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Methylation of Ylidene-Triazenes: Insight and Guidance for 1,3-Dipolar Cycloaddition Reactions

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Reaction of 1,3-dimesitylimidazolylidene (**1**) with *p*-functionalized phenyl azides **2** (**a**: H, **b**: OCH_3, **c**: NO_2) afforded the respective imidazolylidene-triazenes **3** in good yields (65–99 %). Subsequent treatment with methyl iodide produced the corresponding methylated products **4** in near-quantitative yields (99 %). Analysis by NOESY 1D NMR spectroscopy and single-crystal X-ray diffraction revealed that the methylation reaction was regioselective and occurred at the nitrogen atom most distal from the heterocycle. Consistent with the formation of ionic salts, the ^{1}H NMR signals for the imidazole protons in **4** were shifted > 0.5 ppm downfield compared to **1**, indicating the accumulation of positive charge. Similarly, the λ_{max} values recorded for **4** exhibited a much narrower range than those for **3** (16 vs. 77 nm, respectively), suggesting that the frontier orbital energies within the former were dominated by Coulombic effects (i.e., the acquisition of positive charge) as opposed to electronic effects from the electron-donating or withdrawing groups of the aryl azide. Whereas computational analyses revealed that the observed regioselectivity of the methylation reaction may be explained by thermodynamics, kinetic factors (e.g., sterics) may also be important contributors and render one reaction pathway significantly more accessible due to a lower activation energy.

Introduction

Modern chemistry has benefited from the synthetic power and versatility of dipolar cycloaddition and cyclization reactions,[1–4] which have enabled far-reaching advances in many pursuits, from the preparation of unnatural β-amino acids,[5] to the kinetic resolution of stereoisomers,[6] to the functionalization of carbon nanotubes.[7] Alkyne–azide 1,3-dipolar cycloadditions are an especially practical subclass of reactions, given that molecules comprising terminal alkyne[8–10] and azide[11] functionalities are synthetically accessible and often commercially available. Huisgen first described alkyne–azide 1,3-dipolar cycloadditions over 40 years ago,[12] however the low yields of products obtained and the lack of regioselectivity limited the practical scope of this transformation. It was not until 2002 that Sharpless[13] and Meldal[14] reported that the inclusion of catalytic Cu^I facilitates formation of 1,4-disubstituted-1,2,3-triazoles under mild conditions. Since this seminal achievement, copper-catalyzed alkyne–azide "click" couplings have revolutionized a broad swath of scientific disciplines, such as nucleoside and nucleotide functionalization,[15,16] bioimaging,[17,18] drug[19,20] and gene[21] delivery, combinatorial chemistry,[22] as well as the synthesis of complex macromolecular architectures (i.e., ambiphilic block copolymers, star polymers, dendrimers, micelles, etc.).[23–26]

Trisubstituted triazoles have recently received attention as a potentially useful class of nitrogen containing substrates but suffer from challenging synthetic limitations.[27] The preparation of these compounds via 1,3-dipolar cycloaddition chemistry requires either the alkyne or azide to be difunctionalized. Although examples of the former have been reported, their Cu-catalyzed cycloaddition is currently limited to haloalkynes and proceeds by a mechanism that is still being established. Difunctionalized azides are also synthetically daunting targets, however a simpler analogue is an ylidene-triazene (**Y**), the coupling product of an N-heterocyclic carbene (NHC) to an azide,[28–34] which can be viewed as a zwitterion (**Z**) that is suitable to engage in dipolar cycloaddition reactions (Figure 1).

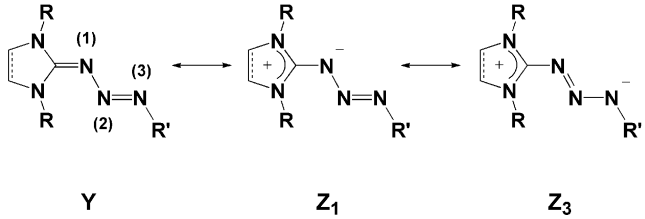

Figure 1. Resonance structures of ylidene-triazenes (**Y**): zwitterions $\mathbf{Z_1}$ and $\mathbf{Z_3}$ feature a formal negative charge at the N^1 and N^3 positions, respectively. R and R′ = alkyl or aryl (see refs.[30–34]).

