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Carbenoid Reactions of 2-Halomethyl-4,6-dimethyl-*s*-triazines

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Reactions of lithium, sodium, and potassium salts of 2,4,6-trimethyl-*s*-triazine (**1**) with 2-halomethyl-4,6-dimethyl-*s*-triazine (**2**) (X = Cl, Br) in glyme have been studied and found to give 1,2-bis(4,6-dimethyl-*s*-triazin-2-yl)ethane (**3**), 1,2-bis(4,6-dimethyl-*s*-triazin-2-yl)ethene (**5**), 1,2,3-tris(4,6-dimethyl-*s*-triazin-2-yl)cyclopropane (**6**), 1,2,3-tris(4,6-dimethyl-*s*-triazin-2-yl)propane (**7**), and 1,2,3,4-tetrakis(4,6-dimethyl-*s*-triazin-2-yl)butane (**8**). It is proposed that product **3** is formed primarily via an S_N2 reaction, whereas the remaining products are formed primarily via carbenoid reactions that are enumerated.

Introduction

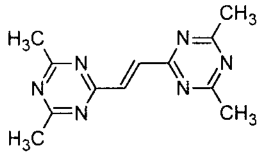
In view of the successful synthesis of a number of heterocyclophanes involving the pyridine ring[1] and the pyrrole ring,[2] it was challenging to consider the possibility of synthesizing a heterocyclophane that contained two *s*-triazine rings connected via two or three ethylene bridges, the latter being $[2_3]$ (2,4,6)-*s*-triazinophane (**4**)[3] analogous to $[2_3]$(1,3,5)cyclophane.[4]

The initial plan, as represented by Scheme 1, was to react the 2,4,6-trimethyl-*s*-triazinyl anion of **1** with the 2-halomethyl-4,6-dimethyl-*s*-triazine (**2**) via an S_N2 reaction to form alkane **3** containing the first ethylene bridge between the two *s*-triazine rings. Possible conversion of compound **3** to the desired heterocyclophane **4** was to be achieved by one of the following routes. (1) The monobromination of the dianion from **3** should enable an intramolecular S_N2 reaction to form the $[2_2]$(2,4)-*s*-triazinophane, and repeating the reactions on the dianion of the latter should give **4**. (2) The dianion of **3** could be dibrominated to give the 4,4′-dibromomethyl derivative of **3**, and the latter, upon treatment with *n*-butyllithium,[1b] should give the $[2_2]$(2,4)-*s*-triazinophane. Repeating the sequence of reactions on the $[2_2]$(2,4)-*s*-triazinophane should give **4**. (3) The reaction with sodium sulfide of the 4,4′,6,6′-tetrabromomethyl derivative formed from **3** should give the trithia-*s*-triazinophane, and the transformation of the latter into **4**, or its corresponding diene, could be achieved by a number of possible routes.[4,5]

During our attempts at the synthesis of **3** by the S_N2 reaction of **1** with **2**, we became aware of the predominance of their carbenoid reactions and the resulting products that we now report.

Results and Discussion

The reaction of **1a** with **2b** in ether gave only a trace amount of product **3**, whereas when glyme was used as the solvent, the reaction of **1a** and **1c** with **2b** gave moderate amounts of **3**. In addition to **3**, we report four other new and interesting products: 1,2-bis(4,6-dimethyl-*s*-triazin-2-yl)ethene (**5**), 1,2,3-tris(4,6-dimethyl-*s*-triazin-2-yl)cyclopropane (**6**), 1,2,3-tris(4,6-dimethyl-*s*-triazin-2-yl)propane (**7**), and 1,2,3,4-tetrakis(4,6-dimethyl-*s*-triazin-2-yl)butane (**8**). All of the above products were identified by ^1H and ^{13}C NMR and elemental analyses, as well as X-ray diffraction studies (excluding compound **3**). X-ray diffraction data showed alkene **5** to be the trans isomer[6] and that the arrangement of the 4,6-dimethyl-*s*-triazine



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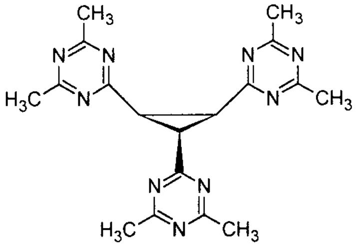

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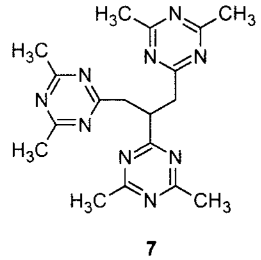

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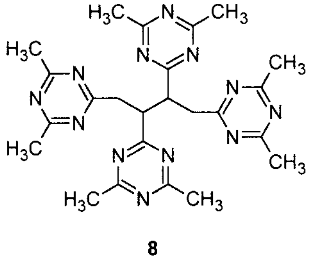

