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Too Short-Lived or Not Existing Species: *N*-Azidoamines Reinvestigated

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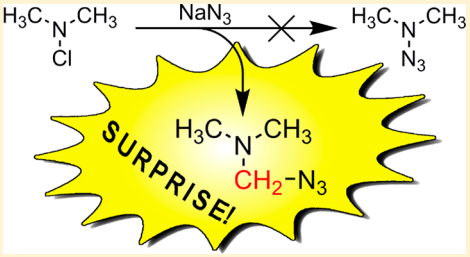
Supporting Information

ABSTRACT: Treatment of *N*-chlorodimethylamine with sodium azide in dichloromethane does not lead to *N*-azidodimethylamine, as thought for more than 50 years. Instead, surprisingly, (azidomethyl)dimethylamine is generated with good reproducibility. A plausible reaction mechanism to explain the formation of this product is presented. The reaction of lithium dibenzylhydrazide with tosyl azide does not result in the creation of an *N*-azidoamine, which can be detected by IR spectroscopy at ambient temperature, as it was claimed previously. Additional experiments with diazo group transfer to lithium hydrazides show that intermediate *N*-azidoamines are very short-lived or their formation is bypassed by direct generation of 1,1-diazenes via synchronous cleavage of two N−N bonds.

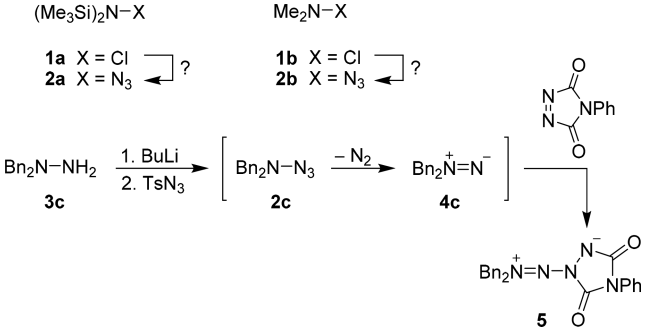


1. INTRODUCTION

The azido unit belongs to the most important functional groups in chemistry because of a variety of applications, particularly in the case of organic azides.[1] Not only carbon but also most elements in the periodic table form a bond to azide;[2] however, only a few of the corresponding covalent compounds are of general interest, for example, as reagents in synthetic chemistry, such as hydrazoic acid,[3] silyl azides,[4] phosphoryl azides,[5] and sulfonyl azides.[5b,6] In particular, azides attached to another nitrogen atom have only rarely been reported.[7a−d] Such azides, in which the azide-bearing additional nitrogen atom is always connected with at least one strongly electron-withdrawing group, turned out to be very unstable. On the other hand, *N*-azidoamines, particularly those derived from nitrogen heterocycles,[7e−o] attracted attention in numerous quantum chemical studies because these compounds are discussed as high energy density compounds (HEDCs).

In the case of *N*-azidoamines, four groups published their results when they tried to generate such azides.[8−11] In 1962, Wiberg and Gieren presented the almost quantitative synthesis of azide **2a** using the reaction of *N*-chloro compound **1a** with lithium azide in tetrahydrofuran (Scheme 1).[8a] Later, it turned out, however, that a mixture of hexamethyldisilazane and 2-azidotetrahydrofuran had been isolated instead of the supposed product **2a**.[8b] Bock and Kompa reported on the treatment of *N*-chlorodimethylamine (**1b**) with sodium azide in dichloromethane, which was claimed to afford, after workup by vacuum distillation, a 25% yield of *N*-azidoamine **2b** that showed an IR signal at 2110 cm^{-1}.[9,12] Anselme and co-workers reacted 1,1-dibenzylhydrazine (**3c**) with butyllithium (1.0 equiv) and then with tosyl azide to obtain products that were most probably derived from the short-lived 1,1-diazene (aminonitrene) **4c**.[10] When the transformation was performed at low temperatures in the presence of 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD), the trapping product **5** was isolated in 65% yield.[10b] The authors postulated the formation of **4c** via intermediate **2c**, which was generated from **3c** and tosyl azide by diazo group transfer. Whereas interception of **4c** with the help of PTAD was successful, the stability of *N*-azidoamine **2c** remained unclear. At first an IR band at 2060 cm^{-1}, which was detected with reduced intensity after workup at room temperature, was assigned to azide **2c**.[10a] Later, it was stated that liberation of dinitrogen already occurred at about −20 °C, and this pointed to lower stability of **2c**.[10b]

Scheme 1. Attempts To Generate *N*-Azidoamines



N-Azidoamines **2b** and **2c** showed slightly divergent azido bands in the IR spectra and quite different thermal stability. Thus, it is not easy to understand that **2b** can be isolated at ambient temperature and **2c** cannot. Attempts to generate nitrogen triazide (N_{10}) from nitrogen trichloride and sodium, lithium, or silver azide resulted in the formation of dinitrogen as the only product.[9b,11,13] To the best of our knowledge, the

