for $C_{18}H_{13}NO_4$: C, 51.33; H, 7.00; N, 7.48. Found: C, 51.39; H, 7.25; N, 7.61.

Methyl **2-Carbomethoxy-3-dimethylaminocrotonate (2).** A mixture of 39.9 g (0.3 mol) of dimethylacetamide dimethyl acetal[22] and 39.6 g (0.3 mol) of dimethyl malonate was left for 1 week at room temperature. The solution was concentrated and the residue distilled (36.2 g; 60%), bp 94–96° (0.01 mm). The distillate which solidified was crystallized twice from ethyl acetate–hexane, mp 62–63.5°; uv max (isooctane) 297 (ϵ 13,900), 236 mμ (ϵ 5300); ir ($CHCl_3$) 1670 (ester C=O) and 1548 cm^{-1} (C=C). *Anal.* Calcd for $C_9H_{15}NO_4$: C, 53.72; H, 7.51; N, 6.96. Found: C, 53.68; H, 7.38; N, 6.92.

Methyl 2-Carbomethoxy-3-(N-methylanilino)acrylate (3). A mixture of 8.70 g (0.05 mol) of methyl 2-carbomethoxy-3-methoxyacrylate[21] and 5.35 g (0.055 mol) of N-methylaniline was kept in an oil bath at 110–120° for 1 hr. The resulting oil was distilled twice (8.3 g; 65%), bp 128° (10^{-3} mm); uv max (isooctane) 298 (ϵ 27,100), 221 mμ (ϵ 10,100); ir 1703 cm^{-1} (ester C=O). *Anal.* Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.67; H, 6.11; N, 5.81.

Methyl 2-Carbomethoxy-3-(N-methylanilino)crotonate (4). A mixture of 9.4 g (0.0357 mol) of methyl 2-carbomethoxy-3-methoxycrotonate[23] and 5.35 g (0.0525 mol) of N-methylaniline was kept in an oil bath at 180° for 1.5 hr. Distillation at 132–133° (10^{-3} mm) gave a yellow oil (3 g; 32%) which was redistilled, bp 129–131° (5×10^{-3} mm); uv max (isooctane) 305 (ϵ 21,500), 235 mμ (ϵ 14,100); ir ($CHCl_3$) 1681 cm^{-1} (ester C=O). *Anal.* Calcd for $C_{14}H_{17}NO_4$: C, 54.75; H, 6.46; N, 5.32. Found: C, 54.81; H, 6.72; N, 5.43.

1-Methyl-2-bis(carbomethoxy)methylenpyrrolidine (5). This compound was prepared in 52% yield according to the procedure given in ref 24 for the preparation of the corresponding bis(carboethoxy) derivative, crystallized from ethyl acetate–hexane, mp 47–48°; uv max (isooctane) 281 (ϵ 17,900), 233 mμ (ϵ 5100); ir ($CHCl_3$) 1672 (ester C=O), 1568 cm^{-1} (C=C). *Anal.* Calcd for $C_{10}H_{15}NO_4$: C, 56.32; H, 6.57; N, 7.09. Found: C, 56.46; H, 6.30; N, 7.20.

1-Benzyl-2-bis(carbomethoxy)methylenpyrrolidine (6). A mixture of 1-benzylpyrrolidine (3.5 g; 0.2 mol) and dimethyl sulfate (25.2 g; 0.2 mol) was heated in an oil bath at 90–100° for 2 hr. To the cold reaction mixture was added a solution of sodium methoxide in 70 ml of methanol (prepared from 4.6 g of sodium) with stirring during 15 min. After keeping the reaction mixture overnight at room temperature the salt was filtered, the methanol was evaporated *in vacuo*, and the residue was distilled at 84° (0.01 mm) to give 1-benzyl-2-pyrrolidone dimethyl acetal (13.5 g; 30%). The above compound (4.57 g; 0.02 mol), 2.64 g (0.02 mol) of dimethyl malonate, and 5 ml of methanol were heated under reflux for 36 hr. Distillation, bp 144–146° (10^{-3} mm), yielded 5.0 g (87%) of product which was crystallized from ethyl acetate–hexane, mp 41–42°; uv max (isooctane) 282 mμ (ϵ 19,500); ir ($CHCl_3$) 1681 cm^{-1} (ester C=O). *Anal.* Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.77; H, 6.49, N, 4.92.

1-Phenyl-2-bis(carbomethoxy)methylenpyrrolidine (7). Triethyloxonium fluoroborate (24.5 g; 0.13 mol) was added to 20 g (0.125 mol) of 1-phenylpyrrolidone in 25 ml of methylene chloride. The mixture was heated in a water bath at 45° for 1 hr, the upper layer was separated, and to the lower layer was added 16.5 g (0.125 mol) of dimethyl malonate. The reaction mixture was kept 48 hr at room temperature and chloroform and water were added. The organic layer was separated, dried ($MgSO_4$), concentrated, and the residue distilled at 188° (0.04 mm) to give 1.5 g (4%), crystallized from ethyl acetate-hexane, mp 104–106.5°; uv max (isooctane 297 (ϵ 12,500), 240 mμ (ϵ 8000); ir ($CHCl_3$) 1683 cm^{-1} (ester C=O). *Anal.* Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.33; H, 6.03; N, 5.33.

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[22] H. Bredereck, F. Effenberger, and G. Simchen, *Angew. Chem.*, **73**, 493 (1961).

[23] Prepared according to the procedure for the corresponding diethyl ester; A. Michael and G. H. Carlson, *J. Amer. Chem. Soc.*, **57**, 165 (1935).

[24] H. Bredereck and K. Bredereck, *Chem. Ber.*, **94**, 2278 (1961).

Internal Rotation in Olefins. II. Thermodynamic and Kinetic Investigation by Nuclear Magnetic Resonance

Youval Shvo and Hana Shanan-Atidi[1]

Contribution from the Department of Chemistry, Tel-Aviv University, Tel-Aviv, Israel. *Received June 9, 1969*

Abstract: Low energy barriers for rotation about carbon–carbon double bonds were discovered in various substituted 1-carbomethoxyacrylonitriles. Rotational rates were found to be within the nmr time scale, and activation energies were determined by variable temperature studies. Thermodynamic as well as kinetic properties of the exchanging diastereomers were investigated by the varying of structural parameters.

