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STRUCTURES OF CARBANIONS, II. EFFECTS OF CATION, CONCENTRATION, AND SOLVENT UPON THE GEOMETRIES OF REACTIONS OF ENOLATE ANIONS

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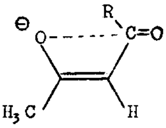
In the preceding paper[1] we reported that O-phosphorylation of the potassium enolates of a variety of substituted ketones gave mixtures consisting predominantly of cis-isomers[2] from reaction in non-polar solvents and predominantly of trans-isomers[2] from reaction in polar solvents. Formation of cis-isomers in non-polar solvents could be attributed either to interaction of the negatively charged oxygen with the polar group (-CN, $-CO_2Et$, $-COCH_3$, or $-PO(OEt)_2$), as in structure I, or to chelation of the anion with the potassium cation, as in structure II. In either case, the cis-configuration of the anion was assumed to be maintained during reaction with the phosphorylating agent, giving rise to the cis-configuration in the product. In polar solvents, on the other hand, the enolates were assumed to consist largely of "free" anions, in which the normal repulsions between the two polar groups on the double bond resulted in a predominantly "trans"-configuration.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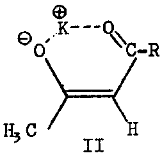
II

In this paper, we present evidence that formation of products of cis-configuration in non-polar solvents is indeed due to chelation of the anion with the metal counterion, while formation of trans-isomers in polar solvents is due to reaction of the "free", unchelated anions. Furthermore, we show that this effect is not limited to phosphorylation reactions, but occurs with a wide variety of reagents which attack the oxygen atom of enolate anions.

Table I lists the trans/cis product ratios for the reactions of various enolates of ethyl acetoacetate with O,O-diethyl phosphorochloridothioate (DECT) in several solvents. All reactions were carried out at 25° in 1.0 molar solution, and the trans/cis ratios obtained by nmr analysis of the vinyl proton peaks.

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Table I

Reaction of DECT with Enolates of Ethyl Acetoacetate

$$CH_3\overset{O}{\overset{\|}{C}}CH_2CO_2C_2H_5 \xrightarrow{Base} CH_3\overset{O^-}{\overset{|}{C}}=CH-CO_2C_2H_5 \xrightarrow{DECT} (EtO)_2\overset{S}{\overset{\|}{P}}-O-C(H_3C)=CH-CO_2C_2H_5$$

Base	Solvent	Trans/Cis
Potassium t-Butoxide	Dimethyl Sulfoxide	9.0
Sodium Methoxide	Dimethyl Sulfoxide	2.2
Potassium t-Butoxide	Dimethyl Formamide	6.5
Potassium Methoxide	Dimethyl Formamide	6.8
Sodium Methoxide	Dimethyl Formamide	1.0
Lithium Methoxide	Dimethyl Formamide	0.25
Tetramethylammonium hydroxide	t-Butanol	15.0
Tetramethylammonium hydroxide	Dimethyl Sulfoxide	21.0

It is clear that changing the cation employed has a great effect on the trans/cis ratios. The smaller cations, which form less ionic salts,[3] give much higher percentages of cis-products. The difference between sodium and potassium is striking, as are the very high percentages of trans-isomers formed when tetramethylammonium salts are used. It has previously been demonstrated that tetraalkylammonium salts exist largely as free ions, even in relatively nonpolar solvents[4], which accords with our hypothesis that trans-isomers are formed from free anions. These results also show that the nature of the basic anion has little effect upon the isomer ratio. Within experimental error, the use of t-butoxide or methoxide as bases gave identical results.

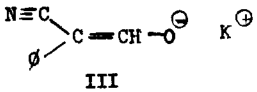
These observations provide strong evidence for the hypothesis that predominant formation of isomers with cis-configurations results from reaction of anions which exist in close association with the counterion. Further support for this hypothesis was obtained from a study of the effect of concentration upon the isomer ratios. If the free ion gives products of trans-configuration, more dilute solutions should give higher percentages of trans-products, since the percentage of free ions in equilibrium with the complexed ions should increase. Table II lists the results of this study, which are completely in accord with this prediction.