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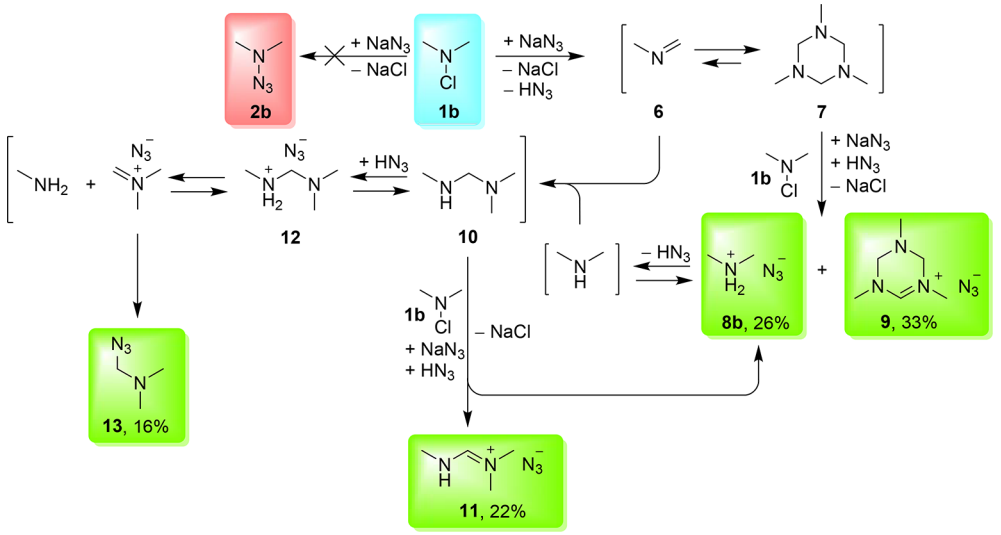
Scheme 2. Reaction of 1b with Sodium Azide in Dichloromethane[a]



[a]Yields based on weighed **1b** and weighed ^{1}H NMR standard.

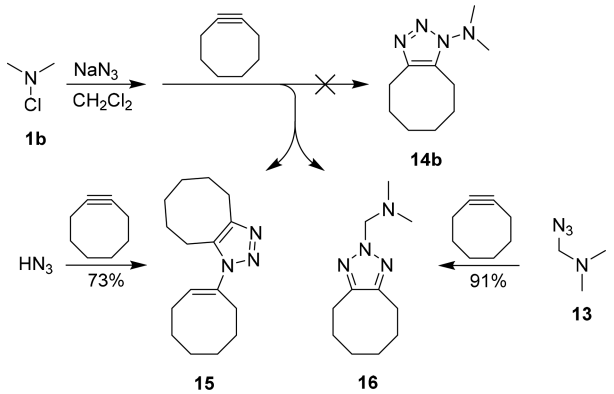
existence of simple *N*-azidoamines has not been further investigated. The wariness of experimenters is possibly based on the explosive properties of **2b**. Bock and Kompa reported on a spontaneous explosion of **2b** (50 mg), which led to a serious injury of a laboratory technician.[9b]

Herein, we describe a corrigendum to the structure of the covalent azide that is formed from **1b** and sodium azide in dichloromethane. Furthermore, we present experiments that indicate that *N*-azidoamines are very short-lived and cannot be isolated and characterized at room temperature.

2. RESULTS AND DISCUSSION

When we repeated the experiments with equimolar amounts of **1b** and sodium azide in dichloromethane (rt, 24 h) several times,[14] we were able to confirm all of the reported[9b,c] phenomena.[15] But after removal of the insoluble sodium salts, we did not obtain any evidence about the formation of *N*-azidoamine **2b**. Instead, we detected the ammonium salt **8b**,[16] the amidinium salts **9**[17] and **11**,[16,18] and the known[19] azide **13**, which were generated with good reproducibility and nearly quantitatively (Scheme 2). The reaction of **1b** with sodium azide was also realized in deuterated dichloromethane to exclude any incorporation of the solvent into one of the products, especially the surprising azide **13**. Diazidomethane[20] was produced in very small traces only; however, a significant proportion of this dangerous azide (22–26% ^{1}H NMR yield based on the azide salt) was formed besides **8b**, **9**, **11**, and **13**, when the experiments were performed with more soluble azide salts such as hexadecyltributylphosphonium azide[21] instead of sodium azide or in the presence of benzyltrimethylammonium chloride. After recondensation[22] of the reaction mixture resulting from **1b** and sodium azide in dichloromethane, **13** was the only (volatile) product. When such a reaction mixture (without recondensation) was treated with cyclooctyne, we did not obtain the trapping product **14b**, although 1-amino-1*H*-1,2,3-triazoles are established as stable substances[23] (Scheme 3). Instead, we obtained the 2*H*-1,2,3-triazole **16** (11% isolated yield based on **1b**), which was formed from **13** by cycloaddition followed by rapid rearrangement of the corresponding 1*H*-1,2,3-triazole, and the product **15** (9% yield) that resulted from hydrazoic acid and cyclooctyne. For comparison, we also prepared **15** and **16** from an excess of cyclooctyne and hydrazoic acid or **13**, respectively.

