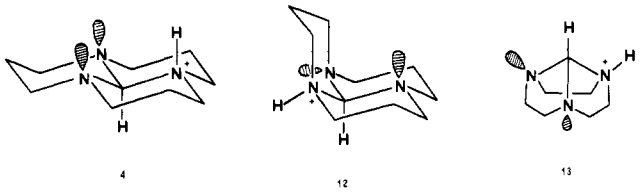
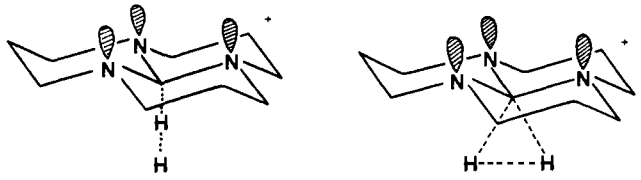


4 12 13

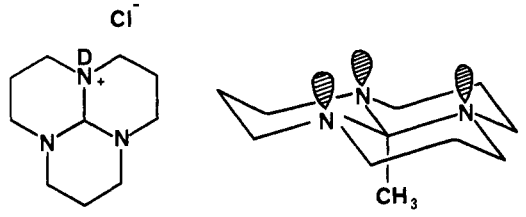
tetrafluoroborate **13**, which melted at 130 °C without decomposition.[12] As a result, we suggest that reaction 2 occurs in two steps: (1) dissociation of ammonium tetrafluoroborate **2a** into orthoamide **1** and tetrafluoroboric acid and then (2) oxidation of orthoamide **1** by the Brønsted acid. Protonation of the central carbon–hydrogen bond of the orthoamide can produce a transition state or intermediate with either the linear configuration **14** or the triangular configuration **15**.[1,2] Although structure **15** assumes



14 15

the C_s symmetry favored by protonated methane,[13] it is destabilized by nonbonded interactions on the protonated face of the molecule.[14] We tentatively favor structure **14** for an additional reason. The direct exchange of hydrogen with superacids (eq 3) is a characteristic reaction of alkanes which is invariably faster than oxidation.[1,2] Structures like carbonium ion **15** readily accommodate this rapid exchange. In contrast, formation of linear ion **14** followed by a virtually irreversible loss of molecular hydrogen would permit oxidation without exchange. In fact, oxidation of orthoamide **1** is much faster than the exchange of hydrogen; orthoamide **1** recovered after partial conversion of deuterioammonium chloride **16** to guanidinium chloride **11** (175 °C, 1 h, $CDCl_3$) contained deuterium in only normal abundance.

$$RD + H^+ \rightleftarrows RH + D^+ \quad (3)$$



16 17

Our results demonstrate unambiguously that the proton can oxidize activated alkanes. Since this particular oxidation requires Brønsted acids of only moderate strength, and since it occurs faster than the exchange of hydrogen, the central carbon–hydrogen bond of orthoamide **1** must be extraordinarily reactive. Mixing of σ_{CH}* with three antiperiplanar lone-pair orbitals accounts for this remarkable activation.[6b] During the reductions of triphenylcarbenium and methyl phenyl glyoxylate by orthoamide **1**, however, the central carbon–hydrogen bond is not broken.[6b] Our present results suggest that this bond is sufficiently reactive, but not readily accessible to bound substrates. They also indicate that if carbon–carbon bonds can be similarly activated, orthoacetamide **17** should transfer methyl with special facility.

(12) Grover, E. R.; Wuest, J. D., unpublished results.
(13) Lathan, W. A.; Hehre, W. J.; Pople, J. A. *J. Am. Chem. Soc.* **1971**, *93*, 808. Gamba, A.; Morosi, G.; Simonetta, M. *Chem. Phys. Lett.* **1969**, *3*, 20. van der Lugt, W. T. A. M.; Ros, P. *Ibid.* **1969**, *4*, 389. Mulder, J. J. C.; Wright, J. S. *Ibid.* **1970**, *5*, 445.
(14) Slutsky, J.; Bingham, R. C.; Schleyer, P. v. R.; Dickason, W. C.; Brown, H. C. *J. Am. Chem. Soc.* **1974**, *96*, 1969.

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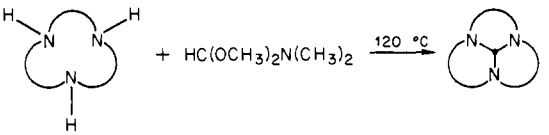
Tricyclic Trisaminomethanes

Sir:

Recent reports from these laboratories have described the synthesis of macrocyclic polyamines[1] and their use in preparing novel polycyclic compounds via an "insertion" reaction, forming three of four bonds to the macrocycle ring.[2] We have found that the macrocyclic cage imparts high stability and unusual reactivity to the central moiety of those systems reported. Although this "macrocyclic effect" has long been recognized and utilized in transition-metal chemistry, it has not been fully exploited by organic chemists. On the basis of examination of models, stable polycyclic trisaminomethanes could be prepared via an exchange reaction and should exhibit novel reactivity dependent on the ring size of the starting macrocycle.

