

A NEW SYNTHESIS OF METHYL KETONES

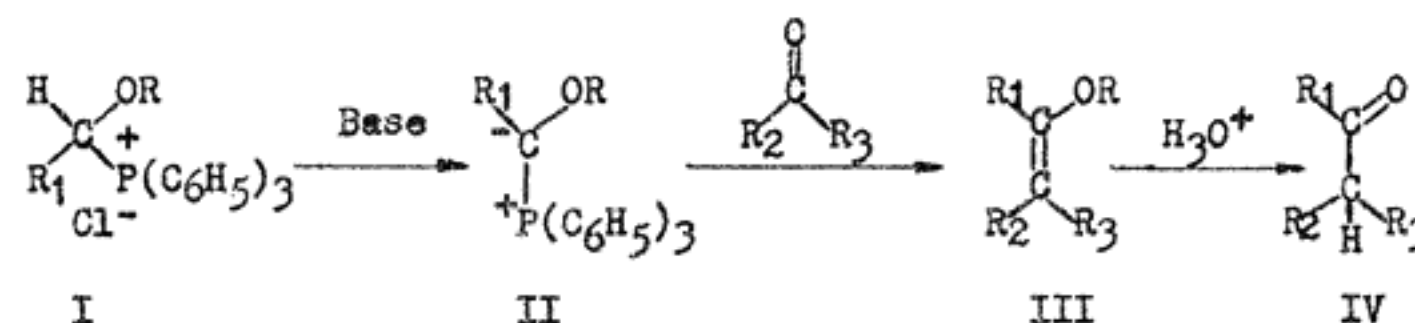
D. Robert Coulsen*

Department of Chemistry

Columbia University, New York 10027

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The Wittig Olefin Synthesis has been ingeniously applied to the synthesis of aldehydes, utilizing the phosphonium salts (I, $R_1=H$, $R=CH_3$, $p-CH_3C_6H_5$, etc.)^{1,2,3}). As a simple extension of this sequence, the synthesis of methyl ketones by way of α -methoxyethyl triphenyl phosphonium chloride (I, $R=R_1=CH_3$) was investigated. It was found that, although an ylid (II, $R=R_1=CH_3$) is involved which is much less stable than those obtained from (I, $R_1=H$, $R=CH_3$, $p-CH_3C_6H_5$, etc.), good to excellent yields of methyl ketones could be realized from representative aldehydes. The ketones studied gave lower yields of the corresponding methyl ketones. This makes attractive the possibility, already noted elsewhere⁴), of a general synthesis of alkyl ketones utilizing the α -halo ethers derived from a variety of aldehydes.



The phosphonium salt (I, $R=R_1=CH_3$) was prepared by dissolving triphenyl phosphine (76.4 g., 0.29 mole) and α -chloroethyl methyl ether⁵) (28.4 g.,

*Present address: Department of Chemistry, University of Chicago, Chicago, Ill.

0.30 mole) in 125 ml. of benzene. After standing 40 hrs. the mixture was filtered and washed with ether giving a white solid (112 g., 88% yield) consisting of the crude phosphonium salt containing one molar equivalent of benzene of crystallization. Attempts to recrystallize this salt resulted in partial or complete conversion to a crystalline dihydrate. Consequently, the salt was characterized as its dihydrate (m.p. 88.4-88.8°C from chloroform-benzene). The NMR spectrum in chloroform gave 8.41 τ , quartet ($J_{\text{PH}}=18$ cps, $J_{\text{HH}}=7$ cps); 6.46 τ , singlet; 3.61 τ , multiplet; 1.50 τ , singlet; intensity ratio 3:3:1:3.5 respectively. The aromatic protons were obscured by the chloroform signal. Anal.: Calculated for $\text{C}_{21}\text{H}_{26}\text{ClO}_3\text{P}$, C=64.18, H=6.66; Found 63.64, H=6.53. However, the crude salt was found sufficiently pure for the following reactions. The salt is slightly hygroscopic on exposure to air but can be stored indefinitely in a sealed container.

The ylid (II, $\text{R}=\text{R}_1=\text{CH}_3$) resulting from treatment of (I, $\text{R}=\text{R}_1=\text{CH}_3$) with base was found to be very unstable at room temperature, the characteristic red color disappearing within a few seconds of formation. Accordingly, the preparation and reaction of this ylid was best carried out at -40°C . The general procedure used for the preparation of the crude enol ethers (III, $\text{R}=\text{R}_1=\text{CH}_3$) was as follows: The phosphonium salt (33 mmoles) was suspended in 40 ml. of glyme at -40°C . under nitrogen. Potassium t-butoxide (33 mmoles) in 15 ml. of glyme was added with stirring over five minutes. At this point a solution of the aldehyde or ketone (30 mmoles) in 5 ml. of glyme was added over five minutes. The mixture was allowed to warm to room temperature over one hour and was then directly distilled.

The distillates obtained were usually quite pure samples of enol ethers in the reactions of the aldehydes. 2-Methoxy-2-nonene obtained from heptaldehyde was a clear liquid of b.p. $50-55^\circ\text{C}/3$ mm. The infra-red spectrum gave bands at 1665 cm^{-1} and 1080 cm^{-1} . Anal.: Calculated for $\text{C}_{10}\text{H}_{20}\text{O}$, C=76.86, H=12.90; Found C=76.64, H=12.90. The geometrical isomers of this

particular enol ether were present in approximately equal amounts as determined by the different chemical shifts of the cis and trans methoxy groups (6.54 τ and 6.58 τ , neat, specific assignments not determined).

The ketones, under these reaction conditions, gave mixtures of enol ethers and unreacted ketone.

The methyl ketones were conveniently prepared from the enol ethers by mixing with one equivalent of water containing 0.5% HCl and enough methanol to effect solution. The solution was heated to boiling and the solvent was then evaporated to give relatively pure samples of ketones in practically quantitative yields. The ketones prepared were characterized by their semicarbazones as shown in Table I.

TABLE I

Carbonyl Compound	Methyl Ketone	Yield ⁶⁾	M.P. of Semicarbazone ⁷⁾	
			Found	Reported
Benzaldehyde	3-Phenyl-2-propanone	88%	185.8-186.3 ⁸⁾	Variable
Cinnamaldehyde	3-Styryl-2-propanone	82	157-157.5	160 ⁹⁾
n-Heptaldehyde	2-Nonanone	57	120.4-120.8	119 ¹⁰⁾
Pelargonaldehyde	2-Undecanone	51	123.5-123.8	122-123 ¹¹⁾
Cyclohexanone	Methyl cyclohexyl ketone	45	171.6-172.6	171-172 ¹²⁾
Cyclopentanone	Methyl cyclopentyl ketone	0 ¹³⁾	-----	-----
2-Octanone	3-Methyl-2-nonanone	15	85.0-85.8	86 ¹⁴⁾

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6. The yields are based on the carbonyl compound and represent overall yields. The yields of methyl ketones obtained from ketones represent the yield of methyl ketone present in a mixture containing the starting ketone.
7. All melting points found are corrected.
8. A mixed melting point determination with authentic material was unde-pressed.
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13. A 50% yield of 2-cyclopentylidene cyclopentanone was instead obtained:
2,4-dinitrophenyl hydrazone, found m.p. 227.5-228°C, reported m.p. 226°C²⁾
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