Scheme 3. Reaction of 1b with Sodium Azide in Dichloromethane Followed by Treatment with Cyclooctyne



Our results demonstrate that the structure of **2b** was erroneously assigned for the real product **13**.[9] In Scheme 2, we propose mechanisms to explain the formation of **8b**, **9**, **11**, and **13** from **1b** and sodium azide.[15] We assume that sodium azide first acts as a base and induces 1,2-elimination[24] of hydrogen chloride from **1b**, which leads to the imine **6**, sodium chloride, and hydrazoic acid. The highly reactive species **6** is known[25] to reversibly trimerize, creating the cyclic aminal **7**. Oxidation of the latter compound with the help of **1b** results in the generation of the final products **8b** and **9**. Equilibration of **8b** with hydrazoic acid and dimethylamine facilitates the addition of this secondary amine to imine **6**, which furnishes the aminal **10**. Such a species is then oxidized with the aid of **1b** to produce **8b** and amidinium salt **11**. If **10** is transformed into the hydrogen azide salt **12**, cleavage of the latter compound and attack of the azide anion leads to *N*-(azidomethyl)-dimethylamine (**13**).

In control experiments, we treated commercially available **7** with **1b** in dichloromethane (rt, 24 h) and obtained the known[17,26] amidinium chloride, including the same cation as amidinium azide **9**, along with dimethylamine hydrochloride.

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When **7** was similarly exposed to **8b**, the covalent azide **13** was formed with 8% yield besides large amounts of unreacted **7**. In this case, **13** was most probably generated via the intermediates **6**, **10**, and **12**. Even treatment of the extremely reactive imine **6**[25a] with **8b** under the same reaction conditions led to the product **13** (7% yield) along with trimer **7** (82%).

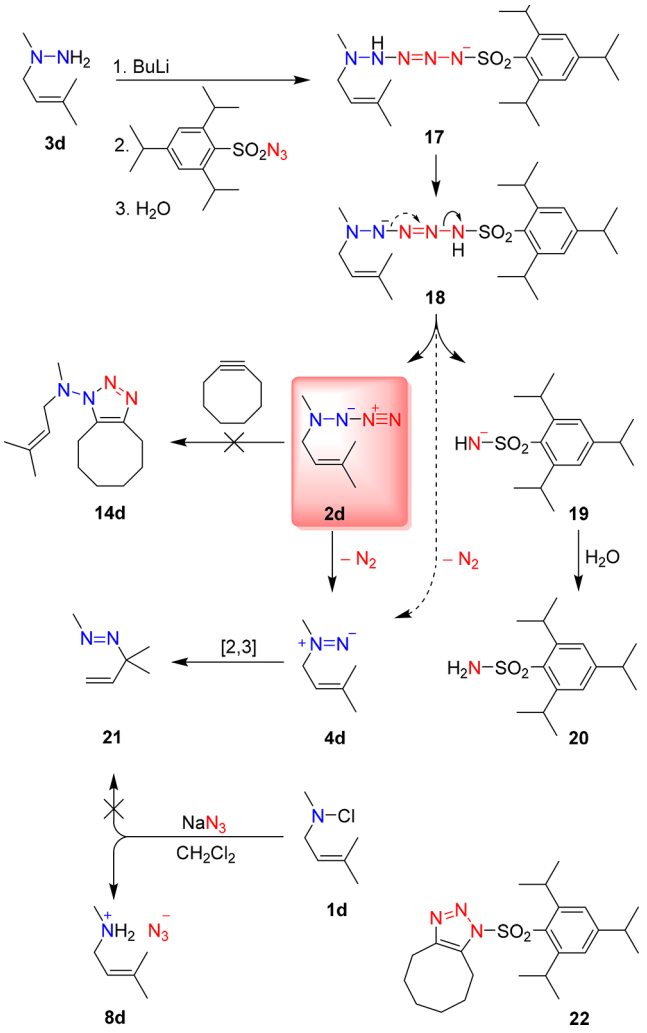
When we repeated the experiments with equimolar amounts of **3c** and butyllithium followed by treatment with tosyl azide (Scheme 1), we were able to confirm all the phenomena, in particular, the IR data, reported by G. Koga and J.-P. Anselm.[10a] However, it turned out that the IR signal at 2060 cm^{-1} did not result from *N*-azidoamine **2c** because it has to be assigned to lithium azide, which was formed as a byproduct after attack of the lithium hydrazide at the sulfur atom of tosyl azide. Consequently, we also detected known[27,28] 1,1-dibenzyl-2-tosylhydrazine that originated from the same reaction. This unwanted side reaction was repressed by using the sterically shielded 2,4,6-triisopropylbenzenesulfonyl azide instead of tosyl azide; in this case, we observed an IR signal at 2060 cm^{-1} with significantly diminished intensity and thus a lower proportion of lithium azide. However, we did not obtain any proof of the existence of the azide **2c**, and our attempts to trap **2c** with the help of cyclooctyne were also in vain.