Table II

Reaction of Ethyl Sodioacetoacetate with DECT in Dimethyl Formamide

Concentration (moles/liter)	Trans/Cis
2.0	0.67
1.0	1.0
0.5	1.7
0.25	2.1

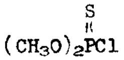
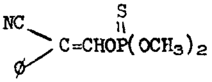
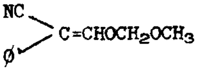
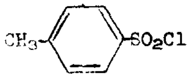
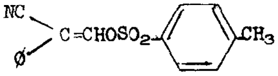
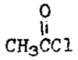
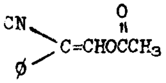
The reactions reported above and in the preceding paper[1] all involve phosphorylation of enolate anions. However, other reagents should similarly give higher amounts of *trans*-products when the reactions are carried out under conditions in which the enolate anions exist predominantly as free ions. We have therefore studied the *trans*/*cis* isomer ratios in the products obtained from reaction of the potassium enolate of 2-phenyl-3-hydroxyacrylonitrile (III) with several different electrophiles. Anion III was employed because the stability of the enolic



III

form of 2-phenyl-3-hydroxyacrylonitrile seemed likely to minimize the probability of reaction at carbon competing with reaction at oxygen. The results of these reactions are presented in Table III.

Table III

Reagent	Product	Solvent	Trans/cis	% yield
 $(CH_3O)_2\overset{S}{\overset{\|}{P}}Cl$		DMSO	2.3:1	63
		t-BuOH	1:7	79
CH_3OCH_2Cl		DMF	2.5:1	48
		t-BuOH	1:5	62
		DMF	1.5:1	64
		t-BuOH	largely *cis*	73
 $CH_3\overset{O}{\overset{\|}{C}}Cl$		DMF	1.8:1	81
		t-BuOH	1:5	84

The configurations of the products listed in Table III were assigned on the basis of the positions of the vinyl proton peaks in the nmr spectra of the products. In all products assigned *trans*-configurations (vinyl hydrogen *trans* to the phenyl group) the vinyl proton singlet lies from 0.2 to 0.3ppm upfield from the position of the peak in the corresponding products assigned *cis*-configuration. Application of the Z values of Pascual et al.[5] to our compounds indicates that the vinyl proton resonances in the *trans*-isomers should lie *ca*. 0.27ppm upfield from those in the *cis*-isomers, in good agreement with our observations.

It can again be seen that the percentage of *trans*-isomers in the products increases as the polarities of the solvents increase. It would be of great interest to compare the *trans*/*cis* ratios obtained from each of the reactions under a given set of conditions. If the ratios were identical for all the reactions, it would provide strong evidence that the isomer ratios in the products are identical with those of the anions in solution. Unfortunately the relatively low yields recorded in Table III prevent precise comparisons, since we cannot be sure that one of the isomers is not selectively destroyed during the reaction of workup. We hope that work now in progress will cast light on this question.

References

1. B. Miller, H. Margulies, T. Drabb, Jr., and R.S. Wayne, Tetrahedron Letters, preceding paper.
2. As was previously defined,[1] *cis*-isomers are those in which the oxygen atom is *cis*- to the polar group on the adjacent vinyl carbon.
3. G.E. Coates, M.L.H. Green, P. Powell, and K. Wade, "Principles of Organometallic Chemistry", Methuen and Co., London, 1968, pp 32-33.
4. S. Winstein, L.G. Savedoff, and S. Smith, Tetrahedron Letters, No. 9, 24 (1960).
5. C. Pascual, J. Meier and W. Simon, Helv. Chim. Acta, 49, 164 (1966).