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[6] Thermal ellipsoid figures and crystallographic data are available in Supporting Information. Atomic coordinates for the following compounds have been deposited with the Cambridge Crystallographic Data Centre: numbers CCDC 177 880 (**5**), CCDC 177 881 (**6**), CCDC 177 882 (**7**), CCDC 177 883 (*meso*-**8**), and CCDC 177 884 (racemate **8**). The coordinates can be obtained upon request from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

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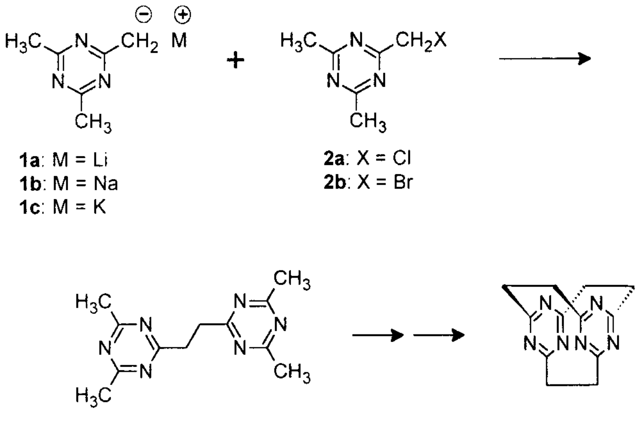
Scheme 1



1a: M = Li
1b: M = Na
1c: M = K

2a: X = Cl
2b: X = Br

3

4

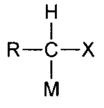
Table 1. Yields of Products from Reactions of 1 with 2

	reactants			relative yields of products (mol %)[a]					absolute
entry	**1**	**2**	*T* (°C)	**3**	**5**	**6**	**7**	**8**	yield (mol %)[b]
1	**1a**	**2a**	25	15		68	17		36
2	**1a**	**2a**	−60	17		65	18		29
3[c]	**1a**	**2a**	25	21		56	23		24
4[d]	**1a**	**2b**	25	44 ± 4	8 ± 2	33 ± 0	16 ± 2		45 ± 4[e]
5	**1a**	**2b**	−60	50	26	7	10	7	56
6	**1b**	**2a**	25	12	6	82			38
7	**1b**	**2a**	−60		11	89			34
8[f]	**1b**	**2b**	25	8 ± 6	59 ± 17	26 ± 9	7 ± 7		39 ± 5[e]
9	**1b**	**2b**	−60	12	73	16			36
10	**1c**	**2a**	25			100			49
11	**1c**	**2a**	−60			100			75
12[f]	**1c**	**2b**	25	38 ± 7	9 ± 9	37 ± 5	16 ± 3		66 ± 2[e]
13	**1c**	**2b**	−60	27		14	19	40	34
14[c]	**1c**	**2b**	25	62		22	16		75

[a] Based upon single runs unless noted otherwise. Precision within 4%. [b] Based upon total moles of triazine ring in each product (**3**, 1 mol; **5**, 2 mol; **6** and **7**, 3 mol; **8**, 4 mol) compared to the total moles of **2**. Uncorrected for any recovered **2** (less than 5%). [c] Rapid addition (10 s vs 25 min). [d] Average of two runs. [e] Based upon a single run. [f] Average of four runs.

rings about the cyclopropane in compound **6** was two up and one down.[6] The structures of **7**, the meso form of **8**, and the (2*S*,3*S*)-enantiomer of racemate **8** were also determined by X-ray diffraction studies.[6] From the above products, it became apparent that the predominant reaction was not the desired substitution reaction but rather the formation of carbenoid species whose reactions led to compounds **5**−**8**, as well as possibly some alkane **3**. The relative and absolute yields of the products are reported in Table 1.

In considering the possible routes for the formation of the above products, the attractive routes, in general, appear to involve a carbene complex or carbenoid species[7] formed by the anion **1** reacting with **2** in the role of a base (α-metalation) to give carbenoid species represented by **9**. Although α-metalation is generally found to be slower than metal−halogen exchange,[8] in this study, the latter simply enabled each species to regenerate the other. It is generally recognized that α-elimination on haloalkanes by an organolithium gives rise to a carbenoid species in most cases rather than a free carbene[7,8d,9] or an isolable carbene.[10] Reported evidence also indicates that the carbenoid species formed by the use of potassium *tert*-butoxide for α-elimination becomes the free carbene only in the presence of 18-crown-6-ether.[11] Therefore, we assumed in this investigation that the use of a sodium or a potassium base for α-metalation in the absence of a crown ether would also yield predominantly carbenoid species and that the presence of glyme as a solvent undoubtedly assisted in the stabilization of the carbenoid species as is reported for tetrahydrofuran[8c,12] and ethyl ether.[7b,9a]



