Chemical Science

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Aryl nitrenium ions from *N*-alkyl-*N*-arylamino-diazonium precursors: synthesis and reactivity†

Cite this: *Chem. Sci.*, 2014, **5**, 699

Chan Woo Huh* and Jeffrey Aubé*

A means of generating an *N*-alkyl-*N*-arylaminodiazonium ion, which then loses nitrogen to form a reactive aryl nitrenium intermediate, is described. In this sequence, a set of triazenyl acetonitriles was synthesized by nucleophilic addition of a nitrile anion to an aryl azide followed by temperature-dependent alkylation at either of two nucleophilic triazenyl nitrogen atoms. An α,α-disubstituted acetonitrile and *N*-arylaminodiazonium moiety (or aryl nitrenium ion upon loss of N_2) are embedded in the resulting 1,3,3-trisubsituted triazene, which undergoes liberation and recombination of these two components under acidic conditions to yield an α-arylated acetonitrile containing an all-carbon-quaternary center. We propose that the *N*-alkyl-*N*-arylaminodiazonium ion loses nitrogen to generate an aryl nitrenium species, which then reacts with an α,α-disubstituted acetonitrile either at the *para*- or *meta*-position of the aromatic ring to afford *p*-alkylaminoaryl acetonitrile derivatives or 3,3-substituted 1-methylindolin-2-imines, depending on the substrates and conditions.

Received 8th October 2013
Accepted 1st November 2013

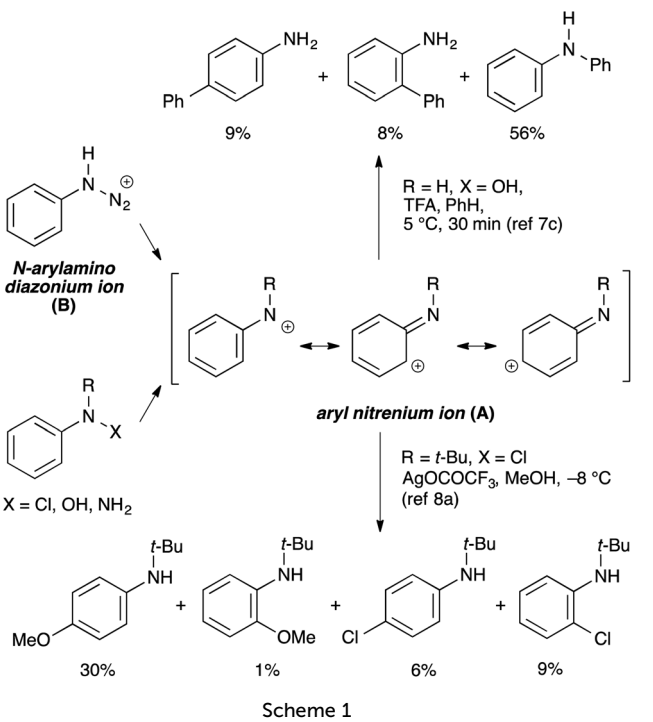
DOI: 10.1039/c3sc52805g

www.rsc.org/chemicalscience

Introduction

Aryl nitrenium ions (**A**),[1] which contain a positive charge spread throughout the aryl ring, are well known but little utilized in fine chemical synthesis. These species can be generated from *N*-arylaminodiazonium ions (**B**),[2,3] hydrazines,[4] hydroxylamines,[5–7] or *N*-chloroanilines.[8] Once generated, nitrenium ions are able to recombine with heteroatomic nucleophiles such as ammonia,[4a] H_2O (the Bamberger rearrangement[5]), chloride,[8] solvents (*e.g.*, methanol[8a,d]); they may also react intramolecularly (Scheme 1).[3,9] Typically, reactions occur at the *para*, *ortho*, or nitrogen atoms of **B**, often leading to mixtures of products.[3c,4c,6,8] However, only a few reports exist of C–C bond-forming reactions of aryl nitrenium ions with external nucleophiles, with those examples limited to Friedel–Crafts-like reactions with aromatic solvent[4c,d,7] or with electron-rich olefins present in large excess.[10] In comparison with most aryl nitrenium ion precursors, *N*-arylaminodiazonium ions (**B**) have the advantage of not having a nucleophilic leaving group that can complicate the reaction outcome (Scheme 1, bottom). Bamberger,[2a] Smith[2b] and Abramovitch[3] have converted aryl azides in acid to *N*-arylaminodiazonium ions and successfully employed them in various intramolecular reactions. These reactions typically require a large excess of strong acid such as sulfuric acid or trifluoromethanesulfonic acid, which constitutes the main drawback of using azides as *N*-arylaminodiazonium ion precursors.

