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SOME STEREOCHEMICAL IMPLICATIONS OF A BI-FUNCTIONAL WITTIG REACTION

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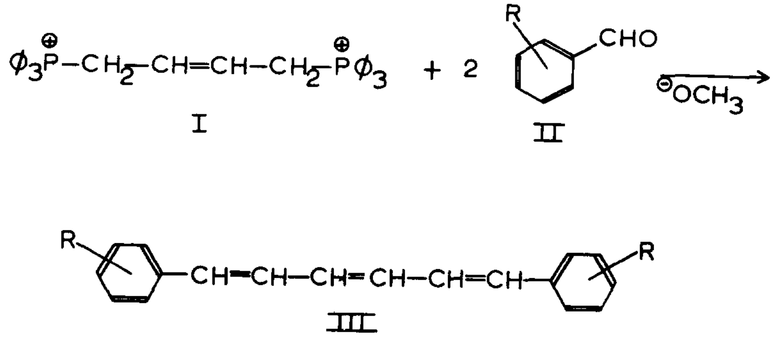
THE stereochemical course of the Wittig reaction has received considerable attention during recent years (1); however, the discussion in all cases has been limited to a consideration of the monofunctional Wittig reagents alone. In this communication we wish to present our observations on the reaction of the bifunctional reagent I with a series of aldehydes (II) and discuss the implication of these results on the stereochemistry of the process of polyene (III) formation.



When the reaction of I with the various aldehydes was carried out in methanol, a rapid formation of a mixture of the stereoisomeric polyenes (III), as indicated by the ultraviolet spectrum of the mixture, was observed, from which the all-trans isomer separated as a pure product. The yields of the all-trans isomers so obtained with the different aldehydes varied considerably with the nature of the substituent R in the aldehyde and on the fact whether the reaction was conducted in the presence or absence of light. The results of the reactions carried out in the dark and in sunlight are described in Table I.

Table I*

Aldehyde	All-trans polyene yield in %	
	light	dark
p-dimethylaminobenzaldehyde	6	-
3,4-dimethoxybenzaldehyde	14	1
p-methoxybenzaldehyde	15	1
p-methylbenzaldehyde	24	8
benzaldehyde	70	2
o-chlorobenzaldehyde	72	30
p-chlorobenzaldehyde	70	10
m-nitrobenzaldehyde	80	60
p-nitrobenzaldehyde	80	45

* Correct micro-analyses have been obtained for all the new compounds described in this table

The data presented in Table I reveals two significant trends in regard to the *all-trans* polyene formation during the Wittig reaction of I, these being, (a) an apparent "light effect" and (b) a polar effect arising from the electronic character of the substituent in the aldehyde, both effects causing an increase in the yield of the *all-trans* product. The nature of the observed "light effect" was readily recognised as the enhancement of the *trans* isomer formation in the stereoisomeric mixture via a rapid light induced cis-trans isomerisation (2). In accord with this concept it was found that the product of the "dark reaction" contained large amounts of the polyenes* after isolation of the *all-trans* isomer, which could be readily converted to a further quantity of the latter by exposure to sunlight. Thus it would appear that the differences in the yields of the *all-trans* compounds formed in the light and in the dark (Table I) reflect for a great part a variation in the stereoisomeric composition of the polyene mixture initially formed during the reaction.

In order to explain the polar influence of the substituents (R) in the aldehydes on the isomer ratio of the polyenes formed, one may extend the general mechanistic considerations which have been developed for the monofunctional Wittig reagents (3) to the present system as well. However, in the latter case it may be further assumed that the addition of the aldehyde moiety to the two sites of the reagent occurs in two separate

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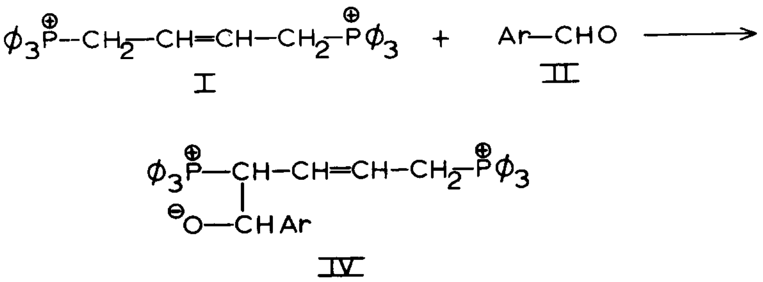
* The residual "polyene system" after isolation of the *all-trans* product probably consists of one or more of the remaining stereoisomeric 1,6-diarylhexatrienes.

steps. Such an assumption would seem to be amply justified in view of the highly unfavourable entropy of activation for a transition state involving a simultaneous attack of the aldehyde at both ends of the reagent.

