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# Conformational Analysis. Effect of a Vicinal Hydroxyl Group on the Methylation Rates of Cyclohexyldimethylamines and *trans*-Decalyldimethylamines

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*Received August 12, 1974*

The rates of methylation of the four 3-dimethylamino-*trans*-2-decahydronaphthols, of the *cis*- and *trans*-2-dimethylaminocyclohexanols, as well as those of the corresponding "parent" amines have been measured as a function of temperature. The rate of the *cis*-3-dimethylamino-*trans*-decahydronaphthol **2** is found to be unusually high for a compound with an axial dimethylamino group and confirms the flattened chair conformation assigned to this compound. The difference in reactivity between axial and equatorial dimethylamino groups seems to be of steric origin (a much more restricted transition state in the former case). An unusual feature of the reaction is that in cases involving an equatorial dimethylamino group the rate constant of the diequatorial isomer is significantly much lower than that of the isomer with an axial hydroxyl group.

Although the reaction of alkyl halides with tertiary amines (Menschutkin reaction) has been extensively studied,[3] there is relatively little information regarding the rates of alkylation of simple conformationally stable exocyclic amines.[4-6] In this work we report the rates of methylation in acetonitrile of the four 3-dimethylamino-*trans*-2-decahydronaphthols (**1**, **2**, **3** and **4**), of the *trans*- and *cis*-dimethylaminocyclohexanols (**5** and **6**), and of the corresponding parent amines (**7**, **8**, and **9**).

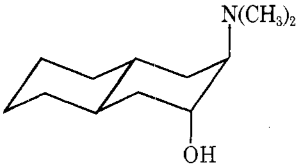
## Results and Discussion

The results of the methylation of the four 3-dimethylamino-*trans*-2-decahydronaphthols (**1–4**), of the *trans*- and *cis*-dimethylaminocyclohexanols (**5** and **6**), of the *trans*- and *cis*-2-decalyldimethylamines (**7** and **8**), and of the cyclohexyldimethylamine are summarized in Table I. The kinetic measurements have been effected in acetonitrile so as to compare them with Allinger's results on *tert*-butylcyclohexylamines. Acetonitrile being in fact a good proton acceptor, it had to be checked that no competition was taking place between the intramolecular H bond and H bond with acetonitrile; to settle this point we have observed the NMR spectra in this solvent and we do not find any variation in half-width band height for the proton $\alpha$ to the substituent. Furthermore, for the compound **2**, deformed by a strong H bond, one finds a value of 22 Hz for the $W_{1/2}$ of the proton $\alpha$ to OH, this value being the same in $CDCl_3$.

The rates constants were evaluated graphically; these values are the average of at least three independant determinations.

The values of $\Delta H^{\ddagger}$ were obtained from the gradient of plots of log $k/T$ against the reciprocal of the absolute temperature; the values of $\Delta S^{\ddagger}$ were obtained from the Eyring equation, i.e., from the gradient of $T$ log $k/T$ against $T$. The precision of the value of $k_2$ is of the order of 1%. The error of the $\Delta S^{\ddagger}$ value is of the order of 1 eu.

First, it may be noted that the compounds in which the dimethylamino group occupies an axial position react more slowly than those in which this group occupies an equatorial position. This is what one would expect, inasmuch as it is experimentally known that axial groups undergo reactions at reduced rates when compared to equatorial groups, in



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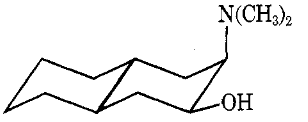

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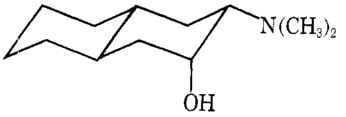

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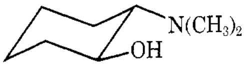

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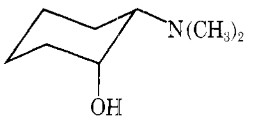

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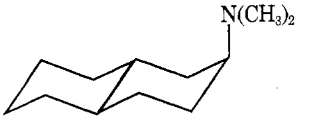

