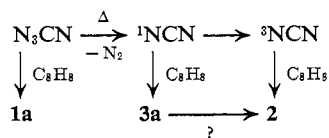


mechanism, depicting the major sources of products, is advanced.



A. G. Anastassiou

Contribution No. 1109

Central Research Department, Experimental Station

E. I. du Pont de Nemours and Company

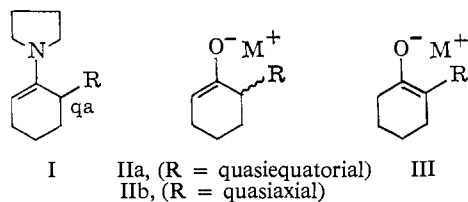
Wilmington, Delaware 19898

Received August 11, 1965

The Stereochemistry of the Anions of 2-Alkylcyclohexanones

Sir:

In previous papers^{1,2} we have demonstrated that the pyrrolidine enamines of 2-substituted cyclohexanones, represented by I, have the substituent R in the quasi-axial position. The preference for this conformation is almost certainly a result of the fact that in the alterna-

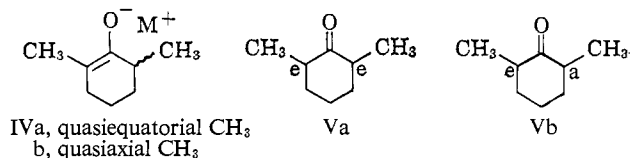


tive quasiequatorial position R would have a nonbonded steric interaction with one of the CH₂ groups on nitrogen.³ We have now extended our studies to investigate whether the solvent has any role in modifying the stereochemistry of the alkyl group in the less substituted enolate anions (II) derived from 2-alkylcyclohexanones.

Aprotic solvents are capable of cation solvation either by a π -orbital or a lone-pair mechanism.⁴ Consequently the solvent shell, which is partly interspersed between the anionic oxygen atom and the cation and partly surrounding them, might interact with the alkyl group when it is in the quasiequatorial orientation (IIa). This nonbonded interaction which would depend on the size of both the solvent shell and the alkyl group should disappear if the alkyl group becomes quasixial (IIb); the latter would of course have a 1,3-diaxial interaction between the methyl group and the hydrogen atom at C-4. If the magnitude of the 1,3-diaxial interaction in IIb and the relative concentrations of IIa and IIb are known for a particular solvent, then the energy associated with the

interaction of the solvent shell and the alkyl group in IIa can be readily calculated.

Since in 2-alkyl substituted ketones the generation of the less substituted enolate anion II is complicated by the concurrent formation of the more substituted anion III,⁵ we selected 2,6-dimethylcyclohexanone as a substrate for our studies. This ketone on treatment with base affords only one enolate anion, IV, which is of course a mixture of conformers IVa and IVb.



The respective concentrations of IVa and IVb in a particular solvent were easily determined by carrying out their protonation with dilute acetic acid, under nonequilibrating conditions, which led to Va and Vb, respectively.⁶ The experimental detail is outlined below.

A solution of V (Va:Vb \sim 92:8 under equilibrating conditions)⁷ in a given aprotic solvent was treated with 2 equiv. of anhydrous potassium *t*-butoxide at room temperature, and the mixture was stirred for 2 hr. under nitrogen. The resulting solution was added dropwise to 50% aqueous acetic acid maintained at 0° and contained in a Morten flask equipped with a high speed stirrer. The amounts of Va and Vb obtained were quantitatively determined by g.l.p.c. The extent of enolate anion formation was determined by quenching an aliquot of the reaction solution with acetic anhydride and determining the amounts of enol acetate (directly representative of enolate anion formed^{8,9}) and starting ketone again by g.l.p.c., and also by treating it with 50% deuterioacetic acid⁵-deuterium oxide (inverse addition) which led to almost exclusively monodeuterated species. Estimates of the concentrations of enolate anion obtained by these two procedures were in good agreement. The results obtained are summarized in Table I.