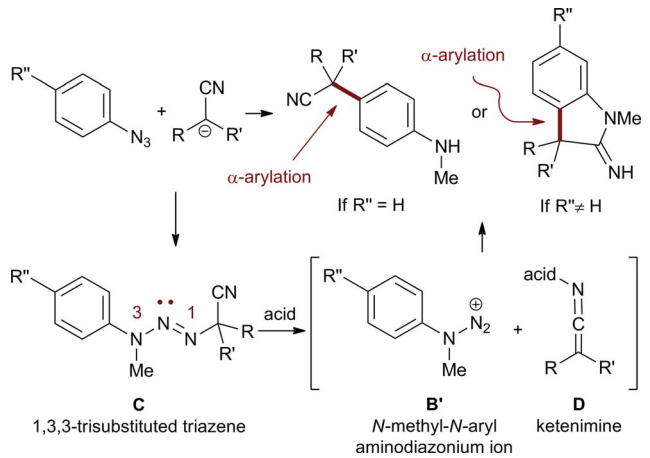
In this paper, we present a new way of generating arylaminodiazonium ions and using them in C–C bond-forming reactions (Scheme 2). The keystone of our method is to form *N*-methyl-*N*-arylaminodiazonium ions **B′** from 1,3,3-trisubstituted triazenyl acetonitrile **C** in a Lewis or Brønsted



Scheme 1

Chemical Methodologies and Library Development Center, University of Kansas, 2034 Becker Dr. Lawrence, KS 66047, USA. E-mail: cwhuh@ku.edu; jaube@ku.edu

† Electronic supplementary information (ESI) available: General procedures, spectral data of previously unknown substrates, reaction optimizations, and crossover experiments. CCDC 923835. See DOI: 10.1039/c3sc52805g



Scheme 2

acid-mediated step that also unleashes a nucleophilic reaction partner **D**. In traditional methods of generating *N*-arylaminodiazonium ions in strong acid, the desired **B** is in an unfavorable equilibrium with the starting aryl azide (Scheme 1). In contrast, using triazenyl acetonitrile **C** as described here requires only 1 equiv. of mild protic acid (TFA) or Lewis acid ($BF_3 \cdot OEt_2$) for a virtually irreversible generation of *N*-methyl-*N*-arylaminodiazonium ion **B′**. As a bonus, the resulting ion **B′** is *N*-methylated, which is not possible *via* the azide protonation method. This overall sequence also represents a conceptually new approach to the α-arylation of nitriles. α-Arylation is a topic of considerable contemporary interest, as evidenced by recently reported methods using transition metal catalysis[11] or, alternatively, nucleophilic addition of an enolate or its equivalent to an activated arene, such as an aryl lead,[12] aryl bismuth,[12] diaryliodonium salt,[13] aryl fluoride,[14] benzyne[15] or diarylsulfoxide.[16]

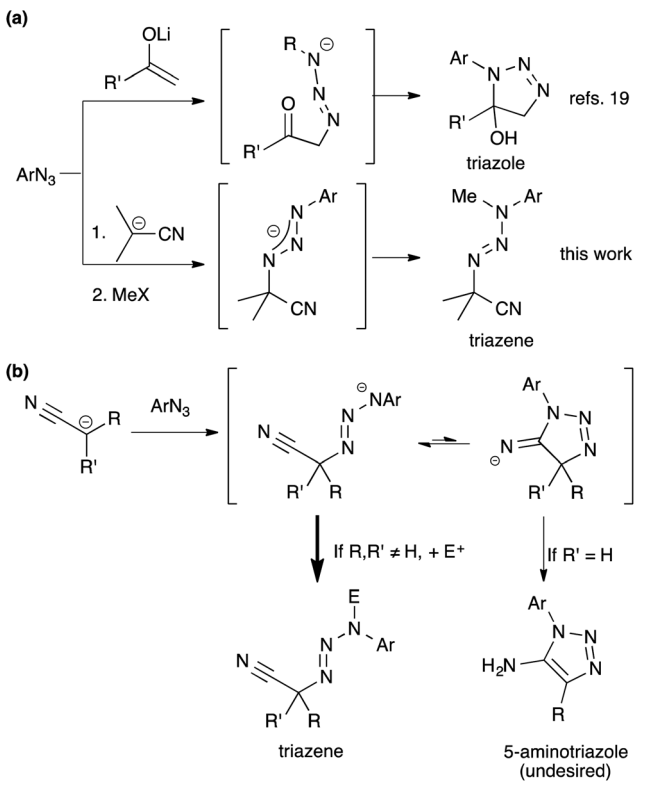
The work described herein combines several synthetic advances: (1) a three-component synthesis of trisubstituted triazenes[17] **C** from α-nitrile anions, in which an unexpected dependence of product type on conditions was noted, (2) the controlled breakdown of 3-aryl-3-alkyl substituted triazenes to useful intermediates **B′** and **D**, (3) the recombination of these intermediates to afford two different kinds of α-arylation products, depending on starting materials and reaction conditions. This work required the consideration of several mechanistic and selectivity issues, which led to insights into the electrophilic chemistry of alkyl azides and the utilization of nitrenium ions for the formation of C–C bonds *via* nonsolvolytic means.