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### Table I
### Second-Order Rates of Methylation in Acetonitrile and Activation Parameters

| Compd | Temp, °C | $k_2$, $10^4$ l. mol$^{-1}$ sec$^{-1}$ | $\Delta G^‡$(273 K), kcal mol$^{-1}$ | $\Delta H^‡$ kcal mol$^{-1}$ | $\Delta S^‡$, eu |
|---|---|---|---|---|---|
| | 0.0 | 0.685 | | | |
| **1** | 10.0 | 1.68 | 21.2 | 12.1 | −33.4 |
| | 20.0 | 2.10 | | | |
| | 0.0 | 2.44 | | | |
| **2** | 10.0 | 5.09 | 20.6 | 11.1 | −34.6 |
| | 20.0 | 10.1 | | | |
| | 0.0 | 62.5 | | | |
| **3** | 10.0 | 115.3 | 18.4 | 9.5 | −32.6 |
| | 20.0 | 217.2 | | | |
| | 0.0 | 6.70 | | | |
| **4** | 10.0 | 14.0 | 19.9 | 9.3 | −38.7 |
| | 20.0 | 25.8 | | | |
| | 0.0 | 5.64 | | | |
| **5** | 10.0 | 11.9 | 19.7 | 10.4 | −34.3 |
| | 20.0 | 23.1 | | | |
| | 0.0 | 64.6 | | | |
| **6** | 10.0 | 128.2 | 18.7 | 9.8 | −32.3 |
| | 20.0 | 241.9 | | | |
| | 0.0 | 1.99 | | | |
| **7** | 10.0 | 4.06 | 21.6 | 10.35 | −41.6 |
| | 20.0 | 7.92 | | | |
| | 0.0 | 237.8 | | | |
| **8** | 10.0 | 488.6 | 17.9 | 8.9 | −32.6 |
| | 20.0 | 895.4 | | | |
| | 0.0 | 154.5 | | | |
| **9** | 10.0 | 364.5 | 20.77 | 11.2 | −35.2 |
| | 20.0 | 719.3 | | | |

cases in which the congestion increases in the product (and hence in the transition state) relative to the starting material.[7-10] In the case of the "parent" amines, the *trans*-2-decalyldimethylamine (**7**) reacts some 120 times more slowly than the corresponding cis isomer (**8**) at the same temperature, and this is in good agreement with the results obtained by Sicher and coworkers.[5] The difference in reactivity between axial and equatorial isomers which amounts to a free-energy difference of about 3 kcal mol$^{-1}$ led Sicher to suggest the possibility of the axial compound reacting through a boat form transition state in which the dimethylamino group was in an equatorial position. A consideration of the activation entropies, however, casts great doubt upon such a transition state for the axial compound. Thus the activation entropy value of −41 eu for the axial compound as compared to that of −32 eu for the equatorial compound is in favor of a much more congested and restricted transition state in the former case, and this would be true only if the transition state in this compound still resembled the initial state. Since the final product in this reaction is still chair, there is no reason to think that the axial isomer undergoes reaction through a boat form transition state.

Secondly, it is observed that all the amino alcohols (with the exception of **2**) react more slowly than the corresponding "parent" amines. Thus in all of the amino alcohols (with the exception of **2**), the overall effect of the vicinal hydroxyl group is a "retarding" effect and can be expressed by the ratio $k_H/k_{OH}$, where $k_H$ and $k_{OH}$ are the rate constants of parent amine and amino alcohol, respectively. The actual magnitude of the rate retardation is, however, found to differ according to the mutual steric positions of the functional groups.

| Compd | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| $k_H/k_{OH}$ | 3 | 0.8 | 4.2 | 39 | 32 | 2.5 |

In the discussion which follows we find it convenient to treat separately the compounds in which the dimethylamino group occupies an equatorial position from those in which this group occupies an axial position.

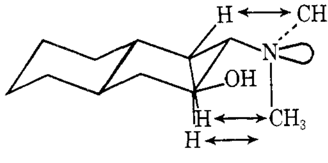
**Compounds with an Equatorial Dimethylamino Group.** We include in this class the *trans*- and *cis*- (**5** and **6**) dimethylaminocyclohexanols because in both compounds the conformational equilibrium is almost totally displaced toward the conformer with the dimethylamino group in an equatorial position.[11] It is thus found that the two trans isomers (**4** and **5**) react more slowly than the corresponding cis isomers (**3** and **6**), and that the ratio $k_H/k_{OH}$ is different in going from the cyclohexane to the decalin series. The smaller retardation ratio in the former (**5** and **6**) case could be due either to an equilibrium not totally displaced or to a more facile deformation of the cyclohexane system. On the other hand, the variation of the ratio $k_H/k_{OH}$ in going from the cis to the trans compounds is almost the same for the two series (2.5:32 and 4.2:39, respectively, for the cyclohexane and decalin series).