When we reacted the known[29] hydrazine derivative **3d** with butyllithium (1.0 equiv) and then with 2,4,6-triisopropylbenzenesulfonyl azide (1 h, −78 °C, then −20 °C), we obtained the sulfonamide **20** and the known[29] azo compound **21** (53% yield) after workup with water or methanol (Scheme 4). We assumed that intermediate **17** was created in the first step, and tautomerism to generate **18** was necessary to induce the cleavage reaction which produced *N*-azidoamine **2d** and the anionic species **19**. Whereas aqueous or methanolic workup transformed **19** into **20**, unstable azide **2d** should liberate dinitrogen to form the short-lived 1,1-diazene **4d** that led to the final product **21** via established [2,3]-sigmatropic rearrangement. We tried to trap **2d** with the help of cyclooctyne in several experiments. Shortly after the lithium hydrazide and the sulfonyl azide were mixed, addition of cyclooctyne resulted in the unwanted formation of **22**,[30] which was identified as the only 1,2,3-triazole product. A 50% yield of **21** but no 1,2,3-triazole compound, such as desired **14d**, was observed when the cycloalkyne was added after nearly complete consumption of the sulfonyl azide. This outcome seems to indicate a very short lifetime of *N*-azidoamine **2d**. Other unstable azides, for example, trimethylsilylethynyl azide[31] with a half-life period of 35 min at −20 °C, can conveniently be trapped with the aid of cyclooctyne to give the corresponding 1,2,3-triazoles in excellent yields.

Our additional experiments with lithium hydrazides derived from other precursors, such as 1,1-dimethylhydrazine and 1,1-diphenylhydrazine, or with other sulfonyl azides, for example, nonafluorobutanesulfonyl azide, were also unsuccessful and did not lead to direct spectroscopic evidence of *N*-azidoamines. Moreover, our attempts to intercept these azido species with the help of cyclooctyne, producing a 1-amino-1,2,3-triazole like **14b**, were in vain. When we treated *N*-chloroamine **1d**[32,33] with sodium azide in dichloromethane, we identified the ammonium salt **8d** as one of the products and excluded the formation of azo compound **21** (Scheme 4). Consequently, the reaction of **1d** with sodium azide did not comprise the generation of **2d** and **4d**.

We interpret the product **21**, which is formed after diazo group transfer to **3d**, as proof of a short-lived 1,1-diazene **4d**.

Scheme 4. Attempts To Generate and Trap the *N*-Azidoamine 2d



However, is it simultaneously a hint about the existence of intermediate **2d**? If the cleavage of the species **18** occurs not only at the N−NH bond but also synchronously at a second N−N bond (see the dashed arrow at the structure of **18** in Scheme 4), the 1,1-diazene **4d** and dinitrogen will be created directly, and the generation of *N*-azidoamine **2d** is bypassed. In this case, any attempt to trap **2d** with retention of all four nitrogen atoms will be unsuccessful.

3. CONCLUSIONS

In summary, we have demonstrated that the claimed synthesis of *N*-azidodimethylamine (**2b**)[9] led in actual fact to the known[19] (azidomethyl)dimethylamine (**13**). The dangerous properties reported[9b] for even small amounts of alleged **2b** should be considered when explosive **13** is handled because distillation of **13** on multigram scale at normal pressure (bp 108−110 °C) was published[19a] without giving any hazard note. Our additional experiments with diazo group transfer to lithium hydrazides show that intermediate *N*-azidoamines cannot be detected directly or trapped with the help of cyclooctyne. Consequently, such azides are very short-lived or their formation is bypassed by direct generation of 1,1-diazenes via synchronous cleavage of two N−N bonds.

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4. EXPERIMENTAL SECTION

General Procedures. *CAUTION! All experiments dealing with the synthesis of small N-chloroamines and/or small azides should be performed with extra safety arrangements because of their potential explosive character. Extra safety arrangements include a safety window-pane and shatter protection gloves. Isolation of highly explosive compounds should be avoided; always handle such substances in diluted solutions. Furthermore, the interaction of chlorinated solvents like DCM with azide salts carries the risk of the formation of highly explosive organic azides such as diazidomethane.*

All reactions dealing with air- or moisture-sensitive compounds were carried out in a dry reaction vessel under a positive pressure of nitrogen. Air- and moisture-sensitive liquids and solutions were transferred via a syringe. All reactions were carried out with freshly distilled, in some cases, dry solvents. Anhydrous solvents were distilled immediately before use.

Dimethylamine hydrochloride, NCS, trisyl chloride, and ^{n}BuLi (2.5 M in hexanes) were obtained commercially from Acros Organics (Belgium). Prenyl bromide, hexahydro-1,3,5-trimethyl-1,3,5-triazine (**7**), and 1,1-diphenylhydrazine hydrochloride were obtained commercially from Sigma-Aldrich (Germany). *N,N*-Dibenzylhydrazine (**3c**) was obtained commercially from TCI (Germany). Tosyl chloride, benzyltrimethylammonium chloride, and *N,N*-dimethylhydrazine were obtained commercially from Merck KGaA (Germany). Methylhydrazine was obtained commercially from Fluka (Germany). QN_3,[21] cyclooctyne,[34] TsN_3,[35] $TrisylN_3$,[36] NfN_3,[37] and activated NaN_3[38] were prepared according to the reported literature.