Results and discussion

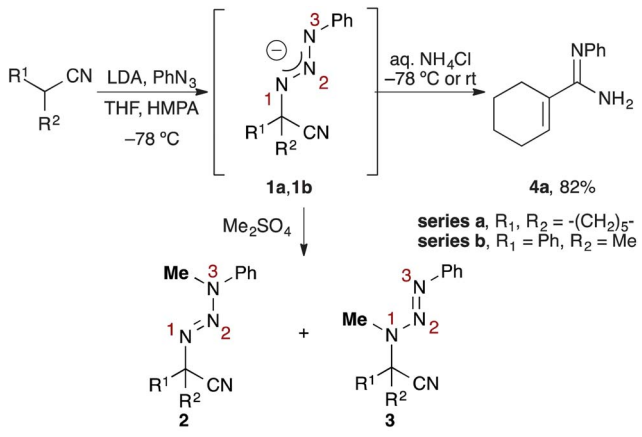
Triazene synthesis from aryl azides

Our first goal was to create an aryl nitrenium precursor that could be reliably generated under conditions consistent with selective reaction with a carbon nucleophile. In principle, a triazene would be suitable provided its decomposition could be directed toward the desired reaction products. We were especially intrigued by the bonus of incorporating both nucleophile (enol equivalent) and electrophile (aminodiazonium ion) precursors in the same triazene *via* capture of the triazenyl anion formed by organometallic addition to an azide with an electrophile to perform an overall 1,3 addition to the azide (Scheme 3a). A number of reactions that afford triazenes from organometallic reagents[18] are known, but all previously reported examples of sequential nucleophilic addition to azides followed by trapping of the resulting anion using enolates[19] or nitrile anions[20] resulted in the formation of cyclic triazoles. We therefore set out to develop a sequence in which the nucleophile and electrophilic reaction partners would be independent of one another and moreover lead to acyclic triazenes. We specifically chose α,α-disubstituted acetonitriles as nucleophiles because the adducts, lacking an additional α-proton for removal, would not cyclize to 5-aminotriazoles (Scheme 3b).

α-(Arylmethyltriazenyl)cyclohexanecarbonitrile isomers **2a** and **3a** were prepared by adding the anion of cyclohexanecarbonitrile to phenyl azide, leading to presumed intermediate **1a** (Scheme 4). We expected that quenching with Me_2SO_4 could occur at either N1 or N3 of the triazenyl anion, and in fact discovered that the outcome depended dramatically on reaction temperature. Quenching at room temperature resulted in methylation on N3 to form triazene **2a**. In contrast, N1 methylation at low temperature (−78 °C, followed by warming to rt) provided the conjugated triazene **3a**. While **3a** was obtained as an oil, **2a** was crystalline and its structure was confirmed by X-ray crystallography (ESI†). When the enolate–azide adduct **1a** was quenched with aqueous NH_4Cl instead of a



Scheme 3

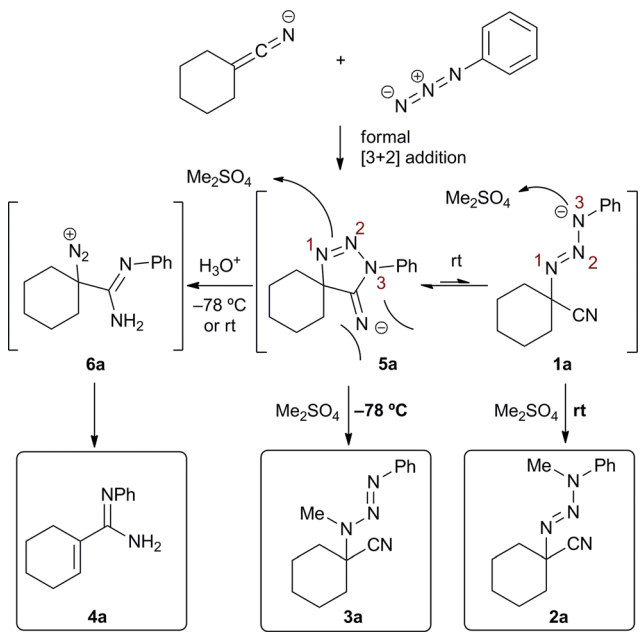


series	quench temp	yield(%)	2	ratio :	3
a	rt	99	93		7
a	−78 °C	94	<2		>98
b	rt	78	>98		<2
b	−78 °C	99	3		97

Scheme 4

methylating reagent, the only observed product was the unexpected cyclohexenecarboxyimidamide **4a**. The same selectivity was also observed using 2-phenylpropionitrile to form **2b** at rt (78%, only isomer observed) and **3b** at −78 °C (99%, 97 : 3 ratio of **3b** : **2b**), respectively.[21]

To explain these results, we propose the initial formation of triazole intermediate **5a** through a formal and probably stepwise[19b] [3 + 2] cycloaddition between the anion and azide (Scheme 5). The formation of amidine **4a** at either −78 °C or rt (82% for both cases) can arise from direct protonation at iminyl anion of **5a** followed by elimination of the resulting α-diazonium compound **6a**. Since no *N*-methyl amidine corresponding to **4a** is obtained upon treatment with a methylating agent, we

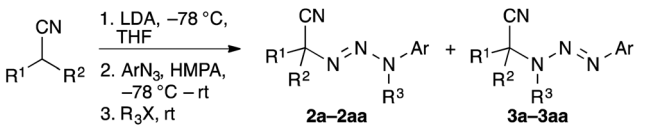


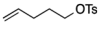
Scheme 5

propose that the hindered iminyl anion moiety in **5a** is unreactive to bulkier alkylating agents. Instead, low-temperature reaction of **5a** leading to product **3a** at −78 °C may be explained from the direct reaction of **5a** at N1 followed by ring opening. The change in site selectivity at room temperature could be due to the formation of triazenyl anion **1a** upon warming, followed by reaction at the unhindered, nucleophilic anionic nitrogen at N3 to form triazene **2a**.

