ACTA CHEMICA SCANDINAVICA 24 (1970) 2075–2083

The Hindered Internal Rotation in Some Enamines

KJELL-IVAR DAHLQVIST and STURE FORSÉN

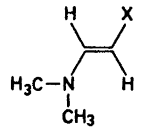
Division of Physical Chemistry, The Lund Institute of Technology, Chemical Center, P.O. Box 740, 220 07 Lund 7, Sweden

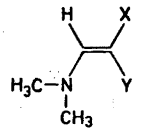
The hindered internal rotation of the *N,N*-dimethyl group in three enamines IV_a, IV_b, and IV_c has been studied by nuclear magnetic resonance (NMR) at 60 and 100 MHz. The interconversion rate has been evaluated by iterative fitting of the theoretical spectra to the experimental spectra using a digital computer. The free energy of activation ($\Delta F^{\ddagger}$) for the hindered internal rotation of the *N*-CH_3 group in the compounds studied is observed to depend on the exocyclic substituent in the following order

$$=C(COOEt)_2 < = O < = C(CN)_2$$

The entropy of activation was found to have large positive values (IV_a, $\Delta S^{\ddagger} = 13.9 \pm 3$ e.u., IV_b, $\Delta S^{\ddagger} = 11.5 \pm 3$ e.u.). The possible sources of these large positive entropies of activation are discussed.

The existence of a high barrier to the internal rotation of the $N(CH_3)_2$ group in simple amides [1–5] and thioamides [6] has been well established by nuclear magnetic resonance (NMR) spectroscopy, and a relatively high barrier to internal rotation for this group has also been found in the enamines $I_a - I_c$ [7,8] and $II_a - II_c$.[9]





I_a: X=CHO
I_b: X=COC_6H_5
I_c: X=$COOC_2H_5$

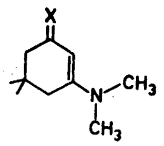
II_a: X=CN; Y=CN
II_b: X=CN; Y=$COOC_2H_5$
II_c: X=H; Y=NO_2

The large barrier to internal rotation around the $-\underset{|}{N}-\underset{|}{C}=$ bond in amides and in compounds such as I and II have sometimes been interpreted in terms of a push-pull conjugative interaction between the electron-donating and

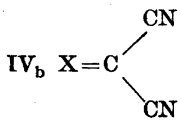
electron-attracting groups at either end of the conjugated system. If the angle of rotation around the $-N-C=$ bond is taken to be the reaction coordinate, the initial state is generally assumed to be the conformation in which the $N(CH_3)_2$ group is almost coplanar with the $-C=C$ trigonal plane, while in the transition state this group is twisted 90° out of this plane. The conjugative interaction between the "lone pair" electrons on the nitrogen atom and the rest of the π-electron system should thus be at a maximum in the initial state and largely destroyed in the transition state.

An interesting question in this connection is whether the $N(CH_3)_2$ group is planar or pyramidal in the transition state. No experimental means at present available can answer this question. Quantum mechanical calculations of CNDO or, preferably, *ab initio* type may on the other hand throw some light on the problem.

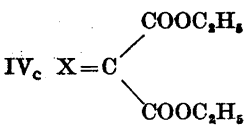
In the present study of substituent effects on the $=C-N-$ barrier in enamines we have chosen compounds of the following type



IV_a X=O



IV_b X=C(CN)(CN)

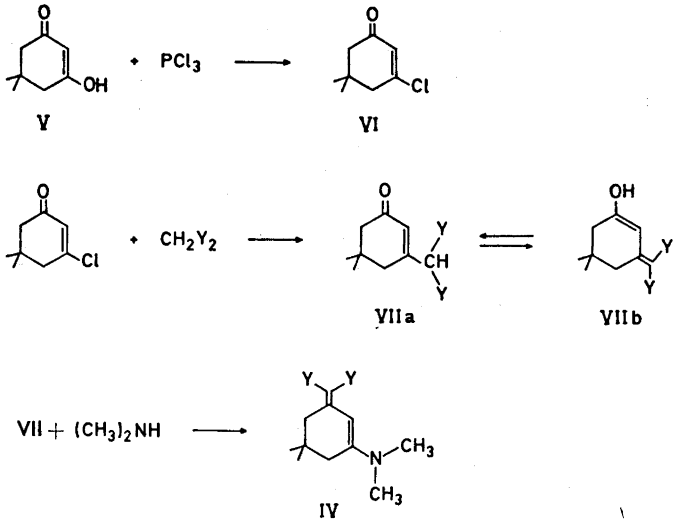


IV_c X=C(COOC$_2$H$_5$)(COOC$_2$H$_5$)

In these compounds the distance between the amino group and the substituent X is so large that steric and inductive interactions between them may be neglected or at least assumed to be the same in all cases. The substituent X is chosen to be symmetrical so that only one conformation is possible at the exocyclic double bond. It may thus be justified to assume that the $=C-N-$ barrier in IV_a-IV_c is mainly determined by conjugative effects.

