Anal. Calcd for $C_{15}H_{26}N_2O_2$: C, 67.63; H, 9.84; N, 10.52; mol wt, 266.4; neut equiv, 133.2. Found: C, 67.44; H, 9.8; N, 10.67; mol wt, 273; neut equiv, 134.

Acknowledgment.—The author is indebted to Donald W. Moore for securing nmr spectra and for helpful discussions.

Bicyclic Bases. Synthesis of 2,5-Diazabicyclo[2.2.1]heptanes[1]

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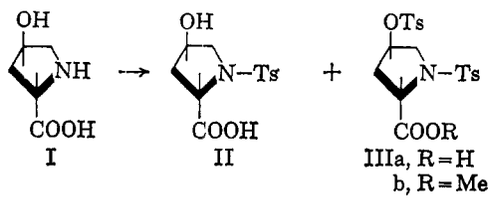
A route to the novel bicyclic system, 2,5-diazabicyclo[2.2.1]heptane, has been elaborated. The starting material, hydroxy-L-proline, was transformed to tritosylhydroxy-L-prolinol, which was then cyclized to 2-tosyl-5-benzyl-2,5-diazabicyclo[2.2.1]heptane with benzylamine. The latter structure was subsequently converted to the parent bicyclic system. Some of the reaction mechanisms leading to the bicyclic compound are discussed, and the nmr spectra of the title compound and its ditosyl derivative are interpreted.

The piperazine ring, which is capable of undergoing conformational inversion,[2] is encountered in a variety of medicinal agents. An approach to investigating the nature of conformational species which are reponsible for biological activity would involve constraining the piperazine ring in a single conformation. One such structure which fulfills the requirements of conformational rigidity is 2,5-diazabicyclo[2.2.1]heptane (XI). We wish to report on the synthesis of XI *via* a novel route which establishes the absolute configuration of this bicyclic system and, moreover, is of general utility in the preparation of other bicyclic structures which are not easily accessible by other methods.

The starting material for the synthesis is hydroxy-L-proline (I), whose absolute stereochemistry[3] is established. In the conception of the synthetic approach to XI, it was desirable to block the basic nitrogen of I with a protective group which would withstand the rigors of reactions employed in the synthetic sequence and also be capable of being removed without affecting other substituents in the molecule. The tosyl group fulfilled these requirements.

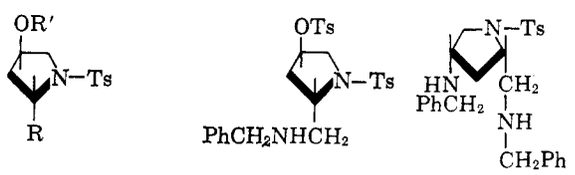
Hydroxy-L-proline (I) was tosylated in aqueous sodium hydroxide solution to afford, in high yield, a mixture of the expected N-tosyl derivative (II) and N,O-ditosylhydroxy-L-proline (IIIa). The identity of IIIa was determined by converting this compound to N,O-ditosylhydroxy-L-proline methyl ester (IIIb). The



same compound[4] was also prepared by tosylation of IV in pyridine solution. The yield of IIIa was increased at the expense of the major product when the reaction time was lengthened. It was found that II could be transformed to IIIa by prolonged exposure to tosyl chloride in aqueous sodium hydroxide solution. Hence, under the experimental conditions, N-tosylation occurred rapidly and this was followed by slow O-tosylation.

Treatment of II with diazomethane gave the methyl ester (IV) which was then reduced to N-tosylhydroxy-L-prolinol (V). It was found that reduction with lithium borohydride produced the highest yield. Attempts to reduce the acid (II) or ester (IV) with lithium aluminum hydride afforded V in much lower yield. Tosylation of V in pyridine solution gave the tritosyl derivative VI. The *trans* stereochemistry of this key intermediate is essential for the subsequent ring closure step since it was expected that displacement of the primary tosyloxy group by an amine nucleophile should produce the transient intermediate, VII, which would then undergo ring closure by internal SN2 expulsion of the secondary tosyloxy substituent.