Having established a practical route to the desired triazene **2a**, we examined the scope of the reaction by preparing a series of α-(aryltriazenyl)acetonitriles (**2b–2aa**) from the corresponding α,α-disubstituted acetonitriles, aryl azides, and a set of alkyl/acylating reagents (Table 1). Thus, generation of a nitrile anion with LDA was followed by addition of an HMPA solution of an aryl azide at −78 °C, and the reaction was allowed to warm to rt over 1 h. Finally, alkylating or acylating (entry 13) reagents were added at room temperature. Although HMPA was not

Table 1 Synthesis of trisubstituted triazenes[a]



	R^1	R^2	Ar	R^3X	Prd	2 + 3[b]	2 : 3[c]
1	−(CH2)5−		Ph	Me_2SO_4	**2a**	99%	93 : 7
2	−(CH2)5−		Ph	MeOTf	**2a**	87%	>98 : 2
3	−(CH2)5−		Ph	MeI	**2a**	88%	91 : 9
4	−(CH2)5−		2-$MeOC_6H_4$	Me_2SO_4	**2c**	89%	94 : 6
5	−(CH2)5−		3-$MeOC_6H_4$	Me_2SO_4	**2d**	77%	95 : 5
6	−(CH2)4−		Ph	Me_2SO_4	**2e**	61%	84 : 16
7	−(CH2)4−		Ph	MeOTf	**2e**	56%	91 : 9
8	Ph	Me	Ph	Me_2SO_4	**2b**	78%	>98 : 2
9	Ph	Me	2-ClC_6H_4	Me_2SO_4	**2f**	97%	84 : 16
10	Ph	Me	3-ClC_6H_4	Me_2SO_4	**2g**	99%	95 : 5
11	Ph	Me	2-$MeOC_6H_4$	Me_2SO_4	**2h**	85%	96 : 4
12	Ph	Me	3-$MeOC_6H_4$	Me_2SO_4	**2i**	85%	97 : 3
13	Ph	Me	Ph	Ac_2O	**2j**	70%	>98 : 2
14	Ph	Me	Ph	Et_2SO_4	**2k**	97%	95 : 5
15	Ph	Me	Ph	Bu_2SO_4	**2l**	94%	65 : 35
16	Ph	Et	Ph	Me_2SO_4	**2m**	68%	>97 : 3
17	Me	Me	Ph	Me_2SO_4	**2n**	72%	91 : 9
18	Me	Me	2-$MeOC_6H_4$	MeOTf	**2o**	60%	96 : 4
19	Ph	Ph	Ph	Me_2SO_4	**2p**	13%	>98 : 2
20	−(CH2)5−		4-MeC_6H_4	Me_2SO_4	**2q**	81%	95 : 5
21	−(CH2)5−		4-$MeOC_6H_4$	Me_2SO_4	**2r**	87%	96 : 4
22	−(CH2)5−		4-*t*-BuC_6H_4	Me_2SO_4	**2s**	92%	95 : 5
23	−(CH2)5−		4-ClC_6H_4	Me_2SO_4	**2t**	82%	95 : 5
24	Ph	Me	3,4-$Me_2C_6H_4$	Me_2SO_4	**2u**	82%	94 : 6
25	Ph	Me	4-MeC_6H_4	Me_2SO_4	**2v**	75%	94 : 6
26	Ph	Me	4-$MeOC_6H_4$	Me_2SO_4	**2w**	78%	96 : 4
27	Ph	Me	4-*t*-BuC_6H_4	Me_2SO_4	**2x**	88%	96 : 4
28	Ph	Me	4-ClC_6H_4	Me_2SO_4	**2y**	94%	95 : 5
29	Ph	Me	4-BrC_6H_4	Me_2SO_4	**2z**	94%	96 : 4
30	−(CH2)5−		Ph		**2aa**	81%	>98 : 2

[a] *Reaction conditions*: (1) α,α-disubstituted acetonitrile (1.0 mmol), THF (0.2 M), LDA (1.05 mmol), −78 °C, 20 min. (2) ArN_3 (1.2 mmol), HMPA (1.0 M), −78 °C to rt, 1 h. (3) RX (1.5 mmol), rt, 1 h. [b] Isolated yield. [c] Determined by crude ^1H NMR integration.

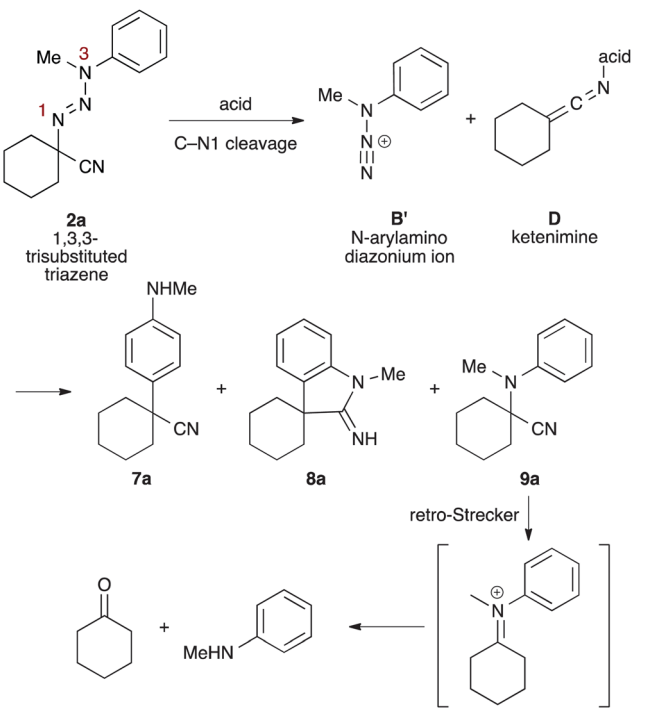
essential, its use slightly increased yields by 5–10%. In most cases, Me_2SO_4 was used as a methylating reagent. MeOTf was later found to be a marginally more selective methylating agent for **2** over **3** (*cf.* entries 1 *vs.* 2 and 5 *vs.* 6). Unlike dibutyl sulfate (entry 15), an alkyl tosylate provided high level of selectivity toward **2**, further broadening the synthetic utility of this reaction (entry 30). The reactions proceeded smoothly except for that involving α,α-diphenylacetonitrile (entry 19), the anion of which failed to react with phenyl azide. In general, these triazenes are stable; some of them have been stored for more than two years without noticeable decomposition.

