Triazene formation *via* reaction of imidazol-2-ylidenes with azides†

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Treatment of N-heterocyclic carbenes (as their free carbenes or generated *in situ*) with alkyl, aryl, acyl or tosyl azides afforded the respective substituted triazenes in excellent yields.

Triazenes[1] have found use as alkylating agents in tumor therapy,[2] as iodo-masking groups in the synthesis of small-[3] and macro-molecules,[4] and in the preparation of N-containing heterocycles.[5] The two most utilized methods of synthesizing triazenes has been through azo coupling of aryl diazonium salts and through the addition of organometallic reagents (RMgBr, RLi, *etc.*) to alkyl azides.[6] Herein, we report a new and operationally simple method of preparing substituted triazenes in high yields *via* the reaction of neutral nucleophilic N-heterocyclic carbenes with alkyl, aryl, acyl and tosylated azides.

Phosphines are well-known to react with azides to afford the corresponding phosphazide which subsequently loses N_2 and yields an azaylide. In the presence of water, the azaylide hydrolyzes to the respective primary amine (*i.e.*, the Staudinger reaction).[7] Spectroscopic studies suggest that imidazolylidenes are principally strong σ-donors with poor π-acceptor capabilities; thus they often share similar reactivity profiles as phosphines.[8] As such, we reasoned that reaction of an azide with an imidazolylidene would ultimately afford a 2-iminoimidazoline in lieu of the azaylide.[9,10] However, as shown in eqn (1), we found that by adding benzyl azide to 1,3-di-*tert*-butylimidazol-2-ylidene (**1**) in tetrahydrofuran at ambient temperature afforded triazine (**2**). Analysis of the crude reaction mixture by ^{1}H NMR spectroscopy indicated that the reaction was essentially quantitative with an estimated product purity of greater than 95% (the material could be further purified chromatographically). Alternatively, we discovered that the free carbene could be generated *in situ* through combination of the more stable and readily accessible 1,3-di-*tert*-butylimidazolium chloride with potassium *tert*-butoxide or sodium hydride and reacted with benzyl azide without suffering any loss in yield of product.
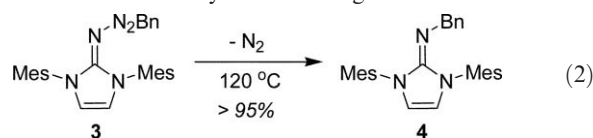

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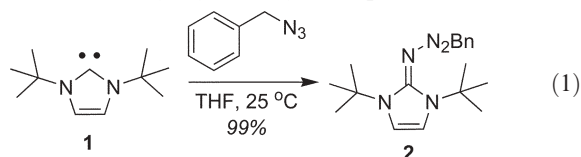
The scope of the reaction between various azides and imidazol-2-ylidenes (generated *in situ* from their respective imidazolium

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halide salts) was investigated;‡ the results are summarized in Table 1. In general, a wide array of alkyl (1°, 2°, 3°), aryl, acyl and tosylated azides were successfully used to triazenate a variety of imidazol-2-ylidenes with N-substituents ranging from methyl to mesityl at ambient temperatures. Reaction periods varied from 2 to 12 h and depended on the solvent (tetrahydrofuran *vs.* toluene) and the size of the N-heterocyclic carbene. Regardless, once the reaction was determined to be complete, unreacted imidazolium and alkali halide salts were precipitated from the reaction mixture using excess hexanes and removed by filtration. Evaporation of the solvent afforded pure product in good to excellent isolated yields (54–94%).

