Polyazapolycyclics by Condensation of Aldehydes with Amines. 3. Formation of 2,4,6,8-Tetrabenzyl-2,4,6,8-tetraazabicyclo[3.3.0]octanes from Formaldehyde, Glyoxal, and Benzylamines[1,2]

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Received June 9, 1992

The condensation of formaldehyde, glyoxal, and benzylamine, in a stoichiometric ratio, leads to 2,4,6,8-tetrabenzyl-2,4,6,8-tetraazabicyclo[3.3.0]octane (**1d**) in methanol solvent with formic acid catalyst. Six phenyl-substituted derivatives of **1d**, as well as 2,4,6,8-tetraisopropyl-2,4,6,8-tetraazabicyclo[3.3.0]octane (**1c**), have been prepared in high yields by this synthetic method. Some of the chemical behavior of the new compounds is discussed.

Few reports of the synthesis of 2,4,6,8-tetraazabicyclo-[3.3.0]octanes substituted only on nitrogen (**1**) have appeared. Three tetraalkyl derivatives (**1a–c**, R = CH_3, C_2H_5, i-C_3H_7, respectively) have been prepared by lithium aluminum hydride reduction of the corresponding substituted glycoluril derivatives (**2a–c**).[3-5] The precursor glycolurils are obtained by condensation of *sym*-dialkylureas with glyoxal or by alkylation of glycoluril itself (**2**, R = H).[6-8] The overall yields in these two-step syntheses are usually low (15–40%).

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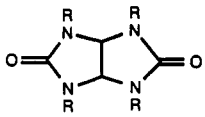

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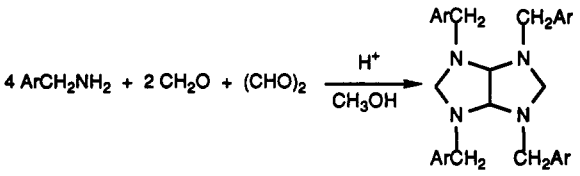
1a, 2a, R = CH_3; **1b, 2b**, R = C_2H_5; **1c, 2c**, R = i-C_3H_7

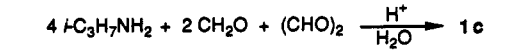
In this report we describe the facile condensation of formaldehyde, glyoxal, and selected primary amines which provide a direct, one-pot, high-yield synthesis of 2,4,6,8-tetrasubstituted-2,4,6,8-tetraazabicyclo[3.3.0]octanes (**1c–j**). This reaction is an extension of our studies of the synthesis of polyazapolycyclic amines by condensation of aldehydes, including glyoxal, with amines.[1,9] With benzylamine the condensation proceeds in methanol solvent at 25 °C using formic acid catalyst, with stoichiometric quantities of amine, formaldehyde, and glyoxal, to yield **1d** in 84% yield. Six substituted benzylamines were also condensed in the same manner to produce high yields (82–90% in five examples) of tetrabenzyltetraazabicyclooctanes **1e–j** (Table I); substituents include 4-methyl, 4-isopropyl, 4-methoxy, 3,4-dimethoxy, 2-chloro, and 4-chloro. These previously unreported compounds separate from the reaction mixture in highly pure crystalline form.



1d, Ar = C_6H_5
1e, Ar = 4-$CH_3C_6H_4$
1f, Ar = 4-(i-C_3H_7)C_6H_4
1g, Ar = 4-$CH_3OC_6H_4$
1h, Ar = 3,4-$(CH_3O)_2C_6H_3$
1i, Ar = 2-ClC_6H_4
1j, Ar = 4-ClC_6H_4

The structure of the tetrabenzyltetraazabicyclooctane **1d** was established by X-ray crystallography. All of the isolated benzyl-substituted bicyclooctanes show similar ^1H and ^{13}C NMR spectra, which support the structure assignments ($CDCl_3$ solvent). Characteristic of the proton spectra in all of the compounds is a singlet near δ 4.5 for the cis-bridgehead CH protons. The ring methylene signals appear as an AB quartet centered near δ 3.4 and 3.8 (J = ~6.6 Hz). In the ^{13}C spectra the bridgehead CH carbons (δ ~85) are shifted downfield slightly more than those of the ring CH_2 carbons (δ ~74). The electron impact mass spectrum of **1d** reveals a weak molecular ion at m/e 474.

