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EFFECT OF EXCESS REACTANT ON THE STERIC COURSE OF CARBONYL OLEFINATION

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It has recently been shown that in the reaction of aldehydes with ylids stabilized by a conjugated CO-group intermediate betaine formation is reversible (1,2). Such reversibility has not yet been demonstrated for unstable ylids (see review (3)). We have attempted to solve this problem, using a stereochemical approach, since the high rate of conversion of the unstable ylids into the betaines makes difficult a kinetic study of the reaction mechanism. We, therefore, investigated the effect of excess initial reactants on the steric course of the reaction between propylidenetriphenylphosphorane (I) and benzaldehyde in the presence of various halogen salts and in various solvents.(see table 1).

It was found that a twofold excess of ylid has no effect on the steric course of the reaction in dimethylformamide solution (cf. runs 1-5). However, in benzene in the presence of LiI an increase in the relative ylid or benzaldehyde content sharply augments the relative yield of the cis isomer (cf. runs 8-10). On the other hand an excess of ylid has a much weaker effect on the stereochemistry of the reaction when the latter is carried out in benzene in the presence of LiCl (runs 6 and 7).

Earlier we had found (4,5) that halogen salts promote the formation of cis β-ethylstyrene when the reaction (A)

TABLE 1. Effect of Reactant Ratio and of Halide on the Steric Course of the Reaction:

$EtCH{=}PPh_3(I) + PhCHO \longrightarrow EtCH{=}CHPh + Ph_3PO$ (A)*

No	Solvent	Halide	Ylid:Aldehyde Ratio	Olefin Yield %	Cis:Trans Ratio
1	DMF	LiCl	1:1	52	73:27
2	DMF	NaCl	1:1	58	75:25
3	DMF	NaCl	2:1	58**	71:29
4	DMF	NaI	1:1	40	74:26
5	DMF	NaI	2:1	94**	73:27
6	Benzene	LiCl	1:1	62	79:21
7	Benzene	LiCl	2:1	86**	88:12
8	Benzene	LiI	1:1	33	35:65
9	Benzene	LiI	2:1	55**	65:35
10	Benzene	LiI	1:2	28***	59:41
11	Ether	LiCl	1:1	70	80:20
12	Ether	LiI	1:1	46	22:78

*Reaction performed at 20° in nitrogen on a 1.5 mMole scale with 0.3 M/l concentrations. Solutions of the ylid (I) in benzene were prepared by reacting BuLi with triphenylpropylphosphonium chloride or iodide. For solutions of the ylid (I) in DMF, BuLi or NaH were used as bases. After mixing, the reactants were stirred for 1 hour. The cis:trans isomer ratio was determined by gas-liquid chromatography, with an accuracy of 2-4 relative percent. Special experiments showed that no isomerization of cis and trans β-ethylstyrene takes place.

**Based on the aldehyde.

***Based on the ylid.

is carried out in benzene. The effect of the halogen salts is due to their behaving as Lewis bases with respect to the phosphoranes or corresponding betaines in which capacity they coordinate with the phosphorus. When the complex (II) reacts with the aldehyde the factor determining the preferential betaine conformation becomes electrostatic repulsion of the electronic shells of the coordinately bound halide and the carbonyl oxygen. The increased probability of cis-olefination under such conditions is due to energy advantage of the erythro betaine (IV), which in this case forms more readily than the threo isomer (III)[*]. At the