Crystallization of 1-benzyl-3-(1,3-dimesitylimidazol-2-ylidene)-triazene (**3**) (see Table 1, entry 6) from ethyl acetate by slow evaporation afforded single crystals suitable for X-ray structure determination. Unexpectedly, as shown in Fig. 1, the triazene was found to be the *Z*-isomer.§ To the best of our knowledge, this is the first example of a non-heteroatom stabilized triazene with a *cis* configuration about the N=N bond.[11] Curiously, when the crystallization was repeated, the *E*-isomer was found (Fig. 2).§ Factors governing the preferential formation of one isomer over the other remain unclear and are currently under investigation. Notably, the triazeno moiety in the *Z* isomer has a shorter N–N single bond (N6–N7, 1.34 Å) and a longer N–N double bond (N7–N8, 1.28 Å) when compared to the *E* isomer (1.36 and 1.26 Å, respectively), which may reflect a long-range interaction between the 2-imino and the benzyl moieties. In both isomers, the exocyclic 2-imino bond is significantly polarized as evidenced by its increased length (1.33–1.34 Å) relative to typical C–N double bonds (1.29 Å).§

Since both *E* and *Z* stereoisomers were discovered in the solid-state, focus shifted toward identifying them in solution. Resonances attributable to discrete isomers of **3** were not resolved at −80 °C in the ^{1}H NMR spectrum (solvent: toluene-d_8).[12] However, we discovered that heating **3** to >120 °C (in DMSO-d_6) cleanly extruded N_2 and formed *N*-benzyl 1,3-dimesityl-2-imino-imidazoline (**4**) in >95% yield (eqn (2)). The scope and mechanism of this reaction is currently under investigation.

$$(2)$$

In summary, we report a simple and effective route to substituted triazines by treatment of imidazol-2-ylidenes with various azides. The utility of this triazenation reaction in the synthesis of small molecules and macromolecular materials will be reported in due course.

Table 1 Synthesis of substituted triazines[a]

Entry	Imidazolium salt	Azide	Product	Isolated yield [b](%)
1	(1,3-dimethylimidazolium iodide)	benzyl azide (PhCH₂N₃)	N₂Bn triazene (1,3-dimethyl)	60
2	(1,3-dimethylimidazolium iodide)	butyl azide	N₂Bu triazene (1,3-dimethyl)	94
3	(1,3-diisopropylimidazolium chloride)	butyl azide	N₂Bu triazene (1,3-diisopropyl)	75
4	(1,3-diisopropylimidazolium chloride)	sec-butyl azide	N₂sBu triazene (1,3-diisopropyl)	81
5	(1,3-diisopropylimidazolium chloride)	phenyl azide	N₂Ph triazene (1,3-diisopropyl)	54
6	(1,3-dimesitylimidazolium chloride)	benzyl azide	N₂Bn triazene (1,3-dimesityl)	83
7	(1,3-dimesitylimidazolium chloride)	adamantyl azide	N₂Ad triazene (1,3-dimesityl)	60
8	(1,3-dimesitylimidazolium chloride)	benzoyl azide	N₂COPh triazene (1,3-dimesityl)	74
9	(1,3-dimesitylimidazolium chloride)	tosyl azide	N₂Ts triazene (1,3-dimesityl)	92

[a] *Reaction conditions*: solvent = THF or toluene, temp = 25 °C, ratios: imidazolium salt (1.00 equiv.)/azide (1.05 equiv.)/KOtBu (0.95 equiv.) or NaH (0.95 equiv.). [b] Isolated yield based on limiting reagent.
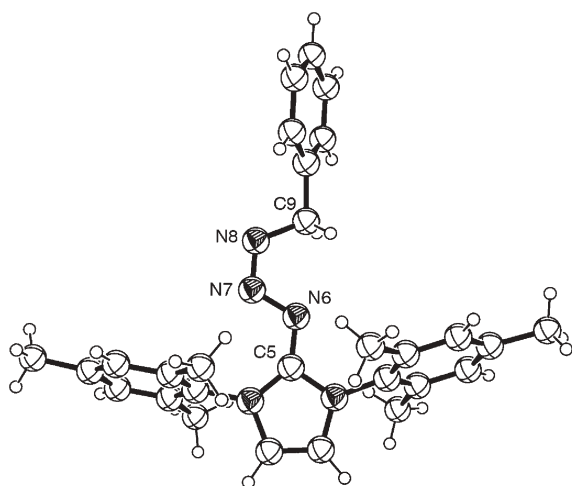