NMR spectra were recorded with a UNITY INOVA 400 FT spectrometer (Varian Inc., Palo Alto, CA) operating at 400 MHz for ^{1}H NMR and 100.6 MHz for ^{13}C NMR; ULTRASHIELD 500 FT spectrometer (Bruker Corp., Billerica, MA) operating at 500 MHz for ^{1}H NMR and 125.8 MHz for ^{13}C NMR; and ASCEND 600 FT spectrometer (Bruker Corp., Billerica, MA) operating at 600 MHz for ^{1}H NMR and 150.9 MHz for ^{13}C NMR. ^{1}H NMR and ^{13}C NMR signals were referenced with the help of the solvent signals and recalculated relative to TMS. Data are presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, m = multiplet, br = broad), coupling constants in hertz (Hz), followed by the number of hydrogen atoms. Assignments of NMR signals were further supported by COSY, TOCSY, HSQC, and HMBC 2D-NMR methods and also by comparison of the data of homologous compounds in several cases. Signal assignment was omitted if it was unclear. IR spectra were measured on a Nicolet iS 5 spectrometer (Thermo Fisher Scientific Inc., Waltham, MA) in a KBr cuvette for liquids. Mass spectra were obtained from a micrOTOF QII spectrometer (Bruker Corp., Billerica, MA) utilizing an electrospray-ionization technique (source = Apollo II ESI) or in the case of compound **1d** on a 15 T solariX FT-ICR-MS (Bruker Corp., Billerica, MA) utilizing an electrospray-ionization technique. Quantitative elementary analyses were performed on a vario Micro cube (Elementar Analyensysteme GmbH, Langenselbold, HE, Germany). Melting points (mp) were measured by the BOETIUS method on a heating apparatus from VEB Analytik Dresden PHMK 74/0032.

N,N-Dimethylamine. Into a 50 mL-two-necked flask was placed *N,N*-dimethylamine hydrochloride (5.3 g, 65.0 mmol) suspended in DCM (15 mL), and finely powdered KOH (10.0 g, 180.0 mmol, 2.7 equiv) was slowly added in portions to hold the temperature between −15 and −5 °C. After the mixture was stirred for 1 h, filtration led to a colorless solution of *N,N*-dimethylamine (14% in DCM (calculated via NMR spectroscopy), 2.6 g of *N,N*-dimethylamine, 58.5 mmol, yield: 90%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ (ppm) = 1.39 (s, 1H, $HN(CH_3)_2$), 2.41 (s, 6H, $HN(CH_3)_2$). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$, 25 °C): δ (ppm) = 38.6 (q, $HN(CH_3)_2$).

*N-Chloro-N,N-dimethylamine (**1b**).*[9] *Method A:* Into a 25 mL-two-necked flask was placed a solution of *N,N*-dimethylamine in DCM (12%, 0.34 g of *N,N*-dimethylamine, 4.0 mmol), and NCS (1.06 g, 8.0 mmol, 2 equiv) was added in small portions to keep the temperature between −15 and −5 °C. After the mixture was stirred for 5 h, volatile components were recondensed at rt/6.8×10^{-3} mbar with the help of an U-tube apparatus. The condensate was dried over $MgSO_4$. Filtration led to a colorless solution of **1b** in DCM (11% in DCM (calculated via NMR spectroscopy), 0.28 g of *N*-chloro-*N,N*-dimethylamine (**1b**), 3.5 mmol, yield: 88%). *Method B:* Into a 250 mL-two-necked flask was placed *N,N*-dimethylamine hydrochloride (10.0 g, 120 mmol) suspended in DCM (20 mL) and the solution cooled to −15 °C. A solution of sodium hypochlorite (13%, 140 mL, 240 mmol, 2 equiv) was added dropwise to hold the temperature below 0 °C. After the solution was stirred for 1 h, the phases were separated, and the aqueous phase was extracted with DCM (5 × 20 mL). The combined organic phases were washed with 1 N sulfuric acid (2 × 40 mL) and dried over Na_2SO_4 or $MgSO_4$. Filtration led to a solution **1b** in DCM (1.83% (calculated via NMR spectroscopy), 4.3 g of *N*-chloro-*N,N*-dimethylamine (**1b**), 54 mmol, yield: 45%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ (ppm) = 2.91 (s, $ClN(CH_3)_2$). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$, 25 °C): δ (ppm) = 54.9 (qq, $^{1}J_{C,H}$ = 137.3 Hz, $^{3}J_{C,H}$ = 5.5 Hz, $ClN(CH_3)_2$).

