Reactions of 1,1-dimethyl-4-substituted semicarbazides with phosgene

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Reactions of 1,1-Dimethyl-4-substituted-semicarbazides with Phosgene

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Reaction of excess phosgene with 1,1-dimethyl-4-phenylsemicarbazide, **3**, gave 3-chloro-1-methyl-4-phenyl-Δ^2-1,2,4-triazolin-5-one, **4**. An investigation into the reaction pathway led to the surprising find that when 1 equiv of phosgene was allowed to react with **3**, 4-(dimethylamino)-1-methyl-3-(phenylamino)-5-(phenylimino)-Δ^2-1,2,4-triazoline, **9**, was obtained. Pathways for the formation of products **4** and **9** involved the conversion of **3** into an *N*-(dimethylamino)carbodiimide, **10**. In the formation of **4**, the carbodiimide reacted with excess phosgene and then underwent an intramolecular von Braun type of N-demethylation. In the formation of **9** the *N*-(dimethylamino)carbodiimide gave an acid-catalyzed self-condensation, cyclization, and N-demethylation. *N*-(Dimethylamino)carbodiimides are highly reactive compounds since they contain both a nucleophilic and an electrophilic center. In the above case, the *N*-(dimethylamino)-*N'*-phenylcarbodiimide, **10**, could not be isolated. When the phenyl group was replaced with a *tert*-butyl substituent, the resulting *N*-*tert*-butyl-*N'*-(dimethylamino)carbodiimide, **16**, showed enough stability to be characterized and, in the presence of phosgene, formed the *tert*-butyl analogue of **4**.

Introduction

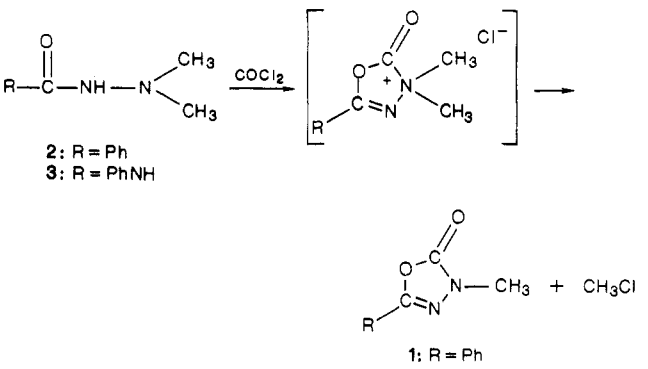
Previously, the oxadiazolinone **1** (R = Ph) had been reported from the reaction of 1,1-dimethyl-2-benzoylhydrazine, **2** (R = Ph), with phosgene (Scheme I).[1] We now report the reaction of 1,1-dimethyl-4-phenylsemicarbazide, **3**, and related semicarbazides.

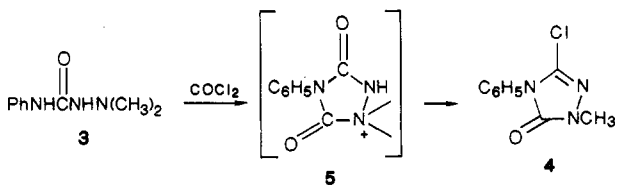
Results

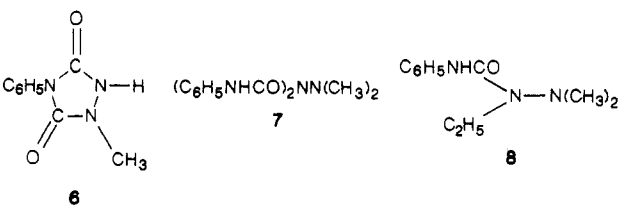
On treatment with excess phosgene, using conditions described by Meyer and Cummings,[1b] 1,1-dimethyl-4-phenylsemicarbazide, **3**, cyclized to form 3-chloro-1-methyl-4-phenyl-Δ^2-1,2,4-triazolin-5-one, **4**, in 92% purified yield. Although imino chlorides are generally reactive,[2] this one is not. Thus, **3** did not react with refluxing ethanolic silver nitrate or with sodium iodide in acetone. It did not react with excess ethanol in trifluoroacetic acid. The chlorine was readily observed by mass spectrometry and was detected by sodium fusion.

