Methyl Sulfate (3b). ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.85 (d, J = 6.8 Hz, 3 H), 0.97 (d, J = 7.4 Hz, 3 H), 1.06 (s, 3 H), 1.09 (s, 3 H), 1.19–1.29 (m, 1 H), 1.49–1.75 (m, 4 H), 1.88–1.96 (m, 1 H, 2.31 (qqd, J = 7.4, 6.8, 4 Hz, 1 H), 2.85–2.94 (m, 2 H), 3.05 (dd, J = 20.9, 9.3 Hz, 1 H), 3.44 (s, 3 H), 3.73 (s, 3 H), 4.23 (br s, 1 H), 4.53 (dd, J = 9.3, 6.7Hz, 1 H), 4.76 (br s, 1 H), 4.77 (ddd, J = 10.7, 6.7, 4 Hz, 1 H), 5.17 (dd, J = 10.7, 9.3 Hz, 1 H); IR ($CHCl_3$) 3090, 2960, 2455, 1650, 1470, 1445, 1395, 1380, 1220, 1000, 895 cm^{-1}.

Acknowledgment. We are pleased to acknowledge support of this work by the National Science Foundation through Grant CHE-8405527.

Registry No. **1a**, 98901-10-1; **1b**, 98876-59-6; **2a**, 98877-34-0; **2b**, 98876-63-2; **3a**, 98876-65-4; **3b**, 98876-67-6; **4a**, 98901-12-3; **4b**, 98876-69-8; **5a**, 98876-71-2; **5b**, 98876-73-4; **6a**, 98876-75-6; **6b**, 98876-77-8; **7a**, 98876-79-0; **7b**, 98876-81-4; **8a**, 98876-83-6; **8b**, 98876-85-8; (±)-**9a**, 98876-87-0; (±)-**9b**, 98876-89-2; (±)-**10a**, 98876-91-6; (±)-**10b**, 98876-93-8; **11a**, 98876-94-9; **11b**, 98876-95-0; **12a**, 98876-97-2; **12b**, 98876-99-4; (±)-**13a**, 98877-01-1; (±)-**13b**, 98877-03-3; **14a**, 98877-05-5; **14b**, 98877-07-7; **15a**, 98877-09-9; **15b**, 98877-11-3; (±)-**16a**, 98877-13-5; (±)-**16b**, 98877-15-7; **17a**, 98877-16-8; **17b**, 98877-17-9; **18a**, 98877-19-1; **18b**, 98877-21-5; **19a**, 98877-23-7; **20a**, 98876-60-9; **20b**, 98876-61-0; **24a**, 98877-40-8; **24b**, 98877-41-9; **25a**, 98877-24-8; **25b**, 98877-25-9; **26a**, 98877-42-0; **26b**, 98877-43-1; (±)-**27a**, 98877-26-0; (±)-**27b**, 98877-27-1; **30a**, 98877-28-2; **30b**, 98877-29-3; (±)-**31a**, 98877-30-6; (±)-**31b**, 98877-31-7; **33a**, 98877-32-8; **33b**, 98877-44-2; (±)-**34a**, 98877-35-1; (±)-**34b**, 98877-36-2; **36a**, 98877-37-3; **36b**, 98877-38-4; **37a**, 98877-39-5; 2-propenyl 4-methylbenzenesulfonate, 4873-09-0.

Supplementary Material Available: Spectral data for N-methyloxazolium salts **2**, **4–19** and their oxazoline precursors (11 pages). Ordering information is given on any current masthead page.

Broadened Scope of Translocative Rearrangements. Substituted 1,2,3-Triazolo[1,5-*a*]-1,3,5-triazines