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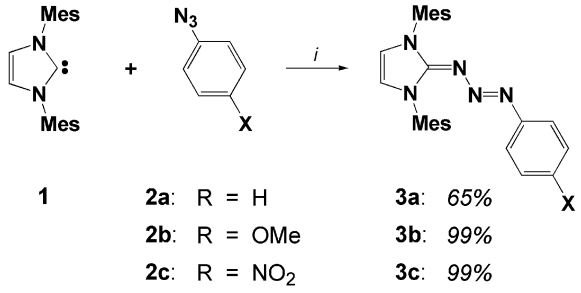
Despite our best efforts, attempts to effect dipolar cycloadditions of various alkynes with ylidene-triazenes have been thus far unsuccessful. Given that the ability of an azide to participate in 1,3-dipolar cycloaddition reactions depends in part on the electron density at the nitrogen atoms,[13,14] we sought to probe the corresponding electron density in ylidene-triazenes via their chemical reactivity towards alkylating agents. Herein we report the synthesis and methylation of a series of imidazolylidene-triazenes, provide a detailed account of their structural and electronic properties, and offer attendant insight and guidance for enabling ylidene-triazenes to engage in 1,3-dipolar cycloadditions.

Results and Discussion

Coupling of 1,3-dimesitylimidazolylidene (**1**) to phenyl azide (**2a**) afforded imidazolylidene-triazene **3a** in good yield (65%, Scheme 1). Using similar methodology, this coupling reaction was also performed with aryl azides bearing electron-donating (OCH_3, **2b**) or electron-withdrawing (NO_2, **2c**) *para*-substituents to afford the corresponding imidazolylidene-triazene **3b** or **3c**, respectively, in excellent yields (99%). Consistent with the loss of carbenoid character at the 2 position, the ^{13}C NMR chemical shifts for **3** (151.5–157.5 ppm, $CDCl_3$; see Table 1) were shifted significantly upfield from that observed in **1** (δ = 219.7 ppm, C_6D_6).[35] Moreover, additional spectroscopic data recorded for **3** were consistent with other ylidene-triazenes previously reported in the literature.[31,32]



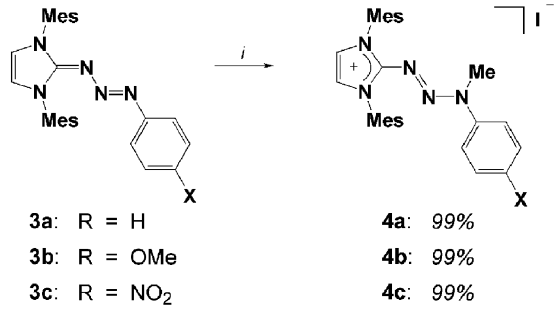
Scheme 1. Synthesis of imidazolylidene-triazenes **3a**–**c**. *i*) THF, room temp., 16 h.

Table 1. Summary of spectroscopic data.[a]

	δ C_2 [ppm]	δ $H_{4,5}$ [ppm]	λ_{max} [nm]
3a	151.5	7.03	368
3b	157.5	6.53	371
3c	156.9	6.69	445
4a	144.6	7.70	367
4b	159.3	7.56	383
4c	146.3	7.71	380

[a] NMR (^1H and ^{13}C) and UV/Vis measurements were performed in $CDCl_3$ and CH_2Cl_2, respectively.

To determine whether the N^1 or N^3 position featured greater negative polarization in the aforementioned ylidene-triazenes, **3** was treated with excess methyl iodide, which afforded **4** in near-quantitative yield (99%, Scheme 2). Upon methylation, the ^1H NMR signals for the 4,5 positions on the imidazole ring were shifted significantly downfield (6.53–7.03 ppm in **3** vs. 7.56–7.70 in **4**, $CDCl_3$; see Table 1), suggesting the acquisition of positive charge and attendant imidazolium character. Interestingly, the values observed for **4** occurred within a narrower range than **3**, which may reflect the alteration of the factors influencing electron density within the imidazole ring. For example, the ylidene moiety in **3a** should experience a greater electron-withdrawing effect by the azide arene than in **3b** ($\Delta\delta$ = 0.50 ppm) due to the presence of the electron donating methoxy group in the latter. However, the addition of a positive charge to the molecule will have a greater effect on the electron density within the imidazole ring than an azide substituent (i.e., Coulombic effects > inductive effects), which is borne out by the smaller chemical shift difference observed between **4a** and **4b** ($\Delta\delta$ = 0.14 ppm).