Acid-promoted decomposition/recombination of triazenes

Triazenes are known to decompose under thermal or acidic conditions.[22,23] We observed that the triazenyl carbonitrile **2** decomposes *via* a previously unknown pathway and that the intermediates resulting from this reaction recombine to generate a new C–C bond (Scheme 6). Thus, attachment of a Lewis or Brønsted acid to the nitrile nitrogen atom is followed by cleavage of the C–N1 bond to afford a reactive *N*-arylaminodiazonium ion **B′** plus an acid-coordinated ketenimine **D**. This contrasts with previously published examples in which acid attachment at the N3 atom of a triazene is followed by cleavage of the N2–N3 bond (see discussion on mechanism below).[23]

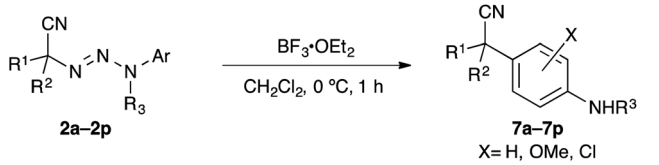
In the second part of this mechanism, *N*-arylaminodiazonium ion **B′** loses N_2 to give the corresponding aryl nitrenium ion, which then recombines with ketenimine **D**. In principle, four possible products are possible, resulting from *ortho*-, *meta*-, *para*-, and *N*-substitution, respectively. We are unaware of previous examples of *meta*-addition and accordingly eliminated it from consideration. In our experiments, products arising from *para*-alkylation (**7a**) were slightly favored over either *ortho*-alkylation, which was followed by cyclization to afford indolinimine **8a**, or *N*-alkylation leading to Strecker product **9a**. This material can be observed spectroscopically but under acidic conditions it undergoes a retro-Strecker reaction to generate *N*-methylaniline and cyclohexanone. Other research groups have also reported the formation of mixed products from aryl nitrenium ions.[7b,c,8b–d]

Initially, the ratios between **7a**, **8a**, and **9a** were comparable and the isolated yield of **7a** was between 7 and 34% (ESI†). In the course of examining various acids, we found that formation of the *ortho*-alkylated and cyclized product **8a** was suppressed (<5%) when $BF_3{\cdot}OEt_2$ was used (Table 2). Under these conditions, the reaction was rapid as evidenced by the cessation of N_2 gas evolution after *ca.* 10 min (although the reactions were allowed to proceed for 1 h). However, we could not find conditions that completely suppressed *N*-alkylation, which limited the overall yields of **7a–p** to 33–67%. The reaction could be carried out using cyclic (entry 1–4), arylalkyl (entry 5–14), dialkyl (entry 15–16), and diaryl (entry 17) acetonitriles. Both electron-withdrawing and donating substituents were tolerated on the aniline moiety. Comparing entries 7 *vs.* 8 and 9 *vs.* 10 shows that an electron-donating group slightly increased the yield, consistent with the intermediacy of a nitrenium ion. Although the triazene substrates were typically purified by column chromatography prior to the rearrangement reaction, direct treatment of the crude triazene with Lewis acid afforded product in a



Scheme 6

Table 2 α-Arylation of **2a–2p**[a]



	2	R^1	R^2	Ar	R^3	Prod	Yield[b]
1	**2a**	$-(CH_2)_5-$		Ph	Me	**7a**	41%
2	**2c**	$-(CH_2)_5-$		2-$MeOC_6H_4$	Me	**7c**	39%
3	**2d**	$-(CH_2)_5-$		3-$MeOC_6H_4$	Me	**7d**	49%
4	**2e**	$-(CH_2)_4-$		Ph	Me	**7e**	35%
5	**2b**	Ph	Me	Ph	Me	**7b**	45%
6	**2b**[c]	Ph	Me	Ph	Me	**7b**	46%
7	**2f**	Ph	Me	2-ClC_6H_4	Me	**7f**	42%
8	**2g**	Ph	Me	3-ClC_6H_4	Me	**7g**	43%[d]
9	**2h**	Ph	Me	2-$MeOC_6H_4$	Me	**7h**	67%
10	**2i**	Ph	Me	3-$MeOC_6H_4$	Me	**7i**	50%
11	**2j**	Ph	Me	Ph	Ac	**7j**	33%
12	**2k**	Ph	Me	Ph	Et	**7k**	51%
13	**2l**	Ph	Me	Ph	Bu	**7l**	49%
14	**2m**	Ph	Et	Ph	Me	**7m**	45%
15	**2n**	Me	Me	Ph	Me	**7n**	40%
16	**2o**	Me	Me	2-$MeOC_6H_4$	Me	**7o**	47%
17	**2p**	Ph	Ph	Ph	Me	**7p**	52%

[a] *Reaction conditions*: **2** (0.25 mmol), CH_2Cl_2 (0.2 M), $BF_3{\cdot}OEt_2$ (0.3 mmol), 0 °C, 1 h. [b] Isolated yield. [c] Crude **2b** was directly treated with $BF_3{\cdot}OEt_2$. Isolated yield over 2 steps. [d] Rt, 1 h.