The results of the table demonstrate conclusively that the solvent shell around the ion pair interacts quite strongly with the adjacent methyl group when the latter is equatorially oriented. To a first approximation it probably can be assumed that a similar effect occurs with the less substituted anions of the simpler 2-alkylcyclohexanones. This has important implications for the alkylation of such systems since the presence of a considerable proportion of IIb in II will undoubtedly slow down axial alkylation⁹ of II by virtue of a steric interaction between the 2-axial alkyl group and the incoming reagent (1,3-diaxial interaction) as in the analogous case of enamines of II.^{1,2} This would of course

(1) F. Johnson and A. Whitehead, *Tetrahedron Letters*, 3825 (1964).

(2) S. K. Malhotra and F. Johnson, *ibid.*, 87, 4027 (1965).

(3) It is important to note (a) that in this system the pair of electrons on nitrogen conjugates with the double bond maintaining planarity and thus ensuring this steric interaction and (b) that the dihedral angle between R and the nitrogen atom is quite small, as can be seen from models.

(4) H. E. Zaugg, B. W. Horrom, and S. Borgwardt, *J. Am. Chem. Soc.*, 82, 2895 (1960); H. E. Zaugg, *ibid.*, 82, 2903 (1960); H. E. Zaugg, D. A. Dunnigan, R. J. Michaels, L. R. Swett, T. S. Wang, A. H. Sommers, and R. W. Denet, *J. Org. Chem.*, 26, 644 (1961); H. E. Zaugg and A. D. Schaefer, *J. Am. Chem. Soc.*, 87, 1857 (1965); H. D. Zook and T. J. Russo, *ibid.*, 82, 1386 (1960); A. J. Parker, *Quart. Rev. (London)*, 16, 163 (1962).

(5) H. O. House and V. Kramar, *J. Org. Chem.*, 28, 3362 (1963); D. Caine, *ibid.*, 29, 1868 (1964).

(6) This protonation was shown to be subject to stereoelectronic control by quenching the enolate anion derived from 2,6-dimethyl-4-*t*-butylcyclohexanone with 50% deuterioacetic acid-deuterium oxide under irreversible conditions. The infrared spectrum of the product showed principal absorption in the C-D stretching region at 2140 cm.⁻¹ (axial C-D).

(7) B. Rickhorn, *J. Am. Chem. Soc.*, 84, 2414 (1962); W. D. Cotterill and M. J. T. Robinson, *Tetrahedron*, 20, 765, 777 (1964).

(8) H. J. Ringold and S. K. Malhotra, *J. Am. Chem. Soc.*, 84, 3402 (1962).

(9) Cf. E. J. Corey and R. A. Snaen, *ibid.*, 78, 6269 (1956).

Table I

Solvent	% enol acetate, ± 2	% Va (<i>cis</i>) ^{a,b}	% Vb (<i>trans</i>) ^{a,b}	Solvent shell-equatorial methyl interaction, kcal./mole ^c
Tetrahydrofuran	67.3	63.7	36.3	0.57
N,N-Dimethylacetamide	66.8	61.7	38.3	0.61
Benzene	46.8	61.6	38.4	0.61
Ether	53.2	59.1	40.9	0.68
Monoglyme	59.9	56.2	43.8	0.76
Diglyme	68.0	55.0	45.0	0.78
Dioxane	55.2	52.4	47.6	0.84
Hexamethylphosphoramide	73.4	50.8	49.2	0.88
Dimethylformamide	65.7	47.8	52.2	0.95
Dimethyl sulfoxide	66.8	44.9	55.1	1.02
Sulfolane	52.4	44.8	55.2	1.02
Triglyme	47.2	38.6	61.4	1.18

^a In these solvents the equilibrium percentage of *cis* (Va) isomer is in the range of 90–92% (cf. ref. 7) as determined by g.l.p.c.

^b Corrected percentages based on the isomeric distribution of free ketone under equilibrating conditions. ^c Based on the assumption that a diaxial 1,3-methyl-hydrogen interaction in cyclohexane has an energy value of 0.9 kcal./mole.

lead to substantially greater alkylation than might be anticipated of the more substituted enolate anion III (which is in equilibrium with II). As one of the controlling influences in enolate anion alkylation, this factor appears not to have been recognized thus far.

Studies along these lines are continuing.¹⁰

Acknowledgment. We wish to thank Mr. D. F. Moakley for technical assistance and Mr. John Flynn for the determination of mass spectra of the deuterated ketones.

