

Formation of *cis*-Substituted Esters by means of Phosphonate Ester Condensations

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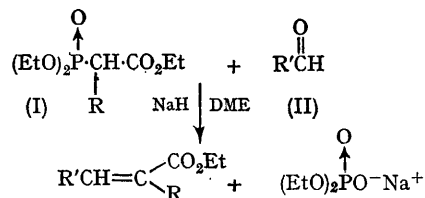
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SEVERAL reports^{1,2} have dealt with the mechanism and stereochemistry of the synthetically invaluable Wittig reaction and it is now well known that stabilized ylids furnish a predominance of *trans*-olefin, while mixtures of isomers (and under certain conditions, mostly the *cis*-isomer)² are obtained from less-stable ylids. The phosphonate modification of the Wittig reaction^{3,4} has been reported to invariably yield a greater preponderance of the *trans*-isomer, even under solvent and structural conditions which should favour formation of the *cis*-isomer.⁵ Two recent reports^{6,7} of the formation of olefin mixtures containing significant amounts of *cis*-isomer, with ketones as the carbonyl compound, have prompted us to report our results.

Condensation of the phosphonate anions of (I; R=Me, Et) with a series of aldehydes produced up to 84% of the *cis*-isomer (see Table). Our method involved the slow addition of a slight excess of the aldehyde to a dimethoxyethane

(DME) solution of the phosphonate carbanion at 15°. The mixture was then stirred for 3 hr. at room temperature, diluted with water, and extracted with ether to yield the mixed esters in 65–95% yield. The reaction mixture was analyzed by n.m.r. spectroscopy⁸ (shown in Table) and v.p.c.[†]

Previously, phosphonate anion condensations which have yielded significant amounts of *cis*-olefins have used ketones as the carbonyl compound,^{6,7} and the results in the Table are the first examples of *cis*-ester formation with aldehydes.



† We have demonstrated that no *cis* ⇌ *trans* equilibration occurs under the reaction conditions, or even in the presence of a large excess of hot phosphonate anion solution. Relatively rapid isomerization of *cis* → *trans*-isomer occurs with sodium hydride in refluxing dimethoxyethane.

Jones and Maisey⁷ have shown that the amounts of *cis*-isomer formed with the anion of (III) were dependent on the structure of the aryl ketone used, particularly on its steric bulk. We have

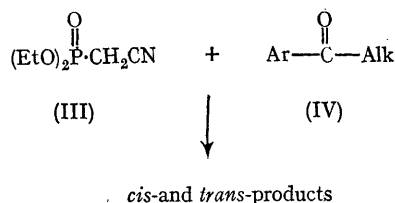
proceed with difficulty, and condensation of (I; R=Prⁱ) with 2-methylpropanal yielded only the *cis*-product in agreement with the trends noted in the Table.

TABLE

Run	R	R'	Position of <i>cis</i> - vinyl proton (p.p.m.)	Position of <i>trans</i> - vinyl proton (p.p.m.)	% <i>cis</i> -isomer
1	H	Pr ⁱ	—	6.84	None detectable
2	H	Bu ^t	—	6.86	"
3	Me	Me	—	6.80	"
4	Me	Et	5.85	6.65	16
5	Me	Pr ⁱ	5.62	6.46	62-73*
6	Me	Bu ⁱ	5.58	6.45	67
7	Me	Bu ^t	5.40	6.68	50
8	Et	Me	5.91	6.75	18
9	Et	Et	5.8	6.68	41
10	Et	Pr ⁱ	5.52	6.42	84*
11	Et	Bu ^t	5.35	6.52	55
12	Me	Mesityl	—	7.52	None detectable

* The % of *cis*-isomer was unchanged when dimethylformamide replaced the 1,2-dimethoxyethane.

systematically varied the size of the R' group in (II) and the R group in (I) and found that when R=H, only the *trans*-ester is formed, even with 2,2-dimethylpropanal. However, when R=Me, the amount of *cis*-isomer increases as R' gets



larger, then decreases again when R' is Bu^t. The same effects are noted in an even more pronounced way with R=Et. Condensations with (I RPrⁱ);=

This condensation makes readily available many less stable, very hindered *cis*-conjugated esters, for further chemical and spectral studies. Separations of the *cis*- and *trans*-isomers can be effected by distillation or by preparative v.p.c.

It is apparent that steric factors are primarily responsible for these trends, probably by hindering rotation in the initially formed betaines. Kinetic studies are in progress to determine more precisely the nature of these steric influences, and these results as well as some applications of the results to some stereoselective syntheses will be reported.

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