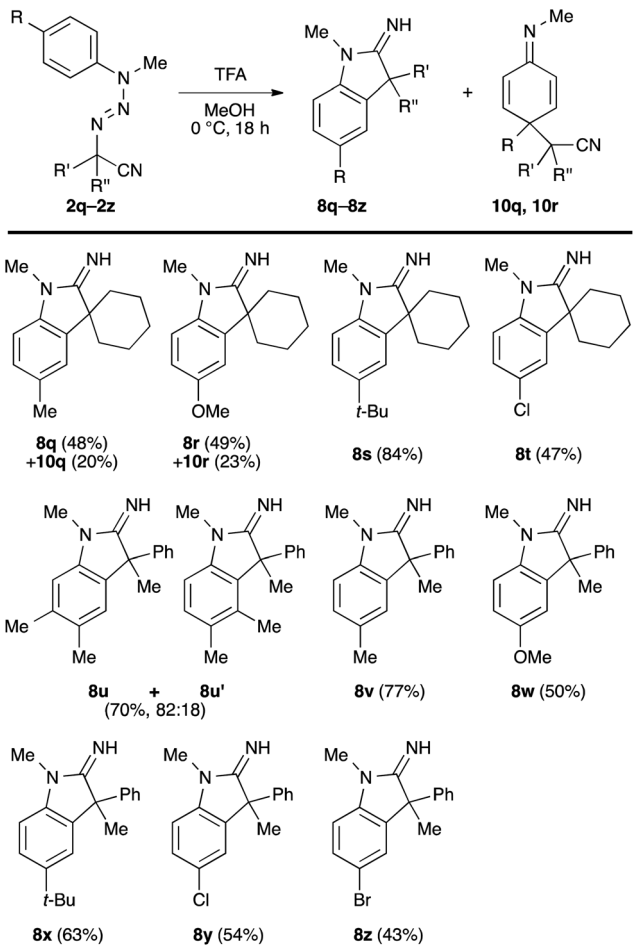
comparable isolated yield (46% over 2 steps for the case of entry 6). In addition to *N*-methylanilines, incorporation of *N*-acetyl (entry 11), ethyl (entry 12), and butyl (entry 13) groups were also successful.

In order to favor *ortho*-selective alkylation of aminodiazonium species, we synthesized *para*-substituted aryl triazene compounds **2q–2z** (Table 1, entry 20–29). Solvent screening for this reaction revealed that using nucleophilic protic solvents diminished *N*-alkylation/retro-Strecker products (ESI†). Thus, treating *para*-substituted aryl triazenes (**2q–2z**) with 2.5 equiv. of trifluoroacetic acid in MeOH (0.2 M) at 0 °C resulted in the formation of spiro- and α,α-disubstituted indolinimines in good to moderate yields (Scheme 7). In a few cases in which a small electron-donating group was present at the *para*-position, a *para*-alkylation product was obtained as a minor product (**10q** and **10r**). Nucleophilic additions at the *para*-position of *para*-substituted aryl nitrenium ions are known.[6,7b,c] In the case of unsymmetrical 3,4-dimethylphenyltriazene substrates, alkylation preferably occurred at the less hindered position (**8u** : **8u′** = 82 : 18). Substrates containing electron-withdrawing groups at the *para*-position afforded product in slightly lower yields as expected from the nitrenium ion mechanism (**8t**, **8y**, **8z**).

