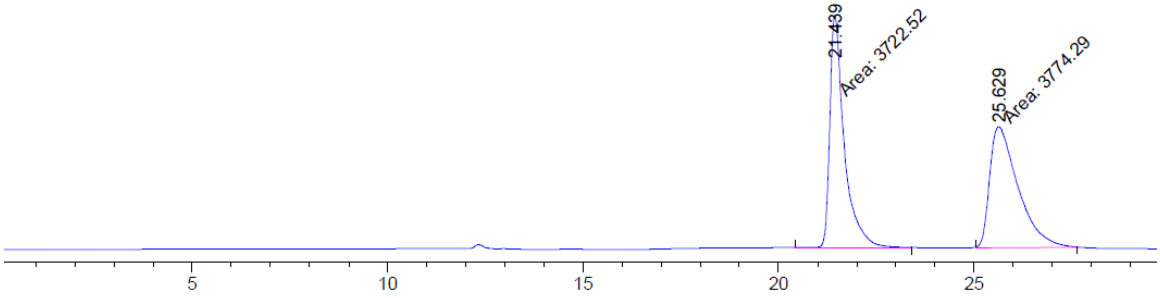
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3e**



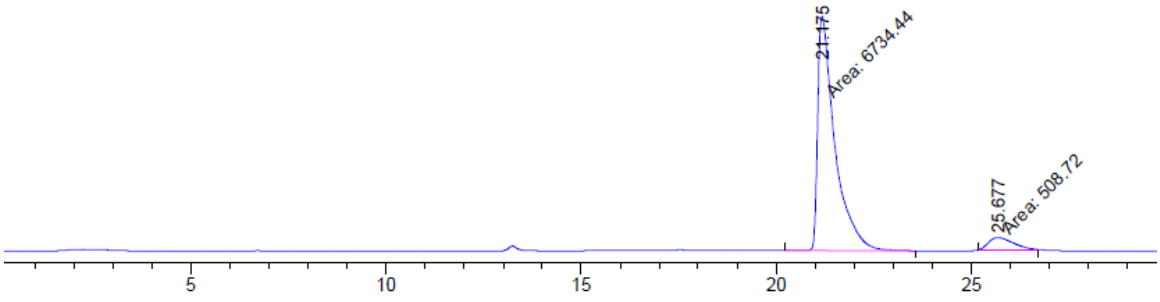
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3e**



HPLC of compound **3e**

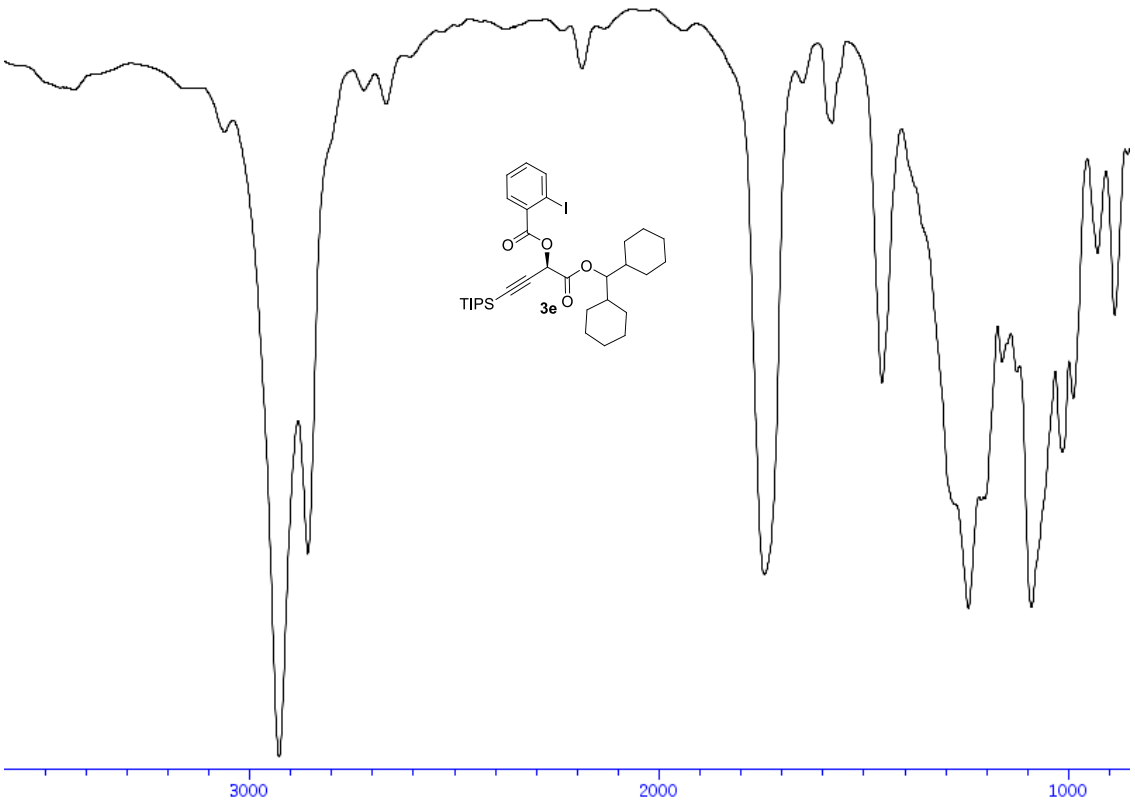


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.439	MM	0.4313	3722.51733	143.84779	49.6547
2	25.629	MM	0.8408	3774.29199	74.81570	50.3453

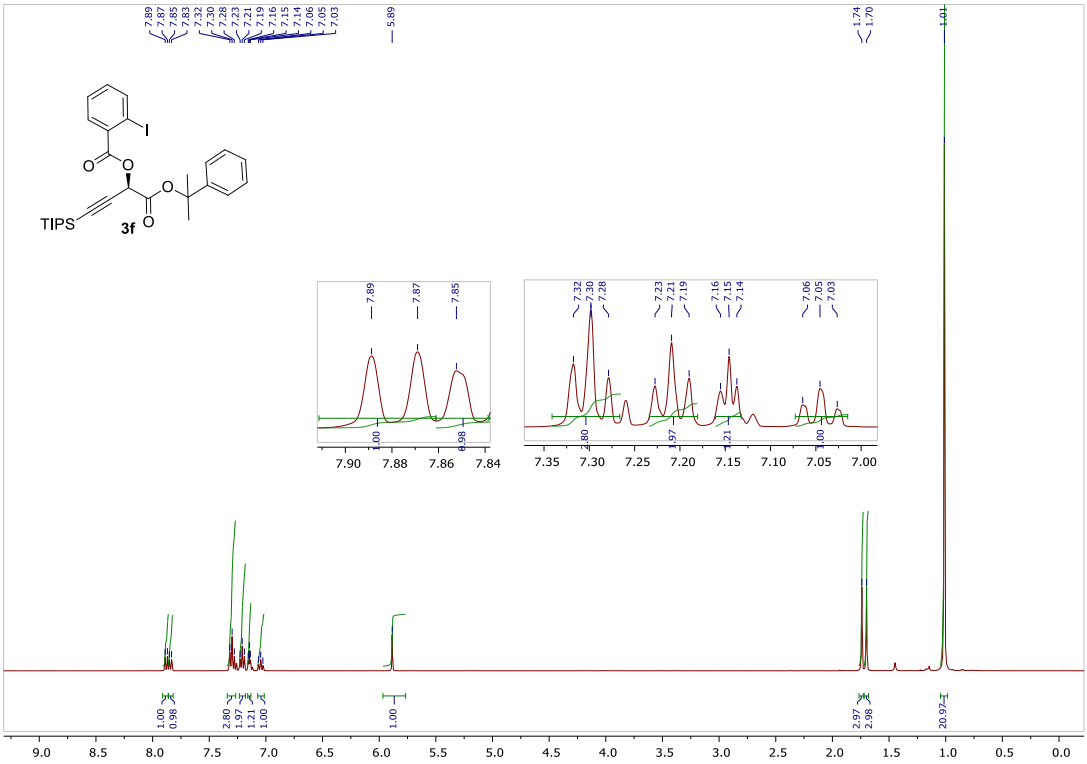


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.175	MM	0.5117	6734.43848	219.32741	92.9765
2	25.677	MM	0.7342	508.72021	11.54773	7.0235

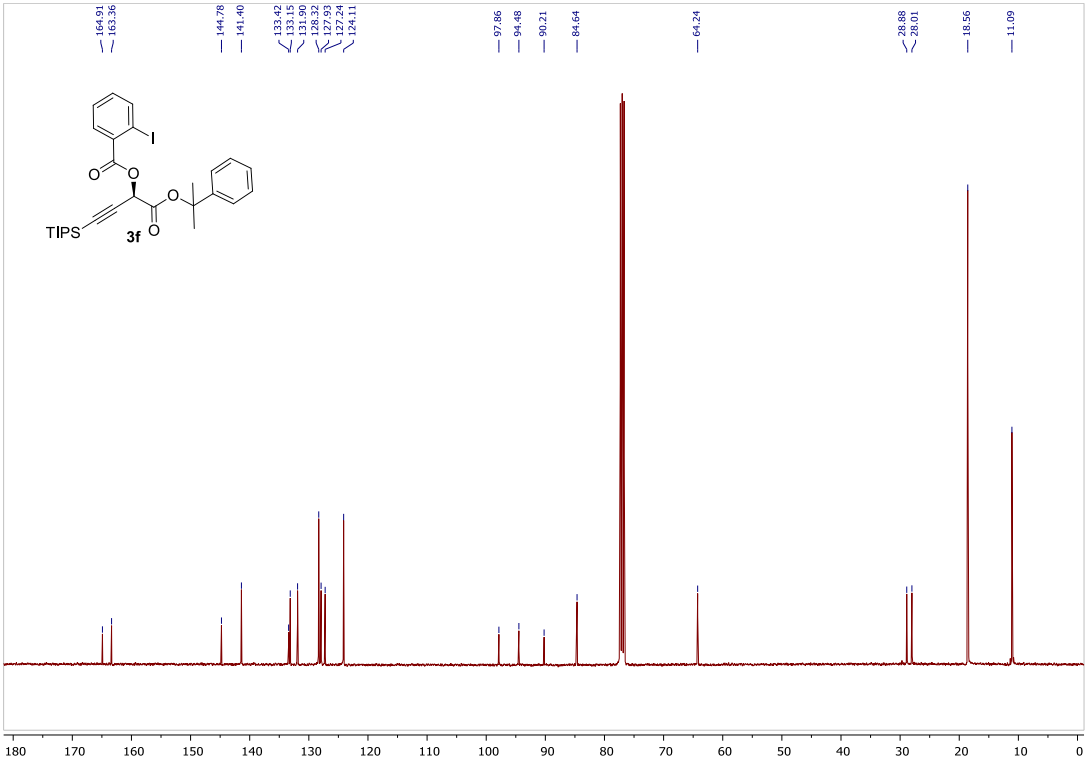
IR of compound **3e**



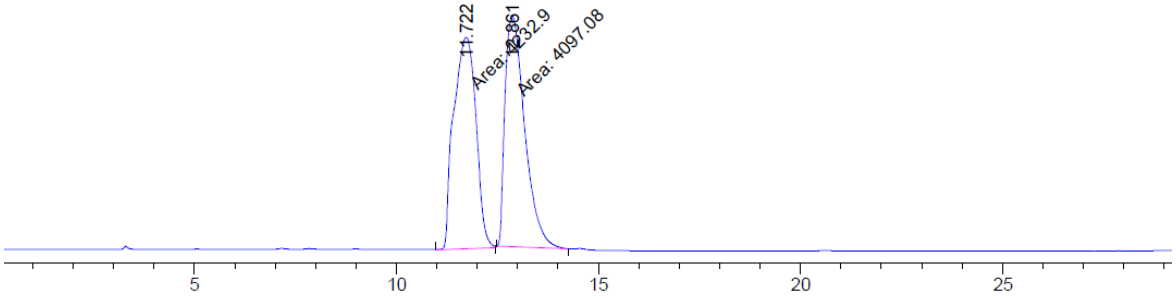
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3f**



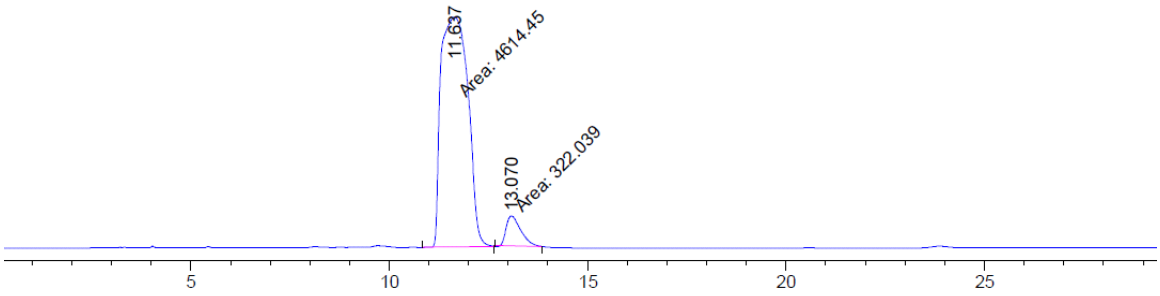
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3f**



HPLC of compound **3f**

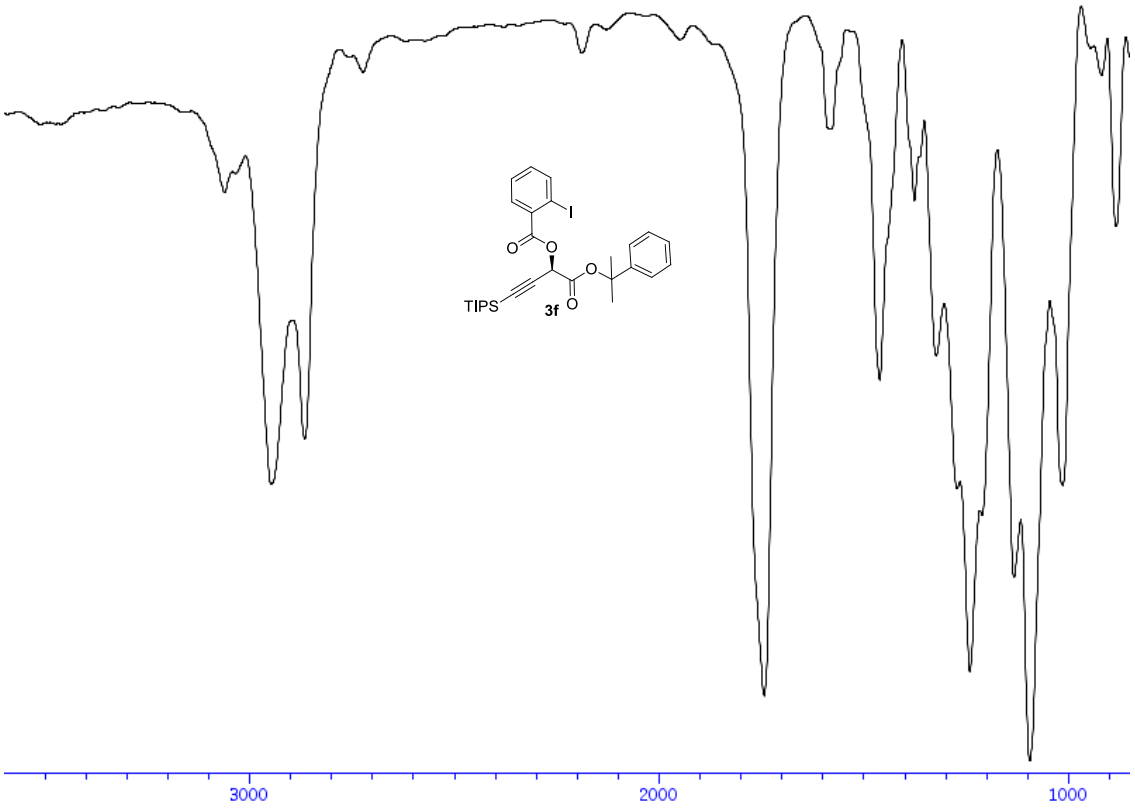


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.722	MM	0.6375	4232.90283	110.65704	50.8153
2	12.861	MM	0.5638	4097.07910	121.12533	49.1847

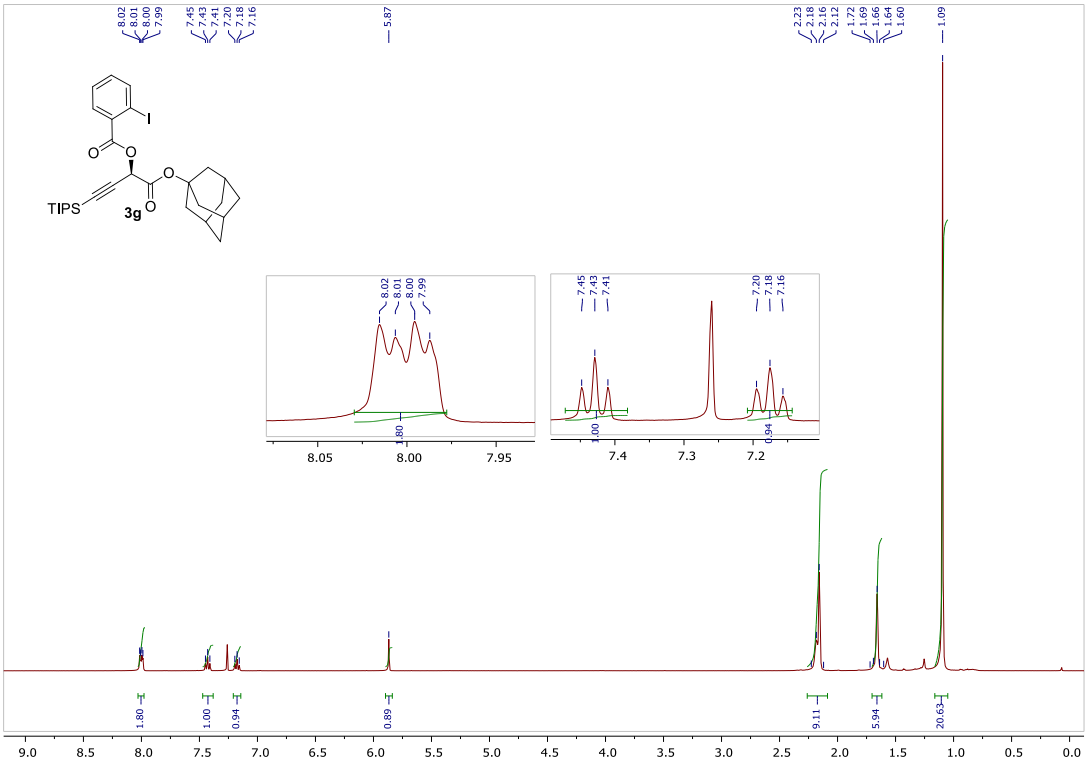


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.637	MM	0.7917	4614.45068	97.14836	93.4764
2	13.070	MM	0.4274	322.03857	12.55725	6.5236

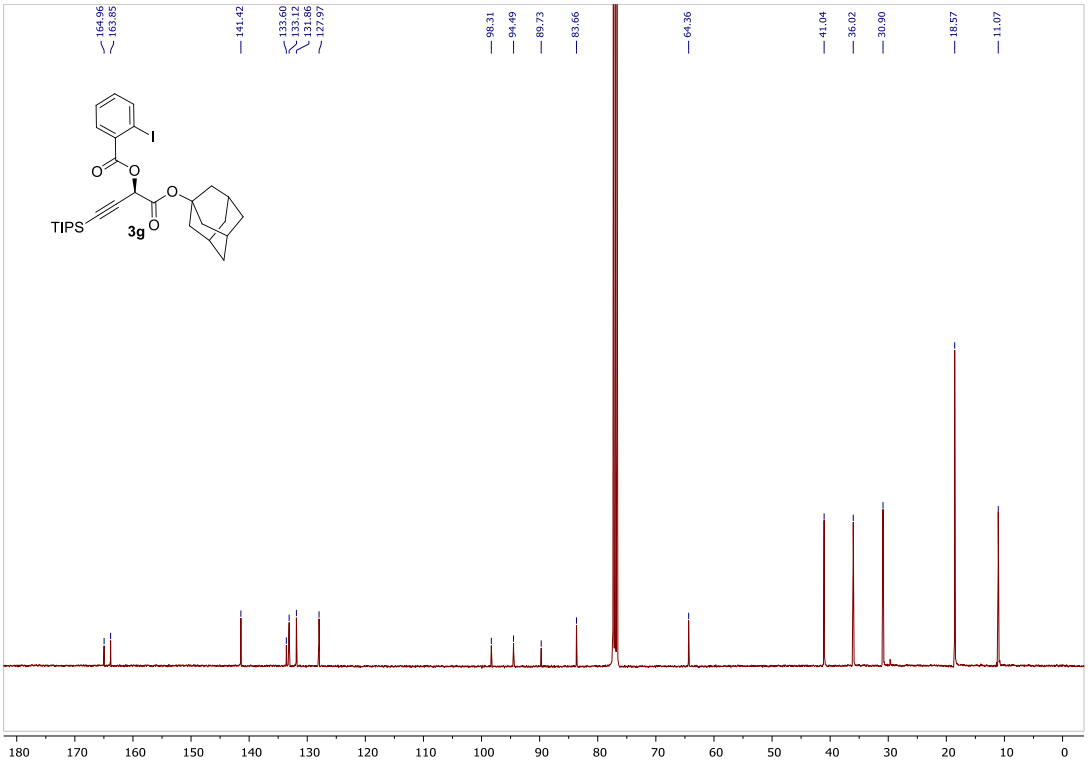
IR of compound **3f**



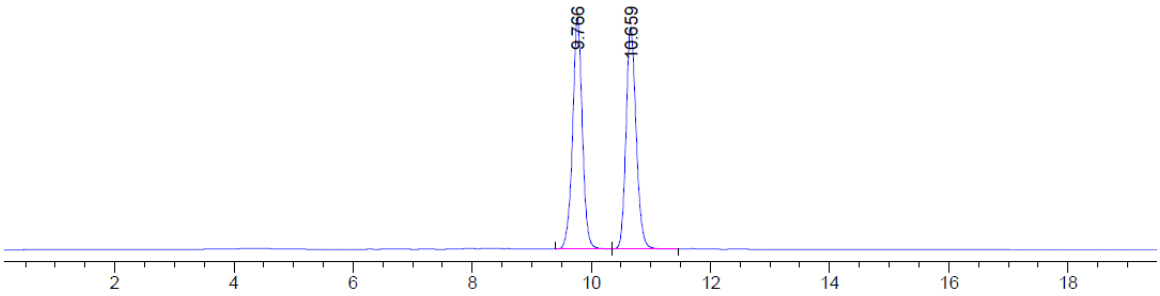
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3g**



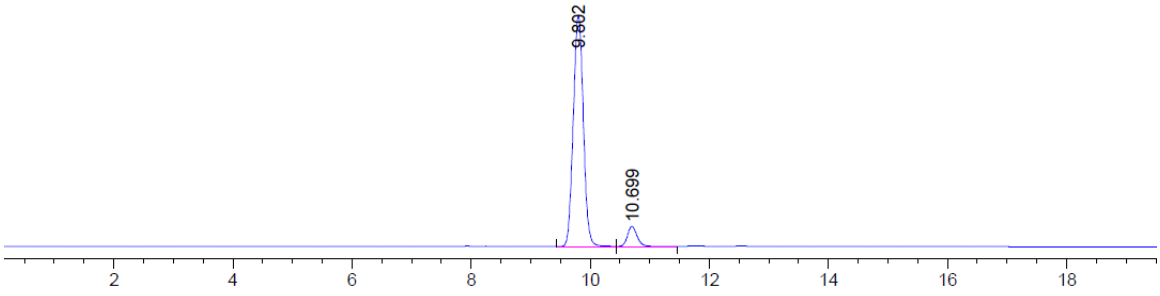
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3g**



HPLC of compound **3g**

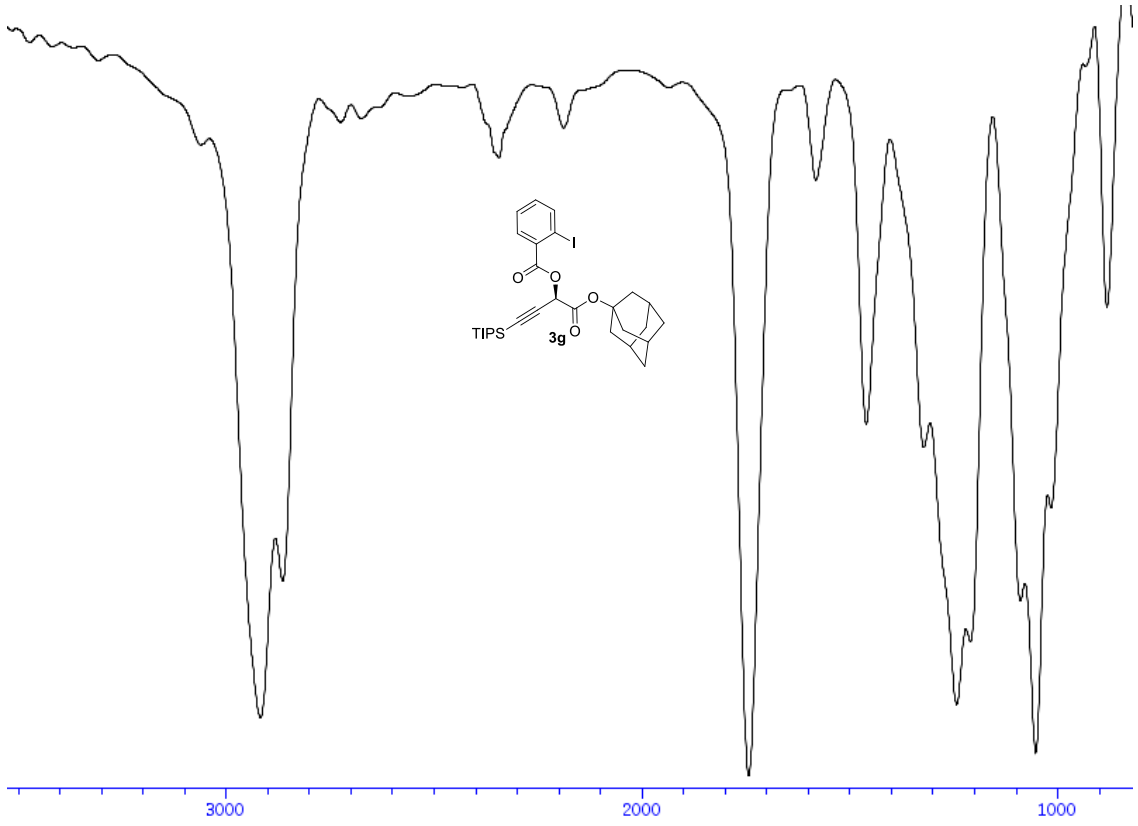


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.766	BB	0.1715	1685.47571	149.57895	50.0315
2	10.659	BB	0.1807	1683.35400	143.63235	49.9685

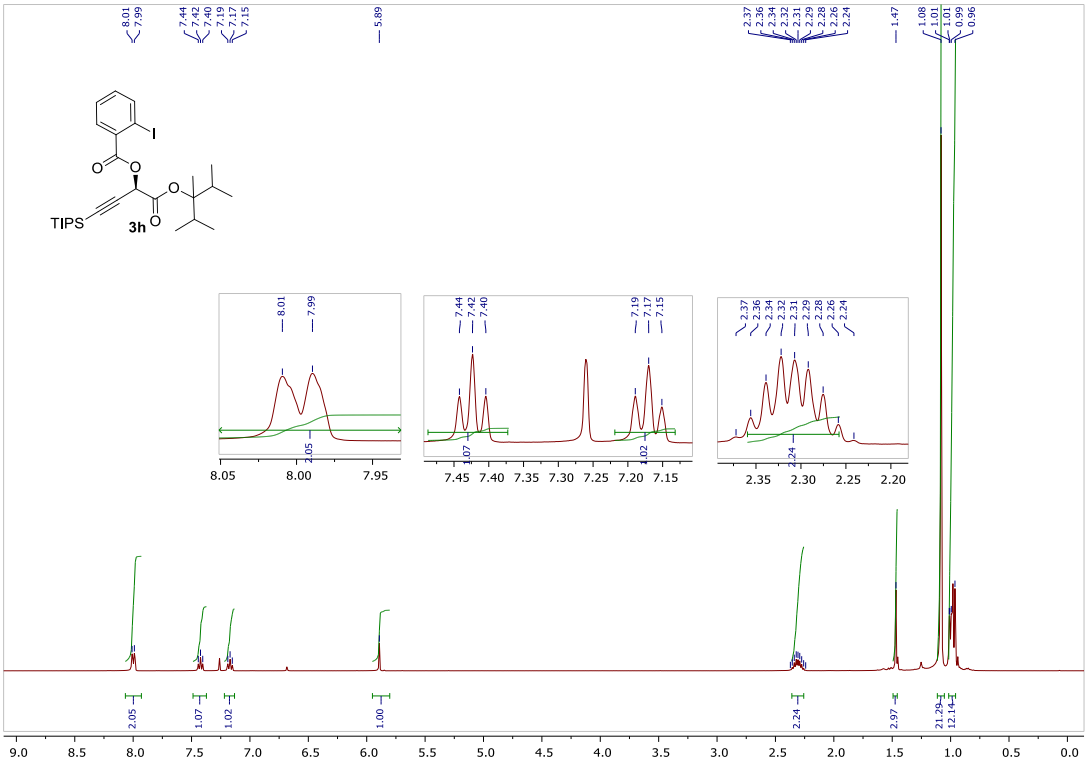


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.802	BV	0.1867	5409.65820	461.60233	92.3678
2	10.699	VB	0.1705	446.98849	39.96426	7.6322

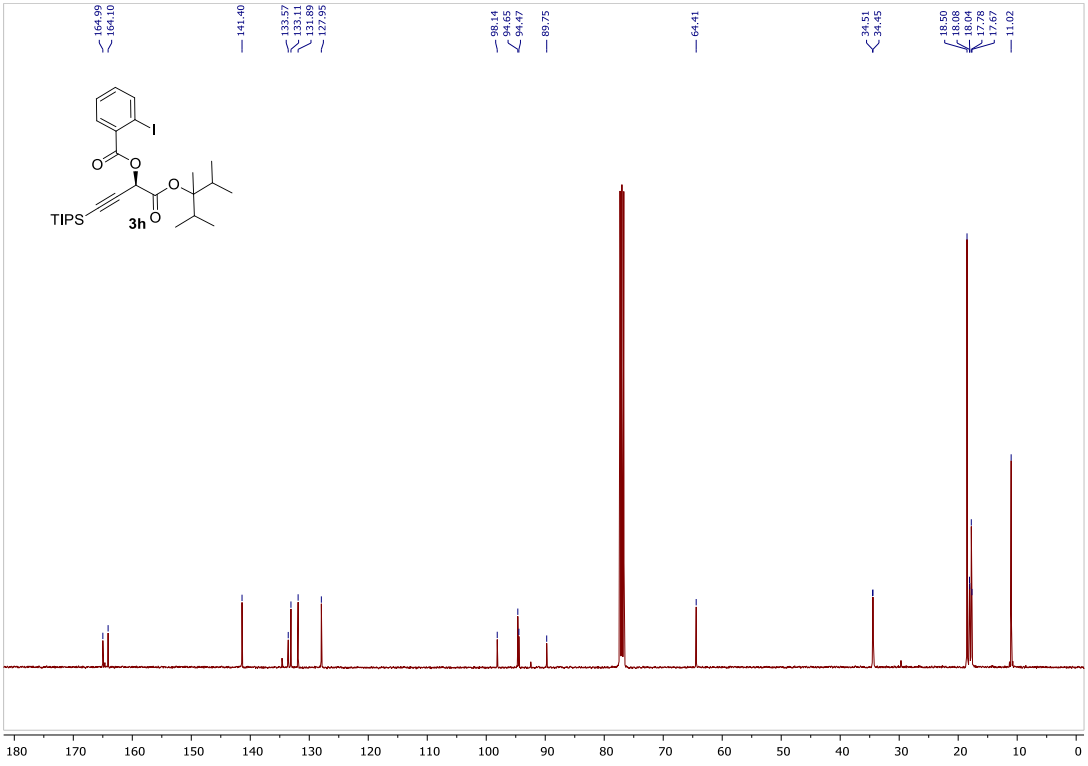
IR of compound **3g**



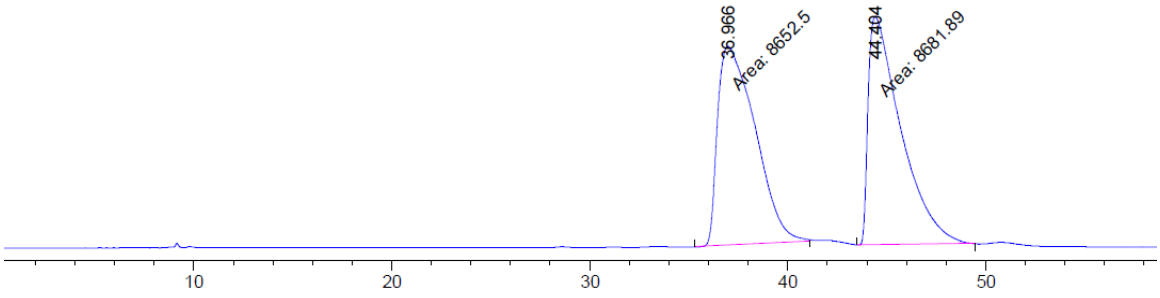
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3h**



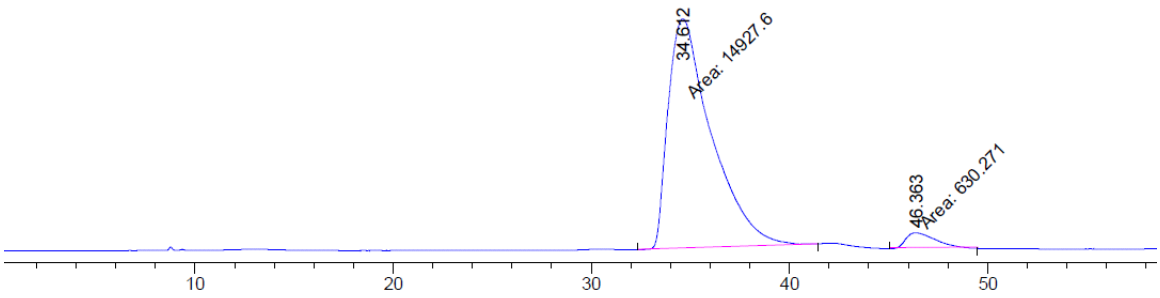
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3h**



HPLC of compound **3h**

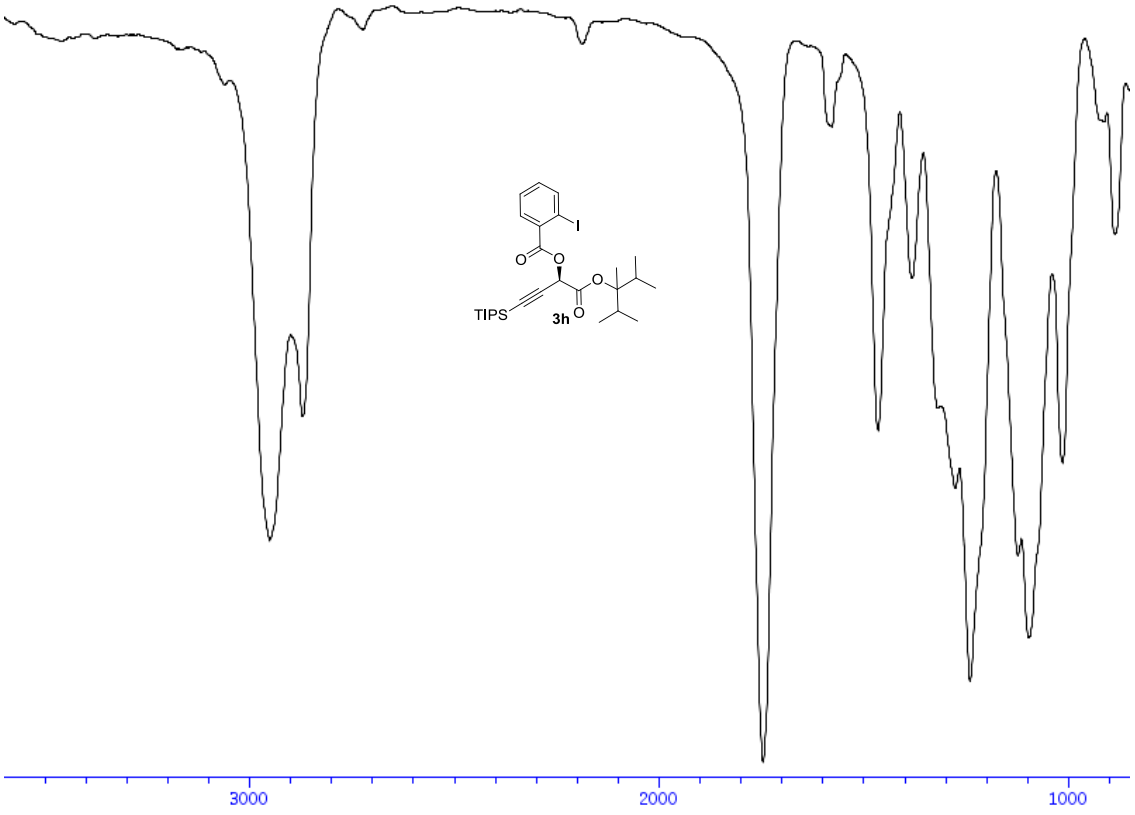


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.966	MM	2.1869	8652.50488	65.94124	49.9152
2	44.404	MM	1.9160	8681.89258	75.52161	50.0848

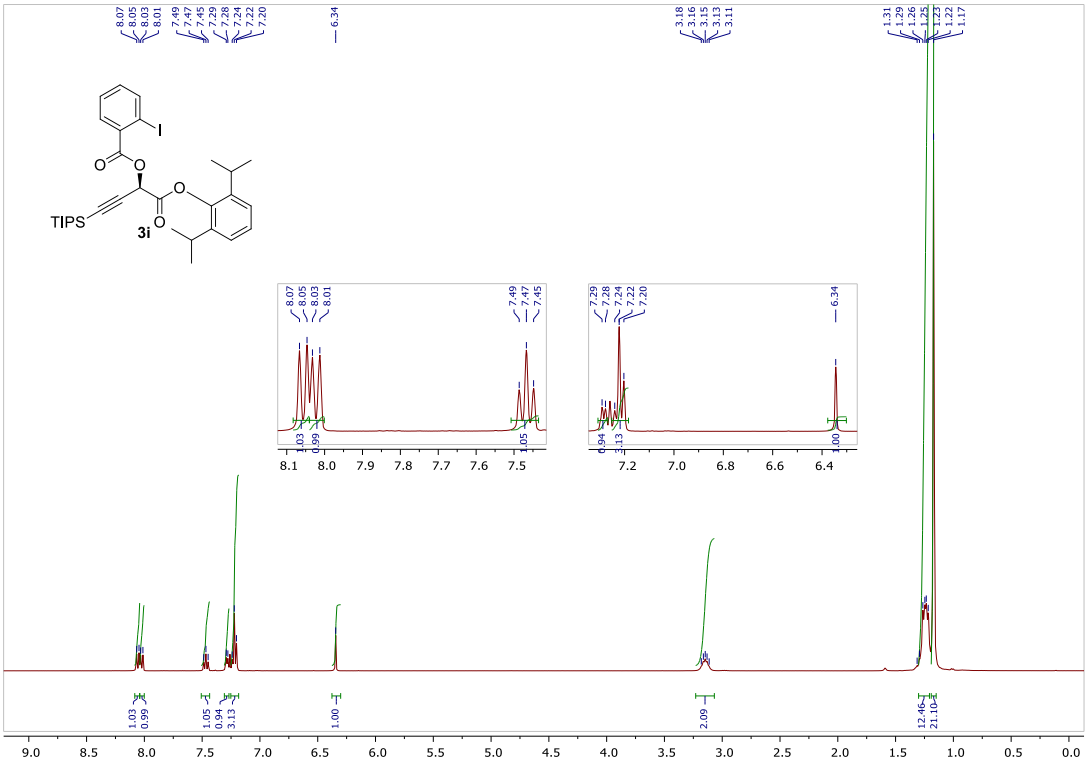


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.612	MM	2.5204	1.49276e4	98.71152	95.9489
2	46.363	MM	1.6453	630.27081	6.38461	4.0511

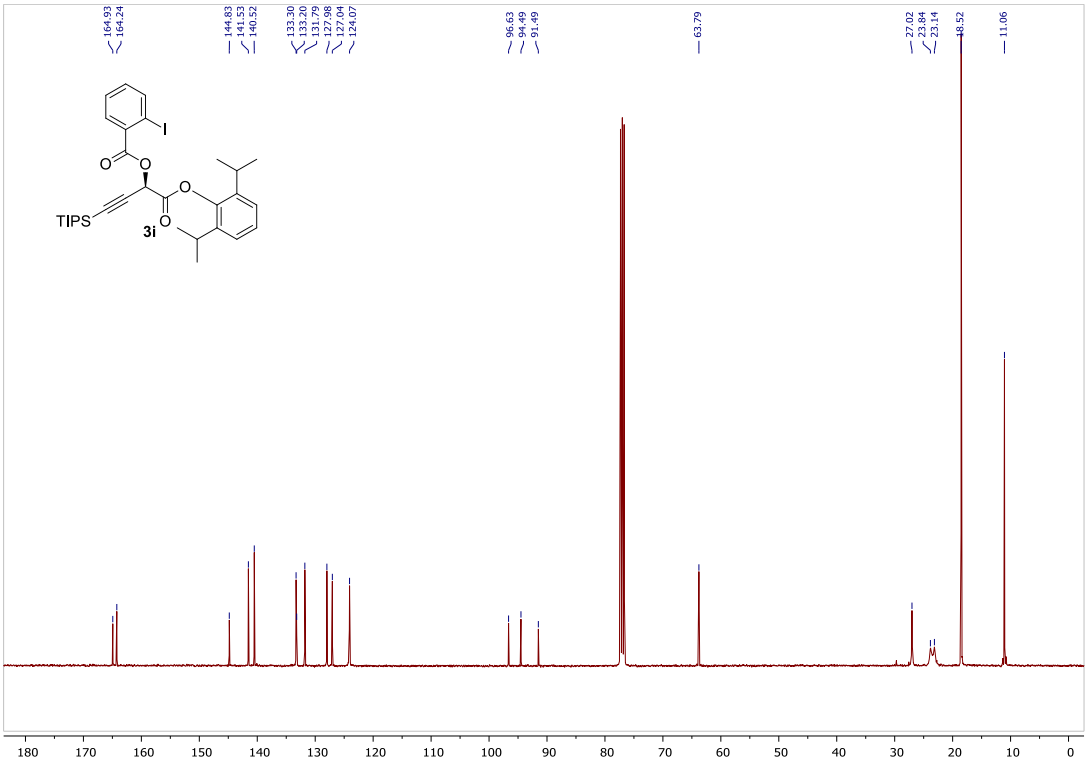
IR of compound **3h**



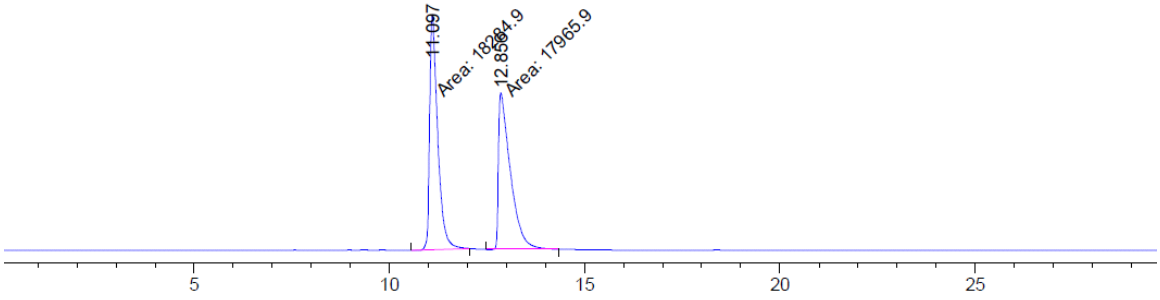
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3i**