The desired 2,5-diazanorbornane derivative (IX) was obtained in 86% yield by refluxing a toluene solution containing 3 equiv of benzylamine and 1 equiv of intermediate VI. Two equivalents of benzylamine acted as a proton acceptor for *p*-toluenesulfonic acid formed in the reaction. Significantly, no compounds corresponding to VII and VIII could be detected in the reaction mixture after approximately 50% of VI had been converted to IX. This suggests that displacement of the primary tosyloxy group by benzylamine proceeds in a rate-determining step to give intermediate VII which then rapidly cyclizes to IX.



IV, R = COOMe; R′ = H
V, R = CH_2OH; R′ = H
VI, R = CH_2OTs; R′ = Ts

VII VIII

In preliminary experiments, N-tosylpiperidine was employed as a model compound to explore the possibility of reductively cleaving the tosyl group in IX by treatment with sodium in liquid ammonia.[5] However, since this method gave yields of piperidine which were not greater than 30%, a more drastic procedure

(1) This investigation was supported in whole by Public Health Service Grant GM 09402 from the Institute of General Medical Sciences.

(2) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, Inc., New York, N. Y., 1965, p 250.

(3) J. P. Greenstein and M. Winitz, "Chemistry of the Amino Acids," Vol. 1, John Wiley and Sons, Inc., New York, N. Y., 1961, p 191.

(4) Y. Fujita, A. Gottlieb, B. Peterkofsky, S. Udenfriend, and B. Witkop, *J. Am. Chem. Soc.*, **86**, 4709 (1964).

(5) Reference 3, Vol. 2, p 1239.

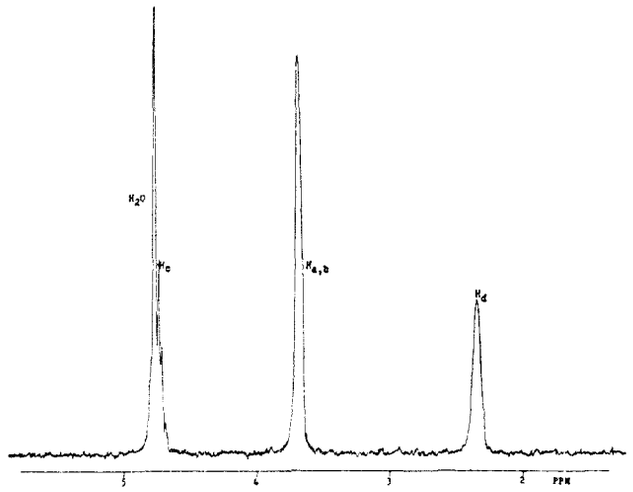


Figure 1.—The nmr spectrum of 2,5-diazabicyclo[2.2.1]-heptane dideuteriochloride in D_2O [sodium 3-(trimethylsilyl)-1-propanesulfonate as internal standard].

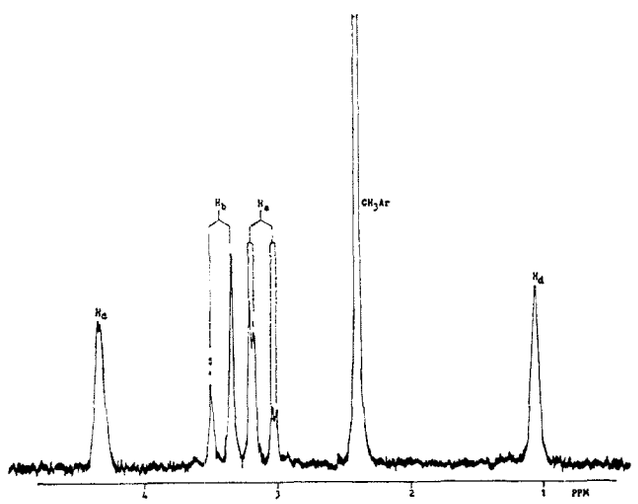
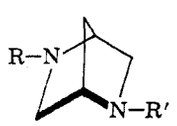