The synthesis of 2,4,6,8-tetraazabicyclo[3.3.0]octanes has been extended to other amines. The reaction of isopropylamine, formaldehyde, and glyoxal produced 2,4,6,8-tetraisopropyl-2,4,6,8-tetraazabicyclo[3.3.0]octane (**1c**). It was necessary to slightly alter the reaction con-



ditions used with the benzylamines, employing water as solvent; pure **1c** crystallized from the reaction mixture in 76% yield. No precipitate of **1c** was observed in methanol solvent, under reaction conditions which led to separation of **1d** from the reaction mixture. Compound **1c** has been prepared previously by lithium aluminum hydride re-

(1) Nielsen, A. T.; Nissan, R. A.; Vanderah, D. J.; Coon, C. L.; Gilardi, R. D.; George, C. F.; Flippen-Anderson, J. *J. Org. Chem.* **1990**, *55*, 1459.
(2) Presented, in part, at the 192nd National Meeting of the American Chemical Society, Anaheim, CA, Sept 12, 1986; ORGN-229.
(3) Nelsen, S. F.; Hintz, P. J. *J. Am. Chem. Soc.* **1972**, *94*, 7114.
(4) Suvorova, L. I.; Epishina, L. V.; Lebedev, O. V.; Khmelnitskii, L. I.; Novikov, S. S. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1979**, 2286.
(5) Koppes, W. M.; Chaykovsky, M.; Adolph, H. G.; Gilardi, R. D.; George, C. F. *J. Org. Chem.* **1987**, *52*, 1113.
(6) Nematollahi, J.; Ketcham, R. *J. Org. Chem.* **1963**, *28*, 2378.
(7) Petersen, H. *Synthesis*, **1973**, 243.
(8) Suvorova, L. I.; Erasko, V. A.; Epishina, L. V.; Lebedev, O. V.; Khmelnitskii, L. I.; Novikov, S. S.; Povstyanoi, M. B.; Krylov, V. D.; Korotkova, G. V.; Lapshina, L. V.; Kulik, A. F. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1979**, 1306.
(9) Nielsen, A. T.; Christian, S. L.; Moore, D. W.; Gilardi, R. D.; George, C. D. *J. Org. Chem.* **1987**, *52*, 1656.

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Table I. Condensation of Benzylamines with Glyoxal and Formaldehyde to 2,4,6,8-Tetrabenzyl-2,4,6,8-tetrazabicyclo[3.3.0]octanes

						elemental analysis					
						calculated			found		
no.	phenyl substitution	mp, °C[a]	yield, %	mol formula	mol weight	C	H	N	C	H	N
1d	None	78–80	84	$C_{32}H_{34}N_4$	474.62	80.97	7.22	11.81	81.14	7.18	11.79
1e	4-CH_3	84–87[b]	88	$C_{36}H_{42}N_4$	542.74	81.47	7.98	10.56	81.42	7.97	11.22
1f	4-*i*-C_3H_7	72–74	54	$C_{44}H_{58}N_4$	642.98	82.19	9.09	8.71	82.38	8.96	8.67
1g	4-CH_3O	111–112	89	$C_{36}H_{42}N_4O_4$	594.73	72.70	7.12	9.42	72.71	7.30	9.03
1h	3,4-$(CH_3O)_2$	127–128	82	$C_{40}H_{50}N_4O_8$	714.83	67.20	7.05	7.84	67.10	7.05	7.86
1i	2-Cl	141–144	90	$C_{32}H_{30}Cl_4N_4$[c]	612.44	62.76	4.94	9.15	62.81	4.84	9.23
1j	4-Cl	95–97	90	$C_{32}H_{30}C_{14}N_4$[d]	612.44	62.76	4.94	9.15	62.81	4.96	9.22

[a] Analytical samples crystallized from acetonitrile. [b] Long prisms (melting point 59–64 °C), which change to feathery needles, melting point 84–87 °C. [c] Calculated for Cl: 23.16%; found 23.21%. [d] Calculated for Cl: 23.16%; found 23.35%.