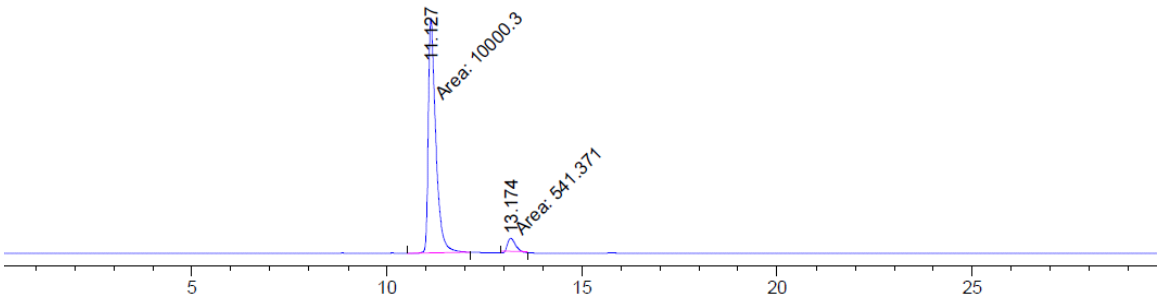
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3i**



HPLC of compound **3i**

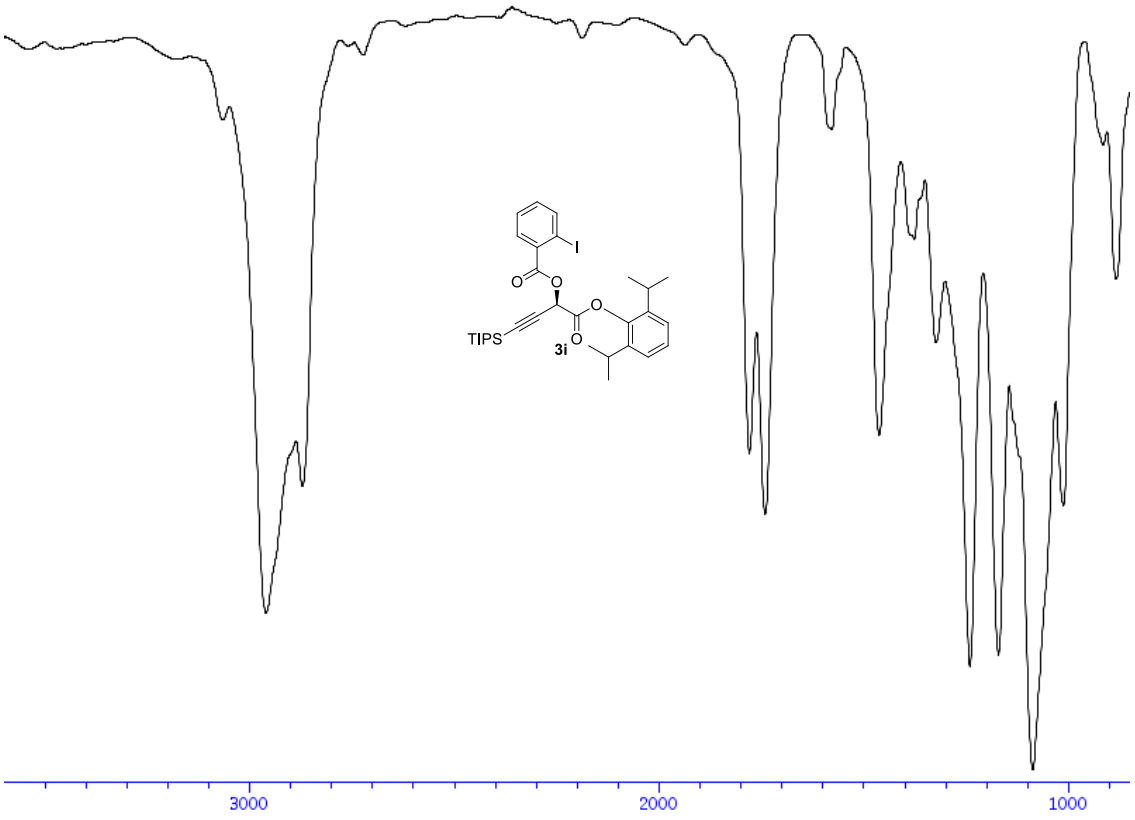


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.097	MM	0.2380	1.82849e4	1280.71191	50.4400
2	12.856	MM	0.3511	1.79659e4	852.89941	49.5600

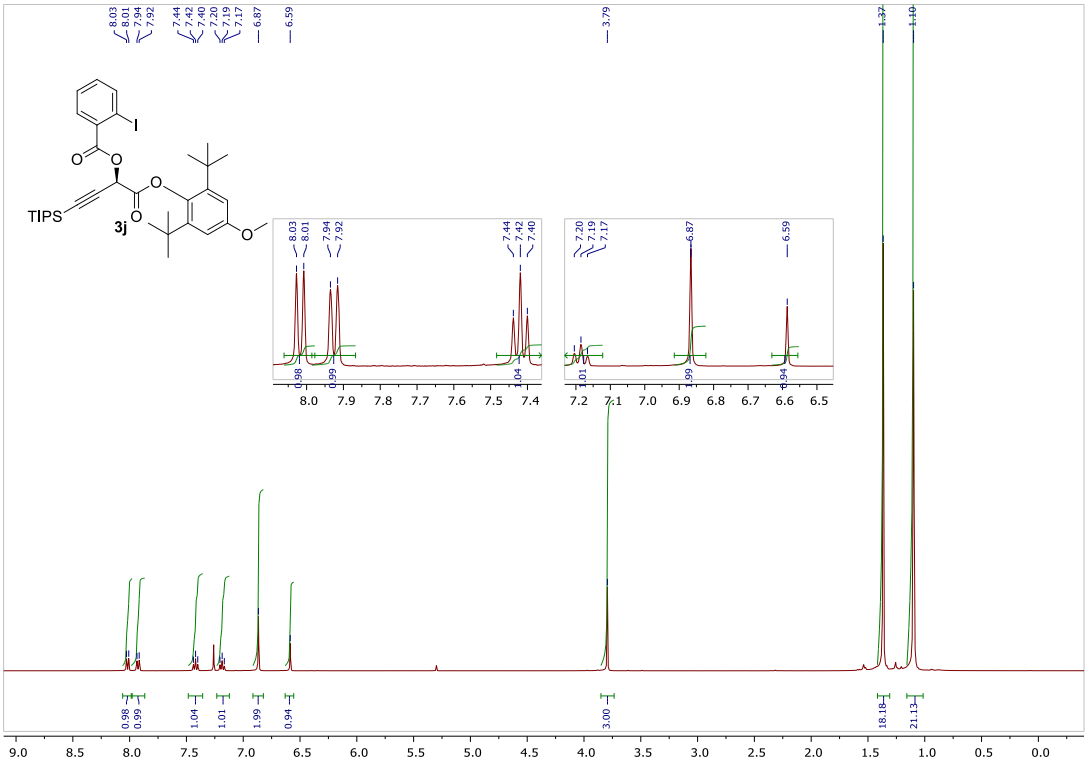


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.127	MM	0.2233	1.00003e4	746.34528	94.8645
2	13.174	MM	0.2161	541.37085	41.75341	5.1355

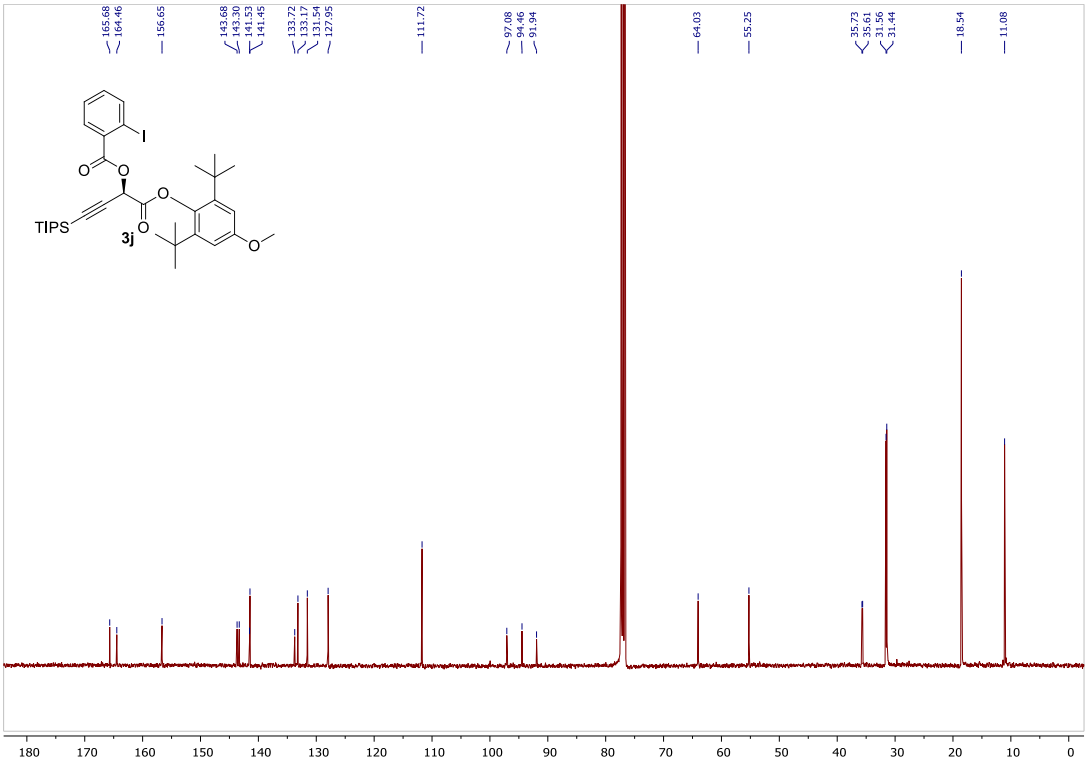
IR of compound **3i**



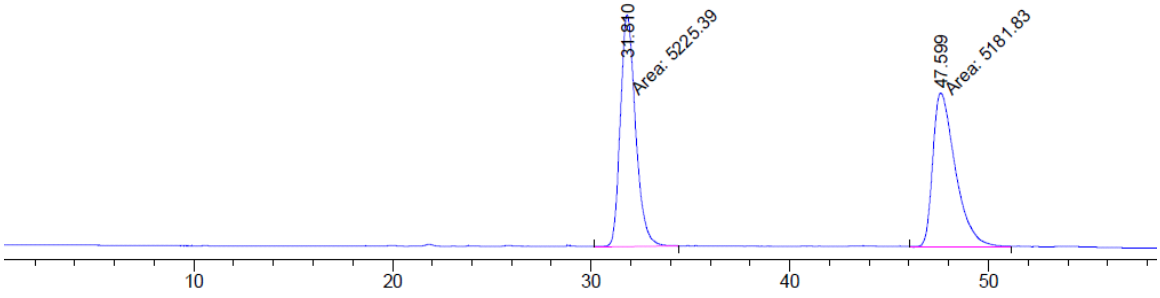
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3j**



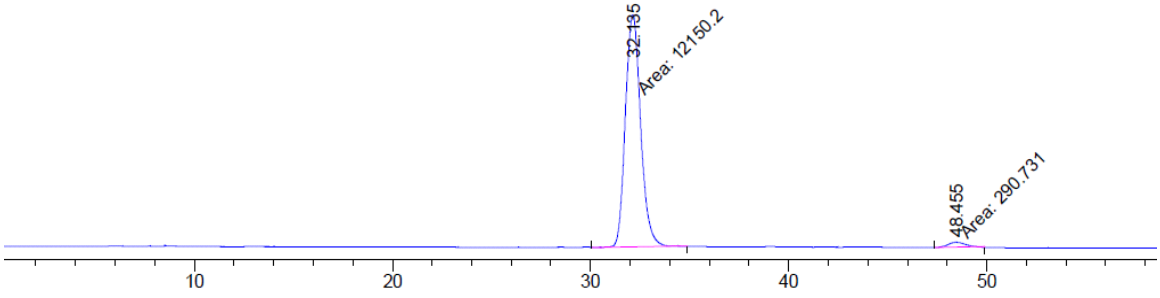
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3j**



HPLC of compound **3j**

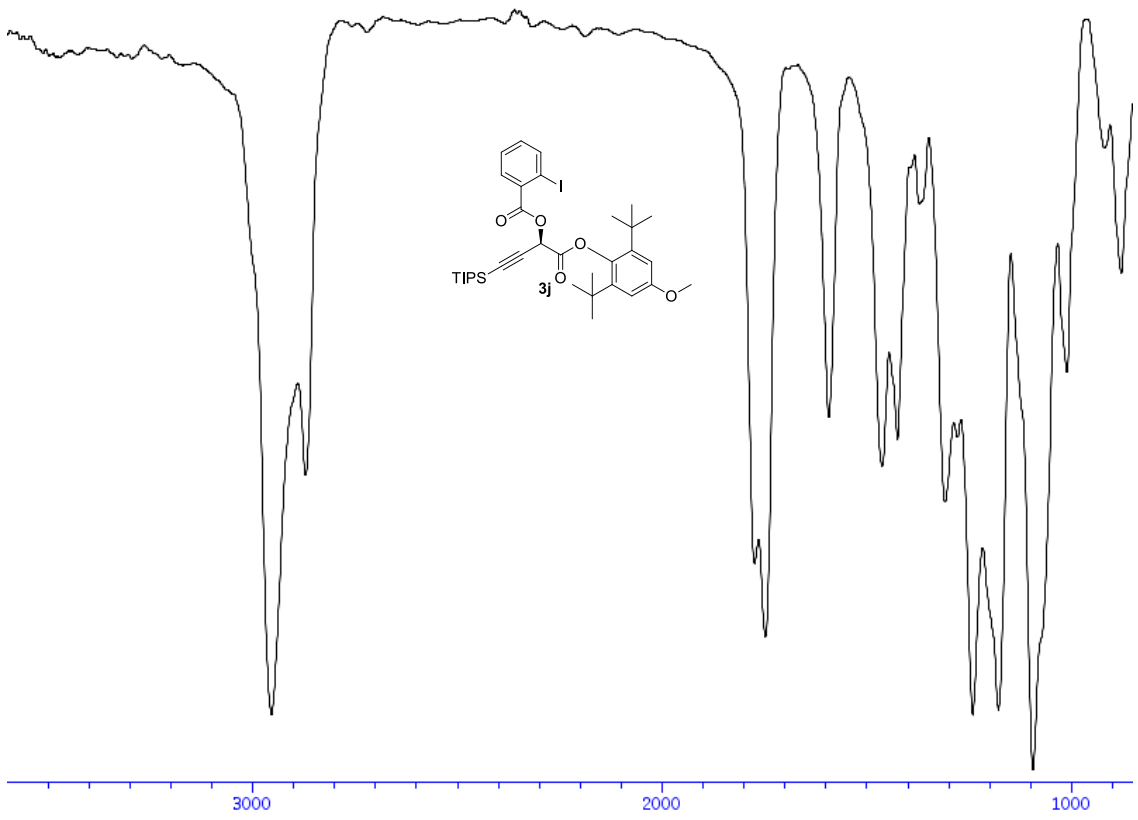


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.810	MM	0.8884	5225.39160	98.03027	50.2093
2	47.599	MM	1.3247	5181.83154	65.19611	49.7907

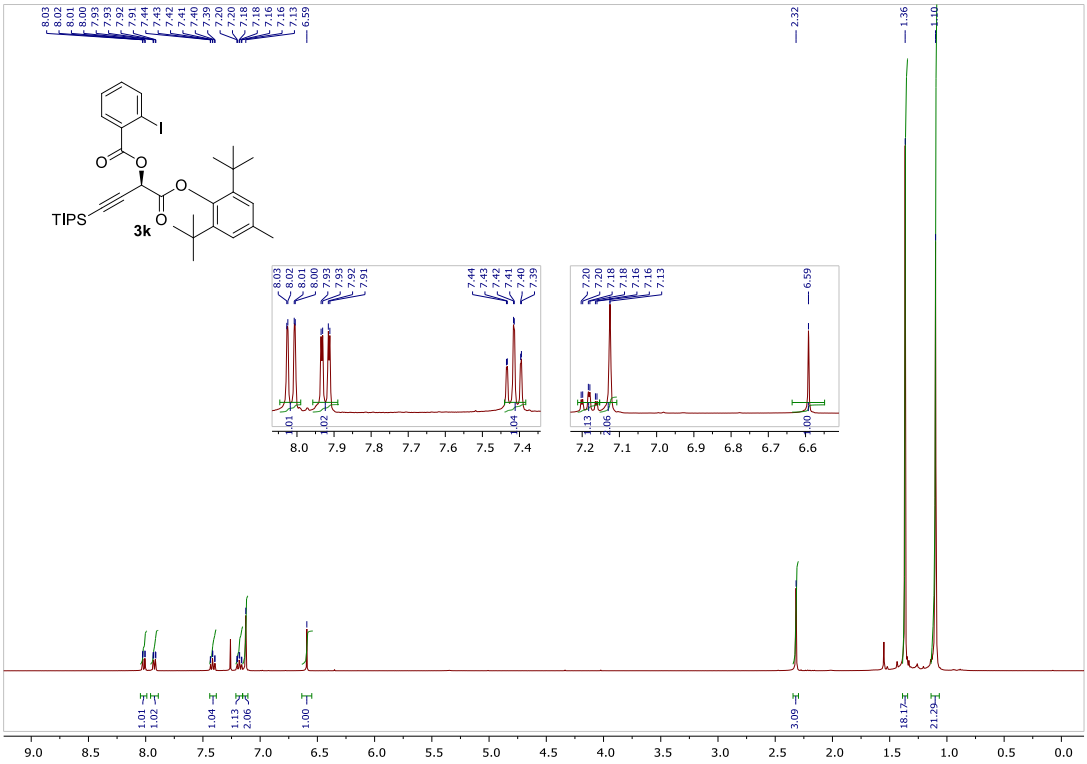


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.135	MM	0.8914	1.21502e4	227.18224	97.6631
2	48.455	MM	1.0099	290.73117	4.79807	2.3369

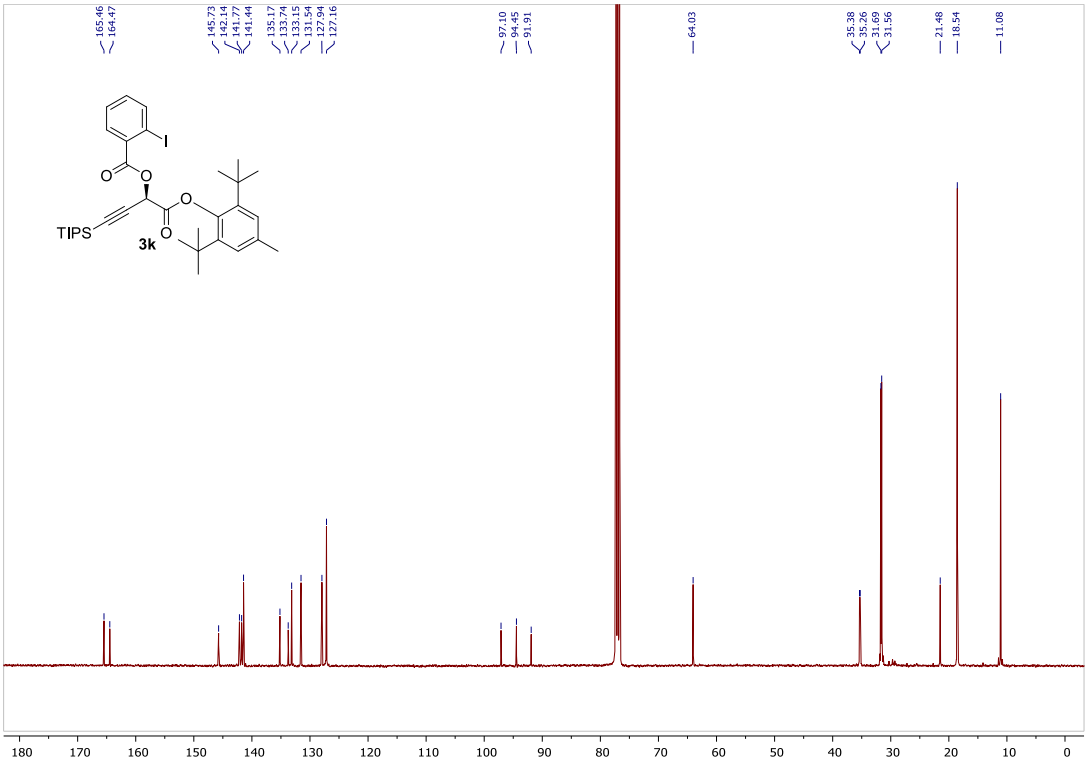
IR of compound **3j**



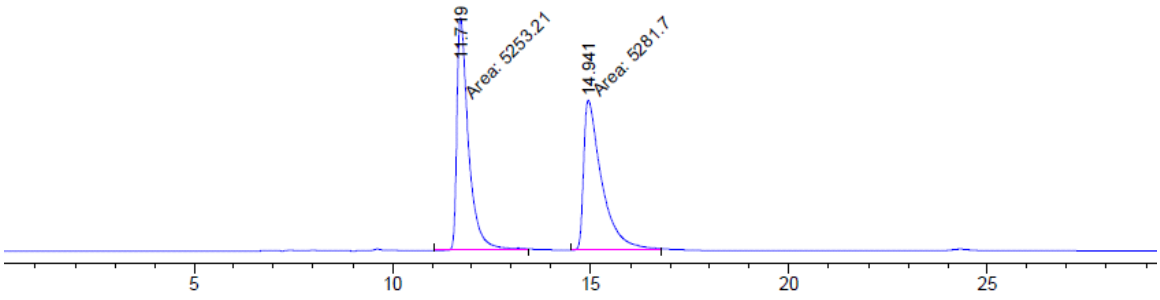
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3k**



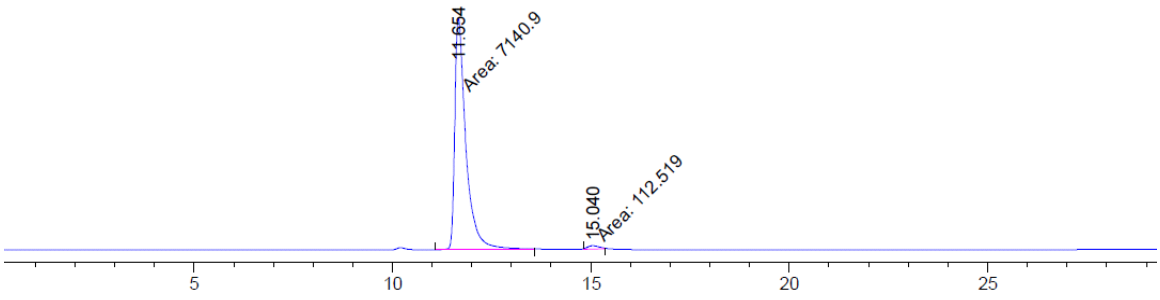
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3k**



HPLC of compound **3k**

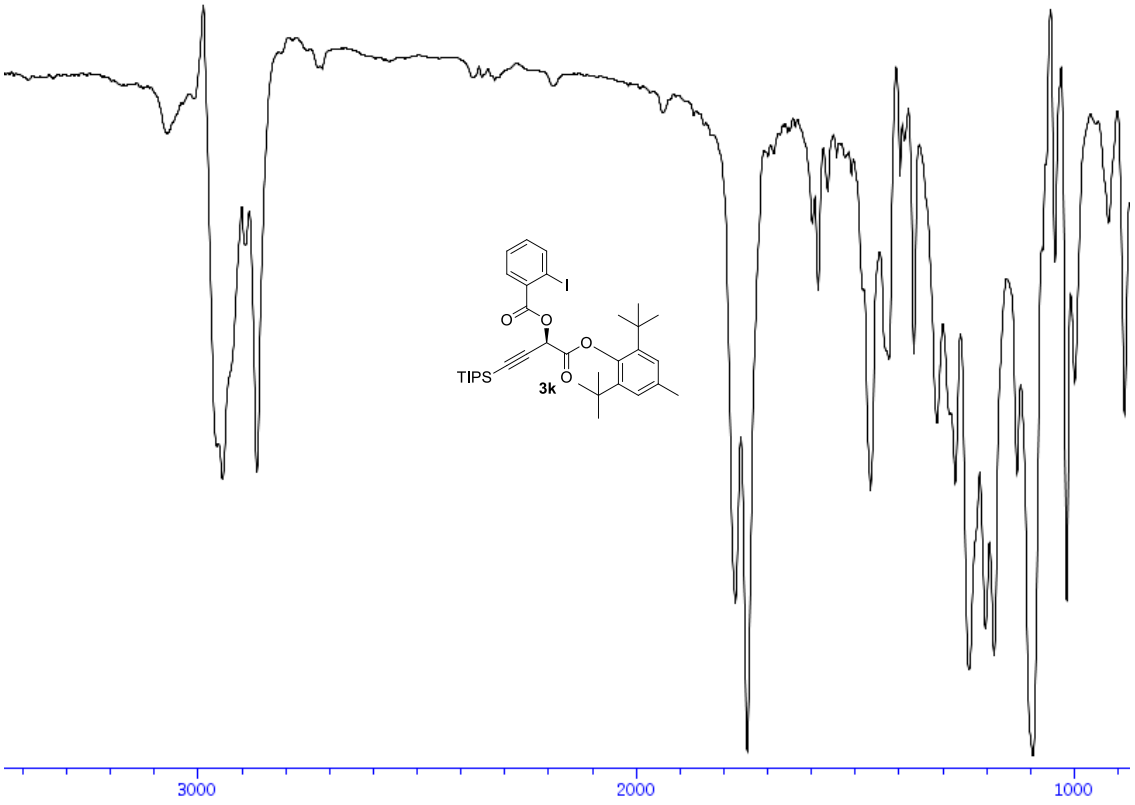


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.719	MM	0.3411	5253.21143	256.71552	49.8648
2	14.941	MM	0.5323	5281.70410	165.38373	50.1352

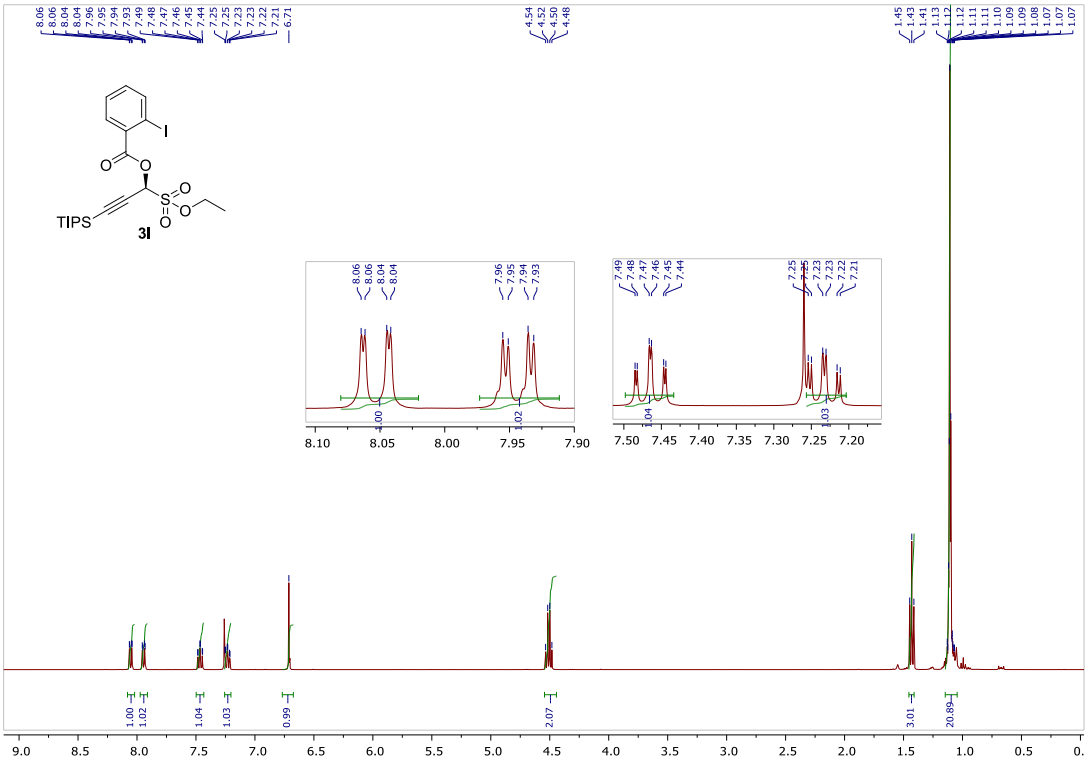


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.654	MM	0.3244	7140.90430	366.86111	98.4487
2	15.040	MM	0.3407	112.51890	5.50450	1.5513

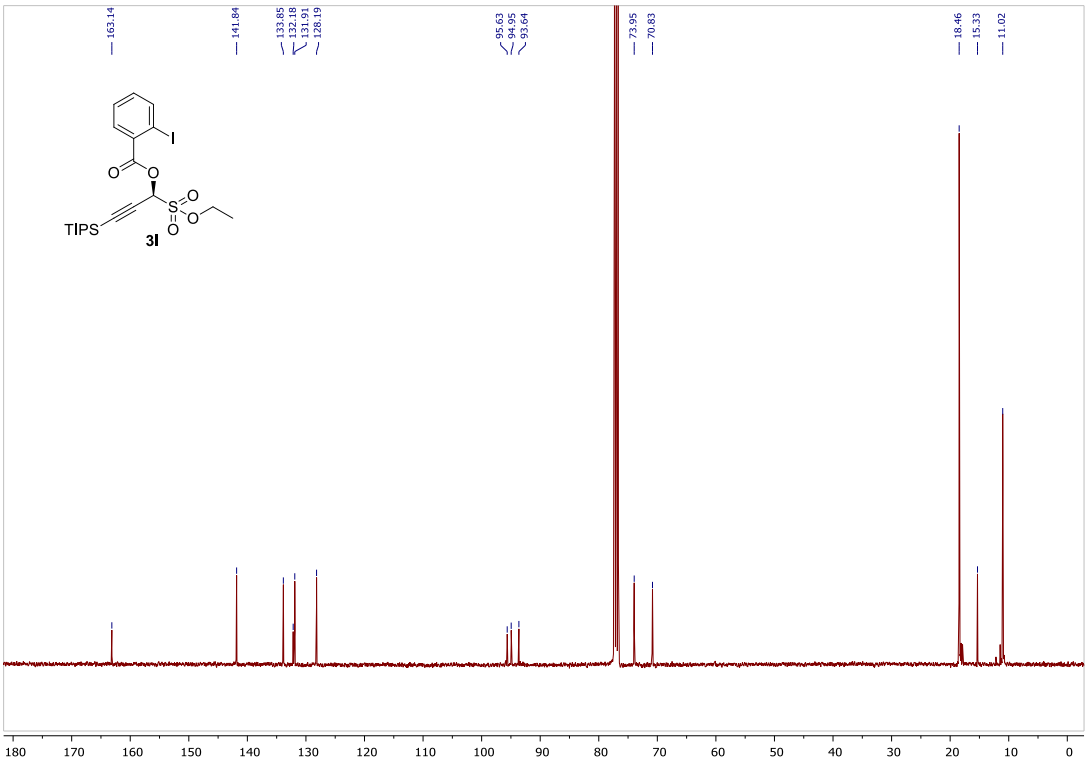
IR of compound **3k**



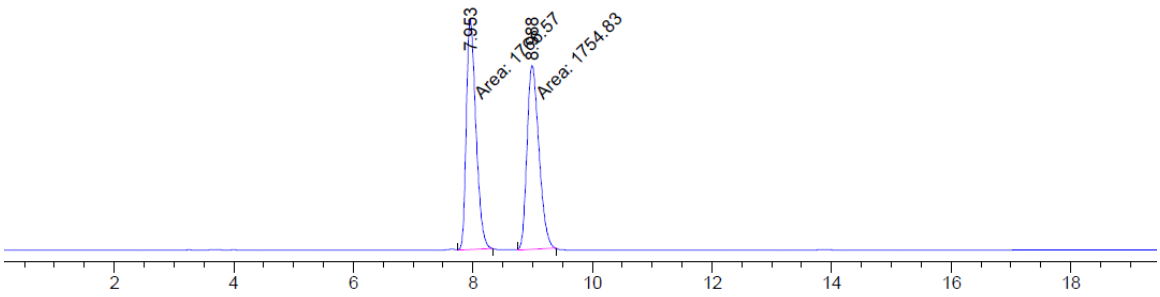
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3l**



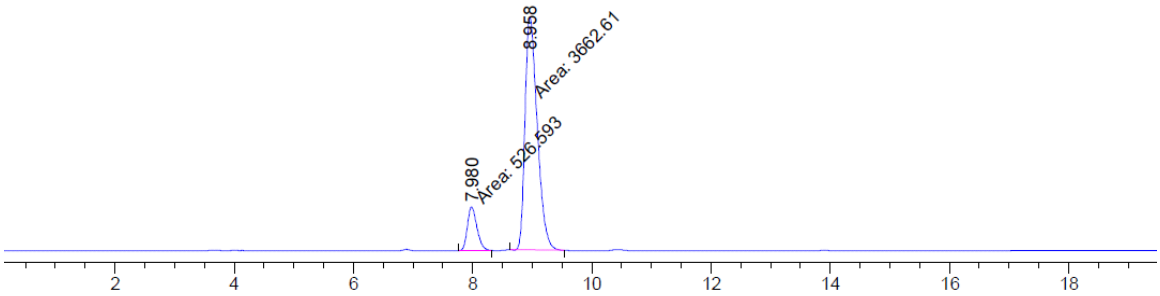
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3l**



HPLC of compound **3l**

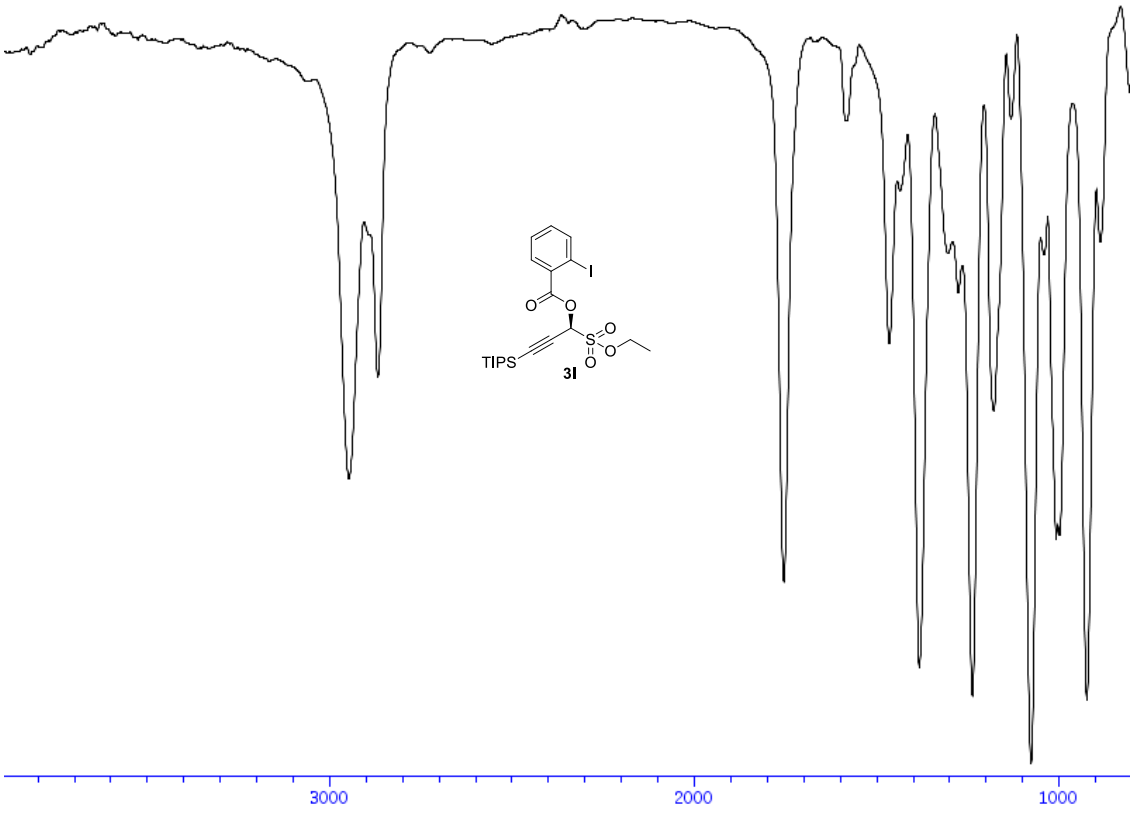


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.953	MM	0.1852	1766.56885	158.95554	50.1667
2	8.988	MM	0.2310	1754.82751	126.59152	49.8333

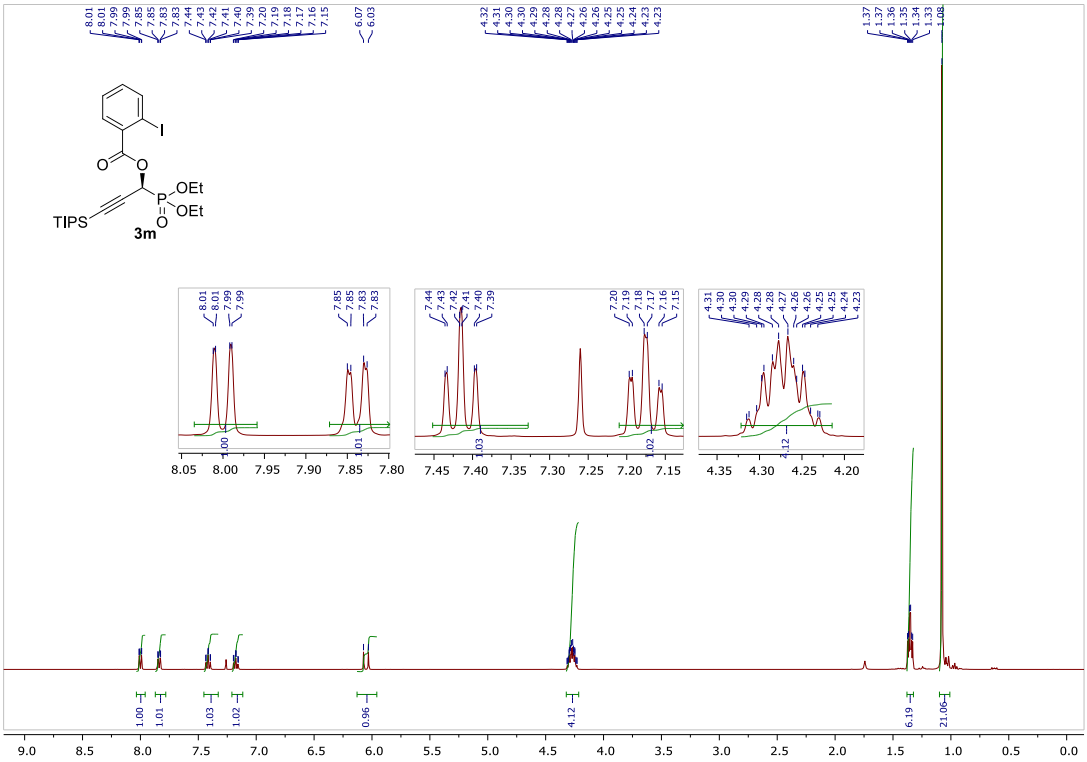


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.980	MM	0.1839	526.59320	47.71982	12.5702
2	8.958	MM	0.2379	3662.61426	256.54730	87.4298

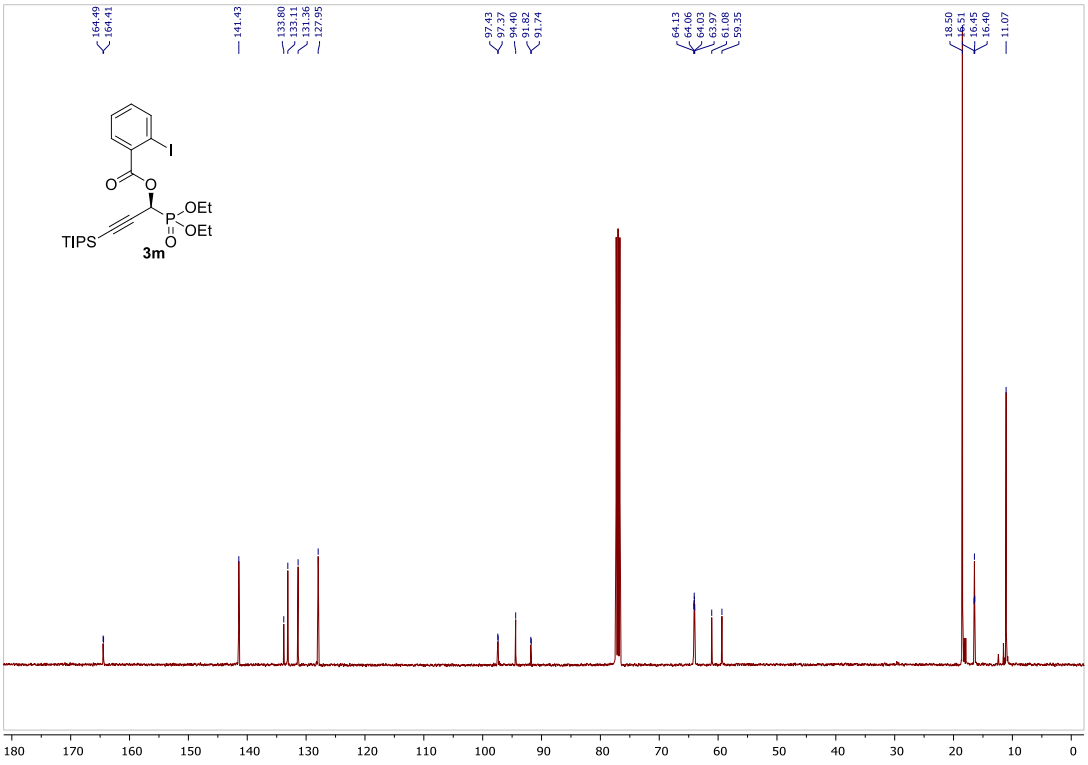
IR of compound **3l**



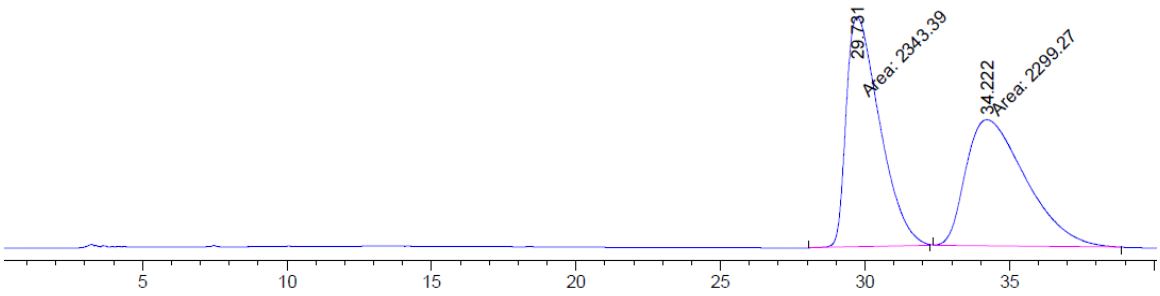
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3m**



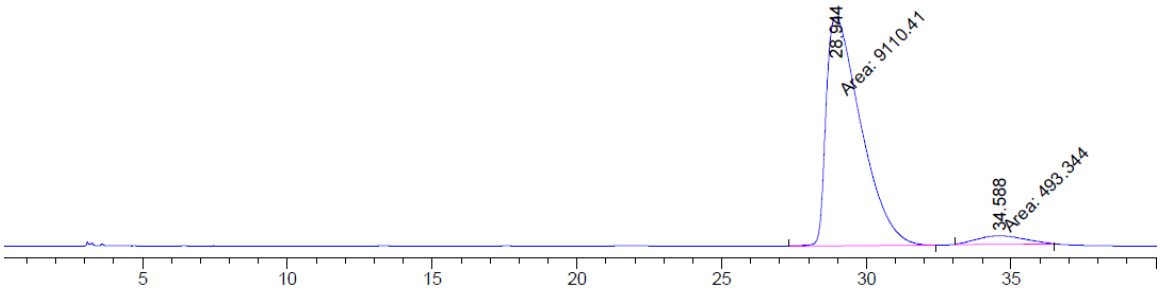
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3m**



