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OXAZOLES FROM ß-ACYLOXY-N,N-BIS(TRIMETHYLSILYL)ENAMINES

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Summary: Sequential addition of methyllithium and acyl chlorides to O-trimethylsilyl acetyltrimethylsilane cyanohydrin affords ß-acyloxy-N,N-bis(trimethylsilyl)enamines which cyclize to 2-substituted-4,5-dimethyloxazoles under thermolysis or trimethylsilyl trifluoromethanesulfonate treatment.

Notwithstanding the substantial literature on oxazole chemistry,[1] preparative efforts in this area continue to be relevant because of the presence of oxazole rings in physiologically active[2] and luminescent[3] materials and the utility of oxazoles in synthetic methodology.[4] Numerous approaches to oxazoles via ring-forming reactions are known,[1] but many of these methods require harshly acidic conditions which would exclude the presence of certain functionalities, or are based on chemistry which would result in isomeric mixtures for any but highly restricted structures. We here present a method for oxazole formation which offers the potential for extensive individual control over the introduction of each of the three possible substituents on the oxazole nucleus.

Scheme 1 outlines our findings thus far. When the O-trimethylsilyl cyanohydrin (2) derived from acetyltrimethylsilane (1) is treated with organolithium reagents, a lithium ß-[bis(trimethylsilyl)amino]enolate (3) is formed by initial attack at the nitrile functionality followed by what we have determined are sequential C $\rightarrow$ N and O $\rightarrow$ N trimethylsilyl group migrations.[5] The existence of this species is evidenced by its silylation to afford 4,[6] but it can also by acylated to form 5. These ß-acyloxyenamines (5a-f) were in turn transformed by flash vacuum pyrolysis, static thermolysis or by trimethylsilyl trifluoromethanesulfonate treatment at ambient temperature into the corresponding oxazoles 6[7] (Table 1). Our ability to prepare 4c and 6b suggests that steric considerations will not be of overriding importance in these preparations. In addition, since a wide variety of acylsilanes,[8] organolithium reagents[9] and acyl chlorides are readily available, we believe that this approach to oxazoles will prove to be quite general.

The following procedures describe the preparation of 2 in synthetically useful quantities, and are typical for the preparations of 4, 5 and 6.

Preparation of 2-Trimethylsiloxy-2-trimethylsilylpropanenitrile (2). A mixture of 14.2 g (123 mmol) acetyltrimethylsilane[10] and 13.4 g (134 mmol) of cyanotrimethylsilane in 150 mL dichloromethane was cooled to -78°C and 0.220 mL (1.14 mmol) of trimethylsilyl