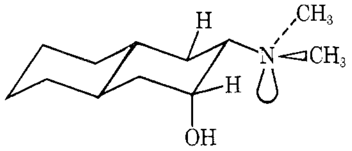
The higher reactivity of the cis compounds as compared to that of the trans compounds is difficult to predict inasmuch as it is known that intramolecular hydrogen bond formation in diequatorial compounds involves a "puckering" of the chair whereas in the cis compounds the approach of the two functional groups involves a flattening of the chair.[12] It would seem, then, in view of this fact, that the diequatorial compounds would undergo reaction more rapidly than the cis compounds, the breaking of the hydrogen bond needing less energy in the former case than in the latter.

However, similar results have been observed in the Menschutkin reaction on the 4-*tert*-butyl-2-methyldimethylcyclohexylamines for which Sicher and coworkers[5] report a higher reactivity for the cis isomer than for the trans isomer. Some findings related to those observed in this reaction are reported in the literature. Thus, Chapman and coworkers[13] have shown that the rate with an equatorial carboxyl group undergoes acid-catalyzed esterification and is much less affected by a vicinal axial group than it is by a vicinal equatorial group. Again, in oxime formation on the 4-*tert*-butyl-2-methyl-1-acetylcyclohexanes, analogous rate relationships have been observed by Heymes and Dvolaitzky.[14]

For all these reactions a number of interpretations have been proposed. Thus, in the Menschutkin reaction on the 4-*tert*-butyl-2-methyldimethycyclohexylamines, Sicher explains the different reactivities of the four isomers from a consideration of conformational energies (*A* values) and arranges them in the following order of stability: $NMe_2$(e) Me(e) > $NMe_2$(e) Me(a) > $NMe_2$(a) Me(e) > $NMe_2$(a) Me(a). The retarding effect due to the introduction of a vicinal methyl group seems then to increase with increasing stability in the ground state. Corresponding considerations of the transition-state energies ought to be envisaged, and according to Sicher,[5] it is probable that the transition states of the four isomers would be deformed, this deformation, or tension equivalent to it, preexisting in the ground states of the two cis and diaxial isomers whereas in the case of the *diequatorial isomer the deformation energy should* be added as part of the activation energy of the reaction.

This interpretation, although attractive, does not seem to explain the whole situation as regards the compounds studied in this paper. Indeed it is unlikely that the same stability order could apply to the compounds under study in this paper inasmuch as intramolecular hydrogen bonding in the cis isomers would tend to stabilize them whereas the opposite would be true in the diequatorial isomer.[12] As we have been able to show that the cis isomer **3** as well as its quaternary ammonium salt exist in a normal nondeformed chair conformation,[15] we think that the low reactivity of the diequatorial isomer **4** is most probably due to steric hindrance in the transition state. Examination of Dreiding models sheds light on this situation. In the intramolecularly hydrogen bonded conformation in this isomer, one of the methyl groups has syn-axial interactions with the two hydrogens in positions 2 and 4 and the other methyl group has a syn interaction with the equatorial hydrogen in position 4, whereas in the cis isomer **3** such syn interactions do *not exist.*





As the third methyl group is introduced to form the quaternary ammonium salt (which is what takes place in the transition state) a much more important steric hindrance to the free rotation of the trimethylammonium group being formed is introduced in the trans compound than in the cis compound. This state of affairs is clearly demonstrated by the calculated activation entropies. While the activation enthalpies are similar (9.54 kcal for isomer **3** and 9.34 kcal for isomer **4**), the activation entropies, on the other hand, differ considerably (−32 eu for **3** and −38 eu for **4**).