Our original idea was that the intermediate for the reaction might be **5**, analogous to that proposed by Meyer and Cummings.[1b] For **4** to form from **5** would require a von Braun type displacement of methyl. Such displacements are well precedented.[1,6] Also required would be the formation of the imino chloride by reaction of the amide group in the heterocycle with excess phosgene. If **5** were the intermediate, the NH at the 2-position of **3** should not be necessary to get a heterocyclic product **6**. That the NH at the 2-position was necessary was established by the observation that **7** and **8** were inert to phosgene.

Scheme I







Still believing that **5** was an intermediate, we treated **3** in the presence of pyridine with 1 equiv of phosgene. Under these conditions 4-(dimethylamino)-1-methyl-3-(phenylamino)-5-(phenylimino)-Δ^2-1,2,4-triazoline, **9**, formed. Low-temperature single-crystal X-ray analysis confirmed this structure for **9** and showed that the unit cell contained two crystallographically independent molecules. These differed only in the orientation of the two

(1) (a) Edwards, L. H. U.S. Patent 4 499 098, 1985. (b) Meyer, R. F.; Cummings, B. L. *Heterocycl. Chem.* **1964**, *1*, 186.

(2) Stone, D. M. Ph.D. Thesis, University of Idaho, 1973. For a review of the reactivity of imino chlorides, see: Bonnett, R. *The Chemistry of the Carbon-Nitrogen Double Bond*; Patai, S., Ed.; Interscience: New York, 1970; Chapter 13.

(3) (a) Neidlein, R.; Heukelbach, E. *Arch. Pharm.* **1966**, *299*, 709. (b) Ulrich, H.; Sayigh, A. A. R. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 704. (c) Eilingsfeld, H.; Neubauer, G.; Seefelder, M.; Weidinger, H. *Chem. Ber.* **1964**, *97*, 1232.

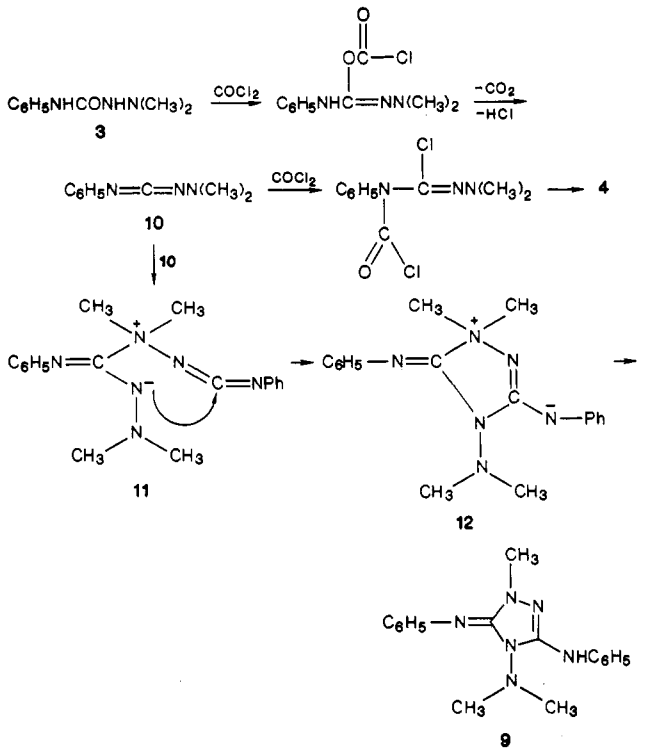
(4) (a) Gross, H.; Zinner, G. *Chem. Ber.* **1973**, *106*, 2315. (b) Zinner, G.; Vollrath, R. *Chem. Ber.* **1970**, *103*, 766. (c) Buyle, R.; Viehe, H. G. *Tetrahedron* **1969**, *25*, 3453. (d) Hartke, K.; Palou, E. *Chem. Ber.* **1966**, *99*, 3155. (e) Ulrich, H.; Sayigh, A. A. R. *J. Org. Chem.* **1963**, *28*, 1427. (f) Eilingsfeld, H.; Seefelder, M.; Weidinger, H. *Angew. Chem.* **1960**, *72*, 836.