*Reaction of **1b** with NaN_3.*[9] To a solution of *N*-chloro-*N,N*-dimethylamine (**1b**) in DCM (2.9%, 1 g, 12.6 mmol **1b**) was added sodium azide (0.8 g, 12.6 mmol, 1 equiv) in a flask connected with a pneumatic apparatus. The mixture was stirred for 24 h cooled by water bath at rt. After 24 h, the reaction mixture was filtered and analyzed by NMR spectroscopy without further purification, obtaining a mixture of **8b** (26%), **9** (33%), **11** (22%), and **13** (16%) in DCM.[14,15]

*Methylmethylenimine (**6**).*[25a] Note: We used the method described in ref 25a since other procedures to prepare **6** (see ref 25b−e) were less successful in our hands. In a vacuum apparatus (see the SI), *N*-methylaminoacetonitrile (2 mL, 1.84 g, 26 mmol) was evaporated at 60 °C/4×10^{-2} mbar through a glass tube (Ø 1 cm, l = 30 cm) over a bed of KO^{t}Bu. The gas flow passed then a first cooling trap cooled with $EtOH/N_{2(liq)}$ at −85 °C and was then recondensed on a cooling finger cooled with liquid nitrogen. On the cooling finger, DCM (3 mL) was first recondensed. After completion of the recondensation, the apparatus was ventilated with dry argon, and warming of the recondensed DCM/**6** mixture was realized with an $EtOH/N_{2(liq)}$ bath at −85 °C. This method led to a solution (7%) of **6** in DCM. The transfer (fast!) into a precooled (−90 °C, $[D_2]$-DCM) NMR tube was executed with a pipet precooled in liquid nitrogen. ^{1}H NMR (600 MHz, $[D_2]$-DCM, −80 °C): δ (ppm) = 3.23 (s, 3H, $H_2C{=}NCH_3$), 7.00−7.10 (m, 1H, $H_2C{=}NCH_3$), 7.30−7.40 (m, 1H, $H_2C{=}NCH_3$). $^{13}C\{^{1}H\}$ NMR (150.9 MHz, $[D_2]$-DCM, −80 °C): δ (ppm) = 50.0 (q, $H_2C{=}NCH_3$), 154.9 (t, $H_2C{=}NCH_3$).

*N-Methyl-N-prenylhydrazine (**3d**).*[29] In a 50 mL-two-necked flask, methylhydrazine (3.7 g, 4.2 mL, 80 mmol, 6 equiv) was emulsified in pentane (10 mL) and at −15 °C with strong stirring treated with prenyl bromide (2.0 g, 1.55 mL, 13 mmol) in hexanes (10 mL). The solution was stirred at this temperature for 4 h and then treated with finely powdered KOH (5 g, 90 mmol). After addition of the base, the solution was stirred for at least 1 h and then filtered. The insoluble salts were then extracted with Et_2O, and the combined organic phases were dried over $MgSO_4$. Removing the solvents on a rotary evaporator led to a pale yellow liquid of *N*-methyl-*N*-(3-methylbut-2-en-1-yl)hydrazine (**3d**, 1.37 g, 12 mmol, yield: 92%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ (ppm) = 1.65 (s, 3H, (*Z*)-$H_3CC{=}$), 1.73 (s, 3H, (*E*)-$H_3CC{=}$), 2.43 (s, 3H, $H_3CN{-}$), 2.73 (br, 2H, $-NH_2$), 3.05 (d, 2H, ^{3}J = 7.1 Hz, $-C\,H_2N{-}$), 5.25 (m, 1H, $-C{=}CH{-}$). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$, 25 °C): δ (ppm) = 18.1 (q, (*Z*)-$H_3CC{=}$), 25.9 (q, (*E*)-$H_3CC{=}$), 48.4 (q, $H_3CN{-}$), 61.0 (t, $-C{=}CHCH_2{-}$), 120.1 (d, $-C{=}CH{-}$), 136.5 (s, $-C{=}CH{-}$).

*N-Chloro-N-methylprenylamine (**1d**).* To a solution of *N*-methyl-*N*-prenylamine (1 g, 10 mmol, traces of Et_2O from synthesis)[33] in DCM (10 mL) was added NCS (1.48 g, 11 mmol, 1.1 equiv) at −20 °C and the mixture stirred for 1 h at −10 °C. Recondensation at rt/6.8×10^{-2} mbar led to a colorless solution of **1d** in DCM (6.8%, 0.98 g **1d**, 7.3 mmol, yield: 73%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ (ppm) = 1.68 (s, 3H, (*Z*)-$H_3CC{=}$), 1.76 (s, 3H, (*E*)-$H_3CC{=}$), 2.89 (s, 3H, $H_3CN{-}$), 3.52 (d, 2H, ^{3}J = 6.8 Hz, $-CH_2N{-}$), 5.30 (m, 1H, $-C{=}CHCH_2{-}$). $^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$, 25 °C): δ

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(ppm) = 18.2 (q, (*Z*)-H_3CC=), 25.9 (q, (*E*)-H_3CC=), 51.6 (q, H_3CN−), 63.4 (t, −C=$CHCH_2$−), 119.7 (d, −C=$CHCH_2$−), 137.8 (s,−C=$CHCH_2$−). HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_6H_{13}NCl$ 134.0731, found 134.0731.