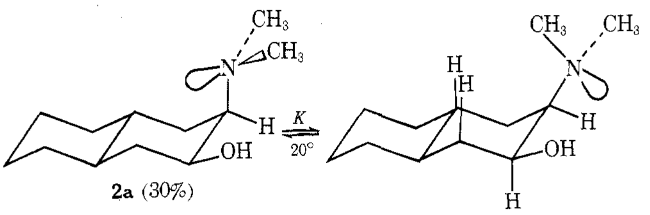
The same reasoning can also apply to the 4-*tert*-butyl-2-methyldimethylaminocyclohexanes of Sicher. Indeed, the hindrance to the free rotation of the trimethylammonium group, as a result of the presence of the vicinal methyl group, should be even greater; the methyl group being bulkier than the hydroxyl group, the retarding effect due to the introduction of a vicinal methyl group, here expressed as the ratio $k_H/k_{CH_3}$ (10 and 227 for the cis and trans isomers, respectively) is much greater than the corresponding ratios observed for the amino alcohols (4 and 39 for the cis and trans isomers, respectively).

This interpretation can thus be rationalized to account for the differences in reactivity observed between cis and trans isomers in this group of reactions. It is evident that kinetic studies evaluating entropy factors ought to be performed to justify the validity of such a generalization.

An approximate evaluation of the steric factors intervening in the transition states of compounds **3** and **4** can be reached by assuming that the activation enthalpy of the reaction consists of two factors, viz., an electronic factor, corresponding to the breaking of the hydrogen bond, and a steric or entropy factor corresponding to the attack by the methyl iodide. Thus, taking 5.8 and 2.0 kcal/mol as the respective hydrogen bond enthalpy values in the cis and trans isomers,[16] and by assuming that the two isomers are *energetically on the same level,*[17] *one shows that the steric* factor is 7.34 kcal/mol in the trans isomer (**4**) whereas it is only 3.7 kcal/mol in the cis isomer (**3**). It is thus found that the steric factor outweighs the electronic factor in the trans isomer, clearly showing the importance of steric factors in the transition state and therefore the validity of our interpretation.[22]

**Compounds with an Axial Dimethylamino Group.** In the case of the diaxial isomer **1** the ratio $k_H/k_{OH}$ is equal to 3. This small value corresponds to a very slight steric hindrance of the hydroxyl group to the attack of methyl iodide by the amine. That this is so is clearly illustrated by comparison with the retarding effect due to a vicinal methyl group in the analogous *tert*-butyl compound, where this effect, expressed as the ratio $k_H/k_{CH_3}$, is only 1.[5] Thus, we attribute the low activity of compound **1** compared to that of the parent amine **7** as solely arising from the inductive effect of the hydroxyl group. By virtue of its tendency to attract electrons, the hydroxyl group will tend to "pull in" the lone-pair electrons toward the nitrogen atom and thereby render it less accessible to attack by the methyl iodide.

The situation in the cis isomer **2** is of particular interest. Thus, it has been shown that compound **2** actually exists as a mixture of two conformers (**2a** and **2b**) in equilibrium,[18] conformer **2a** being in a normal chair form whereas conformer **2b** adopts a flattened chair conformation and is responsible for the bonded hydroxyl band in the infrared spectrum.



**2a** (30%)

**2b** (70%)

The NMR spectrum of the tetradeuterated compound[15] of this isomer shows an unusually high coupling constant between the two protons in positions 2 and 3 for an angle of 60°, this confirming the presence of conformer **2b**. The same type of flattening was observed for the quaternary ammonium salt of the diaxial isomer **1**, it being even more pronounced in the quaternary ammonium salt of isomer **2**, where it results in a "twist chair" conformation.

The ratio here observed, $k_H/k_{OH} = 0.8$, would tempt one to think that the vicinal hydroxyl group had, so to speak, an "accelerating" effect on the reaction of the amine with methyl iodide. This unexpected high reactivity should, however, not come as a surprise and is in fact in agreement with the flattened chair conformation assigned to this compound. Furthermore, the presence of 30% of conformer **2a** (at 20°) should lower the rate constant of conformer **2b**, the observed methylation rate constant being that of the equilibrium mixture.[19] Thus, applying the method independently developed by Eliel[20] and Winstein[21] to this equilibrium, $k_{\text{obsd}} = (k_eK + k_a)/(K + 1)$ where $k_{\text{obsd}}$ is the measured rate constant, $k_e$ and $k_a$ the rate constants of pure equatorial and axial compounds, respectively, and $K$ the equilibrium constant = 2.3 at 20°, and, by assuming that the conformer **2a** has the same rate constant as the diaxial isomer **1**,[23] the calculated rate constant for the conformer **2b** at 20° is found to be $13.6 \times 10^{-4}$ l. mol$^{-1}$ sec$^{-1}$. It is thus found that this conformer **2b** reacts much more quickly than compounds **1** and **7** and slower than the compounds with an equatorial dimethylamino group.