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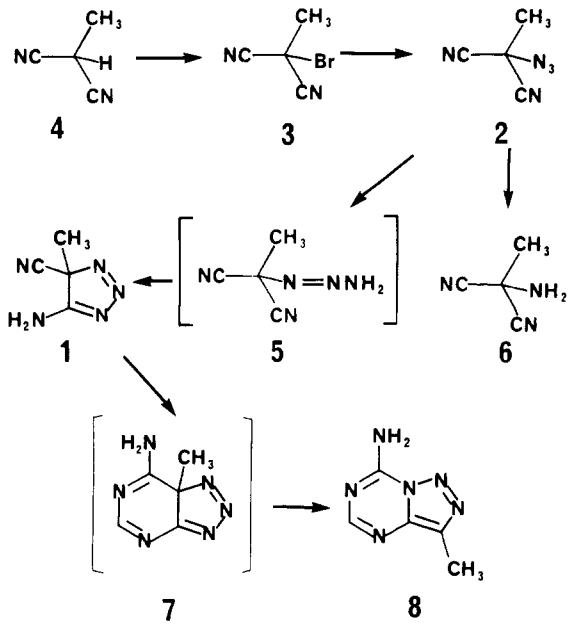
We have previously reported "translocative rearrangements" in which the overall result that occurs during a reaction with formamidine is the removal of a C≡N group from the quaternary carbon of a heterocycle and its translocation to a ring nitrogen two atoms removed, where it becomes attached as a ≥CNH_2 function. Generality has been shown to the extent that 4-substituted 5-amino-4-cyano-4*H*-imidazoles are converted to 8-substituted 4-aminoimidazo[1,5-*a*]-1,3,5-triazines by treatment with formamidine at 20 °C.[1] It was of interest to learn whether the scope of the reaction could be broadened to include the conversion of 4-substituted 5-amino-4-cyano-4*H*-1,2,3-triazoles to 8-substituted 4-amino-1,2,3-triazolo-[1,5-*a*]-1,3,5-triazines. In this category, 5-amino-4-cyano-4-methyl-4*H*-1,2,3-triazole (**1**) was considered a representative candidate for translocative rearrangement.

Scheme I



Several synthetic routes were examined for the preparation of **1**, including approaches through 2-azido-2-cyanopropionitrile (**2**). This proved to be the most acceptable precursor, prepared successfully from 2-bromo-2-cyanopropionitrile (**3**), which was available in turn from the bromination of 2-methylmalononitrile (**4**) (Scheme I).[2] More direct approaches to 2-azido-2-cyanopropionitrile (**2**) from 2-methylmalononitrile (**4**) resulted in diversions. For example, a previous report of the reaction of the sodium salt of 2-methylmalononitrile with *p*-toluenesulfonyl azide in methanol detailed a condensation, rearrangement, and methanolysis that led ultimately to 4-methyl-2-[(4-toluenesulfonyl)amino]-5-imidazolone.[3] The sodium salt of **4**, when treated with benzyl azide in methanol, gave a product consistent with the loss of one cyano group and the formation of the aromatized compound, 5-amino-1-benzyl-4-methyl-1,2,3-triazole. Reaction of the same sodium salt with trimethylsilyl azide in tetrahydrofuran or in methanol did not give promising results. Also, reaction of the highly explosive 2-azido-2-sodiomalonitrile with methyl iodide failed to provide a route to **2**.

The successful synthesis of 5-amino-4-cyano-4-methyl-4*H*-1,2,3-triazole (**1**) was patterned after one described by Hohenlohe–Oehringen for the preparation of 5-amino-4,4-diphenyl-4*H*-1,2,3-triazole.[4] 2-Azido-2-cyanopropionitrile was hydrogenated in ethyl acetate–ethanol using 10% Pd/C catalyst. Ring closure of the putative intermediate[4] triazene **5** or a tautomer gave the substituted triazole **1**. A competing loss of nitrogen from **5** occurred to a nearly equal extent and yielded 2-amino-2-cyanopropionitrile (**6**). The two products, after filtration and evaporation, were readily separable by trituration with chloroform. Filtration followed by a chloroform wash of the insoluble solid afforded analytically pure **1**, while evaporation and distillation of the filtrate provided **6**.

