Novel Structural Effects on the Stereochemistry of the Wittig Reaction with Diethyl Cyanomethylphosphonate

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THE stereochemistry of the olefins produced by the Wittig reaction has been extensively studied;[1] the reaction usually results in a predominance of the *trans*-olefin in the mixture. The stereochemistry of the olefins produced by the reaction of phosphonate carbanions with aldehydes or ketones has not been adequately studied, but the observations that have been made indicate that this reaction results in an even greater predominance of the *trans*-isomer.[2] Attempts to increase the proportion of *cis*-olefin by means of structural and environmental variation have been unsuccessful.[2,3] We now report the stereochemistry of the olefins produced by the Wittig reaction between diethyl cyanomethylphosphonate (I) and each of a series of alkyl phenyl ketones (II b–q). In these reactions the proportion of the *cis*-olefin is dependent on the structure of the ketone.

The ketone (0·1 mole) was added to a filtered solution of the carbanion from diethyl cyanomethylphosphonate (0·15 mole) and sodium hydride (0·15 mole) in 1,2-dimethoxyethane (150

TABLE

			Position of *cis*-olefinic proton (τ)	Position of *trans*-olefinic proton (τ)	*cis–trans* isomer ratio[c]	b.p. (°c/mm.)
(Va)	Ph	H	4·66(*J* 12 c./sec.)	4·26[a](*J* 16 c./sec.)	0·1	—
(Vb)	Ph	Me	4·65	4·44[a]	0·1	—
(Vc)	Ph	Et	4·66	4·53[b]	0·2	72–73/0·2
(Vd)	Ph	Pr^n	4·68	4·55[b]	0·2[h]	87–88/0·4
(Ve)	Ph	Pr^i	4·64	4·75[a]	0·7	78–79/0·1
(Vf)	Ph	Bu^n	4·65	4·56[b]	0·2[g,h]	102–104/0·4
(Vg)	Ph	n-pentyl	4·64	4·53[b]	0·2	109–110/0·5
(Vh)	Ph	cyclopentyl	4·71(*J* 2 c./sec.)	4·80[b]	0·5	116–120/0·5
(Vi)	Ph	cyclohexyl	4·70(*J* 1·5 c./sec.)	4·78[b]	0·6	122–124/0·4
(Vj)	2-methoxyphenyl	Bu^n	4·72[d]	4·72[b,d]	0·4[e]	111–112/0·5
(Vk)	3-methoxyphenyl	Bu^n	4·73	4·58[b]	0·2	146–148/1·8
(Vl)	4-methoxyphenyl	Bu^n	4·76	4·61[b]	0·2	138–140/0·6
(Vm)	4-methoxyphenyl	Bu^t	4·52	4·83[a]	3·0[e]	—
(Vn)	2-methylphenyl	Me	4·52(*J* 1·8 c./sec.)	4·78[a](*J* 1·2 c./sec.)	0·6[e,f]	92–94/1·5
(Vo)	2-methylphenyl	Bu^n	4·60	4·89[b]	0·6[e]	108–110/0·5
(Vp)	3-methylphenyl	Bu^n	4·75	4·60[b]	0·2	110–112/0·5
(Vq)	4-methylphenyl	Pr^n	4·69	4·54[a]	0·2	82–83/0·1