The activation enthalpies for the two isomers (**1** and **2**) are calculated to be 12.1 and 11.1 kcal mol$^{-1}$, respectively, values slightly higher than that of 10.3 kcal mol$^{-1}$ calculated for the parent amine. The activation entropies are, however, found to be more positive for the two isomers (−33 eu for **1** and −34 eu for **2**) as compared to that of −41 eu for the parent amine. The entropy value found for the diaxial compound **1** is quite surprising because, in principle, the transition state of this isomer ought to have the same degree of congestion as that of the parent amine, unless the presence of the vicinal hydroxyl group equally axial brings about a flattening of the substituted ring at the moment of attack by the methyl iodide and thereby places the trimethylammonium group being formed out of the 1,3-syn axial interactions with the axial protons in positions 1 and 10, thus resulting in a much less congested transition state. Such a transition state would indeed be compatible with the flattened chair conformation assigned to the quaternary ammonium of this isomer.[15]

The activation entropy value of −34.6 eu for the isomer **2** agrees quite well with the flattened chair conformation attributed to it; the dimethylamino group, being in a pseudoequatorial position, would be expected to be already free of the syn-1,3-axial interactions. This finding, however, would seem to be incompatible with the almost diequatorial conformation of this isomer; the angle between the amino and hydroxyl groups being smaller than the corresponding angle in the diequatorial isomer **4**, one would expect a much more hindered situation and therefore a much more negative activation entropy value in this case. However, the steric environment in this isomer is different from that of isomer **4** as revealed by examination of molecular models. Thus, intramolecular hydrogen bond formation in this isomer orients the two methyl groups out and away from the syn-axial interactions present in the diequatorial isomer, and since the C–N bond is only pseudoequatorial, the free electron pair is accessible to attack by the methyl iodide. Another possibility could be that of this isomer undergoing reaction through a transition state in which the substituted ring is in a boat form (or further still a twist form). However, a comparison of the activation entropies of this isomer (−34 eu) with that of −32 eu for the other cis isomer **3** seems to render such a transition state unlikely.[24] If, however, such were the case, the entropy of activation of a boat being greater than that of a chair form,[25] other things being equal, the activation entropy of isomer **2** would be expected to become more positive than that of isomer **3**, which, unfortunately, it does not. It would then seem reasonable to conclude that the observed rate constant and the activation entropy value found for this isomer are in agreement with a flattened chair conformation assigned to it and that the transition state is still flattened, the passage into the twist chair conformation of the methiodide salt taking place only after the transition state, as illustrated in Figure 1.[35]

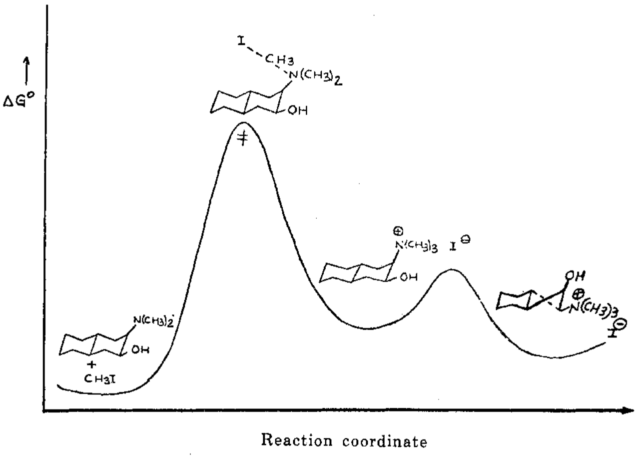


**Figure 1.**

## Conclusion

The influence of the inductive effect of the hydroxyl group on the methylation rate is feeble, since in cases where the hydroxyl group has practically no steric hindrance or no hydrogen bonding (case of the diaxial isomer), the observed retarding effect is relatively small. In cases where there is hydrogen bonding, it is possible to assess the steric effects due to the bulky trimethylammonium group, these effects being more marked in the diequatorial compound **4**. This reaction, very sensitive to small conformational differences around the reaction center, gives evidence for a notable deformation in compound **2**.