HPLC of compound **3m**

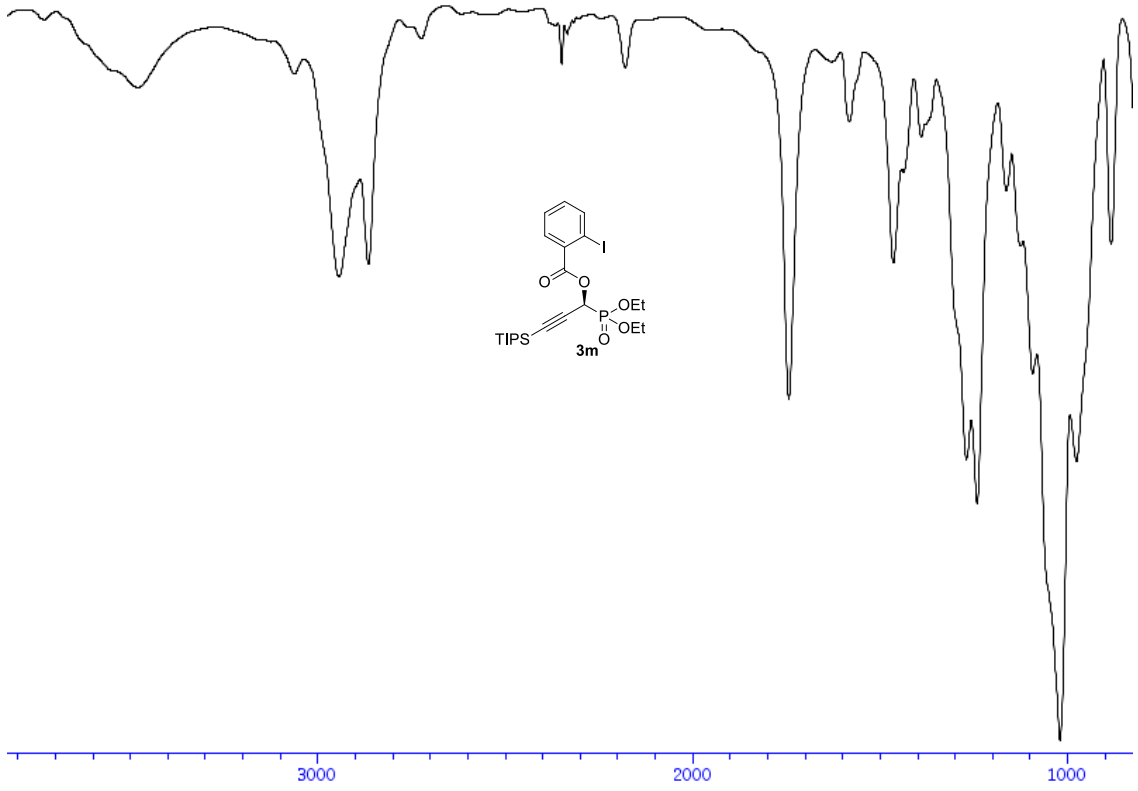


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.731	MM	1.3408	2343.38843	29.12976	50.4751
2	34.222	MM	2.3993	2299.27075	15.97179	49.5249

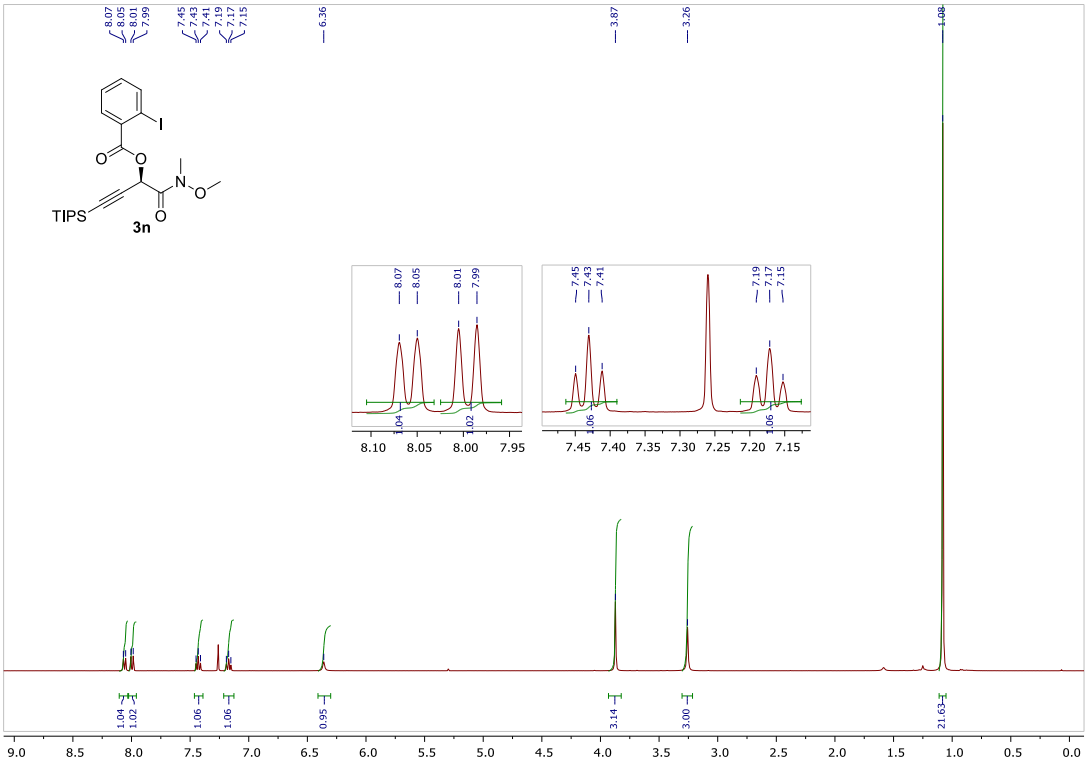


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.944	MM	1.3866	9110.41016	109.50642	94.8630
2	34.588	MM	2.0089	493.34448	4.09298	5.1370

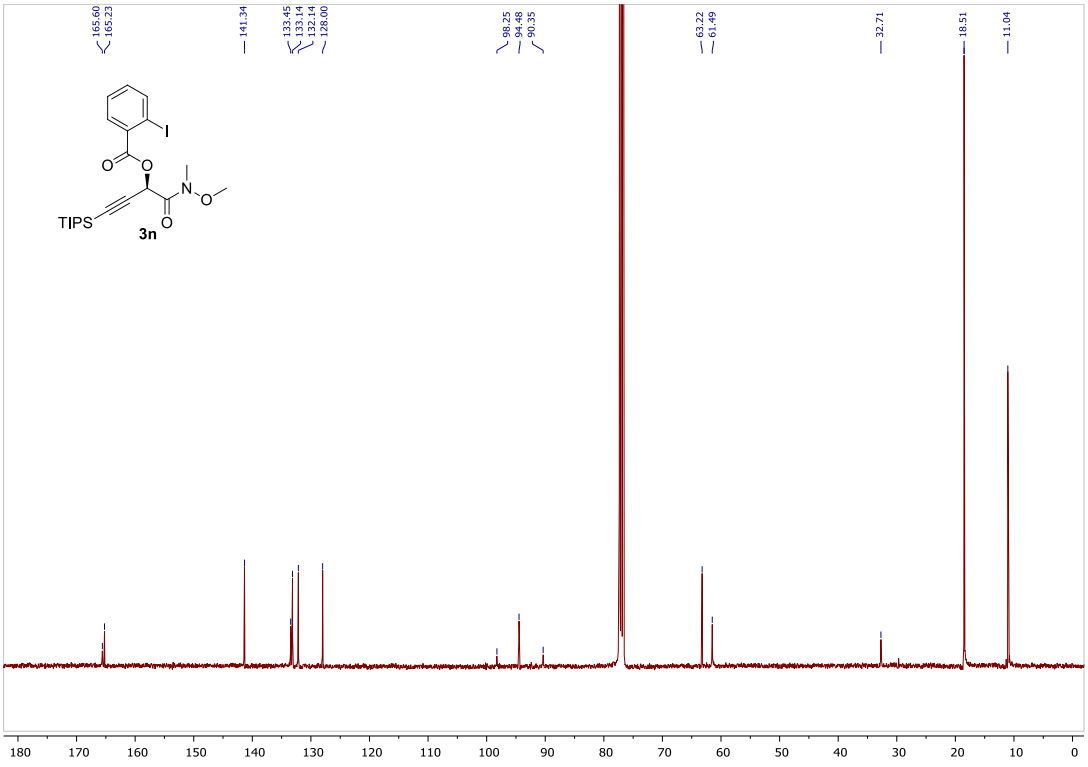
IR of compound **3m**



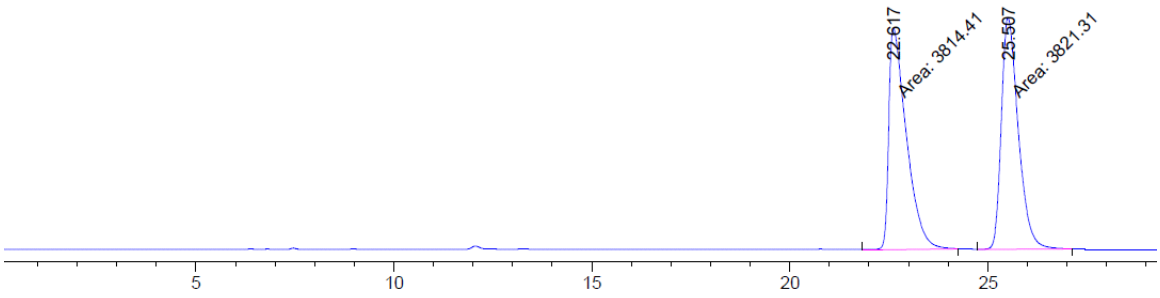
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3n**



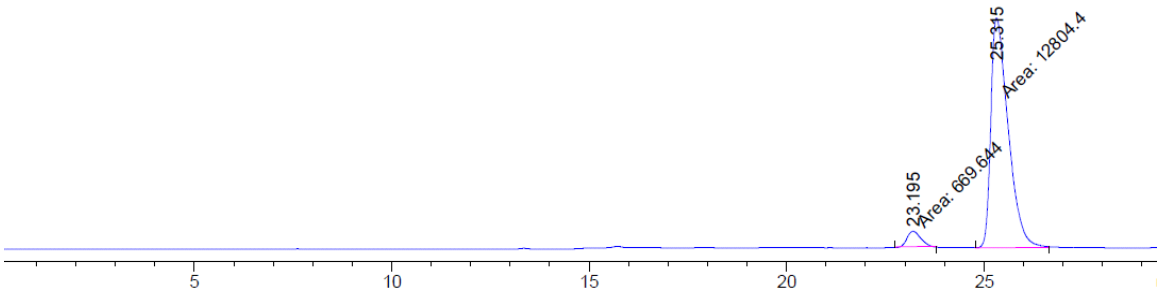
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3n**



HPLC of compound **3n**

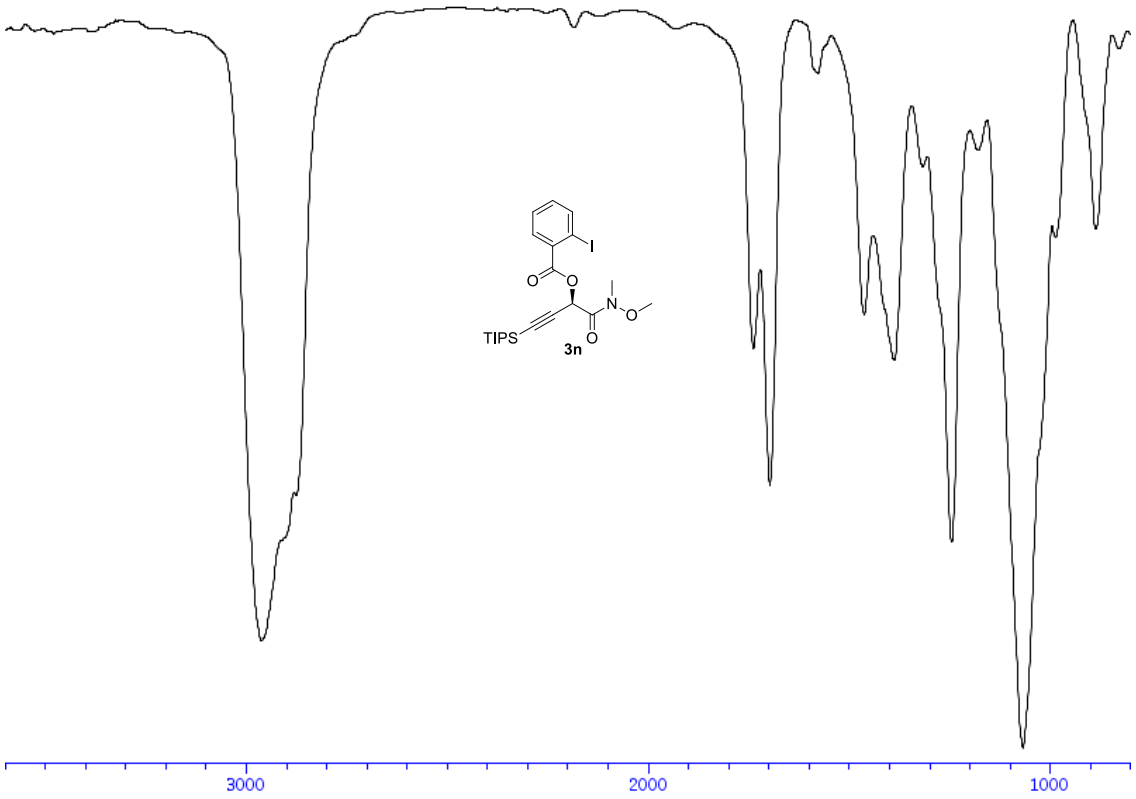


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.617	MM	0.5170	3814.40649	122.97264	49.9548
2	25.507	MM	0.4956	3821.30981	128.51900	50.0452

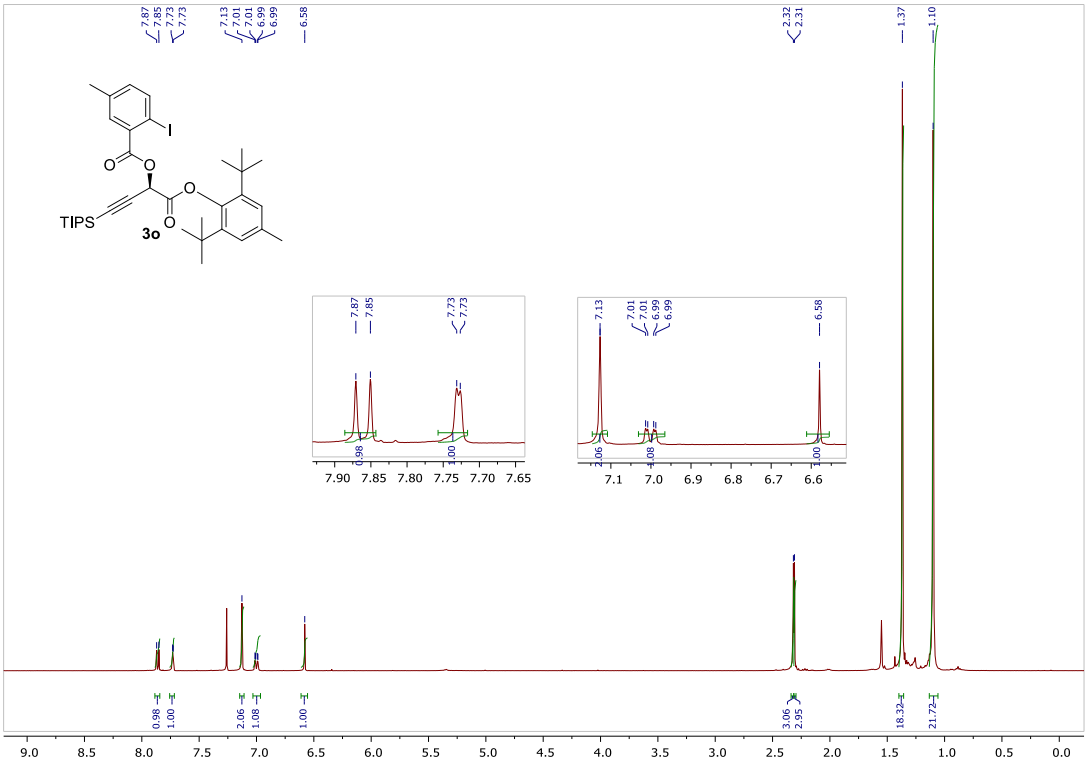


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.195	MM	0.3931	669.64398	28.39186	4.9699
2	25.315	MM	0.5101	1.28044e4	418.38428	95.0301

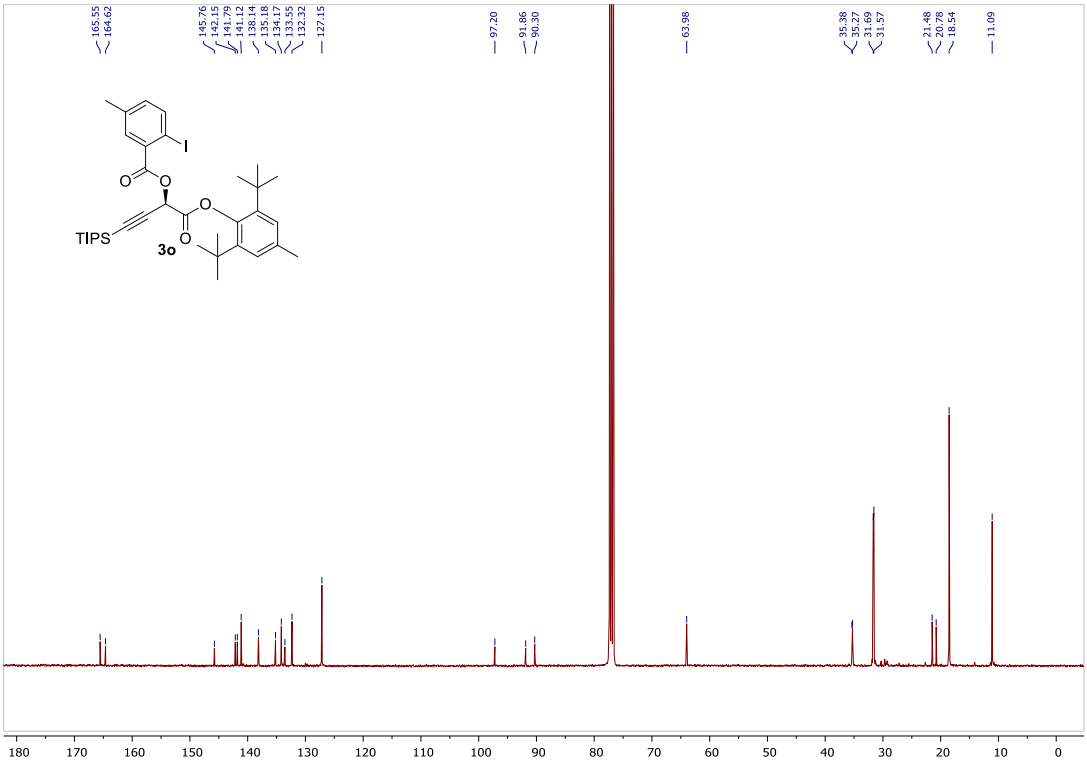
IR of compound **3n**



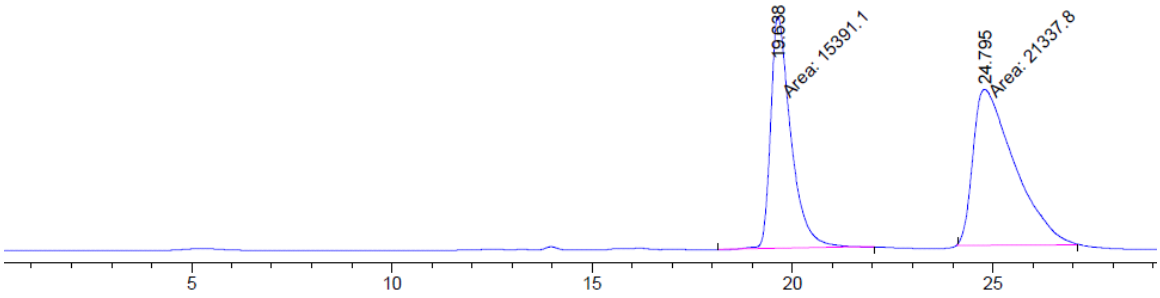
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3o**



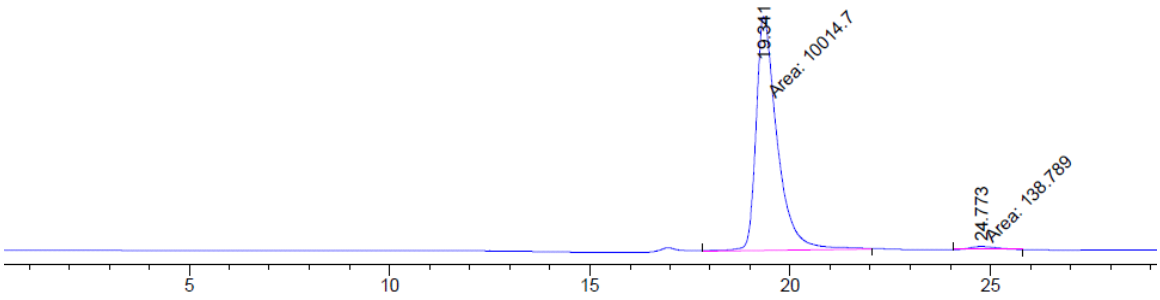
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3o**



HPLC of compound **3o**

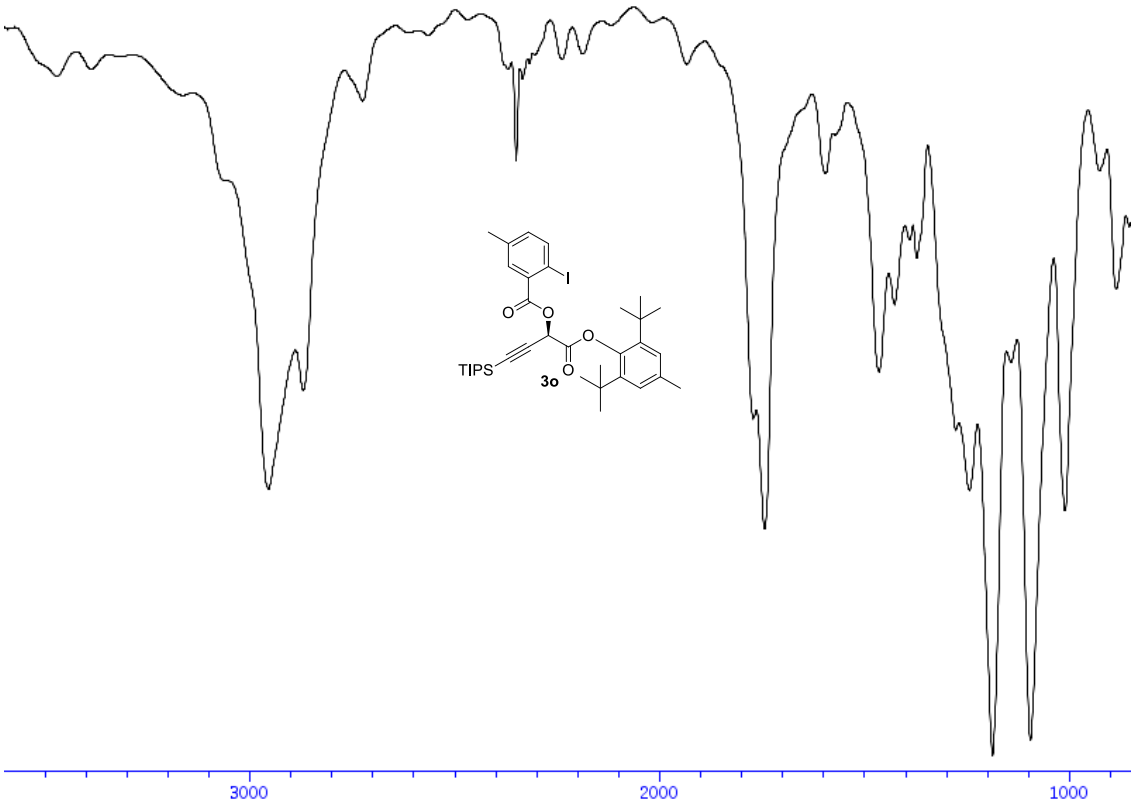


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.638	MM	0.5850	1.53911e4	438.50104	41.9047
2	24.795	MM	1.2058	2.13378e4	294.92432	58.0953

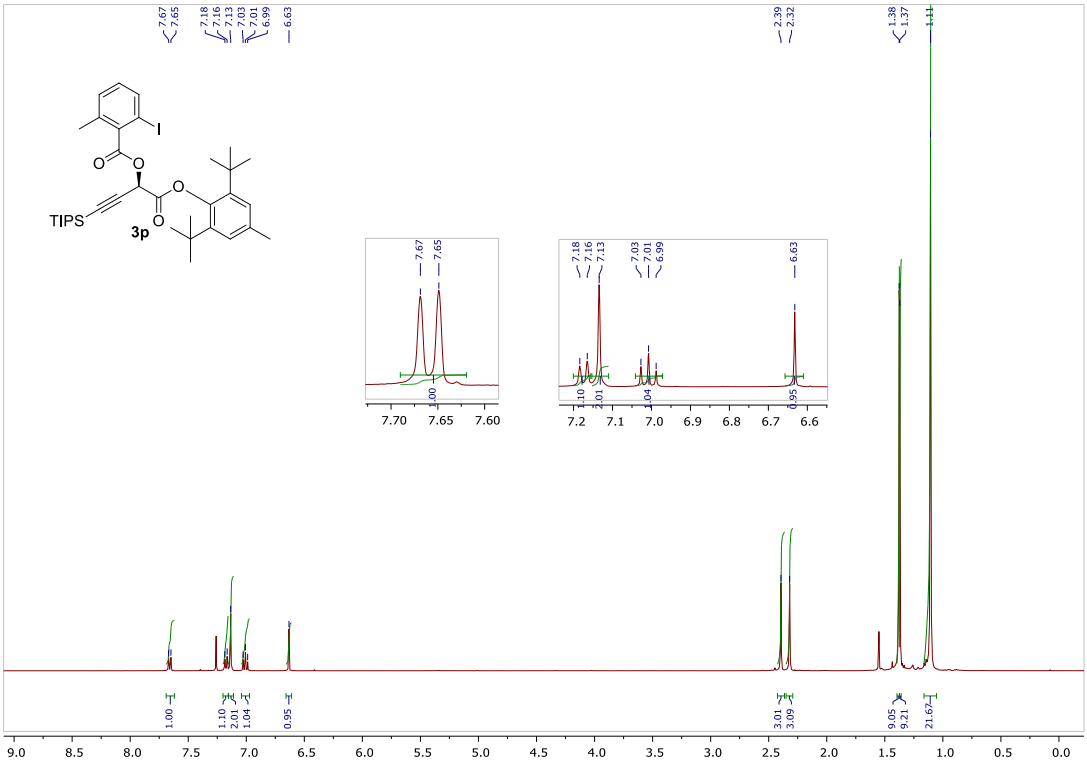


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.341	MM	0.6142	1.00147e4	271.74460	98.6331
2	24.773	MM	0.6950	138.78909	3.32809	1.3669

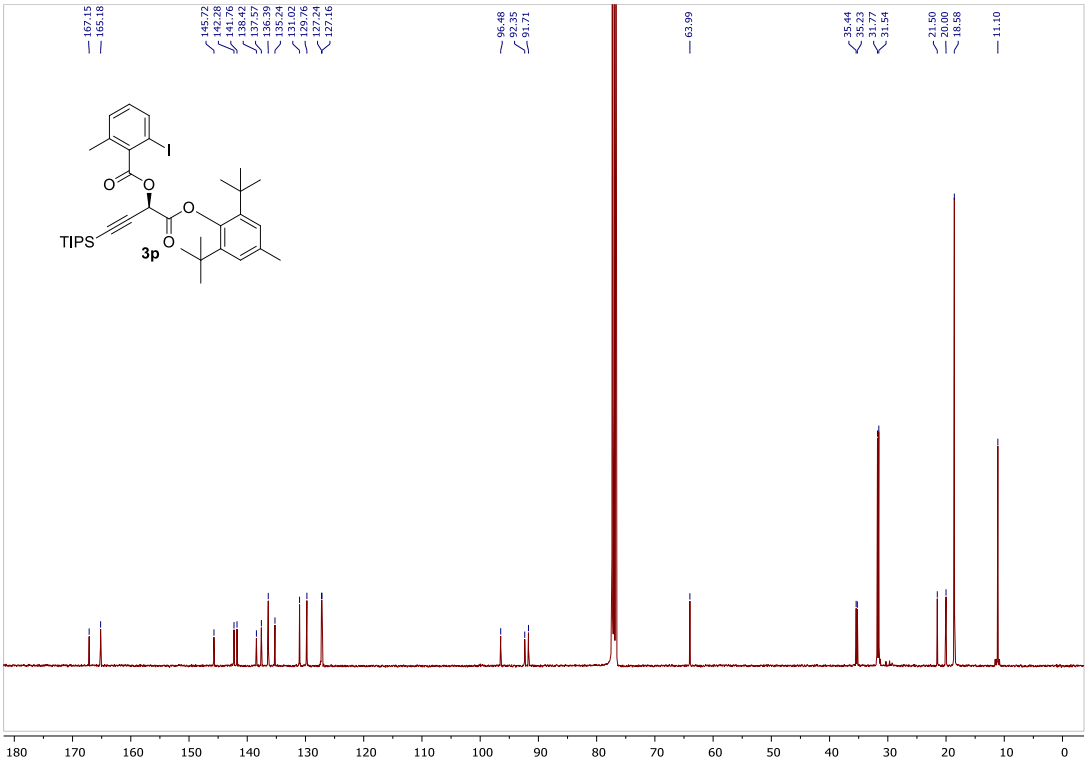
IR of compound **3o**



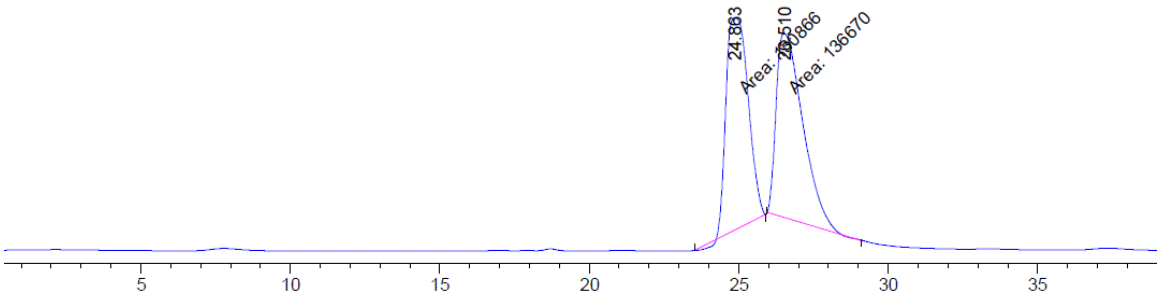
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3p**



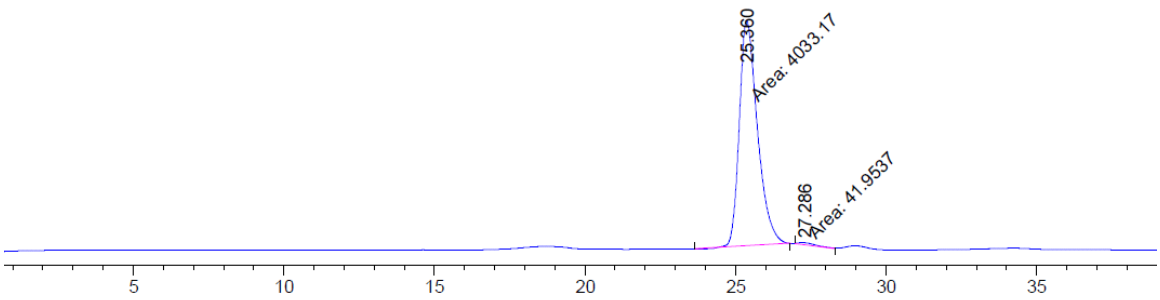
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3p**



HPLC of compound **3p**

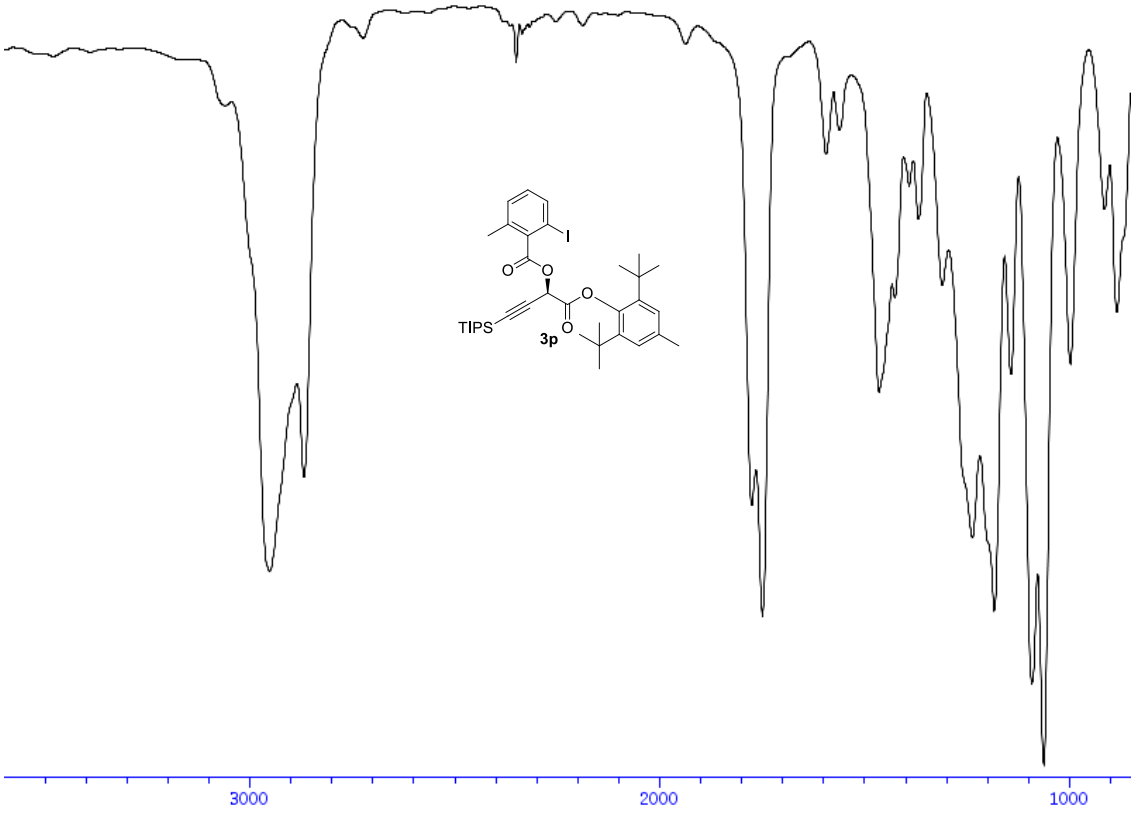


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.863	MM	0.8598	1.30866e5	2536.76318	48.9153
2	26.510	MM	1.0372	1.36670e5	2196.13037	51.0847

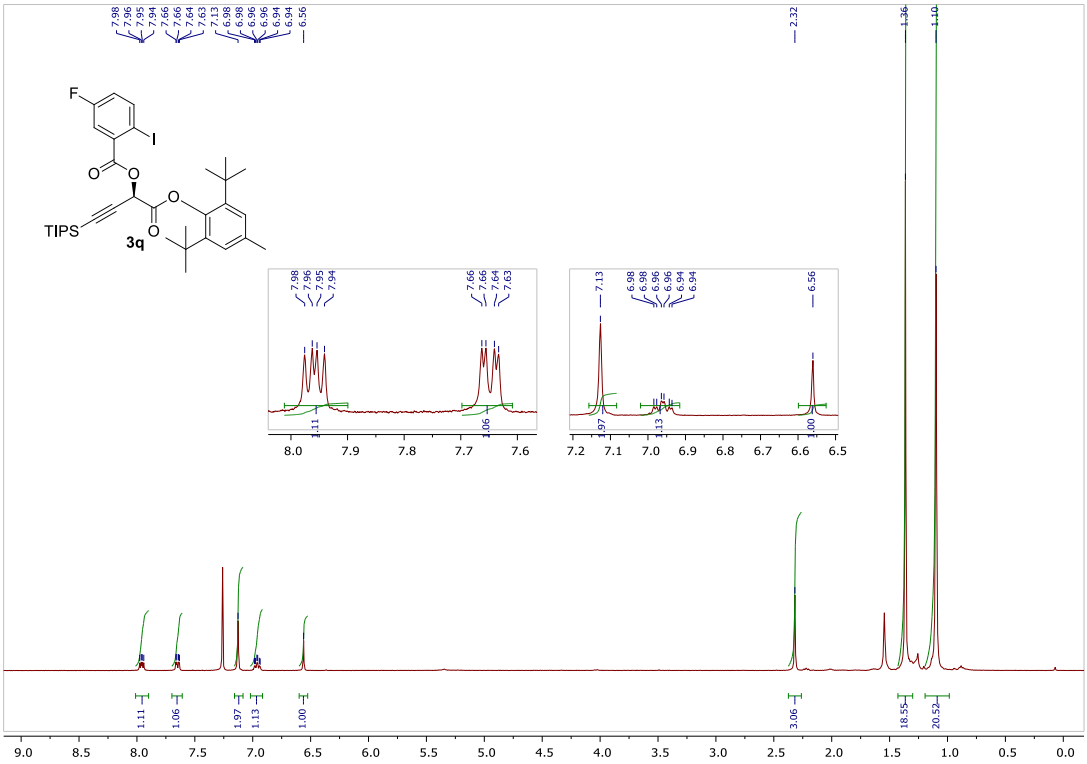


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.360	MM	0.6963	4033.16675	96.53699	98.9705
2	27.286	MM	0.6938	41.95370	1.00781	1.0295

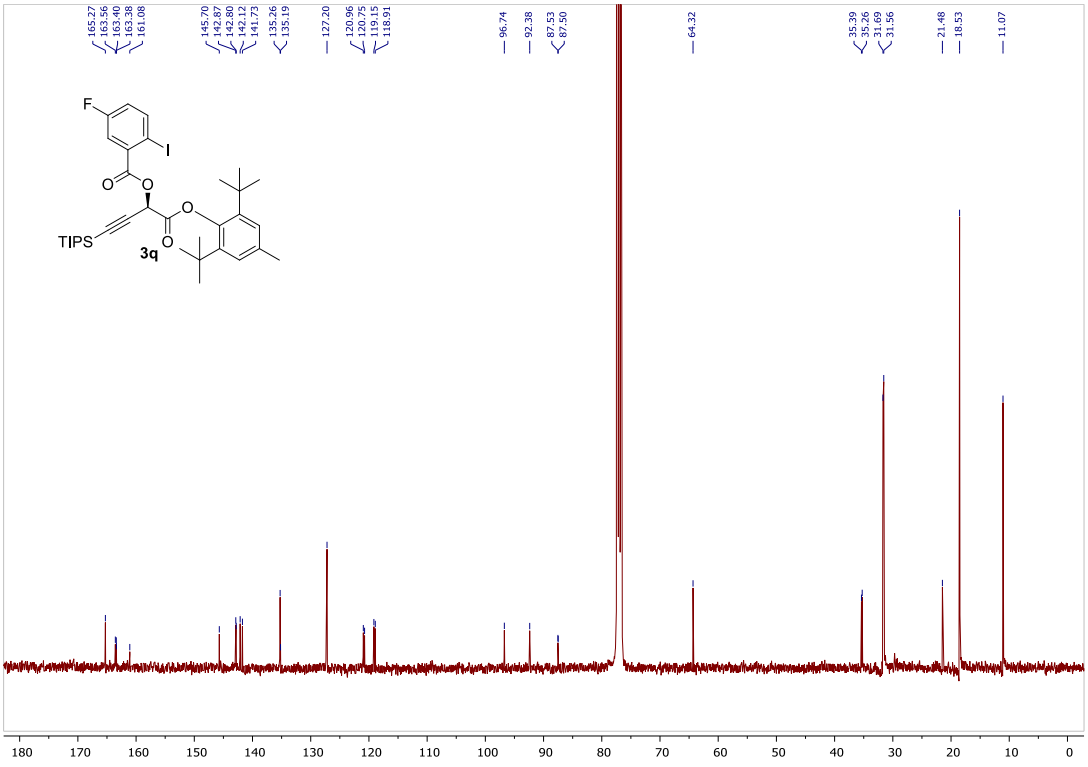
IR of compound **3p**



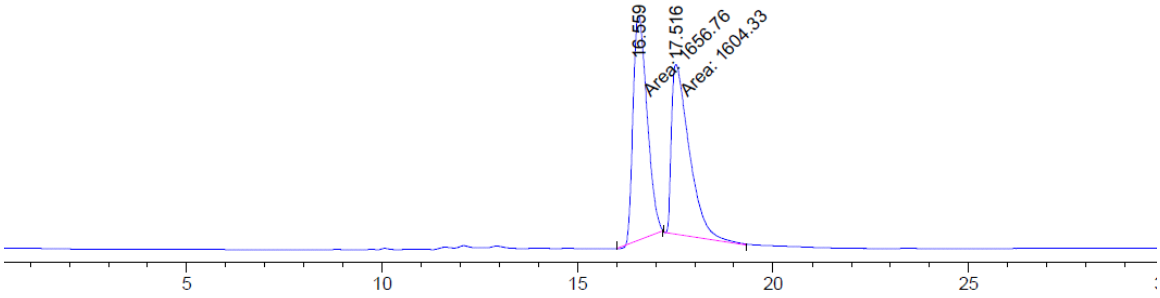
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3q**



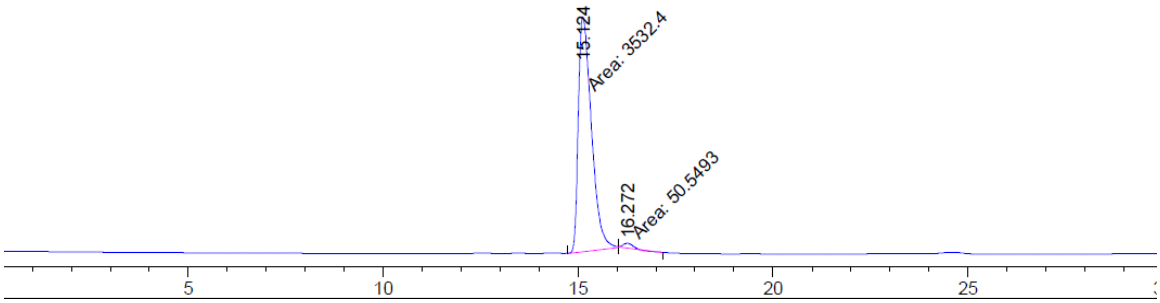
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3q**



