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Reaction of Phosphoranes with Formate Esters. A New Method for Synthesis of Vinyl Ethers[1]

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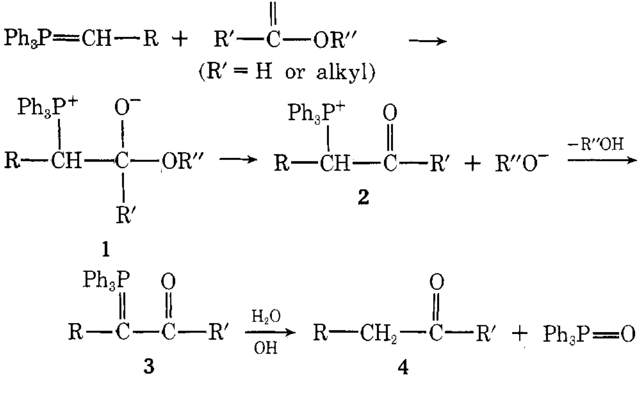
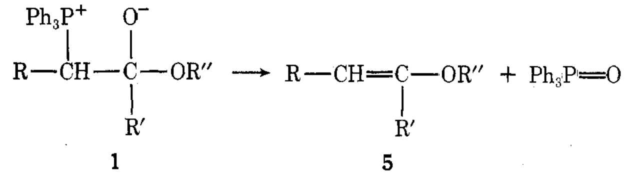
The Wittig reaction between phosphorus ylides and esters of carboxylic acids initially give β-ketoalkylphosphonium salts (**2**), which eliminate R″OH to form the stabilized β-ketoalkylidene phosphoranes (**3**).[2,4] Hydrolytic cleavage of these provides a useful synthesis of corresponding carbonyl compounds (**4**). Ethyl formate is reported to give aldehydes.[3] A reinvestigation of the reaction with formate esters was undertaken with the hope of developing a general method for the synthesis of substituted vinyl ethers instead of the reported aldehydes.[3] This study demonstrates the general feasibility for preparing vinyl ethers by this sequence.

Earlier investigations[2–5] of the mechanism of these acylation reactions indicate an initial nucleophilic attack by the ylide on the carbonyl function to form a betaine (**1**) intermediate. Elimination of OR″ from **1** as alkoxyl ion generates the phosphonium salt **2**. If such elimination is precluded, an alternative course of reaction is elimination of $Ph_3P{=}O$ to form vinyl ether **5**.

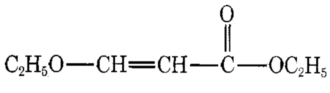




The latter possibility prompted us to explore the role, if any, of the group R′ of the ester function in determining the course of reaction. The reactions were carried out with phosphoranes ($Ph_3P{=}CHR$) that were stabilized (R = CO_2Et), partially stabilized (R = Ph), or reactive (R = alkyl or OCH_3). The esters used were those of formic, acetic, butyric, and benzoic acids and primary, secondary, and tertiary alcohols.

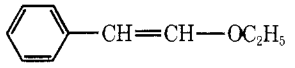
In reactions of phosphoranes with formate esters, where R′ is hydrogen, elimination of $Ph_3P{=}O$ occurred with the formation of vinyl ethers. Reaction conditions and yields depended upon the reactivity of the ylides.

The stable ylide carbethoxymethylenetriphenylphosphorane on refluxing with ethyl formate gave the vinyl ether **6** in 95% yield. A partially stabilized ylide derived from benzyltriphenylphosphonium chloride reacts with ethyl formate at room temperature to give **7** in 90% yield. However, reactive phosphoranes derived from 3-methylbutyltriphenylphosphonium bromide and methoxymethyltriphenylphosphonium chloride react with ethyl formate at room temperature to yield the reported β-formylalkylidene phosphorane.[4] When these reactions were carried out at −78 °C, the 3-methylbutylidenephosphorane gave 22% yield of vinyl ether **8**, but no vinyl ether was obtained from methoxymethylenetriphenylphosphorane at this temperature.



$C_2H_5O{-}CH{=}CH{-}C({=}O){-}OC_2H_5$

6



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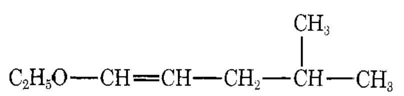
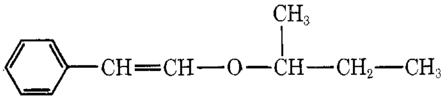


$C_2H_5O{-}CH{=}CH{-}CH_2{-}CH(CH_3){-}CH_3$

8

It appears that in reactive phosphoranes elimination of alkoxyl ion is favored at room temperature. This tendency is reduced at −78 °C and as a result some vinyl ether is formed. In the case of methoxymethylenetriphenylphosphorane, elimination of alkoxyl ion seems to be the only preferred mode of reaction, even at −78 °C. Consequently, no vinyl diether is formed.