When 5-amino-4-cyano-4-methyl-4*H*-1,2,3-triazole (**1**) was treated with formamidine at room temperature, a $C_5H_6N_6$ product was obtained that had spectroscopic properties satisfactory for the assigned structure **8**, which would result by way of the presumed intermediate **7**

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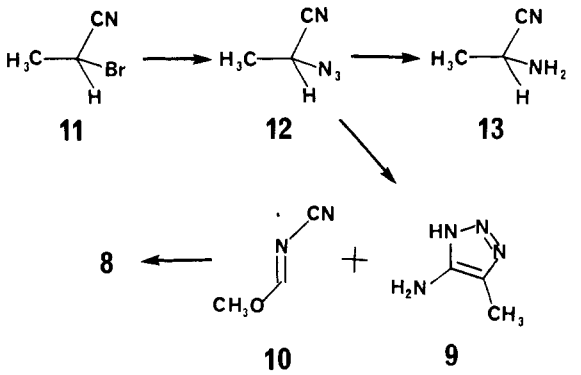
0022-3263/85/1950-4986$01.50/0

Scheme II



(and/or its tautomers). In fact, the physical, spectroscopic, and chromatographic properties of 1 and 8 were directly comparable to those of 5-amino-4-cyano-4-methyl-4*H*-imidazole and its product, 4-amino-8-methylimidazo[1,5-*a*]-1,3,5-triazine, respectively, in the translocative rearrangement initially observed.[1d,e]

Structure 8, 4-amino-8-methyl-1,2,3-triazolo[1,5-*a*]-1,3,5-triazine, was confirmed by an independent synthesis in which 4-amino-5-methyl-1,2,3-triazole (9) was caused to react with methyl *N*-cyanomethanimidate (10),[5] as shown in Scheme II. While a recently reported synthesis of 9 requires the use of trimethylsilyl azide and methyl 2-butynoate as starting materials in a five-step procedure,[6] the presently described synthesis starts with 2-bromopropionitrile (11)[7] in a two-step procedure based upon the methodology used for the preparation of 1 (Scheme I).

Sodium azide in aqueous ethanol brought about the displacement of the bromide from 2-bromopropionitrile (11), providing, after codistillation of the product with water, analytically pure 2-azidopropionitrile (12). Catalytic hydrogenation of 12 with 10% Pd/C in methanol provided a mixture of the desired triazole 9 and 2-aminopropionitrile 13, in direct analogy to the formation of 1 and 6 in Scheme I. The mode of cyclization of 5-amino-4-methyl-1,2,3-triazole (9) with methyl *N*-cyanomethanimidate (10) to 8 is parallel to that of 5-amino-4-methylimidazole to 4-amino-8-methylimidazo[1,5-*a*]-1,3,5-triazine[1a,b] and of 3-aminopyrazole to 4-aminopyrazolo[1,5-*a*]-1,3,5-triazine.[8] Recently, we reported additional examples of cyclization reactions of 10 with aminoheterocyclic compounds,[9] for which the product structures were confirmed by single crystal X-ray analysis. The samples of 4-amino-8-methyl-1,2,3-triazolo[1,5-*a*]-1,3,5-triazine (8) prepared by either the translocative rearrangement (Scheme I) or the direct route (Scheme II) were identical.

Experimental Section

Melting points were determined on a Büchi capillary melting point apparatus and are uncorrected. ^{1}H NMR were recorded on a Varian EM-390, an XL-200, or a Nicolet NTC 360 Fourier Transform (FT) spectrometer, operating at 90, 200, or 360 MHz, respectively. ^{13}C NMR spectra were obtained on a Jeol FX-60 or a Nicolet NTC 360 FT instrument, operating at 15.03 and 90.5 MHz, and are reported in parts per million (ppm) downfield from internal tetramethylsilane. The electron-impact mass spectra were run on a Varian MAT CH-5 low-resolution spectrometer with a 620i computer and a STATOS recorder. Microanalyses were performed by Josef Nemeth and his staff. Infrared spectra were obtained on a Perkin-Elmer 337 spectrometer.

2-Methylmalonodiamide.[1b] This preparation has worked equally well from a 1-g scale to the 500-g scale described below using a catalytic amount of $NaOCH_3$. In a large ground-glass-stoppered bottle, methanol (1.3 L) was saturated during 1 h at 0 °C with NH_3 (approximately 200 mL), and 1 g of $NaOCH_3$ was added. To this solution was then added 500 g (2.87 mol) of diethyl methylmalonate. The bottle was stoppered, clamped, and allowed to stand at ambient temperature for 5 days. The colorless solid was collected, resuspended in hot methanol (300 mL), filtered, and dried, giving 315 g (95%) of 2-methylmalonodiamide, mp 209–213 °C (lit. 208–210 °C,[1b] 216.5 °C[10]). The product was sufficiently pure for further reaction: ^{1}H NMR ($(CD_3)_2SO$) δ 1.1 (d, 3, J = 6 Hz, CH_3), 2.97 (q, 1, J = 6 Hz, CH), 6.93 (4, NH_2).