Scheme 1

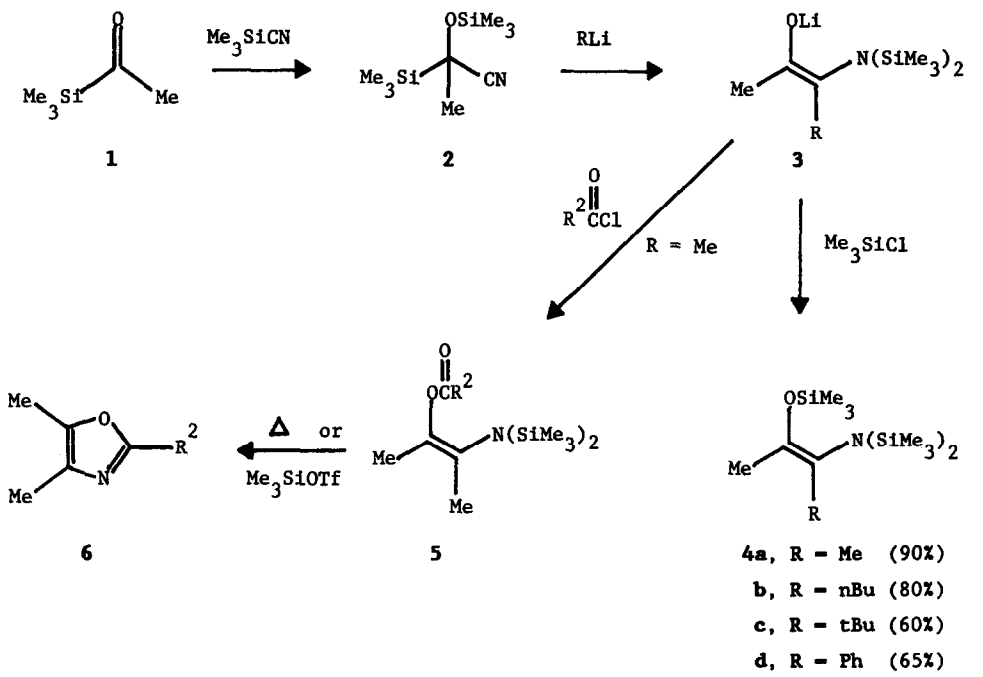

Table 1. Preparation of Acyloxyenamines (5) and Oxazoles (6)[a]

R^2	5	Yield (%)[b]	6	Yield(%)[b]	Method[c]
Me	a	90	a	95	A
tBu	b	78	b	90	C
Ph	c	73	c	75	C
CF_3	d[d]	66	d	95	A
CO_2Et	e	84	e	88	B
OEt	f	62	f	55	B

[a]All new compounds afforded correct C,H analyses; 5e was not analyzed because of thermal lability. See ref. 13 for characterization data on new compounds. [b]Isolated yields. [c]A: Flash vacuum pyrolysis; 14 in x 0.25 in quartz vigreux tube, 575°C, 1 mm Hg. B: Static thermolysis; 6e, 125°C, 16 h; 6f, sealed tube, 150°C, 48 h. [d]Prepared using trifluoroacetic anhydride.

trifluoromethanesulfonate in 15 mL dichloromethane added dropwise. After 2 h at -78°C, pyridine (20 drops) was added and the mixture stirred an additional 5 min. The solution was then poured into saturated $NaHCO_3$, the organic layer dried ($MgSO_4$) and concentrated. Short-path distillation gave 23.1 g (87%) of 2,[11] bp 55-56°C (5 mm Hg). IR: 2210, 1255 cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.14, s, 9H; 0.20, s, 9H; 1.51, s, 3H. ^{13}C NMR ($CDCl_3$): δ -5.0 (SiMe), 1.4 (OSiMe), 23.5 (Me), 61.1 (CCN), 122.9 (CN). Anal. Calcd for $C_9H_{21}NOSi_2$: C, 50.18; H, 9.82. Found: C, 50.31; H, 9.87.

Preparation of Z-2-Trimethylsiloxy-3-[bis(trimethylsilyl)amino]-2-butene (4a). Methyllithium (2.2 mmol) was added to 0.43 g (2.0 mmol) of 2 in 5 mL ether at 25°C.[12] After 2 h, chlorotrimethylsilane (0.24 g, 2.2 mmol) was added, and after an additional 2 h, solvent was removed under vacuum and 30 mL dry pentane added. The mixture was filtered through a glass frit under argon, concentrated and Kügelrohr distilled to give 0.60 g of 4a, bp 70°C (25 mm Hg) which VPC (2 ft SE-30, 135°C) showed to be 92% pure. IR: 1666, 1250 cm^{-1}. ^1H NMR δ 0.04, s, 18H; 0.16, s, 9H; 1.59, q, J = 0.9 Hz, 3H; 1.78, q, J = 0.9 Hz, 3H. ^{13}C NMR δ 1.8 (OSiMe), 2.3 (NSiMe), 18.4 and 22.6 (=CMe), 118.9 (=CN), 138.4 (=CO).

Preparation of Z-2-[2,2-Dimethylpropanoyl)oxy]-3-[bis(trimethylsilyl)amino]-2-butene (5b). Methyllithium (2.2 mmol) was added to 0.43 g (2.0 mmol) of 2 in 20 mL ether at 25°C. After 1 h, 2,2-dimethylpropanoyl chloride (0.27 mL, 2.2 mmol) was added and the mixture stirred overnight. Volatiles were removed under vacuum (1 mm Hg), dry pentane added, and the suspension filtered through Celite under argon. Kügelrohr distillation gave 0.52 g of 5b, bp 50-55°C (1.5 mm Hg) which VPC showed was over 95% pure.

Preparation of 4,5-Dimethyl-2-(1,1-dimethylethyl)oxazole (6b). A solution of 0.26 g 5b (0.83 mmol) in 1 mL chloroform was treated with 0.15 mL (0.78 mmol) of trimethylsilyl trifluoromethanesulfonate. After 64 h at 25°C, the solution was passed through basic alumina and Kügelrohr distilled to give 0.13 g of 6b, bp 35-40°C (50 mm Hg) which VPC showed to be 90% pure.