Figure 2.—The nmr spectrum of 2,5-ditosyl-2,5-diazabicyclo-[2.2.1]heptane in deuteriochloroform (tetramethylsilane as internal standard).

was employed which involved reductive cleavage using hydriodic acid.[6] When IX was refluxed in a mixture of concentrated HI, phosphorus, and acetic acid, compound X was produced, as the dihydriodide salt, in good yield. The fact that X could be converted back to IX by tosylation in pyridine rules out the possibility of rearrangement during the detosylation step. The salt (X·2HI) was resistant to hydrogenolysis using palladium-on-carbon catalyst. However, as the dihydrochloride salt, catalytic hydrogenolysis proceeded smoothly to give the parent structure (XI·2HCl) in high yield.



IX, R = $C_6H_5CH_2$; R′ = Ts
X, R = $C_6H_5CH_2$; R′ = H
XI, R = R′ = H
XII, R = H; R′ = Ts
XIII, R = R′ = Ts

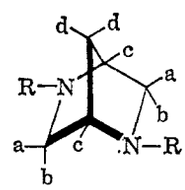
(6) R. B. Woodward, M. P. Cava, W. D. Ollis, A. Hunger, H. U. Daeniker, and K. Schenker, *Tetrahedron*, **19**, 247 (1963).

The possibility of obtaining XI by first removing the benzyl group and then detosylating was explored. Catalytic hydrogenolysis of IX produced the debenzylated intermediate XII. However, although cleavage of the tosyl group did occur on treatment of XII with HI, the dihydriodide salt of XI was not easily isolated in a pure state.

Inasmuch as the starting material for this synthesis possesses the (2*S*:4*R*) stereochemistry and since only the C-4 asymmetric center undergoes inversion during ring closure, the bicyclic system is assigned the (1*S*:4*S*) configuration.

The synthetic route discussed in this communication appears to be generally useful for the preparation of norbornane structures of known absolute configuration in which heteroatoms are part of the bicyclic structure and are located at the 2- and/or 5-position.[7]

Support for the 2,5-diazanorbornane[8] ring system was obtained from nmr analysis of the parent compound (XI) and its ditosyl derivative (XIII). The latter compound was obtained by tosylating XII in pyridine.



XI, R = D·2DCl
XIII, R = Ts

Although XI and XIII are dissymmetric, the *exo*, *endo*, bridgehead, and bridge protons on one-half of the bicyclic system are magnetically equivalent to protons located at similar positions in the second half of the molecule. The nmr spectrum of XI·2DCl in D_2O (Figure 1) is quite simple in that it exhibits signals at 2.35 (H_d), 3.70 (H_a and H_b), and 4.76 ppm (H_c). The bridge protons (H_d) are found upfield relative to H_a, H_b, and H_c because the former are three bonds removed from the protonated nitrogen compared with two bonds for the latter protons. Interestingly, the width at half-height of the signal belonging to H_a and H_b is only 3.5 cps. This is unlike the situation in norbornane where H_{exo} is deshielded relative to H_{endo} by 21–32 cps.[9] Since the geometry of XI is probably almost identical with that of norbornane,[10] the absence of a comparable difference in chemical shift may be related to the presence of nitrogen in this bicyclic system.

The spectrum of XIII (Figure 2) is much more revealing than that of XI·2DCl, because the difference in chemical shift between H_a and H_b is of sufficient magnitude to allow observation of geminal and vicinal coupling. The much larger chemical shift difference may, in part, be due to shielding of H_a by the tosyl group. The quartet centered at 3.11 ppm has been assigned to

(7) We have also prepared bridged piperidine, morpholine, and thiomorpholine derivatives employing a similar synthetic approach. This will be discussed in a future communication.