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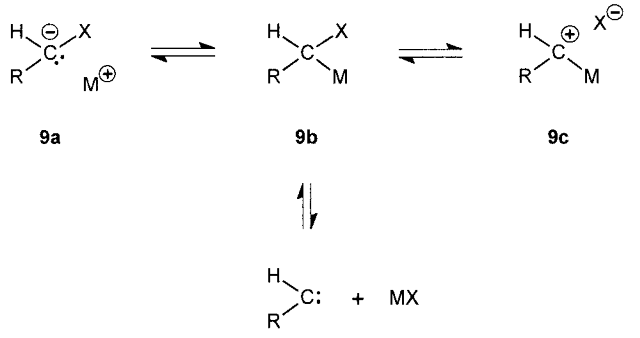
In interpreting the behavior of a carbenoid species such as **9**, it is advantageous to consider it as encompassing a spectrum of species that may be represented by a nucleophilic species (**9a**), an amphophilic or ambiphilic species (**9b**), and an electrophilic species (**9c**) depending upon the degree of bond making or breaking between the carbon, the halogen, and the metal.[8c,9a,12b,13] These species may also give rise to **9d**, the free carbene,[8c,14] which itself may be amphophilic.[13c,d,15] The electron-withdrawing



9a

9b

9c

9d

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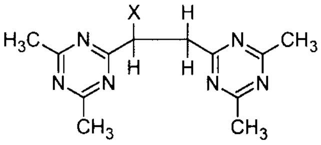
influence of the triazine ring[16] would enhance the removal of the α-hydrogen, stabilize species **9a** and decrease its nucleophilicity, but it would destabilize species **9c** and increase its electrophilicity.[17] However, it is conceivable that species **9c** could be stabilized either by the intramolecular association of the unshared pair of electrons on the neighboring nitrogen with the electron-deficient carbon as has been postulated for the carbomethoxycarbene[18] or by the intermolecular formation of an ylide, which has been shown to form between carbenes and heteroatoms.[19] Due to the heterogeneity of the reaction,[9a,20] temperature dependence, and less significant variables such as the concentration and the rate of addition, some variation in the reproducibility of the yields became apparent. Also, in considering the yield of a given product, one has to do so relative to the competitive formation of the other products.

Formation of Compound 3. As seen from Table 1 (entries 4 and 5 vs 1−3; 8 and 9 vs 6 and 7; and 12−14 vs 10 and 11), alkane **3** was formed in a greater yield in the case of **1** reacting with the bromocompound **2b** than with the chlorocompound **2a**. This would support the formation of **3** primarily via an S_N2 reaction. It is also possible that alkane **3** could arise via a carbenoid species inserting into either the carbon−metal bond of **1**[8c,13f] to give an organometallic precursor of **3** or the carbon−hydrogen bond of 2,4,6-trimethyl-*s*-triazine (formed concurrently with α-metalation). However, evidence for the latter insertion is not supported in the literature.[7a,9a,14]

Formation of Compound 5. Numerous alkenes have been reported as products resulting from possible carbenoid or carbene formations in solution.[12c,21] Alkene **5** could arise as a result of the reaction of the nucleophilic species **9a** reacting with the electrophilic species **9c** or with the amphophilic species **9b** or **9d**, followed by elimination of a molecule of MX (dimerizing α-elimination).[8c,12c] Compound **5** could also arise by the nucleophilic attack of **9a** on **2** (S_N2 reaction) to give intermediate **10** from which the elements of hydrogen halide could be eliminated under the basic conditions of the reaction.[12a] The comparable reaction of benzyl chloride with phenyllithium has been reported to give the phenyl analogue of species **10**.[12a] It is noteworthy that compound **5** was isolated in a significant yield only in the case of **1b** reacting with **2b** (Table 1, entries 8 and 9). However, in the other cases, compound **5**, or its precursor **10**, may have served as a precursor to other products, principally compound **6**, and possibly **7** and **8**. The formation of **5** by the dimerization of two free carbenes is possible, but under the conditions of this investigation, this route is rather unlikely.[8c,22]



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The reaction of sodium hydride with **2b** gave results qualitatively consistent with those of **1b** with **2b** except that essentially no alkane **3** was formed due to the absence of **1b** in the former reaction.