HPLC of compound **3q**

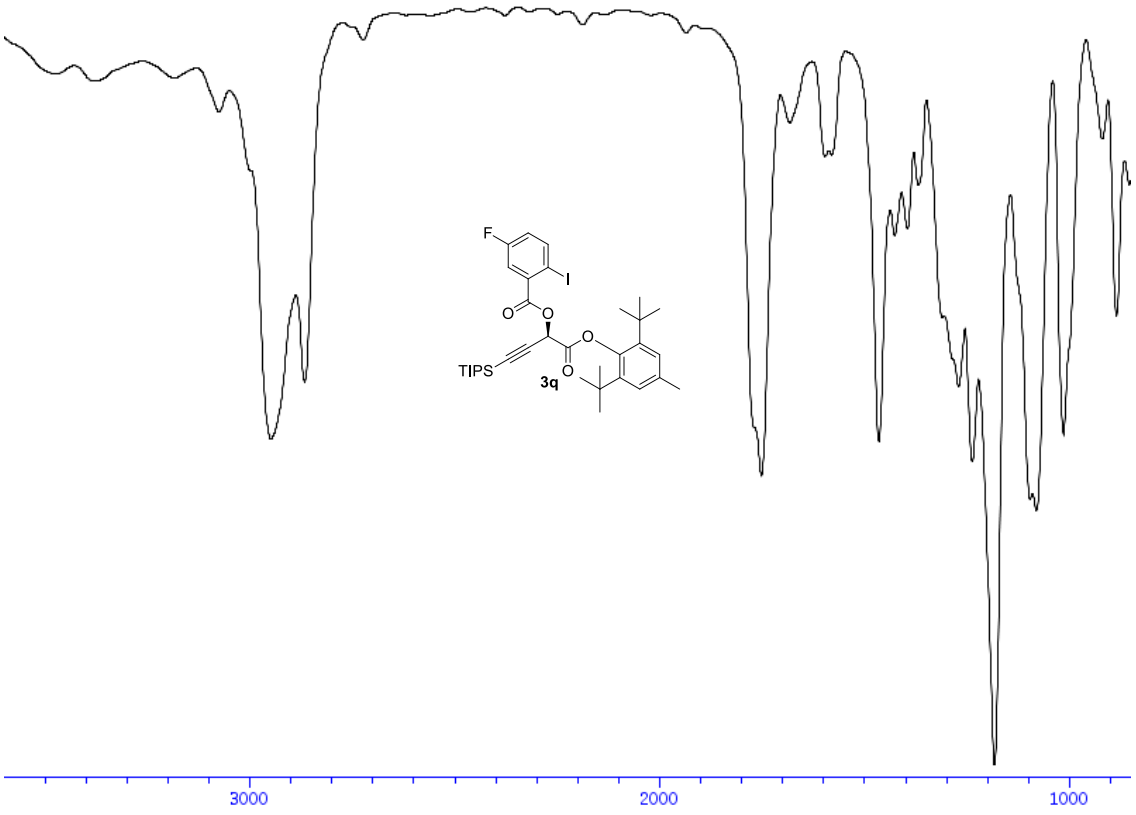


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.559	MM	0.4135	1656.75989	66.78135	50.8038
2	17.516	MM	0.5299	1604.33289	50.45665	49.1962

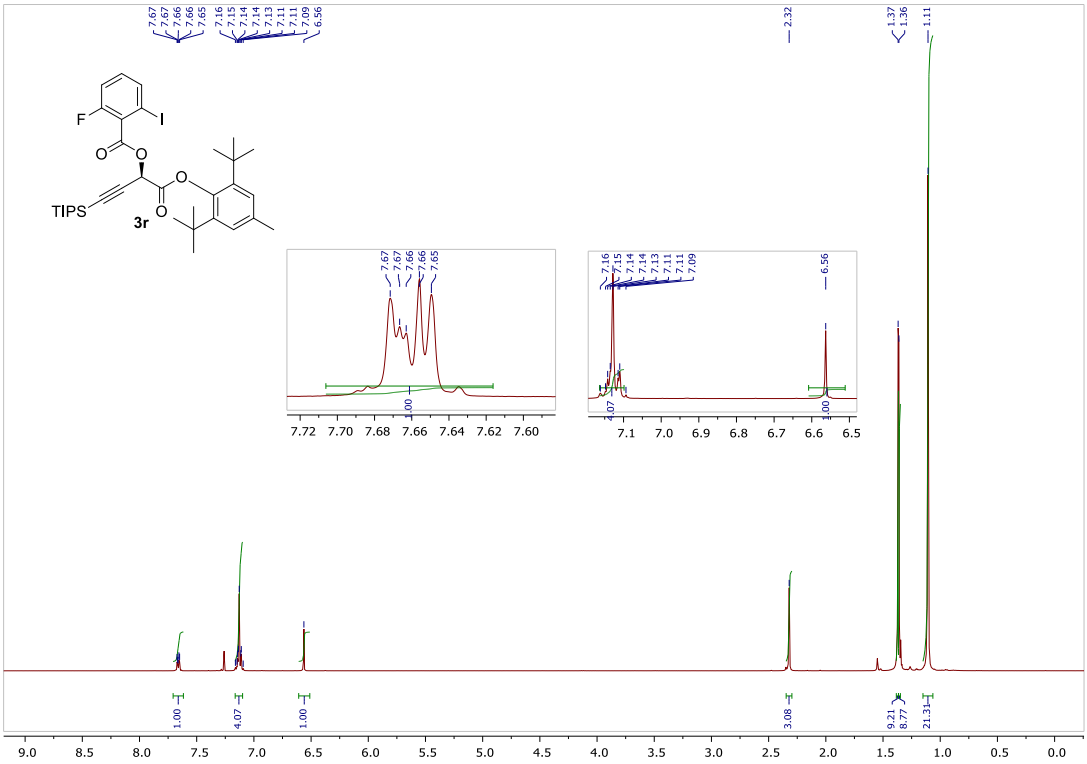


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.124	MM	0.3883	3532.39819	151.60956	98.5892
2	16.272	MM	0.2761	50.54926	3.05192	1.4108

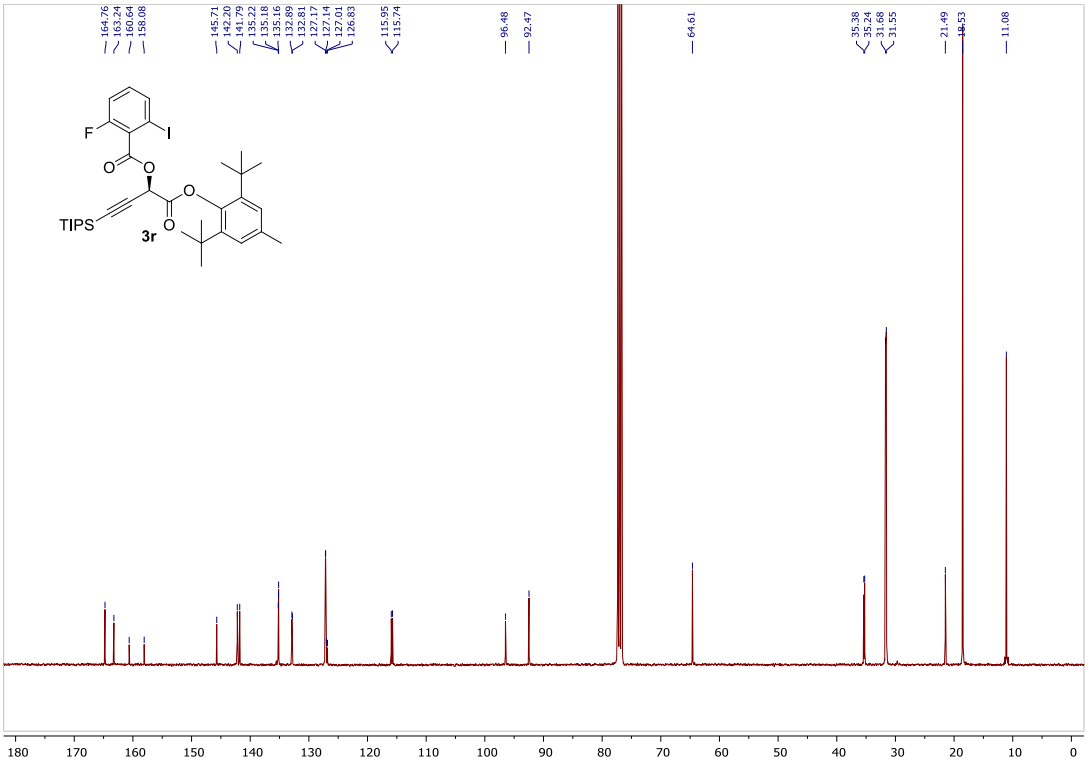
IR of compound **3q**



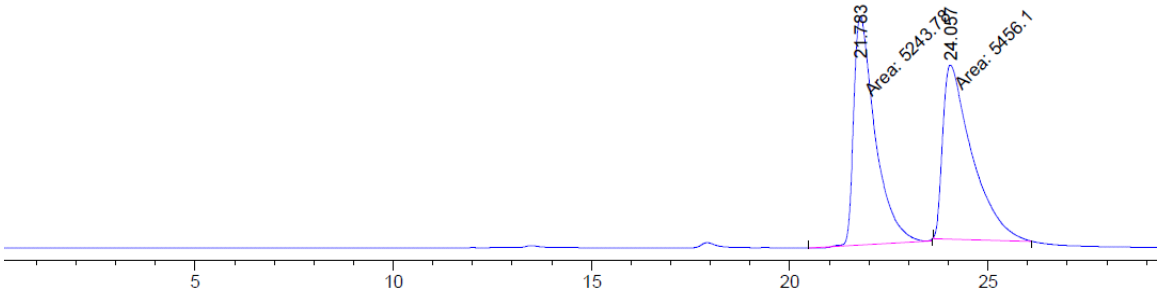
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3r**



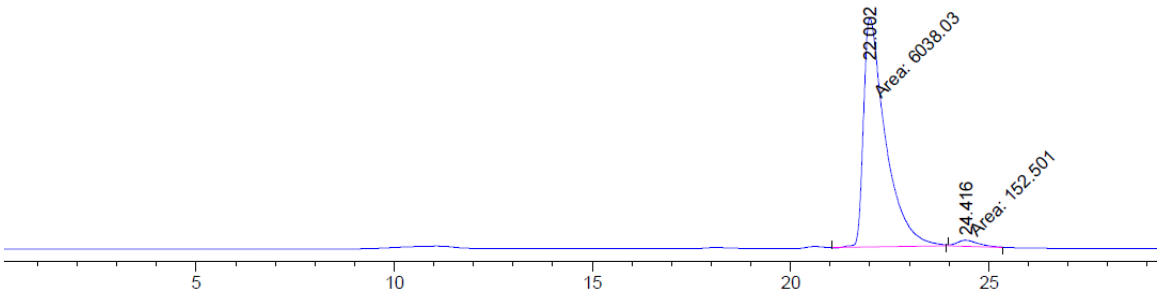
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3r**



HPLC of compound **3r**

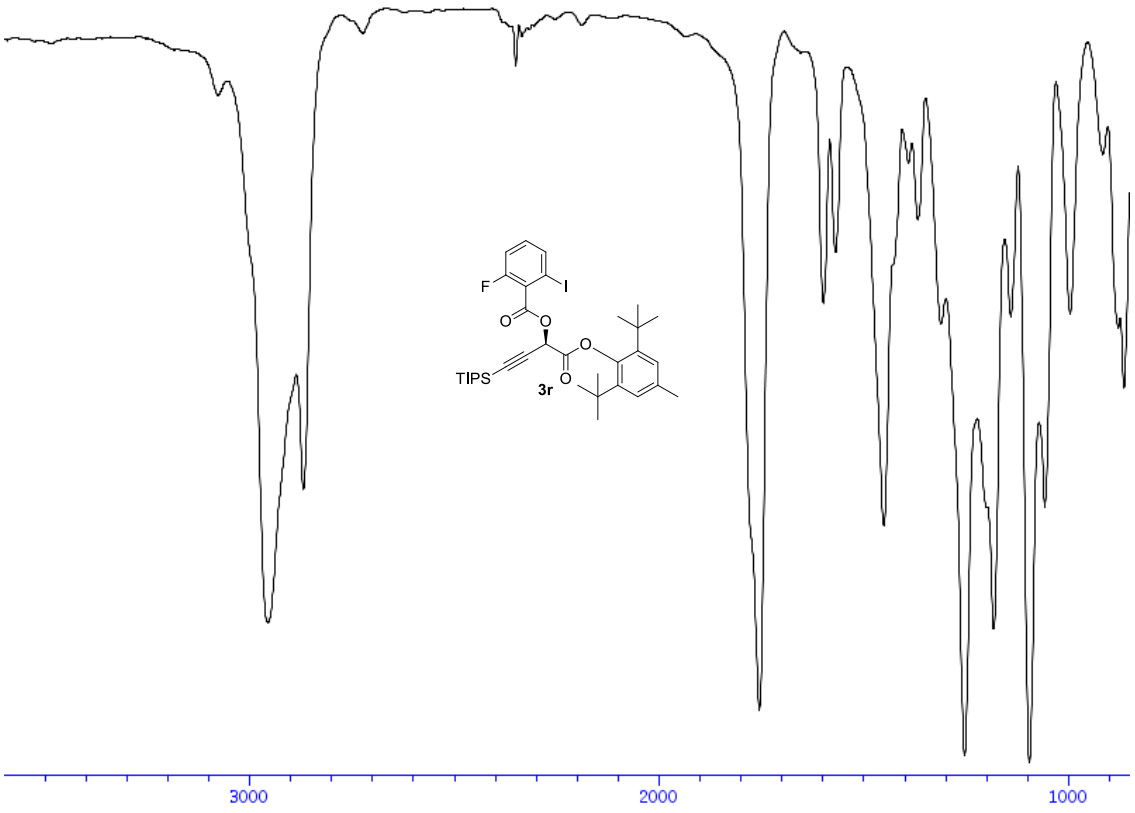


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.783	MM	0.6275	5243.78320	139.26936	49.0078
2	24.057	MM	0.8585	5456.10303	105.92214	50.9922

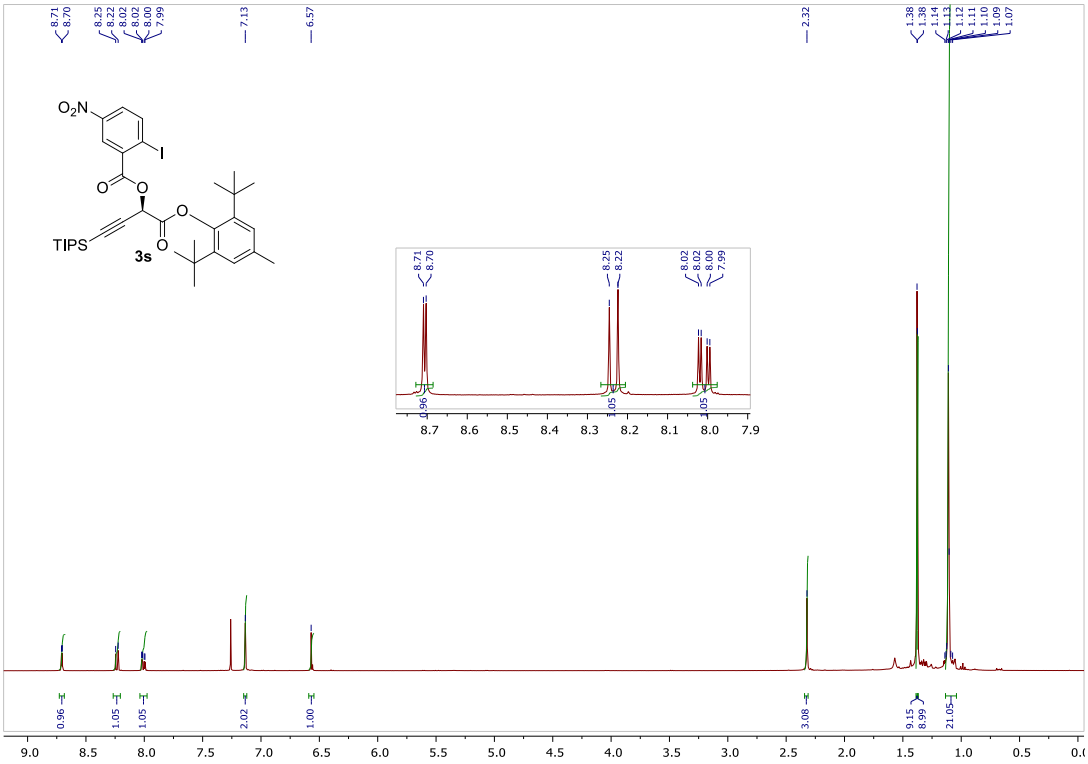


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.002	MM	0.6423	6038.03271	156.67625	97.5365
2	24.416	MM	0.6137	152.50073	4.14182	2.4635

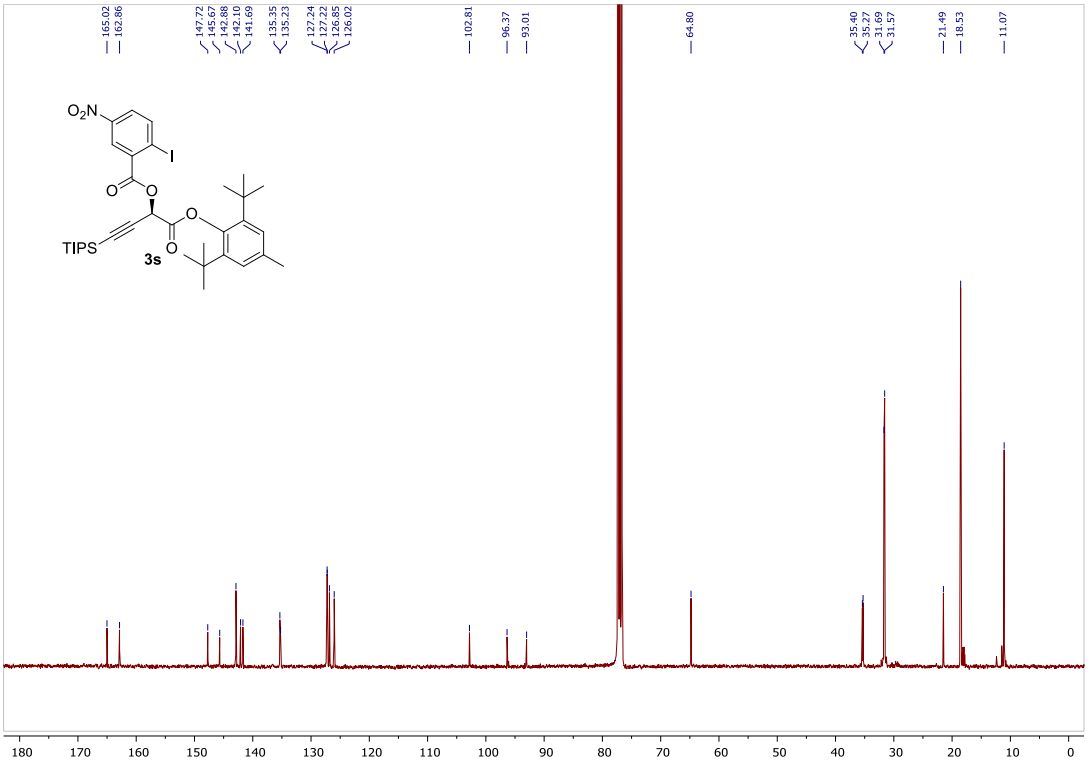
IR of compound **3r**



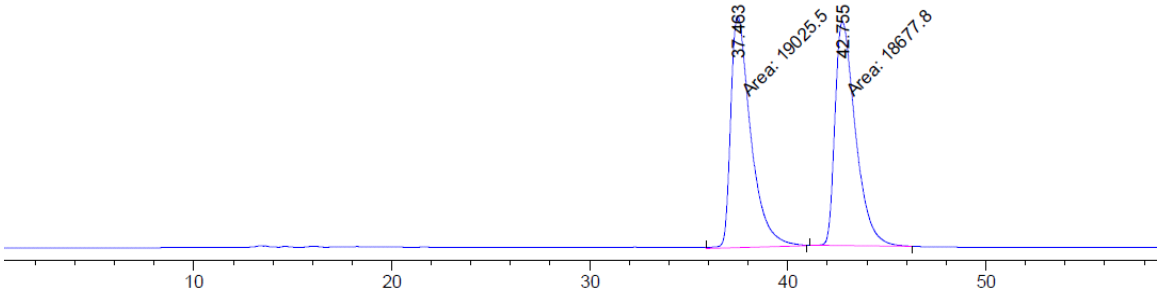
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3s**



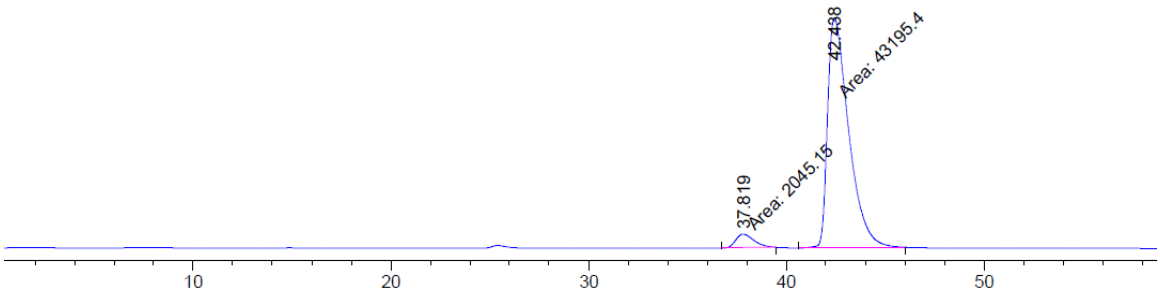
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3s**



HPLC of compound **3s**

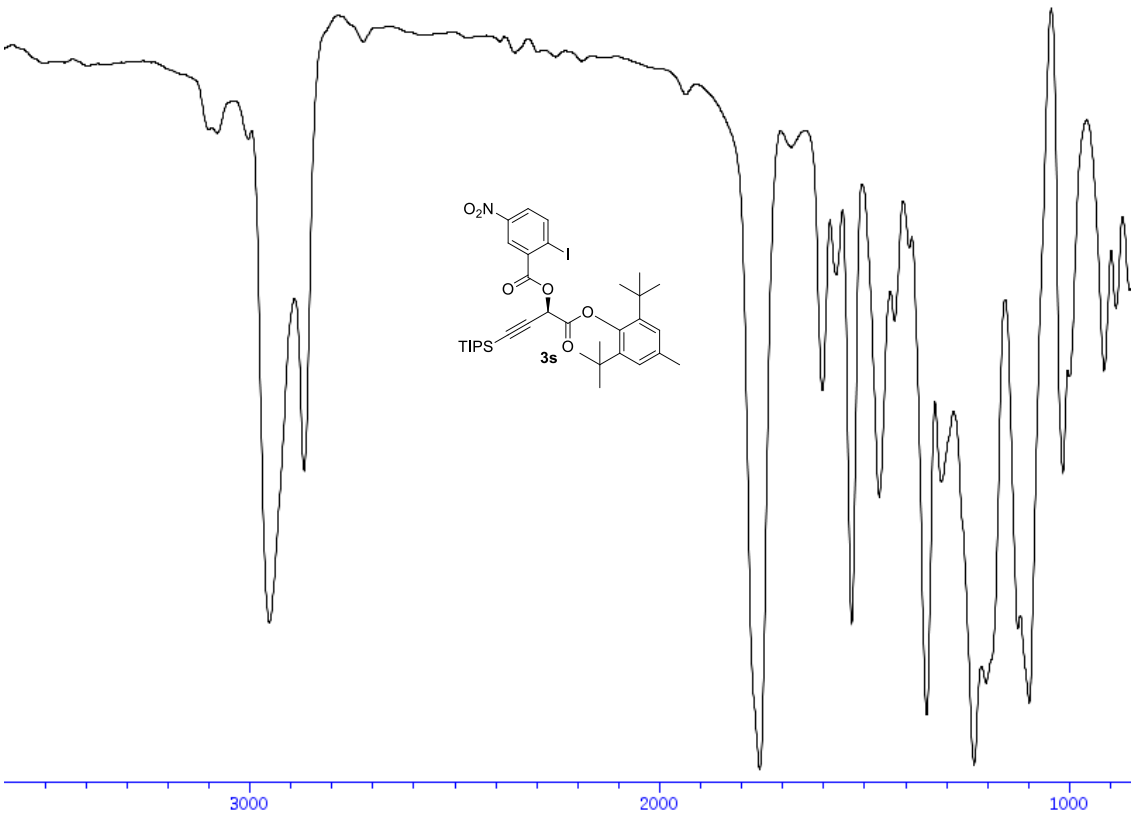


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.463	MM	1.1764	1.90255e4	269.54871	50.4610
2	42.755	MM	1.1967	1.86778e4	260.13611	49.5390

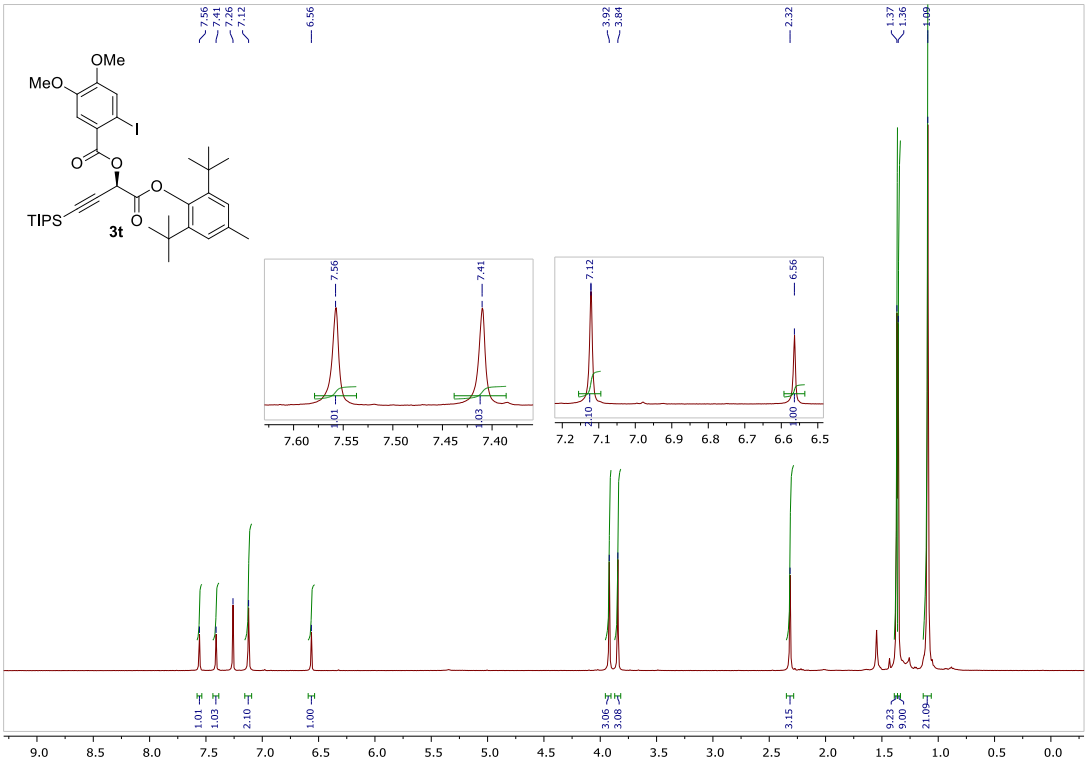


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.819	MM	1.0134	2045.15344	33.63426	4.5206
2	42.438	MM	1.2358	4.31954e4	582.53564	95.4794

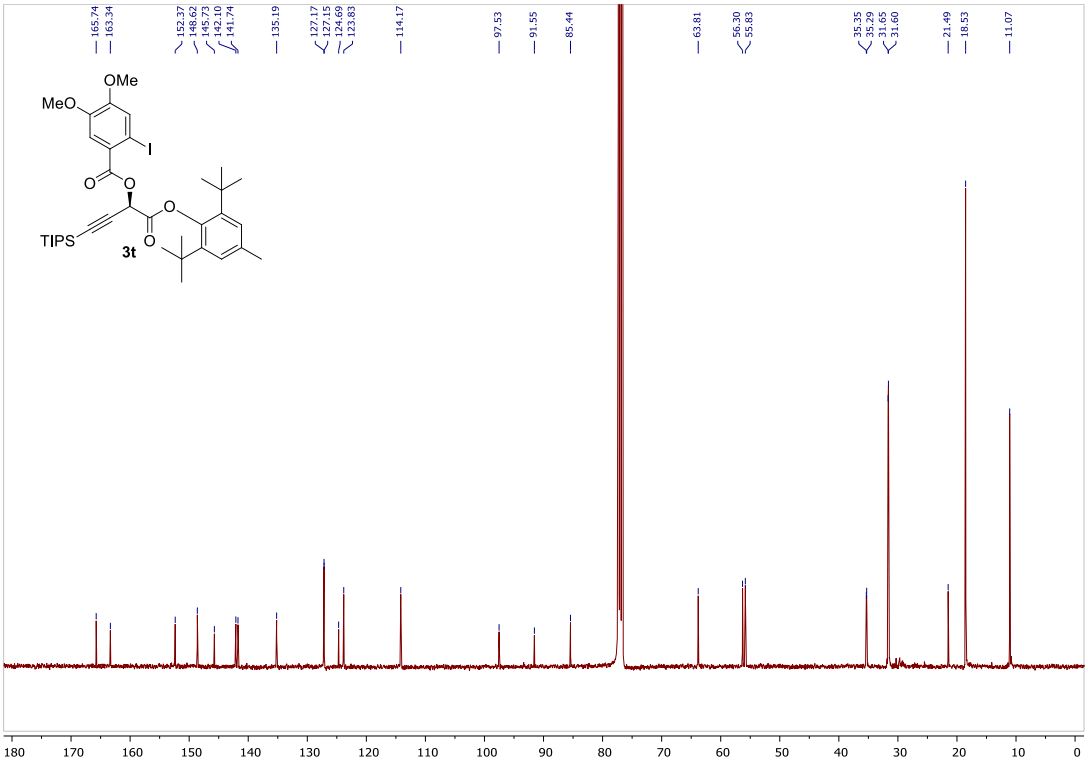
IR of compound **3s**



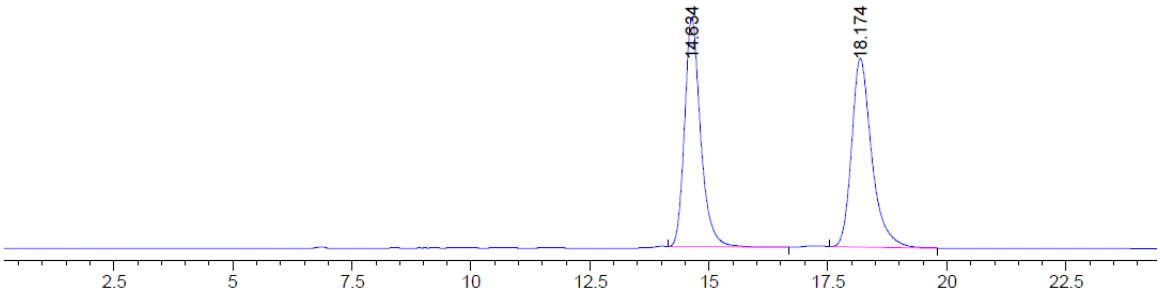
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3t**



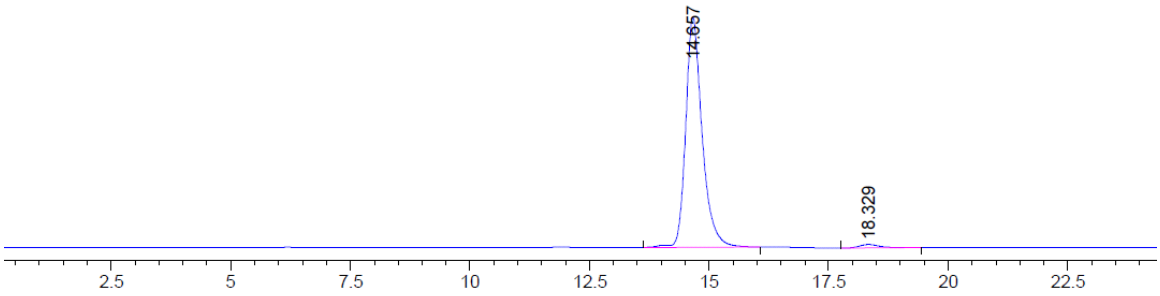
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3t**



HPLC of compound **3t**

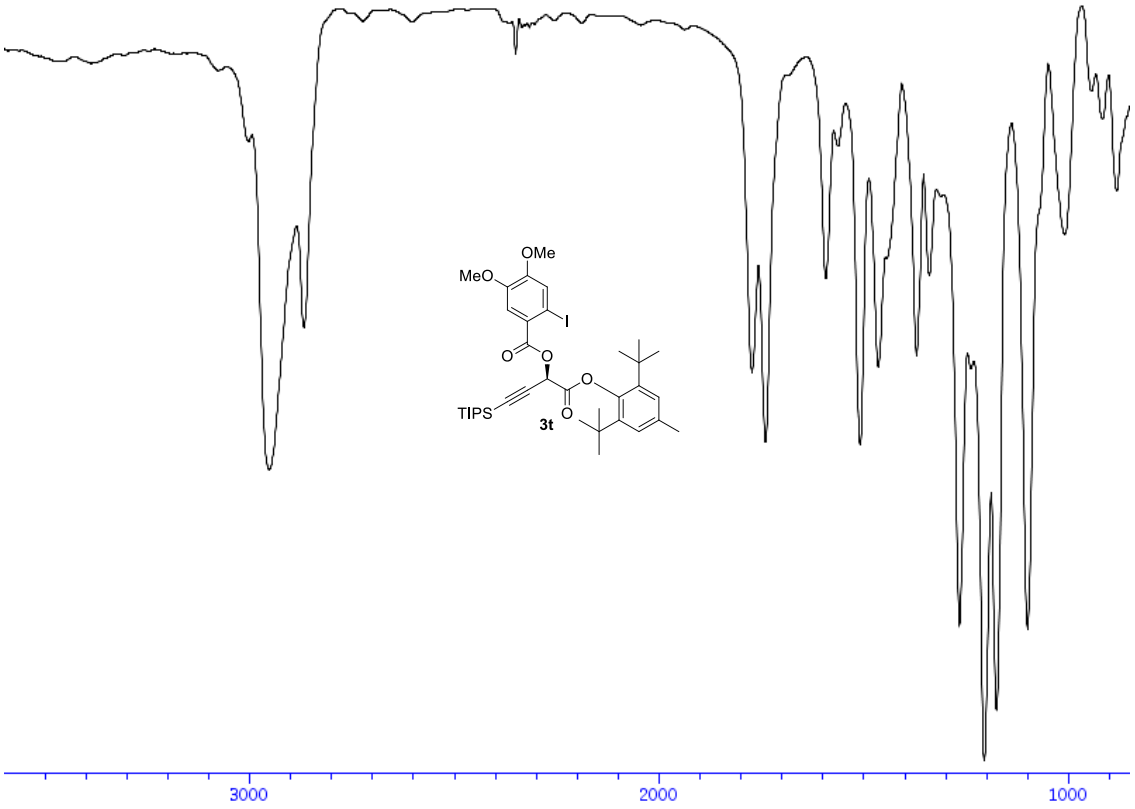


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.634	BB	0.3502	3153.09985	135.13863	49.1663
2	18.174	BB	0.4405	3260.03540	111.04497	50.8337

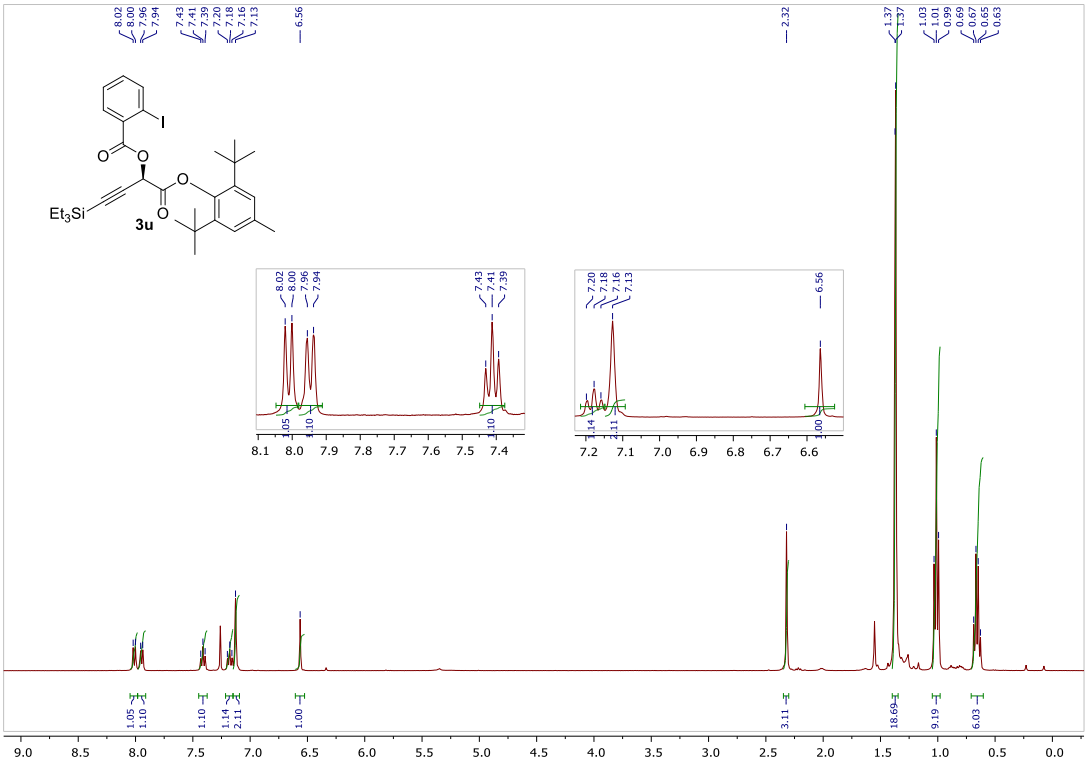


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.657	BB	0.3545	3934.70947	164.85161	98.0256
2	18.329	BB	0.4428	79.25356	2.59110	1.9744

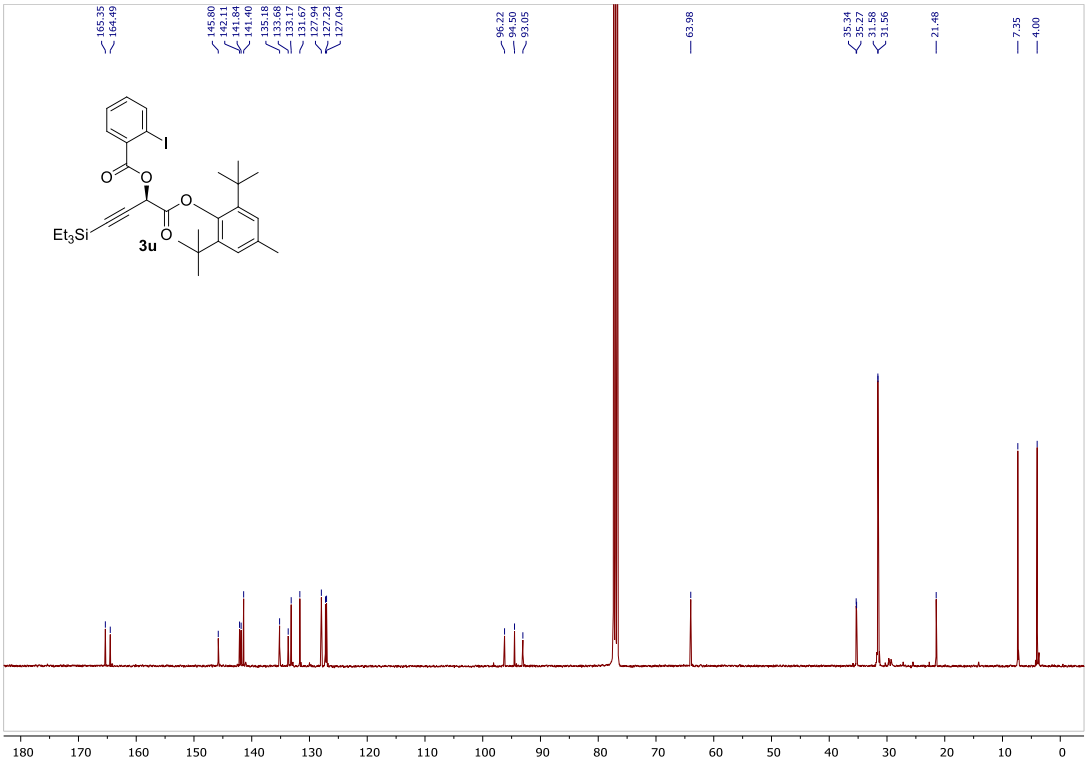
IR of compound **3t**



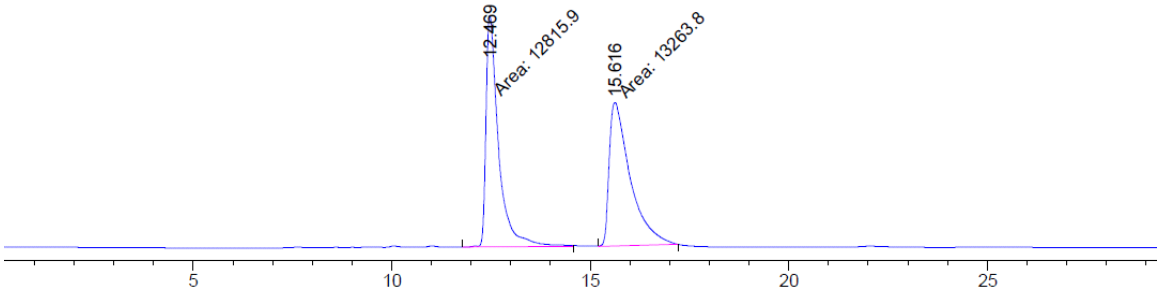
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3u**



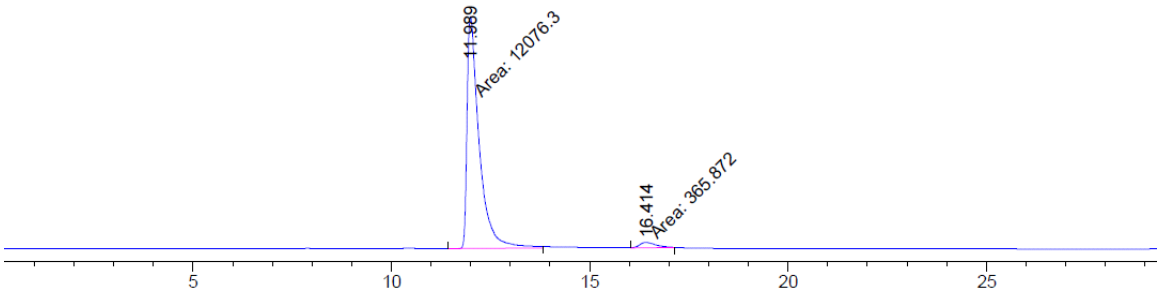
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3u**



HPLC of compound **3u**

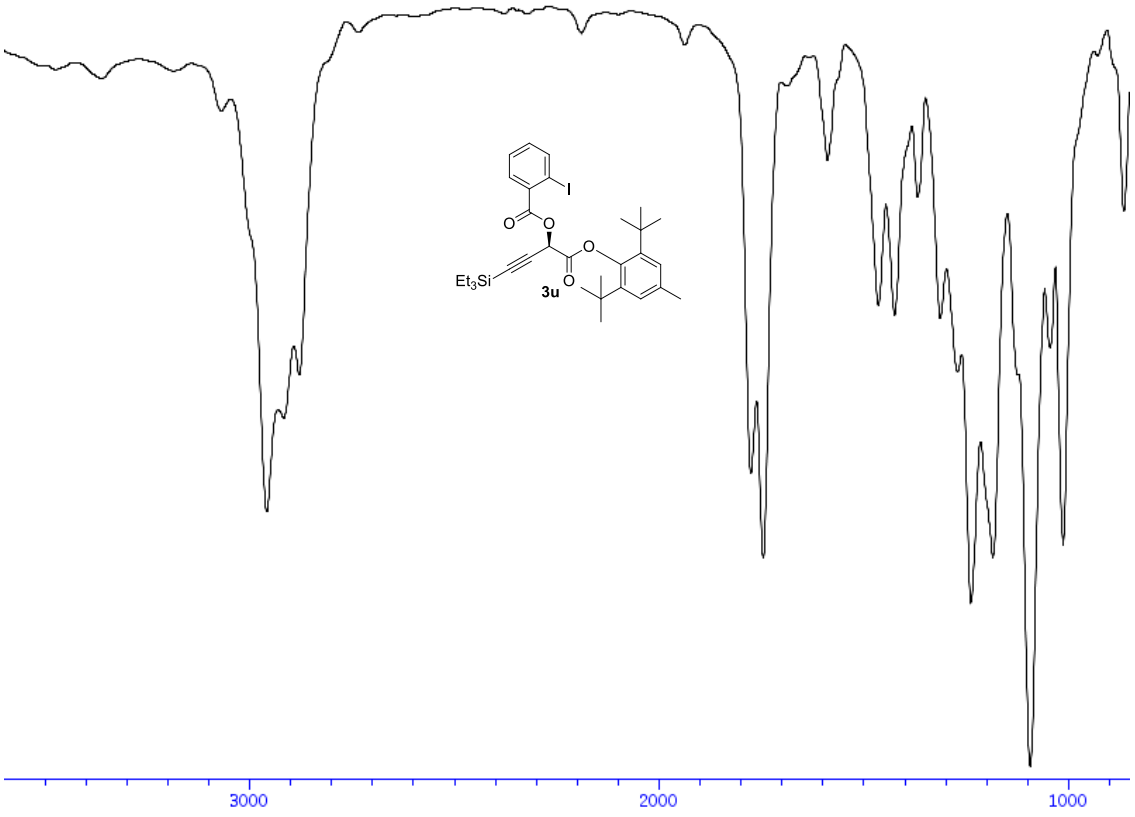


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.469	MM	0.3664	1.28159e4	583.00702	49.1412
2	15.616	MM	0.6114	1.32638e4	361.55771	50.8588

