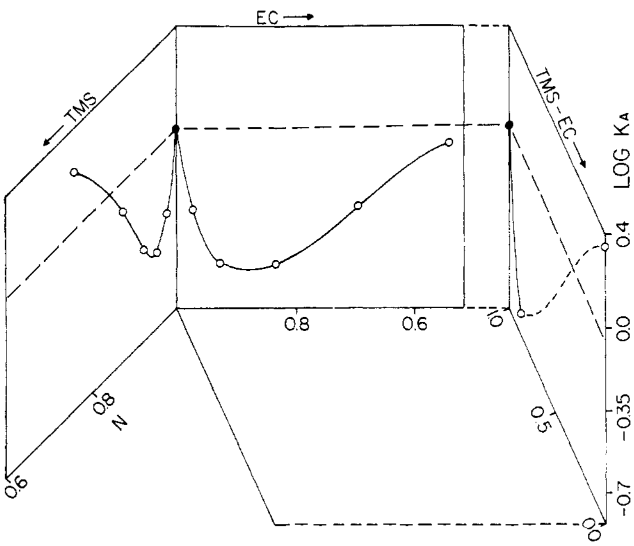

Figure 1. Association of potassium iodide in water and in mixed solvents at 25°.

$$K_A = K^0 \exp(e^2/aDkT) \quad (1)$$

where e is unit charge and K^0 is a geometrical factor which measures excluded volume; according to (1), a plot of log K_A is linear in reciprocal dielectric constant, with K_A increasing as D decreases. The alkali halides in water–dioxane mixtures with D less than about 30 conform to the above model.[2] Until recently, it was impossible to determine association constants with any precision in solvents of higher dielectric constant; integration of the Fuoss–Onsager conductance equation[3] through terms of order $c^{3/2}$ now permits analysis of conductance data at higher concentrations (*e.g.*, to 0.1 *N* for 1:1 salts in water). It was found[3] that the log K_A–$(1/D)$ plots for a variety of 1:1 salts in water–dioxane mixtures was concave down in the range $78.5 \geq D > 30$, becoming linear in the range below 30. Alternatively described, extrapolation of the linear portion of the curve into the region of high dielectric constants gave values for K_A which were too high, as if the first additions of dioxane to water had two effects: the expected increase in K_A due to decreased dielectric constant, and another as yet unexplained one. The latter presumably correlates with the destruction of the water structure as dioxane is added. With dioxane, the dielectric effect dominates, because the dielectric constant of dioxane (2.2) is so low; a relatively small amount of dioxane makes a large change in D. Mixtures of water with several other aprotic solvents of higher dielectric constant (ethylene carbonate (EC) and tetramethylene sulfone (TMS)) were therefore studied, in order to enhance the nonelectrostatic effects. A completely new type of dependence of association on solvent composition was found, as shown in Figure 1, where log K_A for potassium iodide (vertical axis) is plotted against solvent composition (N = mole fraction of water). This surface shows that association in water is decreased by the addition of other solvents which may increase, decrease, or leave unchanged the dielectric constant.

The association constant in water ($K_A = 0.92$) is shown as the solid black point. As TMS is added, D decreases but initially, K_A *also* decreases; the minimum in the log K_A–TMS plane comes at $D \approx 71$ where $K_A = 0.33$. On further addition, K_A then rises, reaching the value 1.6 at $D = 59.4$ ($N = 0.76$, at 68 wt % TMS). Exactly the same pattern is observed when EC is added to water; here K_A again decreases on initial addition of aprotic solvent as D increases, but then on further addition of EC (with accompanying further *increase* of D), K_A *increases*. The minimum in the log K_A–EC plane is at $K_A = 0.24$, at $D \approx 81.5$ and $N \approx 0.87$ (40 wt % EC). Finally, in an anhydrous mixture ($D = 78.64$) of 25.6% TMS–74.4% EC, isodielectric with water, the association constant is 2.25, over twice the water value. Addition of water to this mixture (shown in the projected plane to the right in Figure 1) sharply decreases association, although the dielectric constant is changed but little; at $N = 0.876$, $D = 77.2$, and $K_A = 0.19$. Thus by varying solvent composition at essentially fixed dielectric constant, K_A can be varied up and down by an order of magnitude.