The uncatalyzed exchange reaction between ethyl orthoformate and macrocyclic triamines was unsuccessful. However, when the more reactive dimethylformamide dimethyl acetal was substituted for orthoformate, the exchange reaction (eq 1) proceeded smoothly



(1)

to give the polycyclic trisaminomethanes listed in Table I *in high yield*. The reaction was run with stoichiometric amounts of reactants, either neat or in the presence of inert solvent.[3]

The structures **1–7** were assigned on the basis of their spectral properties and elemental analyses.[4] For example, the 220-MHz ^1H NMR spectrum of **1** exhibited an AA'BB' pattern for the methylene hydrogens. Computer simulation of the pattern gave coupling constants consistent with the expected eclipsed conformation.[5] Compounds **2–6** also exhibited ^1H NMR spectra consistent with their assigned structures.[5]

Apparently anomalous NMR spectra were observed for **7** at room temperature. The methylene protons appeared as a singlet,[5,6] and the hydrogen-decoupled ^{13}C NMR spectrum in CD_2Cl_2 exhibited only two absorptions, δ 101.1 (methine C) and 52.8 (methylene C). However, low-temperature analysis of the 220-

(1) J. E. Richman and T. J. Atkins, *J. Am. Chem. Soc.*, **96**, 2268 (1974); T. J. Atkins, J. E. Richman, and W. F. Oettle, *Org. Synth.*, **58**, 86 (1978).
(2) (a) J. E. Richman and H. E. Simmons, *Tetrahedron*, **30**, 1769 (1974); (b) J. E. Richman, *Tetrahedron Lett.*, 559 (1977); (c) T. J. Atkins, *ibid.*, 4331 (1978); (d) T. J. Atkins and J. E. Richman, *ibid.*, 4333 (1978); (e) *ibid.*, 5149 (1978).
(3) U. S. Patents 4 085 106 and 4 130 715.
(4) Elemental analyses within 0.4% of theory were obtained on all new compounds.
(5) 220-MHz ^1H NMR spectra of the methylene region. **1**: δ 3.08 (6 H, AA', J_{AB} = −10.9 Hz, $J_{AA'} = J_{AB'}$ = 5.9 Hz), 2.80 (6 H, BB', $J_{BB'}$ = 6.1 Hz). **2**: δ 3.35 (2 H, octet), 3.17 (2 H, octet), 3.06–2.91 (4 H, m), 2.79 (2 H, octet), 2.63 (2 H, octet), 1.97 (1 H, dp), 1.09 (1 H, dp). **3**: δ 3.20 (2 H, q), 2.99 (2 H, m), 2.80 (2 H, m), 2.51 (2 H, q), 2.39 (2 H, m), 1.98 (4 H, m), 1.43 (2 H, m). **4**: δ 2.82 (6 H, m), 2.23–1.92 (9 H, m), 1.43 (3 H m). **5**: δ 3.36–2.32 (8 H, m), 2.30 (6 H, s). **6**: δ 3.95 (2 H, m), 3.56 (2 H, m), 3.15 (2 H, m), 3.06 (2 H, m), 2.88 (2 H, m), 2.84–2.71 (4 H, m), 2.64 (2 H, m). **7**: δ 2.90 (16 H, s), 1.54 (1 H, br s) at 100 MHz. Detailed NMR and conformational analyses will be reported in a full paper.
(6) At 100 MHz in C_6D_6, the methylene absorption was δ 2.75, $w_{1/2}$ = 9 Hz. At 220 MHz in $CFCl_3$, they appeared at δ 2.85.

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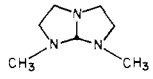
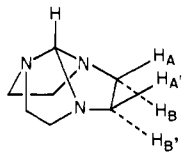
Table I. Polycyclic Trisaminomethanes

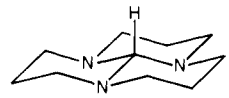
	compd	yield, %	δ methine H
1		88	5.03
2		91	4.04
3		90	2.49
4		90	2.31
5		81	3.74
			
	(6, 7)		
6	X = O	81	4.31
7	X = NH	95	4.45

MHz NMR spectrum in toluene-d_8 showed line broadening, and at −37 °C, two eight-proton multiplets were resolved. At 0 °C in toluene-d_8, five sharp ^{13}C NMR absorptions were resolved, δ 99.8 54.3, 53.8, 51.3, and 49.7. When the sample was warmed to 90 °C, the methylene signals collapsed to a sharp singlet at δ 52.9. All eight equivalent isomers of **7** must interconvert to equilibrate the hydrogens syn to the methine with those anti as well as all the methylene carbons in the localized structure. The isomerization requires carbon–nitrogen bond exchange and methine hydrogen "flipping" through the macrocycle plane. The details of this isomerization are still under investigation.