EXPERIMENTAL

Compound IV_a was prepared directly from dimedone and dimethylamine in benzene at 100°C. Compounds IV_b and IV_c were prepared from dimedone according to the following route



IV_b: Y=CN
IV_c: Y=$COOC_2H_5$

NMR spectra in $CDCl_3$ solution show that compound VII exists in form b if Y=CN and in form a when Y=$COOC_2H_5$.

3-Dimethylamino-5,5-dimethyl-2-cyclohexenone (IV). 4.2 g dimedone, 4 ml dimethylamine and 30 ml benzene were heated in an ampoule at 100°C for 10 h. Evaporation of the solvent gave 4.6 g raw product. Sublimation gave 3.5 g yellow crystals, which upon recrystallization from cyclohexane three times yielded colorless crystals, m.p. 103.7—104.0°C. (Found: C 71.90; H 10.21. $C_{10}H_{12}NO$ requires C 71.81; H 10.24).

3-Dicyanomethyl-5,5-dimethyl-2-cyclohexenone (VII Y=CN). The sodium salt of malononitrile was prepared from 13.2 g malononitrile and 4.8 g sodium hydride in 100 ml dry diglyme. To this solution was added 15.8 g VI [14] and the mixture was stirred at room temperature over night. This mixture was then diluted with 500 ml cold water, acidified and extracted with chloroform. Evaporation of the chloroform and diglyme in vacuum gave 16.5 g crystals after recrystallization from carbon tetrachloride. Further recrystallizations gave pale yellow crystals m.p. 144.7—145.2°C. (Found: C 69.92; H 6.52. $C_{11}H_{12}N_2O$ requires C 70.19; H 6.43).

3-Dicarbethoxymethyl-5,5-dimethyl-2-cyclohexenone (VII Y=COOEt). Compound VII was prepared in the same way as the corresponding cyano compound from 15.8 g VI, 4.8 g NaH, and 32.20 ml diethylmalonate, but stirred at +75°C for 10 h. Distillation of the raw product gave 18.2 g of the desired compound, b.p. 146°/760 mm. (Found: C 63.89; H 7.89; $C_{15}H_{22}O_5$ requires C 63.81; H 7.85).

1-Dicyanomethylene-3-dimethylamino-5,5-dimethylcyclohexene (IVb). 2.80 g VII (Y=CN), 2.00 ml dimethylamine and 20 ml benzene were heated in an ampoule at 100°C for 10 h. Evaporation of the solvent gave 3.5 g dark crystals. Recrystallization from $CHCl_3$:CCl_4 (1:4) gave 2.5 g yellow crystals, which after three further recrystallizations melted at 239.5—240.5°C. (Found: C 72.30; H 8.20. $C_{13}H_{17}N_3$ requires C 72.52: H 7.96).

1-Dicarbethoxy-3-dimethylamino-5,5-dimethylcyclohexene (IVc). Compound IV_c was prepared in the same way as IV_b from 2.82 g VII (Y=COOEt) and 2.00 ml dimethylamine in 20 ml benzene. The raw product (3.2 g) was recrystallized three times from cyclohexane, m.p. 83.5—84.0°C. (Found: C 65.79; H 8.66. $C_{17}H_{27}NO_4$ requires C 65.99; H 8.80).