In a second set of experiments, the partially stabilized ylide benzylidenetriphenylphosphorane was allowed to react with formate esters of *sec*-butyl alcohol and cyclohexanol. The red color characteristic of the phosphorane still remained after 8 h at 50 °C, but on work-up the corresponding vinyl ethers **9** and **10** were obtained in yields of 24 and 27%, respectively. A fourfold excess of formate esters and longer reaction times did not improve the yield. When



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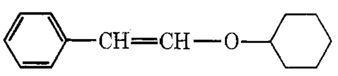

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reactions are carried out for longer periods than 8 h, *trans*-stilbene is formed in appreciable amounts possibly through dimerization of carbene intermediates. Similar results have been reported.[7] The low yields may be attributed in part to steric hindrance of bulky *sec*-alkyl groups. *tert*-Butyl formate, for example, does not react with any of the phosphoranes mentioned.

Our attempts to obtain vinyl ethers from the reaction of stabilized ylides as well as benzylidenetriphenylphosphorane with esters of acetic, butyric, and benzoic acids proved to be unsuccessful under a variety of conditions of temperature and reaction medium. Reactive ylides have been reported to give β-ketoalkylidenephosphoranes.[8]

In all cases, the products are mixtures of cis and trans isomers but the proportions vary depending upon the nature of the ylide. The stable ylide carbethoxymethylenetriphenylphosphorane gave cis and trans vinyl ethers in a 10:90 ratio, while with benzylidenephosphorane the proportion of cis isomer increased to 22% of the product. A cis–trans ratio of 45:55 was observed with the reactive ylide 3-methylbutylidenetriphenylphosphorane. The ratios were based on the vinylic absorptions in the NMR spectra of products.

It appears that substituted vinyl ethers may be conveniently synthesized by reaction of phosphoranes with ethyl formate under suitable conditions, thereby providing a general method for the conversion of alkyl and aralkyl halides to vinyl ethers.

Experimental Section

NMR spectra were recorded on a Varian T-60 instrument in $CDCl_3$. Chemical shifts are reported in δ units from internal Me_4Si, and are followed by parentheses giving multiplicity of signal, coupling constant if applicable, and number of protons. Spin multiplicity is given by s = singlet, d = doublet, t = triplet, q = quartet. All compounds showed satisfactory analytical data (±0.4% for C and H). Boiling points are uncorrected.

2-Carbethoxyethenyl Ethyl Ether (6). Carbethoxymethylenetriphenylphosphorane was prepared according to the published procedure.[9] A mixture of 17.5 g (0.05 mol) of the phosphorane and 40 ml of ethyl formate was heated under reflux for 4 h. The reaction mixture was cooled in ice and the triphenylphosphine oxide formed was separated by filtration. Excess ethyl formate was removed by distillation at atmospheric pressure. Distillation of the residual liquid at 0.5 Torr gave 6.8 g (95% yield) of a pleasant-smelling liquid boiling at 60–61 °C.

NMR spectrum: δ_{Me_4Si} 1.25 and 1.33 (t, t, 3 H, 3 H, $-CH_3$ of the two ethyl groups), 3.9 and 4.1 (q, q, 2 H, 2 H, $-CH_2-$ of the two Et), 4.78 and 5.17 (d, d, J = 7 and 13 Hz, together 1 H, $=CHOEt$), 6.57 and 7.57 (d, d, J = 7 and 13 Hz, together 1 H, $=CHCO_2Et$).

Ethyl Styryl Ether (7). Benzylidenetriphenylphosphorane was generated, according to the method of Corey et al.,[10] from 39.0 g (0.1 mol) of benzyltriphenylphosphonium chloride and 2.6 g (0.11 mol) of sodium hydride in 400 ml of dimethyl sulfoxide. Ethyl formate (15 g, 0.2 mol) was added to the phosphorane and stirred at room temperature for 3 h, during which the red color gradually changed to pale brown. The reaction mixture was thrown into 800 ml of water, the mixture was extracted exhaustively with pentane, and the combined pentane extract was dried over anhydrous $MgSO_4$. Pentane was distilled off under reduced pressure. A clear, colorless liquid boiling at 63 °C (1 mmHg) was obtained in 90% yield (13.3 g).