(8) It is noteworthy that the 2,3-, 1,4-, and 1,7-diazanorbornane derivatives have been reported: S. G. Cohen and R. Zand, *J. Am. Chem. Soc.*, **84**, 586 (1962); Y. S. Shabarov, N. I. Vasil'ev, S. Levina, and R. Y. Levina, *Zh. Obshch. Khim.*, **32**, 2806 (1962); G. R. Pettit and J. Settepani, *Chem. Ind.* (London), 1805 (1964); I. I. Grandberg and A. N. Kost, *Zh. Obshch. Khim.*, **29**, 1099 (1959). To our knowledge, this is the first time XI has been prepared.

(9) J. I. Musher, *Mol. Phys.*, **6**, 93 (1963).

(10) C. F. Wilcox, Jr., *J. Am. Chem. Soc.*, **82**, 414 (1960).

H_a by virtue of its ability to couple with the bridgehead proton (J_{ac} = 2.2 cps) and with H_b (J_{ab} = −9.5 cps), which is seen as a doublet at 3.43 ppm. The fact that H_b exhibits little or no coupling with H_c is predicted by the Karplus equation, when the dihedral angle is about 90°.[11] A similar situation exists for bornane and norbornane derivatives where it has been reported[12] that H_{exo} is coupled while H_{endo} is not coupled with the adjacent bridgehead proton. Since the bridgehead protons are coupled with H_a and H_d, it appears as a broadened singlet (4.34 ppm) whose width at half-height is 4.5 cps. The bridge protons (1.06 ppm) are weakly coupled with H_c and thus give rise to a single peak whose half-width is 4.0 cps.

Experimental Section[13]

Tosylation of Hydroxy-L-proline (I).—Ten grams (0.076 mole) of hydroxy-L-proline (I) was dissolved in 100 ml of 2 *N* sodium hydroxide solution and was shaken for 5 hr with an ether solution containing 17 g (0.089 mole) of tosyl chloride. The aqueous layer was separated, acidified, and refrigerated overnight. The yield of crude product, mp 130–155°, was 20.6 g (95.6%). Recrystallization from ethyl acetate afforded 17.85 g (82%) of II, mp 153–155° (lit.[14] mp 153°), $[\alpha]^{23}D$ −105.4° (*c* 2 %, ethanol) and 138–139.5° (dimorphic modification).

A second product (2.1 g) of the reaction was obtained from the ethyl acetate mother liquor by removing the solvent and crystallizing the residue from 90% ethanol. This product (IIIa), mp 147–148°, $[\alpha]^{23}D$ −42.3° (*c* 2.2%, ethanol), was treated with diazomethane to give N,O-ditosylhydroxy-L-proline methyl ester (IIIb), mp 93–95°, $[\alpha]^{20}D$ −53.8° (*c* 2%, chloroform), lit.[4] mp 94–95°, $[\alpha]^{20}D$ −54.1°, whose nmr and infrared spectra are identical with those of the authentic material.[4]

Tosylation of N-Tosylhydroxy-L-proline.—A solution of 2.85 g (0.01 mole) of N-tosylhydroxy-L-proline (II) in 10 ml of 2 *N* NaOH was shaken for 72 hr at room temperature with an ether solution of 7.62 g (0.04 mole) of tosyl chloride. The ethereal layer was extracted with 10% NaOH solution and the extract was added to the aqueous layer. The combined aqueous solution was cooled and acidified with HCl. The crude product (2.7 g) was crystallized from 90% ethanol to afford 1.91 g of IIIa, mp 147–149°, $[\alpha]^{23}D$ −42.8° (*c* 1.92%, ethanol). The mother liquor from the crystallization yielded 0.405 g of starting material II.