Formation of Compound 6. Most reported cyclopropanation reactions have involved an external alkene added during or after the formation of the carbene or carbenoid species.[23] However, few cases have been reported in which the alkenes generated from the parent carbene or carbenoid species continue to undergo reaction with the remaining carbene or carbenoid species, as in this study, to give cyclopropane products.[21a,c] Thus, in this investigation, compound **6** is most probably formed by a one-step addition reaction of the electrophilic carbenoid species **9c** with alkene **5**. It is interesting to note that the chlorocompound **2a**, in contrast to the bromocompound **2b**, gave much higher yields of the cyclopropane product **6**, indicating that **2a** favors, within each of the three different metal carbenoids, the more electrophilic carbenoid species **9c** (Table 1, entries 1−3 vs 4 and 5; 6 and 7 vs 8 and 9; 10 and 11 vs 12−14). This result is contrary to the trend cited in the literature for CBr_2 and CCl_2 as true carbenes[24] and for bromomethyllithium and chloromethyllithium as carbenoids[9a] but is supported by the report that the fluorenylidenechloromethyllithium carbenoid is less stable (more reactive) than the corresponding bromocarbenoid.[8c] However, an alternative route, consistent with the trend reported in the literature, would be a stepwise addition reaction in which the nucleophilic carbenoid species **9a** would attack the electron-poor alkene **5** in a Michael-type reaction to give an anion (stabilized by the adjacent triazine ring), which then would undergo ring closure by displacing the halide to form compound **6**. Although significant differences exist between alkene **5** and simpler alkenes, evidence to distinguish between the above two mechanisms might be obtained by examining the stereospecificity of the reaction of carbenoid **9** with simple alkenes. It is noteworthy that the reaction of **1b** with **2b** (entry 8) gave a high yield of alkene **5** at 25 °C with a low conversion of **5** to cyclopropane **6**, whereas **1c** with **2b** (entry 12) gave little alkene as a result of most of it presumably being converted to **6** and **7**. Thus, the sodium carbenoid appears to favor the nucleophilic species **9a**, whereas the potassium carbenoid favors the electrophilic species **9c** and

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9d. This trend is also evident in the reactions of **1b** and **1c** with **2a** (Table 1, entries 6 and 10).

Formation of Compound 7. The formation of compound **7** appears to have proceeded most feasibly via the reaction of species **1** with the alkene **5** (Michael-type reaction)[25] or with species **10** (S_N2 reaction). These reactions would lead to a lower yield of **5** and higher yields of **6** and **7**, which was found experimentally (Table 1, entries 1−3 and 12−14). Carbenoid precursors to alkane **3** could conceivably react with carbenoid **9** or compound **2** (S_N2 reaction) to give **7**, but these two alternative reactions are not consistently supported by the experimental results.

The ^{1}H NMR spectrum of compound **7** indicated that the two hydrogens of the methylene groups are diastereotopic due to the presence of the middle prochiral carbon. Presumably, a significant contribution to the nonequivalence of these methylene hydrogens arises from an unequal population of the conformers of **7** at room temperature.[26]

Formation of Compound 8. Both the meso and the racemic forms of **8** were isolated and identified. The formation of a significant amount of **8** was unique to the reaction of **1c** with **2b** at −60 °C, and data at the higher temperature would indicate that **8** was formed at the expense of compounds **3** and **6**, and not of **7** (Table 1, entry 13 vs 12 and 14). This observation would enable one to conclude that the majority of the tetramer **8** was not formed by the trimer **7**, or its precursors, reacting with a monomer but rather from the reaction of two dimeric precursors to compounds **3** and **5**.

It is of interest to compare the above reactions and their products to the reported results of the reaction of benzyl chloride with *n*-butyllithium (α-metalation) in different solvents and at different temperatures.[12a] In this latter study only compounds analogous to compounds **3** and **5** were reported in addition to a derivative of a compound analogous to intermediate **10**. No corresponding cyclopropane, trimer, or tetramer was reported.

Conclusion

Reactions of lithium, sodium, and potassium salts of 2,4,6-trimethyl-*s*-triazinyl anion (**1**) with 2-halomethyl-4,6-dimethyl-*s*-triazine (**2**) (X = Cl, Br) in glyme have been examined semiquantitatively, and the following new compounds have been characterized: 1,2-bis(4,6-dimethyl-*s*-triazin-2-yl)ethane (**3**), 1,2-bis(4,6-dimethyl-*s*-triazin-2-yl)ethene (**5**), 1,2,3-tris(4,6-dimethyl-*s*-triazin-2-yl)cyclopropane (**6**), 1,2,3-tris(4,6-dimethyl-*s*-triazin-2-yl)propane (**7**), and 1,2,3,4-tetrakis(4,6-dimethyl-*s*-triazin-2-yl)butane (**8**). It is proposed that product **3** is formed primarily via an S_N2 reaction, whereas the remaining products are formed primarily via carbenoid reactions. To the best of our knowledge, this is the first reported study of carbenoid reactions facilitated by the *s*-triazine ring.