The NMR spectra were recorded between −90°C and +60°C using a Varian A60 NMR spectrometer equipped with a variable temperature probe and a V-6040 variable temperature controller, and a Varian HA 100 NMR spectrometer equipped with a variable temperature probe and a V-4343 variable temperature controller. The shifts were measured by the sideband technique using Hewlett Packard low frequency oscillators models 202A and 202C. The resolution of the spectrometer was adjusted so as to always obtain the same line-width (0.35 Hz) for the signals in the triplet from the traces of $CDHCl_2$ in the solvent. The NMR measurements used in the lineshape analysis were carried out using a 10 wt. % solution of the compounds in CD_2Cl_2 containing 5 wt. % TMS. The solvents were of commercial quality and used without further purification. The temperatures were obtained from the temperature dependent shift between the methylene and the hydroxyl protons in ethylene glycol dissolved to 50 wt. % in acidified CD_3OD. This solution was placed in a capillary which in turn was centered in the middle of the sample tube by means of two teflon plugs. The temperature dependent shift between the methylene and the hydroxyl protons in this glycol solution was calibrated against a copper-constantan thermocouple in a separate experiment according to a procedure described elsewhere.[10] The temperatures measured in this way are estimated to be accurate to about ±0.5°C.

Evaluation of the interconversion rate. The interconversion rate was evaluated according to the theory of Gutowsky, McCall and Slichter (GMS).[11] At slow interconversion rates, the two N-CH_3 groups were found to have unequal line-widths, probably due to unequal unresolved spin coupling constants to the ring protons. The equations describing the exchange broadening were therefore modified to take into account spin couplings to the interchanging protons. The lineshape function, v, is thus dependent on seven parameters according to eqn. (1)

$$v = f(J_1,J_2,J_3,J_4,\delta\nu,T_2,\tau) \quad (1)$$

In this equation J_1 and J_2 are the spin couplings from the ring protons to the low field N-CH_3 group, and J_3 and J_4 are the corresponding spin couplings to the high field N-CH_3 group. T_2 is the spin-spin relaxation time for the two N-CH_3 groups, $\delta\nu$ is the peak separation in the absence of exchange, and τ is the mean lifetime for the exchanging CH_3 protons at each site.

The parameters in eqn. (1) were obtained by iterative curve-fitting of theoretical spectra to experimental ones according to the method of least squares using the computer program LETAGROP VRID,[12] which was adapted for the Swedish computer TRASK. The various parameters in eqn. (1) were evaluated in the following way: The spin coupling constants, J_1, J_2, J_3, J_4 were determined by iteration of these together with T_2 and $\delta\nu$ so as to obtain the best fit between theoretical and experimental spectra in the limit of slow interconversion. These spin coupling constants were assumed to be temperature independent and therefore used for all higher temperatures. In the fast interconversion limit where τ no longer affects the line-width, T_2 was iterated in the curve-fitting procedure while the rest of the parameters in eqn. (1) were kept constant. The T_2 values obtained in this region were found to be about 30 % larger than those found at low temperatures, although the resolution of the spectrometer was kept constant as described in the experimental part. The spin-spin relaxation time for the intermediate temperatures were obtained from linear interpolation between those for the high and low temperatures.

The temperature dependence of the chemical shift difference $\delta\nu$ between the two dimethylamino signals was studied at several temperatures down to 30°C below the lowest temperature used in the determination of τ. No significant variation of $\delta\nu$ with the temperature was, however, observed. The difference between the largest and the smallest value of $\delta\nu$ in this region was less than 0.2 to 0.3 Hz. In the temperature region below the coalescence temperature $\delta\nu$ as well as τ were determined by computer analysis of the exchange broadened spectra using values for T_2 and J_1 to J_4 appropriate to each temperature (see above). Neither in this temperature region was any systematic temperature dependence found for $\delta\nu$. The difference between the largest and the smallest values of $\delta\nu$ was only about 0.1 to 0.2 Hz. For temperatures above the coalescence temperature the spectrum contains too little information to allow simultaneous determination of both $\delta\nu$ and τ, and thus only τ was iterated using the mean value of $\delta\nu$ determined below the coalescence temperature. Values of the parameters $\delta\nu$, T_2, and spin coupling constants for the N-CH_3 group in IV_a and IV_b are summarized in Table 1.

Table 1. Summary of the parameters $\delta\nu$, T_2, and spin coupling constants for compounds IV_a and IV_b at 60 and 100 MHz.

Compound	Resonance frequency MHz	t °C	$\delta\nu$[a] Hz	T_2 sec	Spin coupling constants
IV_a	60	−50	8.8	0.22	
	60	+10		0.30	$J_1=J_2=0$ [b]
	100	−45	14.4	0.20	$J_3=J_4=0.4$ [c]
	100	+10		0.27	
IV_b	60	−15	4.0	0.37	
	60	+40		0.44	$J_1=J_2=0.0$ [b]
	100	−10	6.3	0.30	$J_3={}_4J=0.5$ [c]
	100	+50		0.40	

[a] The chemical shift difference between the two N-CH_3 signals.
[b] Spin coupling constants to the low field N-CH_3 signal.
[c] Spin coupling constants to the high field N-CH_3 signal.

