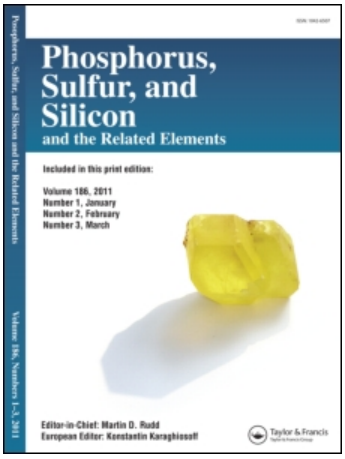

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A STUDY OF REACTIONS BETWEEN CARBOETHOXYMETHYLENETRIPHENYL-PHOSPHORANE AND ALKYL DIBROMIDES

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Carboethoxymethylenetriphenylphosphorane **1** reacts with 1,4-dibromobutane and 1,5-dibromopentane under transylidation conditions in refluxing anhydrous benzene affording the cyclization products, 1-carboethoxycyclopentyl and 1-carboethoxycyclohexyltriphenylphosphonium bromides, **6**, which by alkaline hydrolysis produce the corresponding cycloalkylcarboxylic acids and esters.

Phosphorane **1** and its phosphonium salt **5** formed in the transylidation step also lead to 3-carboethoxy-3-triphenylphosphoranyliden-2-oxopropanetriphenylphosphonium bromide (**9**) as a secondary reaction product.

Key words: Phosphoranes; transylidation; alkylation; cycloalkyltriphenylphosphonium salts; cycloalkylcarboxylic acids.

INTRODUCTION

The alkylation of phosphoranes[1] has served two main purposes. It has been utilized as a route to more complex phosphoranes which often are virtually unavailable by the normal salt method. Such phosphoranes can be used in the Wittig reaction for the preparation of 1,1-disubstituted alkenes. The second main role for the alkylation of phosphoranes is as a convenient source of a carbanion species used to form a carbon-carbon bond followed by the removal of the phosphorus group. Bestmann[2] has prepared a series of aliphatic carboxylic acids by alkylation of carbomethoxy methylenetriphenylphosphorane followed by hydrolysis of both the resulting phosphorane and the ester group.

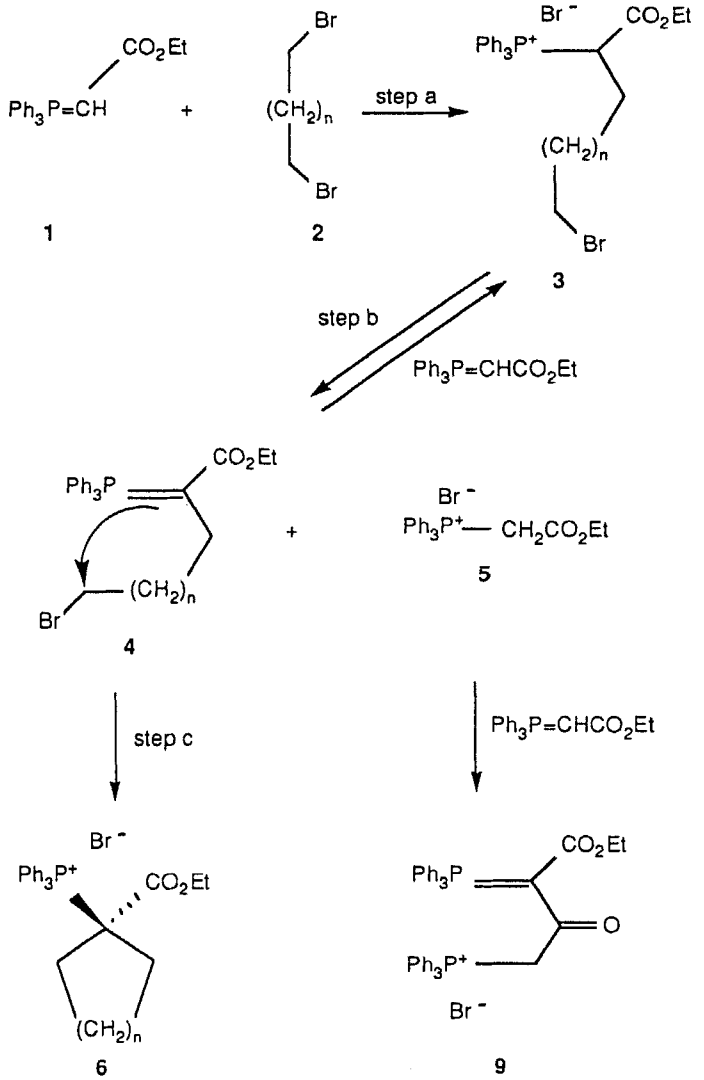
We were interested in exploring whether carboethoxymethylene triphenylphosphorane might undergo reaction with dibromides, thus providing a synthetic route to cyclopentyl and cyclohexylcarboxylic acids or their corresponding esters which are important intermediates in organic synthesis.