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[2] R. M. Fuoss, *Rev. Pure Appl. Sci.*, **18**, 125 (1968).

[3] R. M. Fuoss and K. L. Hsia, *Proc. Natl. Acad. Sci. U. S.*, **57**, 1550; **58**, 1818 (1967).

The 3,7-Transannular C–H Insertion Reaction in the Pyrolysis of the Sodium Salt of Pseudopelletierine Tosylhydrazone. A Simple and Novel Synthesis of N-Methylnorazaadamantane[1]

Sir:

Proximity effects in the transannular reactions of medium-sized rings have been well documented. Postulated intermediates include carbonium ions, carbanions, radicals, and carbenes.[2] Extreme cases of proximity would be expected in transannular reactions between C-3 and C-7 positions in bicyclo[3.3.1]nonane ring systems and their heterocyclic analogs, where a twin-chair conformation has been postulated.[3] Studies on the transannular reactions in such ring systems seem to be limited to solvolytic reactions to nonheterocyclic analogs.[5] We wish now to report a facile 3,7-transannular C–H insertion reaction in a 9-methyl-9-azabicyclo[3.3.1]nonane ring system using base-promoted decompositions of the tosylhydrazone (Ib) of pseudopelletierine (Ia), which has been postulated to prefer a double-chair conformation in the ground state.[4]

The dry sodium salt (Ic) of Ib, obtained readily by treatment of Ib-hydrochloride (mp 236–238° dec) with

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[1] The Synthesis of Adamantane Derivatives. VI. For the previous paper in this series, see T. Sasaki, S. Eguchi and T. Toru, *Tetrahedron Lett.*, 4135 (1968).

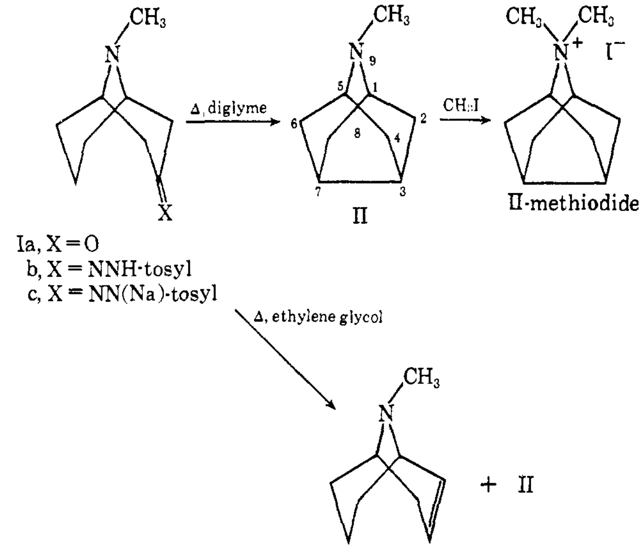
[2] (a) For an excellent review on transannular reactions in medium-sized rings, see A. C. Cope, M. M. Martin, and M. A. Mckervey, *Quart. Rev.* (London), **20**, 119 (1966); (b) for recent papers on transannular carbene reactions, see A. C. Cope and S. S. Hecht, *J. Amer. Chem. Soc.*, **89**, 6920 (1967); S. Oida and E. Ohki, *Chem. Pharm. Bull.* (*Tokyo*), **15**, 545 (1967).

[3] For example, see (a) N. L. Allinger, J. A. Hirsch, M. A. Miller, I. J. Tyminski, and F. A. Van-Catledge, *J. Amer. Chem. Soc.*, **90**, 1199 (1968), and references cited therein; (b) see also references quoted in ref 4.