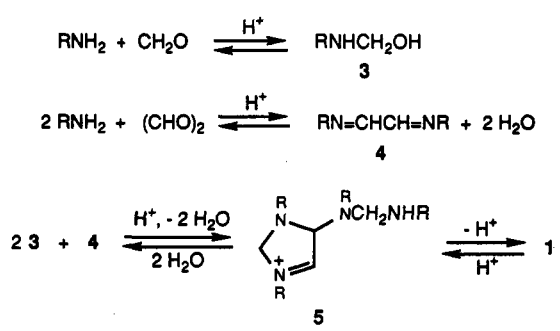
duction of tetraisopropylglycoluril (2c) (77% yield); 2c was obtained by condensation of *sym*-diisopropylurea with glyoxal (50% yield).[5] The proton ^1H NMR spectrum of our sample is in agreement with reported data[5] and the spectra of 1d–j.

The condensation of *tert*-butylamine with formaldehyde and glyoxal under reaction conditions which led to 1c did not produce a bicyclooctane (1, R = *t*-C_4H_9). Also, it has been reported that condensation of *sym*-di-*tert*-butylurea with glyoxal does not produce a tetra-*tert*-butylglycoluril (2, R = *t*-C_4H_9).[5] The only other known tetraalkyl-substituted 2,4,6,8-tetraazabicyclo[3.3.0]octanes are the methyl and ethyl compounds 1a,b which are thermally stable, distillable liquids.[3,4]

We have also extended the new synthesis to two silyl-substituted derivatives, 1k (R = $(CH_3)_3SiCH_2CH_2$) and 1l (R = $(C_6H_5)_2(CH_3)SiCH_2CH_2$). Compound 1k was prepared in methanol solvent (57% yield) with added formic acid by the same procedure employed with the benzyl-substituted derivatives 1d–j. However, compound 1l was prepared in 17% yield from 2-(diphenylmethylsilyl)-ethylamine hydrochloride by a different procedure. The amine salt reactant was neutralized by addition of 2 molar equiv of potassium carbonate, and the reaction was conducted in acetonitrile solvent for 48 h at 25 °C; no acid catalyst was added. In the preparations of 1k and 1l these products remained in solution throughout the reaction and were isolated by removal of solvents and purification by elution chromatography on silica gel; prolonged contact with silica gel caused their decomposition. Thus, it would appear that the reaction could have wide scope and apply to numerous amines as precursors for preparing derivatives of 1, probably including methylamine and ethylamine to yield 1a and 1b. Also, since the reaction to produce 1l (in low yield) occurred at higher pH than that used in the other preparations, the reaction should be applicable to acid-sensitive amine reactants and products 1. The major limitation appears to apply to the amine structure, which cannot incorporate excessive steric crowding about the amino group, as in *tert*-butylamine.

The 2,4,6,8-tetraazabicyclo[3.3.0]octanes 1a–l are quite stable neat at ambient temperature. However, in solution they decompose at rates which vary with the pH, concentration of added acid, solvent (including water content), and structure of the compound. The decomposition is accelerated by acid or water. This behavior had been examined previously for the tetraisopropyl compound 1c.[5] Solutions in dichloromethane which were exposed to the atmosphere decomposed completely over a 72-h period. Addition of a small amount of acetic acid accelerated the decomposition to a half-life of less than 10 min. However, 1a (R = CH_3) was found to be stable under these conditions. We have observed that the ^1H NMR spectrum of 1c in $CDCl_3$ solution changes after 18–60 h at 25 °C to

Scheme I



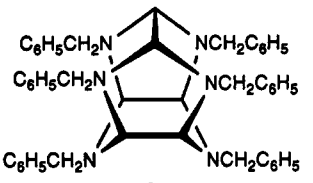
reveal new signals, attributable to *N*-(hydroxymethyl)diisopropylamine (3, R = *i*-C_3H_7, Scheme I) and *N*,*N*′-diisopropyl-1,2-ethanediimine (4, R = *i*-C_3H_7), in agreement with previously reported chemical shift values.[10] These data also agree with a ring-opening mechanism,[5] producing 5 by N-protonation of 1 (Scheme I). Degradation of 5 can follow rapidly by reaction with adventitious moisture.