*(E)-1-Methyl-2-(2-methylbut-3-en-2-yl)diazene (**21**).*[29] To a solution of **3d** (0.2 g, 1.8 mmol) in dry THF (1 mL) was added ″BuLi (2.5 M in hexanes, 1.1 mL, 3.4 mmol, 1.5 equiv) at −78 °C. The mixture was stirred for 1 h and then treated with trisyl azide (0.6 g, 1.9 mmol, 1.1 equiv) in dry THF (1 mL) at −78 °C. The suspension was then stirred for another 1 h and finally treated with water/THF (0.1 mL/0.5 mL) when the temperature reached −20 °C. Compound **21** (107.0 mg, 0.95 mmol, yield: 53%, calculated by internal naphthalene standard) was obtained after filtration in THF/hexanes with **20** and some further unknown impurities. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ (ppm) = 1.31 (s, 6H, $(H_3C)_2C$−), 3.76 (s, 3H, H_3CN=N−), 5.10−5.17 (m, 2H, H_2C=CH−), 5.98 (dd, ^3J = 17.8 Hz, ^3J = 10.5 Hz, 1H, H_2C=C*H*−). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 25 °C): δ (ppm) = 24.5 (q, $(H_3C)_2C$−), 57.0 (q, H_3CN=N−), 71.0 (s, $(H_3C)_2C$−), 113.3 (t, H_2C=CH−), 143.0 (d, H_2C=CH−).

1,3,5-Trimethyl-2,3,4,5-tetrahydro-1,3,5-triazin-1-ium Chloride.[17] To a solution of 7 (2.2 mL, 2 g, 15.5 mmol) in DCM (10 mL), cooled with a water bath to rt, was added NCS (2.5 g, 18,5 mmol, 1.2 equiv) in small portions. The mixture was stirred overnight and then filtered. Removing the solvent on a rotary evaporator led to a pale yellow oil. The crude product was then washed in a flask several times with DME (approximately 10 times) with the help of an ultrasonic bath to remove succinimide and then four times with Et_2O. Removing the solvents was done each time by decantation, and after the last washing step drying was done at reduced pressure (ventilation with dry Ar!). Compound **9** was gained as a white, strongly hygroscopic solid (1.03 g, 6.3 mmol, yield: 41%). ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ (ppm) = 2.55 (s, 3H, $-CH_2N(CH_3)CH_2-$), 3.23 (s, 6H, $-CHNCH_3$), 4.26 (s, 4H, $-CH_2-$), 9.23 (s, 1H, −C*H*=). $^{13}C\{^1H\}$ NMR (150.9 MHz, $CDCl_3$, 25 °C): δ (ppm) = 39.5 (qm, $^1J_{CH}$ = 140.6 Hz, $-CHNCH_3$), 40.4 (qquin, $^1J_{CH}$ = 136.2 Hz, $^3J_{CH}$ = 5.2 Hz, $-CH_2N(CH_3)CH_2-$), 66.9 (tm, $^1J_{CH}$ = 156.2 Hz, $-CH_2-$), 153.5 (dm, $^1J_{CH}$ = 198.9 Hz, −CH=). Note: Using NBS (3.31 g, 18.5 mmol, 1.2 equiv) instead of NCS as oxidizing reagent led to the corresponding bromide (2.31 g, 11.1 mmol, yield: 72%).

*(E)-1-(Cyclooct-1-en-1-yl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (**15**).* A HN_3 solution (1.53 M in $CDCl_3$, 0.70 mL, 1 equiv) was treated with cyclooctyne (230 mg, 2.14 mmol, 2 equiv) at 0 °C. Within 1 h, the solution was allowed to warm to rt and was then stirred for an additional 24 h. The solvent and unreacted HN_3 were then removed in vacuo to obtain **15** as a colorless oil (202 mg, 0.78 mmol, yield: 73%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ (ppm) = 1.40−1.52 (m, 4H), 1.58−1.80 (m, 12H), 2.25−2.35 (m, 2H), 2.53−2.64 (m, 2H), 2.70−2.80 (m, 2H), 2.84−2.94 (m, 2H), 5.74 (t, $^3J_{C,H}$ = 8.5 Hz, 1H, $-CH_2CH$=C−). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 25 °C): δ (ppm) = 22.0 (t), 24.4 (t), 25.3 (t), 25.5 (t), 26.0 (t), 26.1 (t), 26.1 (t), 27.7 (t), 28.0 (t), 28.2 (t), 29.3 (t), 30.2 (t), 128.4 (d, $-CH_2CH$=C−), 133.0 (s), 137.0 (s, $-CH_2CH$=C−), 144.2 (s). An assignment of all CH_2 signals was not possible. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{16}H_{26}N_3$ 260.2121, found 260.2128. Anal. Calcd for $C_{16}H_{25}N_3$: C, 74.09; H, 9.71. Found: C, 73.77; H, 9.87.