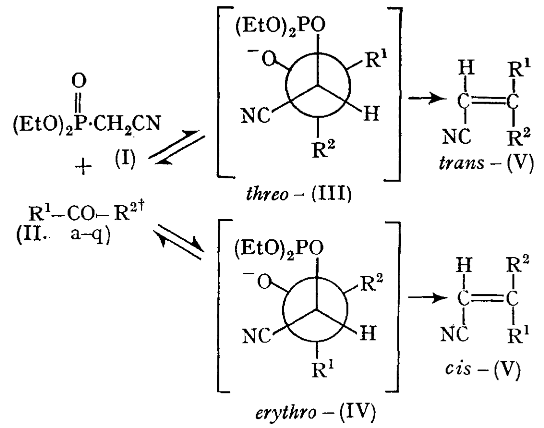
[a] In $CDCl_3$ with added Me_4Si as standard;
[b] In CCl_4 with added Me_4Si as standard;
[c] Approximated to the nearest whole number;
[d] Signal unresolved;
[e] Isomeric composition of crude olefin was confirmed by g.l.c. (2%, XE-60, 150—200°);
[f] The *trans*-isomer was isolated by preparative g.l.c. and used to confirm that no isomerisation of this *trans*-olefin occurred either during g.l.c. or in the presence of the carbanion of diethyl cyanomethylphosphonate under the reaction conditions described in text;
[h] The *cis–trans* isomer ratio was unchanged when dimethylformamide was used in place of 1,2-dimethoxyethane.

ml.) at 20°. The exothermic reaction increased the temperature of the mixture to about 50°. After 3 hr. the mixture was diluted with water and extracted with ether. Evaporation of the ethereal extract gave the crude olefin in almost quantitative yield. The isomeric composition of the crude olefin was determined by analysis of its n.m.r. spectrum and the results are shown in the Table.

In most of the *trans*-isomers, the olefinic proton is deshielded by the phenyl ring and olefinic proton resonance is observed at lower field than in the *cis*-isomer. Olefinic proton resonance in the *cis*-isomer is further characterised by fine structure due to the larger allylic coupling (*J* 1—2 c./sec.) of this configuration.[4] However, when the alkyl group is branched (Ve,h,i,m) or the *ortho*-position of the phenyl ring is substituted with a methyl group (Vn,o), the olefinic proton resonance of the *trans*-isomer is observed at higher field than that of the *cis*-isomer.

In these cases, it is considered that for steric reasons the phenyl ring is twisted out of the plane of the double bond and deshielding of the olefinic proton in the *trans*-isomer is reduced. In the case of (Vj) in which the *ortho*-position of the phenyl ring is substituted with a methoxy-group there is a less pronounced steric effect and the olefinic signals of the *cis*- and *trans*-isomers coincide.

The tabulated results show that the modified Wittig reaction between diethyl cyanomethylphosphonate and alkyl phenyl ketones yielded predominantly *trans*-olefins provided that the alkyl



† R^1=substituted or unsubstituted phenyl; R^2=alkyl.

group was unbranched and that the phenyl ring was unsubstituted in the *ortho*-position. However, when the alkyl group was secondary (Ve,h,i) the reaction yielded a substantial proportion of *cis*-olefin and when the alkyl group was tertiary (Vm) the *cis*-olefin became the major product of the reaction. When the phenyl ring was substituted in the *ortho*-position by methyl or methoxyl (Vj,n,o) the reaction yielded a substantial proportion of *cis*-olefin whereas in the case of corresponding substitution in the *meta*- or *para*-position (Vk,l,p,q) the reaction yielded predominantly *trans*-olefin.

These observations are consistent with the view that the rate of formation of the *threo*-betaine (III) is usually greater than that of the *erythro*-betaine (IV) which is more sterically hindered. Similarly, the rate of decomposition of the *threo*-betaine to the *trans*-olefin (V) is usually greater than that of the *erythro*-betaine to the *cis*-olefin (V) because the *threo*-betaine is less sterically hindered and provides better conjugative stabilisation of the incipient double bond in the transition state. Branching of the alkyl chain increases steric hindrance in the *threo*-betaine. The rate of formation of the *threo*-betaine and the rate of its decomposition to the *trans*-olefin are thus reduced. *ortho*-Substitution of the phenyl ring decreases the conjugative stabilisation of the incipient double bonds in the transition states, and since conjugative stabilisation is usually greater in the transition state leading to the *trans*-olefin, the proportion of the *trans*-olefin in the reaction mixture is decreased.

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