Scheme 2. Synthesis of N^3-methylated imidazolylidene-triazenes **4a**–**c**. *i*) 2.5 equiv. MeI, CH_2Cl_2, room temp., 16 h.

Primacy of Coulombic over inductive factors was also apparent in the UV/Vis spectroscopic profiles of **3** vs. **4** (Table 1). For example, imidazolylidene-triazenes **3** may be viewed as a donor–acceptor systems,[31] where the moiety derived from the imidazolylidene functions as a donor and the moiety derived from the azide as an acceptor. As such, **3c** exhibited a significantly longer λ_{max} than in **3a** and **3b** (445, 368, and 371 nm, respectively). Although methylation of **3c** (to obtain **4c**) produced a significant hypsochromic shift in the measured λ_{max} ($\Delta\lambda$ = 65 nm), methylation of **3a** or **3b** had a relatively minimal effect ($\Delta\lambda \leq$ 12 nm). Collectively, these results suggested to us that (*i*) the electron density distributions in imidazolylidene-triazenes **3** are influenced by the electron-donating or -withdrawing character of the azide, and (*ii*) the positive charge acquired by these molecules upon reaction with methyl iodide dominates the electronic topology of their alkylated derivatives **4**.

Despite the information about the electronic properties of **4** provided by the aforementioned NMR and UV/Vis spectroscopic measurements, these data did not enable unambiguous determination of the position of the *N*-methyl group (i.e. N^1 vs. N^3). Therefore, NOESY experiments were conducted on **4c** to determine which protons were proximal to those in the *N*-methyl substituent, and thus elucidate the absolute structure of these molecules. Assuming that **4c** was

methylated at the N^3 position (see Figure 2), the diagnostic ^1H NMR signals will be for the protons at: the *meta*-aryl position within the mesityl rings (*a*), the 4,5 positions on the imidazole ring (*b*), the *ortho*-aryl protons on the nitrophenyl ring (*c*), the *N*-methyl group (*d*), and the *ortho*-methyl substituents on the mesityl rings (*e*) (see Figure 2, middle spectrum). Saturation of the transition assigned to the *N*-methyl protons (*d**, negative peak; top trace) afforded two positive peaks (*c* and *e*), which indicated that the *N*-methyl group was in close proximity to the nitrophenyl and mesityl rings. Conversely, irradiation of the signal attributed to the mesityl *ortho*-methyl groups (*e**; negative peak, bottom trace) revealed two strong positive peaks (*a* and *b*) that were assigned to the nearest neighboring protons derived from the imidazolylidene fragment. Collectively, the results suggested to us that the methyl group in **4c** was located at the N^3 position. In further support of this notion, irradiation at *d* did not enhance the signal associated with the *N*-mesityl methyl or aryl protons (*a* and *e*), results that would have been expected if the methyl group was located at the N^1 position.