[4] For conformational studies of Ia and its derivatives, see C.-Y. Chen and R. J. W. Le Fèvre, *J. Chem. Soc.*, *B*, 539 (1966), and references cited therein; H. S. Aaron, C. P. Ferguson, and C. P. Rader, *J. Amer. Chem. Soc.*, **89**, 1431 (1967); W. D. K. Macrosson, J. Martin, and W. Parker, *Tetrahedron Lett.*, 2589 (1965).

[5] For example, see M. A. Eakin, J. Martin, W. Parker, S. C. Egan, and S. H. Graham, *Chem. Commun.*, 337 (1968), and references cited therein.

Scheme I



sodium methoxide in methanol, was decomposed by refluxing in diglyme at 165° for 2 hr (Scheme I). Products were distilled together with diglyme, and from the distillates a basic component was isolated as its picrate (mp 308–310°) or methiodide (mp > 320°), in a total yield of *ca.* 80%. Both the picrate and the methiodide were uniform on tlc[6] and gave satisfactory analyses. *Anal.* Calcd for picrate $C_{15}H_{18}N_4O_7$: C, 49.18; H, 4.95; N, 15.30. Found: C, 49.57; H, 4.83; N, 15.31. Calcd for methiodide $C_{10}H_{18}NI$: C, 43.02; H, 6.50; N, 5.02. Found: C, 42.96; H, 6.63; N, 5.17. The structure of this base was assigned as N-methylnorazaadamantane (II), 9-methyl-9-azatricyclo[3.3.1.0^{3,7}]nonane, from the spectral data: the nmr spectrum of II-picrate in $(CD_3)_2SO$ at 100 MHz (Figure 1a) showed signals at τ 6.28 (2 H) assignable to bridgehead protons adjacent to nitrogen atom, 7.22 (3 H) to N-methyl protons, 7.36 (*ca.* 2 H)[7] to bridgehead protons at C-3 and C-7, and a multiplet centered at τ 8.16 (8 H) to methylene protons, all supporting structure II. The nmr spectrum of a free base of II in $CDCl_3$ at 60 MHz had signals at τ 6.87 (2 H, broad singlet, two bridgehead protons at C-1 and -5), 7.59 (3 H, singlet, N-methyl protons), 7.72 (2 H, singlet, two bridgehead protons at C-3 and C-7), 8.12 and *ca.* 8.54 (8 H, unsymmetrical broad AB quartet with $J_{AB}/\Delta\tau$ = *ca.* 0.45, methylene protons), also supporting the structure. The mass spectrum of II-methiodide at 70 eV had the molecular ion peak at *m/e* 279 (1.7% relative to the base ion peak at *m/e* 42) and other main fragmented ion peaks at *m/e* 152 (54.7), 142 (82.3), 137 (92.5), 127 (90.5), 111 (34.3), 110 (25.1), 108 (28.4), 96 (97.1), 95 (95.7), 94 (92.4), 41 (58.1), and 39 (46.1). These fragmentations could be explained similarly to those of Ia[8] and some tropane alkaloids,[9] except peaks at *m/e* 41 and 39 which might be characteristic to this ring system.[10]

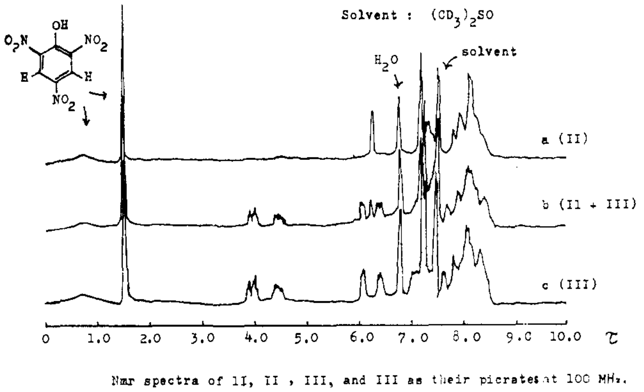


Figure 1. Nmr spectra of II, II + III, and III as their picrates at 100 MHz.