Anal. Calcd for $C_{19}H_{21}NO_7S_2 \cdot 0.5H_2O$: C, 50.88; H, 4.94; N, 3.12. Found: C, 51.13; H, 5.26; N, 3.08.

N-Tosylhydroxy-L-proline Methyl Ester (IV).—A cold solution of 2.1 g (0.0073 mole) of compound II in 15 ml of methanol was treated with an ethereal solution of diazomethane until a pale yellow color persisted. The solvent was removed and the residue was crystallized from benzene and petroleum ether (bp 60–68°). The yield of IV, mp 97.5–99°, $[\alpha]^{23}D$ −116.5° (*c* 1.86%, ethanol), was 2.02 g (91.8%). The infrared spectrum exhibited bands at 2.70 (OH), 5.72 (COOMe), 7.42, and 8.61 μ (N-Ts).

Anal. Calcd for $C_{13}H_{17}NO_5S$: C, 52.16; H, 5.72; N, 4.67. Found: C, 52.49; H, 5.75; N, 4.57.

N-Tosylhydroxy-L-prolinol (V).—A solution of 25 g (0.087 mole) of IV in 340 ml of dry tetrahydrofuran was cooled to 0°, and 10 g (0.454 mole) of lithium borohydride was added. The reaction mixture was stirred for 7 hr and allowed to stand at room temperature for 12 hr. After cooling with ice and addition of 170 ml of water followed by 65 ml of dilute HCl (1:1), the reaction mixture was heated on a water bath for 30 min, cooled to room temperature, and extracted with ethyl acetate. The extract was washed with 100-ml portions of 2 *N* NaOH, 2 *N* HCl, and finally water. It was then dried over sodium sulfate, concentrated, and cooled. The yield of V, mp 131–133°, $[\alpha]^{23}D$ −43.4° (*c* 1.86%, ethanol), was 19.4 g (86%). The infrared spectrum included bands at 2.96 and 3.10 μ (OH).

Preparation of V was also carried out by reduction of the ester (IV) or the acid (II) with lithium aluminum hydride in tetrahydrofuran solution. The yields of product were 42 and 56%, respectively.

Anal. Calcd for $C_{12}H_{17}NO_4S$: C, 53.12; H, 6.32; N, 5.16. Found: C, 53.32; H, 6.32; N, 5.29.

Tritosylhydroxy-L-prolinol (VI).—To a cooled solution of 28.6 g (0.15 mole) of tosyl chloride in 60 ml of pyridine there was added 19.2 g (0.071 mole) of N-tosylhydroxy-L-prolinol (V). The mixture was refrigerated at 10° for 72 hr and then poured into 500 ml of chilled 2 *N* HCl. The product was filtered off, washed with cold water, and recrystallized from ethanol. The yield of VI, mp 134.5–136°, $[\alpha]^{23}D$ −52.5° (*c* 1.92%, acetone), was 35.8 g (87.6%). The infrared spectrum showed some new bands at 7.32 and 8.55 μ which could be attributed to O-Ts. Hydroxyl bands were absent.

Anal. Calcd for $C_{26}H_{29}NO_8S_3$: C, 53.87; H, 5.04; N, 2.42; S, 16.59. Found: C, 53.63; H, 4.95; N, 2.41; S, 16.82.

2-Tosyl-5-benzyl-2,5-diazabicyclo[2.2.1]heptane (IX).—A solution of 11.59 g (0.02 mole) of compound VI and 6.42 g (0.06 mole) of benzylamine was refluxed for 50 hr in 40 ml of toluene. The reaction mixture was cooled to room temperature and filtered, and the solvent was removed at reduced pressure. The residue was recrystallized from ethanol and dried *in vacuo*. The yield of IX, mp 122–124°, $[\alpha]^{23}D$ +28.8° (*c* 1.64%, acetone), was 5.92 g (86.3%). The infrared spectrum showed bands at 7.45, 8.64 (N-Ts), and 14.32 μ (benzyl).