The tetrabenzyl derivatives 1d–j, in contrast to the isopropyl compound 1c, are much more stable in $CDCl_3$ solution. However, they decompose in acidic media. The unsubstituted tetrabenzyl compound 1d was examined most extensively. It is almost completely decomposed within 24 h at 25 °C in dichloromethane containing 10% acetic acid; *N*-(hydroxymethyl)benzylamine (3, R = $C_6H_5CH_2$) was isolated as a product. Under the same conditions in a short parallel run of 15 min, 62% of 1d was recovered. Thus, the relative stability of the tetrasubstituted bicyclooctanes 1 in acidic media varies with substituents in the order: $CH_3 > C_6H_5CH_2 > i\text{-}C_3H_7$.

Available data from the present investigation, as well as previous work on the condensation of amines with glyoxal,[1,10,11] suggest that the glyoxal diimine 4 is an important intermediate in the synthesis, as well as the degradation of 1. The diimine can react stepwise with 2 mol of amine and formaldehyde, or with the methylolamine 3, to produce the monocyclic imidazoline cation 5, which upon proton loss yields 1 (Scheme I). The observed ring-opening of 1 could occur stepwise with loss of amine and formaldehyde, or by a direct cleavage leading to 3.

The stability of the related hexabenzylhexaazaisowurtzitane (6)[1] in acidic media was observed to be slightly greater than that of 1d; 82% of 6 was recovered after 15 min treatment of 6 at 25 °C with dichloromethane containing 10% acetic acid. Compound 6 is formed in 64% yield from benzylamine and glyoxal in methanol solvent with formic acid catalyst. The mechanism of its formation involves trimerization of *N*,*N*-dibenzyl-1,2-ethanediimine

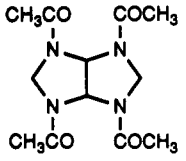
(10) Kliegman, J. M.; Barnes, R. K. *Tetrahedron* 1970, *26*, 2555.
(11) Kliegman, J. M.; Barnes, R. K. *J. Org. Chem.* 1970, *35*, 3140.



6

(4, R = $C_6H_5CH_2$) under conditions virtually identical to those employed in the preparation of **1d**.[1] However, no evidence was found for the presence of **6** in the product reaction mixture containing **1d**.

The reductive acetylation of **1d** was examined in an attempt to convert it into 2,4,6,8-tetraacetyl-2,4,6,8-tetraazabicyclo[3.3.0]octane (**7**). This compound has been synthesized previously by reaction of 4,5-diacetoxy-1,3-diacetylimidazolidine with *N,N'*-methylenebisacetamide in refluxing acetonitrile solvent with *p*-toluenesulfonic acid catalyst.[5] Hydrogenation of **1d** in acetic anhydride solvent (50 psi, Pd/C catalyst) led to ring cleavage with formation of 1,1,2,2-tetra-*N*-acetyl-1,1,2,2-tetra-*N*-benzyl-1,1,2,2-tetraaminoethane (**8**, 4.3% yield) as the only isolable crystalline product.



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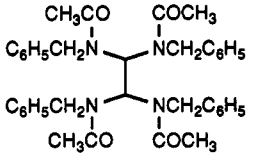

8

Experimental Section

Chemical shift measurements were determined at 30 °C unless otherwise stated, and are referenced to external standard tetramethylsilane. Melting points were determined on a Kofler hot stage and are uncorrected.