Lastly, the study of the substitution reaction (Menschutkin reaction) of these amino alcohols helps to explain the results in elimination reactions (Hofmann,[26] Wittig, Cope[27]).

## Experimental Section

Melting points were taken on a Dr. Tottoli melting point apparatus and are uncorrected. Composition and homogeneity of liquid samples were monitored by a Barber-Colman gas chromatograph series 5000 using an 8-ft Carbowax 20M over 3% Anakrom column. Microanalyses were performed by the Microanalysis Laboratories, Montpellier. The compounds used in this study were synthesized by standard stereospecific routes, from starting materials of known conformation. The pseudo-first-order rate constants for the methylation in acetonitrile with a 500-fold excess of methyl iodide were measured by means of a conductimetric bridge.[28-31] These were converted to second-order constants by the simple relation $k_2 = k_1/[CH_3I]$, where $[CH_3I]$ is the molar concentration of methyl iodide.

The enthalpies $\Delta H^‡$ and entropies $\Delta S^‡$ of activation were calculated directly from the experimental kinetic data by the method of least squares with the aid of the expression given by Cagle and Eyring.[32]

***trans*-Δ²-Octalin.** this compound was prepared by the diene condensation of *p*-benzoquinone and butadiene according to the method of Johnson,[33] bp 77° (14 mm) [lit.[32] bp 59° (8 mm)]. VPC showed that this compound was homogeneous.

**2,3-Epoxy-*trans*-decalin** was prepared by reaction of the *trans*-Δ²-octalin with *p*-nitroperbenzoic acid, bp 106° (22 mm) [lit.[32] bp 105° (21 mm)].

**3(a)-Dimethylamino-*trans*-2(a)-decahydronaphthol (1).** This compound was prepared directly from the epoxide by reaction with an alcoholic solution of dimethylamine, mp 76–78°. Anal.

Calcd for $C_{12}H_{23}NO$: C, 73.04; H, 11.75; N, 7.10; O, 8.11. Found: C, 73.36; H, 11.36; N, 7.16; O, 8.68.[31]

**3(a)-Dimethylamino-*trans*-2(e)-decahydronaphthol (2).** This compound came from 3(a)-amino-*trans*-2(a)-decahydronaphthol, which was converted to the cis isomer by the usual method, i.e., via the oxazoline. Dimethylation of the amino alcohol gave the *N,N*-dimethylamino compound **2**, mp 40–41°. Anal. Calcd for $C_{12}H_{23}NO$: C, 74.04; H, 11.75; N, 7.10; O, 8.11. Found: C, 73.96; H, 11.43; N, 7.25; O, 8.30.[31]

**3(e)-Dimethylamino-*trans*-2(a)-decahydronaphthol (3)** was obtained by reduction of 3(e)-amino-*trans*-2-decalone chloride over platinum oxide, followed by dimethylation of the amino alcohol, mp 61–62°. Anal. Calcd for $C_{12}H_{23}NO$: C, 73.04; H, 11.75 ; N, 7.10; O, 8.11. Found: C, 72.91; H, 11.39; N, 7.28; O, 8.35.[31]

**3(e)-Dimethylamino-*trans*-2(e)-decahydronaphthol (4).** This compound was prepared from 3(e)-hydroxy-*trans*-2(e)-decalinecarboxylic acid according to a known procedure, mp 51–52°. Anal. Calcd for $C_{12}H_{23}NO$: C, 73.04; H, 11.75; N, 7.10; O, 8.11. Found: C, 73.23; H, 11.31; N, 7.18; O, 8.26.[34]

***trans*-2-Dimethylaminocyclohexanol (5).** This compound was prepared from 1,2-epoxycyclohexane by a method identical with that used for compound **1**, bp 105–106° (25 mm). Anal. Calcd for $C_8H_{17}NO$: C, 67.13; H, 11.96; N, 9.79; O, 11.26. Found: C, 66.97; H, 11.92; N, 9.81; O, 11.30.