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5. Details to appear elsewhere.
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12. Initially at -78°C for other organolithium reagents.
13. **5a**: IR 1746 cm^{-1}; ^1H NMR δ 0.09, s, 18H; 1.67, s, 3H; 1.86, s, 3H; 2.08, s, 3H. ^{13}C NMR δ 2.2, 16.1, 21.2, 22.6, 128.2, 137.9, 168.9. **5b**: IR 1738 cm^{-1}; ^1H NMR δ 0.07, s, 18H; 1.22, s, 9H; 1.70, s, 3H; 1.80, s, 3H. ^{13}C NMR δ 2.2, 16.0, 22.9, 27.3, 38.7, 127.3, 138.1, 176.6. **5c**: IR 1726 cm^{-1}. ^1H NMR δ 0.06, s, 18H; 1.76, s, 3H; 1.98, s, 3H; 7.5, m, 3H and 8.05, m, 2H. ^{13}C NMR δ 2.2, 16.3, 22.9, 128.3, 128.5, 129.9, 130.7, 132.9, 138.2, 164.8. **5d**: IR 1788 cm^{-1}. ^1H NMR δ 0.08, s, 18H; 1.74, s, 3H; 1.95, s, 3H. ^{13}C NMR δ 1.9, 15.3, 22.7, 114.6 (q, J = 286 Hz), 130.9, 137.4, 155.4, (q, J = 42 Hz). **5e**: IR 1773, 1750 cm^{-1}. ^1H NMR δ 0.07, s, 18H; 1.34, t, J = 7 Hz; 1.71, s, 3H; 1.92, s, 3H; 4.33, q, J = 7Hz. ^{13}C NMR δ 2.0, 13.9, 15.6, 22.6, 62.9, 129.9, 137.6, 156.0, 157.9. **5f**: IR 1752 cm^{-1}. ^1H NMR δ 0.08, s, 18H; 1.29, t, J = 7 Hz, 3H; 1.68, s, 3H; 1.90, s, 3H; 4.17, q, J = 7 Hz, 3H. ^{13}C NMR δ 2.1, 14.3, 15.7, 22.6, 63.7, 129.0, 137.5, 153.2. **6a**: Wiley, R.H. *J. Org. Chem.* **1947**, *12*, 43. ^1H NMR δ 2.0, s, 3H; 2.14, s, 3H; 2.31, s, 3H. ^{13}C NMR δ 9.7, 11.0, 13.7, 130.1, 142.5, 158.6. **6b**: Bowie, J.H.; Donaghue, P.F.; Rodda, H.J. *J. Chem. Soc (B)* **1969**, 1122. ^{13}C NMR δ 9.8, 11.1, 28.6, 33.3, 129.4, 142.1, 168.5. **6c**: Friedman, B.S.; Sparks, M.; Adams, R. *J. Am. Chem. Soc.* **1937**, *59*, 2262. ^{13}C NMR δ 10.1, 11.3, 125.8, 127.9, 128.6, 129.6, 131.9, 143.4, 159.1. **6d**: ^1H NMR δ 2.12, s, 3H; 2.30, s, 3H. ^{13}C NMR δ 10.0, 11.0, 116.6 (q, J = 270 Hz), 132.3, 146.6, 148.2 (q, J = 44 Hz). **6e**: Jaworski, T.; Mizerski, T. *Pol. J. Chem.* **1981**, *55*, 47 (*Chem. Abstr.* **1981**, *95*, 169045). IR 1733 cm^{-1}. ^1H NMR δ 1.39, t, J = 7 Hz, 3H; 2.14, s, 3H; 2.30, s, 3H; 4.41, q, J = 7 Hz, 2H. ^{13}C NMR δ 10.2, 11.1, 14.2, 62.3, 133.8, 147.7, 150.0, 155.9. **6f**: ^1H NMR 1.38, t, J = 7 Hz, 3H; 1.96, s, 3H; 2.09, s, 3H; 4.34, q, J = 7 Hz, 2H. ^{13}C NMR δ 9.7, 11.4, 66.6, 128.9, 137.3, 159.9.

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