2,4,6,8-Tetrabenzyl-2,4,6,8-tetraazabicyclo[3.3.0]octane (1d). To a solution of benzylamine (21.4 g, 0.20 mol) and formic acid (0.45 g of 88% aqueous solution, 0.0086 mol) in methanol (200 mL) at 0 °C was added dropwise formaldehyde (8.1 g of 37% aqueous formaldehyde solution, 0.10 mol) during 3 min, while the solution temperature was kept below 8 °C. Glyoxal (7.25 g of 40% aqueous glyoxal solution, 0.050 mol) was then added dropwise during 3 min, while the temperature was kept below 7 °C. The clear solution, after standing at 0 °C overnight, was stored at 25 °C for 7 d. The crystalline product which had precipitated was removed by filtration and washed with cold methanol to yield 17.12 g of **1d**. Concentration of the filtrate to a volume of 15 mL deposited a second crop of crystals (2.83 g; total yield of **1d**, 19.95 g, 84% yield, both crops mp 78–80 °C). Recrystallization from acetonitrile (CH_3CN) did not alter the melting point (elemental analyses in Table I). **1d**: ^1H NMR ($CDCl_3$) δ 7.24–7.51 (m, 20 H, C_6H_5), 3.92 (s, 8 H, CH_2 of benzyl), 3.51, 3.85 (AB q, J = 6.49 Hz, 8 H, ring CH_2), 4.57 (s, 2 H, ring CH); ^{13}C NMR ($CDCl_3$) δ 126.72, 128.13, 128.35, 139.78 (C_6H_5), 55.57 (CH_2 of benzyl), 85.24 (ring CH), 73.93 (ring CH_2); X-ray crystal structure data are included in the supplementary material; mass spectrum (EI) m/z 474 (M^+, 0.3), 383 (1.6), 264 (3.9), 249 (7.0), 237 (13.0), 225 (1.1), 159 (9.1), 91 (100); mass spectrum (CI, CH_4) m/z 441 (0.7), 355 (1.5), 249 (1.2), 237 (12.5), 235 (15.8), 159 (67.5), 145 (41.7), 119 (98.6), 106 (100).

The same procedure was employed in the synthesis of the substituted tetraazabicyclooctanes **1e–j** from formaldehyde, glyoxal, and 4-methyl-, 4-isopropyl-, 4-methoxy-, 3,4-dimethoxy-, 2-chloro-, and 4-chlorobenzylamines, respectively (see summary in Table I). ^1H and ^{13}C NMR data for **1e–j**, which are similar to **1d**, are summarized in supplementary material (Tables II and III).

The stability of the tetrabenzyl derivative **1d** in acid solutions was examined. To a sample of **1d** (0.50 g) in CH_2Cl_2 (10 mL) was added formic acid (0.16 g of 88% aqueous solution). After standing for 10 min at 25 °C, the solution was extracted once with excess saturated $NaHCO_3$ solution. The CH_2Cl_2 solution was dried with anhydrous $MgSO_4$ and concentrated to dryness to yield 0.41 g (82%) of recovered **1d**.

In a parallel experiment with 0.50 g of **1d** in which acetic acid (1.05 g) was employed in CH_2Cl_2 (10 mL) and the solution was allowed to stand at 25 °C for 15 min, 62% of reactant **1d** was recovered. An identical run at 25 °C for 24 h gave 0.14 g of an oil, identified as *N*-(hydroxymethyl)benzylamine by comparison of its ^1H NMR spectrum with that of an authentic sample: ^1H NMR ($CDCl_3$) δ 7.37 (s, 5 H, C_6H_5), 3.64 (s, 2 H, $C_6H_5CH_2N$), 3.38 (s, 2 H, NCH_2O); the spectrum of the acid-treated oil fraction also revealed the complete absence of reactant **1d**.

When the above procedure was repeated with 0.50 g of hexabenzylhexaazaisowurtzitane (**6**) under the same conditions (1.05 g of acetic acid in 10 mL of CH_2Cl_2, 25 °C, 24 h), the product isolated (0.48 g) revealed a ^1H NMR spectrum ($CDCl_3$ solvent) indicating much degradation, but the presence of some reactant **6**; crystallization from methanol gave 4 mg of recovered **6**. In a parallel run, a shorter reaction time (15 min) produced 82% recovery of **6** (identified by ^1H NMR and melting point comparison with an authentic sample).

The procedure used for preparation of compounds **1d–j** was also used for the preparation of 2,4,6,8-tetrakis[2-(trimethylsilyl)ethyl]-2,4,6,8-tetraazabicyclo[3.3.0]octane (**1k**) from 2-(trimethylsilyl)ethylamine;[12] the product **1k** did not precipitate from the reaction mixture. The clear yellow solution, which had stood at 25 °C for 9 days, was poured into water and extracted with CH_2Cl_2. After drying the combined extracts with anhydrous $MgSO_4$ and concentration to dryness, the crude product was purified by rapid chromatography on silica gel (elution with ethyl acetate/hexane) to yield low-melting, slightly oily crystals (57% yield): ^1H NMR ($CDCl_3$) δ 4.03 (s, 2 H, ring CHCH), 3.55, 3.31 (AB q, J = 6.37 Hz, 4 H, ring CH_2), 2.52–2.74 (m, 8 H, CH_2CH_2Si), 0.63–0.85 (m, 8 H, CH_2CH_2Si), –0.02 (s, 36 H, CH_3). When allowed to remain on the silica gel column for 12–18 h, compound **1k** was completely destroyed.