While the investigation of the diester compounds, presented in the preceding publication,[2] has yielded kinetic information regarding the isomerization process about the C=C bond, thermodynamic as well as kinetic data were obtained in the present study. The structure of the presently investigated compounds (Table I) may be arrived at by a single structural modification in the compounds of the preceding publication,[2] namely, the substitution of one carbomethoxy group by a nitrile. Again, two kinds of kinetic processes which occur within one molecule were discovered. The observed nmr phenomena could be unambiguously identified with the rotational process about the carbon–carbon double bond and about the nitrogen-to-sp^2 carbon bond (nitrogen rotation). In most of the compounds which are listed in Table I the rates of these processes are within the nmr time scale.

Consideration of the above-mentioned two types of rotational processes in the compounds of the present investigation leads to an equilibrium system depicted in Figure 1. Since all double-bond substituents are structurally different, the maximum number of diastereomeric species possible in the above equilibrium is four.

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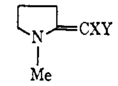
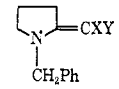
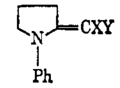
[1] H. Shanan-Atidi, M.S. Thesis, Tel-Aviv University, Tel-Aviv, Israel, 1968.

[2] Y. Shvo and H. Shanan-Atidi, *J. Amer. Chem. Soc.*, **91**, 6683 (1969).

Table I. Nmr[a] and Activation Data for Rotation about the C=C Bond

Compd no.	Compound, X = CO_2Me; Y = CN	Signal observed	$\Delta\nu$,[b] cps	T_c, °C	K_{eq}	ΔG^*, kcal/mol	Solvent
1	$H(Me_2N)C{=}CXY$	All	0		$\leqslant 10^{-2}$		C_2HCl_2 $(CD_3)_2CO$ C_6H_5Br
2	$Me(Me_2N)C{=}CXY$	=CMe	15.0	13.5	0.77 (−25°)	14.9; 14.8	CH_2Cl_2
		NMe_2	15.3	14.0	0.75 (−60°)	14.9; 14.8	CH_2Cl_2
3	$H(PhMeN)C{=}CXY$	All	0		$\leqslant 10^{-2}$		CH_2Cl_2 $(CD_3)_2CO$ C_6H_5Br
4	$Me(PhMeN)C{=}CXY$	=CMe	27.9	77.0	0.44 (32°)	18.3; 17.8	C_6H_5Br
5		All	0		$\leqslant 10^{-2}$		CH_2Cl_2 $(CD_3)_2CO$ C_6H_5Br
6		All	0		$\leqslant 10^{-2}$		CH_2Cl_2 $(CD_3)_2CO$ C_6H_5Br
7		OMe	25.0[c]	82	0.058 (32°)	18.6; 18.0	$CDCl_3$

[a] Nmr spectra were determined at a frequency of 100 Mc unless specified otherwise. [b] These values are maximum chemical shift separation. [c] Spectrum was recorded at 60 Mc.

Thus, when $R_1 = R_2$ the equilibrium constants for the exchange I ⇆ II and III ⇆ IV are identical, while when $R_1 \neq R_2$ all four equilibrium constants are different. All the species presented in Figure 1 are diastereomerically related, and their equilibrium concentrations would of course depend on their free-energy differences. Thus, by following the changes in the equilibrium constants with the corresponding changes in molecular structure, nmr investigation can yield aside from kinetic parameters also thermodynamic information about the systems under investigation. The relationship between structure, and both kinetic and thermodynamic properties of the systems under consideration, are of value in understanding molecular structure and may provide a basis for prediction of these properties in other systems.

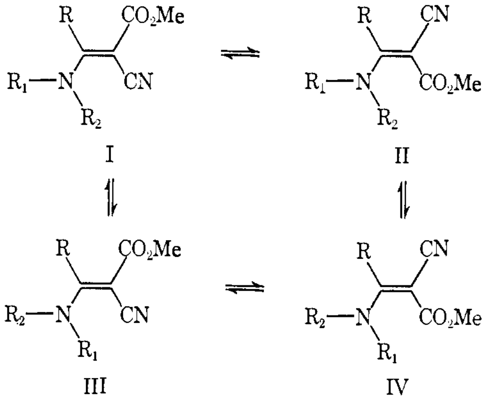


Figure 1.

The study of an equilibrium system, such as the one presented in Figure 1, by nmr requires the *simultaneous* fulfillment of two conditions: (a) the rates of exchange should of course be within nmr time scale; (b) the equilibrium concentrations of the exchanging species should be within the sensitivity limit of nmr instrumentation, which is estimated at *ca.* 1%. It follows that the observation of *one* signal from two species, exchanging at rates which are on the nmr time scale implies that the maximum limiting value of the equilibrium constant is *ca.* 10^{-2} and the corresponding upper limit of the free energy difference is 2.7 kcal/mol at 25°. Even though the value of the above equilibrium constant can be increased by raising the temperature of measurement, thus enabling the observation of signals from less stable species, the exchange rates at elevated temperatures may rise to values which are out of nmr time scale. In conclusion, even though an nmr technique is an ideal tool for obtaining kinetic and thermodynamic information about an equilibrium system such as the one presented in Figure 1, it is limited by the magnitude of both the kinetic and thermodynamic properties of the system.

Results and Discussion

The kinetic and thermodynamic parameters for the rotation process about the C=C bond and for the nitrogen rotational process are listed in Tables I and II, respectively. The chemical shifts of the compounds under investigation are presented in Table III. The exchange rates at the coalescence temperature (T_c), involving equally populated sites were determined from the Gutowsky–Holm relationship.[3] The rates, at the coalescence temperatures of two unequal intensity signals were determined from eq 1–3,[4] where δ = max-

$$[(\delta^2\tau^2 - 2)/3]^3/\delta^2\tau^2 = (\Delta p)^2 \qquad (1)$$

imum chemical shift separation in radians. $\Delta P = p_b$

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[3] H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, 25, 228 (1956).

[4] Equation 1 was derived from R. M. Lynden-Bell in "Progress in NMR Spectroscopy," Vol. 2, J. W. Emsley, J. Feeney, and L. H. Sutcliffe, Ed., Pergamon Press, Oxford, 1967, p 163. The detailed derivation and application of eq 1 is described by H. Shanan-Atidi and K. H. Bar-Eli, *J. Chem. Phys.*, in press.