2-Methylmalononitrile (4).[1b] In a 5-L flask, a 1.03-mol sample of 2-methylmalonodiamide (120 g), P_2O_5 (Fisher) (300 g), and sand (150 g) were mixed for 20 min. The mixture made clumps at first but was reduced to a powder by rolling it over and over. The product was distilled under aspirator vacuum through a bulb-to-bulb apparatus into an ice-cooled receiver over a 1-h period by strong heating of the mixture without stirring. Clogging of the receiver adapter was prevented by warming with a heat gun. The reaction mixture turned orange during the distillation and swelled greatly. The distillation was concluded when the still-pot was nearly filled with a thick, orange mass. The product was distilled at 90–100 °C/15 torr to give 60 g (73%) (generally 70–80% on scales from 0.2 g to 120 g.) of a clear, colorless oil that crystallized immediately: mp 33–34 °C. Recrystallization of the product, if desired, was by dissolving in ether, adding pentane until the solution became cloudy, and cooling to −10 °C. The colorless needles that separated were washed with pentane: mp 34–34.5 °C (lit.[1b] 32–34 °C); ^{1}H NMR ($CDCl_3$) δ 1.71 (d, 3, J = 7 Hz, CH_3), 3.82 (q, 1, J = 7 Hz, CH); IR (neat, melt) 3006 w, 2930 vs, 2255 s, 1455 vs, 1380 w, 1293 w, 1260 w, 1123 vs, 1065 vs, 1027 vs, 915 w, 785 vw, 575 w cm^{-1}.

2-Bromo-2-cyanopropionitrile (3).[2] *Caution*: Compound 3 is a very potent lachrymator. 2-Methylmalononitrile (42.1 g, 0.526 mol) was melted and then suspended in 300 mL of water. Bromine (124.8 g, 40 mL, 0.78 mmol) was added, and the flask was stoppered. The reaction mixture was stirred for 11 h in a lighted hood, and sodium sulfite ($Na_2SO_3 \simeq$ 30 g) was added in portions until the solution became colorless. The mixture was separated, and the aqueous layer was extracted with 2 × 50 mL of CH_2Cl_2. The combined organic layers were washed with 2 × 30 mL of water and then dried with $MgSO_4$. Evaporation at 30 °C on a rotary evaporator (rinsed thoroughly immediately afterwards with acetone) afforded a light yellow oil that was distilled through a 12-in. Vigreux column at 65–67 °C/15 torr and provided 78 g (95%) of pure 3: mp −4 °C; IR (neat) 3008 w, 2930 w, 2250 vw, 1445 vs, 1360 s, 1181 vs, 1110 vs, 1040 vs, 940 w, 816 w, 789 s, 605 w cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.36 (s).

2-Azido-2-cyanopropionitrile (2). Sodium azide (5.6 g) was dissolved in 25 mL of water and 85 mL of acetone was added, followed by cooling to 0 °C. To this suspension, compound 3 (11.4 g) in 18 mL of acetone was added dropwise over 15 min. The mixture was stirred for 3 h and then allowed to warm to ambient temperature. Water (15 mL) was added, and the product was codistilled at 96–100 °C. The oil layer was separated, washed with 2 × 5 mL of water, and dried with $MgSO_4$: yield 4.2 g (48%) of pure 2. After initial removal of 2 from unreacted 3 by codistillation with water, distillation of 2 (52–54 °C/15 torr) provides repurification of a stored sample; IR (neat) 3003 w, 2920 m, 2400 br w, 2250 vw, 2140 vs, 2110 sh, 1455 m, 1395 m, 1210 br, vs, 1172 sh, 1130 m, 1070 w, 920 w, 880 m, 735 w, 635 w cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.57 (d, 3, J = 7 Hz, CH_3), 4.27 (q, 1, J = 7 Hz, CH); ^{13}C NMR ($CDCl_3$) δ 112.3 (C≡N), 49.5 (C-N_3), 25.7 (CH_3); mass spectrum (EI), m/z (relative intensity) 102 (M^+ + 1, 0.7), 121 (M^+, 11), 92 (M^+ − 29, 4), 91 (M^+ − 30, 5), 80 (M^+ − 41, 4), 79 (M^+ − 42, 37), 78 (M^+ − 43, 23), 77 (M^+ − 44, 4), 67 (M^+ − 54, 15), 66

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(M^+ - 55, 8), 53 (M^+ - 68, 30), 52 (M^+ - 69, 100), 51 (M^+ - 70, 24), 43 (M^+ - 78, 13).