(5) (a) Vaughan, W. R.; Carlson, R. D. *J. Am. Chem. Soc.* **1962**, *84*, 769. (b) von Braun, J. *Chem. Ber.* **1900**, *33*, 1438. (c) For a review, see: Hageman, H. A. *Org. React.* **1953**, *7*, 198.

(6) For similar cyclizations using phosgene, see: (a) Maryanoff, B. E.; Molinari, A. J.; McComsey, D. F.; Maryanoff, C. A.; Wooden, G. P.; Olofson, R. A. *J. Org. Chem.* **1983**, *48*, 5074. (b) Maryanoff, B. E.; Molinari, A. J.; Wooden, G. P.; Olofson, R. A. *Tetrahedron Lett.* **1982**, *23*, 2829. (c) Lunsford, C. D.; Cale, A. D., Jr. U.S. Patent 3 337 580, 1967. (d) Clarke, R. L.; Mooradian, A.; Lucas, P.; Slauson, T. J. *J. Am. Chem. Soc.* **1949**, *71*, 2821.

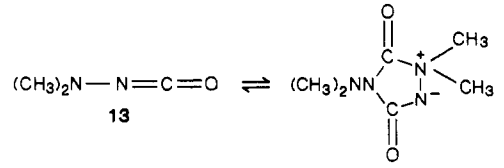
0022-3263/89/1954-1048$01.50/0

Scheme II

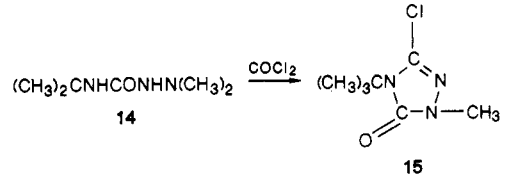


phenyl groups relative to the five-membered ring. The structure of **9** suggested that an intermediate in its formation might be the carbodiimide, **10** (Scheme II). It is known that carbodiimides are formed when ureas are treated with phosgene.[3] Further, the addition of phosgene to carbodiimides is well established.[7] Formation of **4** from carbodiimide, **10**, involves addition of an equivalent of phosgene to **10** followed by an intramolecular von Braun reaction. Formation of **9** requires intermolecular reaction of the nucleophilic dimethylamino group of **10** with the electrophilic group of a second molecule of **10** forming the zwitterion **11**. In turn the nucleophilic nitrogen attacks the electrophilic carbodiimide group of **11** to form a second zwitterion **12**. Finally a von Braun dealkylation and a protonation of the nitrogen anion give **9**. Although direct evidence for the key intermediate, **10**, could not be obtained, it is a logical choice.

A similar but reversible intermolecular dimerization has been suggested for (dimethylamino)isocyanate, **13**, by Wadsworth and Emmons.[8]



In order to examine the effect of an alkyl substituent in place of the aromatic group on **3**, the 4-*tert*-butyl-1,1-dimethylsemicarbazide, **14**, was treated with excess phosgene, and the triazolinone **15** was obtained in 96% yield. Gas chromatographic analysis of this reaction



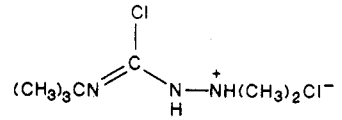
showed the presence of an intermediate peak, which formed immediately upon addition of phosgene and gradually decreased as the amount of **15** increased. The following evidence was accumulated that this intermediate was *tert*-butyl(*N*,*N*-dimethylamino)carbodiimide, **16**.

$$(CH_3)_3CN{=}C{=}NN(CH_3)_2$$

16

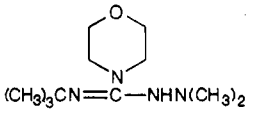
First, the infrared spectrum of the reaction medium showed a strong band at 2100 cm^{-1} corresponding to the carbodiimide group. Second, **16** was prepared and shown to have the same retention time on gas chromatography. Third, treatment of **16** with 1 equiv of phosgene gave **15**.