Table II. Nmr[a] and Activation Data for the Nitrogen Rotation

Compd no.	Signal observed	$\Delta\nu$,[b] cps	Temp, °C	K_{eq}	ΔG^*, kcal/mol	Solvent
1	NMe_2	7.0	58.0	1	17.6	C_6H_5Br
2	NMe_2	18.0	−35.0	1	12.1[c]	CH_2Cl_2
	NMe_2	15.8	−12.0	1	14.8[c]	CH_2Cl_2
3	=CH	11.0	−37.5	0.29	12.8; 12.2	$(CD_3)_2CO$
4	All	0		(−55°)		C_6H_5Br
				$\leqslant 10^{-2}$		CH_2Cl_2
						$(CD_3)_2CO$

[a] Nmr data were obtained at 100 Mc. [b] These values are maximum chemical shift separation of the observed signals. [c] This value may be inaccurate since two exchange processes are occurring simultaneously (see Figure 2c).

Table III. Chemical Shift Data[a]

Compd no.	Chemical shift δ, ppm: CO_2Me	NMe	C-3 Me or H	Pyrrolidine protons[b]
1	3.72	3.37, 3.25	7.70	
2	3.70	3.20	2.47	
3	3.79	3.79	8.03	
3[c]	3.84, 3.70	3.78, 3.55		
4	3.70	3.66, 3.36	2.30, 2.12	
5	3.70	3.42		3.69, 3.30, 2.02
6	3.67	5.06 (NCH_2Ph)		3.48, 3.36, 1.90
7	3.65, 3.24			3.89, 3.49, 2.13

[a] Recorded at room temperature in $CDCl_3$ relative to an internal TMS standard. [b] Each signal integral is equivalent to two protons. [c] Determined in CH_2Cl_2 at −65°.

— p_a when p_a and p_b are the molar fractions of the two exchanging diastereomers a and b. τ_a and τ_b are the

$$\tau^{-1} = \tau_a^{-1} + \tau_b^{-1} \qquad (2)$$

$$p_a\tau_a^{-1} = p_b\tau_b^{-1} \qquad (3)$$

lifetimes of a and b. The values of p_a and p_b were determined by integration of the appropriate nmr signals. The free energies of activation at T_c were calculated from the Eyring activation function taking the transmission coefficient as unity.

Only one signal for the carbomethoxy group and one for the vinylic H have been observed at various temperatures and in different solvents in the nmr spectrum of **1** (Table I). The spectrum of compound **2**, however, shows doubling of the vinylic methyl and carbomethoxy signals upon cooling, and its dependence on the temperature is depicted in Figures 2a, b. The doubling of these signals, with unequal intensities, can be interpreted only in terms of a rotational process about the C=C bond which results in the exchange of the two unequally populated diastereomers (**2a**) and (**2b**). Also, the rotational rate of the nitrogen atom is slowed down at low temperature, and consequently all four signals of the diastereotopic[5] NMe groups in **2a** and **2b** are being observed (Figure 2c). This four-line system exhibits three distinct coalescence temperatures as can be seen from the spectra in Figure 2c. Such a behavior reflects the occurrence of three different kinetic processes, which are well separated as far as their nmr phenomena are concerned. Two of them are associated with the nitrogen rotation in the two diastereomers (**2a**) and (**2b**), and are indeed expected to follow different energy paths. They can be identified in the nmr spectra (Figure 2c), since the nitrogen rotational process must necessarily be associated with the coalescence of two *equal* intensity signals (T_c = −35 and −12°; Table II and Figure 2c). The third coalescence which involves two *unequal* in-

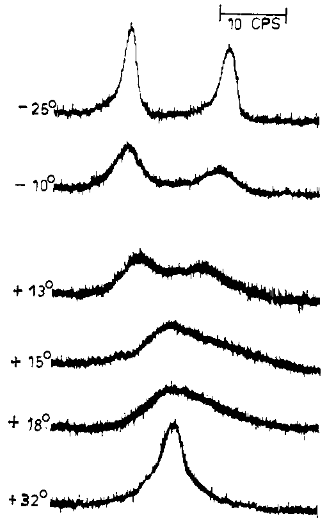

Figure 2a. Variable temperature nmr spectra of methyl 3-dimethylamino-2-cyanocrotonate (**2**). (Magnetic field is increasing from left to right); $=CCH_3$ signal.

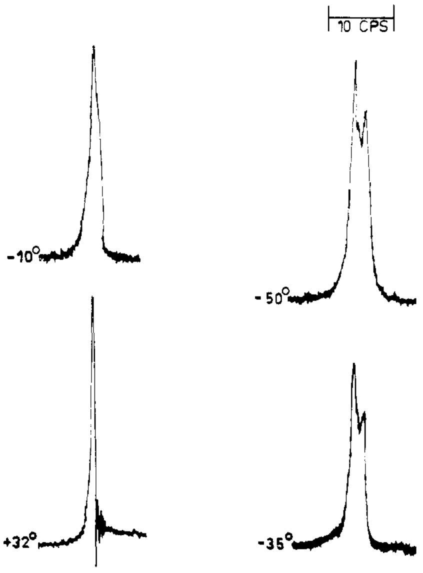

Figure 2b. Variable temperature nmr spectra of compound **2**; CO_2CH_3 signal.

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[5] K. Mislow and M. Raban in "Topics in Stereochemistry," Vol. 1, N. L. Allinger and E. L. Eliel, Ed., Interscience Publishers, New York, N. Y., 1967, p 19.

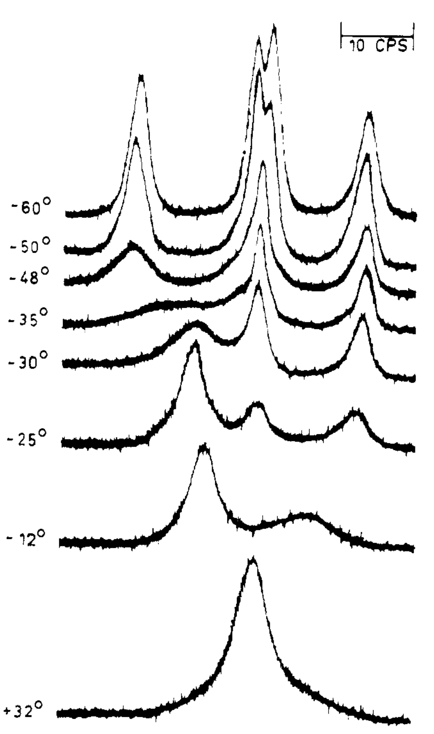
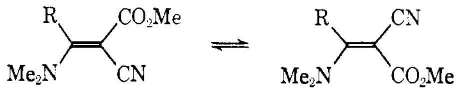


Figure 2c. Variable temperature nmr spectra of compound **2**; $N(CH_3)_2$ signal.

tensity lines must therefore be related to the rotation about the C=C bond which results in the exchange **2a** $\rightleftharpoons$ **2b** (T_c = 14.0°; Table I). The above two NMe signals and the vinylic Me signals (Figure 2a) possess an identical intensity ratio, and from their spectral behavior identical ΔG^* values were determined (Table I), as indeed is anticipated.