Experimental Section

Melting points and boiling points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 200 and 50 MHz, respectively. Proton and carbon chemical shifts were referenced to residual solvent protons and the solvent, respectively. Elemental analyses were performed by Desert Analytics, Tucson, AZ. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Ether and glyme were distilled prior to use from sodium benzophenone ketyl and lithium aluminum hydride, respectively. 2,4,6-Trimethyl-*s*-triazine was prepared by the method of Schaefer and Peters.[27] Compound **2a** was prepared by the method of Campaigne and Tullar using NCS.[28]

Preparation of 2-Bromomethyl-4,6-dimethyl-*s*-triazine (2b). The general procedure of Glaze was followed.[29] *n*-Butyllithium in hexane (1.6 M, 0.160 mol) was added dropwise under argon to a stirred solution (−78 °C) of 2,4,6-trimethyl-*s*-triazine (18.74 g, 0.152 mol) in ether (750 mL). The bright-yellow suspension was allowed to warm to room temperature and then transferred (80 min) under argon to a stirred solution (0 °C) of bromine (8.7 mL, 0.17 mol) in pentane (400 mL). The flask was covered with foil and allowed to warm to room temperature overnight. The cream-colored mixture was cooled (0 °C); ice water (25 mL) was added dropwise, and the phases were separated. The aqueous phase was extracted with ether (150 mL); the organic phase was extracted with ice water (10 mL), and the combined organic phases were dried ($MgSO_4$) in the dark. The solution was filtered and evaporated under reduced pressure to give a red-orange liquid, which was distilled to afford 19.8 g (64%) of **2b**: bp 60−68 °C (0.15 Torr) (lit.[30] 93−95 °C (10 Torr)).

Reaction of 1c with 2b. Isolation of 3 and 5. A 35 wt % dispersion of KH in mineral oil (802 mg KH, 20.0 mmol) was washed under argon with dry benzene (3 × 4 mL) and covered with glyme (50 mL). To the stirred suspension was added a solution of 2,4,6-trimethyl-*s*-triazine (2.43 g, 19.7 mmol) in glyme (20 mL). The slurry was stirred at room temperature until all the hydride had reacted (2 h or longer) to give a red-orange mixture. The slurry was then transferred (18 min) under argon to a magnetically stirred solution of **2b** (3.89 g, 19.2 mmol) in glyme (70 mL) at room temperature. The reaction mixture was stirred for approximately 15 h; the brick-red slurry was filtered, and the filtrate was evaporated under reduced pressure to give 4.30 g of a viscous red residue. A portion (0.76 g) of the above viscous residue was eluted on neutral alumina (17.3 g) with 50% ether/pentane to give 0.12 g of solid, which was separated into approximately equal amounts of compound **3** and compound **6** by the sublimation of **3**. Resublimation of **3** gave an analytical sample: mp (sealed) 147−149 °C; IR (KBr) 2960, 2920, 1515, 1380 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.54 (s, 12H), 3.33 (s, 4H); ^{13}C NMR ($CDCl_3$) δ 25.8, 35.5, 176.1, 177.9. Anal. Calcd for $C_{12}H_{16}N_6$ (244.30): C, 59.00; H, 6.60; N, 34.40. Found: C, 58.97; H, 6.57; N, 34.30.

In a comparable run, the above viscous residue yielded light-orange crystals with time. Some of the crystals were removed, washed with pentane and water, dissolved in CH_2Cl_2, and dried ($MgSO_4$). The resulting solution was filtered and evaporated to afford a solid that was recrystallized from absolute ethanol (2×) and from dichloromethane/ether (2×) to give an analytical sample of **5**: mp (sealed) 229−230 °C; IR (KBr) 2970, 1500, 1425, 1375, 970 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.63 (s, 12H), 7.99 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 25.8, 138.8, 170.0, 176.8. Anal. Calcd for $C_{12}H_{14}N_6$ (242.28): C, 59.49; H, 5.82; N, 34.69. Found: C, 59.47; H, 5.59; N, 34.45.

Reaction of 1c with 2a. Isolation of 6. A 35 wt % dispersion of KH in mineral oil (736 mg KH, 18.4 mmol) was

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washed under argon with dry benzene (4 × 3 mL) and covered with glyme (50 mL). To the stirred suspension was added a solution of 2,4,6-trimethyl-*s*-triazine (2.10 g, 17.1 mmol) in glyme (10 mL). The slurry was stirred until all the hydride had reacted (2 h or longer) to give an orange-rust mixture. The slurry was transferred (25 min) under argon to a stirred solution of **2a** (2.69 g, 17.1 mmol) in glyme (115 mL) at room temperature. The dark reaction mixture was stirred for approximately 15 h and filtered through Celite, and the major amount of solvent was removed under reduced pressure to yield a red-black residue. A portion (0.67 g) of the residue was eluted on neutral alumina (1 × 19 cm) to afford 0.10 g of crude **6**. The crude **6** was recrystallized (3×) from pentane to give a pure sample of **6** for X-ray diffraction and elemental analysis: mp 99−100 °C; IR (KBr) 2960, 1510, 1420, 1375 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 2.43 (s, 12H), 2.57 (s, 6H), 3.54 (d, $J = 5.7$ Hz, 2H), 3.81 (t, $J = 5.7$ Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 25.5, 25.7, 33.4, 37.1, 174.0, 175.6, 175.9, 176.3. Anal. Calcd for $C_{18}H_{21}N_9$ (363.43): C, 59.49; H, 5.82; N, 34.69. Found: C, 59.67; H, 5.76; N, 34.89.