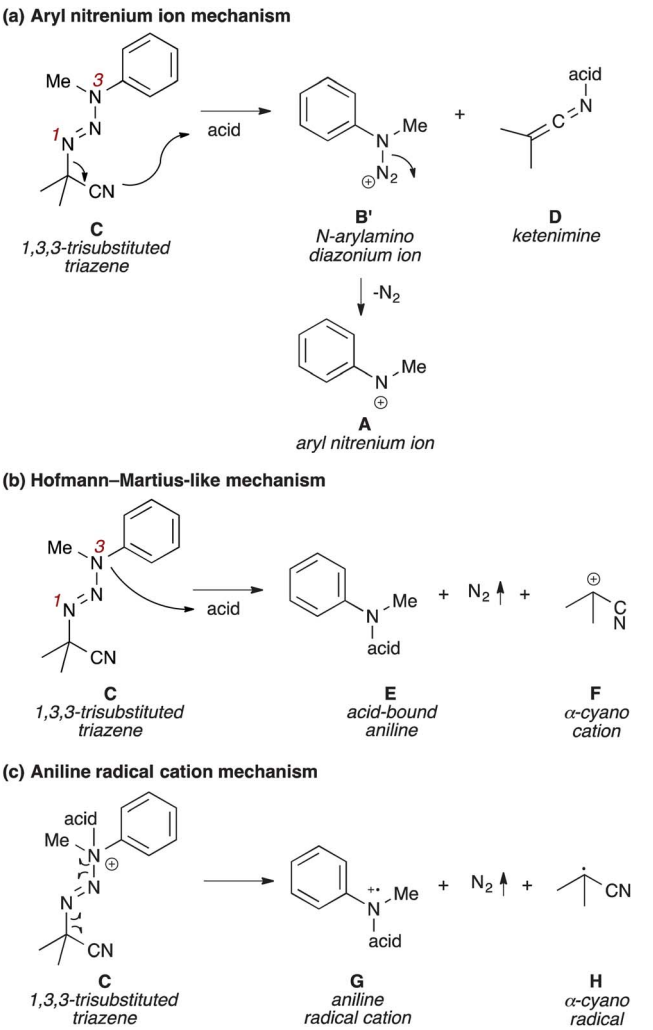
Mechanism

We sought to gain additional insight into the mechanisms behind the decomposition and recombination of triazene **C** (Scheme 8). We have already discussed the aryl nitrenium ion mechanism, in which acid bound to the carbonitrile initiates the decomposition to *N*-arylaminodiazonium ion **B′** and nucleophilic ketenimine species **D** (Scheme 8a; *cf.* Scheme 2). A second possibility involves acid attachment at the triazene N3 atom, which would incur N2–N3 bond cleavage and result in the formation and recombination of an anilinic nucleophile **E** and an α-cyano cation **F**. Such a mechanism is reminiscent of the Hofmann–Martius reaction of α-arylated anilines (Scheme 8b)[24] and protonation at the sp^3 nitrogen of triazenes is commonly accepted in the acid-promoted decomposition of triazenes.[23] A third possibility is a radical mechanism, which would involve the protonation of the aniline nitrogen followed by homolytic cleavage of the N–N bond to form an aniline radical cation **G** and an α-cyano radical **H** (Scheme 8c).

Two observations are inconsistent with a radical mechanism. First, aniline radical cations are known to form dimerized or polymerized products,[25] neither of which was observed in any



Scheme 7



Scheme 8

of our experiments. Secondly, we prepared **2aa** as a probe compound with the expectation that an *N*-radical species formed would undergo rapid cyclization.[22e,26] Upon treating this material with $BF_3 \cdot OEt_2$, α-arylation product **7aa** as well as retro-Strecker product **11** were obtained in comparable yields to those reported above with no products arising from radical cyclization being found (Scheme 9a).[27]

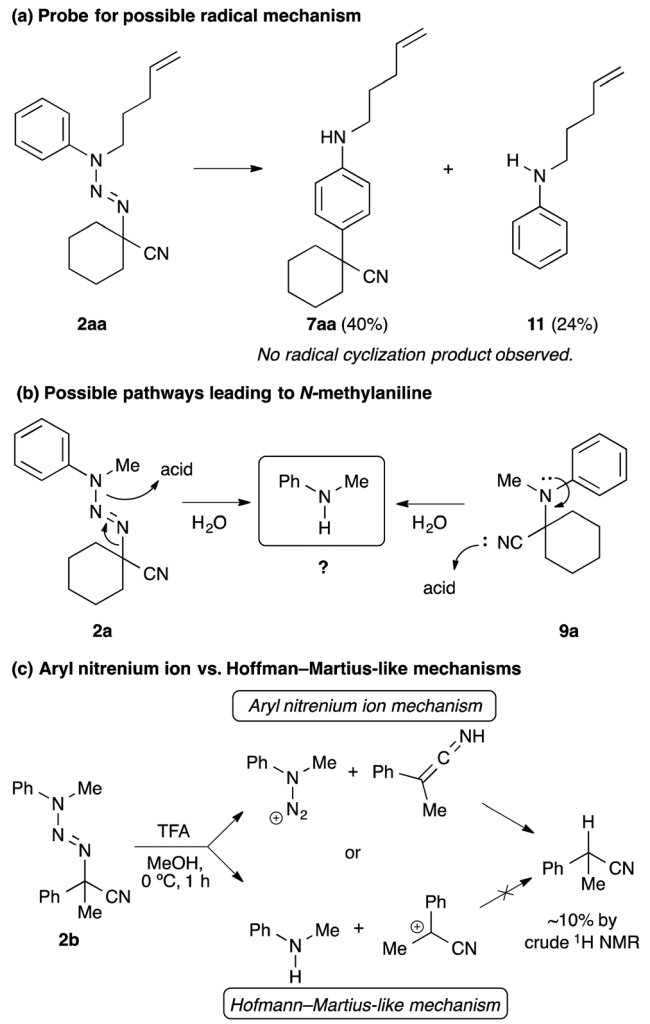
This leaves us with one of the two ionic mechanisms (Scheme 8a/b). We initially suspected a Hofmann–Martius-like mechanism (Scheme 8b) since we had detected *N*-methylaniline (or protonated **E**) in the crude reaction mixture. Although an α-cyano cation **F** essential to this mechanism is energetically unfavorable, such species have been previously reported.[28] However, *N*-methylaniline could also arise from retro-Strecker decomposition of **9a** (Scheme 9b, also see Scheme 6). To determine whether the latter was possible, we treated **2b** with acid and showed that *N*-methylaniline and acetophenone were formed under these conditions in a *ca.* 1 : 1 ratio.[29] This shows that the *N*-methylaniline observed in the reaction mixture could arise from either the decomposition of triazene **2b** or the *N*-alkylated product **9b**, leaving both of the mechanisms in Scheme 8a and b as reasonable possibilities.