1a, R = H   1b
2a, R = Me   2b

The activation value for the exchange **2a** $\leftrightarrows$ **2b** was determined from the variable temperature nmr spectra of 2 (14.9, 14.8 kcal/mol) and the equilibrium constant, (0.77) from integration of the appropriate signals (Table I). This is in contrast to the situation concerning compound **1** where no signals multiplicity could be observed upon varying the temperature and the solvent, and consequently the above parameters could not be determined. From the results of the previous publication[2] it is anticipated that the barrier for the exchange **1a** $\leftrightarrows$ **1b** would be higher than that for **2a** $\rightleftharpoons$ **2b**, since substitution of Me by H would result in an increase in ΔG^* for rotation about the C=C bond. It follows therefore that the exchange rates **1a** $\rightleftharpoons$ **1b** must also be within the nmr time scale. Therefore, the observation of only one set of signals at various temperatures in the spectrum of **1** must be a consequence of a large free-energy difference between **1a** and **1b**. The concentration of the undetected less stable isomer of **1**, is less than 1%, and a minimum value of 10^{-2} is assigned to the equilibrium constant under consideration (Table I).

For subsequent discussion, it is necessary to identify the configuration of the prevailing isomer in the equilibrium system of **1**. Simple steric considerations dictate that **1a** should be more stable than **1b** inasmuch as the trigonal carbomethoxy group has larger steric requirements than the linear nitrile. This conclusion is substantiated by chemical-shift arguments. The average chemical shifts of the NMe_2 signals in methyl 3-dimethylamino-1-carbomethoxyacrylate are 2.98 ppm,[6] and 3.31 ppm in compound **1** (Table III). Thus, substitution of one CO_2Me by CN results in a significant deshielding (0.33 ppm) of the NMe_2 signal. It has been found[7] that homoallylic hydrogens ($C{=}C{-}N{-}CH_3$) are being deshielded to a larger extent by a neighbor-anisotropy effect of a *cis* CN than by a *cis* CO_2Me. In other words, the substitution of a CO_2Me group by CN in a position *cis* to the NMe_2 group should result in deshielding of the latter protons, which is indeed our experimental observation. Consequently, **1a** must represent the configuration of the prevailing isomer in the equilibrium system of **1**. Further support to the above assignment is the observed *shielding* of the NMe_2 signal (0.11 ppm; Table III) in proceeding from compound **1** to **2**. The two configurations **2a** and **2b** are known to be almost equally populated (K_{eq} = 0.77; Table I), and the above shielding reflects therefore the increase in the population of **2b** at the expense of **2a** which results in the exchange of a CN group *cis* to the NMe_2, by a CO_2Me group.

The two activation values found for compound **2** indicate a difference of 0.1 kcal/mol (Table I) in the free energy of the two configurations. That **2a** is still more stable than **2b** can be deduced from the chemical shifts and the relative intensities of the two NMe signals in Figure 2c at −60°. The low field NMe doublet (the first and third signal at low field), which by previous argument must be assigned to **2a** (*cis* NMe_2 and CN), has a larger integrated intensity than that of the high field signal which is necessarily assigned to **2b**.[8] Therefore, the higher ΔG^* value (14.9 kcal/mol) must be related to the change **2a** $\rightarrow$ **2b** while the lower (14.8 kcal/mole) to **2b** $\rightarrow$ **2a**. From the previous discussion, a minimum limiting value of *ca.* 2.7 kcal/mol can be assigned to the free-energy difference between **1a** and **1b** ($K_{eq} \leqslant 10^{-2}$; Table I), the former being more stable than the latter. This value is strikingly different from the corresponding free energy difference of **2a** and **2b** (0.1 kcal/mol). This difference in the diastereomeric stabilities must be associated with variations in steric factors accompanying the substitution of H by Me on C-3. Upon such a replacement the more stable isomer **1a** is being destabilized to a larger extent (*cis* $CH_3 \leftrightarrow CO_2Me$ interaction) than **1b** (*cis* $CH_3 \leftrightarrow$ CN interaction). Consequently, the above substitution diminishes the free-energy difference between the two diastereomers, as indeed is reflected by the observed increase in K_{eq} upon proceeding from **1** to **2** (Table I).

The interpretation of the nmr spectra of compounds **3** and **4** poses a somewhat complicated problem. In principle, since the nitrogen atom is nonsymmetrically substituted, each compound may exist as an equilibrium mixture of four diastereomers with different populations, as depicted in Figure 1 ($R_1 \neq R_2$). The nmr spectra of **3** and **4** each exhibit two unequal intensity

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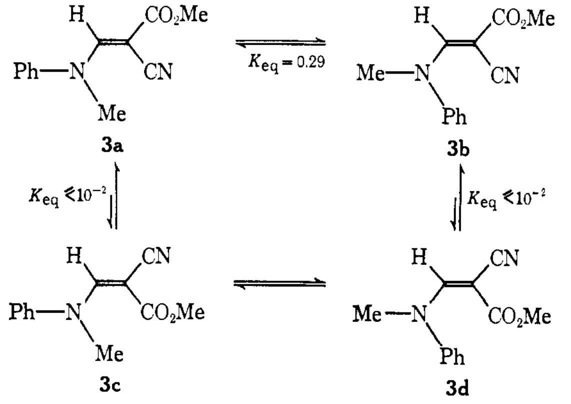
(6) Compound 1, Table I in ref 2.

(7) T. Hayashi, I. Hori, H. Baba, and H. Midorikawa, *J. Org. Chem.*, **30**, 695 (1965).