(10) Ringold and co-workers (private communication) have found in the case of the potassium enolate derived from 2-methylandro-4-ene-3,17-dione in *t*-butyl alcohol solution that the steric interaction of the equatorial methyl group and the solvated ion pair (as in IIa) destabilizes the enolate by almost 2 kcal./mole.

Sudarshan K. Malhotra, Francis Johnson

The Dow Chemical Company, Eastern Research Laboratory
Wayland, Massachusetts

Received August 30, 1965

The Role of Vibrational Excitation in Hydrogen-Deuterium Exchange. Nascent Molecules at Room Temperature

Sir:

Kinetic studies of a variety of homogeneous gas-phase H-D exchange reactions at elevated temperatures in shock tubes have led to an unexpected and novel conclusion: that the exchange rate is limited by the rate of populating critical vibrational levels.¹⁻³ The implication of this mechanism, which accounts for the shock-tube data in detail, is that for the strictly bimolecular process the relative kinetic energy of transla-

(1) A. Lifshitz, C. Lifshitz, and S. H. Bauer, *J. Am. Chem. Soc.*, **87**, 143 (1965).

(2) S. H. Bauer and E. L. Resler, Jr., *Science*, **146**, 1045 (1964).

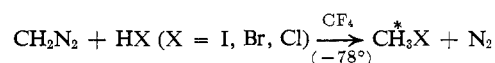
(3) S. H. Bauer and E. Ossa, presented before the Division of Physical Chemistry, at the 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept. 1965, Abstract No. 115.

tional motion along the line of centers of the colliding pair is of little consequence. The transition probability for exchange is high only when the four-center transition state is generated by the association of a pair of molecules, one of which is in a high enough vibrational level. The vibrational excitation mechanism (a) accounts for the observed diverse power rate expressions, such as that for H₂ + D₂

$$\frac{d(\text{HD})}{dt} = k_p(\text{D}_2)^{0.66}(\text{H}_2)^{0.38}(\text{Ar})^{0.93}$$

(b) accounts for the narrow range of activation energies for exchange (for example, with ammonia it is approximately 39 kcal./mole, with hydrogen 42 kcal./mole, with methane 52 kcal./mole; (c) permitted the *a priori* calculation of the pre-exponential factor for the exchange rate between hydrogen and deuterium from the observed vibrational relaxation times,⁴ to within a factor of five. Further, an extension of this mechanism to the reactions C₂N₂ + H₂ → 2HCN and C₂N₂ + D₂ → 2DCN predicted that the rate of the latter is severalfold faster than that of the former. We found that DCN/HCN = 6 (1050°K.), 3 (1130°K.), 1.6 (1200°K.).

While the indirect evidence is impressive, it is difficult to demonstrate directly that the exchange rate is insensitive to the relative translational energy of the colliding pair. In contrast, the demonstration of the second half of the postulate, that vibrational excitation in the absence of any significant translational contribution is sufficient for exchange, has now been made. In this proof we utilized the very interesting reaction reported recently by Hassler and Setser⁵ on the homogeneous gas phase reaction of diazomethane with mineral acids. They found that



Their explorations showed that whereas CH₃I^{*} is sufficiently activated (approximately 60 kcal./mole) to decompose unimolecularly to CH₃ + I, in CH₃Br^{*} and CH₃Cl^{*} the bond-dissociation energies for the corresponding C-X bonds are greater than the available excitation energy and avoid decomposition. *No radicals could be detected in these mixtures.* These facts we accept without further tests; however, our analytical data indirectly support their conclusions.

We found that when the reaction between diazomethane and HBr (or HCl) was carried out at room temperature using D₂ or CD₄ as diluents, a significant fraction of the alkyl halides appeared as CH₂DX. This is due to H-D atom exchange which occurs at room temperature between the nascent, vibrationally activated CH₃X^{*} and either D₂ or CD₄. Were the energy released during the reaction to appear as relative translational energy of the two product molecules, only 23% (≈14 kcal./mole) could be carried by the methyl bromide, and this is insufficient for exchange activation. Further evidence for this conclusion was provided by the reaction between diazomethane and DX

(4) J. H. Kiefer and R. W. Lutz, *Phys. Fluids*, **8**, 1393 (1965), and private communication.

(5) J. C. Hassler and D. W. Setser, *J. Am. Chem. Soc.*, **87**, 3793 (1965).