We were unable to separate **16** from the reaction medium of **14** with 1 equiv of phosgene and pyridine.[10] A different approach for isolation of **16** was as follows: Equimolar amounts of phosgene and **14** were allowed to react without adding a base to tie up the 2 equiv of hydrogen chloride that form as a byproduct. The hydrogen chloride reacted with **16** to form a white solid dihydrochloride, which was stable under nitrogen. We suggest the structure **17** for the dihydrochloride as shown based on the



following spectra: IR (N–H) 3156 and 2382 cm^{-1}; NMR NCH_3 at δ 3.08 ppm (s, 6 H) compared to NCH_3 at δ 2.33 ppm for **14** and δ 2.22 ppm for the morpholine derivative, **18**, of **17**. The position of the C=N in **17** is speculative, but the ^{13}C NMR chemical shifts of the central *tert*-butyl carbons were 48.98 ppm for **14**, 55.66 ppm for **16**, and 55.28 ppm for **17**.

A morpholine derivative, **18**, formed when **17** was treated with an excess of 1,4-diazabicyclo[2.2.2]octane (DABCO), which formed an insoluble white salt. The solution was then treated with morpholine.



The *N*-*tert*-butyl-*N'*-(dimethylamino)carbodiimide, **16**, was easily obtained from the salt, **17**, by the addition of solid sodium hydrogen carbonate, filtration of the resulting inorganic salts, and vacuum distillation of the product. The liquid *N*-(dimethylamino)carbodiimide, **16**, was characterized by IR (carbodiimide peak) frequency and ^{13}C NMR (N=C=N carbon at 144.81 ppm) compared to 140.2 and 139.9 ppm reported for diisopropyl- and dicyclohexylcarbodiimides.[11] Although **16** was more stable than

(7) For reviews of the reactivityof carbodiimides, see: (a) Mikolajczyk, M.; Kielbasinski, P. *Tetrahedron* **1981**, *37*, 233. (b) Kurzer, F.; Douraghi-Zadeh, K. *Chem. Rev.* **1967**, *67*, 107.

(8) Wadsworth, W. S.; Emmons, W. D. *J. Org. Chem.* **1967**, *32*, 1279.

(9) The compound *N*-(dimethylamino)-*N'*-*tert*-octylcarbodiimide has been reported to have limited stability: Wadsworth, W. S., Jr.; Emmons, W. D. *J. Org. Chem.* **1964**, *29*, 2816.

(10) Gas chromatographic analysis of the reaction mixture showed that the *N*-(dimethylamino)carbodiimide, **23**, was the major constituent (72%). The remainder of the mixture was the starting semicarbazide, **21**, and the cyclic product, **22**.

(11) Levy, G. C.; Lichter, R. L.; Nelson, G. L. *Carbon-13 Nuclear Magnetic Resonance Spectroscopy*, 2nd ed.; John Wiley and Sons: New York, 1980; p 163.

the phenyl analogue, it solidified upon standing. The solid does not have the carbodiimide peaks in the IR and ^{13}C NMR, but we have been unable to characterize it at this time.

When **16** was treated with 1 equiv of phosgene, **17** was obtained. The identity of the intermediate peak observed in the GC analysis of the conversion of **14** into **15** was confirmed to have the same retention time as the cabodiimide **16**. In order to ensure that the peak observed was not a decomposition product of **16**, the high-resolution mass spectral analysis of **16** was performed as GC/HRMS using similar chromatographic conditions.

Experimental Section

General. ^1H and ^{13}C NMR spectra were obtained, in the indicated solvent, from either an IBM NR/300 FTNMR or a JEOL FX90Q spectrometer; reported chemical shifts are in ppm (δ) relative to either $CHCl_3$ (δ 7.26) or TMS (δ 0.00). Infrared spectra were recorded on a Digilab Qualimatic FTIR instrument using NaCl plates. MS and GC/MS measurements were made with a VG 7070HS mass spectrometer coupled to a Hewlett-Packard Model 5880A gas chromatograph. Melting points were determined by using a Thomas-Hoover apparatus and were corrected. Elemental analyses were carried out by Desert Analytics, Tucson, AZ.

Materials. Unless indicated otherwise, reagents were purchased from Aldrich Chemical Co., Inc., Milwaukee, WI. Solvents were glass distilled and were obtained from either Burdick and Jackson Laboratories, Inc., Muskegon, MI, or from EM Science, Cherry Hill, NJ. Phosgene gas was acquired in lecture bottles from Matheson Gas Products, Newark, CA.