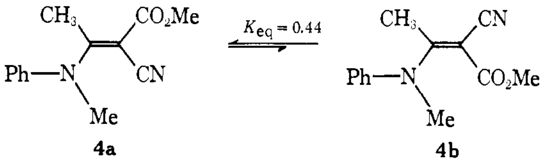
(8) The population ratio was determined by integrating the lowest and highest field signals (Figure 2c).

signals for every group in the molecule, which coalesce to singlets by the usual pattern. Therefore, for each of the above two compounds, only two out of the four possible exchanging diastereomers are observed. The question arises, now, whether this exchange is due to the rotation about the C=C bond or to the nitrogen rotational process. It should be noted that the spectral phenomena associated with these two processes are equivalent, and do not by themselves provide a basis for the identification of the above two processes. According to the following arguments, it is concluded that the nmr phenomenon observed with compound **3** is associated with the kinetic process of nitrogen rotation ($\Delta G^* = 12.8$ and 12.2 kcal/mol; Table II) while that observed with compound **4** is associated with the process of rotation about the C=C bond ($\Delta G^* = 18.3$, 17.8 kcal/mol; Table I). The above two sets of activation parameters cannot both be assigned to the rotation process about the C=C bond in compounds **3** and **4**. This follows since the only structural difference between **3** and **4** is a Me *vs.* H substitution at C-3, which has been noted[2] to depress the energy barrier for rotation about the C=C bond to an appreciable extent (*ca.* 9 kcal/mol). Thus, we would anticipate that $\Delta G^*(3) > \Delta G^*(4)$ which is in variance with the above experimental results. Similarly, both activation parameters cannot be assigned to the nitrogen rotational process, since in all cases the substitution of H by CH_3 on C-3 is accompanied by a decrease in ΔG^* for the above process (compare compounds **1** and **2**, Table II, and relevent data in the previous publication[2]). Thus, since $\Delta G^*(4) > \Delta G^*(3)$ such an assignment must also be ruled out. It follows that each activation parameter of the above two compounds must be assigned to a different rotational process. Such an assignment can be achieved employing compound **2** as a comparison model. Two structural parameters are varied upon proceeding from compound **2** to **3**. The first variation constitutes substitution of H by Me on C-3 and the second, substitution of Me by Ph on the nitrogen atom. In the previous publication[2] it was established that both kinds of variations are accompanied by increment in ΔG^* for rotation about the C=C bond, the first by 6.5–9.4 kcal/mol and the second by *ca.* 3.8 kcal/mol. It follows that the energy barrier for rotation about the C=C bond in **3** must be considerably higher than in **2**. Inasmuch as the experimental value $\Delta G^*(3) < \Delta G(2)$, the former cannot be assigned to the above rotational process. Consequently, the nmr phenomenon which is observed with compound **3** must be assigned to the nitrogen rotational process (Table II), and that with compound **4**, to the process of rotation about the C=C bond (Table I). The magnitude of the difference between the activation parameters of **2** and **4** (Table I) is *ca.* 3.1 kcal/mol, and is the change that would be anticipated for the replacement of Me by Ph on the nitrogen atom (3.8 kcal/mol), as was found in the preceding publication.[2]



From the above conclusions, the total equilibrium system of compound **3** may be represented by the four exchanging stereoisomers **3a–3d**. The geometry of the minimum energy conformations with respect to the nitrogen rotational process may be safely assumed to be essentially planar as in the analogous amide systems. It is now desired to determine the relative stabilities of the above four exchanging species. The experimental equilibrium constant of **3** (0.29) which has been argued to be related to the nitrogen rotational process, is assigned to the pair **3a** ⇌ **3b** rather than to **3c** ⇌ **3d**. This follows since the presence of **3d** should result in an observable shielding[2] of the CO_2Me signal, *vida infra.* Since no such shielding was observed (compare **2** and **3** in Table III), the concentration level of **3c** and **3d** must be considered to be less than 1% ($K_{eq} \leqslant 10^{-2}$). The conformation **3a** should predominate in the equilibrium system **3a** ⇌ **3b** ($K_{eq} = 0.29$), since in the nmr spectrum of **3** (at −65°) the low field NMe signal (3.78 ppm) is of higher integrated intensity than that of the high field signal (3.55 ppm, Table III). This is based on the assumption that the nitrile is more effective in deshielding the NMe group in **3a** than in **3b**. Consequently the activation value of 12.8 kcal/mol is assigned to the process **3a** → **3b** and that of 12.2 kcal/mol to **3b** → **3a**. On the basis of steric considerations, it would have been predicted that **3a** is the most stable configuration in the above four-species equilibrium system, in agreement with our experimental finding. The shift of the equilibrium from the pair **3c**, **3d** toward **3a**, **3b** reflects the larger steric requirements of the trigonal CO_2Me *vs.* the linear CN group.

Regarding compound **4** it has been argued that the signals multiplicity (doubling) detected in its nmr spectrum is due only to the rotation about the C=C bond, and an equilibrium constant ($K_{eq} = 0.44$) for the exchange **4a** ⇌ **4b** was determined by integration of the appropriate signals. It follows that for the nitrogen rotational process $K_{eq} \leqslant 10^{-2}$. The average chemical shift of the carbomethoxy group in **4** is 3.70 ppm, identical with the shift of the same group in **2** (Table III). This must indicate that in the prevailing conformation with respect to the nitrogen substituents the phenyl group is in an *s-trans* position with respect to the double bond, as depicted in **4a** and **4b**, and the remote carbomethoxy group is unaffected by its magnetic anisotropy.[2] Turning now to the configuration of the double-bond isomers of **4**, it is noted that the low field NMe signal of **4** (3.66 ppm) is of higher integrated intensity than the high field signal (3.36 ppm). Therefore, **4a** is thermodynamically more stable than **4b** inasmuch as the former is populated to a larger extent than the latter, and the

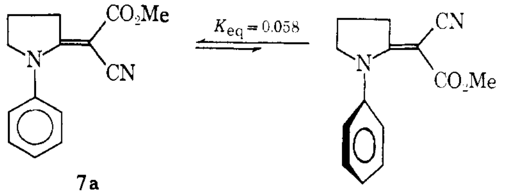


activation value of 18.3 kcal/mol is assigned to the change **4a** → **4b** and 17.8 kcal/mol to the reverse process.

It is instructive to compare the equilibrium constants between diastereomers which result from rotation about the C=C bond in compound **3** ($K_{eq} \leqslant 10^{-2}$) and **4** ($K_{eq} = 0.44$). It is apparent that substitution of H by Me on C-3 diminishes the free energy difference between the two exchanging diastereomers. Indeed an analogous thermodynamic behavior has already been encountered with compounds **1** and **2** which are structurally related to **3** and **4**, respectively, as far as C-3 substitution is concerned. An interpretation of this phenomenon, based on differential steric interactions has already been suggested.