Reaction of 1a with 2a. *tert*-Butyllithium in pentane (1.7 M, 17.0 mmol) was added dropwise under argon to a stirred solution (−78 °C) of 2,4,6-trimethyl-*s*-triazine (2.09 g, 17.0 mmol) in glyme (40 mL). The bright-yellow slurry was allowed to warm to room temperature overnight and then transferred (22 min) under argon to a stirred solution of **2a** (2.69 g, 17.0 mmol) in glyme (70 mL) at room temperature. After 7 days, the reaction mixture was filtered through Celite; the filtercake was washed with CH_2Cl_2 (5 × 25 mL), and the filtrates were combined. A portion (100 mL) of the filtrates was evaporated, and the residue was dried under vacuum to a constant mass (1.03 g). The residue was dissolved in CH_2Cl_2 (45 mL), extracted with cold, saturated NH_4Cl (4 × 5 mL), dried ($MgSO_4$), filtered, and evaporated to afford a residue that was dried under vacuum to a constant mass (0.49 g). The residue was then dissolved in a measured amount of CH_2Cl_2 to give a solution with an approximate concentration of 10 mg/mL. Three aliquots (2 mL) were removed, dried under vacuum, and dissolved in $CDCl_3$ for quantitative GC and NMR analyses using bibenzyl as an internal reference.

The above reaction was repeated using 2,4,6-trimethyl-*s*-triazine (1.96 g, 15.9 mmol), *tert*-butyllithium in pentane (1.7 M, 15.7 mmol), and **2a** (2.48 g, 15.8 mmol). However, in this case, the solution of **2a** was cooled in a dry ice/acetone bath before the addition of the slurry. The resulting mixture was then maintained below −60 °C (internal) for 6−8 h before being warmed to room temperature. After 2 days, the reaction mixture was filtered through Celite; the filtercake was washed with CH_2Cl_2 (4 × 25 mL), and the filtrates were combined. A portion (100 mL) of the filtrates was removed and worked up as described for the reaction of **1a** with **2a**.

The above original reaction was repeated using 2,4,6-trimethyl-*s*-triazine (1.91 g, 15.5 mmol), *tert*-butyllithium in pentane (1.7 M, 15.6 mmol), and **2a** (2.44 g, 15.5 mmol). However, in this case, the slurry was added rapidly (10 s) to the solution of **2a** at room temperature. After 3 days, the reaction mixture was filtered through Celite; the filtercake was washed with CH_2Cl_2 (4 × 25 mL), and the filtrates were combined. A portion (100 mL) of the filtrates was removed and worked up as described for the reaction of **1a** with **2a**.

Reaction of 1a with 2b. *tert*-Butyllithium in pentane (1.7 M, 16.5 mmol) was added dropwise to a stirred solution (−78 °C) of 2,4,6-trimethyl-*s*-triazine (2.03 g, 16.5 mmol) in glyme (40 mL) under argon. The suspension was allowed to warm to room temperature. After 2 days, the bright-yellow slurry was transferred (31 min) under argon to a stirred solution of **2b** (3.33 g, 16.5 mmol) in glyme (70 mL) at room temperature. After 3 days, the reaction mixture appeared to be homogeneous. A portion of the solution (50 mL) was evaporated to afford a residue that was dried under vacuum to a constant mass. To the residue was added CH_2Cl_2 (50 mL); the resulting suspension was filtered through Celite, and the filtercake was washed with CH_2Cl_2 (2 × 10 mL). The filtrates were combined and worked up as described for the reaction of **1a** with **2a**.

The above reaction was repeated using 2,4,6-trimethyl-*s*-triazine (2.02 g, 16.4 mmol), *tert*-butyllithium in pentane (1.7 M, 16.3 mmol), and **2b** (3.31 g, 16.4 mmol). However, in this case, the solution of **2b** was cooled in a dry ice/acetone bath before the addition of the slurry. The resulting mixture was maintained below −60 °C (internal) for 6−8 h before being warmed to room temperature. After 4 days, the reaction mixture was filtered through Celite; the filtercake was washed with CH_2Cl_2 (3 × 25 mL), and the filtrates were combined. A portion (75 mL) of the filtrates was removed and worked up as described for the reaction of **1a** with **2a**.

Reaction of 1b with 2a. 2,4,6-Trimethyl-*s*-triazine (2.14 g, 17.4 mmol), dissolved in glyme (20 mL), was added under argon to a magnetically stirred suspension of dry (95%) sodium hydride (417 mg NaH, 17.4 mmol) in glyme (50 mL) with gentle heating. The mixture was heated (79 °C) for 7 days and cooled to room temperature, and the deep-red slurry was transferred (25 min) under argon to a stirred solution of **2a** (2.74 g, 17.4 mmol) in glyme (70 mL) at room temperature. After 6 days, the reaction mixture was filtered through Celite; the filtercake was washed with CH_2Cl_2 (4 × 25 mL), and the filtrates were combined. A portion (75 mL) of the filtrates was removed and worked up as described for the reaction of **1a** with **2a**.