Crystal Structure Analysis of 9. A single crystal was mounted on a Nicolet R3m/E diffractometer equipped with a graphite monochromator on a LT-2 low-temperature device. Lattice constants of this triclinic crystal were determined to be a = 10.738 (5) Å, b = 12.197 (5) Å, c = 13.386 (7) Å, α = 88.93 (4)°, β = 88.70 (4)°, and γ = 68.13 (3)° with Mo Kα radiation (0.710688 Å). Data collection at 123 K yielded 3179 unique reflections.[12] Structure solution via direct methods and subsequent difference Fourier synthesis yielded the positions of the C, N, and H atoms of the two crystallographically independent molecules.[13] Least-squares refinement with hydrogen atoms included at calculated positions gave a final R value of 0.0693 for data with $|F| \geq 3\alpha(F)$.

General Method for the Preparation of Semicarbazides 3, 7, 8, 14. A 250-mL flask was charged with the appropriate isocyanate (100 mmol was used in all cases except **7** where 200 mmol was necessary) dissolved in benzene (75 mL). The mixture was cooled to 0 °C (ice/H_2O) under a nitrogen atmosphere. A 100-mL flask containing 110 mmol of either 1,1-dimethylhydrazine (in the synthesis of **3**, **7**, and **14**) or 1,1-dimethyl-2-ethylhydrazine[14] (in the synthesis of **8**) dissolved in benzene (25 mL) was added, via cannula, over a 15-min period. The cold bath was removed, and the mixture was stirred for an additional 30 min. Removal of the solvent (rotovap) left the crude product, which was recrystallized from the solvent indicated.

1,1-Dimethyl-4-phenylsemicarbazide (3) (93%): white needles from CCl_4; mp 107–108 °C (lit.[15] mp 108 °C); IR (KBr, cm^{-1}) 3314, 3264, 3209, 3110, 2990, 2954, 2858, 1682, 1592, 1530, 1449, 1158, 755, 698; ^1H NMR ($CDCl_3$) δ 2.59 (s, 6 H), 5.45 (broad s, 1 H), 7.02–7.54 (m, 5 H), 8.15 (broad s, 1 H); MS m/z (relative intensity) 179 (M^+, 13.1), 136 (19.0), 119 (6.7), 60 (100).

1,1-Dimethyl-2,2-bis(phenylcarbamoyl)hydrazine (7) (96%): white prisms from anhydrous ethanol; mp 123.5–124.5 °C (lit.[2] mp 121 °C); IR (Nujol, cm^{-1}) 3264, 1719, 1656, 1592, 1555, 1504, 1442, 1174, 752, 692; ^1H NMR ($CDCl_3$) δ 2.91 (s, 6 H), 6.90–7.50 (m, 10 H); MS m/z (relative intensity) 298 (M^+, 0.8), 179 (40.2), 136 (13.8), 119 (100), 93 (58.7), 91 (36.0), 60 (75.1).

1,1-Dimethyl-2-ethyl-4-phenylsemicarbazide (8) (27%): recrystallized from hexane; mp 87–87.5 °C; IR (melt, cm^{-1}) 3351, 2988, 2952, 2865, 1684, 1675, 1601, 1589, 1520, 1446, 1307, 1149, 924, 752, 694; ^1H NMR ($CDCl_3$) δ 1.28 (t, 3 H), 2.57 (s, 6 H), 3.40 (q, 2 H), 6.96–7.55 (m, 5 H), 8.55 (broad s, 1 H); MS m/z (relative intensity) 207 (M^+, 9.8), 164 (15.9), 119 (25.4), 93 (31.6), 87 (100), 59 (88.9). Anal. Calcd for $C_{11}H_{17}N_3O$: C, 63.64; H, 8.27; N, 20.27. Found: C, 63.63; H, 8.25; N, 20.38.