Anal. Calcd for $C_{19}H_{22}N_2O_2S$: C, 66.64; H, 6.48; N, 8.18. Found: C, 66.36; H, 6.47; N, 8.14.

N-Benzyl-2,5-diazabicyclo[2.2.1]heptane Dihydriodide (X).—A mixture of 45 ml of hydriodic acid, 54 ml of glacial acetic acid, 10.5 ml of water, 5 g (0.0146 mole) of IX, and 2.4 g of red phosphorus was refluxed for 3.5 hr and then left at room temperature overnight. The mixture was filtered and the residue was washed a few times with glacial acetic acid and then with water. The filtrate was removed *in vacuo* and the residue was freed from remaining HI by repeated distillation with 50-ml portions of glacial acetic acid. The residue was crystallized from glacial acetic acid to yield the crude dihydriodide salt. Recrystallization from water and glacial acetic acid yielded 4.95 g (76.1%) of X·2HI, mp 252–256° dec, $[\alpha]^{23}D$ −6.1° (*c* 2.7%, water). The infrared spectrum possessed no bands characteristic of the N-tosyl group (7.45 and 8.64 μ). The product (X) could be reconverted to intermediate IX by treatment with tosyl chloride.

Anal. Calcd for $C_{12}H_{16}N_2 \cdot 2HI$: C, 32.45; H, 4.09; N, 6.31. Found: C, 32.48; H, 4.23; N, 6.67.

2,5-Diazabicyclo[2.2.1]heptane Dihydrochloride (XI).—A solution of 4 g (0.009 mole) of X in 60 ml of water was treated with 1 drop of 10% solution of sodium bisulfite, refluxed for 15 min with 2 equiv of silver chloride, and filtered. The filtrate was treated with 10 ml of 2 *N* HCl and 1 g of 10% palladium-on-carbon catalyst, and hydrogenated at 40 psi for 20 hr. The mixture was filtered and the solvent was removed *in vacuo*. The residue was crystallized from absolute ethanol to afford 1.52 g (85%) of XI·2HCl, mp 272–278° dec, $[\alpha]^{23}D$ +41° (*c* 1.17%, water). The infrared spectrum showed the absence of the benzyl band at 14.32 μ.

Anal. Calcd for $C_5H_{10}N_2 \cdot 2HCl$: C, 35.10; H, 7.07; N, 16.38. Found: C, 35.07; H, 7.25; N, 16.65.

N-Tosyl-2,5-diazabicyclo[2.2.1]heptane (XII).—A solution of 0.91 g (0.00266 mole) of compound IX in a mixture of 10 ml of ethanol and 4 ml of 1 *N* HCl was treated with 0.2 g of 10% palladium-on-carbon catalyst and shaken at a hydrogen pressure of 40 psi for 5 hr. After the reaction mixture was filtered, solvent was partially removed *in vacuo* and the remaining aqueous solution was cooled and rendered basic with NaOH solution. The crystalline product was collected, washed with water, and dried. The yield of XII, mp 130–132°, $[\alpha]^{23}D$ +19.3° (*c* 2%, chloroform), was 0.59 g (87%). The infrared spectrum included bands at 3.05 (NH) and 8.62 μ (N-Ts). The band at 14.32 μ (benzyl) was absent.

Anal. Calcd for $C_{12}H_{16}N_2O_2S$: C, 57.12; H, 6.39; N, 11.10. Found: C, 57.62; H, 6.65; N, 10.81.

N,N-Ditosyl-2,5-diazabicyclo[2.2.1]heptane (XIII).—To a solution of 0.23 g (0.0012 mole) of tosyl chloride in 1 ml of pyridine there was added a solution of 0.25 g (0.001 mole) of XII in 2 ml of pyridine. The solution was left at room temperature

(11) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

(12) F. A. L. Anet, *Can. J. Chem.*, **39**, 789 (1961), and references cited therein.

(13) All melting points are corrected.