RESULTS AND DISCUSSION

With the above purpose in mind we allowed the stabilized title phosphorane **1** (1 molar solution in anhydrous benzene) to react with 1,4-dibromobutane **2** ($n = 2$) in a 2:1 molar ratio (transylidation conditions) for 9 hours at reflux. The white precipitate which formed was a mixture of the cyclization product, carboethoxy-

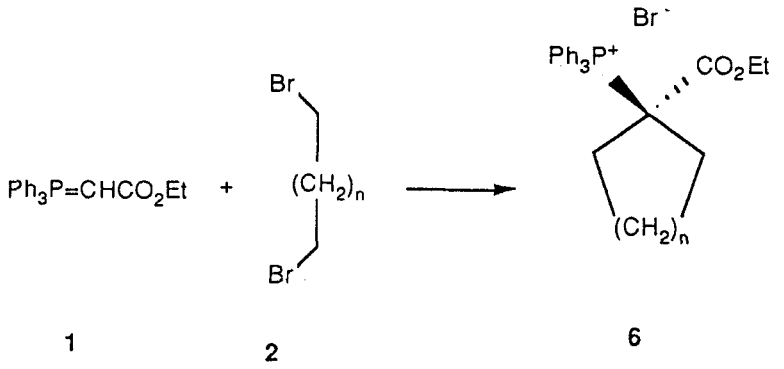
cyclopentyltriphenylphosphonium bromide **6** (n = 2, 37%) and the unexpected phosphorane-phosphonium salt **9** (see Scheme 1). These products were separated by fractional crystallization from chloroform-ethyl acetate. The benzene filtrate of the reaction mixture was concentrated under vacuum, affording a residue which yielded an additional 3% of cyclopentylphosphonium salt **6** and 35.5% of the starting phosphorane.

In order to optimize the reaction conditions, the reaction time and the concentration of the phosphorane **1** were modified. The results, shown in Table I, indicate that the best conditions are 20 hours of reflux and 1 M concentration of the starting phosphorane. We made the phosphorane **1** react with 1,5-dibromopentane **2** (n = 3) under the same conditions.