1,1-Dimethyl-4-*tert*-butylsemicarbazide (14) (93%): colorless prisms from hexane; mp 90–91.5 °C; IR (melt, cm^{-1}) 3378, 3200, 2962, 2661, 2825, 2782, 1684, 1525, 1448, 1362, 1238, 1218, 1162; ^1H NMR ($CDCl_3$) δ 1.21 (s, 9 H), 2.33 (s, 6 H), 5.38 (broad s, 1 H), 5.88 (broad s, 1 H); ^{13}C NMR ($CDCl_3$) δ 29.01 (*tert*-butyl-CH_3), 47.24 (NCH_3), 48.98 (*tert*-butyl-C), 157.34 (C=O); MS m/z (relative intensity) 159 (M^+, 0.4), 144 (0.3), 99 (0.2), 84 (2.5), 60 (100), 57 (12.1), 45 (20.4). Anal. Calcd for $C_7H_{17}N_3O$: C, 52.80; H, 10.76; N, 26.39. Found: C, 52.64; H, 11.12; N, 26.73.

3-Chloro-1-methyl-4-phenyl-Δ^2-1,2,4-triazolin-5-one (4). A dry 250-mL round-bottomed flask, equipped with magnetic stirring bar, sintered-glass gas inlet tube (Teflon sleeved), and efficient reflux condenser, was charged with **3** (1.897 g, 10.6 mmol). Dichloromethane (170 mL) was added, and the mixture was brought to reflux. Phosgene was introduced through the inlet tube beneath the surface of the liquid (ca. 10 mL/min). After 20 min, the initially colorless solution had turned to pale yellow. The reaction was monitored by TLC (silica gel with ethyl acetate elution) and allowed to reflux until no starting material could be detected (4 h). The reaction mixture was cooled to room temperature, added to 500 mL of 5% $NaHCO_3$, and stirred for 1 h, and the layers were separated. The organic portion was washed with 5% $NaHCO_3$ (2 × 150 mL) and once with brine (200 mL), dried (Na_2SO_4), and filtered, and the solvent was removed under reduced pressure, leaving an off-white solid (2.49 g). TLC showed the presence of a base-line contaminant, which was easily removed by column chromatography (silica gel with ethyl acetate elution). The resulting solid (2.05 g, 92%) was recrystallized from CCl_4; mp 134–134.5 °C: IR (Nujol, cm^{-1}) 1715, 1710, 1599, 1534, 762, 692; ^1H NMR ($CDCl_3$) δ 3.42 (s, 3 H), 7.19–7.45 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 32.51 (NCH_3), 126.67, 129.05, 129.23, 131.56 (aromatic), 132.39 (CCl), 152.00 (C=O); MS m/z (relative intensity) 211 (M + 2, 32.2), 209 (M^+, 100), 174 (1.5), 140 (12.2), 138 (37.4), 119 (13.6), 117 (16.8), 90 (28.5), 77 (50.7), 65 (21.0), 51 (24.9), 43 (19.8). Anal. Calcd for $C_9H_8N_3OCl$: C, 51.57; H, 3.85; N, 20.04. Found: C, 51.31; H, 3.88; N, 19.91.

4-(Dimethylamino)-1-methyl-3-(phenylamino)-5-(phenylimino)-Δ^2-1,2,4-triazoline (9). A 500-mL round-bottomed flask, equipped with magnetic stirring bar, was charged with **3** (4.357 g, 24.3 mmol). The flask was evacuated three times to 0.10 mmHg and then filled with nitrogen. Dichloromethane (250 mL) and pyridine (3.93 mL, 48.6 mmol) were added via syringe, and the solution was cooled to 0 °C (ice/H_2O). Phosgene gas was condensed at −78 °C (2-propanol/CO_2) into a 100-mL three-necked round-bottomed flask under a flow of nitrogen. Phosgene (1.74 mL, 24.3 mmol) was then added via syringe. A deep red color formed immediately and faded slowly. The mixture was allowed to warm to room temperature and stirred for 24 h. The solvent was removed with a rotovap until approximately 75 mL remained. The reaction mixture was washed with H_2O (2 × 100 mL) and brine (100 mL). The aqueous washings were extracted with dichloromethane (75 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was removed, leaving a white solid (3.13 g, 10.2 mmol, 83.6%), which was recrystallized from anhydrous ethanol; mp 141–141.5 °C: IR (KBr, cm^{-1}) 3372, 3170, 3141, 2960, 1668, 1627, 1601, 1586, 1555, 1400, 1300, 740, 685, 505; ^1H NMR (DMSO-d_6/TMS) δ 2.89 (s, 3 H), 3.01 (s, 6 H), 6.69–7.69 (m, 10 H), 8.50 (broad s, 1 H); MS m/z (relative intensity) 308 (M^+, 7.7), 265 (100), 220 (23.9), 146 (13.7), 188 (31.6), 104 (27.1), 91 (15.3), 77 (51.2), 65 (9.7), 51 (16.6). Anal. Calcd for $C_{17}H_{20}N_6$: C, 66.21; H, 6.54. Found: C, 66.19; H, 6.48.