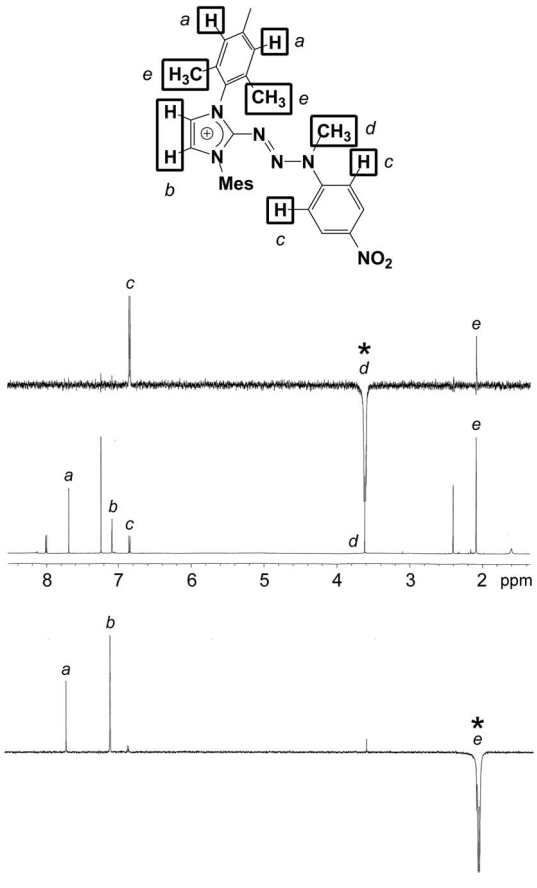


Figure 2. Summary of NOESY 1D NMR experiments ($CDCl_3$, 600 MHz, mixing time = 0.8 s) used to confirm methylation at the N^3 position in **4c** (see top structure, italicized lowercase letters indicate labelling scheme). Saturating the transition for the *N*-methyl group (*d**, top spectrum) afforded strong, positive peaks at *c* and *e*. Conversely, irradiation of the mesityl *ortho*-methyl substituents (*e**, bottom spectrum) afforded strong, positive peaks at *a* and *b*.

To obtain greater insight into the structure and bonding within the aforementioned imidazolylidene-triazenes and their N^3-methylated derivatives, single crystals of **3c** and **4c**, respectively, were subjected to X-ray diffraction (see Figures 3 and 4, respectively). In agreement with the ^1H NMR chemical shifts for these compounds, the N4–C1–N5 angle in **3c** was more obtuse than in **1** [106.67(18) vs. 101.4(2)°, respectively],[36] reflecting its loss of carbenoid character, and was within the range of values observed for other ylidene-triazenes previously reported (105.4–108.5°).[31,32] Similarly, the N1–N2 distance was longer in **3c** [1.337(2) Å] and the N1–N2–N3 angle more acute [110.92(17)°] than the cor-

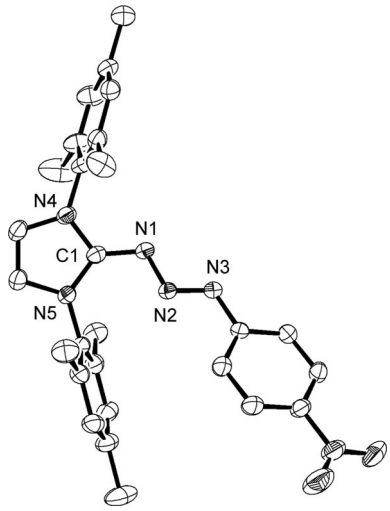


Figure 3. ORTEP diagram showing 50% probability thermal ellipsoids and selected atom labels for **3c**. Hydrogen atoms and solvent molecules have been omitted for clarity. Selected bond lengths [Å] and angles [°]: N1–C1 1.348(3), N1–N2 1.337(2), N2–N3 1.286(2), N4–C1–N5 106.67(18), N1–N2–N3 110.92(17), N5–C1–N1–N2 24.2(2).

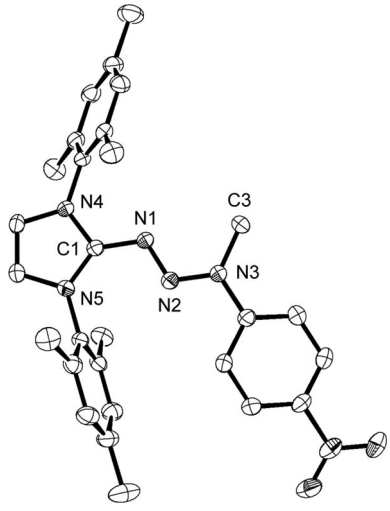


Figure 4. ORTEP diagram showing 50% probability thermal ellipsoids and selected atom labels for **4c**. Counteranion, hydrogen atoms and solvent molecules have been omitted for clarity. Selected bond lengths [Å] and angles [°]: N1–C1 1.372(3), N1–N2 1.283(3), N2–N3 1.322(3), N3–C3 1.464(3), N4–C1–N5 107.2(2), N1–N2–N3 113.6(2), N5–C1–N1–N2 8.2(2), N1–N2–N3–C3 2.6(2).