The above reaction was repeated using 2,4,6-trimethyl-*s*-triazine (2.07 g, 16.8 mmol), dry (95%) sodium hydride (406 mg NaH, 16.9 mmol), and **2a** (2.66 g, 16.9 mmol). However, in this case, the solution of **2a** was cooled in a dry ice/acetone bath before the addition of the slurry. The resulting mixture was maintained below −60 °C (internal) for 6−8 h before being warmed to room temperature. After 3 days, the reaction mixture was filtered through Celite; the filtercake was washed with CH_2Cl_2 (2 × 25 mL), and the filtrates were combined. A portion (75 mL) of the filtrates was removed and worked up as described for the reaction of **1a** with **2a**.

Reaction of 1b with 2b. 2,4,6-Trimethyl-*s*-triazine (2.03 g, 16.5 mmol), dissolved in glyme (20 mL) was added under argon to a stirred suspension of dry (95%) sodium hydride (375 mg NaH, 15.6 mmol) in glyme (50 mL). The slurry was heated (81 °C) for 7 days, cooled to room temperature, and transferred (20 min) under argon to a stirred solution of **2b** (3.31 g, 16.4 mmol) in glyme (70 mL) at room temperature. After 2 days, the reaction mixture was filtered through Celite; the filtercake was washed with CH_2Cl_2 (5 × 25 mL), and the filtrates were combined. A portion (100 mL) of the filtrates was removed and worked up as described for the reaction of **1a** with **2a**.

The above reaction was repeated using 2,4,6-trimethyl-*s*-triazine (2.01 g, 16.3 mmol), dry (95%) sodium hydride (399 mg NaH, 16.6 mmol), and **2b** (3.31 g, 16.4 mmol). However, in this case, the solution of **2b** was cooled in a dry ice/acetone bath before the addition of the slurry. The resulting mixture was maintained below −60 °C (internal) for 6−8 h before being warmed to room temperature. After 2 days, the reaction mixture was filtered through Celite; the filtercake was washed with CH_2Cl_2 (5 × 25 mL), and the filtrates were combined. A portion (100 mL) of the filtrates was removed and worked up as described for the reaction of **1a** with **2a**.

Reaction of 1c with 2a. A 35 wt % dispersion of KH in mineral oil (710 mg KH, 17.7 mmol) was washed under argon with dry benzene (5 × 4 mL) and then covered with glyme (50 mL). To the stirred suspension was added a solution of 2,4,6-trimethyl-*s*-triazine (2.26 g, 18.4 mmol) in glyme (20 mL). After 2 days, the rust-colored slurry was transferred (40 min) under argon to a stirred solution of **2a** (2.79 g, 17.7 mmol) in glyme (70 mL) at room temperature. After 2 days, the reaction mixture was filtered through Celite; the filtercake was washed with CH_2Cl_2 (3 × 25 mL), and the filtrates were combined. A portion (75 mL) of the filtrates was removed and worked up as described for the reaction of **1a** with **2a**.

The above reaction was repeated using 2,4,6-trimethyl-*s*-triazine (1.99 g, 16.1 mmol), potassium hydride (647 mg KH, 16.1 mmol), and **2a** (2.57 g, 16.3 mmol). However, in this case, the solution of **2a** was cooled in a dry ice/acetone bath before the addition of the slurry. The resulting mixture was maintained below −60 °C (internal) for 6−8 h before being warmed to room temperature. After 3 days, the reaction mixture was filtered through Celite; the filtercake was washed with CH_2Cl_2 (4 × 25 mL), and the filtrates were combined. A portion (100 mL) of the filtrates was removed and worked up as described for the reaction of **1a** with **2a**.

Reaction of 1c with 2b. Isolation of 7. A 35 wt % dispersion of KH in mineral oil (644 mg, KH, 16.1 mmol) was washed under argon with dry benzene (4 × 4 mL) and then covered with glyme (50 mL). To the stirred suspension was added a solution of 2,4,6-trimethyl-*s*-triazine (2.05 g, 16.6 mmol) in glyme (20 mL). After 2 days, the rust-colored slurry was transferred (20 min) under argon to a stirred solution of **2b** (3.35 g, 16.6 mmol) in glyme (70 mL) at room temperature. After 2 days, the reaction mixture was filtered through Celite; the filtercake was washed with CH_2Cl_2 (5 × 25 mL), and the filtrates were combined. A portion (125 mL) of the filtrates was removed and worked up as described for the reaction of **1a** with **2a**.