4-*tert*-Butyl-3-chloro-1-methyl-Δ^2-1,2,4-triazolin-5-one (15). A 250-mL round-bottomed flask, equipped with magnetic stirring bar, was charged with **14** (2.887 g, 18.2 mmol). The flask was evacuated three times to 0.10 mmHg and then filled with nitrogen. Dichloromethane (100 mL) and pyridine (5.9 mL, 73 mmol) were added via syringe and the mixture was cooled to 0 °C (ice/H_2O).

(12) Campana, C. F.; Shepard, D. F.; Litchman, W. M. *Inorg. Chem.* **1981**, *20*, 4039.
(13) Sheldrick, G. M. SHELXTL, Revision 4.1; Nicolet Inst. Corp., Madison, WI, 1985.
(14) Hinman, R. L. *J. Am. Chem. Soc.* **1956**, *78*, 1645.
(15) Renouf, E. *Ber.* **1880**, *13*, 2169.

Phosgene (2.6 mL, 36 mmol) was added as described in the synthesis of **9**. The solution was allowed to warm to room temperature and stirred for 20 h. Due to the partial water solubility of the product, the reaction was worked up in the following way: a solid mixture of $NaHCO_3$ (10.8 g, 119 mmol) and anhydrous $MgSO_4$ (10.0 g, 83.0 mmol) was added to the reaction and stirred, vigorously, for 1 h. The solid was filtered, the solvent was removed with a rotovap, and the residue was subjected to a high vacuum (room temperature, 0.01 mmHg) for several hours. A 3.30-g residue of the product (96%) was recrystallized from water; mp 72–74 °C: IR (melt, cm^{-1}) 2981, 2942, 2916, 1718, 1524, 1388, 1373, 1348, 1257, 1211, 1148, 746, 626; ^1H NMR ($CDCl_3$) δ 1.70 (s, 9 H), 3.39 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 28.91 (*tert*-butyl-CH_3), 31.88 (NCH_3), 59.71 (*tert*-butyl-C), 131.83 (CCl), 152.68 (C=O); MS *m/z* (relative intensity) 191 (M + 2, 2.8), 189 (M^+, 7.6), 176 (0.3), 174 (0.6), 135 (31.1), 133 (90.7), 57 (100). Anal. Calcd for $C_7H_{12}N_3OCl$: C, 44.33; H, 6.38; N, 22.16; Cl, 18.69. Found: C, 44.17; H, 6.47; N, 21.90; Cl, 18.86.

Gas Chromatographic Analysis of the Conversion of 14 into 15. A Hewlett-Packard Model 5890A gas chromatograph using a thermal conductivity detector and coupled to a Hewlett-Packard Model 3390A recorder and integrator was used. The column was an HP-5 (cross-linked 5% PhMe silicone) 30 m × 0.53 mm (megabore) × 2.65 μm film thickness. Helium, scrubbed to remove moisture and oxygen, was used as the carrier gas at a total flow rate of 29 mL/min. Corrections for different response factors of the TCD toward **14** and **15** were determined by using a known concentration of benzophenone as an internal standard. Aliquots (50 μL) were removed and diluted with dichloromethane (2 mL). They were quenched with anhydrous K_2CO_3 (100 mg). Retention times were as follows: dichloromethane, 0.84 min; pyridine, 2.44 min; *N*-(dimethylamino)carbodiimide (**16**), 6.69 min; semicarbazide (**14**), 10.27 min; cyclized product (**15**), 12.09 min; benzophenone, 15.2 min.