RESULTS AND DISCUSSION

The activation parameters for the $=C-N-$ rotation in the compounds

IV_a, IV_b, and IV_c are given in Table 2 and plots of ln $(1/\tau)$ *vs.* $10^3/T$ are shown in Figs. 1 and 2. For IV_c only $\Delta F_{T_c}^{\ddagger}$ (T_c is the coalescence temperature for the N-CH_3 signals) could be determined since the whole spectrum became broadened at temperatures below T_c, probably due to slow ring inversion. For this compound the value of $\Delta F_{T_c}^{\ddagger}$ was calculated from the coalescence temperature using the equation $2\pi\tau\delta\nu=\sqrt{2}$ and is therefore somewhat uncertain. The τ values used in the evaluation of E_a for IV_a and IV_b are mean values of five spectra at each temperature. At the coalescence temperature the difference between the highest and the lowest τ values in the five measure-

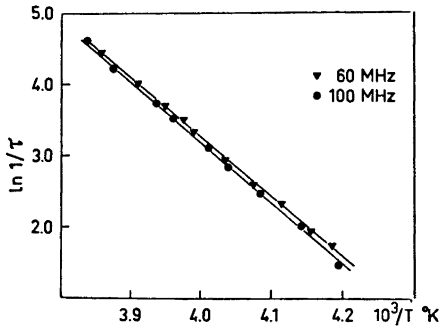


Fig. 1. Plots of ln$(1/\tau)$ *versus* $1/T$ for compound IV_a.

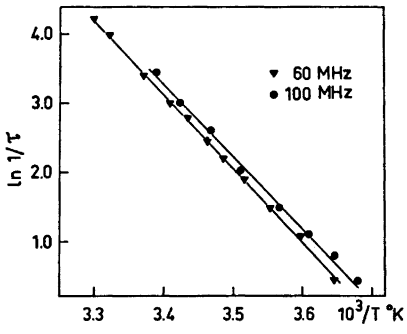


Fig. 2. Plots of ln$(1/\tau)$ *versus* $1/T$ for compound IV_b.

ments was generally not more than 2–4 %, while for the longest and shortest τ values used this difference was about 10 %.

Compounds IV_a and IV_b were investigated at both 60 and 100 MHz in order to obtain some indication of the magnitude of the experimental errors in the determination of the $=C-N-$ barrier for these substances. The activation parameters given in Table 2 were calculated assuming only random errors, which are probably lower than the "true" errors. A comparison between the values for E_a and $\Delta H^{\ddagger}$ obtained at 60 and 100 MHz indicates that a more realistic value for the errors in E_a and $\Delta H^{\ddagger}$ would be $\pm 0.50-0.70$ kcal/mol, while a realistic value for the error in $\Delta F^{\ddagger}$ might be *ca.* 0.2 kcal/mol. Using the error limits for $\Delta H^{\ddagger}$ and $\Delta F^{\ddagger}$ estimated above, the error in $\Delta S^{\ddagger}$ is calculated to be about $\pm 2-3$ e.u. These assumptions about the errors in the activation parameters are supported by other investigations of a similar nature.[10,13]

Table 2. Summary of activation parameters for the hindered $-N-C=$ rotation in compounds IV_a, IV_b, and IV_c. The errors given for these parameters were calculated assuming only random errors.

Compounds	Resonance frequency MHz	T °K	E_a kcal/mol	$\Delta H^{\ddagger}$ kcal/mol	$\Delta F^{\ddagger}_{298}$ kcal/mol	$\Delta S^{\ddagger}$ e.u.
IV_a	60	298.2	16.73 ± 0.06	16.14 ± 0.06	12.30 ± 0.13	13.23 ± 0.64
	100	298.2	16.94 ± 0.12	16.34 ± 0.12	12.30 ± 0.19	13.89 ± 1.04
IV_b	60	298.2	20.38 ± 0.40	19.79 ± 0.40	15.24 ± 0.59	15.36 ± 3.32
	100	298.2	21.10 ± 0.19	20.50 ± 0.19	15.31 ± 0.29	17.47 ± 1.61
IV_c	60	203.5	—	—	11.4 ± 0.5	—