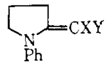
The two pyrrolidine derivatives **5** and **6** exhibit in their nmr spectra single lines for the carbomethoxy group and the nitrogen substituents, when examined both at high (150°) and low (−95°) temperatures and in a variety of solvents (Table I). On the other hand the NPh pyrrolidine derivative (**7**) exhibits two unequal intensity lines (5.5/94.5) for the carbomethoxy group. From the coalescence temperature of these two signals (*ca.* 82°), the corresponding activation energies were calculated. Because of the low intensity of one of the signals (5.5%) in the nmr spectrum of **7**, it was desired to ascertain rigorously its association in the exchange process. To this end, the high intensity (94.5%) CO_2Me signal in the nmr spectrum of **7** was saturated by an external rf field at 60° with simultaneous tracing of the low intensity signal, which revealed the disappearance of the latter. This must indicate that two signals are indeed involved in a common exchange process.[9] Since it has already been demonstrated that substitution of an alkyl by a phenyl group on the nitrogen atom is accompanied by an increase in ΔG^* for rotation about the C=C bond, it must be concluded that the activation values of **5** and **6** are lower by *ca.* 3.1 kcal/mol than the corresponding value of **7**. Consequently, the lack of signals multiplicity in the nmr spectra of **5** and **6** is attributed to a large free-energy difference between the two diastereomers ($K_{eq} \leqslant 10^{-2}$). The configuration of the exclusively prevailing isomers of **5** and **6** can be ascertained from chemical shift considerations. A comparison of the chemical shifts of the nitrogen substituents in **5** and **6** (Table III) with those of the corresponding diesters in the preceding publication[10] reveals that the replacement of CO_2Me by CN is accompanied by deshielding of these N-substituents by 0.57 and 0.67 ppm, respectively. These rather large differential shifts must again indicate that the nitrile group is in a *cis* position with respect to the nitrogen atom in the more stable configurations of **5** and **6**.

The configuration of the two exchanging isomers of **7** could be readily established by the inspection of the chemical shifts of the carbomethoxy group. The two unequal intensity signals (5.5/94.5) have been observed at 3.65 and 3.24 ppm (Table III); the higher field signal being of lower intensity. It is apparent from chemical shift analysis in the previous publication,[2] that the high field signal must be related to the configuration depicted in **7b**. The upfield shift (0.41 ppm) with respect to the low field signal is attributed to the diamagnetic field component originating from the necessarily twisted phenyl ring in **7b**. Since the high field signal is of lower intensity, the predominating isomer in the above equilibrium is **7a**, and the activation parameter for the change **7a** → **7b** is 18.6 kcal/mol while that for **7b** → **7a** is 18.0 kcal/mol. From the equilibrium data of Table I it is evident that the isomer with the vinyl nitrogen atom and the carbomethoxy group in a *cis* position is more stable in **7** ($K_{eq} = 0.058$) than in **5** and **6** ($K_{eq} \leqslant 10^{-2}$). This must be the outcome of the smaller steric requirements of the twisted phenyl ring in **7** as compared with the tetrahedral nitrogen substituents in **5** and **6**.



7a **7b**

Table IV. Comparison of Activation Data for Rotation about the C=C Bond

Entry	Compound	X = Y = CO_2Me ΔG_T^*, (kcal/mol)[a]	X = CO_2Me; Y = CN ΔG_T^*, (kcal/mol)
1	Me(Me_2N)C=CXY	<9.1 (−95°)	14.9; 14.8 (13.5°)
2	Me(PhMeN)C=CXY	10.0 (−76°)	18.3 17.8 (77°)
3		13.7 (5°)	18.6; 18.0 (82°)

[a] The values in this column were taken from Table I in the preceding publication.[2]

We are now in a position to evaluate and interpret the kinetic consequences associated with substitution of a carbomethoxy group by nitrile in the systems under investigation. From the relevant data collected in Table IV, it is clear that substitution of CO_2Me by CN is accompanied by a significant increment in ΔG^* values for rotation about the C=C bond (*ca.* 6–8 kcal/mol). It is noted, however, that in each pair the activation parameters were determined at widely different temperatures which casts doubt on the significance of the results from such comparisons, inasmuch as entropy terms may possibly offset the above relationships. From trial calculations it becomes apparent that only in the case where the entropies of activation of the diesters (X = Y = CO_2Me) are positive and very large (*ca.* +20 eu) and those of the nitrile derivatives (X = CO_2Me; Y = CN) are negative and very small (*ca.* −20 eu) would the relative magnitude of the ΔH^* values of the two types of compounds be inverted. The above hypothetical relationship between the entropies of activation of the two types of compounds seems illogical in the light of the process, and the nature of the ground and transition states under consideration.[11] Thus, it may safely be concluded that only part of the observed increments in ΔG^* values upon substitution of CO_2Me by CN (Table IV) could possibly originate from $T\Delta S$ terms; the rest must be due to increments in

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[9] I. C. Calder, P. J. Garratt, and F. Sondheimer, *Chem. Commun.*, 41 (1967).

[10] Compounds **5** and **6**, Table III in ref 2.

[11] It is logical to assume that with both types of compounds entropy is gained in proceeding from the more rigid planar ground state to the orthogonal transition state.

the enthalpies of activation. In the previous publication[2] it has been argued that the transition state for the rotational process about the C=C bond is of a dipolar nature with a positive charge at C-3 and a negative charge at C-2. In such a case the relative magnitude of the electronic effects which are associated with the nitrile and ester groups may be judged from their respective σ values (σ (CN) = 0.66; σ (CO_2Me) = 0.52).[12] Consequently, a more extensive electron delocalization is anticipated upon substitution of CO_2Me by CN, since σ (CN) > σ (CO_2Me). In turn, such a replacement would diminish the C=C bond order, and one may arrive at the conclusion that the above substitution should be accompanied by a decrease in the energy barrier for rotation about the C=C bond. But such a conclusion is in clear variance with the experimental results in Table IV, where the opposite relationships have been consistently observed. Obviously, such an approach is unacceptable as indeed has been pointed out in the previous publication,[2] since only a ground-state property (bond order) is being considered. If now both the ground and transition states are analyzed, and the above mentioned σ values relationship is applied, both the ground and transition state must be lowered, but the former to a larger extent, than the latter (Figure 3a), in order to account for the increment in ΔG^* which accompanies the substitution of CO_2Me by CN. This implies that the ground state for the rotational process under consideration is more polar than the transition state. Such a conclusion is in variance with our previous arguments claiming a heteropolar transition state due to charge separation. If, however, the above two σ values are separated into their inductive and resonance components,[12] it turns out that $\sigma_R(CO_2Me) = +0.20$ and $\sigma_R(CN) = +0.07$; thus, the relative magnitudes of the σ_R values of the two groups are inverted with respect to their total σ values. With this relationship established, the experimental results may be properly interpreted by raising the transition state upon substitution of CO_2Me by CN (Figure 3b), since in light of the relative magnitude of the σ_R values, the latter group less effectively delocalizes the negative charge than the former (in the transition state for rotation). The ground state must of course also be raised, but to a smaller extent (Figure 3b), or even be lowered, since resonance stabilization is by far more important in the charged transition state than in the essentially neutral ground state. In view of the above analysis, it should in principle be possible to establish a relationship between σ_R values and energy parameters for the process under consideration. Activation energies for various other systems could be predicted from such a relationship.