responding features observed in the solid state structure (not shown) of **2c** (1.127 Å and 173.4°),[37] consistent with the reduction of formal bond order (2.5 to 1.5) upon incorporation of **2c** into **3c**. Collectively, the metric parameters for the ylidene–triazene linkage in **3c** [N1–C1 1.348(3) Å, N1–N2 1.337(2) Å, N2–N3 1.286(2) Å, N1–N2–N3 110.92(17)°] were in good agreement with other reported ylidene-triazenes that have been crystallographically characterized (N1–C1 1.329–1.356 Å, N1–N2 1.328–1.370 Å, N2–N3 1.261–1.295 Å, N1–N2–N3 109.4–116.2°) and suggested to us that the electronic topology within this framework was largely independent of the chemical identity of the various *N*- and *C*-substituents.

As shown in Figure 4, analysis of **4c** by single-crystal X-ray diffraction unambiguously confirmed that the methyl group was affixed to the N^3 position.[36] Although no analogues to **4c** have been reported in the literature to the best of our knowledge, there are related molecules that belong to the broader class of N^1,N^2,N^3-trisubstituted triazenes.[38–47] Despite substantial variation in the chemical identity of the *N*-substituents, the bond lengths observed within the N_3–R (where R is a variety of alkyl groups) fragments of these previously reported N^1,N^3,N^3-trisubstituted triazenes did not vary significantly (N1–N2 1.266–1.288 Å, N2–N3 1.304–1.343 Å, N3–C3 1.435–1.466 Å) and encompassed the values observed for **4c** [N1–N2 1.283(3) Å, N2–N3 1.322(3) Å, N3–C3 1.464(3) Å]. Similarly, the N1–N2–N3 angle and N1–N2–N3–C3 torsion in **4c** [113.6(2) and 2.6(2)°, respectively] were consistent with the corresponding angles observed in other trisubstituted triazene systems (111.3–114.6 and 0.1–4.0°, respectively).[38–47] Interestingly, the fact that these structural features are so highly conserved suggested to us that the bonding within N^1,N^3,N^3-trisubstituted triazenes is determined primarily by the N_3–CH_3 fragment and largely independent of the chemical identity of the other *N*-substituents.

Having obtained structural information for both **3c** and **4c**, we compared their metric parameters to discern the changes in bonding that accompanied methylation. Whereas the N4–C1–N5 angle for **3c** [106.67(18)°] did not change significantly upon conversion to **4c** [107.2(2)°], the N1–N2–N3 angle was more obtuse in the latter [110.92(17)° for **3c** vs. 113.6(2)° for **4c**], possibly due to the steric effects between N1 and C3. Interestingly, the bond lengths within the C1–N1–N2–N3 linkage in **3c** and **4c** reflect the alteration of bonding that occurs upon methylation (Scheme 2). For example, the CN_3 linkage in **3c** can be formally represented as C=N–N=N, featuring terminal double bonds and an internal single bond (**2**–**1**–**2**, Figure 5); **4c** can be viewed as C–N=N–N, where the terminal and internal bond orders are 1 and 2, respectively (**1**–**2**–**1**). Indeed, conversion of **3c** to **4c** afforded an elongation of N1–C1 [1.348(3) to 1.372(3) Å], a contraction of N1–N2 [1.337(2) to 1.283(3) Å], and a larger N2–N3 distance [1.286(2) to 1.322(3) Å]. Therefore, we conclude that an alteration of bond order occurs upon methylation of **3c**, whereby its alternating "double–single–double" CN_3 structure (**2**–**1**–**2**) is inverted upon formation of **4c**, which exhibits a "single–double–single" CN_3 structure (**1**–**2**–**1**).

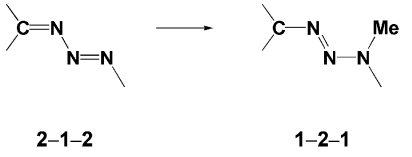


Figure 5. Bond order within the CN_3 fragment in: (left) an ylidene-triazene (**2**–**1**–**2**, C=N–N=N) compared to (right) an N^3-methylated derivative (**1**–**2**–**1**, C–N=N–N).