As seen from Table 2 the activation parameters are sensitive to the nature of the exocyclic substituent X. As steric and inductive effects for the $N(CH_3)_2$ group may be assumed to be almost the same for IV_a-IV_c the magnitude of the activation parameters given in Table 2 may be correlated with the strength of the conjugative interaction between the dimethylamino group and the substituent X. In view of such an interpretation the present investigation thus indicates a greater "push-pull" interaction between the cyano and $N(CH_3)_2$ groups than between the ester and $N(CH_3)_2$ groups in enamines of this type. This is in agreement with the data for compounds II_a and II_b given by Mannschreck and Koelle [8] and also indicated by the larger Hammett σ_p value for the CN group ($\sigma_p(CN) = 0.66$) than for the $COOC_2H_5$ group ($\sigma_p(COOC_2H_5) = 0.44$).[14]

The entropy of activation $\Delta S^{\ddagger}$ for the hindered rotation of the $N(CH_3)_2$ group in IV_a and IV_b was found to be very large (*cf.* Table 2). This is very interesting in the light of the assumption of a zero entropy of activation for

hindered internal rotations which is sometimes made.[15] Careful NMR investigations of the $=C-N-$ rotation in simple amides have indeed given activation entropies around zero.[14] The high $\Delta S^{\ddagger}$ values made us suspect some systematic error in our evaluation of the activation parameters, and we thus rechecked the various steps in the evaluation of τ and recalibrated the temperature dependent shift in the "glycol" capillary from which the sample temperature was obtained. However, no evidence for hidden systematic errors in the evaluated activation parameters was found and the entropy of activation is probably significant to about ± 3 e.u., as estimated above.

A possible explanation for the large entropies of activation might be a temperature dependence in the activation enthalpy $\Delta H^{\ddagger}$. A linear temperature dependence in $\Delta H^{\ddagger}$ is, however, impossible to distinguish from a change in the entropy of activation.

If we assume

$$\Delta H^{\ddagger} = \Delta H_0^{\ddagger} - \alpha T \tag{2}$$

$\Delta S^{\ddagger}$ is then evaluated as

$$\Delta S^{\ddagger} = \frac{\Delta H_0^{\ddagger} - \alpha T - \Delta F^{\ddagger}}{T} \tag{3}$$

from which it follows that

$$\Delta S^{\ddagger} + \alpha = \frac{\Delta H_0^{\ddagger} - \Delta F^{\ddagger}}{T} \tag{4}$$

To account for an apparent $\Delta S^{\ddagger}$ value of $+15$ e.u. the total change in $\Delta H^{\ddagger}$ over a temperature interval of *ca.* 50°C need only be 0.75 kcal/mol. For the determination of a temperature dependence in $\Delta H^{\ddagger}$, from a nonlinear $\ln(1/\tau) - 1/T$ plot, the NMR method is not well suited due to the relatively large errors in the evaluation of τ and the short temperature region in which τ can be determined.

The positive entropy of activation may also originate in a solvent-solute and/or a solute-solute interaction which makes the initial state more structurally "rigid" than the transition state. As a change in the entropy of activation would also lead to a change in the free energy of activation, we have investigated $\Delta F^{\ddagger}$ for IV_a at T_c in different solvents and at different concentrations (see Table 3). These studies show that $\Delta F_{T_c}^{\ddagger}$ is very little affected by a change of the solvent or by a change of the solute concentration. One exception is methanol in which $\Delta F_{T_c}^{\ddagger}$ is about 1 kcal/mol larger than in the other solvents investigated. In methanol solutions of IV_a, on the other hand, the solvent-solute interactions are expected to be exceptionally strong due to the possibility of hydrogen bonding between the OH protons of the solvent and the carbonyl group of the solute. Judged from these studies of solvent and concentration effects, it seems likely that a solvent-solute and solute-solute stabilization of the initial state compared to the transition state is of minor importance for the magnitude of the entropy of activation associated with the $-N-C=$ rotation in enamines, at least as long as no specific interactions such as hydrogen bonds are involved.

Table 3. The free energy of activation $\Delta F_{T_c}^{\ddagger}$ for the $-\overset{|}{N}-\overset{|}{C}=$ rotation in IV_a measured in different solvents at various concentrations.