2,4,6,8-Tetraisopropyl-2,4,6,8-tetraazabicyclo[3.3.0]octane (1c). To a solution of isopropylamine (2.36 g, 0.040 mol) and formic acid (50 mg of 88% solution) in water (10 mL) was added dropwise formaldehyde (1.62 g, of 37% aqueous formaldehyde, 0.020 mol) (below 10 °C). Glyoxal (1.45 g of 40% aqueous solution, 0.010 mol) was then added dropwise (below 10 °C). Some crystals, mixed with oil, appeared within a few hours after mixing the reactants. After storage at 0 °C for 8 d, the crystalline product was filtered and washed with water to yield 2.13 g (76%) of **1c** as chunky prisms, mp 40–42 °C. Recrystallization from CH_3CN gave long, needle-shaped prisms: mp 38–40 °C (64% recovery); ^1H NMR ($CDCl_3$) δ 4.34 (s, 2 H, ring CH), 3.60, 3.39 (AB q, J = 6.72 Hz, 4 H, CH_2), 2.95 (septet, J = 6.44 Hz, 4 H, CH of i-C_3H_7), 1.05 (d, J = 6.44 Hz, 12 H, CH_3), 1.01 (d, J = 6.44 Hz, 12 H, CH_3). A similar ^1H NMR spectrum in CD_2Cl_2 has been reported for **1c** (described as a low-melting white solid).[5] ^{13}C NMR δ 81.94 (ring CH), 64.70 (ring CH_2), 49.05 ($CH(CH_3)_2$), 22.56, 19.45 (magnetically nonequivalent CH_3 groups). Anal. Calcd for $C_{16}H_{34}N_4$: C, 68.03; H, 12.13; N, 19.84. Found: C, 68.12; H, 12.19; N, 19.86. When *tert*-butylamine was substituted for isopropylamine, no tetraazabicyclo[3.3.0]octane product was isolated. The procedure employed for the preparation of the tetrabenzyl compounds **1d–j** (methanol solvent) when used with isopropylamine gave no precipitate of **1c**.

A sample of **1c** in $CDCl_3$ after standing at 25–30 °C for 60 h was observed to have a ^1H NMR spectrum different from that of pure **1c**; weak signals of **1c** remained (~11 mol % of the mixture based on integrals). Strong, new NMR signals appeared at δ 7.92 (s, CH), 3.50 (septet, J = 6.36, CH), 1.20 (d, J = 6.36, CH_3) of *N,N'*-diisopropyl-1,2-ethanediimine (**4**, R = i-C_3H_7, ~32%) [reported for this compound: ^1H NMR ($CDCl_3$) δ 7.97 (s, CH), 3.50 (septet, J = 7.0), 1.18 (d, J = 7.0)[10]] and at δ 3.46 (s, CH_2 of i-$C_3H_7NHCH_2OH$, ~57%) with i-C_3H_7 signals near δ 2.83 (septet, J = 6.52 Hz, CH) and 1.05 (d, J = 6.52 Hz, CH_3). The ^{13}C NMR of the solution of **1c** in $CDCl_3$ after 60 h revealed weak signals of **1c** in addition to strong signals at δ 159.6, 61.1, and 23.66 (CH=N, CH, and CH_3, respectively, of *N,N*-diisopropyl-1,2-ethanedimine) and at δ 68.45, 49.70, and 19.81 (CH_2, CH, and CH_3,

(12) Sommer, L. H.; Rockett, J. *J. Am. Chem. Soc.* **1951**, *73*, 5130.

respectively, of i-$C_3H_7NHCH_2OH$); only traces of other signals are seen in the spectrum. In a parallel experiment a sample which had stood in $CDCl_3$ at 25 °C for 18 h produced nearly identical spectra. Shift assignments were confirmed by examination of coupled spectra.