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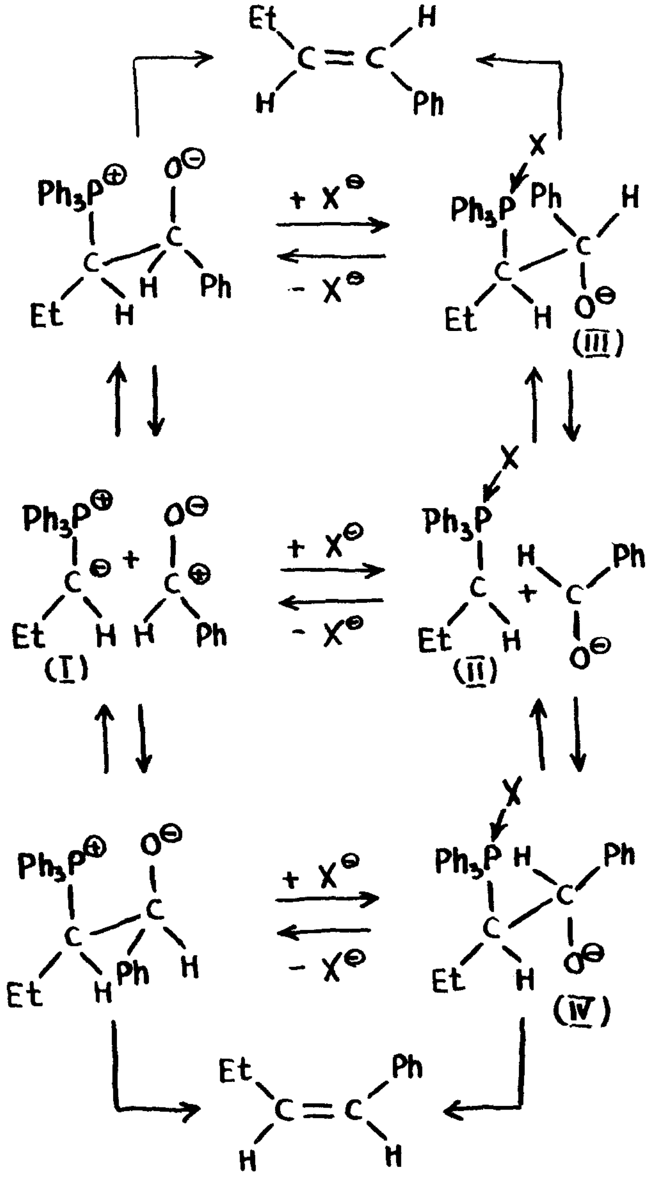
[*] H.O.House et al. (6) expressed the belief that when the Wittig reaction is carried out in the presence of a metal halide the increase in relative yield of the cis isomer (4,5) is due only to the influence of the Lewis acid (coordination of the cation with the carbonyl oxygen) and is independent of the nature of the Lewis base. This is in variance with a number of facts we have observed in studying the stereochemistry of carbonyl olefination. Thus we have found that in dimethylformamide in the presence of LiCl, NaCl and KCl the stereochemistry of the reaction $PhCH{=}PPh_3$(V) + $OCHEt \longrightarrow PhCH{=}CHEt + Ph_3PO$ is independent of the cation species (cis:trans ratio 39:61, 38:62 and 39:61), whereas when the reaction is carried out in benzene in the presence of LiCl, LiBr or LiI the cis:trans isomer ratio increases from Cl^- to I^- (20:80, 26:74 and 42:58, respectively). At the same time, the transition from LiCl to LiI is in a number of cases accompanied by a considerable fall in the over-all reaction rate (cf. Table 1). Since the solubility (very low) of the lithium halides in benzene solution of the phosphorane (V) is of the same order of magnitude these facts cannot be explained by solubility differences of the halides but serve to confirm the existence of coordination of the ylids and betaines with Lewis bases and show that the effect of the latter on the stereochemistry of the reaction cannot be ignored. Naturally, the stereochemistry of the Wittig reaction in certain cases can depend not only on the Lewis bases, but also on the Lewis acids coordinating with the carbonyl compounds. This problem which we have been studying for some time will be the subject of a separate communication.


+ X⊖
- X⊖
X
(I)
(II)
(III)
(IV)

same time the halogen ions, in particular iodine ions, diminish the over-all rate of the reaction (cf. runs 6 and 8 or 11 and 12) by sterically hindering accessibility to the phosphorus of the betaines (III) and (IV) and simultaneously increasing its electron density. As a result the iodine ions increase the reversibility of the reaction and, when the second stage (transformation of the betaine to the olefin) occurs sufficiently slowly as compared with the first stage, equilibrium is established between the diastereomeric betaines. Therefore, in low polar solvents lithium iodide lowers the stereospecificity of the reaction (A). The effect of excess reactant on the steric course of the reaction, increasing the stereospecificity, is due to suppression of the reversible decomposition of the betaines. Consequently the change in the steric direction of carbonyl olefination in the presence of excess reactant is a direct confirmation of the reversibility of betaine formation in the case of unstabilized ylids.

In combination with other cis directing factors of the Wittig reaction (polar solvents, inorganic salts) the use of excess ylid allows one to achieve practically complete cis olefination of some aldehydes with non-stabilized phosphorylids (see review (7)). It should, however, be noted that the stereochemical influence of all these factors is greatly dependent on the solubility of the ylids, betaines and their complexes with the inorganic salts. In some cases cis olefins are formed in sufficiently high yield also when the reaction is carried out without excess of reactant. Thus in the reaction $EtCHO + Ph_3P{=}CHEt \longrightarrow EtCH{=}CHEt + Ph_3PO$ in dimethylformamide at 20° in the presence of LiCl, LiBr or LiI the cis:trans ratios of the hexenes were respectively 96:4, 94:6 and 95:5, even though the reaction was carried out with equivalent amounts of ylid and aldehyde.

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