Anal. Calcd for $C_4H_3N_5$: C, 39.67; H, 2.48. Found: C, 39.49; H, 2.54.

5-Amino-4-cyano-4-methyl-4*H*-1,2,3-triazole (1). A solution of a freshly distilled sample of **2** (1.2 g) in 75 mL of absolute ethanol and 50 mL of ethyl acetate was deoxygenated with N_2 and 120 mg of 10% Pd/C was added. Hydrogenation for 4 h resulted in a pressure drop of 6 psi from 45 psig initial in a 500-mL hydrogenation bottle. The solution was filtered through Celite and evaporated to provide 1.02 g of crude, yellow product. The sample was crystallized from 5 mL of ethanol, 20 mL of chloroform, and 15 mL of cyclohexane: 406 mg (34%) as an off-white powder, mp 144–145 °C dec. Recrystallization from acetonitrile provided an analytically pure, colorless product, mp 153–154 °C dec; IR (KBr) 3330 vs, 3075 vs, 2750 w, 2235 w, 1655 vs, 1570 s, 1455 m, 1400 m, 1200 s, 1038 s, 1115 s, 995 s, 955 vs, 938 s, 858 w, 813 m, 735 m, 710 w, 664 m, 595 m, 545 m, 503 m cm^{-1}; ^1H NMR ($(CD_3)_2SO$) δ 1.74 (s, 3, CH_3), 9.0 (br, 2, NH_2); ^{13}C NMR ($(CD_3)_2SO$) δ 20.33 (CH_3), 75.74 (4-C), 113.86 (C≡N), 176.04 (5-C); mass spectrum (FD), m/z (relative intensity) 125 (M^+ + 2, 5), 124 (M^+ + 1, 100), 124 (M^+, 6), 122 (M^+ - 1, 5), 96 (M^+ - 27, 6), 95 (M^+ - 28, 3), 94 (M^+ - 29, 11), 80 (M^+ - 43, 16), 79 (M^+ - 44, 7), 69 (M^+ - 54, 3).

Anal. Calcd for $C_4H_5N_5$: C, 39.02; H, 4.09; N, 56.88. Found: C, 39.18; H, 3.90; N, 56.89.

2-Amino-2-cyanopropionitrile (6). The mother liquor from the crystallization of **1** was evaporated on a rotary evaporator, and the residual oil was distilled to provide 2-amino-2-cyanopropionitrile (**6**) (35% yield) that was identical with an authentic sample.[1b]

4-Amino-8-methyl-1,2,3-triazolo[1,5-*a*]-1,3,5-triazine (8). Method A. A sample of **1** (0.061 g, 0.5 mmol) was combined with formamidine acetate (0.061 g, 0.54 mmol) and dissolved in 8 mL of anhydrous ethanol. A solution of sodium ethoxide from 12 mg of sodium (0.52 mmol) and 4 mL of ethanol was added dropwise and slowly over a 1-h period. After the reaction had been stirred for 9 h, a colorless crystalline product was obtained by filtration followed by an ethanol wash. The product was vacuum dried: 0.025 g (33%) of **8**, mp 221–222 °C. The same mp was found for samples recrystallized from methanol or ethanol. IR (KBr) 3245 s, 3060 m, 1710 vs, 1600 m, 1590 s, 1540 s, 1370 s, 1310 m, 1270 s, 1190 s, 1150 w, 1015 s, 905 m, 790 w, 796 m, 758 m, 675 w, 605 m, 560 w, 549 w cm^{-1}; ^1H NMR ($(CD_3)_2SO$) δ 2.47 (s, 3, CH_3), 8.17 (s, 2, 2-H), 9.09 (br, 2, NH_2); ^{13}C NMR ($(CD_3)_2SO$) δ 9.25 (CH_3), 131.39 (8-C, $^2J_{8\text{-}CCH_3}$ = 7.15 Hz), 141.17 (8a-C, $^3J_{8a\text{-}C\text{-}2\text{-}H}$ = 12.3 Hz, $^3J_{8a\text{-}CCH_3}$ = 3.9 Hz), 149.10 (4-C, $^3J_{4\text{-}C\text{-}2\text{-}H}$ = 11.4 Hz), 154.63 (2-C, $^1J_{2\text{-}C\text{-}2\text{-}H}$ = 204.2 Hz);[11] mass spectrum (EI), m/z (relative intensity) 151 (M^+ + 1, 2), 150 (M^+, 18), 122 (M^+ - 28, 5), 96 (M^+ - 54, 5), 95 (M^+ - 55, 12), 81 (M^+ - 69, 14), 80 (M^+ - 70, 13), 54 (M^+ - 96, 26), 53 (M^+ - 97, 33), 52 (M^+ - 98, 14), 42 (M^+ - 107, 100), 42 (M^+ - 108, 38).