(14) E. W. McChesney and W. K. Swann, *J. Am. Chem. Soc.*, **59**, 1116 (1937).

for 22 hr and was then poured into water. The mixture was acidified with HCl and the oil which separated was extracted into chloroform. The chloroform solution was evaporated under reduced pressure, leaving a glassy product which was crystallized from ethanol. The yield of XIII, mp 122–123°, $[\alpha]^{23}D$ −70° (*c* 2%, chloroform), was 0.38 g (98%). The infrared spectrum showed strong bands at 7.45 and 8.65 μ (N–Ts), whereas the band at 3.05 μ (N–H) was absent.

Anal. Calcd for $C_{19}H_{22}N_2O_4S_2$: C, 56.14; H, 5.46; N, 6.89. Found: C, 56.02; H, 5.72; N, 6.81.

Stereoselectivity in the N-Methylation of Certain Azabicyclic Systems[1]

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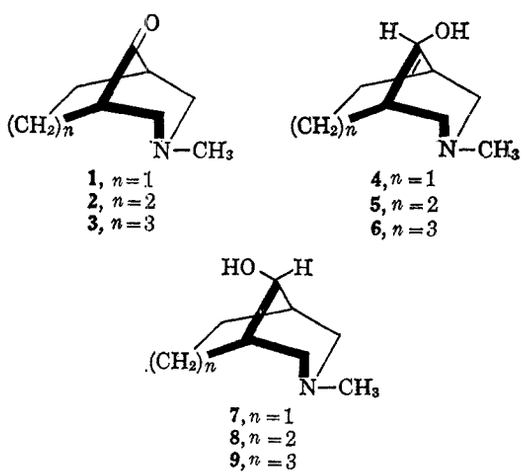
Received October 1, 1965

The reactions of the N-methyl azabicyclic ketones **1–3** and alcohols **4–9** with trideuteriomethyl *p*-toluenesulfonate have been examined to determine the degree of stereoselectivity with which the trideuteriomethyl group is introduced to form a quaternary ammonium salt. The predominant stereoisomer in these cases comprised from 60 to 90% of the mixture of quaternary ammonium salts; the predominant reaction path was shown to be the same for both the ketones and the alcohols. The preferred direction of attack at nitrogen is assigned as *syn* to the oxygen function.

The availability of the amino ketones **1–3** as well as the corresponding β (**4–6**) and α (**7–9**) secondary alcohols[2] prompted us to study the degree of stereospecificity which would be associated with the N-alkylation of these amines. Studies of the addition reactions of ketones **1–3**[2c,3] have demonstrated that steric hindrance at the carbonyl group from the methylene chain increased in a regular manner as the chain was lengthened from two carbon atoms (as in **1**) to three and then to four atoms (as in **3**). It was of interest to learn whether a similar steric effect might be observed for reactions at the nitrogen atom[4,5] and also whether the stereochemistry of reaction at the nitrogen atom might be influenced by the nature or steric arrangement of the oxygen function (*i.e.*, ketone, α alcohol, or β alcohol).[6]



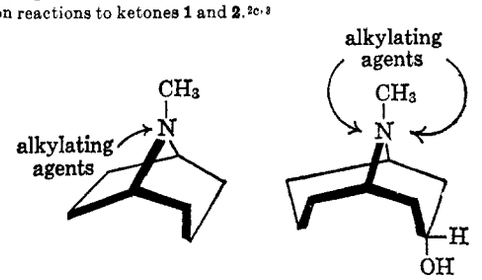
1, $n=1$ **2**, $n=2$ **3**, $n=3$

4, $n=1$ **5**, $n=2$ **6**, $n=3$

7, $n=1$ **8**, $n=2$ **9**, $n=3$

To examine these possibilities, each of the amines **1–9** was allowed to react with trideuteriomethyl *p*-toluenesulfonate in acetone solution to form trideuterio derivatives of the known[2a,2c] dimethylammonium *p*-toluenesulfonates **10–18** in which the methyl group introduced by N-alkylation was labeled with deuterium.[7,8] The stereoselectivity of the alkylation of amines **1–7** could be determined from the nmr spectra of the corresponding salts **10–16** because the nmr signals for the two N-methyl groups appeared as separate singlets.[2a,c] The proportions of isomers present in the salt **17** (in which the two N-methyl signals coincided) could be established by catalytic oxidation[9] to the corresponding keto derivative **11**.