***N*-[4-Morpholino(*tert*-butylimino)methyl]-*N'*,*N'*-dimethylhydrazine (18).** A 500-mL round-bottomed flask was charged with the semicarbazide **14** (8.461 g, 53.2 mmol) and dichloromethane (150 mL). The solution was cooled to 0 °C (ice/H_2O), and phosgene gas was bubbled into the mixture (ca. 10 mL/min) until the total volume had reached approximately 250 mL. The solution was allowed to warm to room temperature, with stirring, under a stream of nitrogen for 20 h. After 20 h, most of the solvent had been removed, leaving behind a very thick colorless oil. Residual dichloromethane and phosgene were removed with a vacuum of 0.01 mmHg at room temperature, leaving the *N*-*tert*-butyl-*N'*-(dimethylamino)chloroformamidine hydrochloride, **17**, as a white solid: IR (Nujol, cm^{-1}) 3156, 2451, 2382, 2341, 1608, 1525, 1365, 1288, 1161, 1046, 965, 622, 598; ^1H NMR ($CDCl_3$) δ 1.36 (s, 9 H), 3.08 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 27.75 (*tert*-butyl-CH_3), 48.40 (NCH_3), 55.28 (*tert*-butyl-C), 143.84 (CCl); MS *m/z* (relative intensity) (no molecular ion detected), 141 (4.2), 116 (18.4), 112 (5.9), 85 (100), 60 (16.6), 58 (58.0), 57 (30.6), 43 (73.8).

The solid, **17**, was transferred, under nitrogen, into a 250-mL flask. Dichloromethane (100 mL) and purified DABCO (11.94 g, 106.0 mmol) were added, and the mixture was stirred for 4 h. Morpholine (4.64 mL, 53.2 mmol) was added via syringe, and the solution was stirred for 1 h. The salt was removed by filtration, and the product was isolated by column chromatography (silica gel, acetone elution). Removal of the solvents left **18** as a clear liquid (10.051 g, 44.1 mmol, 83%); bp 193 °C: IR (neat, cm^{-1}) 3276, 2963, 2854, 1611, 1391, 1364, 1121, 1010, 951; ^1H NMR ($CDCl_3$) δ 1.15 (s, 9 H), 2.22 (s, 6 H), 2.96 (t, 4 H), 3.60 (t, 4 H), 5.44 (broad s, 1 H); ^{13}C NMR ($CDCl_3$) δ 28.60 (*tert*-butyl-CH_3), 46.89 (NCH_3), 49.33 (NCH_2), 51.60 (*tert*-butyl-C), 65.81 (OCH_2), 164.31 (N=C); MS *m/z* (relative intensity) 228 (M^+, 28.2), 168 (4.0), 157 (5.4), 115 (17.6), 110 (15.6), 87 (19.7), 86 (61.1), 57 (50.9), 42 (98.8), 41 (100); HRMS calcd for $C_{11}H_{24}N_4O$ 228.195 01, found 228.194 96.

***N*-*tert*-Butyl-*N'*-(dimethylamino)carbodiimide (16).** To a solution of hydrochloride, **17** (13.46 g, 63.2 mmol), in 100 mL of CH_2Cl_2 was added a solid mixture of $NaHCO_3$ (20 g, 240 mmol) and anhydrous $MgSO_4$ (10 g, 80 mmol) over a 5-min period, and the mix was stirred for 30 min. The solid was removed by filtration, and the solvent was removed under reduced pressure, leaving **16** as a colorless liquid. Pure **16** was obtained after vacuum distillation (5.733 g, 40.7 mmol, 64%); bp 150 °C (760 mmHg) (lit.[9] bp 65 °C (15 mmHg)): IR (neat, cm^{-1}) 2972, 2858, 2779, 2105, 2074, 1466, 1367, 1236, 1167, 961, 774, 638; ^1H NMR ($CDCl_3$) δ 1.41 (s, 9 H), 2.69 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 29.58 (*tert*-butyl-CH_3), 47.74 (NCH_3), 55.66 (*tert*-butyl-C), 144.81 (N=C=N); MS *m/z* (relative intensity) 141 (M^+, 1.1), 98 (7.9), 85 (17.8), 83 (42.2), 67 (2.8), 57 (100); HRMS calcd for $C_7H_{15}N_3$ 141.1266, found 141.1247.

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Supplementary Material Available: Details of the data collection and structure analysis, final positional and thermal parameters, as well as important bond distances and angles (13 pages). Ordering information is given on any current masthead page.