***cis*-2-Dimethylaminocyclohexanol (6).** This compound was prepared from 1,2-epoxycyclohexane by a method similar to that used for compound **2**, mp 72–73°. Anal. Calcd for $C_8H_{17}NO$: C, 67.13; H, 11.96; N, 9.79; O, 11.26. Found: C, 67.24; H, 11.99; O, 11.36.

**2-*trans-N,N*-Dimethylamino-*trans*-decalin (7).** This compound was prepared by reduction of *trans*-2-decalone oxime over platinum oxide. Dimethylation and purification via the hydrochloride salt (mp 235–236°) gave compound **7**. VPC showed that the compound was homogeneous. Anal. Calcd for $C_{12}H_{23}N$: C, 79.4; H, 12.60.

***2-cis-N,N*-Dimethylamino-*trans*-decalin (8)** was prepared by reaction of *trans*-decalytosylate with sodium azide, followed by dimethylation of the resulting amine (mp of hydrochloride salt 225°). VPC showed that the compound was homogeneous. Anal. Calcd for $C_{12}H_{23}N$: C, 79.6; H, 12.8.

***N,N*-Dimethylaminocyclohexane (9)** was prepared from the corresponding amine which was commercially available, bp 82° (19 mm).

**Kinetic Measurements.** The method used in the determination of rate constants was the same as that used by Allinger. Each compound ($5 \times 10^{-4}$ mol) was dissolved in 100 ml of acetonitrile (Merck purified by distillation from magnesium sulfate under nitrogen) and stored under nitrogen. Resistance measurements were made on 5-ml aliquots of the standard solution to which was added carefully weighed (approximately 0.5 ml) methyl iodide, using a Philips conductivity bridge, Model G.M. 4249. Dry nitrogen was passed through the solution during each run. The temperature control was such that no variation was greater than 0.1°. In order to better correlate the exposed results we have brought rate-constant values determined at different but close temperatures, at 0, 10 and 20°, by Arrhenius extrapolation (the experimental values are given in ref 1).

**Acknowledgments.** We are grateful to Professor N. L. Allinger of Georgia University for kindly communicating to us the kinetic details and for numerous suggestions and helpful discussion and to Professor Winternitz for help in the preparation of this manuscript.

**Registry No.**—**1**, 2454-63-9; **2**, 1204-73-5; **3**, 18289-82-2; **4**, 25690-15-7; **5**, 15910-74-4; **6**, 20431-82-7; **7**, 20184-40-1; **7** HCl, 38506-08-0; **8**, 19432-46-3; **8** HCl, 38506-06-8; **9**, 98-94-2; 2,3-epoxy-*trans*-decalin, 21399-51-9; 3(a)-amino-*trans*-2(a)-decahydronaphthol, 15875-02-2; 3(e)-amino-*trans*-2-decalone, 54003-43-9; cyclohexylamine, 108-91-8; 1,2-epoxycyclohexane, 286-20-4; *trans*-2-decalone oxime, 15876-37-6; *trans*-2-decalyltosylate, 54053-73-5.

## References and Notes

(1) Taken from the Doctorat de Specialité Thesis of J.G.S., submitted to the Faculté des Sciences et Techniques du Languedoc in fulfillment of the requirements for the Doctorat de Specialité, March 22, 1974.

(2) Assistant Laboratory Technician.

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(23) To a first approximation this assumption seems reasonable and it can be assumed that the diaxial isomer **1** and conformer **2a** will be subjected only to the inductive effect of the hydroxyl group and will thus have the same reactivity toward methyl iodide.

(24) The difference between these two values is evidently very small and goes in fact in the order of the error on the value of entropy. Thus, that difference is in good agreement with the more congested transition state in the case of the cis isomer with the amino group in pseudoaxial position; otherwise the boat transition state would be driven to a value of $\Delta S^\ddagger$ of approximately −27 eu.

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(35) We are thankful to a suggestion of one of the referees of this paper, who suggests that the difference in reactivity between the amine **7** and the amino alcohol **2** is coming from the difference in solvation in the transition state; the solvation would, in fact, be less due to electrostatic stabilization with the amino alcohol than with the amine. If this effect can come into play, it would, however, be difficult to measure; the authors do not think that it can explain the difference in reactivity, for it will intervene also in the case of the isomers in which $-N(Me)_2$ is equatorial, for which the $\Delta S^\ddagger$ values between amine and amino alcohols are not found to be so very different.