The chemical shift of the methine protons in the series **1–4** varies over 2.7 ppm (Table I). The downfield shift of the methine hydrogens[7] of **1** and **2** can be ascribed to a dramatic anomeric effect of the nitrogen lone pairs.[8] The methine hydrogen of **1**



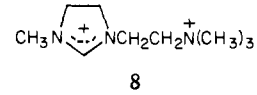
1



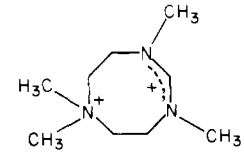
4

is highly deshielded by combined eclipsing interactions with all three lone pairs. The downfield methylene hydrogen absorption has been assigned to the exo-hydrogen, based on lone pair deshielding. The trans,trans,trans three-chair conformation of **4** places all nitrogen lone pairs anti to the methine hydrogen. The presence of Bohlmann bands[9] at 4.0 μm in the IR spectrum provides evidence for this conformation. With a high population of this lowest energy conformation,[10] the methine absorption of **4** appears at a much higher field than that of **1** or **2**. Compounds **1** and **4** may be the ultimate models for monitoring the anomeric effect of nitrogen lone pairs in syn (0° dihedral angle) and anti (180° dihedral angle) conformations.

When the trisaminomethane moiety was incorporated into a small macrocyclic cage, as in **1**, its reactivity differed markedly from the model bicyclic analogue **5**. For example, when **5** was treated with excess methyl iodide, the trisaminomethane opened as expected to give a mixture of the formamidinium cations **8** and **9**,[4,11] resulting from double alkylation at the ring and bridgehead nitrogens, respectively.



8



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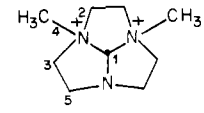

10

However, when **1** was treated with either methyl iodide or methyl fluorosulfate, the dication **10**[4] was formed. Compound **10** exhibited no IR absorptions near 6 μm; its ^1H NMR spectrum showed the methine hydrogen at δ 6.51 and a methyl singlet (6 H) at δ 2.96, and its ^{13}C NMR spectrum (D_2O) had absorptions at δ 106.8 (C_1), 53.9 (C_2), 52.2 (C_3), 41.9 (C_4), and 41.5 (C_5). In comparison, **1** had ^{13}C NMR absorptions (D_2O) at δ 93.2 and 41.9. Clearly, the tricyclic integrity of **1** has been preserved after alkylation. In addition, **1** was stable in water whereas **5** gave a vigorous exotherm with complete loss of the trisaminomethane moiety. The enhanced stability of **1** can be attributed to the high energy required to open one carbon–nitrogen bond to give an excessively strained formamidinium cation.

Thus, these readily available polycycles exhibited remarkable conformational effects and unusual reactivity. Further explorations of the chemistry of this novel class of compounds will be presented in a full paper.

(7) The methine hydrogen of tris(dimethylamino)methane absorbs at δ 3.02 in C_6D_6; see: H. Weingarten and W. A. White, *J. Am. Chem. Soc.*, **88**, 850 (1966).

(8) For an empirical correlation of the ^1H NMR shift with amine and ether conformations, see: C. C. Price, *Tetrahedron Lett.*, 4527 (1971).

(9) (a) F. Bohlmann, *Angew Chem.*, **69**, 641 (1957); (b) T. A. Crabb, R. F. Newton, and D. Jackson, *Chem. Rev.*, **71**, 109 (1971).

(10) Calculations indicate this conformation to be ca. 6 kcal/mol more stable than the corresponding cis,cis,trans three-chair conformation: D. A. Pensak, private communication.

(11) The mixture of salts of **8** and **9** had IR absorptions in the 6 μm region and NMR absorptions at δ 8.46 and 8.16 in the ^1H NMR spectrum and at δ 147–150 in the ^{13}C NMR spectrum.

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Transfer of Hydrogen from Orthoamides. Synthesis, Structure, and Reactions of Hexahydro-6b*H*-2a,4a,6a-triazacyclopenta[*cd*]pentalene and Perhydro-3a,6a,9a-triazaphenalene

Sir:

The transfer of a proton and two electrons from one molecule to another is a common but puzzling process.[1] Important examples are enzymatic and nonenzymatic reductions involving 1,4-dihydropyridines.[2] Despite extensive study, not all the factors which promote these transfers have been identified. To provide

(1) For reviews, see: Nenitzescu, C. D. *Carbonium Ions* **1970**, *2*, 463. Deno, N. C.; Peterson, H. J.; Saines, G. S. *Chem. Rev.* **1960**, *60*, 7. Stewart, R. "Oxidation Mechanisms", W. A. Benjamin: New York, 1964. Nenitzescu, C. D. *Usp. Khim.* **1957**, *26*, 399.

(2) For references, see: Sund, H. *Biol. Oxid.* **1968**, 603. *Enzymes 3rd Ed. 11*, 1. Kill, R. J.; Widdowson, D. A. *Bioorg. Chem.* **1978**, *4*, 239. Sigman, D. S.; Hajdu, J.; Creighton, D. J. *Ibid.* **1978**, *4*, 385.

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