Solvent	Conc. % by weight	T_c °K	$\delta\nu^b$ Hz	$\Delta F^{\ddagger}$ kcal/mol
CCl_4:$CHCl_3$ (8:1)	5	240	9.0	12.2
	20	240	9.0	12.2
Pyridine	5	241	8.8	12.2
	20	242	8.5	12.2
Acetone (d_6)	5	240	13.3	12.1
	20	240	13.1	12.1
DMSO (d_6):CH_2Cl_2 (1:1)	5	248	11.3	12.5
	20	249	11.0	12.5
Methanol	5	260	9.5	13.4
	20	260	9.7	13.4

[a] Calculated from τ values obtained by the formula $2\pi\delta\nu\tau = \sqrt{2}$.
[b] The chemical shift difference between the two N-CH_3 signals.

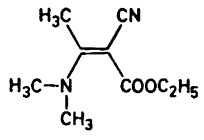
Another possible explanation for the large positive entropies of activation would be the existence of a low frequency vibration in the transition state not present in the initial state. The vibrational contribution to the entropy, S_ν, for each vibrational degree of freedom, is given by equation *5*, valid for a harmonic oscillator with the frequency ν (cm^{-1}).

$$S_\nu = R\left[\frac{u}{e^u - 1} - \ln\,(1 - e^u)\right] \qquad (5)$$

In this equation R = the gas constant = 1.987 cal mol^{-1} $deg.^{-1}$; $u = hc\nu/kT$; h = Planck's constant; k = Boltzmann's constant; c = the velocity of light and T = the temperature in °K.

According to eqn. 5 the entropy associated with vibrational frequencies larger than 500 cm^{-1} is less than 0.7 e.u. at 300°K and in order to obtain a vibrational contribution to the entropy of the order of 13 – 15 e.u. eqn. 5 predicts frequencies in the range $\sim 1 < \nu < \sim 50$ cm^{-1}. It seems somewhat unlikely to us that there should exist a vibration in the transition state with a frequency as low as 1 to 50 cm^{-1}. It is, however, not possible to test this hypothesis unless proper model compounds for the transition state are found.

Positive entropies of activation of the same magnitude have recently also been found for the $=\overset{|}{C}-\overset{|}{N}-$ rotation in the structurally similar noncyclic enamine VIII.[16]



VIII

Acknowledgements. The authors wish to thank Dr. R. E. Carter for linguistic criticism and valuable discussions. The cost of the NMR spectrometer was defrayed by grants from the *Knut and Alice Wallenberg Foundation.*

REFERENCES

1. Gutowsky, H. S. and Holm, C. H. *J. Chem. Phys.* **25** (1950) 228.
2. Fryer, C. W., Conti F. and Franconi, C. *Ric. Sci. Chim.* **8** (1965) 788.
3. Rodgers, M. T. and Woodbrey, J. C. *J. Phys. Chem.* **66** (1962) 540.
4. Inglefield, P. T., Krakower, E., Reeves, L. W. and Stewart, R. *Mol. Phys.* **15** (1968) 65.
5. Rabinovitz, M. and Pines, A. *J. Am. Chem. Soc.* **91** (1969) 1585.
6. Sandström, J. *J. Phys. Chem.* **71** (1967) 2318.
7. Kramer, H. E. A. and Gompper, R. *Z. physik. Chem. (Frankfurt)* **43** (1964) 292.
8. Kramer, H. E. A. and Gompper, R. *Z. physik. Chem. (Frankfurt)* **43** (1964) 349.
9. Mannschreck, A. and Koelle, U. *Tetrahedron Letters* **1967** 863.
10. Drakenberg, T., Dahlqvist, K.-I. and Forsén, S. *Acta Chem. Scand.* **24** (1970) 694.
11. Gutowsky, H. S., McCall, D. V. and Slichter, C. P. *J. Chem. Phys.* **21** (1953) 279.
12. Ingri, N. and Sillén, L. G. *Acta Chem. Scand.* **16** (1962) 173.
13. Drakenberg, T., Dahlqvist, K.-I. and Forsén, S. *To be published.*
14. McDaniel, D. H. and Brown, H. C. *J. Org. Chem.* **23** (1958) 420.
15. Binsch, G. In Eliel, E. L. and Allinger, N. L. *Topics in Stereochemistry,* Interscience, New York 1968, Vol. 3, p. 97.
16. Dahlqvist, K.-I. **24** (1970) 1941.

Received December 13, 1969.