SCHEME 1

TABLE I

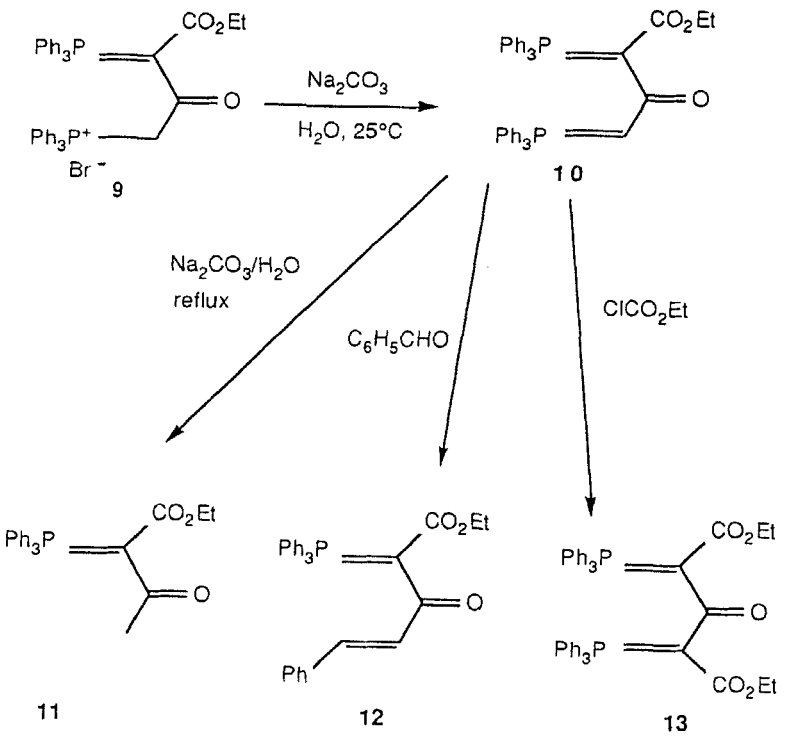


1 2 6

Concentration of phosphorane **1**	Reaction time (h)	**6** Yield %
1 M	9	40 (n = 2)
		12 (n = 3)
	20	50 (n = 2)
0.1 M	30	6 (n = 2)

The chemical structure of **9** is unambiguously established by elemental and spectroscopic analysis, and further chemical transformations (Scheme 2): a) reaction of phosphorane-phosphonium salt **9** with base to produce the diphosphorane **10** (66%); b) hydrolysis of **10** to yield ethanoylcarboethoxymethylenetriphenylphosphorane **11** (88%); c) Wittig reaction of **10** with benzaldehyde to form cinnamoylcarboethoxymethylenetriphenylphosphorane **12** (48%); d) regioselective reaction of **10** with ethyl chloroformate to obtain the ketodiester diphosphorane **13**.

A likely mechanism which can explain these results involves a number of well known reactions. The first step (Scheme 1) is assumed to be an intermolecular alkylation reaction, in which the phosphonium salt intermediate **3** is formed by nucleophilic attack of the phosphorane **1** on the dibromide. Step **b** is a transylidation reaction in which the phosphorane **1** reacts as a base with the phosphonium salt intermediate **3**. This equilibrium is unfavorable for the formation of the phosphorane intermediate **4**, because the basicity of this species is equal to or higher than the basicity of phosphorane **1**.[2] The progress of the reaction could be determined mainly by the displacement of step **c**, which is favored by the low solubility of the cycloalkylphosphonium salt **6** in the apolar solvent. Analysis of molecular models indicates the presence of strong steric interactions, mainly in the cyclohexylphosphonium salt **6** (n = 3). This factor may explain the low yield of the cyclohexyl derivative **6** (n = 3) in relation to the cyclopentyl analogue **6** (n = 2). No references have been found so far in the literature regarding the synthesis of ring systems in which the triphenylphosphonium group is attached directly to an endocyclic tertiary carbon atom through cyclization reactions. Synthesis of carboethoxycyclopropyl and carboethoxycyclobutyltriphenylphosphonium salts has been reported making use of the reaction of cyclopropylidene and cyclobutylidenetriphenylphosphorane with ethyl chloroformate.[3]