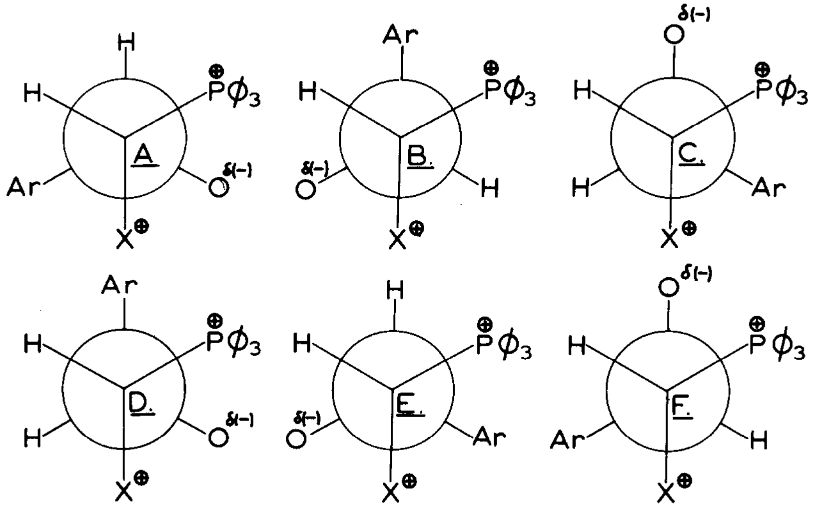


$$\underset{\text{I}}{\phi_3\overset{\oplus}{P}-CH_2-CH=CH-CH_2-\overset{\oplus}{P}\phi_3} + \underset{\text{II}}{Ar-CHO} \longrightarrow$$

$$\underset{\text{IV}}{\phi_3\overset{\oplus}{P}-\underset{\overset{|}{{}^{\ominus}O-CHAr}}{CH}-CH=CH-CH_2-\overset{\oplus}{P}\phi_3}$$

The possible steric alignments for the transition state for the betaine (IV) formation in the first step of the reaction can be represented by the six Newman structures A to F. Three of these, A, B and C would form betaines which would eventually collapse to a <u>cis</u> double bond while D, E and F would result in the formation of a <u>trans</u> olefinic linkage.

An examination of the molecular models of these structures clearly indicates that the Ar-X interaction in the transition state is less pronounced than that arising from the steric requirements for the proximity of the Ar and the $P\emptyset_3$ groups, thus suggesting structures A and F to be the sterically most favoured representations of the transition states eventually leading to the formation of the cis and trans linkage respectively.



$$X = -CH{=}CH-CH_2-\overset{\oplus}{P}\phi_3$$

It has been recently pointed out that the electronic factors operating in the transition state of the betaine formation may have a profound influence on the ultimate stereochemistry of the Wittig reaction (4,5,6).

A similar consideration of the Newman structures A and F would argue in favour of structure A in which the partial negative charge on the carbonyl oxygen of the approaching aldehyde molecule is electrostatically stabilised by the two flanking positive phosphorus atoms. The presence of electron attracting substituents in the aldehyde system would, however, decrease the negative charge on the oxygen atom by suppression of the contribution of the $\text{R-CH}^{+}\text{---O}^{-}$ structure in the ground state of the molecule and thereby reduce the significance of structure A with respect to F. Thus the formation of the trans olefinic linkage at the expense of the cis bond would be the anticipated trend in the reaction of reagent I with a series of aldehydes possessing increasingly electronegative substituents, which expectation is clearly borne out by the results presented in Table I. It may be pointed out that the above considerations do not permit us at this stage to draw any conclusions concerning the stereochemistry of the reaction at the second site of the reagent. However, one may expect that the second step of the reaction may be similar in behaviour to that of a monofunctional system. Some preliminary results of the reaction of bis trialkylphosphonium salts appear to support the general conclusions regarding the operation of the stereoelectronic effects observed in the reaction of the bifunctional Wittig reagent I.

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