Fig. 1 ORTEP representation of the X-ray crystal structure of (Z)-1-benzyl-3-(1,3-dimesitylimidazol-2-ylidene)triazene (**3**), showing non-hydrogen atoms as 50% thermal ellipsoids. Selected bond distances (Å) and angles (°): C5–N6 1.330(3), N6–N7 1.342(4), N7–N8 1.278(3), N8–C9 1.431(5); C5–N6–N7 114.7(3), N6–N7–N8 116.2(2), N7–N8–C9 116.4(2); N6–N7–N8–C9 2.3(5).
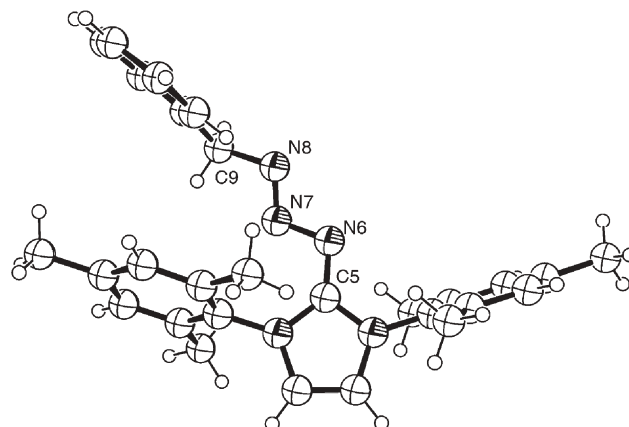

Fig. 2 ORTEP representation of the X-ray crystal structure of (E)-1-benzyl-3-(1,3-dimesitylimidazol-2-ylidene)triazene (**3**), showing non-hydrogen atoms as 50% thermal ellipsoids. Selected bond distances (Å) and angles (°): C5–N6 1.339(3), N6–N7 1.370(2), N7–N8 1.261(2), N8–C9 1.468(2); C5–N6–N7 109.4(2), N6–N7–N8 112.1(2), N7–N8–C9 109.8(2); N6–N7–N8–C9 179.2(2).

Notes and references

‡ *Representative procedure* for the synthesis of 1-benzyl-3-(1,3-dimesityl-imidazol-2-ylidene)triazene: Benzyl azide (0.79 mmol, 105 mg) was added in one portion using a 1 mL syringe to a slurry of mesityl imidazolium chloride (0.53 mmol, 180 mg) in dry THF (3 mL). In one portion, KO*t*Bu (0.58 mmol, 65 mg) was added to the reaction vessel and the resulting mixture was stirred under argon for 2 h. Excess hexanes (1 mL) were then added and the reaction mixture was filtered through Celite. The crude product was concentrated and purified using flash chromatography (70% EtOAc–hexanes) to afford the product as pale yellow crystals (192 mg, 83%). Crystals suitable for X-ray analysis were grown by slow evaporation from ethyl acetate. R_f = 0.33 (70% EtOAc–hexanes); ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.18–7.09 (m, 3H), 6.89 (br s, 6H), 6.44 (s, 2H), 4.04 (s, 2H), 2.28 (s, 6H), 2.14 (s, 12H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 152.1, 138.5, 138.3, 135.6, 124.3, 128.9, 128.8, 127.8, 126.3, 116.0, 65.4, 21.0, 18.0; HRMS calc. for C$_{28}$H$_{31}$N$_5$ [M + H$^+$]: 438.2658; found: 438.2659.