Based on our experimental findings, we speculated that selective methylation of **3** at the N^3 vs. N^1 position may reflect a thermodynamic preference beyond simple steric considerations. To test this hypothesis, we performed RHF calculations on **3c** and **4c** using the 6-31G(*) basis set on all atoms.[48] The HOMO of **3c** was found to be consistent with the **2**–**1**–**2** formulation derived from the crystal structure (see Figure 6). In agreement with our hypothesis, the total energy of the (observed) N^3-methylated imidazolylidene-triazene was lower than the hypothetical N^1 isomer by 6.4 kcal/mol (structure not shown). In addition being thermodynamically favored, formation of the former may be driven by kinetic factors as well (e.g. the activation barrier for N^1-methylation may be higher due to steric crowding from the *N*-mesityl groups).

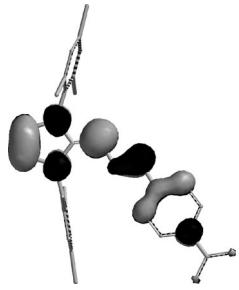


Figure 6. HOMO for **3c** determined by RHF calculations using the 6-31G(*) basis set on all atoms.

Conclusions

In sum, the synthesis and methylation of a series of imidazolylidene-triazenes was accomplished. Analysis by NMR and UV/Vis spectroscopy indicated that the electronic changes (such as the deshielding of imidazole ring and perturbation of the frontier orbitals) that accompanied *N*-methylation were derived primarily from Coulombic effects. Both NOESY NMR and single-crystal X-ray diffraction revealed that the methyl group was located at the N^3 position. Interestingly, the metric parameters observed for an ylidene-triazene and its methylated derivative were consistent with their formal bond orders (i.e., C=N–N=N and C–N=N–N, respectively). Whereas computational methods indicated a thermodynamic preference for the N^3-methyl isomer (vs. the N^1-methyl isomer), steric congestion and other kinetic factors may contribute to the observed regioselectivity as well.

Collectively, our findings demonstrate that ylidene-triazenes feature the requisite formal charges to engage in 1,3-dipolar cycloaddition reactions but do not exhibit the necessary distribution thereof. Decreasing the steric congestion at the N^1 position might circumvent the kinetic obstacles to reactivity at this atom (e.g., employ imidazolylidenes with *N*-methyl in lieu of *N*-mesityl substituents); however, such ylidene-triazenes are often unstable.[49] Alternatively, destabilizing any negative charge build-up at the N^3 position via judicious choice of electron-donating substituents may favor reactivity at the N^1 position and enable ylidene-triazenes to engage in dipolar cycloaddition reactions. Efforts toward achieving this goal are underway and will be described in due course.

Experimental Section

Materials and Methods: 1,3-Dimesitylimidazolylidene (**1**)[35] and aryl azides (**2**)[50,51] were prepared as described previously. Solvents were dried and degassed by a Vacuum Atmospheres Company solvent purification system (model 103991) and stored over 3 Å molecular sieves in a nitrogen-filled glove box. ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded using a Varian 300, 400 or 500 MHz spectrometer. All NOESY 1D NMR spectra were collected on a 600 MHz NMR (mixing time = 0.8 s). Chemical shifts δ (in ppm) are referenced to tetramethylsilane using the residual solvent as an internal standard. For ^{1}H NMR: $CDCl_3$, 7.24 ppm. For ^{13}C NMR: $CDCl_3$, 77.0 ppm. Coupling constants (*J*) are expressed in Hertz (Hz). FT-IR spectra were recorded using Perkin–Elmer Spectrum BX system. High-resolution mass spectra (HRMS) were obtained with a VG analytical ZAB2-E instrument (ESI or CI). All syntheses were performed under inert atmosphere unless specified otherwise.

General UV/Visible Spectroscopic Considerations: UV/Visible absorption spectra were recorded on a Perkin–Elmer Lambda 35 spectrometer. All room-temperature measurements were made using matched 6Q Spectrosil quartz cuvettes (Starna) with 1 cm path lengths and 3.0 mL of sample solution volumes. Absorption spectra were acquired in CH_2Cl_2 under ambient conditions for all complexes. Extinction coefficients (ε) were determined from Beer's law measurements using 10, 20, 30 and 40 μM concentrations of the analyte.