Experimental Section

General. The chemical shifts and $\Delta\nu$ values reported in Tables I-III were obtained from measurements of the spectra on a Varian A60-A or HR-100 spectrometer employing solutions of approximately 10-20% by volume. The spectrometers were equipped with variable temperature probes. The coalescence temperatures are accurate to 2°, $\Delta\nu$ values are averages of at least three tracings and are accurate to 0.1 cps, and chemical shifts are accurate to 1 cps and integrations to 3%. Ultraviolet spectra were recorded on a Cary 14 spectrometer and infrared spectra on a Perkin-Elmer grating spectrometer, Model No. 337.

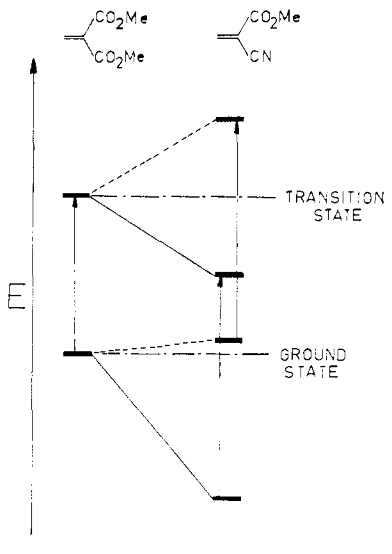

Figure 3. Energy level diagram of thermal ground and transition states: (a) —, energy changes predicted according to σ(CN) > σ(CO_2Me); (b) – – –, energy changes predicted according to σ_R(CO_2Me) > σ_R(CN).

Methyl 3-Dimethylamino-2-cyanoacrylate (1).[13] Formamide dimethyl acetal[14] (13.2 g; 0.11 mol) and methyl cyanoacetate (9.9 g; 0.1 mol) were mixed. A crystalline product separated after a few minutes, and crystallized from ethyl acetate-hexane (12 g; 90%): mp 102-103°; uv max (isooctane) 297 (ϵ 21,000), 240 mμ (ϵ 8,000); ir ($CHCl_3$) 1703 (ester C=O), 1605 (C=C), and 2197 cm^{-1} (C≡N). *Anal.* Calcd for $C_7H_{10}N_2O_2$: C, 54.53; H, 6.54; N, 18.17. Found: C, 54.55; H, 6.81; N, 17.90.

Methyl 3-Dimethylamino-2-cyanocrotonate (2). Dimethylacetamide dimethyl acetal[15] (19.95 g; 0.15 mol) and methyl cyanoacetate (14.85 g; 0.15 mol) were mixed. After 0.5 hr the resulting oil was distilled, bp 115-116° (10^{-3} mm). The distillate was crystallized from ethyl acetate-hexane (21.4 g; 85%): mp 59-61°; uv max (isooctane) 301 mμ (ϵ 18,000); ir ($CHCl_3$) 1692 (ester C=O), 1558 (C=C), and 2187 cm^{-1} (C≡N). *Anal.* Calcd for $C_8H_{12}N_2O_2$: C, 57.13; H, 7.19; N, 16.66. Found: C, 57.20; H, 7.36. N, 16.83.

Methyl 3-(N-Methylanilino)-2-cyanoacrylate (3). Methyl 3-methoxy-2-cyanoacrylate[16] (10.08 g; 0.075 mol) and N-methylaniline (8.02 g; 0.075 mol) were heated in an oil bath at 180° for 1 hr. The resulting oil was distilled, the fraction which boiled at 170-184° (10^{-3} mm) was collected and crystallized from ethyl acetate-hexane (8.9 g; 55%): mp 94-96°; uv max 304 mμ (ϵ 24,600), shoulder 230 mμ (ϵ 6,000); ir ($CHCl_3$) 1703 (ester C=O), 1586 (C=C) and 2203 cm^{-1} (C≡N). *Anal.* Calcd for $C_{12}H_{12}N_2O_2$: C, 66.60; H, 5.56; N, 12.95. Found: C, 66.71; H, 5.78; N, 13.05.

Methyl 3-(N-Methylanilino)-2-cyanocrotonate (4). Methyl 3-methoxy-2-cyanocrotonate[16] (7.75 g; 0.05 mol) and N-methylaniline (5.35 g; 0.05 mol) were heated in an oil bath at 180° for 2.5 hr. After cooling, the resulting oil was crystallized from ethyl acetate-hexane, (4.6 g; 40%): mp 96-98°; uv max (isooctane) 306 mμ (ϵ 18,400); ir ($CHCl_3$) 1700 (ester C=O), 1533 (C=C), and 2200 cm^{-1} (C≡N). *Anal.* Calcd for $C_{13}H_{14}N_2O_2$: C, 67.84; H, 6.13; N, 12.17. Found: C, 67.66; H, 5.90; N, 12.10.

1-Methyl-2-(cyanocarbomethoxymethylene)pyrrolidine (5). 1-Methyl-2-pyrrolidone diethyl acetal[14] (5.19 g; 0.03 mol) and methyl cyanoacetate (2.49 g; 0.03 mol) were mixed. The solid which separated was crystallized from chloroform-petroleum ether (4.15

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[12] R. W. Taft in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley & Sons, Inc., New York, N. Y., 1956, p 595.

[13] This compound was mistakenly reported in ref 14, and is actually the corresponding ethyl ester derivative as can be verified from the elemental analysis on p 27, ref 14.

[14] H. Meerwein, W. Florian, N. Schön, and G. Stopp, *Ann. Chem.*, 641, 1 (1961).

[15] H. Bredereck, F. Effenberger, and G. Simchen, *Angew. Chem.*, **73**, 493 (1961).

[16] F. Arndt, H. Schloz, and M. Frobel, *Ann. Chem.*, **521**, 95 (1931).

g; 77%): mp 113–115°; uv max (isooctane) 284 mμ (ε 21,000); ir ($CHCl_3$) 1695 (ester $C{=}O$), 1576 ($C{=}C$), and 2190 cm^{-1} ($C{\equiv}N$). *Anal.* Calcd for $C_9H_{12}N_2O_2$: C, 59.98; H, 6.71; N, 15.55. Found: C, 60.23; H, 7.00; N, 15.63.