(4) Investigations[5] of the stereochemistry of N-alkylation of tropane (i) and granatanol (ii) have led to the generalizations summarized in the accompanying formulas. These stereochemical results parallel the results of addition reactions to ketones **1** and **2**.[2c,3]



i ii

(5) For studies of the N-alkylation of tropane and granatanine derivatives, see (a) G. Fodor, J. Toth, and I. Vincze, *Helv. Chim. Acta*, **37**, 907 (1954); (b) G. Fodor, J. Toth, and I. Vincze, *J. Chem. Soc.*, 3504 (1955); (c) O. Kovacs, G. Fodor, and M. Halmos, *ibid.*, 873 (1956); (d) G. Fodor, K. Koczka, and J. Lestyan, *ibid.*, 1411 (1956); (e) G. Fodor, I. W. Vincze, and J. Toth, *ibid.*, 3219 (1961); (f) C. H. MacGillavry and G. Fodor, *ibid.*, 597 (1964); (g) G. Fodor, F. Uresch, F. Dutka, and T. Szell, *Collection Czech. Chem. Commun.*, **29**, 274 (1964); (h) G. L. Closs, *J. Am. Chem. Soc.*, **81**, 5456 (1959); (i) H. L. Holmes in "The Alkaloids," Vol. 1, R. H. F. Manske and H. L. Holmes, Ed., Academic Press Inc., New York, N. Y., 1950, pp 271–374; (j) G. Fodor, *Tetrahedron*, **1**, 86 (1957); (k) G. Fodor in "The Alkaloids," Vol. 6, R. H. F. Manske, Ed., Academic Press Inc., New York, N. Y., 1960, pp 145–177.

(6) For example, the hydroxyl function in the β isomers **4–6** might be expected to solvate the leaving group during alkylation at nitrogen and, consequently, favor attack of the alkylating agent from the direction *syn* to the hydroxyl function. For a possible example of this sort of directional effect in a carbon alkylation, see F. J. McQuillin and R. B. Yeats, *J. Chem. Soc.*, 4273 (1965), and earlier papers cited.

(7) Since our earlier studies[2c] had demonstrated that even in the presence of the much better nucleophile, iodine ion, these quaternary salts did not undergo rapid reversal (by a displacement by iodide ion at an N-methyl group) at temperatures below 200°, we are confident that the *p*-toluenesulfonate salts obtained in this study are the result of kinetically controlled processes.

(8) The use of trideuteriomethyl iodide to study the stereoselectivity of alkylation of N-methylaziridine derivatives has recently been reported by A. T. Bottini and R. L. Van Etten, *J. Org. Chem.*, **30**, 575 (1965).

(9) For a recent review, see K. Heyns and H. Paulsen in "Newer Methods of Preparative Organic Chemistry," Vol. 2, W. Foerst, Ed., Academic Press Inc., New York, N. Y., 1963, p 303.

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(2) (a) H. O. House, P. P. Wickham, and H. C. Müller, *J. Am. Chem. Soc.*, **84**, 3139 (1962); (b) H. O. House and H. C. Müller, *J. Org. Chem.*, **27**, 4436 (1962); (c) H. O. House, H. C. Müller, C. G. Pitt, and P. P. Wickham, *ibid.*, **28**, 2407 (1963).

(3) H. O. House and W. M. Bryant, III, *ibid.*, **30**, 3634 (1965).