We favor the *N*-aryldiazonium ion (**B′**) → aryl nitrenium ion (**A**) mechanism (Scheme 8a) because the positive charge is in the aryl nitrenium intermediate **A** is extensively stabilized by the phenyl group.[30] In seeking to differentiate the aryl nitrenium ion mechanism from a Hofmann–Martius-like mechanism involving α-cyano cation **F**, we treated **2b** with TFA in methanol (Scheme 9c). Analysis of the crude ^{1}H NMR spectrum indicated formation of *ca.* 10% of α-methylphenylacetonitrile. This compound cannot be formed according to the Hofmann–Martius mechanism (it would require a reduction of the cation), but it can be formed under the second aryl nitrenium ion mechanism *via* tautomerization of the ketenimine intermediate. This is more consistent with the aryl nitrenium mechanism as opposed to one involving an α-cyano cation.

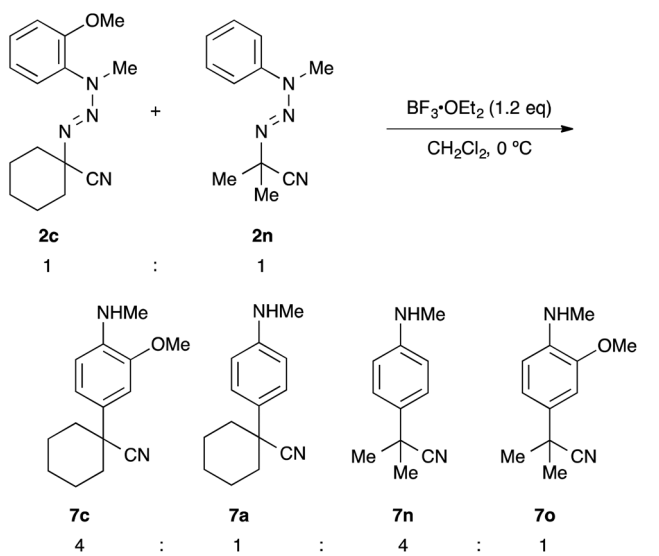
A crossover experiment with a 1 : 1 mixture of **2c** and **2n** was performed. The product distribution from ^{1}H NMR analysis on the crude mixture indicated that *ca.* 80% of the products were self-recombination products, with 20% arising from crossover (Scheme 10). This is consistent with that the *ca.* 60% of the decomposed fragments arising from the given triazene remained in proximity to one another to recombine.

Although aryl azides can be converted to *N*-phenyl-aminodiazonium salts (**B** in Scheme 1) by strong acid,[2a,b] the direct generation of *N*-methyl-*N*-phenylaminodiazonium salts **B′** (*N*-methylated; Scheme 2) has not been previously reported. This represents a clear advancement of using a triazene as an aminodiazonium precursor, as verified by the result that no α-arylated acetonitrile was observed when we combined phenyl azide in sulfuric acid with 3 equiv. of α-methylphenylacetonitrile. Thus, although the crossover experiments establish that the reactive intermediates generated in this process can react outside their initial solvent cage to some extent, there is considerable practical value to generating both species from a common triazene precursor.

Finally, we note that, unlike the readily acid-labile triazene **2a**, the isomeric **3a** undergoes much slower acid decomposition



Scheme 9



Scheme 10

to unidentified products. Specifically, no recombined product was obtained for **3a**. At this point, we have not pursued the synthetic application of **3** in acid-promoted reactions, although one cannot rule out its utility in other applications.

Conclusions

These studies describe (1) the generation of a trisubstituted triazene by α-cyano anion addition followed by electrophilic trapping, (2) the discovery that the regiochemistry of the trapping event depends remarkably on conditions, which have been analyzed on the basis of a spirocyclic 1-phenyl-1*H*-1,2,3-triazol-5(4*H*)-imine anionic intermediate **5a**, (3) that 3-alkyl-3-aryltriazenes can be converted into *N*-arylaminodiazonium ions, useful but previously uninvestigated precursors to nitrenium ions. Furthermore, we have discovered (4) that the recombination of such *N*-arylaminodiazonium ions with a nonsolvent nucleophile is possible (here, with a recycled ketenimine corresponding to the original nitrile reaction partner in the first step), (5) the product profile depends on aryl substitution, and finally (6) that the overall sequence results in two new α-arylation reactions yielding products with α-all-carbon quaternary centers without the need for transition metals. Although the yields of the overall arylation reactions are modest, the rich chemistry of triazenes introduced here provides a platform for additional studies in the areas of nitrenium ion and triazene chemistry.

Acknowledgements

This work was supported by the National Institute of General Medical Sciences (P50 69663). Also, we acknowledge Dr Victor Day for X-ray crystallography (NSF-MRI CHE-0923449) and Benjamin Neuenswander for HRMS.

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30 We thank an anonymous referee of an earlier version of this paper for initially suggesting this mechanism.