2,4,6,8-Tetrakis[2-(diphenylmethylsilyl)ethyl]-2,4,6,8-tetraazabicyclo[3.3.0]octane (11). To a suspension of 2-(diphenylmethylsilyl)ethylamine hydrochloride[12] (0.944 g, 3.6 mmol), anhydrous K_2CO_3 (1.00 g, 7.23 mmol), and freshly activated 4-Å molecular sieves (5 g) in ahydrous CH_3CN (30 mL) was added a solution of 40% aqueous glyoxal (0.128 g, 0.883 mmol) in ethanol (3 mL) with ice-bath cooling. Formaldehyde (0.143 g, 1.76 mmol of 37% aqueous solution) in CH_3CN (5 mL) was then added. After standing at 25 °C for 48 h, the mixture was filtered and the filtrate concentrated under reduced pressure to yield 0.41 g of an oil which was purified by chromatography on silica gel (elution with ethyl acetate/hexane) to yield 0.155 g (17%) of **11** as a colorless, viscous oil: ^1H NMR ($CDCl_3$) δ 7.15–7.50 (m, 40 H, C_6H_5), 3.83 (s, 2 H, ring CH), 3.49, 3.24 (AB q, J = 6.48 Hz, 4 H, ring CH_2), 2.5–2.71 (m, 8 H, CH_2CH_2Si), 1.10–1.31 (m, 8 H, CH_2CH_2Si), 0.49 (s, 12 H, CH_3). Anal. Calcd for $C_{64}H_{74}N_4Si_4$: C, 75.98; H, 7.37; N, 5.54. Found: C, 74.15; H, 7.22; N, 5.32. Like **1k**, compound **11** is decomposed by prolonged contact with silica gel.

1,1,2,2-Tetra-*N*-acetyl-1,1,2,2-tetra-*N*-benzyl-1,1,2,2-tetraaminoethane (8). 2,4,6,8-Tetrabenzyl-2,4,6,8-tetraazabicyclo-[3.3.0]octane (**1d**, 2.0 g, 4.21 mmol), acetic anhydride (100 mL), and 10% Pd/C catalyst (1.0 g) were shaken with hydrogen in a Parr apparatus (45 °C, 50 psi, 6 h). The catalyst was filtered off and the filtrate concentrated to remove volatiles, leaving an oil mixed with solid. The product was dissolved in CH_2Cl_2 (20 mL) and extracted twice with saturated $NaHCO_3$ solution, twice with 1 N HCl, and once with water. After drying with anhydrous $MgSO_4$, the CH_2Cl_2 solution was concentrated to dryness to yield an oil mixed with solid. Trituration with methanol (10 mL) and storage at 0 °C deposited crystalline **8**: 0.113 g, 4.3% yield; mp 175–177 °C; recrystallization from CH_3CN gave flat, rhombic prisms, mp 183–186 °C (42% recovery); ^1H NMR (DMSO-d_6) δ 7.4 (s, 20 H, C_6H_5), 6.5 (s, 2 H, CH), 4.8 (s, 8 H, CH_2), 2.0 (s, 12 H, CH_3). Anal. Calcd for $C_{38}H_{42}N_4O_4$: C, 73.76; H, 6.84, N, 9.06. Found: C, 74.55; H, 6.91; N, 8.73.

Acknowledgment. We are indebted to Richard S. Miller and the Office of Naval Research for support of this work.

Supplementary Material Available: Tables of atomic coordinates, bond distances and angles, anisotropic thermal parameters, ^1H NMR and ^{13}C NMR spectra, and Figure S1 (molecular structure and numbering scheme) (12 pages); observed and calculated structure factors (15 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Dimethyldioxirane Oxidation of Primary Amines

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Received June 26, 1992

Several primary amines **2** have been oxidized with dimethyldioxirane (**1**) under a variety of conditions. Mixtures of dimeric nitrosoalkanes **4** and oximes **5** were typically obtained with solutions of the oxidant in excess. In several instances, nitrones **12** were found as byproducts in these reactions. In situ oxidations using oxone in buffered aqueous acetone solutions also gave nitrosoalkanes **4** and oximes **3** as important products; in addition, oxaziridines **11** were obtained in significant amounts in biphasic procedures containing methylene chloride. The corresponding nitroalkanes **5** were not formed in major amounts in either oxidation procedure, unless large excesses of oxidant were used. These results are discussed in terms of the several competing processes which occur under the different reaction conditions.