NMR spectrum: δ_{Me_4Si} 1.25 (t, 3 H, CH_3 of Et), 3.75 (q, 2 H, $-CH_2-$ of Et), 5.18 and 5.8 (d, d, J = 7 and 13 Hz, together 1 H, $=CHOEt$), 6.1 and 6.93 (d, d, J = 7 and 13 Hz, together 1 H, $=CHC_6H_5$), 7.08 (broad s, 5 H, C_6H_5-).

4-Methyl-1-pentenyl Ethyl Ether (8). A suspension of 20.7 g (0.05 mol) of 3-methylbutyltriphenylphosphonium bromide in 250 ml of anhydrous ether was stirred with 21 ml of a 2.4 M solution of *n*-butyllithium (0.05 mol) at room temperature in an atmosphere of N_2. After 0.5 h it was cooled in a bath of dry ice–acetone for 10 min. A solution of 4.1 g (0.055 mol) of ethyl formate in 10 ml of ether was slowly added with stirring. The red color discharged slowly. The reaction mixture was allowed to warm to room temperature. About 10 ml of alcohol was added and the slurry filtered. The filtrate was washed with water, dried with $MgSO_4$, and solvent removed by distillation at atmospheric pressure. The residue was distilled from a small flask and 1.4 g (22% yield) of compound **8** was obtained as a colorless liquid boiling at 132–133° (760 mm).

NMR spectrum: δ_{Me_4Si} 0.9 [d, 6 H, methyls of $-CH(CH_3)_2$], 1.23 (t, 3 H, $-CH_3$ of OEt), 1.73 and 1.85 (m, m, together 3 H, $-CH-$ and $-CH_2-$ of C-4 and C-3 respectively), 3.66 and 3.73 (q, q, together 2 H, $-CH_2-$ of OEt, trans and cis isomers, respectively), 4.27, 4.37, 4.60, and 4.82 (t, t, t, t, together 1 H, J = 7 and 13 Hz, respectively, $=CHCH_2$ cis and trans), 5.93, 6.17 (d, d, together 1 H, J = 7 and 13 Hz, respectively, $-CH=$ of $EtOCH=$).

***sec*-Butyl styryl ether (9) and cyclohexyl styryl ether (10)** were prepared by the same procedure used for making compound **7** from 0.05 mol of the benzylidenetriphenylphosphorane and obtained in 24 and 27% yields, respectively.

Registry No.—(*E*)-**6**, 5941-55-9; (*Z*)-**6**, 40648-44-0; (*E*)-**7**, 20565-86-0; (*Z*)-**7**, 13294-31-0; (*E*)-**8**, 16969-14-5; (*Z*)-**8**, 16969-29-2; (*E*)-**9**, 57967-99-4; (*Z*)-**9**, 14371-22-3; (*E*)-**10**, 57901-31-2; (*Z*)-**10**, 57901-32-3; carbethoxymethylenetriphenylphosphorane, 1099-45-2; ethyl formate, 109-94-4; benzylidenetriphenylphosphorane, 16721-45-2; 3-methylbutyltriphenylphosphonium bromide, 28322-40-9.

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Europium Shift Reagents. The Assignment of Aryl Stereochemistry in 6,6-Diarylbicyclo[3.1.0]hexan-3-*exo*-ols

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As part of our studies on remote electronic interactions, we have studied the stereoselectivity of cylopropanation by substituted diarylcarbenoids.[1] The assignment of endo/exo aryl stereochemistry on the isomeric 6-phenyl-6-arylbicyclo[3.1.0]hex-2-ene products was a tremendous problem that could not be solved by uv spectroscopy,[2] ^{13}C NMR,[2] or OH-π bonding studies[3] on alcohol derivatives. CNDO calculations indicated that photoelectron spectroscopy would not be helpful.[2] Although ^1H NMR has been used to study the stereochemistry of various 6,6-disubstituted bicyclo[3.1.0]hexane derivatives[4] and a great number of phenylcyclopropanes,[5] the small (ca. 0.1 ppm) but regular shifts of the center of each aryl pattern seen here were not definitive. Europium shift reagents have been applied to a variety of stereochemical problems[6] and the necessary alcohol derivatives could be readily prepared[3] via hydroboration of the bicyclic olefins (eq 1). We therefore present a europium shift reagent study that clearly defines the aryl stereochemistry in 6,6-diarylbicyclo[3.1.0]hexan-3-*exo*-ols (**3**) and suggests the principal conformation of the 5 ring. We