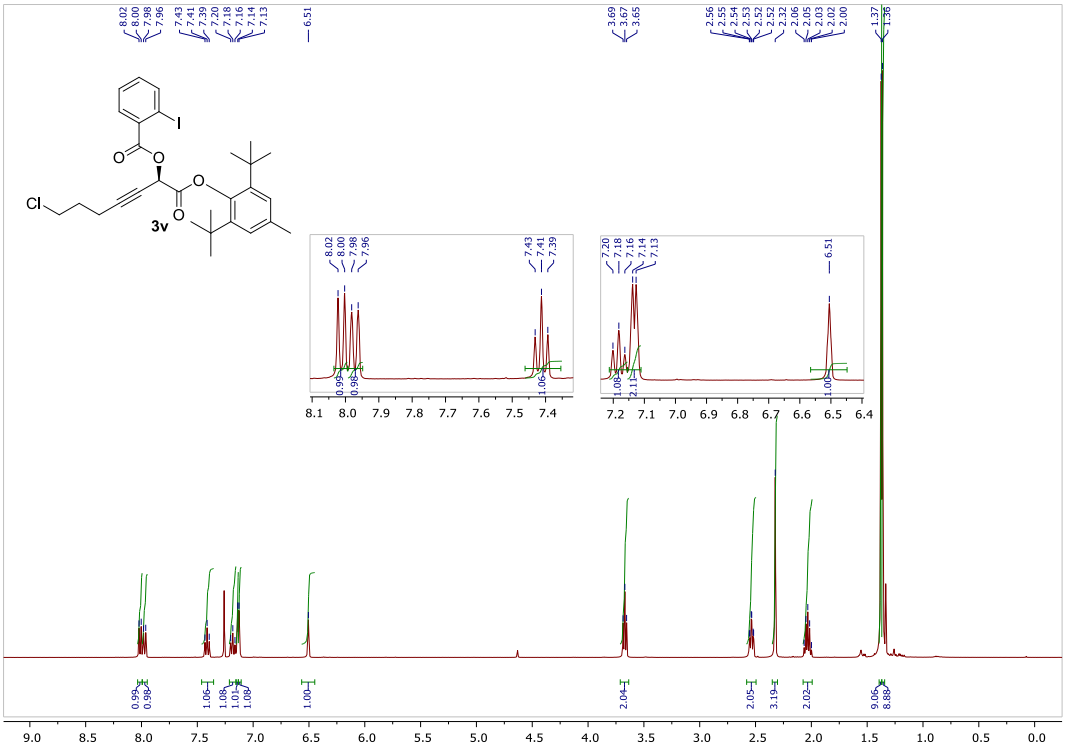


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.989	MM	0.3535	1.20763e4	569.38245	97.0594
2	16.414	MM	0.4844	365.87164	12.58844	2.9406

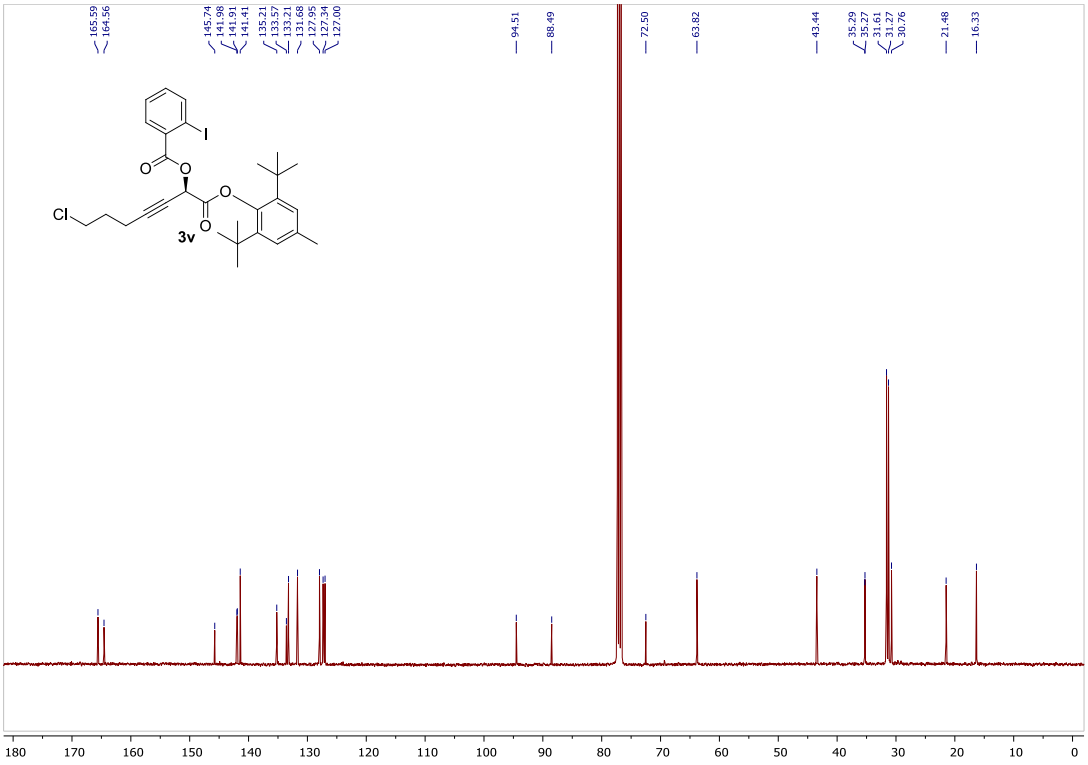
IR of compound **3u**



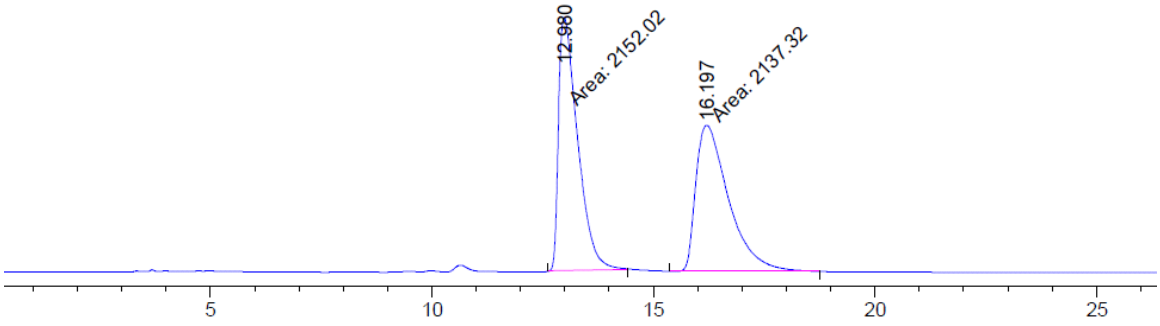
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3v**



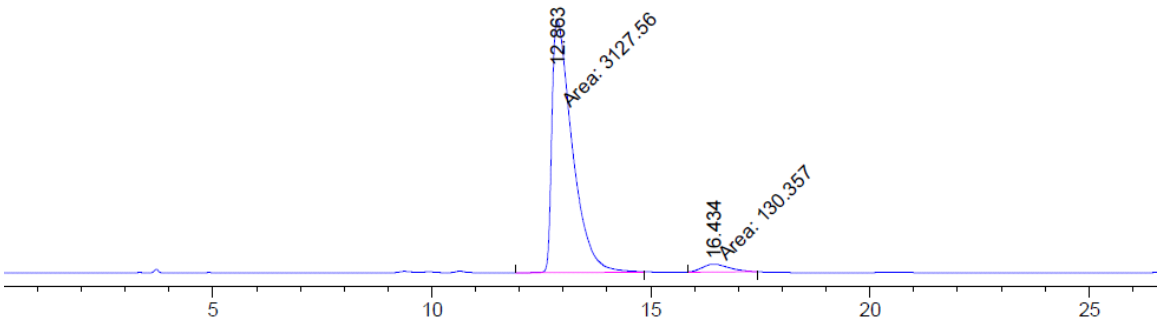
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3v**



HPLC of compound **3v**



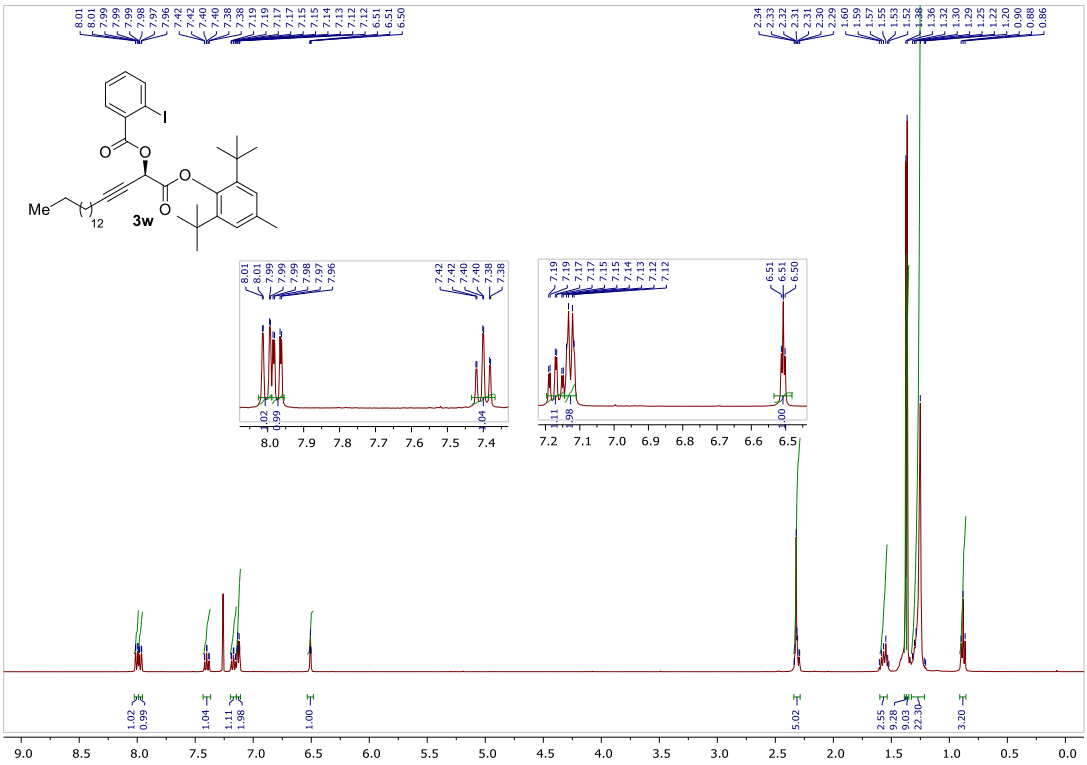
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.980	MM	0.4980	2152.01904	72.02358	50.1713
2	16.197	MM	0.8582	2137.32422	41.50692	49.8287



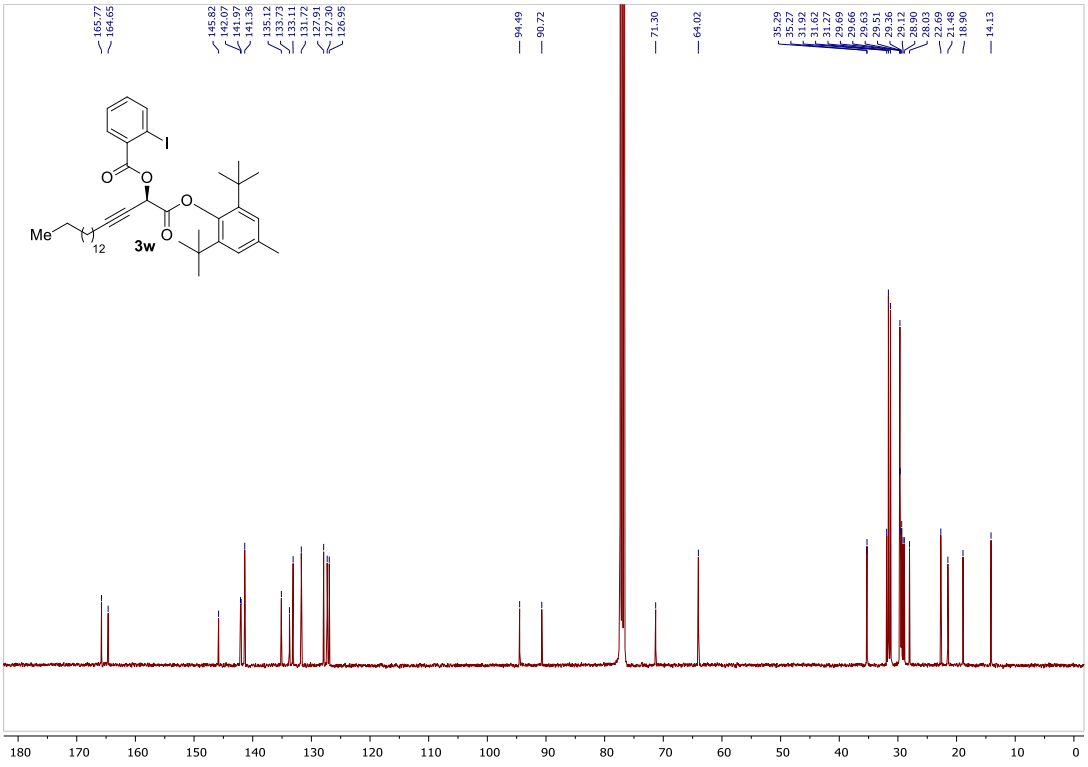
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.863	MM	0.5394	3127.56006	96.62812	95.9988
2	16.434	MM	0.7331	130.35664	2.96369	4.0012

IR of compound **3v**

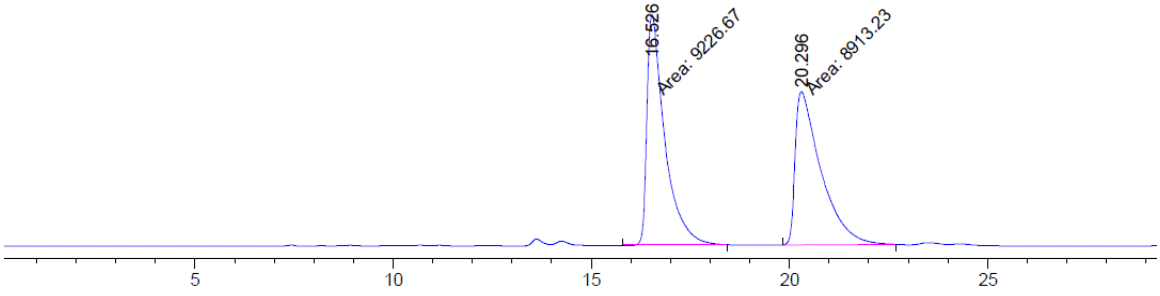
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3w**



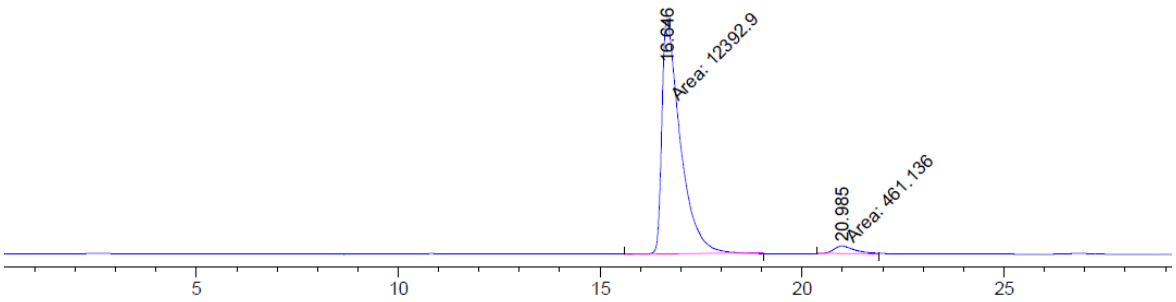
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3w**



HPLC of compound **3w**

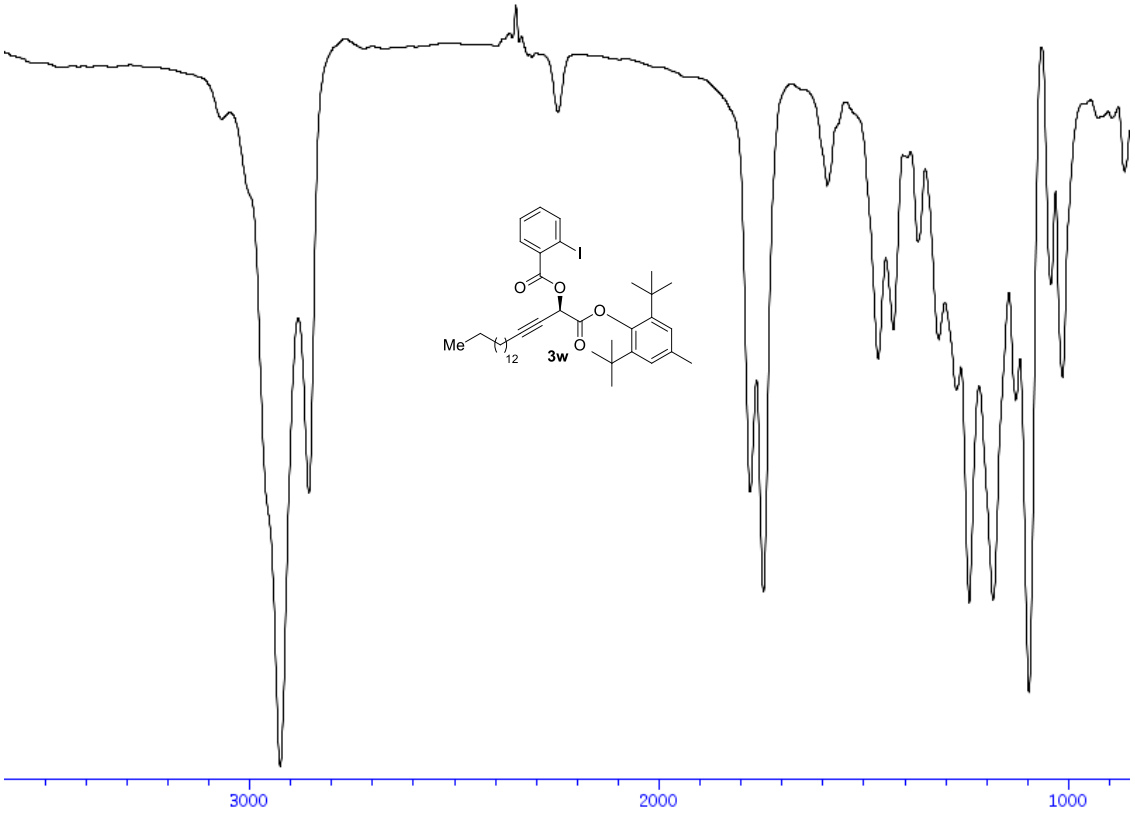


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.526	MM	0.5197	9226.67188	295.90186	50.8640
2	20.296	MM	0.7544	8913.22949	196.90375	49.1360

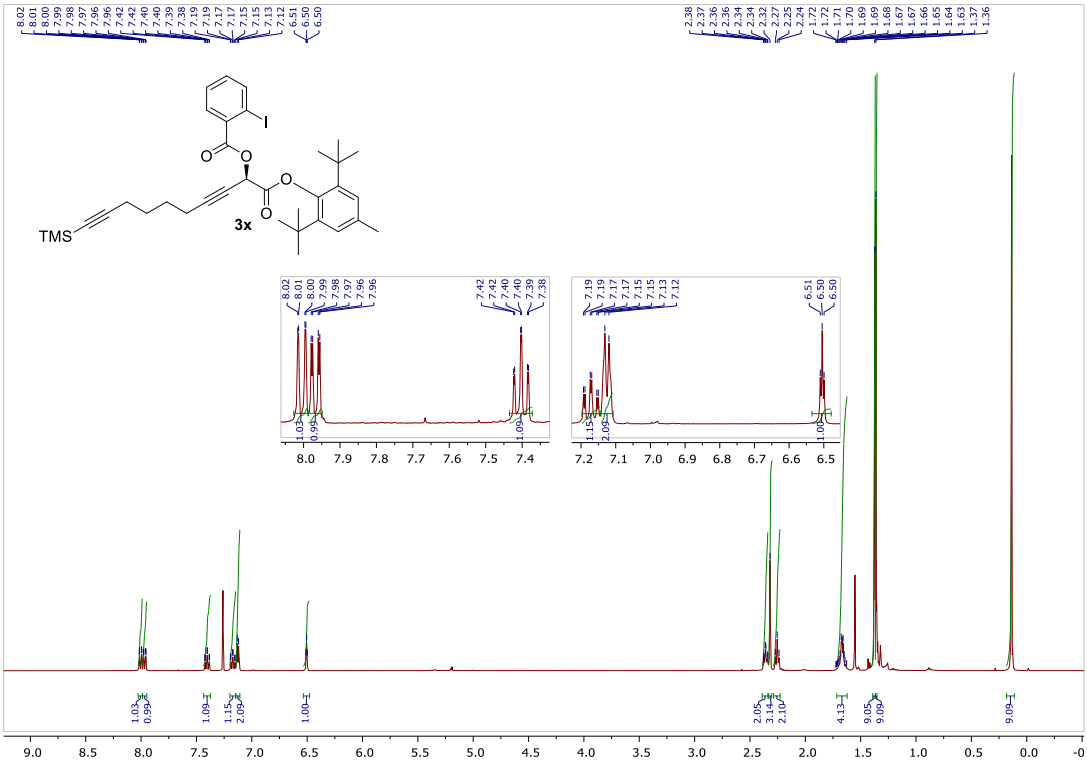


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.646	MM	0.5272	1.23929e4	391.78439	96.4125
2	20.985	MM	0.6259	461.13568	12.27846	3.5875

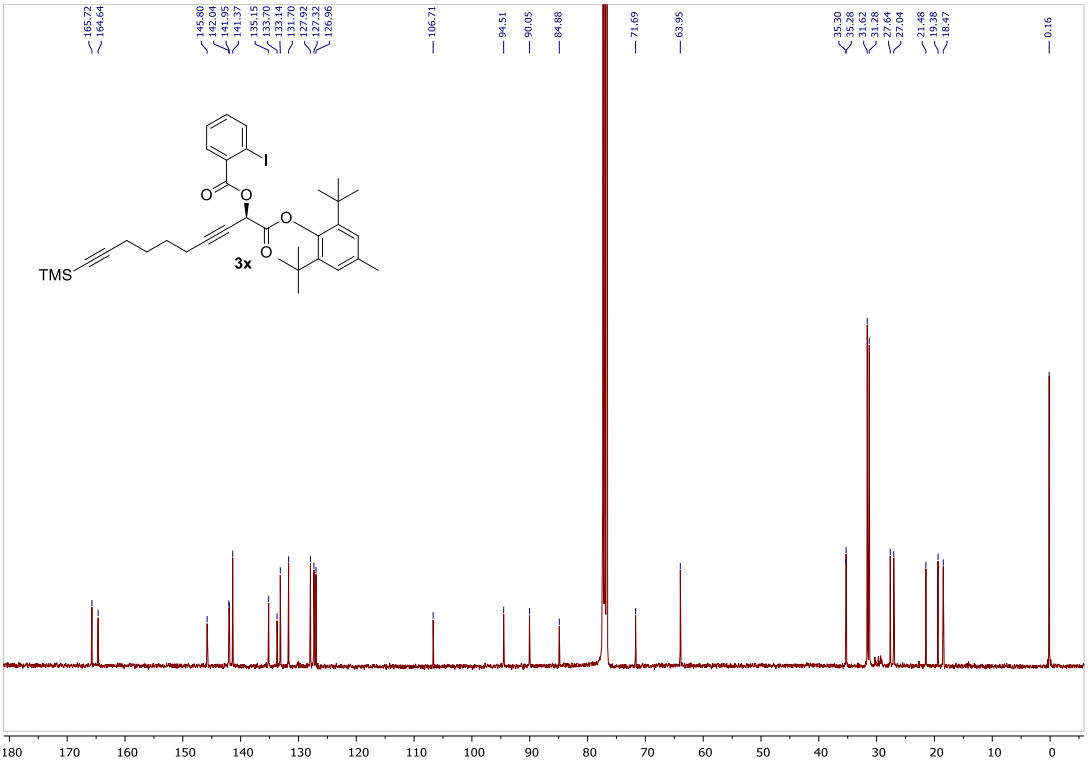
IR of compound **3w**



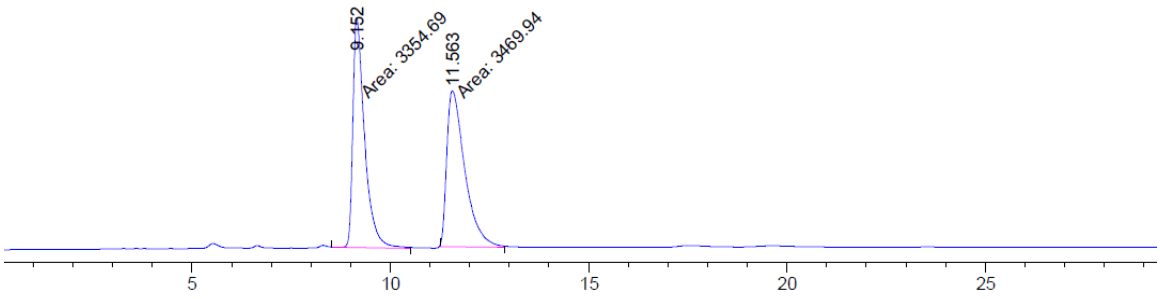
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3x**



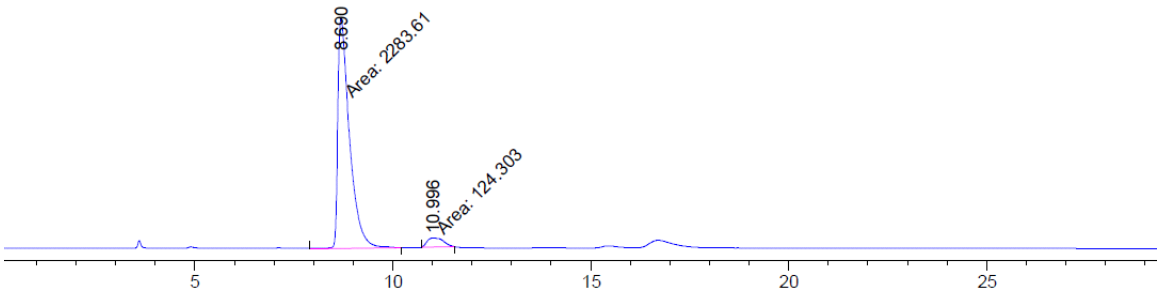
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3x**



HPLC of compound **3x**

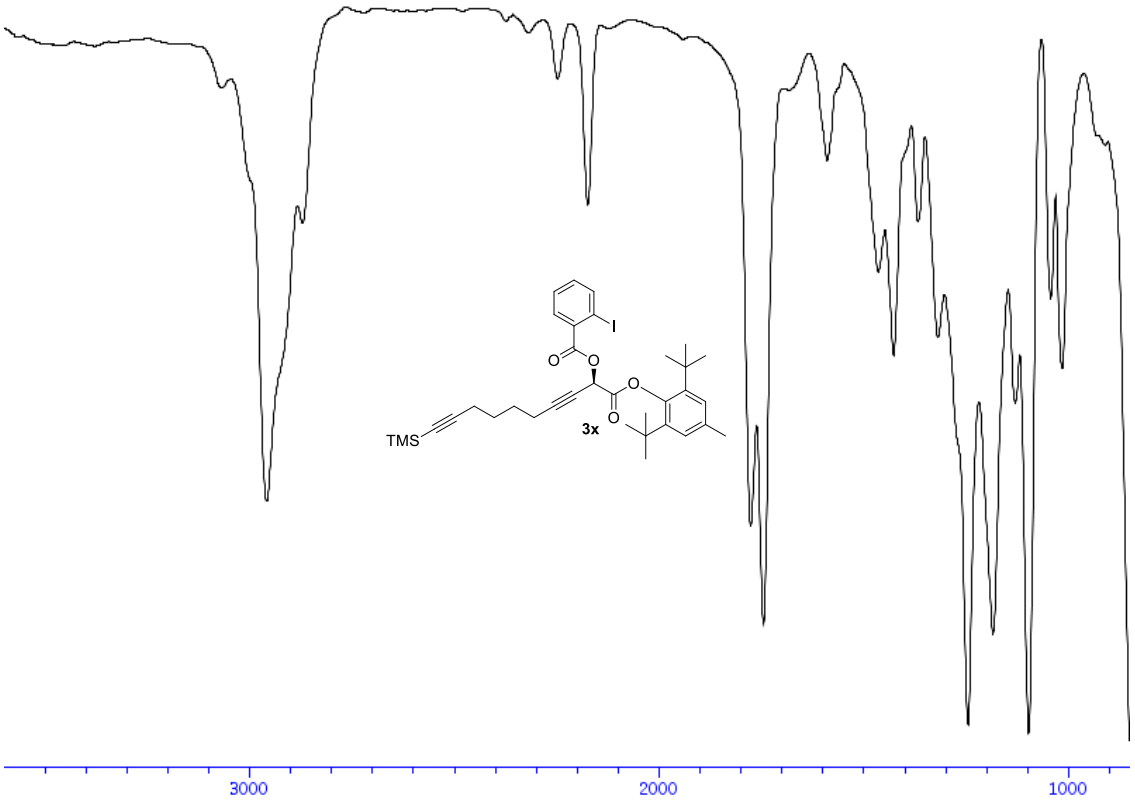


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.152	MM	0.3442	3354.68921	162.45605	49.1556
2	11.563	MM	0.5250	3469.94458	110.15355	50.8444

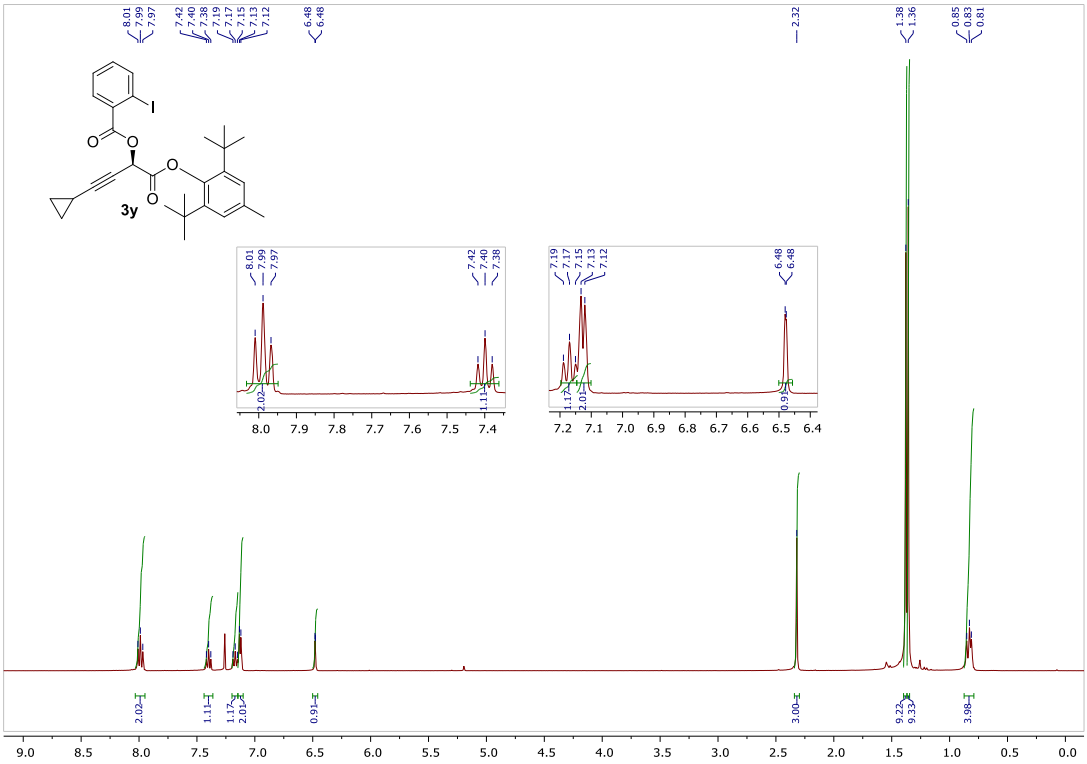


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.690	MM	0.3430	2283.60596	110.96562	94.8377
2	10.996	MM	0.4781	124.30341	4.33306	5.1623

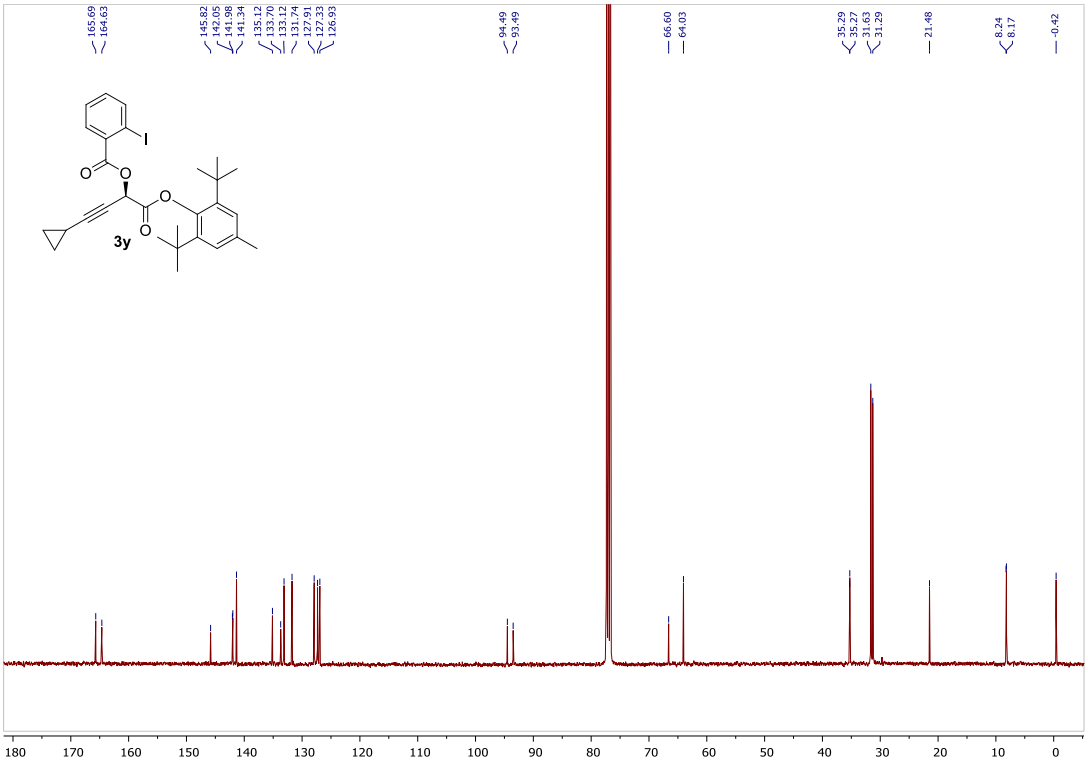
IR of compound **3x**



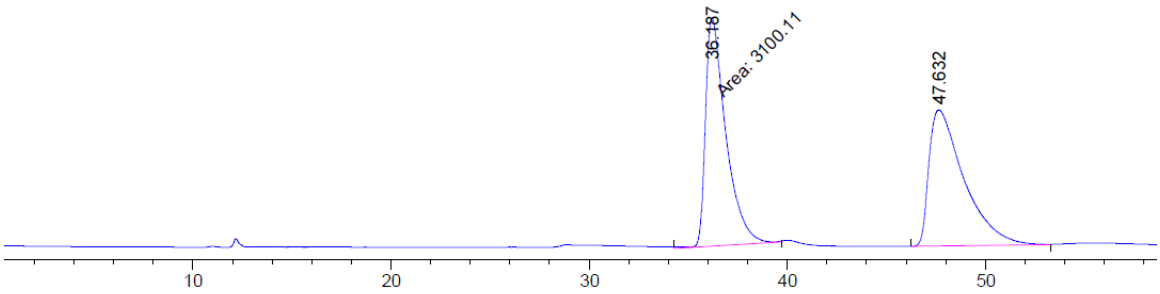
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3y**



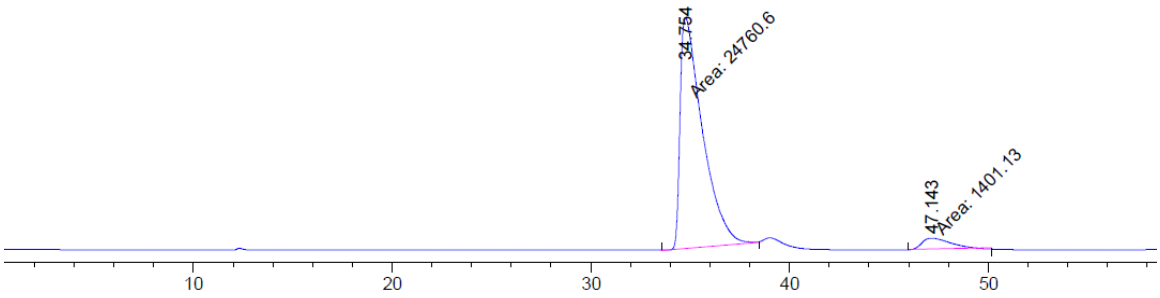
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3y**



HPLC of compound **3y**

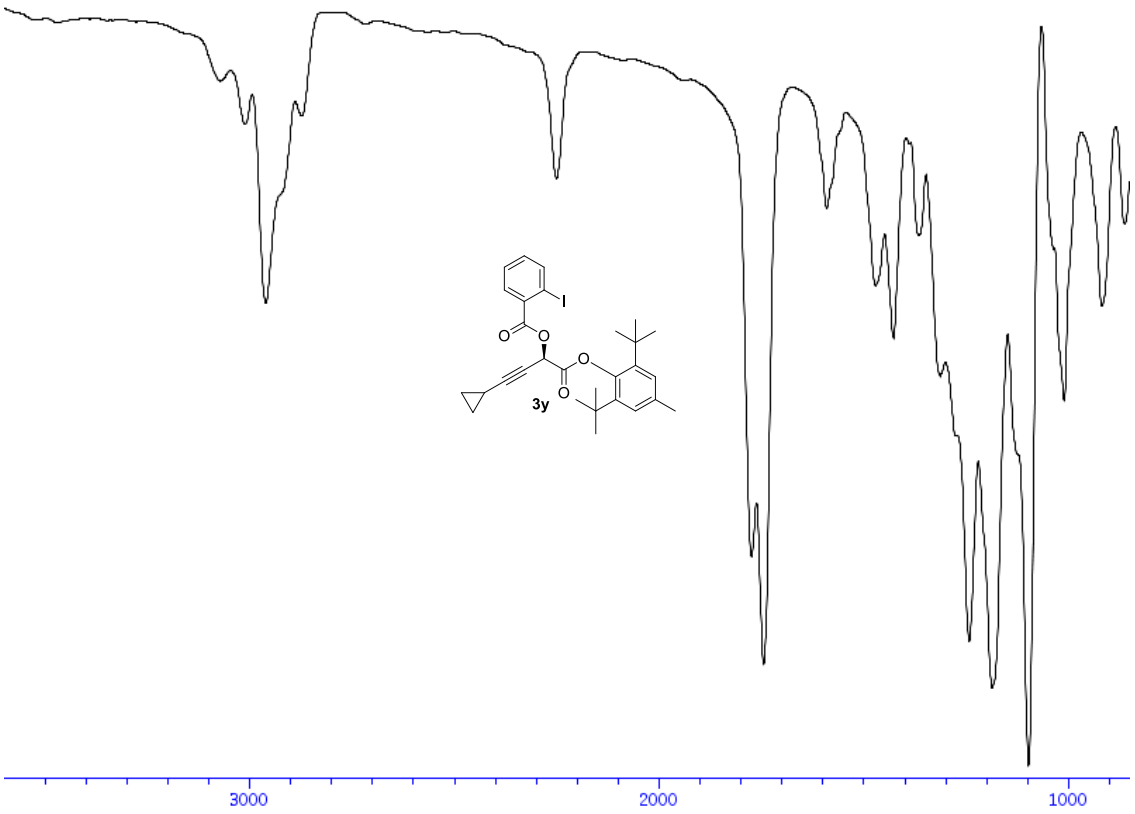


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.187	MM	1.1902	3100.11206	43.41235	49.4924
2	47.632	BB	1.7160	3163.70801	25.81199	50.5076

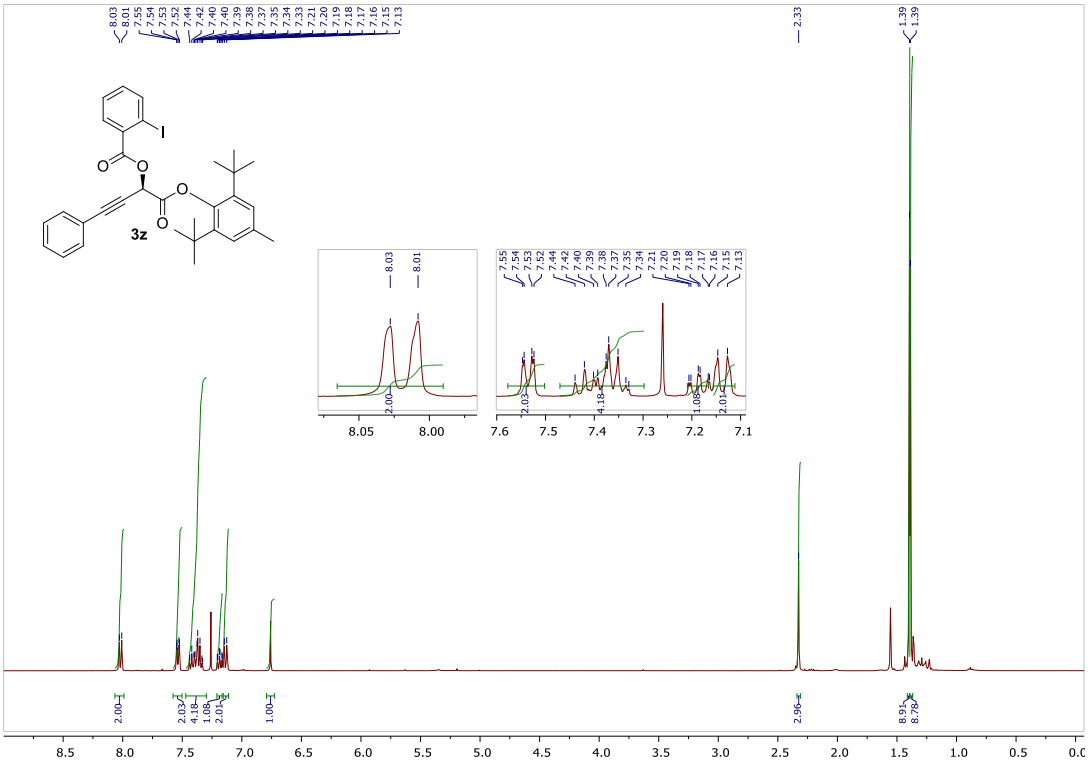


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.754	MM	1.3018	2.47606e4	317.00549	94.6443
2	47.143	MM	1.5879	1401.13440	14.70628	5.3557