Although amines are readily oxidized by a range of reagents, there is a lack of general methodology for specific oxidative transformations of primary amines.[1] Soon after the introduction of dimethyldioxirane[2] (**1**) as a powerful but selective oxidant, its applications to this problem were examined. Several papers report efficient conversions of primary amines to the corresponding nitro compounds by this reagent, which can be either prepared and used separately or generated in situ.[3-7] Solutions of **1** have also been utilized for the controlled oxidation of amino sugars and esters of amino acids to the corresponding hydroxylamines.[8] Interestingly, complications associated with the nitroso compounds of intermediate oxidation state have not generally been a problem with this reagent, although nitroso dimers and oximes (common products with other oxidants[1,9]) were noted in a few instances.[5,6,8] Observations made during a study of the oxidation of allenic amines by **1**[10] suggested that this situation is not universal and prompted a study of primary amines bearing primary and secondary alkyl substituents. In these cases, tautomerization of the intermediate nitrosoalkanes to oximes is

(1) Rosenblatt, D. H.; Burrous, E. P. In *The Chemistry of Functional Groups: Supplement F. The Chemistry of Amino, Nitroso, Nitro Compounds and their Derivatives*; Patai, S., Ed.; Wiley Interscience: New York, 1982; p 1085.

(2) Curci, R. In *Advances in Oxygenated Processes*; Baumstark, A. L., Ed.; JAI Press: Greenwich, CT, 1988; Vol. 2, Chapter 1. Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187. Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205.

(3) Murray, R. W.; Jeyaraman, R.; Mohan, L. *Tetrahedron Lett.* **1986**, *27*, 2335.

(4) Murray, R. W.; Rajadhyaksha, S. N.; Mohan, L. *J. Org. Chem.* **1989**, *54*, 5783.

(5) Zabrowski, D. L.; Noormann, A. E.; Kenneth, R. B. *Tetrahedron Lett.* **1988**, *28*, 4501.

(6) Eaton, P. E.; Wicks, G. E. *J. Org. Chem.* **1988**, *53*, 5353.

(7) For related oxidations of secondary amines, see: Murray, R. W.; Singh, M. *Tetrahedron Lett.* **1988**, *29*, 4677. Murray, R. W.; Singh, M. *Synth. Commun.* **1989**, *19*, 3509. Murray, R. E.; Singh, M. *J. Org. Chem.* **1990**, *55*, 2954.

(8) Wittman, M. D.; Malcohm, R. L.; Danishefsky, S. J. *J. Org. Chem.* **1990**, *55*, 1981. Galik, J.; Wong, H.; Krishnan, B.; Vyas, D. M.; Doyle, T. W. *Tetrahedron Lett.* **1991**, *32*, 1851.

(9) (a) Zajac, W. W.; Walters, T. R.; Woods, J. M. *Synthesis* **1988**, 808. (b) Zajac, W. W.; Walters, T. R.; Darcy, M. G. *J. Org. Chem.* **1988**, *53*, 5856. (c) Baer, H. H.; Lee Chiu, S. H. *Can. J. Chem.* **1973**, *51*, 1812. (d) Burckard, P.; Fleury, J.; Weiss, F. *Bull. Soc. Chim. Fr.* **1965**, *10*, 2730. (e) Robinson, C. H.; Milewach, L.; Hofer, P. *J. Org. Chem.* **1966**, *31*, 524. (f) Kahr, K.; Berther, C. *Chem. Ber.* **1960**, *93*, 132. (g) Sakaue, S.; Sakata, Y.; Nishiyama, Y.; Ishii, Y. *Chem. Lett.* **1992**, 289. (h) Gilbert, K. E.; Borden, W. T. *J. Org. Chem.* **1979**, *44*, 659. (i) Emmons, W. D. *J. Am. Chem. Soc.* **1957**, *79*, 5528. (j) Keinan, E.; Mazur, Y. *J. Org. Chem.* **1977**, *42*, 844.

(10) Crandall, J. K.; Reix, T., manuscript in preparation.

0022-3263/92/1957-6759$03.00/0 © 1992 American Chemical Society