Postdoctoral Fellowship (to R.S.P.), and Johnson Matthey, Inc., for a generous loan of rhodium. The NMR facilities were supported in part through the University of Chicago Cancer Center Grant NIH-CA-14599.

Registry No. 1, 63439-10-1; 2, 63372-77-0; 3, 96502-52-2; 4, 96502-53-3; (OEP)RhCH$_2$C$_6$H$_5$, 57650-51-8; (OEP)RhBr, 63372-78-1; PhCH=CH$_2$, 100-42-5; C$_6$H$_5$CH$_2$Br, 100-39-0.

On the Reported High Barrier to Nitrogen Inversion in Azetidine (Trimethylenimine)

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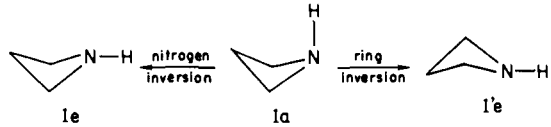
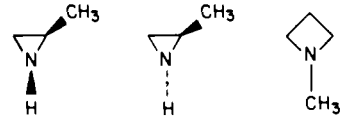
A paper by Friedman, Chauvel, and True (FCT) states that two separate (chemically shifted) NH resonances with unequal areas (ca. 3:1) are observed in the ^{1}H NMR spectrum of azetidine (I) at room temperature and that the free energy barrier to nitrogen inversion is about 17.9 kcal/mol.[1] This would require that *both* ring inversion and nitrogen inversion in nonplanar I be slow on the dynamic NMR time scale under these conditions, since *either* of the above processes is sufficient to cause exchange of the NH proton between the quasi-axial and quasi-equatorial sites, as can be seen from the structures Ia, Ie, and I'e.[2] Thus, both



Ie Ia I'e

free energy barriers must be more than 17 kcal/mol. However, it is known from other investigations quoted by FCT that the barrier to ring inversion in azetidine is at best only a few kilocalories per mole. Furthermore, the methylene chemical shifts of I in CCl_4 are known[3] and are quite different from those reported by FCT.

A consideration of the data reported by FCT shows that the compound that they studied must be 2-methylaziridine (II). The



IIc IIt III

250-MHz ^{1}H NMR spectrum of this compound in CCl_4 has been measured and analyzed previously.[4] The chemical shifts and integration are consistent with those given by FCT, except for the NH proton signals whose chemical shifts are about 1–1.5 ppm to lower fields in CCl_4 than are those in the gas phase. These chemical shifts are expected to be influenced by hydrogen bonding and thus to depend on both concentration and solvent. The conformational ratio (IIt:IIc) is 2:1 in the liquid phase and the small difference from the gas-phase value (3:1) is again not unexpected.

The free energy barrier to nitrogen inversion found by FCT is very close to that in aziridine itself ($\Delta G^{\ddagger} = 17.2 \pm 0.1$ kcal/mol in either the gas[5] or the liquid phase[6]) and much higher than that in 1-methylazetidine (III) ($\Delta G^{\ddagger} = 10.0$ kcal/mol in the liquid phase[7]). At present, the barrier to nitrogen inversion in I remains unknown,[8] but its value should be similar to that in its *N*-methyl derivative, III.[9]

(1) Friedman, B. R.; Chauvel, J. P., Jr.; True, N. S. *J. Am. Chem. Soc.* **1984**, *106*, 7638–7639.

(2) FCT correctly point out that both fast ring and nitrogen inversions are required for the β-CH$_2$ protons in Ia and Ie to give a single averaged chemical shift. However, the four lines that they ascribe to the β-protons at room temperature collapse to two lines and not to one line at high temperatures. Thus, their conclusion that there is "complete exchange" of these protons is not borne out by their published spectra. The NH proton has only two possible sites which are shown in Ia and Ie, and thus its behavior is different from that of the β-protons.

(3) Higgins, R. H.; Cromwell, N. H.; Paudler, W. W. *J. Heterocycl. Chem.* **1971**, *8*, 961–966. The chemical shifts of the α- and β-protons in I in CCl_4 solution, with tetramethylsilane as the internal reference, are δ 3.53 and 2.33, respectively, whereas the chemical shifts reported by FCT for these protons are between δ 1 and 2. These latter high-field shifts point to unusual shielding, such as occurs in a three- but not in a four-membered ring.

(4) Lopez, A.; Gauthier, M. M.; Martino, R.; Lattes, A. *Org. Magn. Reson.* **1979**, *12*, 418–428. In the major conformer (IIt), the assignments are as follows: CH$_3$, δ 1.04, J = 5.5 Hz; CH$_2$, δ 0.96 and 1.66; CH, δ 1.89; NH, δ 0.61. In the minor conformer (IIc), the CH$_3$ and NH protons are at δ 1.23 and 0.08, respectively, and the other protons lie between δ 1.2 and 1.4.

(5) Carter, R. E.; Drakenberg, T.; Bergman, N.-Å. *J. Am. Chem. Soc.* **1975**, *97*, 6990–6996.

(6) Nakanishi, H.; Yamamoto, O. *Tetrahedron* **1974**, *30*, 2115–2121. Skaarup, S. *Acta Chem. Scand.* **1972**, *26*, 4190–4192.

(7) Lambert, J. B.; Oliver, W. L., Jr.; Packard, B. S. *J. Am. Chem. Soc.* **1971**, *93*, 933–937.

(8) The barrier to nitrogen inversion in piperidine can be observed in solution, but special care must be taken to prevent NH exchange: Anet, F. A. L.; Yavari, I. *J. Am. Chem. Soc.* **1977**, *99*, 2794–2796.

(9) Professor, N. S. True (personal communication) has informed me that the compound studied by them was indeed 2-methylaziridine (see Additions and Corrections; True, N. S. *J. Am. Chem. Soc.*, in press.)

A Diacridine Derivative That Binds by Bisintercalation at Two Contiguous Sites on DNA

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When two DNA-intercalating chromophores are joined by a linker chain, the nature of this chain becomes a major constraint upon bisintercalative binding.[1-3] Results for derivatives of 9-aminoacridine indicate that compounds with polymethylene or amide-containing linker chains as short as 8.8 Å undergo bisintercalative binding.[1-6] Such compounds (e.g., **1** and **2**) must intercalate at contiguous sites, with one chromophore on either side of the same base pair, in violation of the "excluded-site" principle proposed as a thermodynamic limitation in some theoretical models of the binding of monointercalators and observed in practice for such compounds.[5,7]

However, monointercalative binding of a related bis(acridine) hydrazine **3** was indicated in a recent study.[2] Also, NMR studies show that **1** and **2** bind to the oligodeoxyribonucleotide d(A-T)$_5$-d(A-T)$_5$ by monointercalation,[6] suggesting that bisintercalation of chromophores joined by flexible chains is condition dependent.

Molecules where the chromophores are held by a rigid framework in a suitable orientation can show an increased propensity for intercalative binding. The quinoxaline chromophores of triostin A are known to both intercalate DNA[8] (although not

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(2) King, H. D.; Wilson, W. D.; Gabbay, E. J. *Biochemistry* **1982**, *21*, 4982.

(3) Atwell, G. J; Leupin, W.; Twigden, S. J.; Denny, W. A. *J. Am. Chem. Soc.* **1983**, *105*, 2913.

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