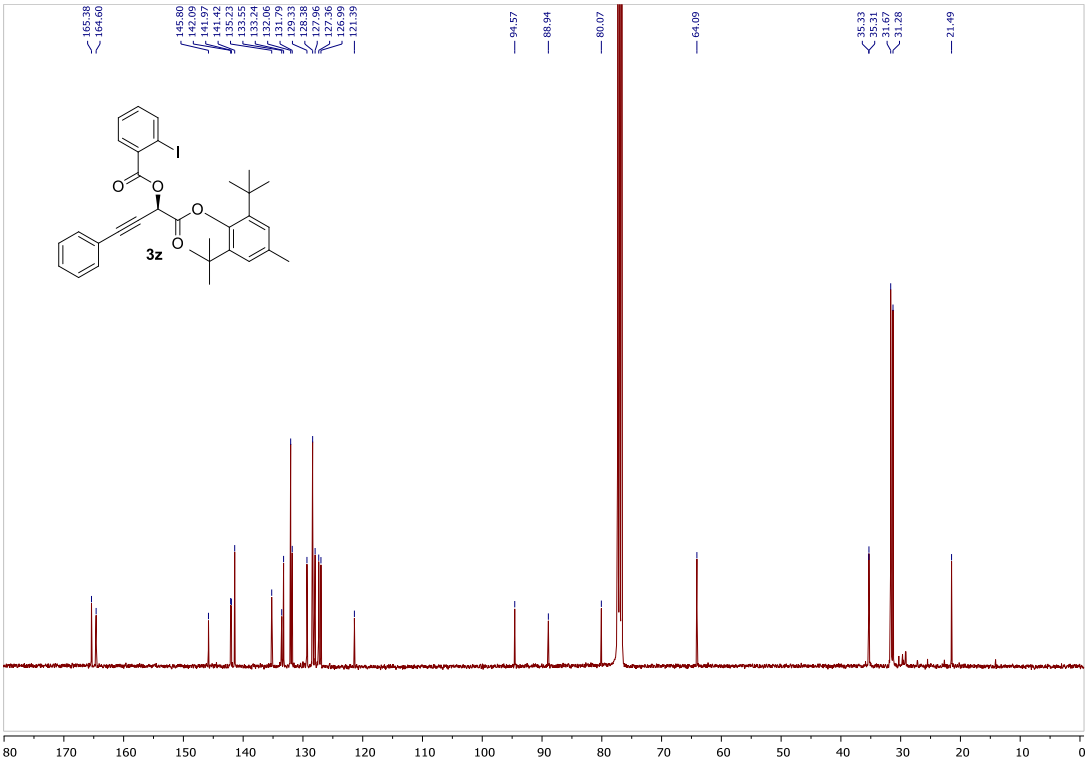
IR of compound **3y**



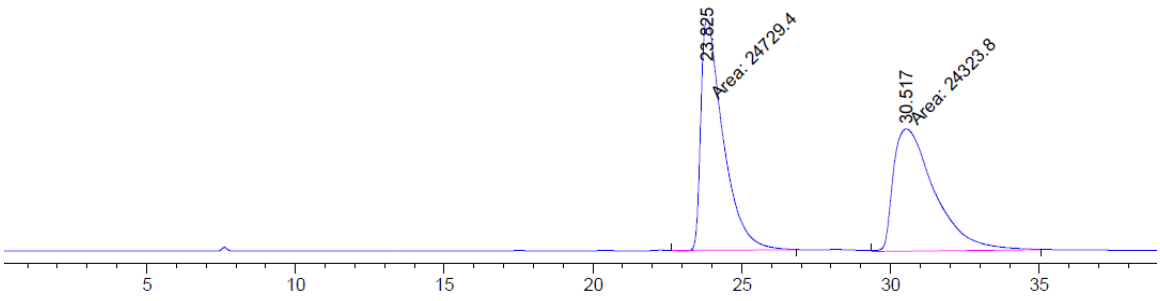
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3z**



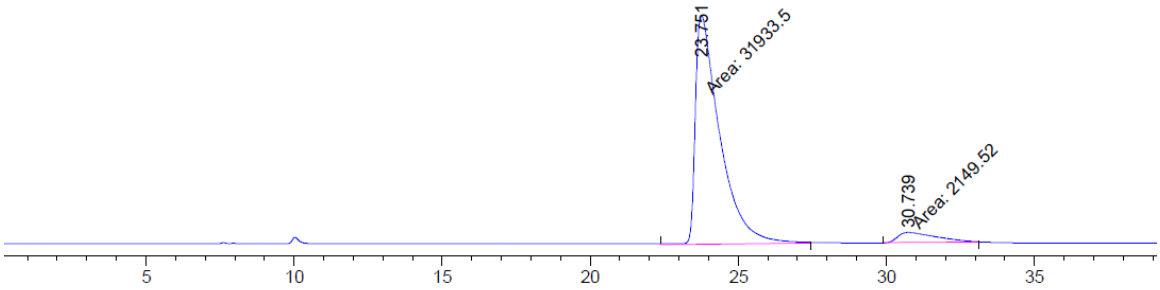
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3z**



HPLC of compound **3z**

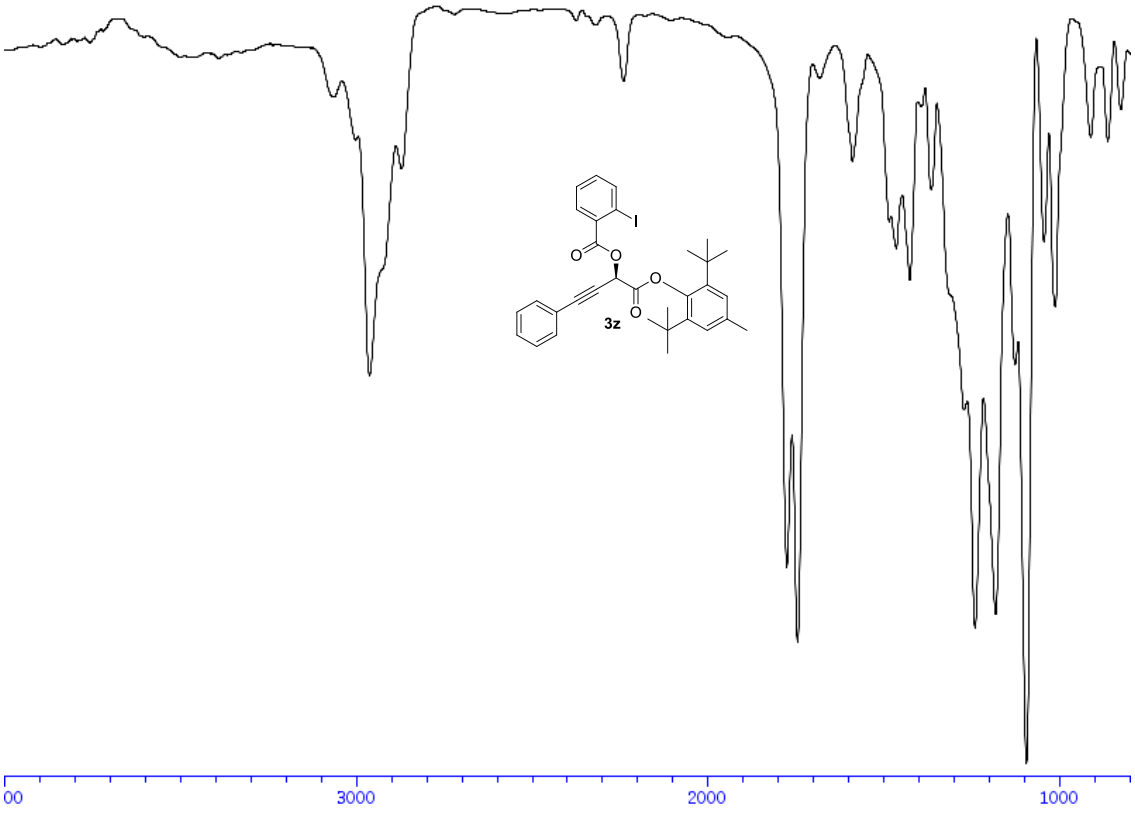


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.825	MM	0.8655	2.47294e4	476.20676	50.4134
2	30.517	MM	1.6116	2.43238e4	251.55571	49.5866

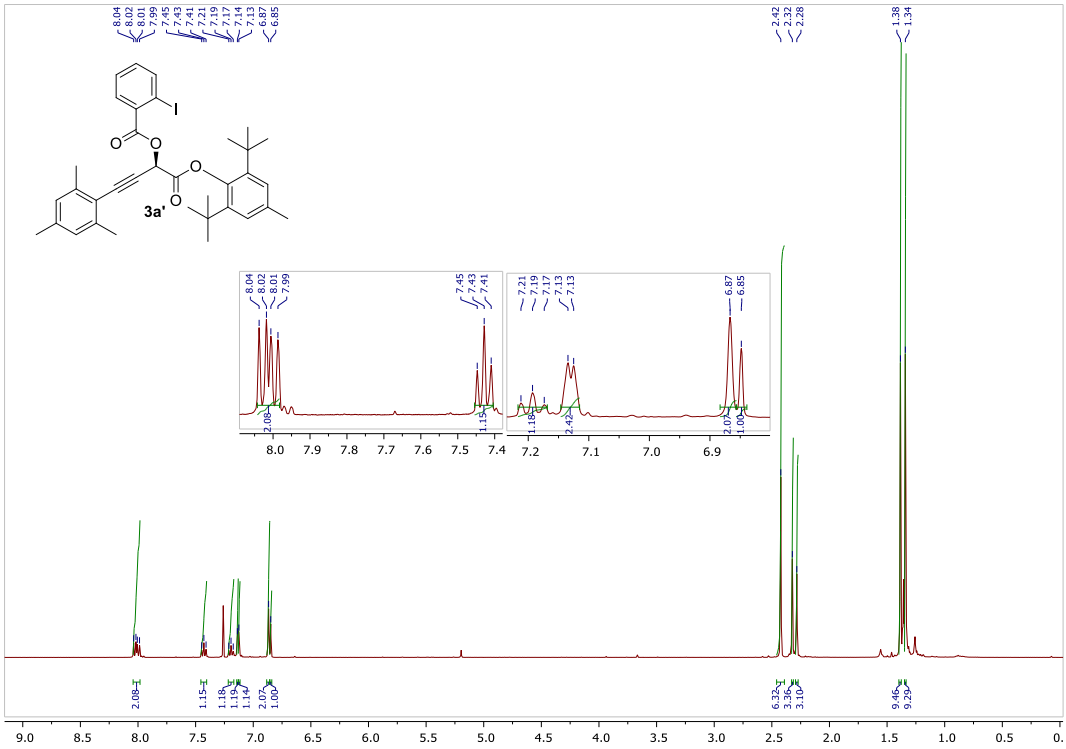


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.751	MM	0.9585	3.19335e4	555.26276	93.6933
2	30.739	MM	1.4983	2149.52466	23.91120	6.3067

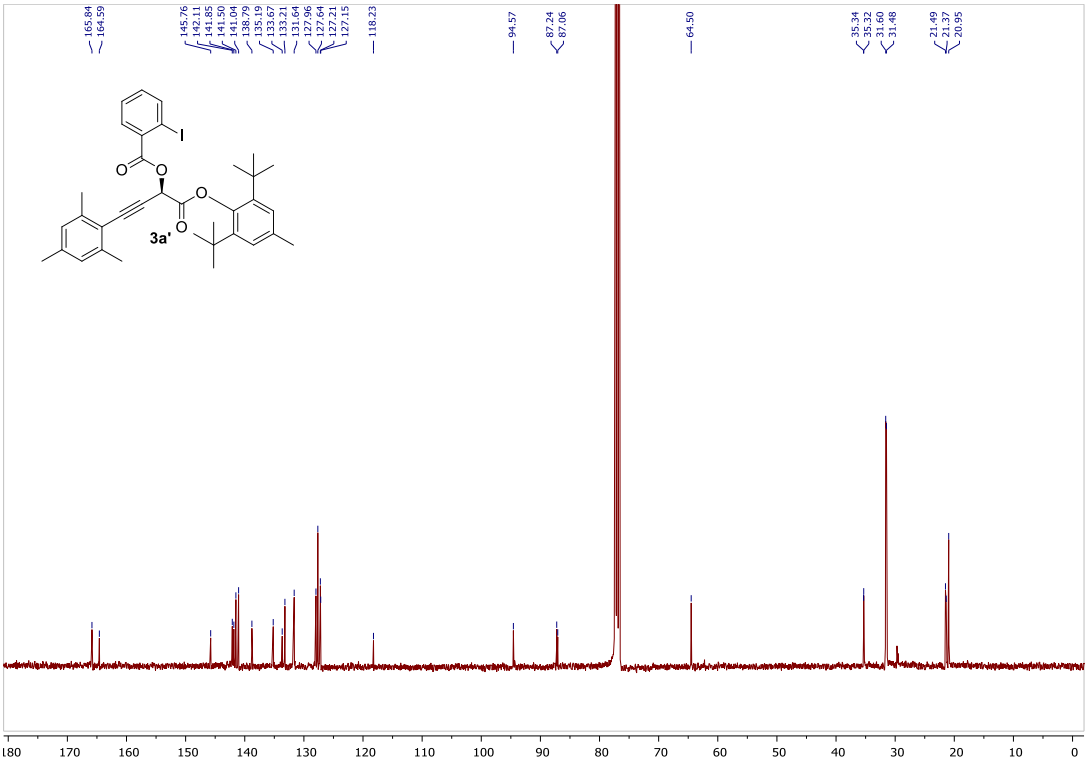
IR of compound **3z**



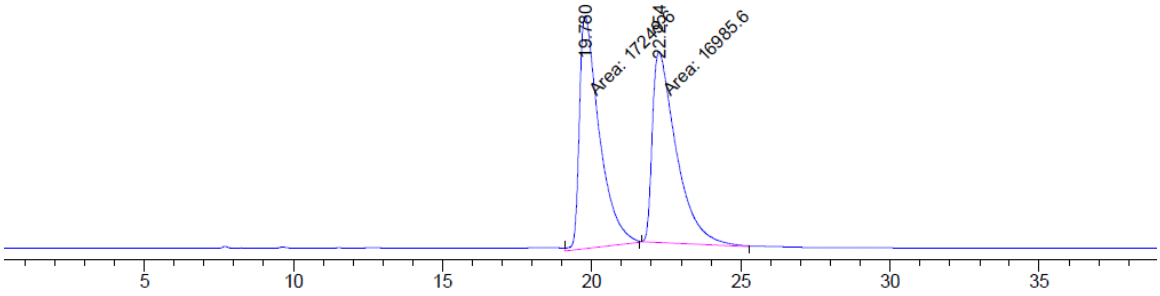
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3a'**



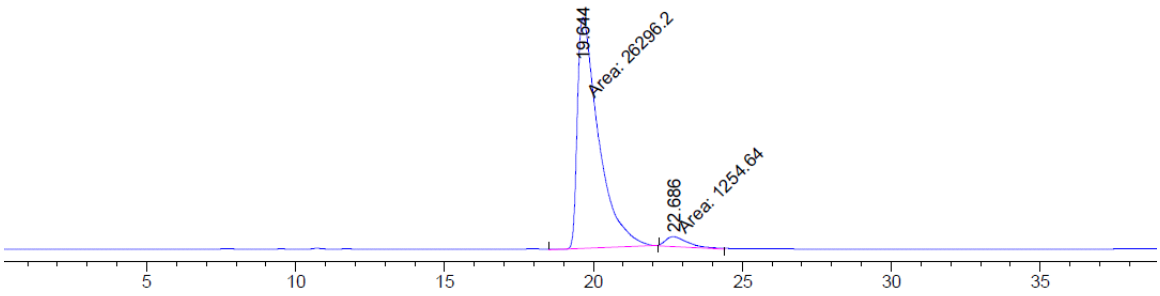
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3a'**



HPLC of compound **3a'**

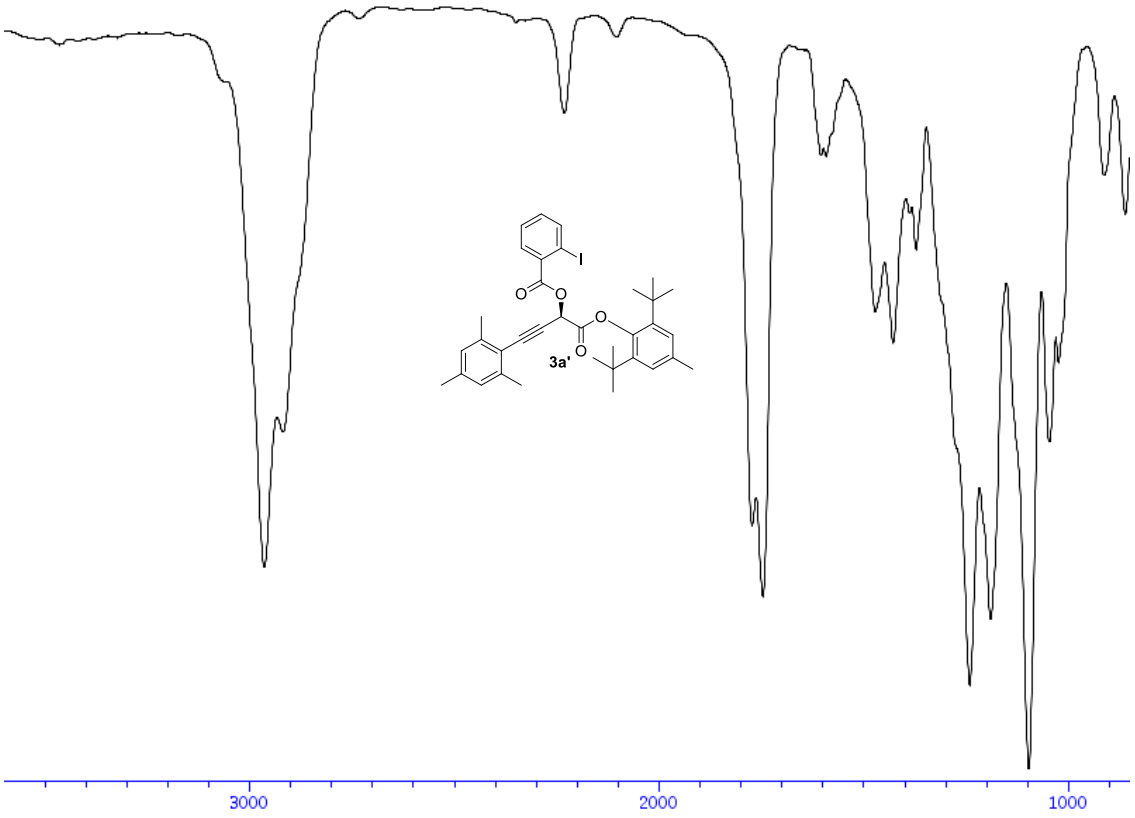


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.780	MM	0.7715	1.72496e4	372.64279	50.3855
2	22.254	MM	0.9279	1.69856e4	305.10339	49.6145

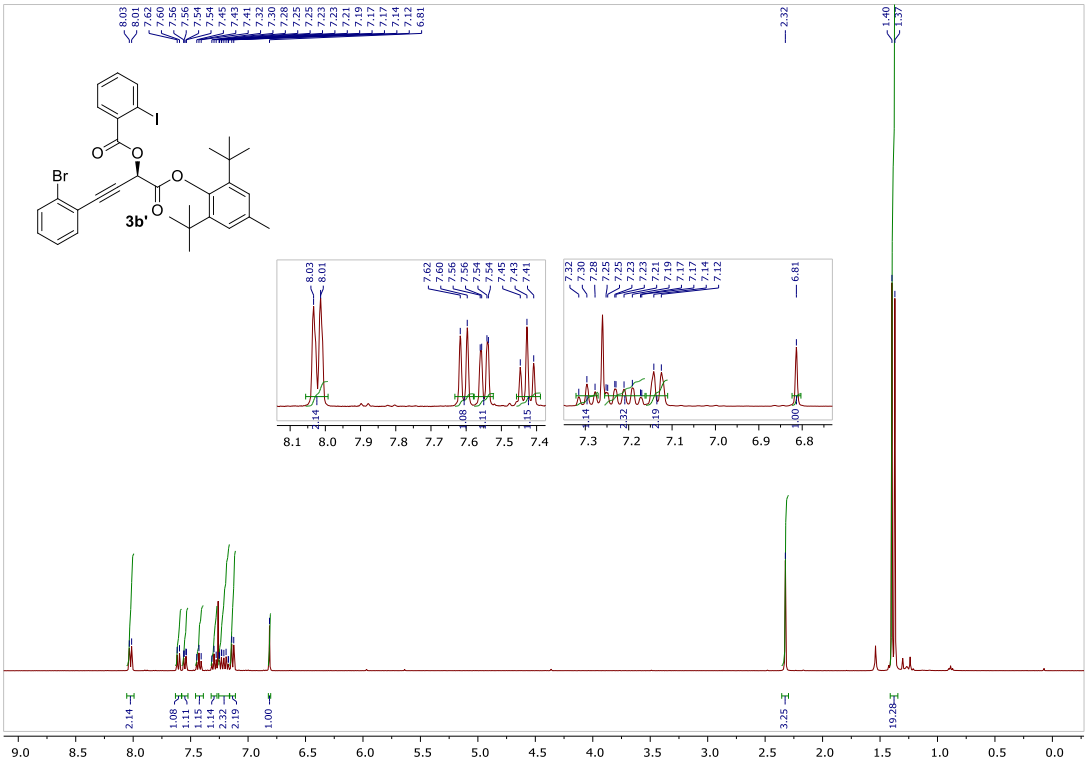


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.644	MM	0.8265	2.62962e4	530.26599	95.4461
2	22.686	MM	0.9022	1254.64221	23.17749	4.5539

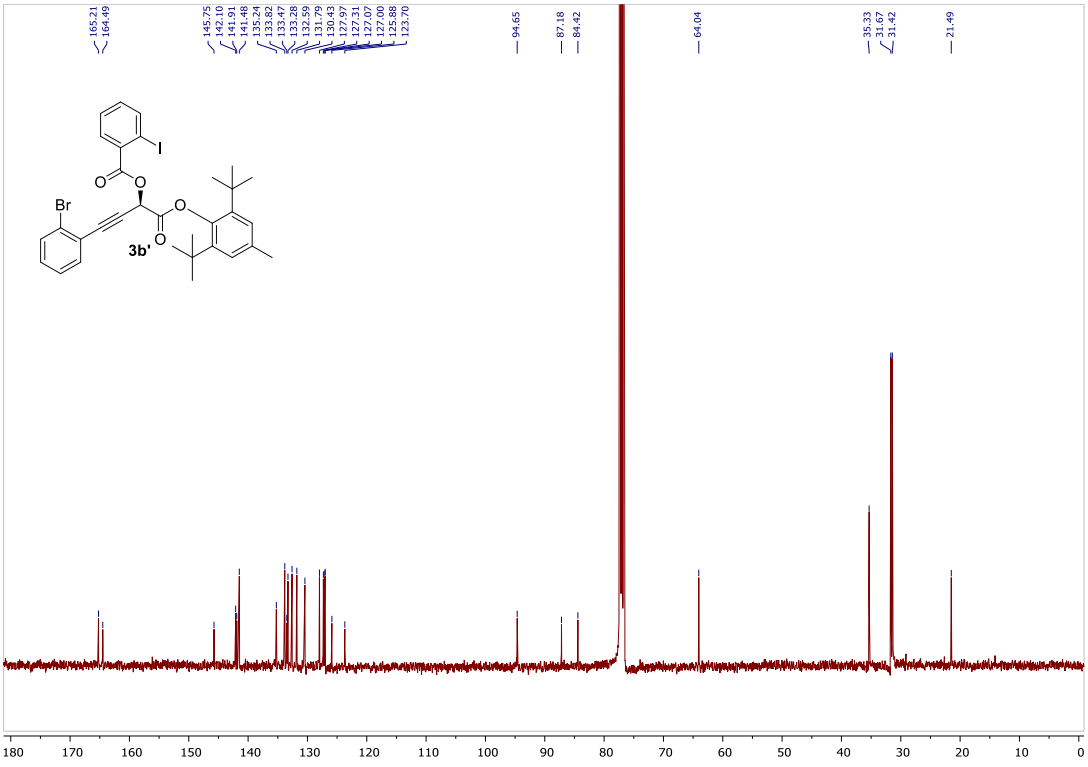
IR of compound **3a'**



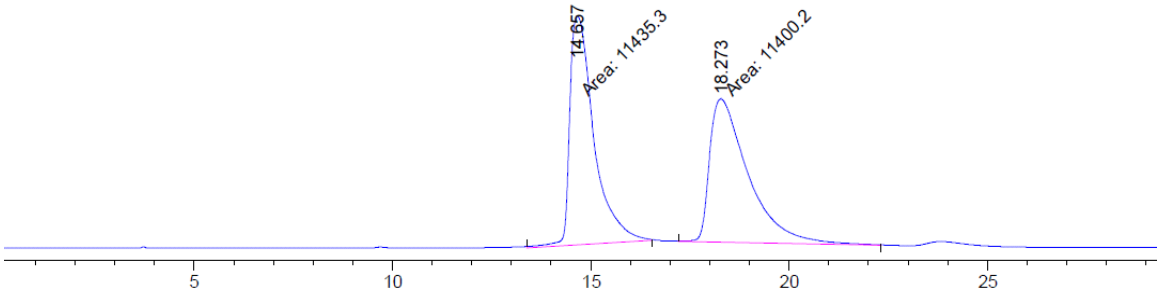
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3b'**



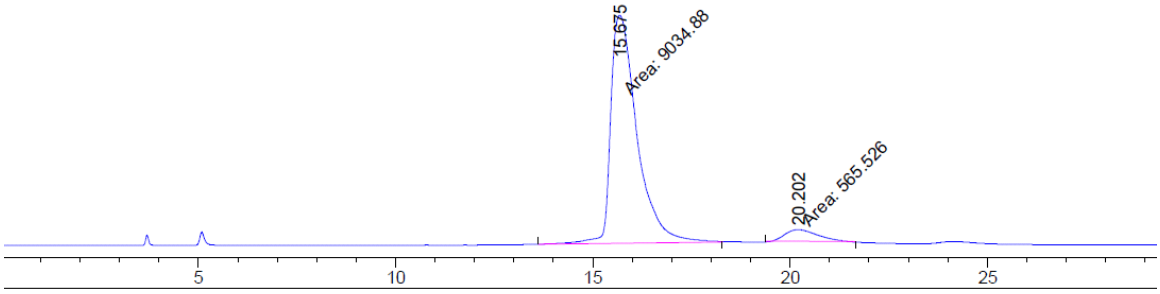
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3b'**



HPLC of compound **3b'**

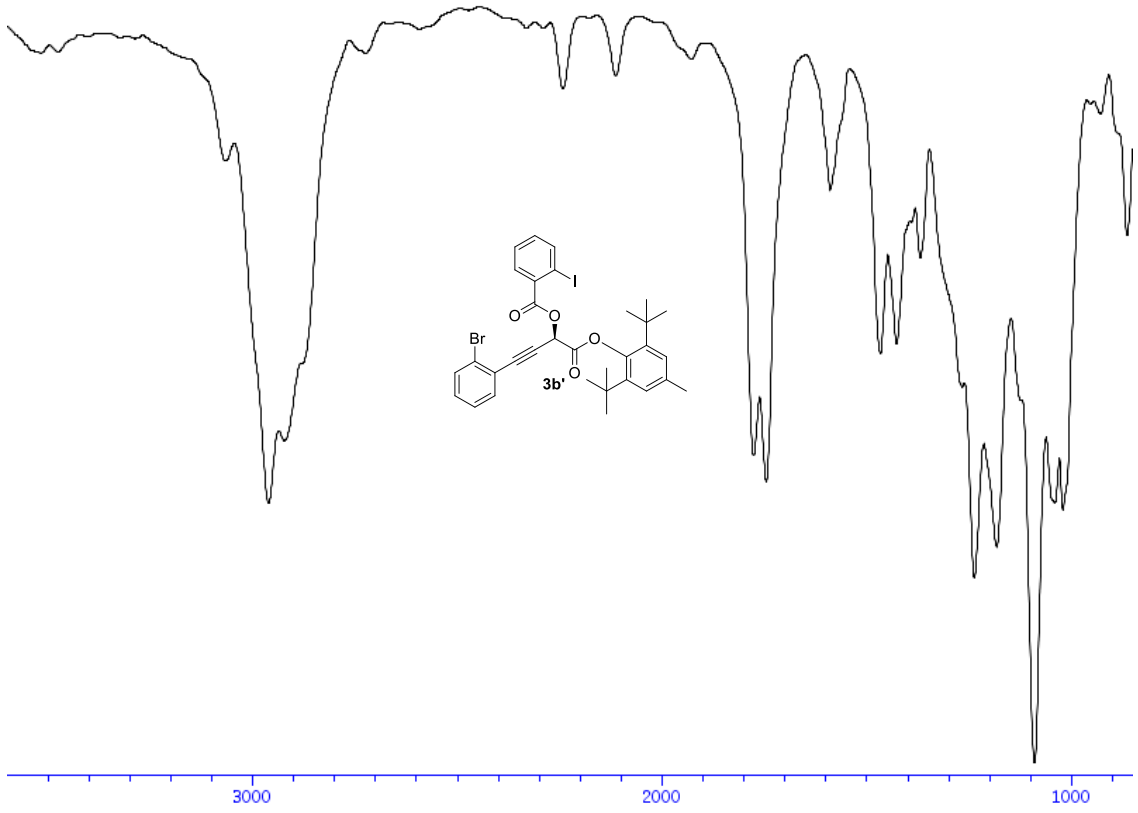


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.657	MM	0.7064	1.14353e4	269.80692	50.0768
2	18.273	MM	1.1262	1.14002e4	168.71158	49.9232

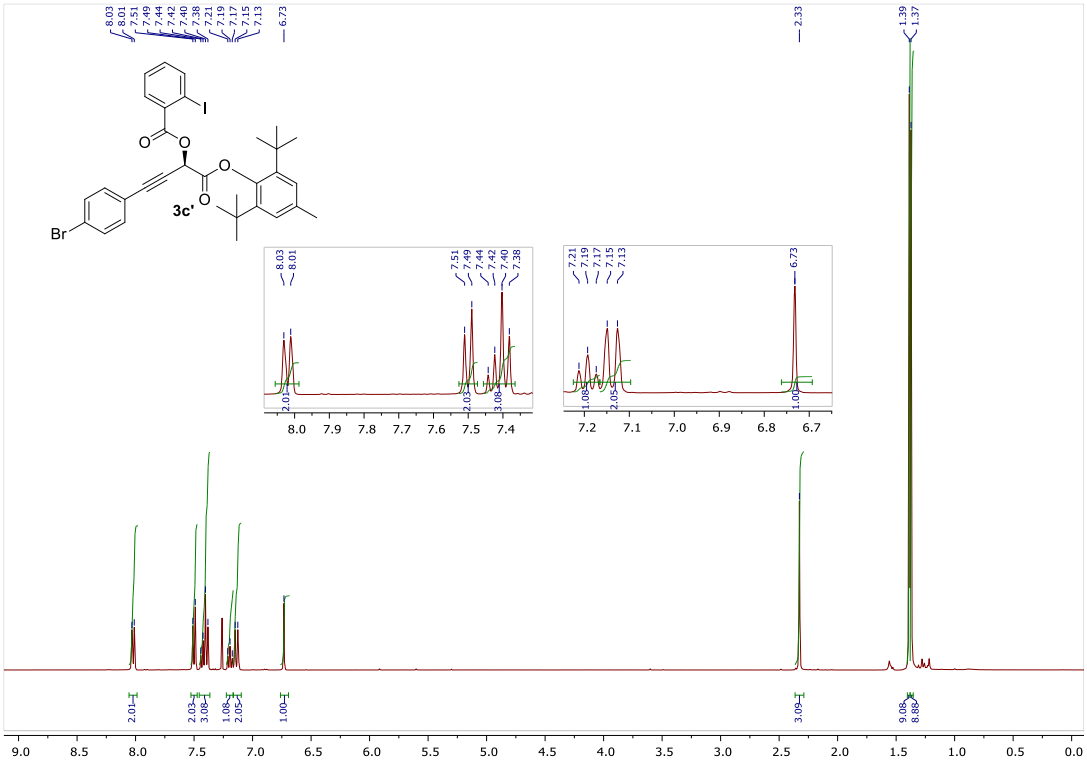


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.675	MM	0.7748	9034.88184	194.35129	94.1094
2	20.202	MM	0.9468	565.52563	9.95541	5.8906

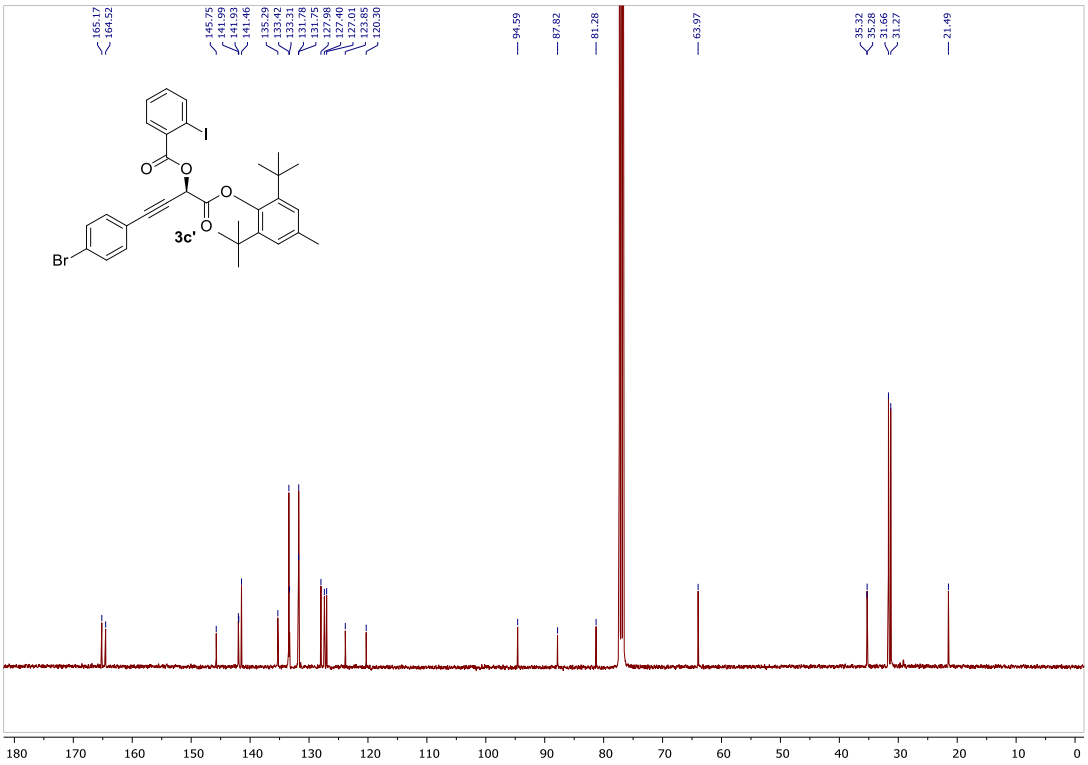
IR of compound **3b'**



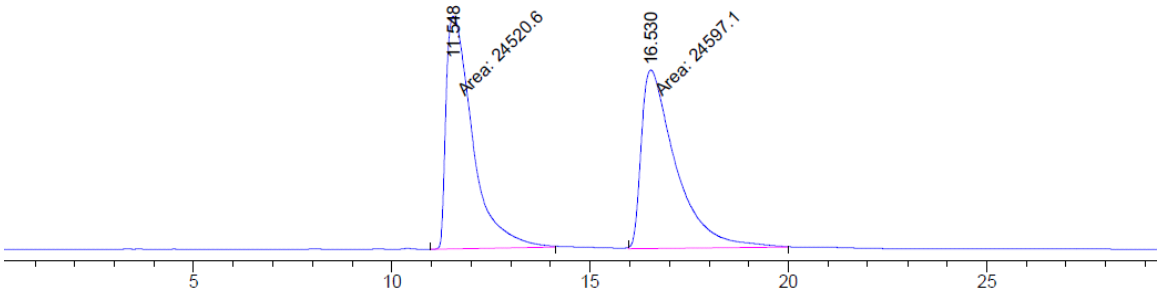
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **3c'**



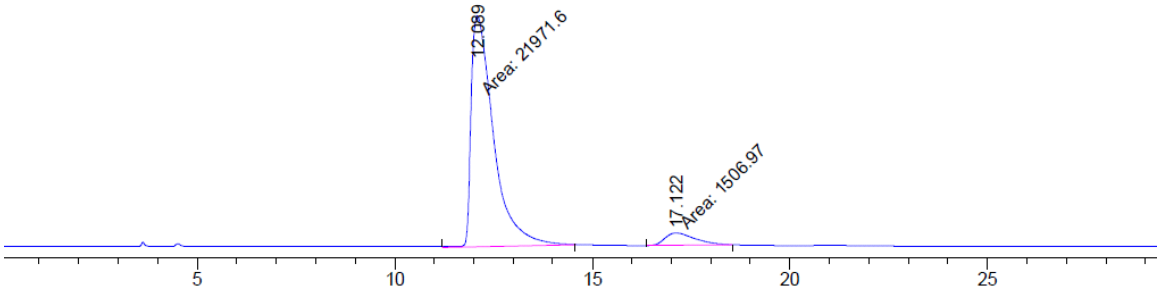
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **3c'**



HPLC of compound **3c'**

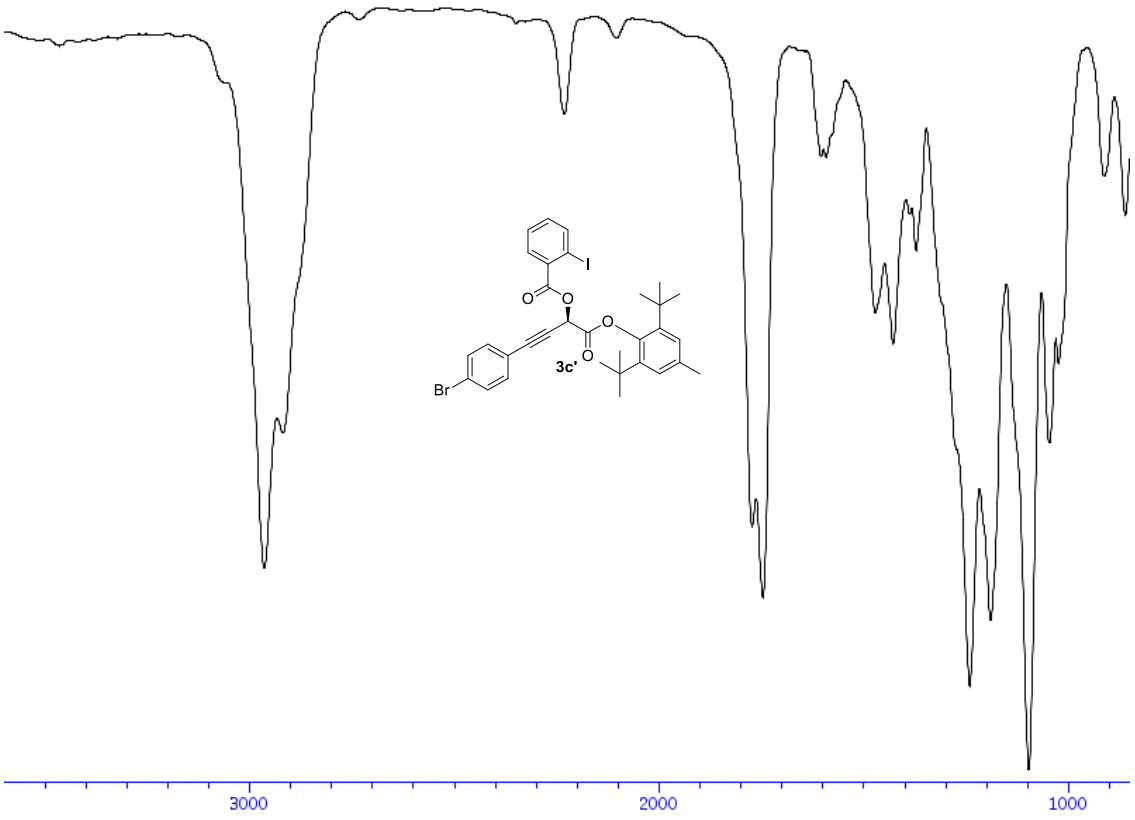


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.548	MM	0.7750	2.45206e4	527.31091	49.9221
2	16.530	MM	1.0133	2.45971e4	404.57532	50.0779

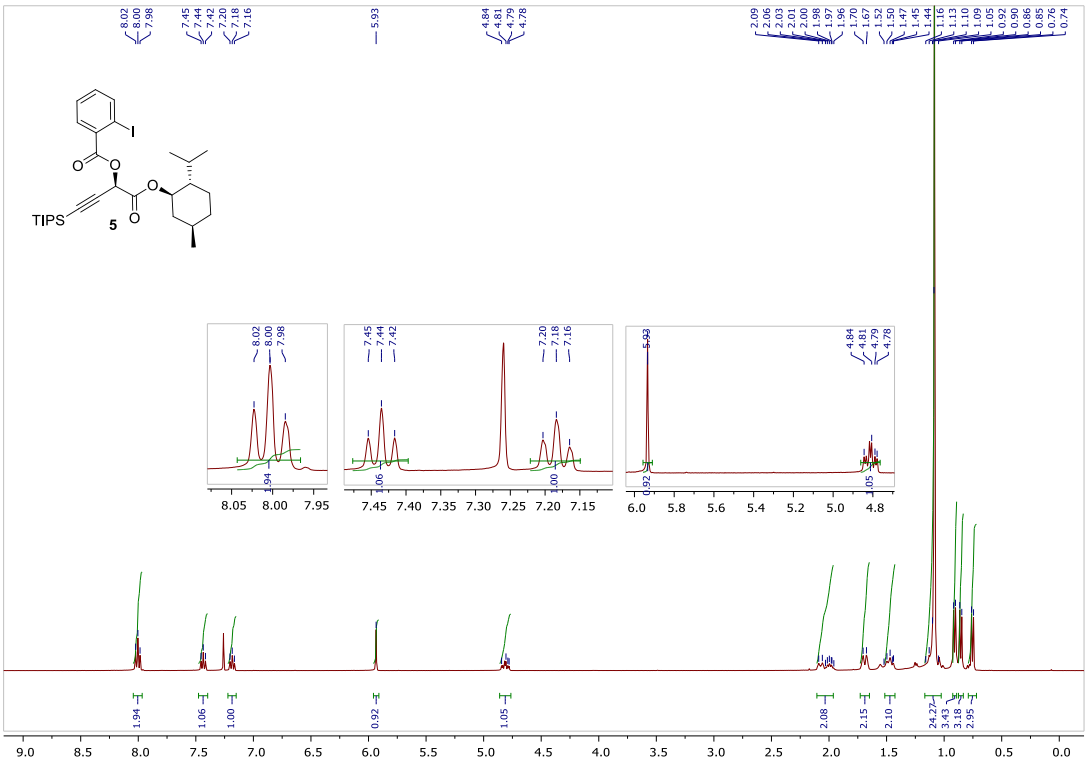


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.089	MM	0.6585	2.19716e4	556.14374	93.5815
2	17.122	MM	0.8669	1506.96521	28.97096	6.4185