*1-(4,5,6,7,8,9-Hexahydro-2H-cycloocta-1,2,3-triazol-2-yl)-N,N-dimethylmethanamine (**16**).* Into a 25 mL-flask, cooled with H_2O to rt, a solution of **13** in Et_2O (12.3%, 1.0 g of *N*-azidomethyl-*N*,*N*-dimethylamine (**13**), 10.0 mmol)[19e] was slowly treated with cyclooctyne (1.5 mL, 1.3 g, 12.0 mmol, 1.2 equiv) and stirred overnight. Volatile components were then removed in vacuum, and the residue was worked up via flash chromatography (silica 60, eluent: ethyl acetate, R_f = 0.31). Compound **16** was obtained as a colorless oil (1.9 g, 9.1 mmol, yield: 91%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ (ppm) = 1.44 (m, 4H, $-NCCH_2CH_2CH_2-$), 1.72 (m, 4H,$-NCCH_2CH_2CH_2-$), 2.34 (s, 6H, $(H_3C)_2N-$), 2.80 (m, 4H, $-NCCH_2-$), 5.02 (s, 2H,$-NCH_2-$). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 25 °C): δ (ppm) = 23.6 (tm,$^1J_{C,H}$ = 127 Hz, $-NCCH_2CH_2CH_2-$), 25.4 (tm, $^1J_{C,H}$ = 123 Hz, $-NCCH_2CH_2CH_2-$), 28.8 (tm, $^1J_{C,H}$ = 125 Hz, $-NCCH_2CH_2CH_2-$), 42.2 (qm, $^1J_{C,H}$ = 134 Hz, $(H_3C)_2N-$), 75.1 (tm, $^1J_{C,H}$ = 152 Hz, $-NCH_2-$), 146.0 (s, $-NCCH_2-$). HRMS (ESI-TOF) *m*/*z*: $[M - H]^+$ calcd for $C_{11}H_{19}N_4$ 207.1604, found 207.1609.

*1-((2,4,6-Triisopropylphenyl)sulfonyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (**22**).* In a 10 mL-flask, cooled with NaCl/ice/water, was dissolved trisyl azide (0.5 g, 1.6 mmol) in THF (3 mL) and the solution slowly treated with cyclooctyne (0.25 g, 2.4 mmol). After the solution was stirred for 1 h, all volatile components were removed under reduced pressure. After TLC (silca 60, eluent: hexanes/Et_2O = 5:1), **22** was gained as a white solid (0.65 g, 1.6 mmol, yield: 100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.16 (d, 12H, ^3J = 6.6 Hz, *o*-$CH(CH_3)_2$), 1.26 (d, 6H,^3J = 6.7 Hz, *p*-$CH(CH_3)_2$), 1.36−1.45 (m, 4H, $-CH_2-$), 1.68−1.75 (m, 4H, $-CH_2-$), 2.85−2.88 (m, 2H,$-CH_2-$), 2.93 (sept, 1H, ^3J = 6.7 Hz, *p*-$CH(CH_3)_2$), 3.01−3.05 (m, 2H, $-CH_2-$), 4.01 (sept, 2H,^3J = 6.6 Hz, *o*-$CH(CH_3)_2$), 7.22 (s, 2H, $-CH_{aromat}-$). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 21.6 (t, $-CCH_2-$), 23.4 (q, *p*-$CH(CH_3)_2$), 24.4 (q, *o*-$CH(CH_3)_2$), 24.5 (t,$-CH_2-$), 24.9 (t, $-CCH_2-$), 25.6 (t,$-CH_2-$), 26.5 (t,$-CH_2-$), 28.7 (t,$-CH_2-$), 29.8 (d, *o*-$CH(CH_3)_2$), 34.3 (d, *p*-$CH(CH_3)_2$), 124.3 (d, $-CH_{aromat}-$), 129.7 (s, $-CSO_2-$), 134.5 (s,$-CCH_2-$), 145.7 (s, $-CCH_2-$), 152.5 (s, $-CCSO_2-$), 155.8 (s, −CHC−CH−). Mp: 94−95 °C. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{23}H_{36}N_3O_2S$ 418.2523, found 418.2538.

N′,N′-Dibenzyl-4-methylbenzenesulfonohydrazide.[27] In a 50 mL flask, a mixture of triethylamine (2.91 mL, 2.12 g, 21 mmol, 1 equiv), tosyl chloride (4 g, 21 mmol, 1 equiv), and 1,1-dibenzylhydrazine (4.45 g, 21 mmol, 1 equiv) in DCM (30 mL) was refluxed for 4 h and then stirred overnight. The resulting solution was then washed with 10% HCl (4 × 20 mL) and water (4 × 20 mL) and then dried over $MgSO_4$. After the solvent was removed, the desired product was gained after flash chromatography (silica 60, eluent: petroleum ether/DCM/NEt_3 = 13/6/1, R_f = 0.53) as a beige solid (4.85 g, 13.2 mmol, yield: 63%) with small impurities. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.41 (s, 3H, $-C_{arom}-CH_3$), 3.74 (s, 4H, $-CH_2-$), 5.60 (s, 1H, −N*H*−), 7.15−7.21 (m, 6H), 7.25−7.30 (m, 6H), 7.74 (d, 2H, *J* = 8.3 Hz). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 21.5 (q, $-C_{arom}CH_3$), 59.8 (t, $-CH_2-$), 127.6 (d), 128.2 (d), 128.4 (d), 129.3 (d), 129.7 (d), 135.0 (s), 135.4 (s), 143.5 (s).

■ ASSOCIATED CONTENT

Supporting Information

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Experimental details for new reactions and printed IR and NMR spectra (PDF)

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T.P. performed the experimental work and prepared the Supporting Information. K.B. wrote the manuscript.

Notes

The authors declare no competing financial interest.

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DEDICATION

This work is dedicated to Professor Ernst Schaumann on the occasion of his 75th birthday.

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