General Procedure for the Synthesis of 3: To a solution of **1** (50 mg, 0.16 mmol) in THF (3 mL) was added phenyl azide **2** (0.16 mmol) in one portion and the reaction was allowed to stir at room temperature. After 16 h, the solvent was removed under reduced pressure, and the residual solids were then washed with hexanes and dried to afford the desired imidazolylidene-triazene **3**.

3a: Yield 45 mg (65%), m.p. 252 °C. ^{1}H NMR ($CDCl_3$, 300.14 MHz): δ = 7.06–6.99 (m, 2 H, NC*H* and 5 H, Ph-*H*) 6.57 (br. s, 4 H, Mes*H*), 2.36 (s, 6 H, 4-CH_3), 2.16 (s, 12 H, 2,6-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ = 151.6, 151.3, 138.5, 135.0, 134.1, 129.2, 127.9, 125.3, 121.3, 116.7, 21.0, 17.9 ppm. IR (KBr): $\tilde{\nu}$ = 1530 (s), 1491 (m), 1481 (m), 1458 (m), 1382 (s), 1176 (m), 1156 (m), 852 (w) cm^{-1}. UV/Vis (CH_2Cl_2): λ_{max} = 368 nm, ε = 2.01×10^4 M^{-1} cm^{-1}. HRMS: [M + H]$^+$ calcd. for $C_{27}H_{30}N_5$ (424.56): 424.2501; found 424.2498.

3b: Yield 74 mg (99%), m.p. 259 °C. ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ = 6.98 (m, 4 H, Mes-*H*), 6.55–6.52 (m, 4 H, Ph-*H* and 2 H, NC*H*), 3.73 (s, 3 H, O-CH_3), 2.35 (s, 6 H, 4-CH_3), 2.16 (s, 12 H, 2,6-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ = 157.7, 151.5, 145.2, 138.4, 135.1, 129.2, 116.5, 113.2, 55.2, 21.0, 17.9 ppm. IR (KBr): $\tilde{\nu}$ = 1608 (w), 1557 (m), 1501 (s), 1426 (s), 1340 (s), 1294 (w), 1233 (w), 1189 (w), 1109 (w), 1029 (w), 854 (w) cm^{-1}. UV/Vis (CH_2Cl_2): λ_{max} = 371 nm, ε = 2.04×10^4 M^{-1} cm^{-1}. HRMS: [M + H]$^+$ calcd. for $C_{28}H_{31}N_5O$ (453.58): 453.2529; found 453.2526.

3c: Yield 74 mg (99%), m.p. 279 °C. ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ = 7.87 (d, ^1J = 9.3 Hz, 2 H, *meta*-Ph-*H*), 7.02 (s, 4 H, Mes-*H*), 6.69 (s, 2 H, NC*H*), 6.58 (d, ^1J = 9.2 Hz, 2 H, *ortho*-Ph-*H*), 2.38 (s, 6 H, 4-CH_3), 2.15 (s, 12 H, 2,6-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 125.59 MHz): δ = 156.9, 151.2, 144.4, 139.2, 134.7, 133.6, 129.4, 124.1, 121.0, 117.7, 21.1, 17.8 ppm. UV/Vis (CH_2Cl_2): IR (KBr): $\tilde{\nu}$ = 1558 (m), 1522 (s), 1502 (s), 1421 (w), 1324 (s), 1288 (s), 1259 (m), 1182 (s), 1154 (s), 1102 (s), 854 (m) cm^{-1}. λ_{max} = 445 nm, ε = 2.65×10^4 M^{-1} cm^{-1}. HRMS: [M + H]$^+$ calcd. for $C_{27}H_{29}N_6O_2$ (469.56): 469.2352; found 469.2347.

General Procedure for the Synthesis of 4: To a solution of **3** (66 μmol) in CH_2Cl_2 (5 mL) was added methyl iodide (10 μL, 0.16 mmol, 2.5 equiv.) under ambient conditions, and the reaction was allowed to stir at room temperature. After 16 h, the solvent was removed under reduced pressure, and the residual solids were then washed with Et_2O and dried to afford the desired N^3-methylated imidazolylidene-triazene **4**.