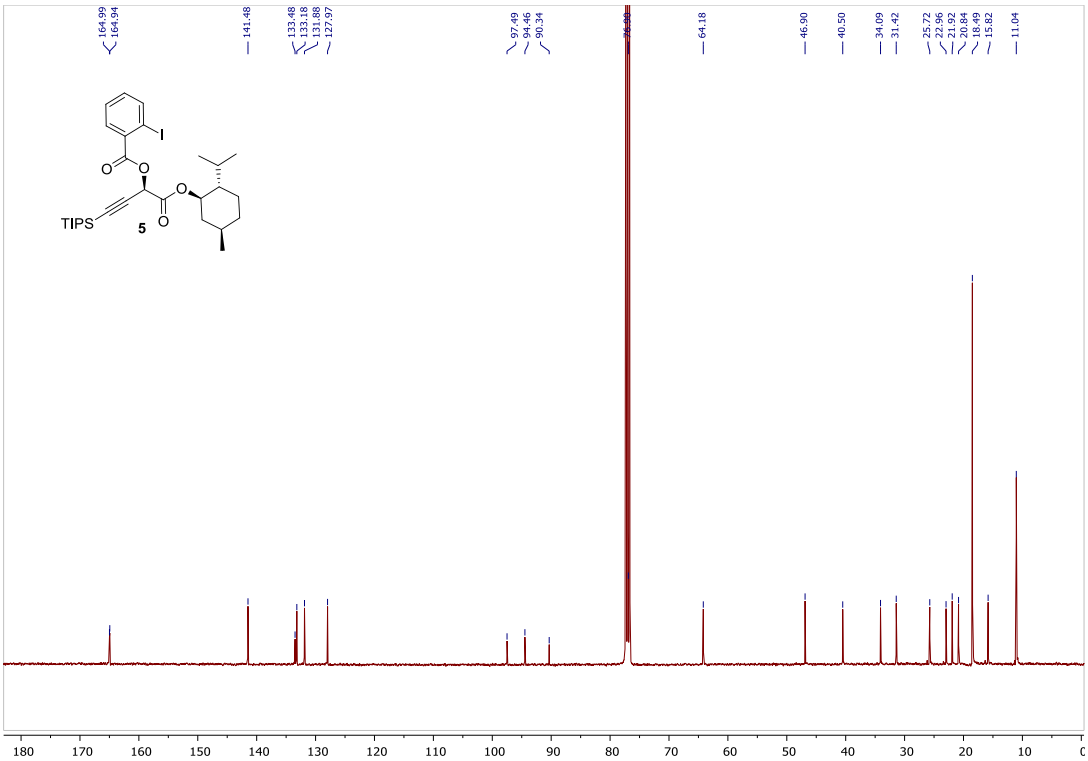
IR of compound **3c'**



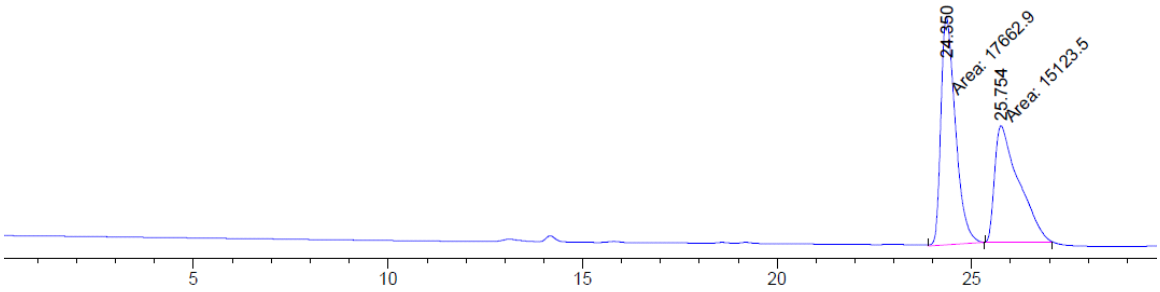
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **5**



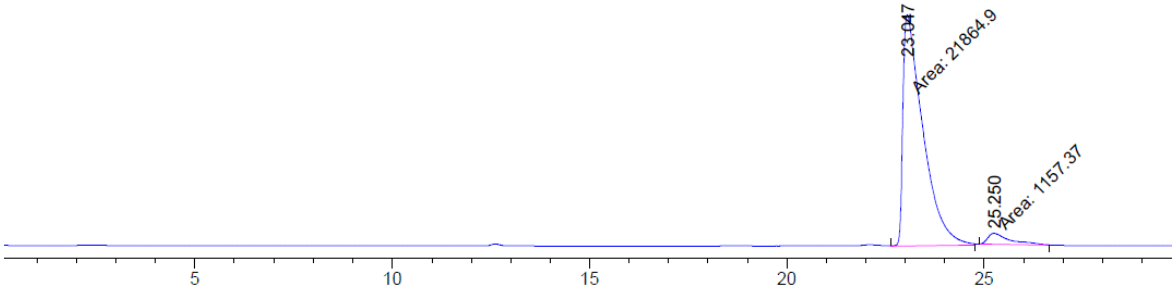
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **5**



HPLC of compound **5**

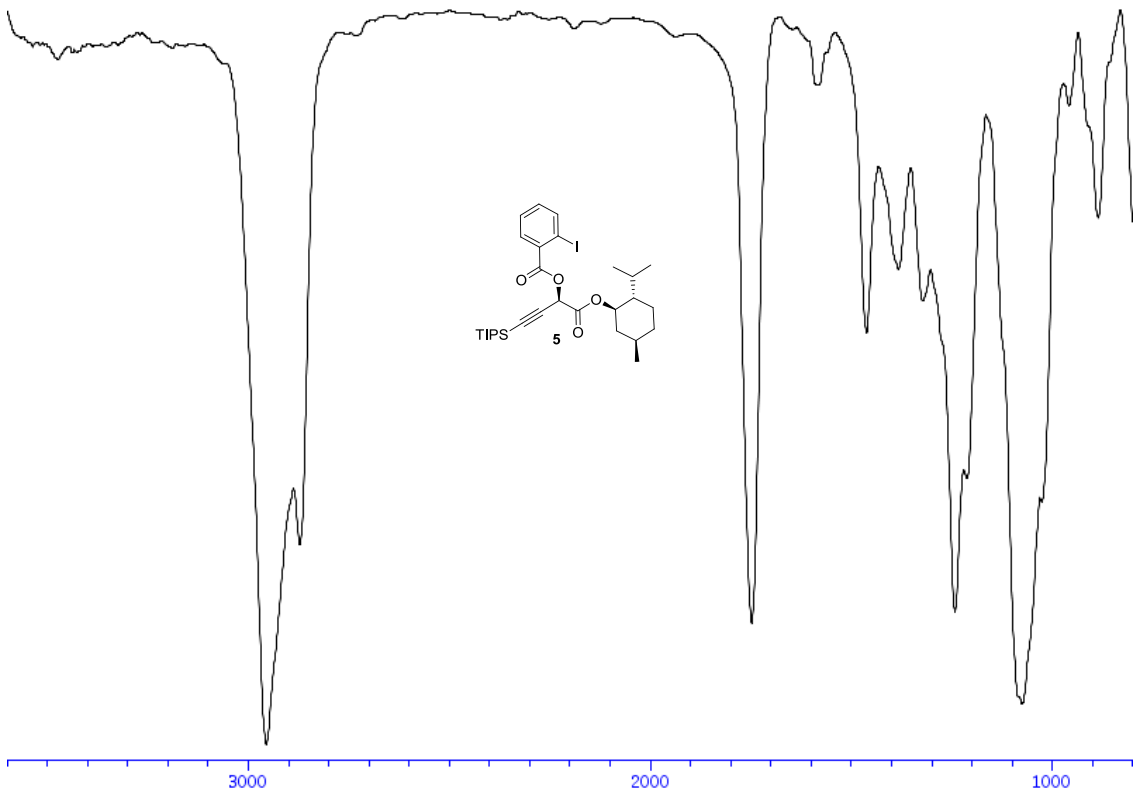


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.350	MM	0.4302	1.76629e4	684.30103	53.8726
2	25.754	MM	0.7216	1.51235e4	349.31091	46.1274

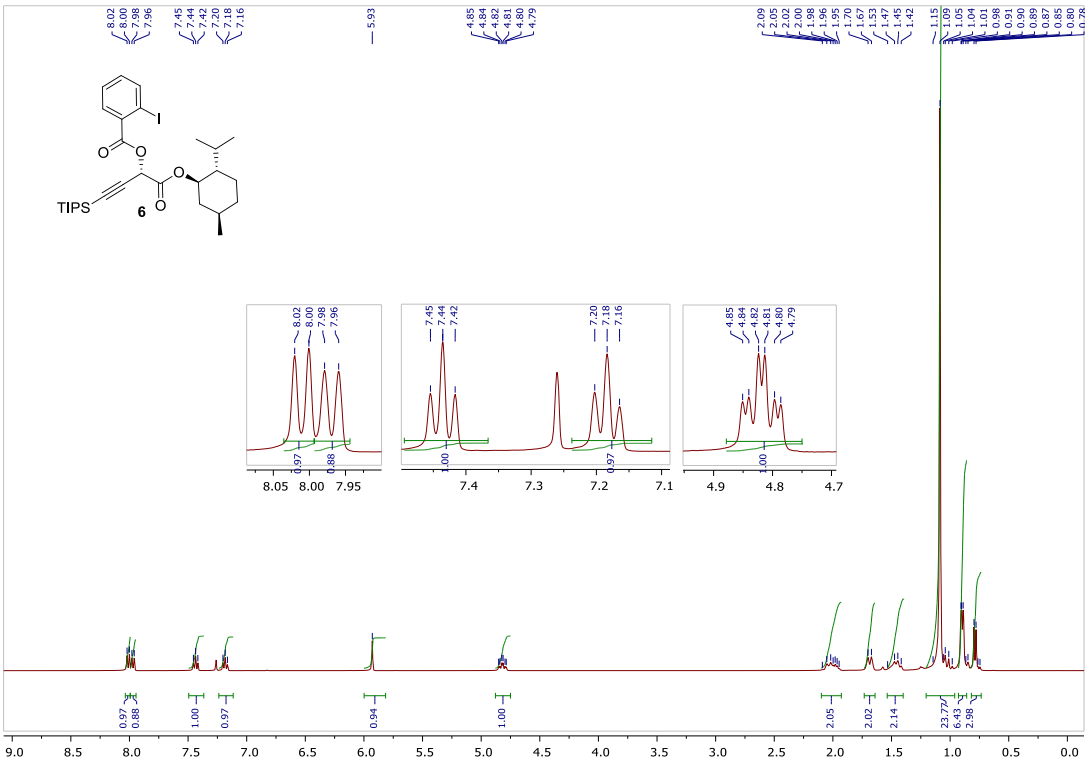


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.047	MM	0.5856	2.18649e4	622.31567	94.9728
2	25.250	MM	0.6533	1157.37305	29.52432	5.0272

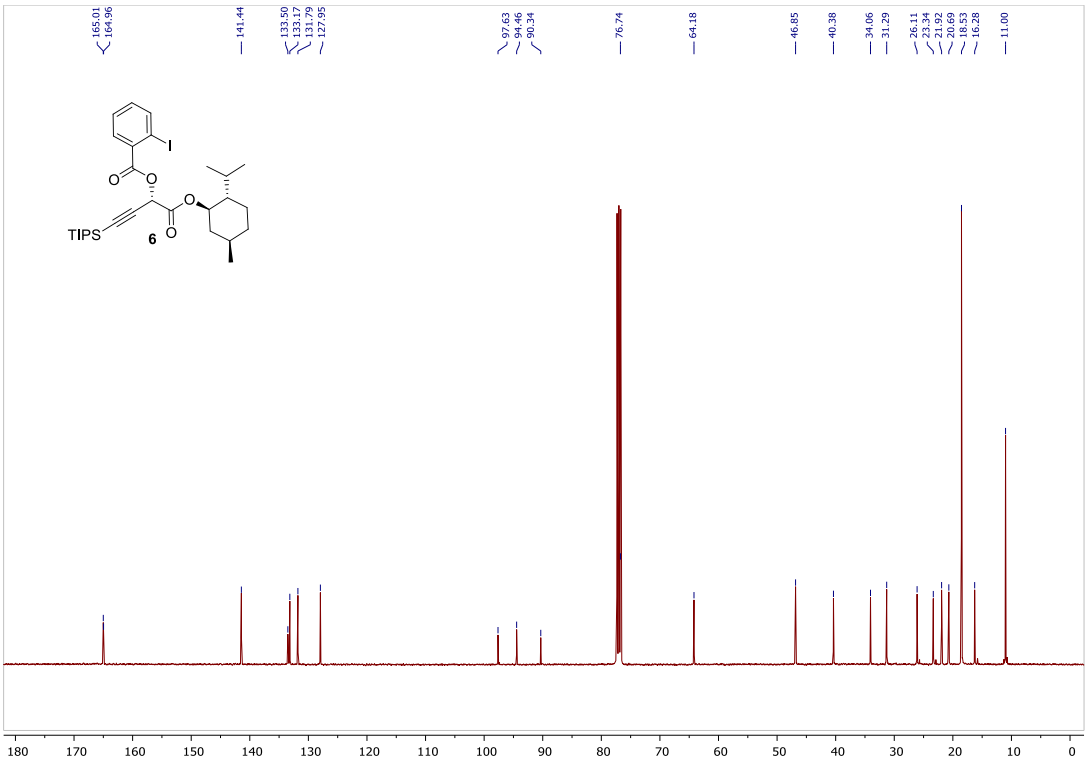
IR of compound **5**



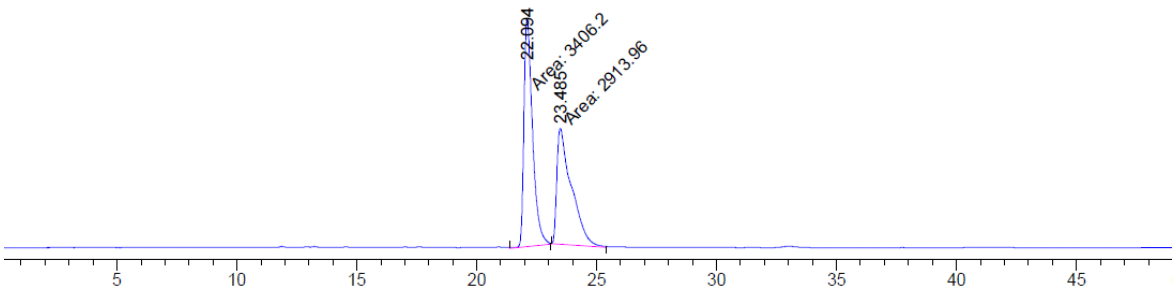
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **6**



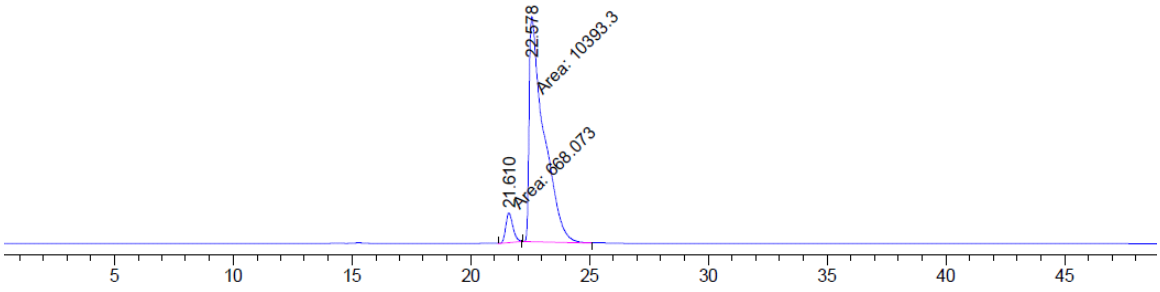
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **6**



HPLC of compound **6**

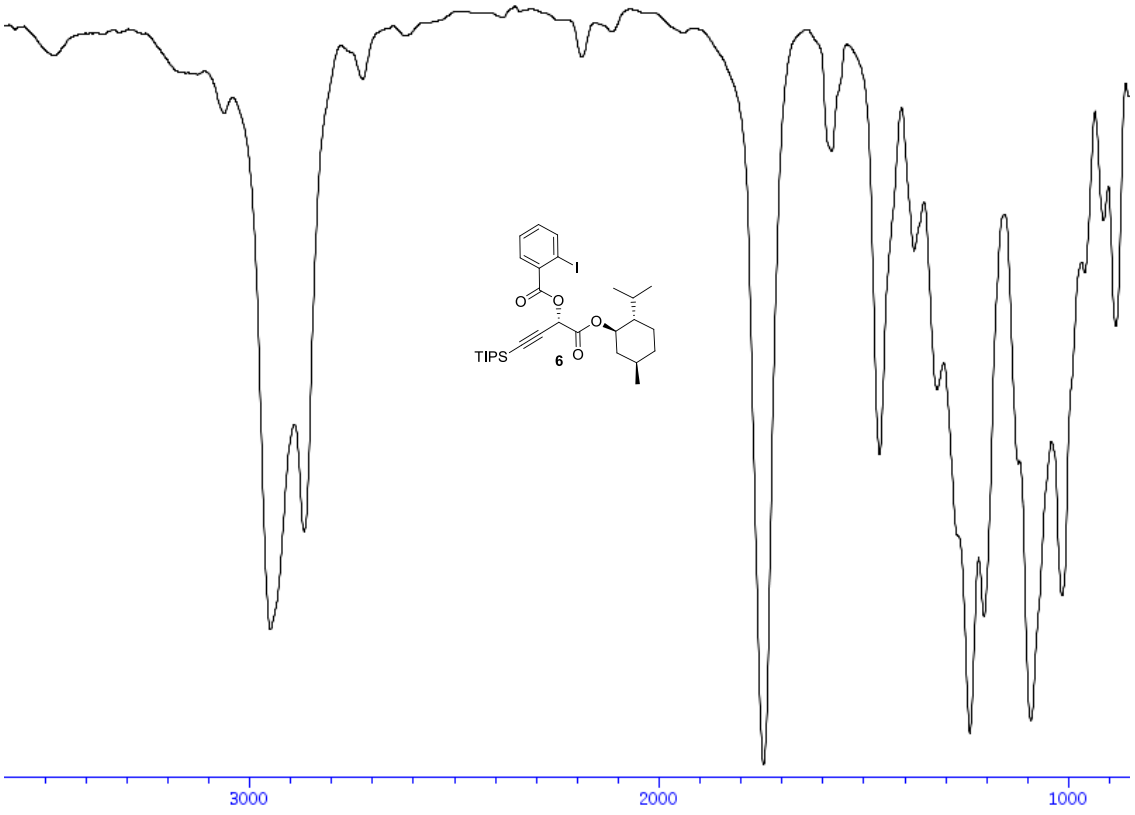


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.094	MM	0.4161	3406.20142	136.43030	53.8943
2	23.485	MM	0.6995	2913.95581	69.42936	46.1057

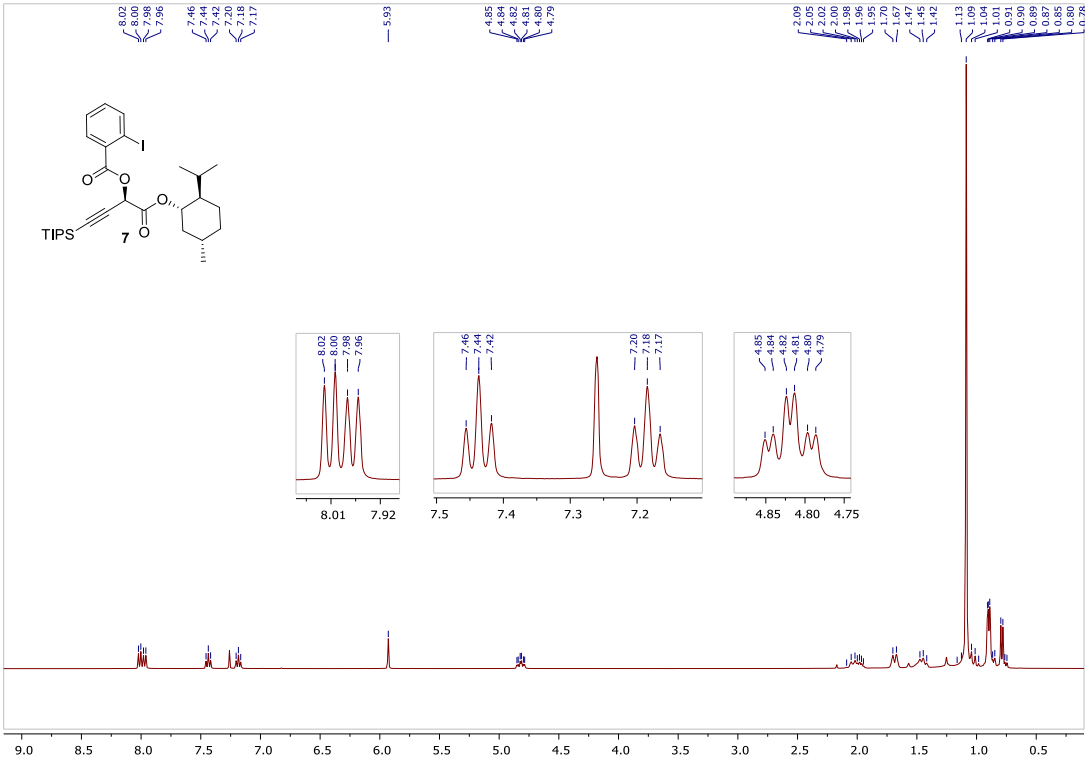


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.610	MM	0.3488	668.07349	31.92639	6.0397
2	22.578	MM	0.7185	1.03933e4	241.08705	93.9603

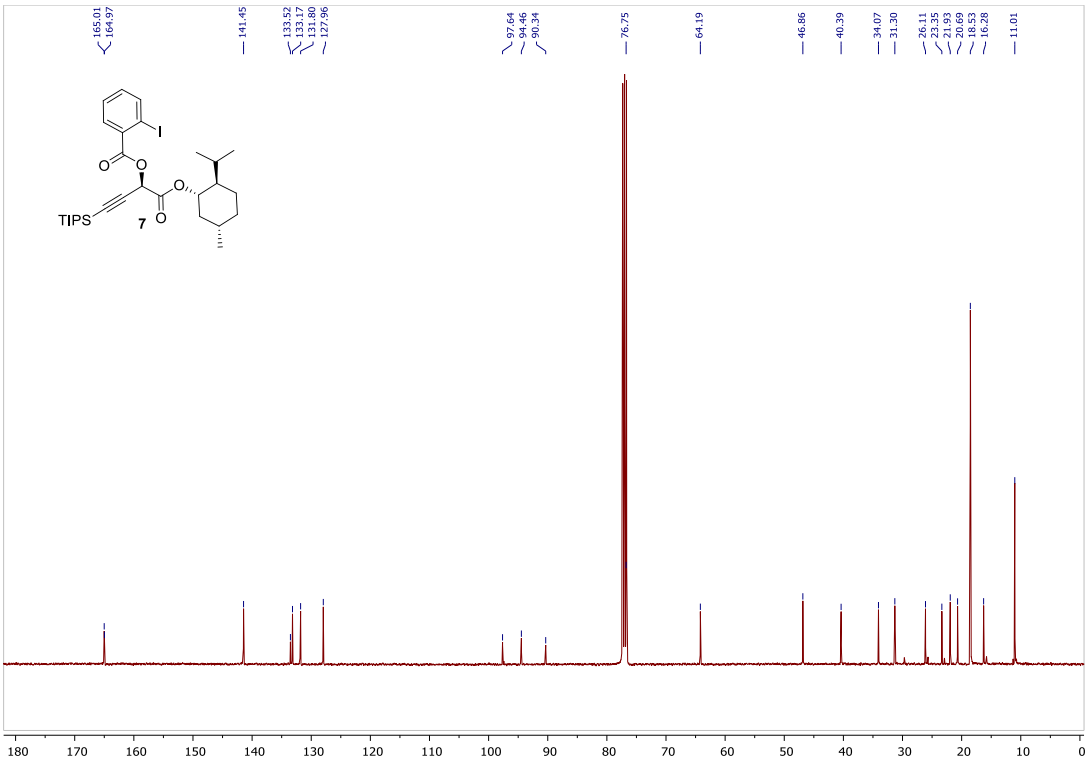
IR of compound **6**



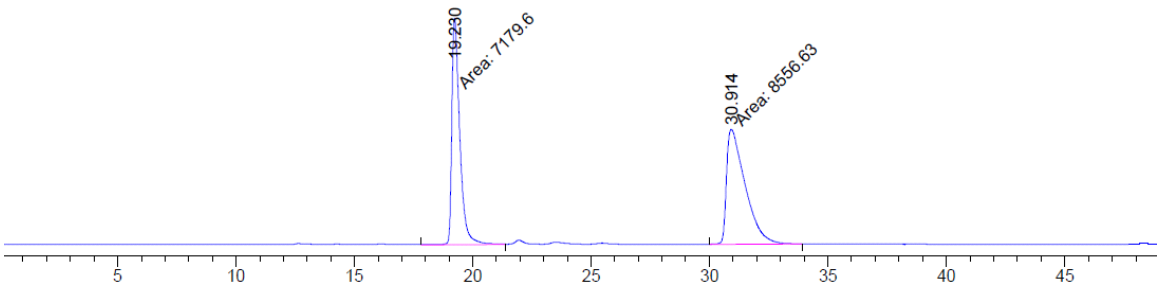
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **7**



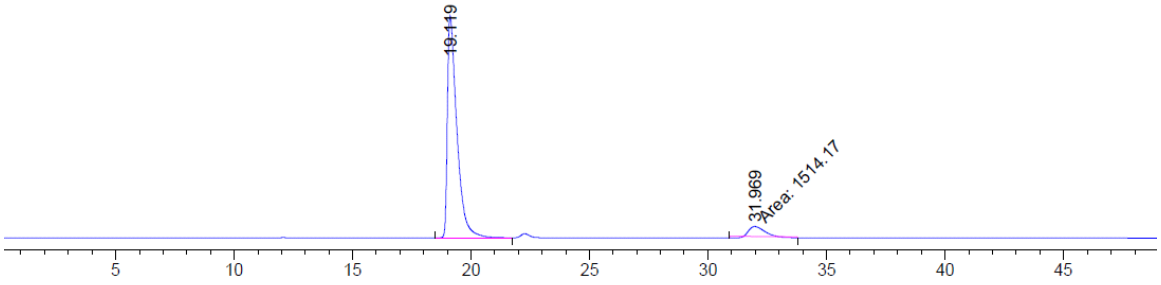
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **7**



HPLC of compound **7**

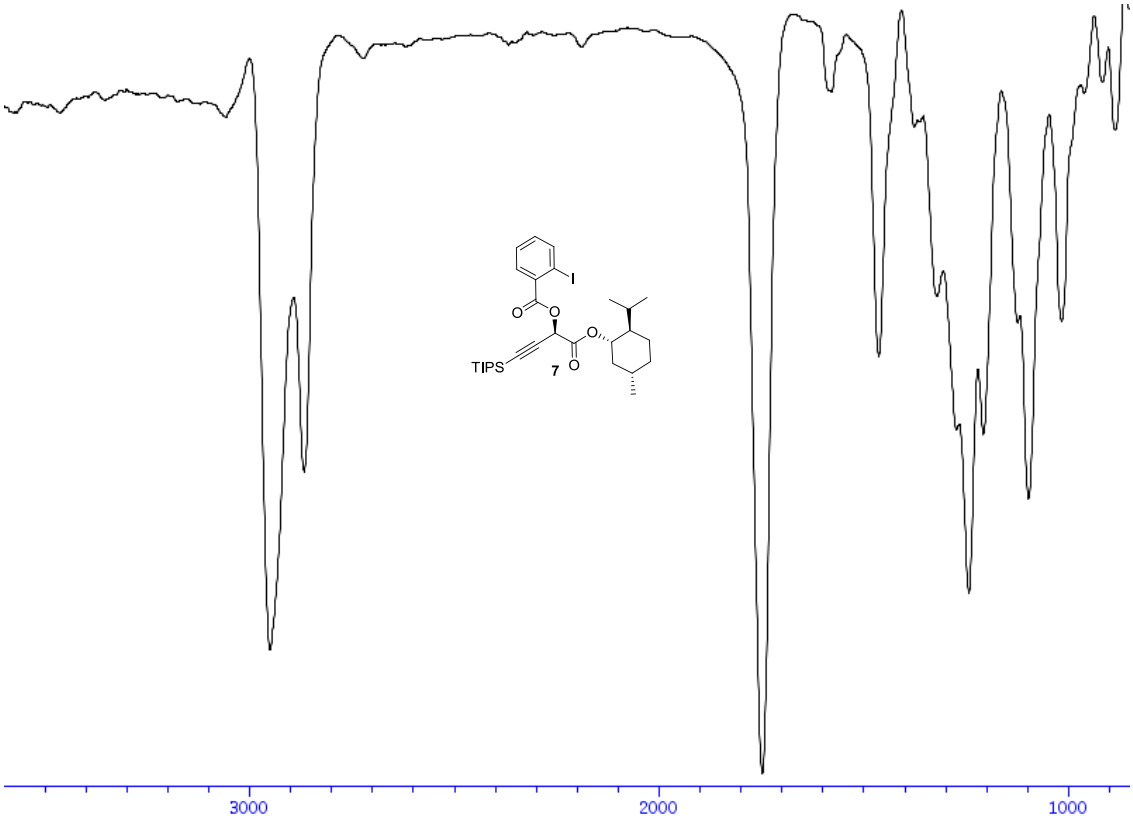


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.230	MM	0.3877	7179.59961	308.63159	45.6247
2	30.914	MM	0.9098	8556.62891	156.75209	54.3753

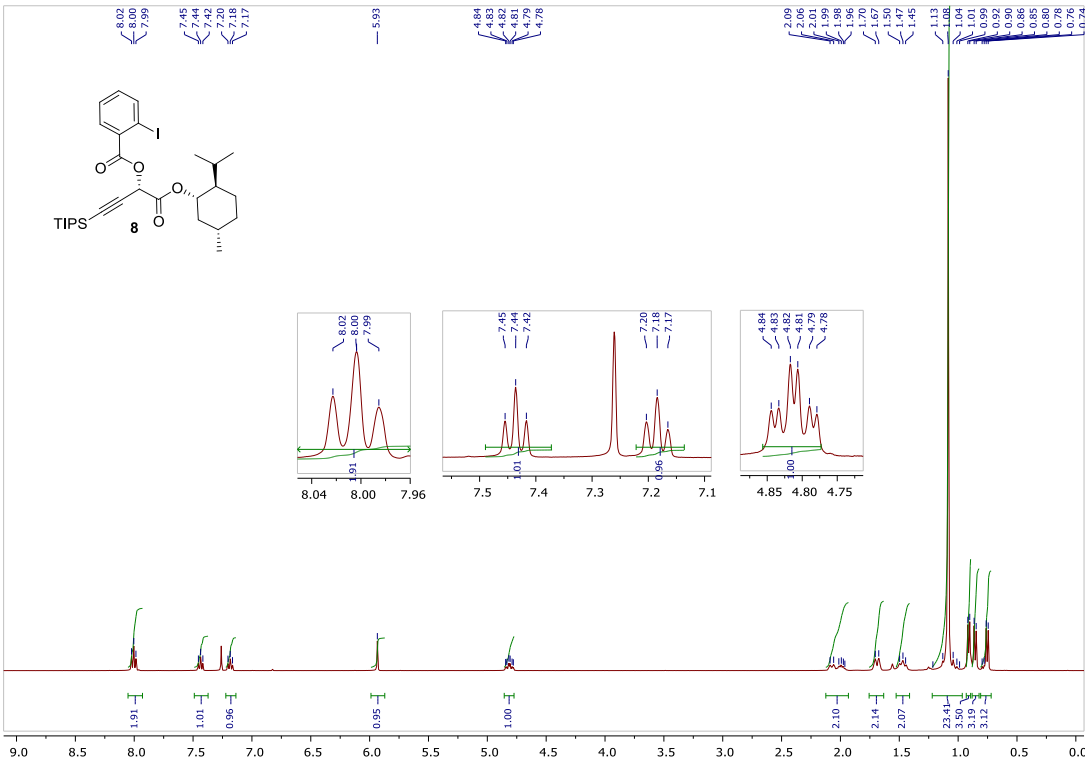


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.119	BB	0.4048	2.17780e4	787.04730	93.4992
2	31.969	MM	0.7256	1514.17175	34.77738	6.5008

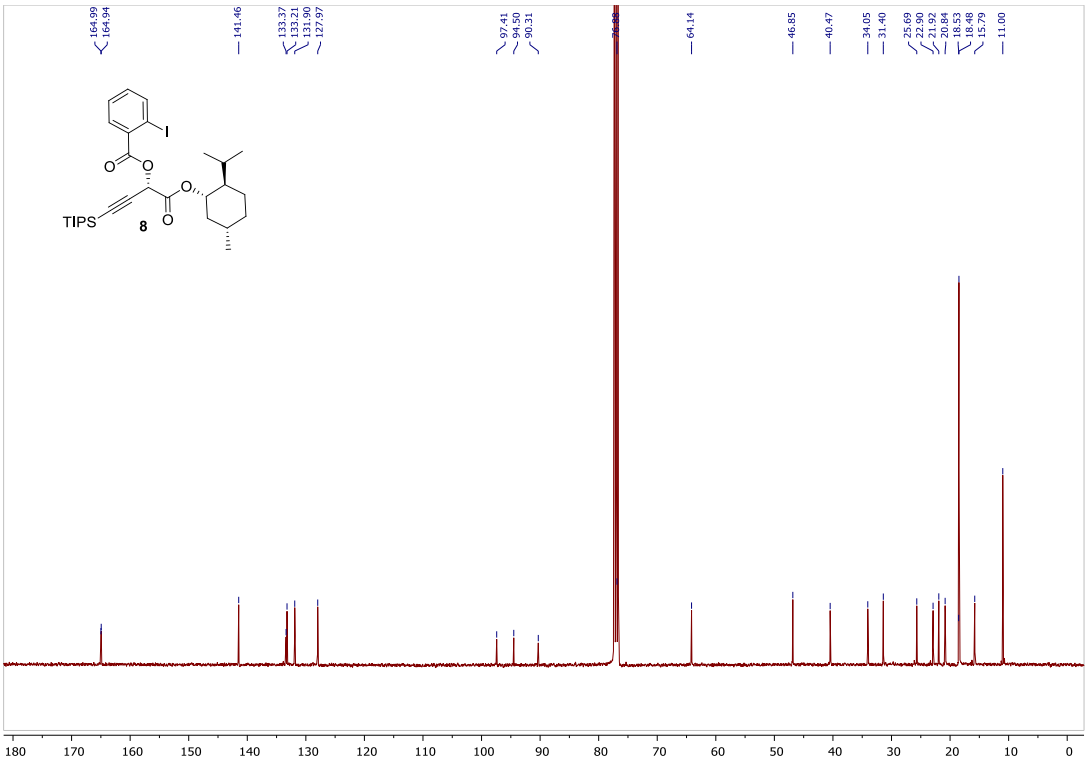
IR of compound **7**



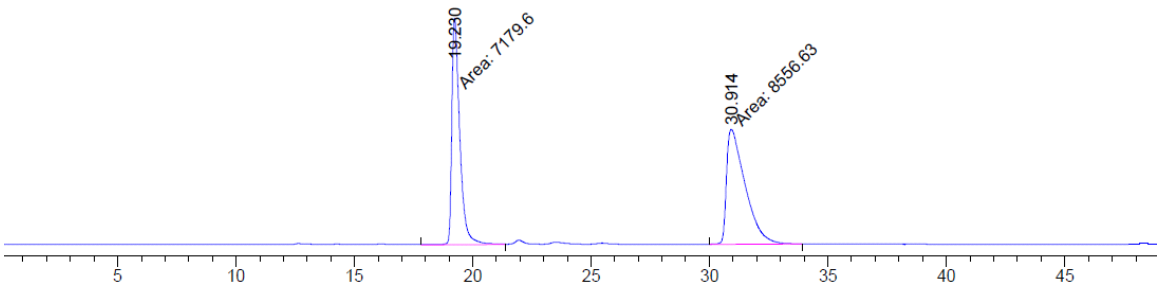
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **8**



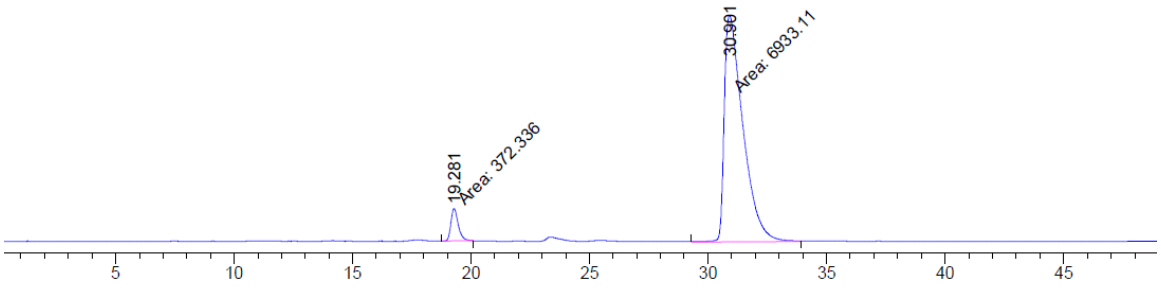
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **8**



HPLC of compound **8**

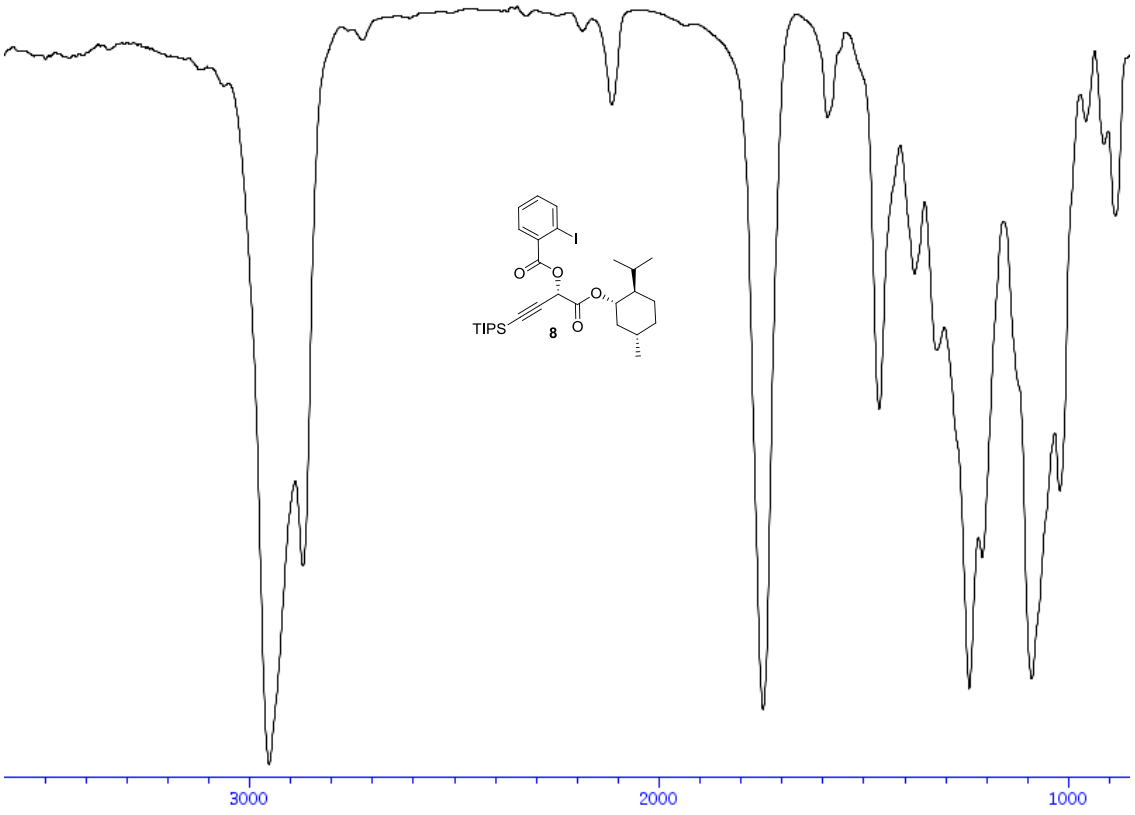


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.230	MM	0.3877	7179.59961	308.63159	45.6247
2	30.914	MM	0.9098	8556.62891	156.75209	54.3753

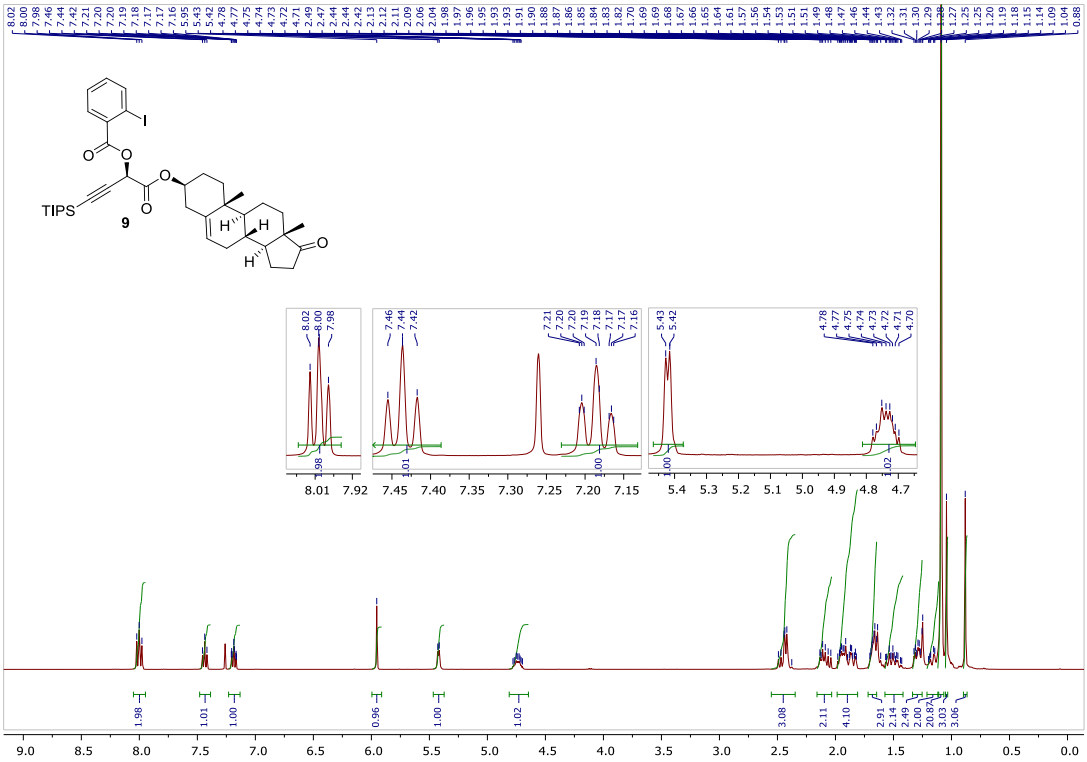


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.281	MM	0.3432	372.33646	18.07934	5.0967
2	30.901	MM	0.9124	6933.11133	126.64017	94.9033

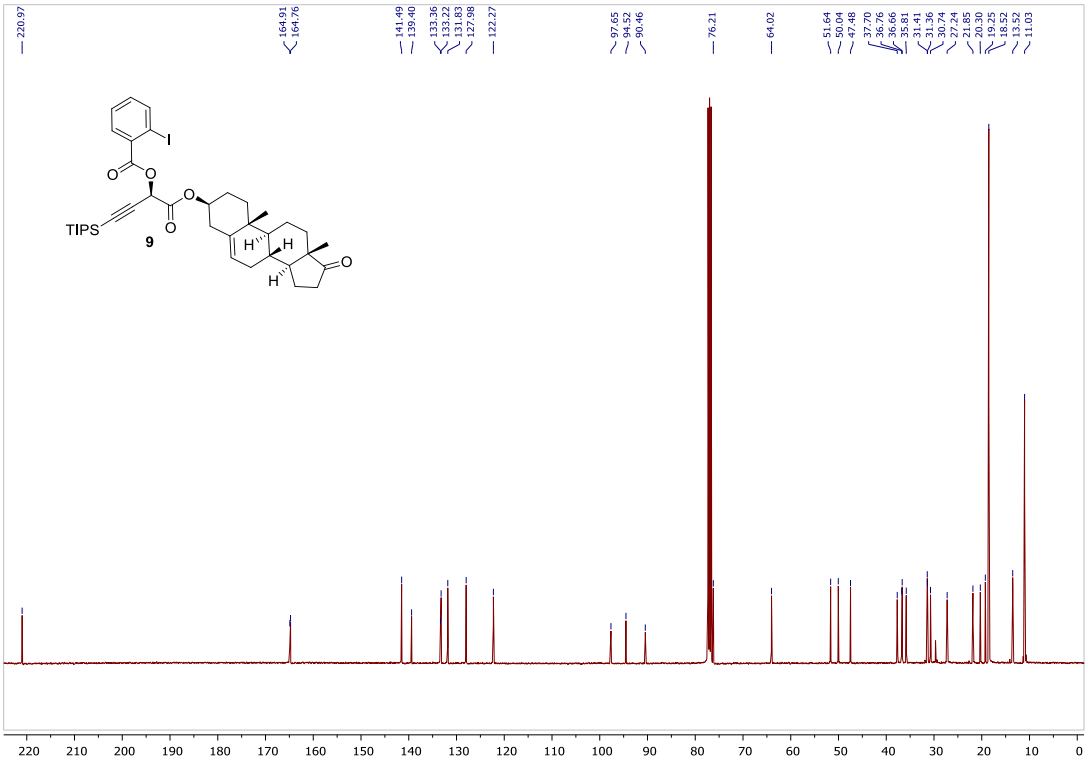
IR of compound **8**



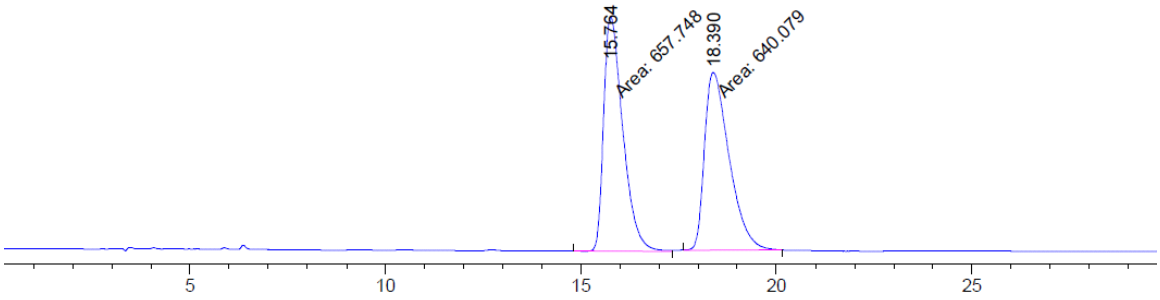
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **9**