§ *Crystal data* for (*Z*)-1-benzyl-3-(1,3-dimesitylimidazol-2-ylidene)triazene (**3**) (C$_{28}$H$_{31}$N$_5$): M = 437.58, T = 153 (2) K, triclinic, space group $P\bar{1}$, a = 9.1191(1), b = 15.4148(2), c = 18.4677(3) Å, α = 104.680(1), β = 92.260(1), γ = 90.110(1)°, V = 2509.10(6) Å^3, Z = 4, D_c = 1.158 Mg m^{-3}, μ = 0.070 mm^{-1}, λ = 0.71073 Å, θ_{max} = 27.48°, 19912 measured reflections, 11357 independent reflections, 612 refined parameters, GOF = 1.152, $R[F^2 > 2\sigma(F^2)]$ = 0.0576, $wR(F^2)$ = 0.1163. The intensity data were collected on a Nonius Kappa CCD diffractometer. The structure was solved by direct methods using SIR97^{13} and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-97.^{14} The hydrogen atoms were calculated in ideal positions with isotropic displacement parameters set to 1.2U_{eq} of the attached atom (1.5U_{eq} for methyl hydrogen atoms). There were two crystallographically unique molecules in the asymmetric unit. In one molecule, the orientation of the triaza portion was disordered about two orientations. The disorder was modeled by assigning the variable x to the site occupancy factors of one component of the disorder composed of atoms N6, N7, N8 and C9. The site occupancy factor of the alternate component, composed of atoms N6A, N7A, N8A and C9A, had a site occupancy factor of $1 - x$. A common isotropic displacement parameter was assigned to the relevant atoms while refining x. The variable, x, refined to 0.82(2). The geometry of the disordered moieties were restrained to be approximately equal throughout the refinement. The atoms of the minor component of the disorder were refined isotropically.

Crystal data for (*E*)-1-benzyl-3-(1,3-dimesitylimidazol-2-ylidene)triazene (**3**) (C$_{28}$H$_{31}$N$_5$): M = 437.58, T = 153 (2) K, monoclinic, space group $P2_1/c$, a = 14.6396(3), b = 12.1965(2), c = 28.0462(5) Å, β = 90.634(1)°, V = 5007.40(16) Å^3, Z = 8, D_c = 1.161 Mg m^{-3}, μ = 0.070 mm^{-1}, λ = 0.71073 Å, θ_{max} = 25.00°, 16441 measured reflections, 8809 independent reflections, 596 refined parameters, GOF = 1.002, $R[F^2 > 2\sigma(F^2)]$ = 0.0525, $wR(F^2)$ = 0.0974. The intensity data were collected and the structure was solved and refined as above. The hydrogen atoms were also calculated as above. There were two crystallographically unique molecules in the asymmetric unit. These two molecules differed only slightly in conformation.

The crystal structure of (*E*)-1-benzoyl-3-(1,3-dimesitylimidazol-2-ylidene)triazene (**3**) was also determined. *Crystal data* for C$_{28}$H$_{29}$N$_5$O: M = 451.56, T = 153(2) K, orthorhombic, space group $P2_12_12_1$, a = 14.0109(3), b = 14.0230(3), c = 12.6469(2) Å, V = 2484.80(8) Å^3, Z = 4, D_c = 1.207 Mg m^{-3}, μ = 0.076 mm^{-1}, λ = 0.71073 Å, θ_{max} = 27.48°, 5434 measured reflections, 5434 independent reflections, 308 refined parameters, GOF = 1.191, $R[F^2 > 2\sigma(F^2)]$ = 0.0511, $wR(F^2)$ = 0.1018. The intensity data were collected and the structure was solved and refined as above. The

hydrogen atoms were also calculated as above. Selected bond distances (Å) and angles (°): C5–N6, 1.355(3), N6–N7 1.328(2), N7–N8 1.295(2), N8–C9 1.414(3); C5–N6–N7 110.4(2), N6–N7–N8 112.3(2), N7–N8–C9 110.4(2); N6–N7–N8–C9 −173.1(2).

CCDC 275071–275073. See http://dx.doi.org/10.1039/b508679e for crystallographic data in CIF or other electronic format.

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