Anal. Calcd for $C_5H_6N_6$: C, 40.00; H, 4.03; N, 55.97. Found: C, 39.80; H, 4.01; N, 55.93.

2-Bromopropionamide. Ethyl-2-bromopropionate (Aldrich) (10.0 g, 60 mmol) was dissolved in 65 mL of methanol, 30 mg of sodium methoxide was added, and the solution was cooled to 0 °C and saturated with NH_3 during 12 min. A silicone stopper was wired on, and the flask was allowed to remain in the ice bath for 4.5 h. The solvent was then removed at 30 °C on a rotary evaporator, and the product was recrystallized by dissolving the solid in 200 mL of ether at reflux and decanting the solution away from the gummy residue. The product was obtained upon addition of 40 mL of low-boiling petroleum ether. The crystals were collected and washed with pentane: 2.8 g of amide, mp 116–118 °C. The mother liquor was concentrated, and 1.9 g additional of 2-bromopropionamide, mp 117–120 °C, was obtained for a total of 4.7 g (52%) (Yields range from 40 to 68%.), sufficiently pure for the following reaction. A sample was recrystallized from $CHCl_3$: mp 123–125 °C (lit.[12] 123 °C); IR (mineral oil) 3050–3400 br, 1640 s, 1425 m, 1200 s, 730 br cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.95 (d, 3, CH_3), 4.46 (q, 1, CH), 6.25 (br, 2, NH_2).

2-Bromopropionitrile (11). 2-Bromopropionamide (20.05 g, 0.132 mol), P_2O_5 (32.8 g, 0.231 mol), and sand (27 g) were shaken together for 5 min. The mixture was heated strongly and the product was distilled into an ice-cooled receiver under aspirator vacuum. 2-Bromopropionitrile was collected at 46 °C/15 torr: 16.9 g (96%). *Caution*: the reaction vessel cracked unless ethanol was added prior to cleaning with water. IR (neat) 2990 vs, 2935 m, 2855 w, 2245 vs, 1445 vs, 1385 vs, 1295 w, 1187 vs, 1082 vs, 987 vs, 868 m, 844 s, 665 w, 628 s cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.0 (d, 3, CH_3), 4.40 (q, 1, CH).

2-Azidopropionitrile (12). Sodium azide (12.4 g, 0.191 mol) (Sigma) was dissolved in 25 mL of water in a 250-mL round-bottomed flask. 2-Bromopropionitrile (**11**) (14.8 g, 0.111 mol) dissolved in 12 mL of ethanol was added slowly to the sodium azide solution over a 5-min period. The mixture was heated at reflux for 35 min and then 30 mL additional of water was added. The product was codistilled with water. The oil layer was separated from the fraction that distilled from 96 to 100 °C and was combined with a 50 mL ether extract of the combined aqueous distillate. The product was washed with water and was dried with $MgSO_4$. Removal of the solvent provided **12**: 7.9 g (74%) of analytical purity; IR (neat) 3000 w, 2950 w, 2470 br w, 2250 w, 2150 vs, 2100 sh, 1455 m, 1395 m, 1310 br m, 1230 s, 1085 s, 1020 s, 1008 sh, 883 s, 718 w cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.60 (d, 3, J = 7 Hz, CH_3), 4.30 (q, 1, J = 7 Hz, CH); ^{13}C NMR ($CDCl_3$) δ 117.3 (C≡N), 46.6 (CN_3), 18.6 (CH_3); mass spectrum (EI) m/z 96 (M^+), 81 (M^+ - 15), 67 (M^+ - 29), 54 (M^+ - 42), 53 (M^+ - 43), 43 (M^+ - 53), 27 (M^+ - 69).