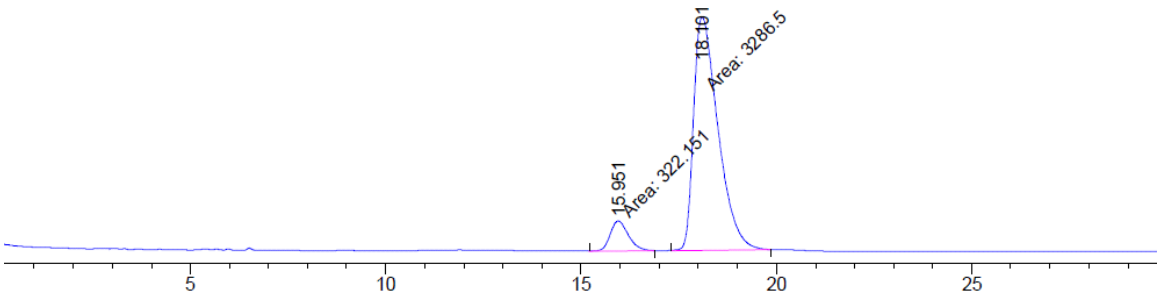
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **9**



HPLC of compound **9**

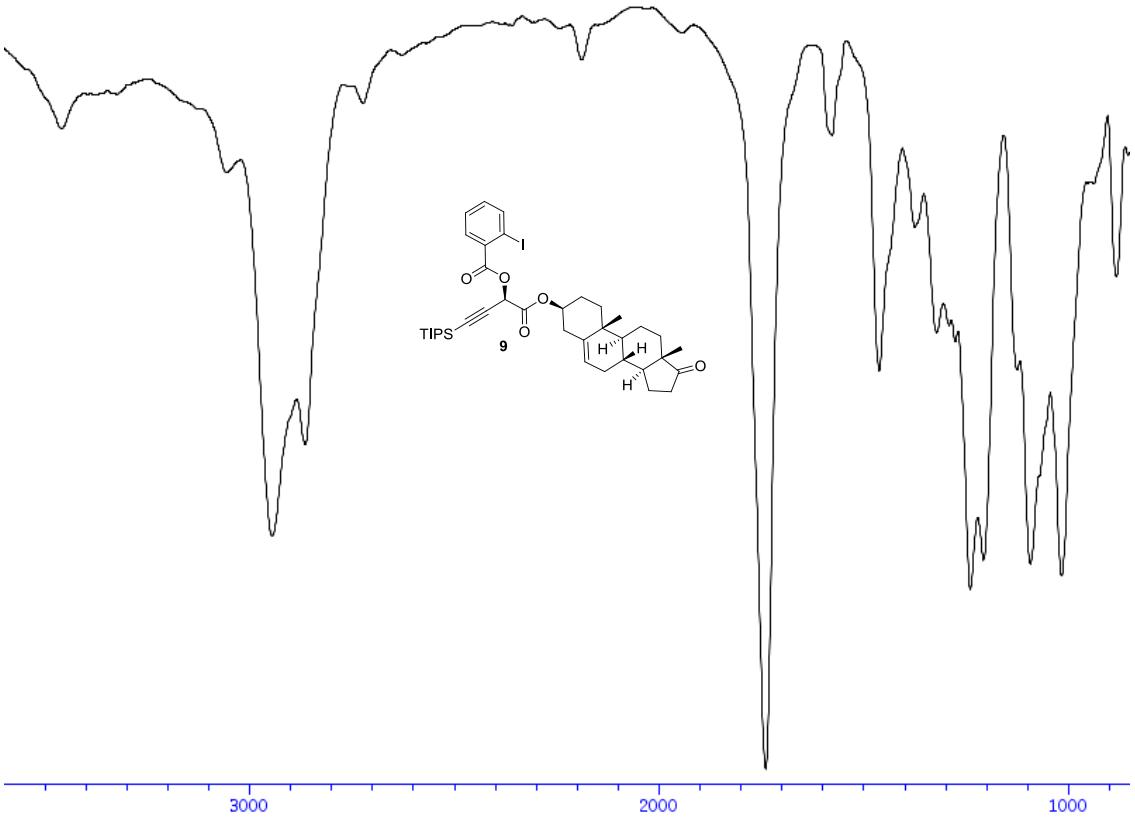


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.764	MM	0.5688	657.74847	19.27251	50.6807
2	18.390	MM	0.7311	640.07910	14.59236	49.3193

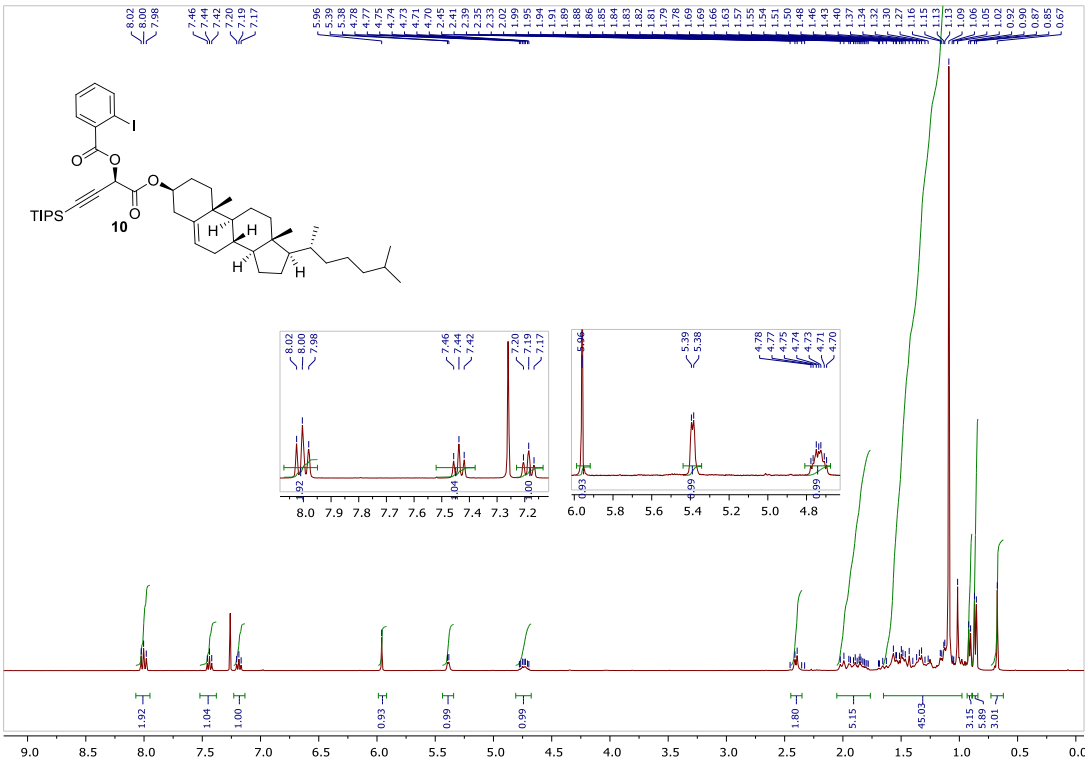


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.951	MM	0.5474	322.15079	9.80873	8.9272
2	18.101	MM	0.7227	3286.49536	75.79417	91.0728

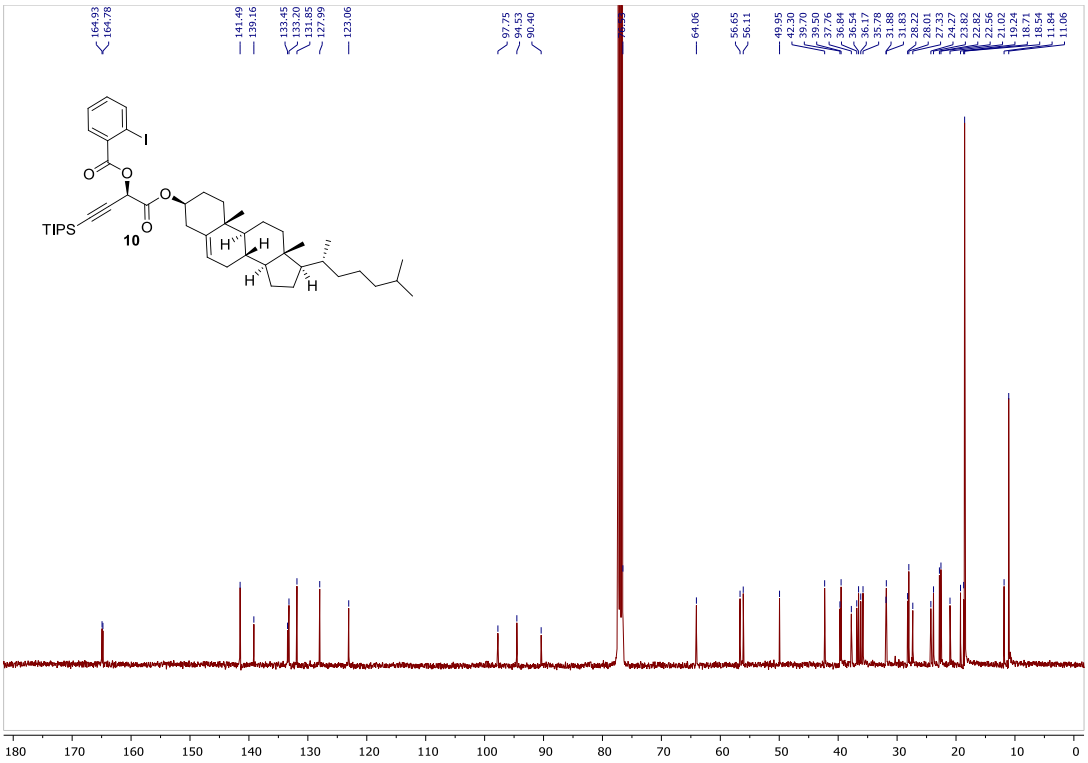
IR of compound **9**



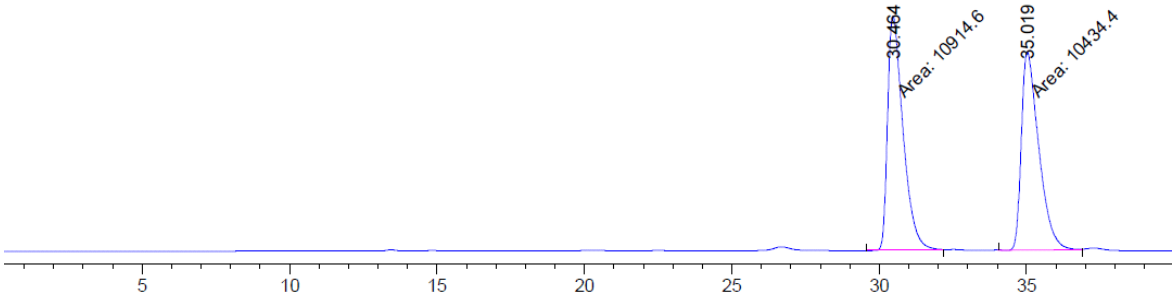
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **10**



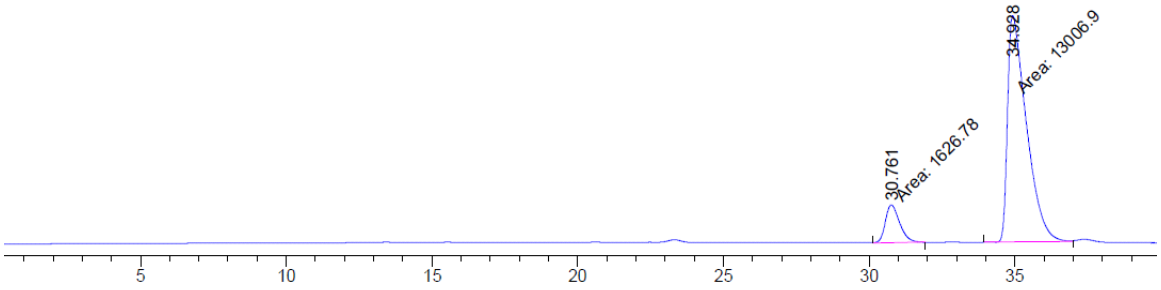
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **10**



HPLC of compound **10**

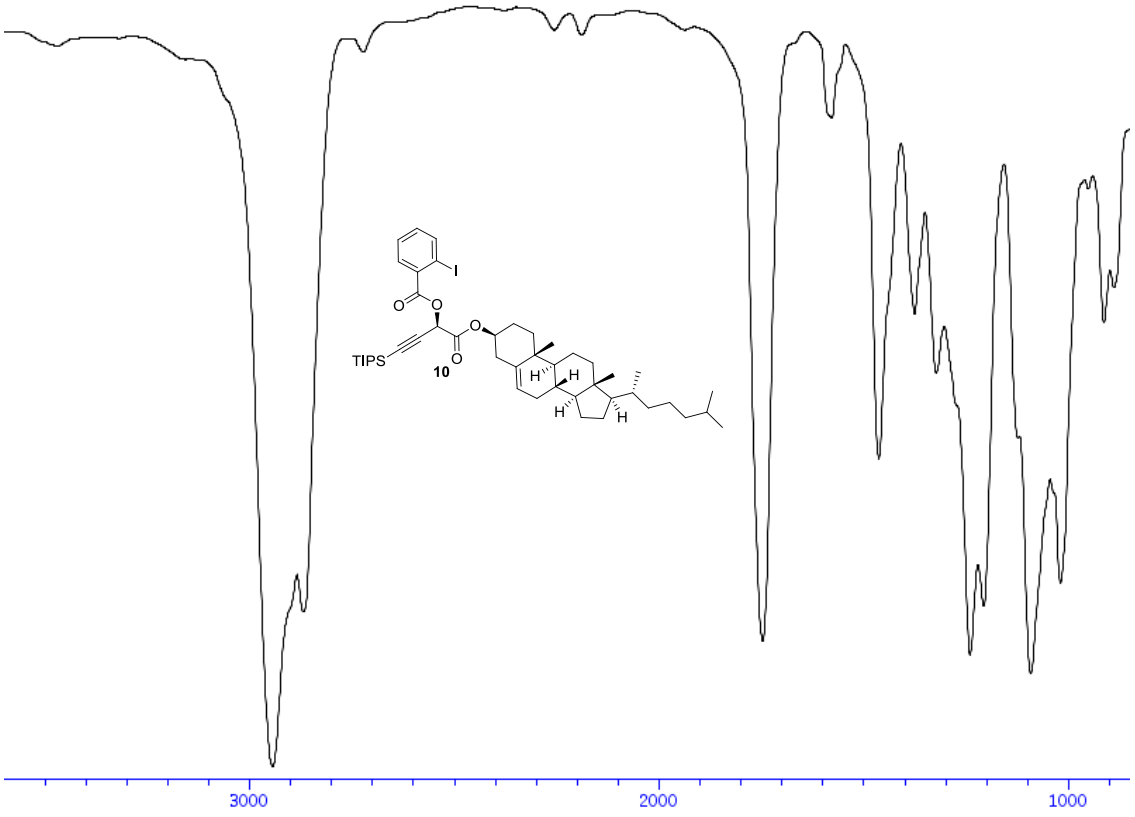


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.464	MM	0.6066	1.09146e4	299.90860	51.1248
2	35.019	MM	0.6850	1.04344e4	253.86644	48.8752

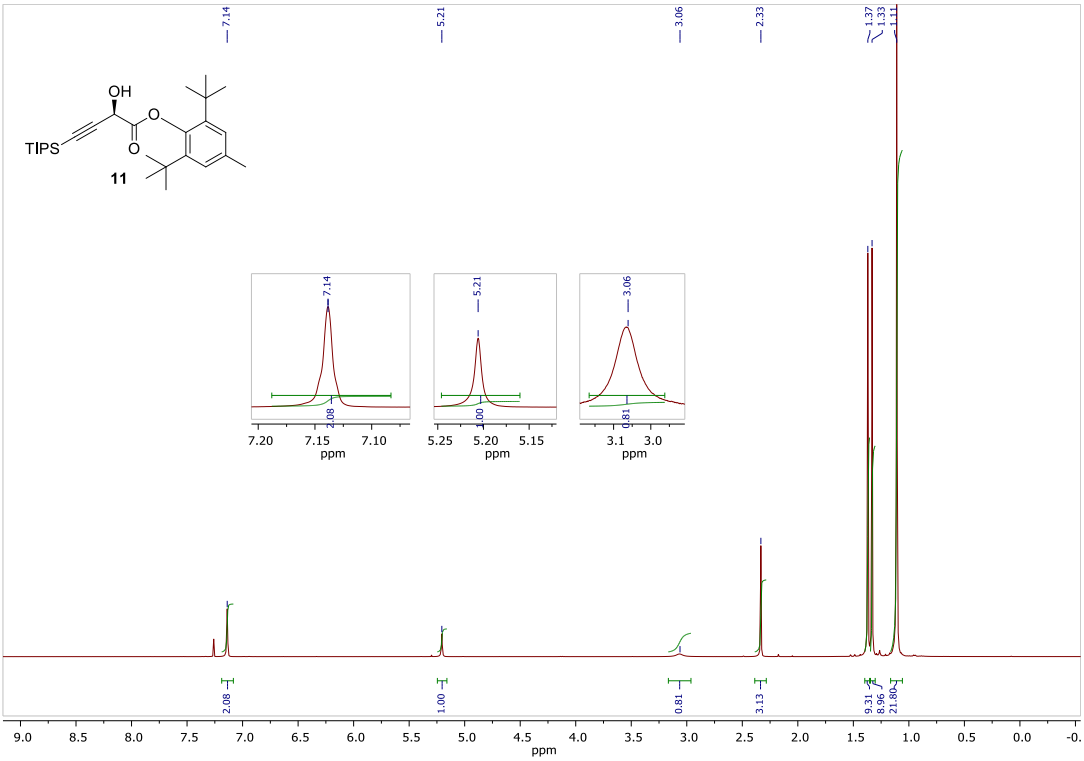


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.761	MM	0.5656	1626.77930	47.93273	11.1167
2	34.928	MM	0.7532	1.30069e4	287.81146	88.8833

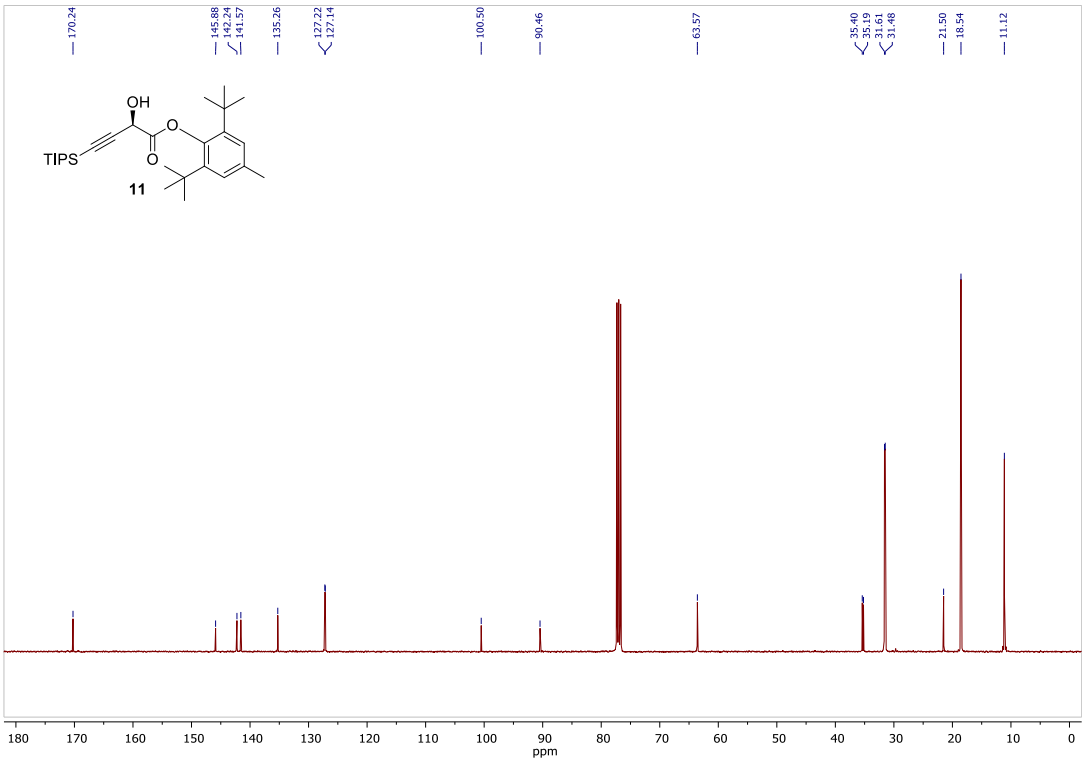
IR of compound **10**



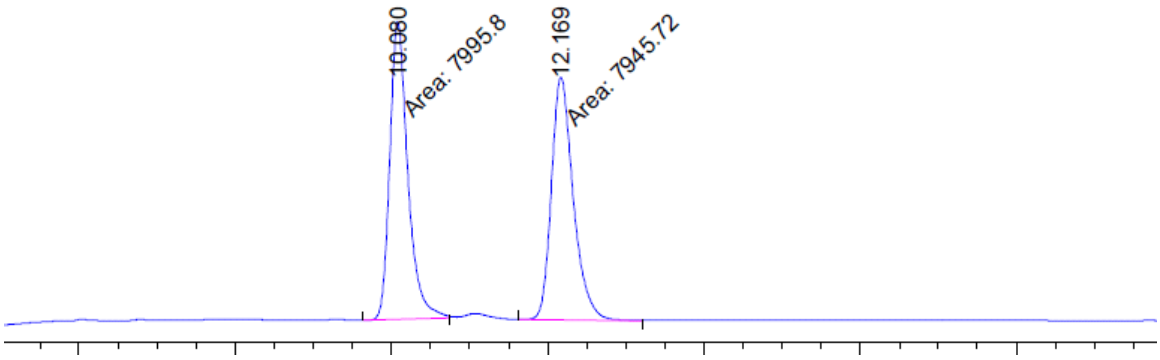
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **11**



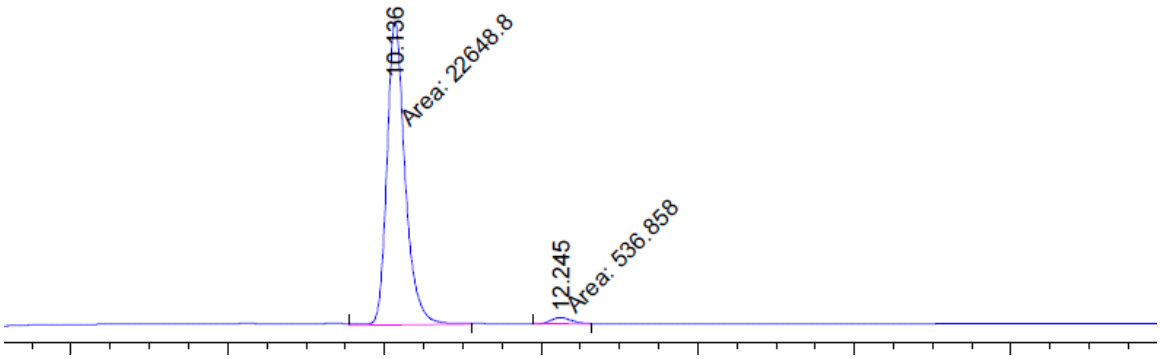
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **11**



HPLC of compound **11**

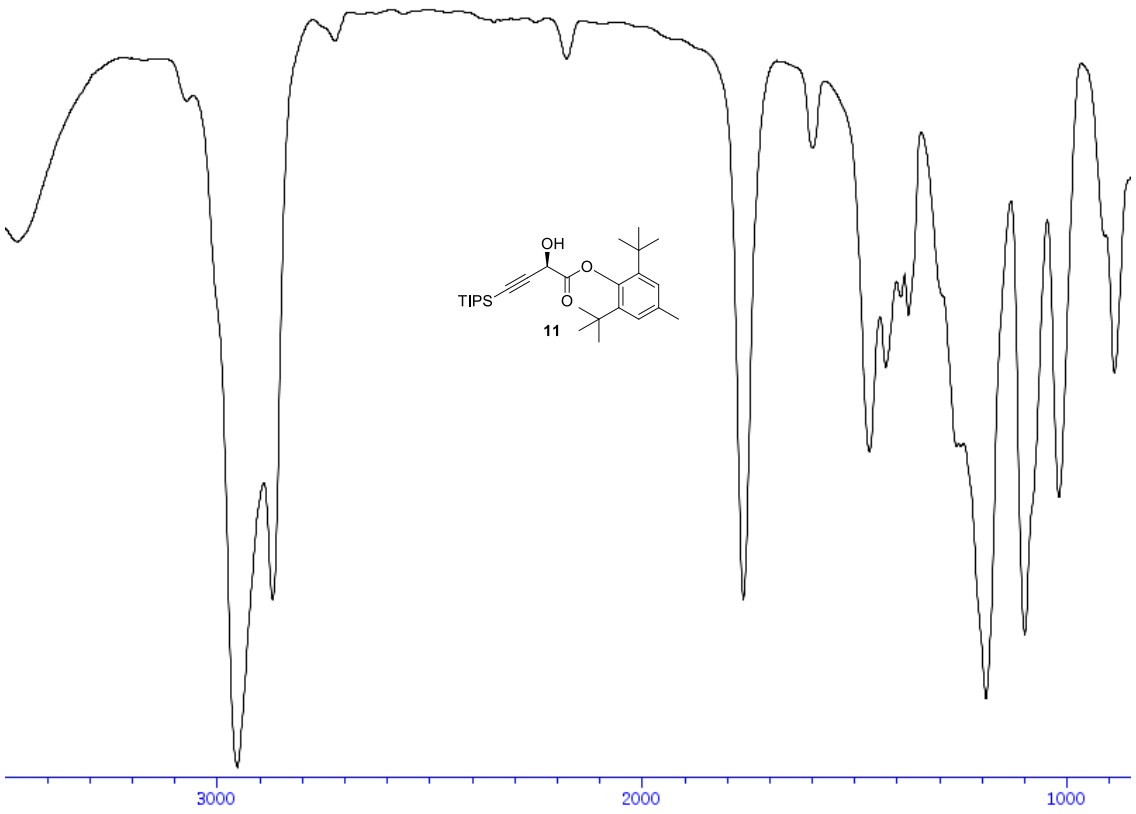


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.080	MM	0.2676	7995.80225	498.05582	50.1571
2	12.169	MM	0.3262	7945.71973	406.01230	49.8429

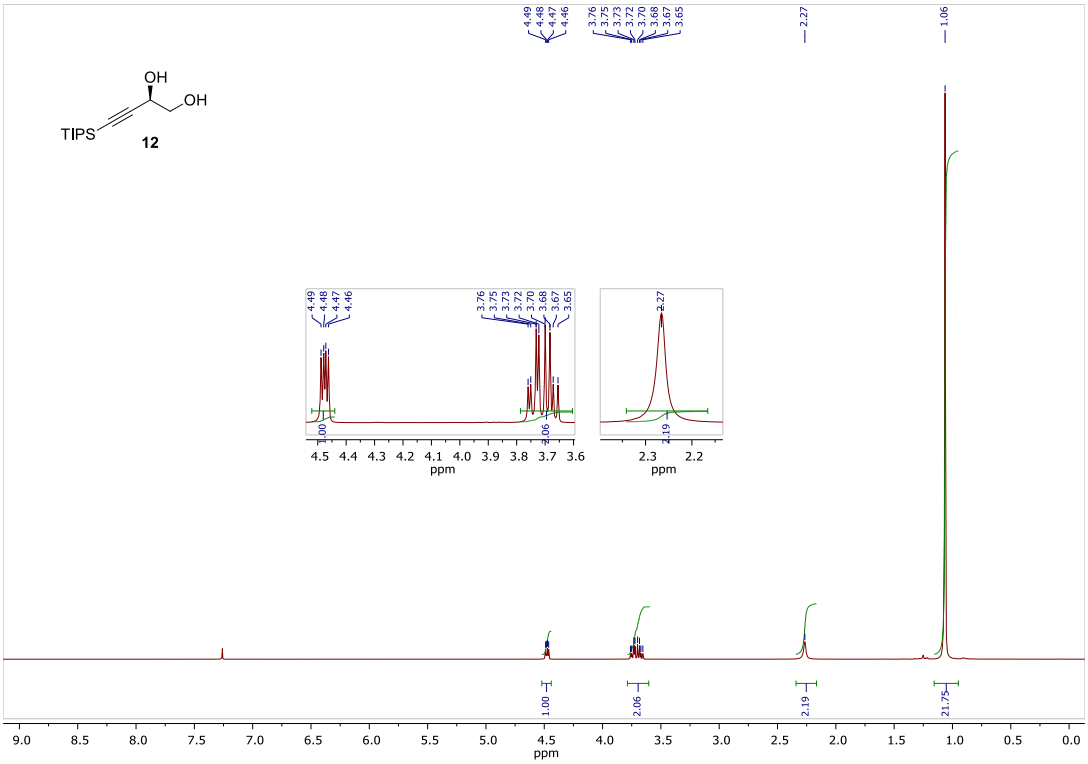


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.136	MM	0.2686	2.26488e4	1405.55713	97.6845
2	12.245	MM	0.2999	536.85846	29.83269	2.3155

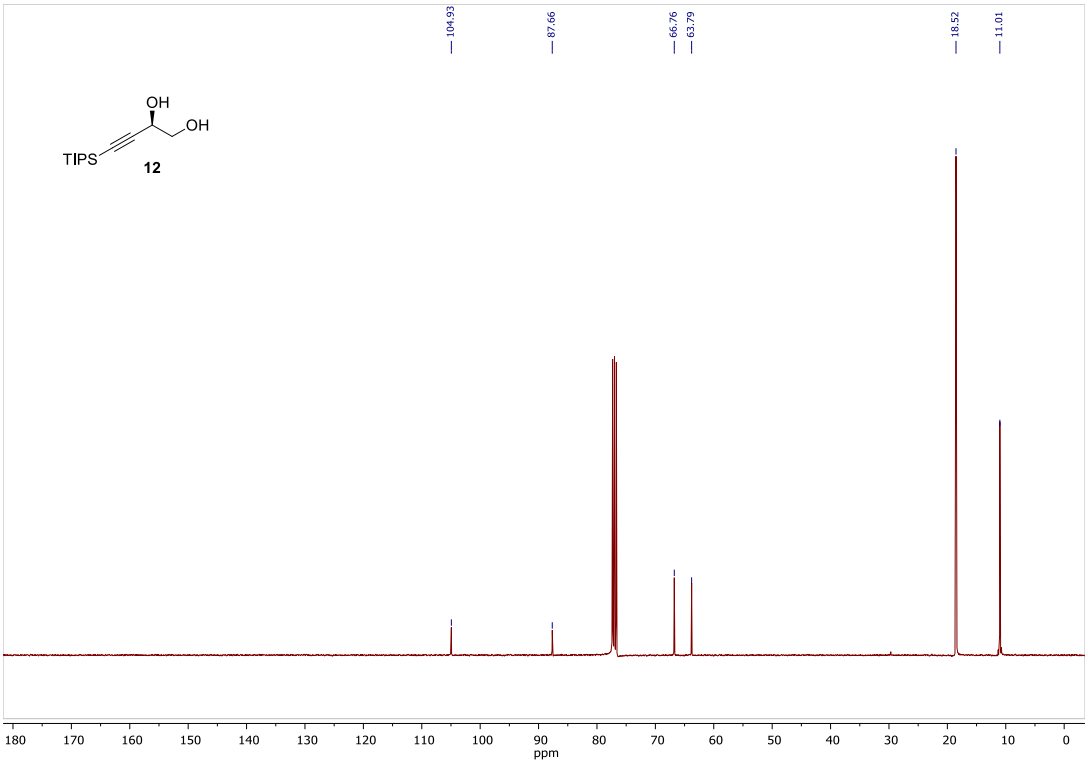
IR of compound **3a**



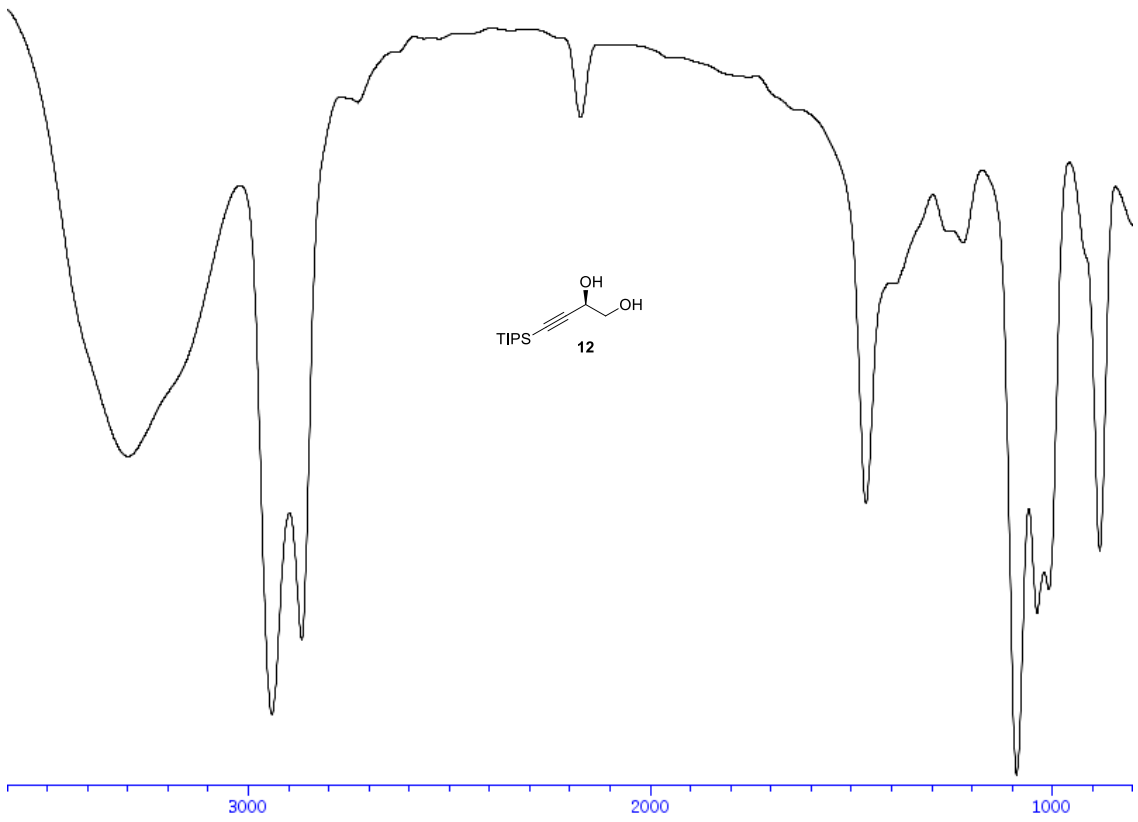
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **12**



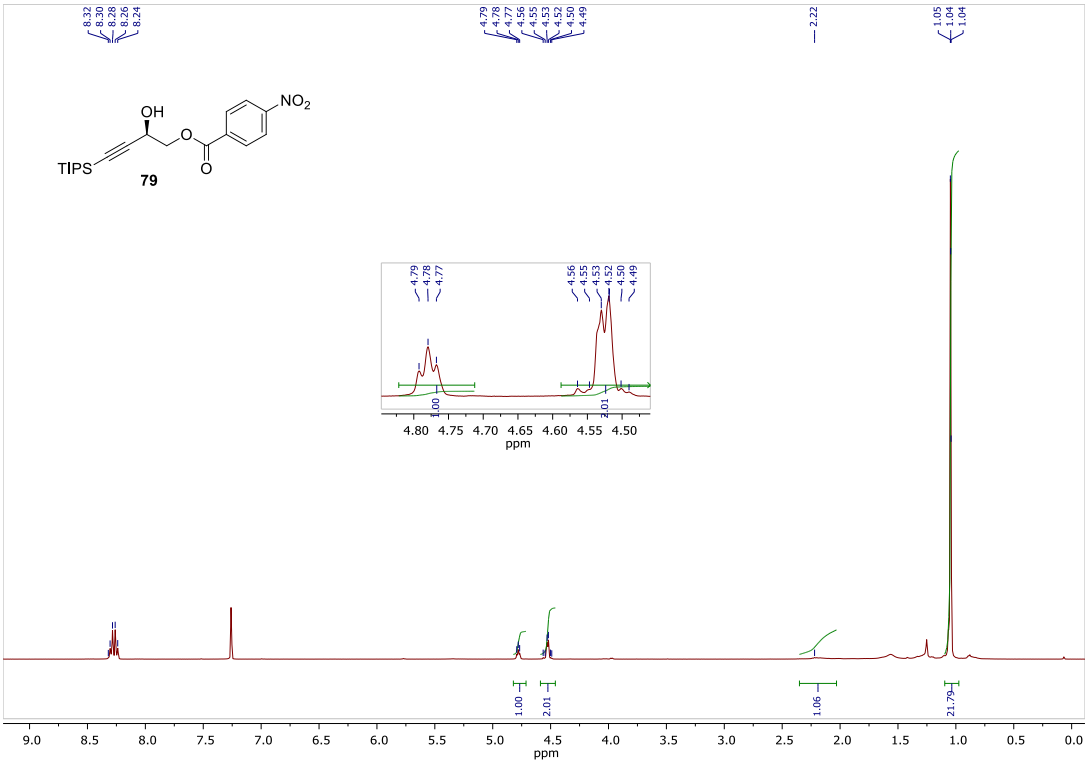
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **12**



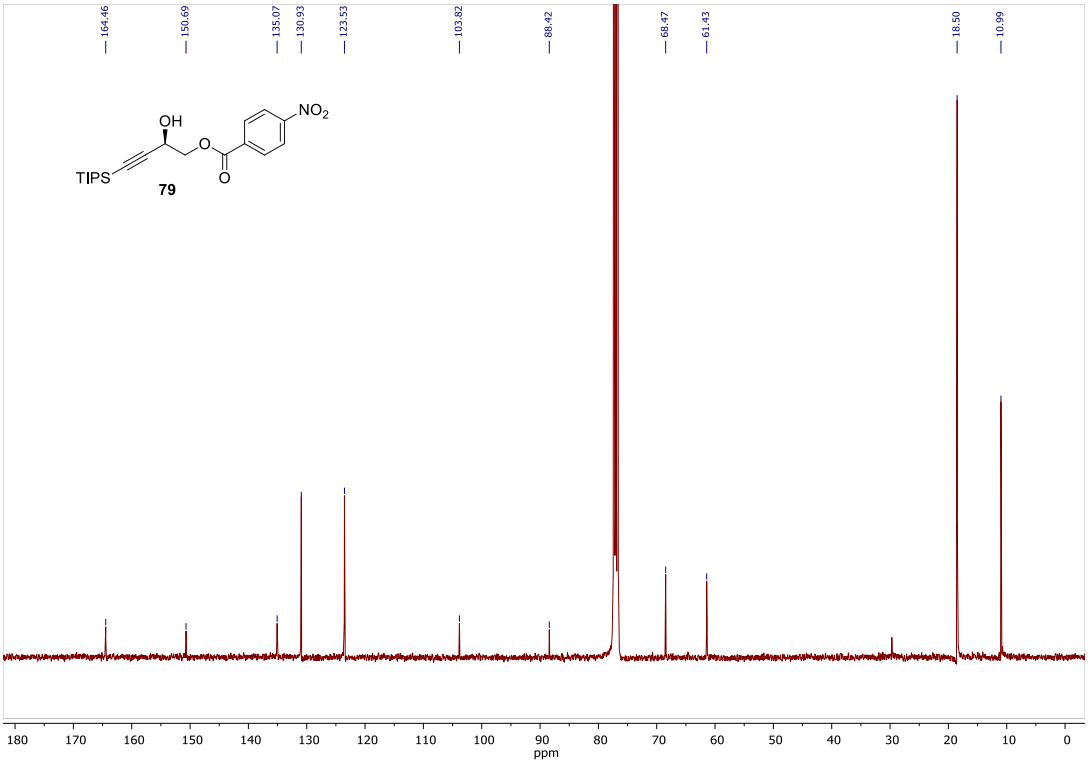
IR of compound **12**



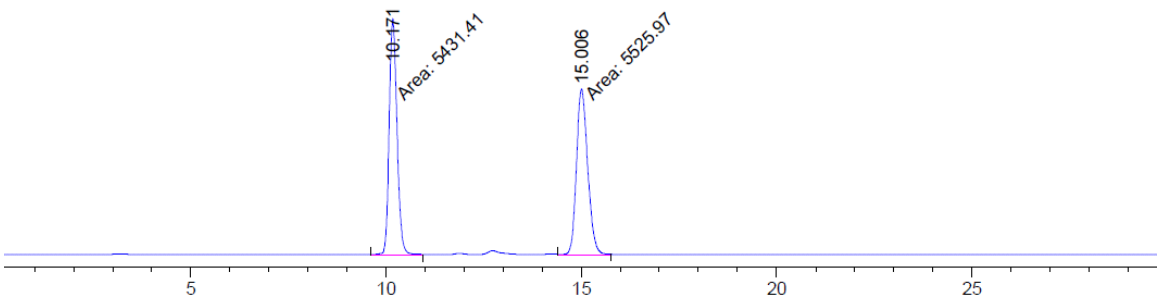
^{1}H-NMR (400 MHz, $CDCl_3$) of compound **79**



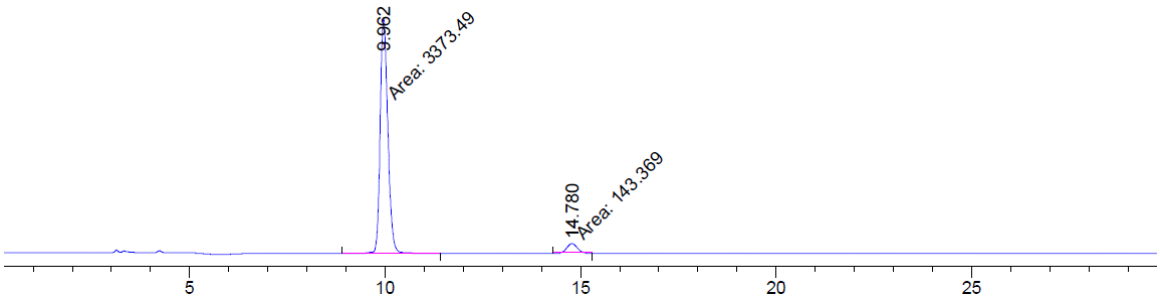
^{13}C-NMR (100 MHz, $CDCl_3$) of compound **79**



HPLC of compound **79**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.171	MM	0.2336	5431.41455	387.46164	49.5685
2	15.006	MM	0.3382	5525.96729	272.29950	50.4315



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.962	MM	0.2256	3373.48682	249.19731	95.9234
2	14.780	MM	0.2686	143.36926	8.89486	4.0766

IR of compound **79**