Decomposition of Ic in ethylene glycol afforded a basic product which was isolated as its picrate (mp 302–307° dec) in 46% yield. This product was analyzed as a mixture of 76.5% of olefin III and 23.5% of II on the basis of tlc[6] and analytical and spectral data. *Anal.* Calcd for $C_{15}H_{18}N_4O_7$: C, 49.18; H, 4.95; N, 15.30. Found: C, 49.38; H, 4.65; N, 15.46. The relative yields were calculated on the basis of the relative integral ratio of the nmr signals (Figure 1b) at τ 6.27 due to II and 3.92, 4.40, 6.08, and 6.41 due to III (picrate, mp 299–302° dec)[11] which was isolated by chromatography on neutral alumina from the mixture.

In pyrolytic decompositions of Ic,[12] the observed exclusive formation of II in aprotic diglyme and even in protic ethylene glycol as well as the higher ratio of C–H insertion product to the olefinic product compared with other cyclic systems[13] support the idea that the C–H carbene insertion reactions in this ring system are governed by proximity effects between the C-3 and C-7 positions.[3,5]

From a synthetic viewpoint, such a facile transannular C–H insertion reaction in bicyclo[3.3.1]nonane ring systems may provide a general route to certain tricyclic ring systems.[14]

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[6] Tlc (thin layer chromatography) was carried out on alumina and silica gel plates by using benzene–methanol mixtures as developing solvents and iodine as a developing reagent.

[7] This signal was analyzed as an AB quartet with $J_{AB}/\Delta\tau$ = 0.50 in spite of the expected molecular symmetry of II, since II-picrate is assumed reasonably to be asymmetrical enough to produce such nonequivalence of these bridgehead protons; in agreement with this assumption, the signal at τ 7.72 due to protons at C-3 and C-7 of free base II appeared in a singlet; *cf.* M. van Gorkom and G. E. Hall, *Quart. Rev.* (London), **22,** 14 (1968).

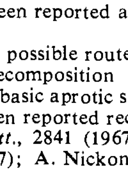
[8] R. D. Guthrie and J. F. McCarthy, *J. Chem. Soc.*, *C*, 1207 (1966).

[9] E. C. Blossey, H. Budzikiewicz, M. Ohashi, G. Fodor, and C. Djerassi, *Tetrahedron*, **20,** 585 (1964).

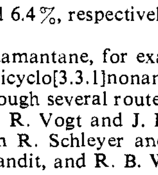
[10] Detailed discussions on the fragmentations of II and its derivatives will be published as a full paper in the future.

[11] R. Willstätter and E. Waser, *Ber.*, **44,** 3423 (1911).

[12] Although in the pyrolytic decompositions any formation of other possible insertion products like i and ii was not observed in diglyme and ethylene glycol, in the photolytic decomposition of Ic in ether a mixture of i and ii (*ca.* 3:2) was isolated in 26.5% yield after chromatography, further studies on which are still in progress.



i



ii

[13] In the decomposition of cyclooctyl tosylhydrazone in ethylene glycol, the relative yields of an olefinic and a transannular insertion product have been reported as 83.5 and 6.4%, respectively; see ref 2a, p 145.

[14] Another possible route to noradamantane, for example, will be supplied by decomposition of the bicyclo[3.3.1]nonan-3-one tosylhydrazone in a basic aprotic solvent, though several routes to this compound have been reported recently: B. R. Vogt and J. R. E. Hoover, *Tetrahedron Lett.*, 2841 (1967); P. von R. Schleyer and E. Wiskott, *ibid.*, 2845 (1967); A. Nickon, C. D. Pandit, and R. B. Williams, *ibid.*, 2851 (1967).

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