1-Benzyl-2(cyanocarbomethoxymethylene)pyrrolidine (6). 1-Benzyl-2-pyrrolidone dimethyl acetal was prepared by heating 1-benzylpyrrolidone (35 g; 0.2 mol) and dimethyl sulfate (25.2 g) in an oil bath at 90–100° for 2 hr. To the above reaction mixture a methanolic solution of NaOMe (4.6 g of Na in 70 ml of MeOH) was added during 15 min, with ice-cooling and stirring. The mixture was left overnight at room temperature, the salt was filtered, and the filtrate was concentrated *in vacuo*. The resulting oil was fractionated by vacuum distillation, (13 g), bp 84° (0.01 mm).

Methyl cyanoacetate (3.80 g; 0.038 mol) and 1-benzyl-2-pyrrolidone dimethyl acetal (9.27 g; 0.042 mol) were mixed. The reaction mixture solidified immediately (exothermic), and the solid was crystallized from ethyl acetate–hexane (8.25 g; 85%): mp 126–128; uv max (isooctane) 286 mμ (ε 23,800); ir ($CHCl_3$) 1692 (ester $C{=}O$), 1553 ($C{=}C$), and 2181 cm^{-1} ($C{\equiv}N$). *Anal.* Calcd for $C_{16}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.42; H, 6.19; N, 10.92.

1-Phenyl-2-(cyanocarbomethoxymethylene)pyrrolidine (8). 1-Phenyl-2-pyrrolidone diethyl acetal was prepared by reacting 1-phenylpyrrolidone with triethyl oxoniumfluoroborate according to the general procedure given in ref 14, 62% yield, bp 113–114° (0.15 mm).

Methyl cyanoacetate (4.95 g; 0.050 mol) and 1-phenyl-2-pyrrolidone diethyl acetal (12.9 g; 0.055 mol) were mixed and left for 50 hr at room temperature. A solid was obtained by addition of hexane, crystallized from ethyl acetate (6.15 g; 51%): mp 164–65°, uv max (isooctane) 292 mμ (ε 15,900), shoulder 237 mμ (ε 3800); ir ($CHCl_3$) 1697 (ester $C{=}O$), 1547 ($C{=}C$), and 2198 cm^{-1} ($C{\equiv}N$). *Anal.* Calcd for $C_{14}H_{14}N_2O_2$: C, 69.40; H, 5.83; N, 11.56. Found: C, 69.62; H, 5.78; N, 11.43.

Studies on Oxime Hydrochlorides. IV. Nuclear Magnetic Resonance Studies of the Stereochemistry of 2-Substituted Cyclohexanone Oximes and Their Hydrochlorides. Conformation Change Caused by Protonation and Hydrogen Bonding

Hazime Saitô, Isao Terasawa, Masaji Ohno, and Kenkichi Nukada

Contribution from the Basic Research Laboratories, Toyo Rayon Co., Ltd., Kamakura, Japan. Received March 11, 1969

Abstract: The configuration and conformation of 2-substituted cyclohexanone oximes and their hydrochlorides are investigated by means of ir and nmr spectroscopy. They include the compounds with substituents, OMe (I), OEt (II), Cl (III), Me (IV), OH (V), $OCOCH_3$ (VI), OCOPh (VII), piperidinyl (VIII), and morpholinyl (IX). The *E* isomer is predominant in compounds IV, V, VIII, and IX, whereas less than 20% of the *Z* isomer appears in the rest. In all the compounds except IV and V, the substituent is axially oriented. The substituent of V is held in the equatorial position in nonpolar solvents by the intramolecular hydrogen bond formed between the nitrogen atom of the hydroxyimino group and the hydroxyl substituent. No other type of intramolecular hydrogen bond is observed. The presence of the hydrogen bond is confirmed by the low wave-number shift in OH-stretching frequency under extremely dilute conditions. In V, the substituent shows an axial preference in polar solvents. A variation of the conformation and configuration is observed in some hydrochlorides. In the hydrochloride of IV the substituent turns to the axial position and, at the same time, the *Z* isomer appears because of the conversion from the *E* isomer. The substituents are partly equatorial in the hydrochloride of I, II, and III in the *E* isomer, while no appreciable change is observed in the *Z* isomer. This conformation change is interpreted in terms of electrostatic attraction between the lone-pair electrons of the substituent and the positive charge on the nitrogen atom due to the formation of the hydrochloride. The downfield shift of methyl signals is discussed in terms of the excess dipole moment of the nitrogen atom.

A number of conformational studies of 2-substituted cyclohexanones have been reported.[1-12] Allinger and his coworkers[1,2] showed that conformational energies of 2-alkyl compounds are about 2 kcal/mol in favor of the equatorial position. Studies of the conformation equilibria of 2-halocyclohexanones by infrared,[3,4] ultraviolet,[5,6] dipole moment,[7,8] optical dispersion,[9,10] and nmr measurements[11,12] have revealed that the substituents are axially oriented in nonpolar solvents and that the population of the equatorial substituent increases in polar media.

However, except for Chow's work,[13] no attention has been paid to the stereochemistry of 2-substituted cyclohexanone oximes. If the molecular backbone is in the chair form, there are four possible isomeric forms of 2-substituted cyclohexanone oxime (Figure 1). Destabilizing factors such as steric or electrostatic repulsions between the substituent and hydroxyl groups should be

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(1) N. L. Allinger and H. M. Blatter, *J. Amer. Chem. Soc.*, **83**, 994 (1961).

(2) N. L. Allinger, H. M. Blatter, L. A. Freiberg, and F. M. Karkowski, *ibid.*, **88**, 2999 (1966).

(3) E. J. Corey, *ibid.*, **75**, 2301 (1953).

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(5) N. L. Allinger and J. Allinger, *J. Amer. Chem. Soc.*, **80**, 5476 (1958).

(6) N. L. Allinger, J. Allinger, L. A. Freiberg, R. T. Czaja, and N. A. Lebel, *ibid.*, **82**, 5876 (1960).

(7) N. L. Allinger, J. Allinger, L. W. Chow, and G. L. Wang, *J. Org. Chem.*, **32**, 552 (1967).

(8) N. L. Allinger, J. Allinger, and N. A. Lebel, *J. Amer. Chem. Soc.*, **82**, 2926 (1960).

(9) C. Djerassi and W. Klyne, *ibid.*, **79**, 1506 (1957).

(10) C. Djerassi, L. E. Geller, and E. H. Eisenbraun, *J. Org. Chem.*, **25**, 1 (1960).

(11) E. W. Garbisch, *J. Amer. Chem. Soc.*, **86**, 1780 (1964).

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(13) Y. L. Chow, *ibid.*, **43**, 2711 (1965).