A portion of the above solution (15 mL) was removed and evaporated to afford a residue (0.25 g) that was eluted on neutral alumina (1 × 21 cm) with 2% methanol/ether. Selected fractions were combined and distilled in a Kugelrohr distillation apparatus to afford 14 mg of **7**: bp 162 °C (0.3 Torr); mp 148−153 °C; IR (neat) 2920, 1525 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.48 (s, 12H), 2.50 (s, 6H), 3.18 (dd, J = 6.5, 15.4 Hz, 2H), 3.47 (dd, J = 7.7, 15.4 Hz, 2H), 4.20 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 25.6_7, 25.7_1, 41.9, 43.9, 175.9_6, 175.9_9, 176.9, 179.8. Anal. Calcd for $C_{18}H_{23}N_9$ (365.44): C, 59.16; H, 6.34; N, 34.50. Found: C, 58.95; H, 6.11; N, 34.36.

The above reaction was repeated using 2,4,6-trimethyl-*s*-triazine (1.97 g, 16.0 mmol), potassium hydride (645 mg KH, 16.1 mmol), and **2b** (3.23 g, 16.0 mmol). However, in this case, the potassium salt was added rapidly (10 s) to the solution of **2b** at room temperature. After 3 days, the reaction mixture was filtered through Celite; the filtercake was washed with CH_2Cl_2 (4 × 25 mL), and the filtrates were combined. A portion (100 mL) of the filtrates was removed and worked up as described for the reaction of **1a** with **2a**.

Isolation of 8. The above reaction was repeated using 2,4,6-trimethyl-*s*-triazine (1.96 g, 15.9 mmol), potassium hydride (638 mg KH, 15.9 mmol), and **2b** (3.22 g, 15.9 mmol). However, in this case, the solution of **2b** was cooled in a dry ice/acetone bath before the addition of the slurry. The resulting mixture was maintained below −60 °C (internal) for 6−8 h before being warmed to room temperature. After 1 day, the reaction mixture was filtered through Celite; the filtercake was washed with CH_2Cl_2 (5 × 25 mL), and the filtrates were combined. A portion (100 mL) of the filtrates was removed and evaporated to afford a residue that was dried under vacuum to a constant mass (1.05 g). The residue was dissolved in CH_2Cl_2 (20 mL), and 10 mL of the solution was removed and worked up as described for the reaction of **1a** with **2a**. The remaining solution was evaporated to a minimum volume and eluted on neutral alumina (21.2 g) with ether. Selected fractions were combined and recrystallized from dichloromethane/ethanol (2×) to obtain a sample of **8** for elemental analysis: mp 198−200 °C; IR (KBr) 2980, 2940, 1540, 1440 cm^{-1}. Anal. Calcd for $C_{24}H_{30}N_{12}$ (486.62): C, 59.24; H, 6.21; N, 34.55. Found: C, 59.26; H, 5.96; N, 34.43.

The crystals of **8** were visually separated into the racemic and meso forms. *meso*-**8**: mp 174−175 °C; ^1H NMR ($CDCl_3$) δ 2.43 (s, 12H), 2.48 (s, 12H), 3.14 (dd, J = 3.9, 16.5 Hz, 2H), 3.57 (dd, J = 9.6, 16.5 Hz, 2H), 4.17 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 25.6_6, 25.7_3, 39.3, 49.1, 175.8, 177.0, 178.7. Racemic **8**: mp 203−205 °C; ^1H NMR ($CDCl_3$) δ 2.43 (s, 12H), 2.47 (s, 12H), 3.30 (dd, J = 4.1, 16.5 Hz, 2H), 3.73 (dd, J = 9.6, 16.5 Hz, 2H), 4.32 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 25.6_9, 25.7_5, 37.3, 48.1, 175.8, 177.3, 178.8.

Reaction of NaH with 2b. An 80 wt % dispersion of NaH (213 mg NaH, 8.90 mmol) was washed with dry benzene (4 × 5 mL) and then covered with glyme (50 mL). To the stirred suspension, under argon, was added (20 s) a solution of **2b** (1.81 g, 8.95 mmol) in glyme (20 mL). After 5 days, the mixture was filtered through Celite, and the filtrate was evaporated to yield 1.11 g of yellow-orange solid. A small amount of the solid was washed with water to give a white solid. The water was removed via pipet, and the solid was dissolved in CH_2Cl_2 (25 mL), dried ($MgSO_4$), and filtered through Celite. A portion (1 mL) of the resulting solution was evaporated under vacuum to afford a solid that was dissolved in $CDCl_3$ and analyzed via ^1H NMR. Relative mol %: **3**, 2; **5**, 61; **6**, 37.

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Supporting Information Available: ^1H and ^{13}C spectra for compounds **3**, **5**−**7** (^1H only), *meso*-**8**, racemate **8**, a mixture of *meso*- and racemate **8**, and a mixture of **7** and **8**, and crystallographic data and thermal ellipsoid figures for compounds **5**−**7**, *meso*-**8**, and racemate **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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