Anal. Calcd for $C_3H_4N_4$: C, 37.51; H, 4.19; N, 58.32. Found: C, 37.50; H, 3.96; N, 58.26.

4-Amino-5-methyl-1,2,3-triazole (9). A solution of **12** (3.0 g) in 50 mL of methanol was deoxygenated with nitrogen in a 500-mL hydrogenation bottle and then hydrogenated over 10% Pd/C (0.32 g) from 43 to 36 psig during 1 h. The solution was filtered through Celite and evaporated. The oil was dissolved in $CHCl_3$ and the solution was decanted from a small amount of sticky, grey material. Crystallization at −10 °C gave 4-amino-5-methyl-1,2,3-triazole (**9**): 0.55 g (18%); mp 99.5–101.5 °C. Recrystallization from $CHCl_3$ provided pristine colorless, crystalline **9**, mp 104–105 °C (lit.[6] 102–104 °C); ^1H NMR ($CDCl_3$) δ 2.07 (s, 3, CH_3), 4.75 (br s, 2, NH_2, exchangeable with D_2O), 13.08 (br s, 1, NH, exchangeable with D_2O); mass spectrum (EI), m/z 98 (M^+), 69 (M^+ - 29), 57 (M^+ - 41), 42 (M^+ - 56), 38 (M^+ - 60).

2-Aminopropionitrile (13). The mother liquor from the crystallization of **9** was evaporated to give 1.3 g of oil which was found to be 2-aminopropionitrile (**13**) with traces of **12**. Purification by chromatography (silica gel, elution with chloroform–acetone 1:1) gave a sample that was identical by IR with authentic material; mass spectrum (EI), m/z 70 (M^+), 69 (M^+ - 1), 55 (M^+ - 15), 42 (M^+ - 28), 28 (M^+ - 42).

4-Amino-8-methyl-1,2,3-triazolo[1,5-*a*]-1,3,5-triazine (8). Method B. A solution of **9** (0.097 g, 0.99 mmol) in 10 mL of methanol was treated dropwise via syringe with a solution of methyl *N*-cyanomethanimidate (0.13 g, 1.56 mmol) in 2 mL of methanol over a 10-min period and stirred at reflux for 12 h. The mixture was then stirred for 3 days at ambient temperature. The colorless solid that separated was collected and washed with methanol: yield 0.088 g (58%); mp 221–221.5 °C. This compound was found to be identical, by TLC in several solvent systems and by ^1H and ^{13}C NMR, IR, and mass spectra, with **8** prepared by Method A. Elemental analyses were equally acceptable.

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(11) The ^{13}C NMR spectra for 4-amino-8-methylimidazo[1,5-*a*]-1,3,5-triazine in reference 1b and analogous compounds in reference 1a should have the assignments for 2-C and 6-C reversed. A 6-deuterio derivative was prepared by using trimethyl [1-^{2}H]orthoformate in place of trimethyl orthoformate as in reference 1b, which provided a sample for unequivocal ^{13}C NMR assignments in the methyl-substituted species and, by analogy, for ^{13}C assignments in the analogues in reference 1a. ^1H NMR spectral assignments were reported correctly for these compounds.