4a: Yield 31 mg (99%), m.p. 208 °C. ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ = 7.70 (s, 2 H, NC*H*), 7.23–7.20 (m, 3 H, Ph-*H*), 7.08 (s, 4 H, Mes-*H*), 6.56 (d, ^1J = 6.9 Hz, 2 H, N–Ph–*H*), 3.50 (s, 3 H, N-CH_3), 2.40 (s, 6 H, 4-CH_3), 2.10 (s, 12 H, 2,6-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ = 144.6, 141.8, 140.7, 133.9, 130.8, 129.7, 129.1, 127.9, 122.6, 118.9, 36.1, 21.0, 17.6 ppm. IR (KBr): $\tilde{\nu}$ = 1608 (w), 1557 (m), 1501 (s), 1426 (s), 1340 (s), 1233 (m), 1189 (w), 1109 (w), 1029 (w), 854 (w) cm^{-1}. UV/Vis (CH_2Cl_2): λ_{max} = 367 nm, ε = 1.66×10^4 M^{-1} cm^{-1}. HRMS: [M + H]$^+$ calcd. for $C_{28}H_{32}N_5$ (438.59): 438.2658; found 438.2652.

4b: Yield 39 mg (99%), m.p. 222 °C. ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ = 7.56 (s, 2 H, NC*H*), 7.06 (s, 4 H, Mes-*H*), 6.70 (d, ^1J = 9.2 Hz, 2 H, Ph-*H*), 6.52 (d, ^1J = 9.2 Hz, 2 H, Ph-*H*), 3.78 (s, 3 H, O-CH_3), 3.49 (s, 3 H, N-CH_3), 2.39 (s, 6 H, 4-CH_3), 2.08 (s, 12 H, 2,6-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 125.59 MHz): δ = 159.3, 145.0, 140.7, 135.4, 134.1, 131.1, 129.8, 122.3, 120.7, 114.3, 55.6, 36.6, 21.1, 17.7 ppm. IR (KBr): $\tilde{\nu}$ = 1604 (w), 1553 (m), 1508 (s), 1429 (s), 1354 (s), 1294 (w), 1254 (w), 1178 (w), 1028 (w), 832 (w) cm^{-1}. UV/Vis (CH_2Cl_2): λ_{max} = 383 nm, ε = 1.71×10^4 M^{-1} cm^{-1}. HRMS: [M + H]$^+$ calcd. for $C_{29}H_{34}N_5O$ (468.61): 468.2763; found 468.2762.

4c: Yield 39 mg (99%), m.p. 238 °C. ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ = 8.01 (d, ^1J = 9.2 Hz, 2 H, *meta*-Ph-*H*), 7.71 (s, 2 H, NC*H*), 7.10 (s, 4 H, Mes-*H*), 6.88 (d, ^1J = 9.2 Hz, 2 H, *ortho*-Ph-*H*), 3.64 (s, 3 H, N-CH_3), 2.41 (s, 6 H, 4-CH_3), 2.09 (s, 12 H, 2,6-CH_3) ppm. ^{13}C NMR ($CDCl_3$, 125.59 MHz): δ = 146.3, 145.9, 143.9, 141.3, 133.9, 130.8, 130.1, 124.7, 123.4, 119.4, 36.4, 21.2, 17.7 ppm. IR (KBr): $\tilde{\nu}$ = 1606 (w), 1593 (m), 1558 (m), 1522 (s), 1505 (s), 1429 (s), 1390 (m), 1324 (s), 1314 (s), 1272 (m), 1182 (m), 1099 (m), 856 (m) cm^{-1}. UV/Vis (CH_2Cl_2): λ_{max} = 380 nm, ε = 1.87×10^4 M^{-1} cm^{-1}. HRMS: [M + H]$^+$ calcd. for $C_{28}H_{31}N_6O_2$ (483.58): 483.2503; found 483.2502.

Supporting Information (see also the footnote on the first page of this article): Crystallographic tables ORTEP diagrams for **4a** and **4b**, ^{1}H and ^{13}C NMR spectra.

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