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C-Hydroxy- and *C*-Methylchlorins. A Convenient Route to Heme *d* and Bonellin Model Compounds

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Although the majority of heme-containing proteins found in nature possesses iron porphyrins as the prosthetic group, a significant number of organisms have now been shown to contain pyrrolic macrocycles based on C-substituted chlorins and isobacteriochlorins. Examples include bonellin (1) isolated from the green echurian worm *Bonellia viridis*,[1] Faktor I from the B_{12}-producing *Clostridium tetanomorphum*,[2] heme *d* (which has just been determined[3] to have a structure derived from **2**) of *Escherichia coli*, heme d_1 from *Pseudomonas aeruginosa*,[4] and sirohydrochlorin of nitrite and sulfite reductases as well as a B_{12} intermediate.[5] The principal difference between these macrocycles and the unsubstituted hydroporphyrins is that the C-substituted compounds can resist dehydrogenation (back to porphyrin) and, therefore, are better suited for undertaking the redox processes with which they may be associated in vivo. As the structures of these unique molecules are being elucidated, it has become timely to investigate the chemistry and to identify their functional roles in their respective host systems. To realize such goals, however, requires workable quantities of materials which are often difficult to obtain from natural sources.

Several rational approaches toward the synthesis of *C*-alkylchlorins have been described very recently.[6-8] Unfortunately these lengthy and demanding syntheses do not seem to lend themselves easily as a serviceable route at providing the compound. Short and reliable syntheses thus far have not been available at producing functionalized C-substituted chlorins for general reactivity and biomimetic studies. This paper presents a very simple solution to this problem and, in addition, reports for the first time, several purified and well-characterized vicinal dihydroxychlorin containing the core structure of heme *d*.

Dihydroxychlorin was first discussed by Fischer who reacted porphyrin with hydrogen peroxide in concentrated sulfuric acid and obtained what he thought at first was the dihydroxy adduct.[9] This product was later determined to contain only one oxygen.[10] It was not until 1960s that the keto-*gem*-dialkylporphyrin (oxochlorin) structure was characterized.[11-13] The acidic hydrogen peroxide oxidation, which yields not only oxochlorins but diketo- (dioxoisobacteriochlorins and dioxobacteriochlorins) and triketoporphyrins arising from pinacolic rearrangements, has prevented the isolation of the expected dihydroxy intermediate. Fischer, however, demonstrated that hydroxylation of type IX porphyrins can be achieved with osmium tetraoxide although the resultant isomeric dihydroxychlorins were not individually identified.[10,14]

In an effort to synthesize **2**, we added 1.2 equiv of OsO_4 to 2,4-dimethyldeuteroporphyrin IX dimethyl ester[15] in CH_2Cl_2. The reaction was quenched after 20 h to yield the two dihydroxychlorins **3a** (37%) and **4a** (8%), plus the unreacted porphyrin (30%). Increasing the amount of OsO_4 and lengthening the reaction time invariably led to the formation of tetrahydroxybacteriochlorin at the expense of the dihydroxy product. A similar reaction was tested on dimethyl 5,8-dimethyl-1,2,3,4-tetraethylporphinedipropionate.[16] With this porphyrin apparently for steric reasons, the dihydroxylation occurred favorably at the "southern" pyrroles affording nearly 1:1 ratio of **3b** and **4b**. Treating the dihydroxychlorin **3b** in CH_2Cl_2 with 70% $HClO_4$ cleanly produced the rearranged ketones **5b** and **6b** in equal amount. The two isomers were separated by chromatography and their structures were determined by nuclear Overhauser enhancements (NOE) on the proton resonances. Selective irradiation of the methyl substituents resulted in NOEs (>5%) at the adjacent positions; by determining the nearest meso protons, it is possible to assign the structures unambiguously. Similar reaction and characterization were applied successfully for the tetramethyl homologues **5a** and **6a**. It is interesting to note that the NH protons of **5b** and **5a** should appear as two peaks while they remain as singlet in **6a** and **6b**. It is not evident whether an alteration of the tautomeric patterns or structural distortions is a possible cause for the splitting of the NH resonance.

The oxochlorin **6a** reacted sluggishly with methylenetriphenylphosphorane. The excess Wittig reagent present in the reaction invariably converted the ester group into the β-keto methylphosphonium salt.[17] Thus the methyl ester **6a** was first hydrolyzed in aqueous KOH, and the carboxyl groups were protected as the carboxylate ion during the Wittig reaction.[18] The resultant methylenechlorin was esterified and then hydrogenated quantitatively to the methylchlorin **8** with PtO_2 in formic acid.

The dihydroxychlorin isomers **3a**/**4a** and **3b**/**4b** have almost identical visible absorption spectra whose overall features are indistinguishable from that of the common dihydroporphyrins or the methylchlorin **8**. The di-

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