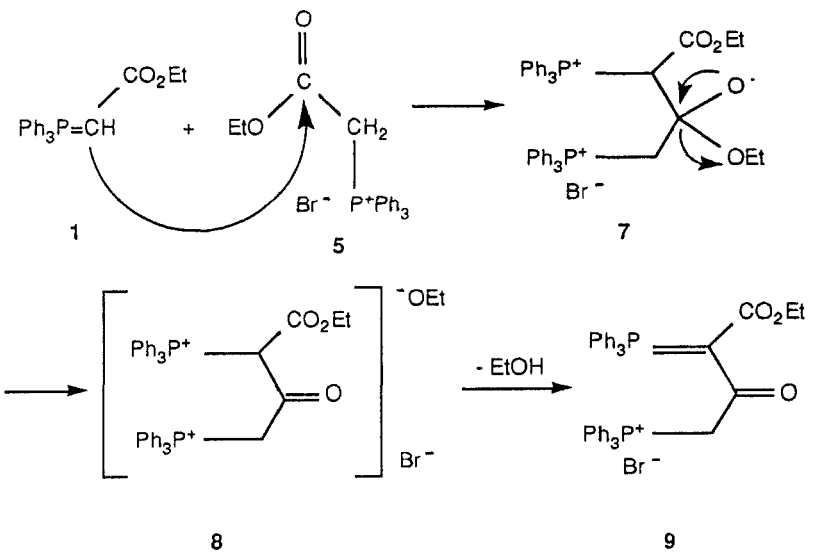


SCHEME 2

Under alkylation conditions, a nucleophilic reaction between phosphorane **1** and the ester moiety of carboethoxymethyltriphenylphosphonium bromide **5** takes place yielding the mixed phosphoranephosphonium salt **9**. The independent formation of this compound by reaction of the phosphorane **1** and the phosphonium salt **5** under the same conditions described for the alkyl dibromide reactions, supports the proposed mechanism described in Scheme 3. Furthermore, the same reaction is observed using *N*,*N*-dimethylformamide as solvent. The wide synthetic application of transylidation reactions in which phosphorane **1** coexists with its conjugated acid, the phosphonium salt **5**, confers great value to this unreported reaction.

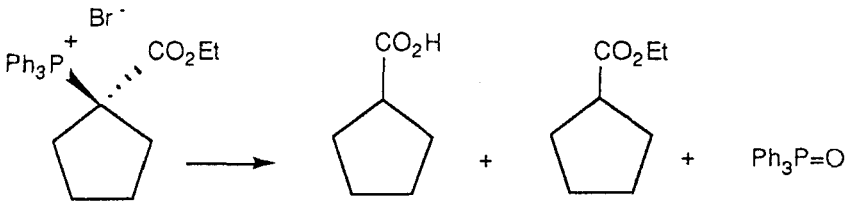
It has been stated that reactions between stabilized phosphoranes such as **1** and esters give Wittig olefination products[4,5] whereas reactive phosphoranes give rise to β-ketophosphoranes.[6,7] With stabilized phosphoranes it was suggested that the electron withdrawing group also stabilizes and encourages the formation of the double bond of the product.[6] Factors such as the absence of metal salts and higher reaction temperatures could also play a role in the different outcome of the reaction with stabilized phosphoranes. It has also been concluded that electron withdrawing groups attached to the ester carbonyl increase the tendency to form the olefinic product.[7]

However, in contrast to the above mentioned work, our results show that β-ketophosphoranes (i.e., **9**) can be formed by the reaction of stabilized phosphoranes (i.e., **1**) with compounds possessing an electron withdrawing group next to the



SCHEME 3

TABLE II



Molar ratio NaOH: 6	Yield %			
	Acid **14**	Ester **15**	$Ph_3P{=}O$	**6**
Catalytic ratio[a]	0	7.5	14.0	67
1:1[b]	22.6	35.2	69.8	0
2:1[b]	64.7	18.5	97.0	0

[a] Catalytic ratio NaOH: 6 = 1:36; 10 h reflux.
[b] 20 h reflux.

ester carbonyl (i.e., **5**), at higher temperatures, in the absence of metal salts, and in solvents of widely differing polarities.

We assume that phosphorane **1** gives rise to a carbonyl nucleophilic addition on phosphonium salt **5** in order to form an oxyanion betaine **7**. In this intermediate the interaction of the oxyanion with both triphenylphosphonium groups could disfavor the oxaphosphetane formation necessary for the obtainment of a Wittig product, allowing, instead the generation of the β-ketophosphorane **9**. It is also possible to consider a steric effect favoring this reaction.

The synthesis of cycloalkylcarboxylic acids and esters was carried out by an alkaline hydrolysis of the cycloalkylphosphonium salt **6**. 1-Carboethoxycyclopentylphosphonium bromide **6** (n = 2) showed great stability under hydrolytic conditions. This process was studied in aqueous sodium hydroxide solutions. The results are summarized in Table II, and show that the best conditions for removal of the triphenylphosphorus group are at reflux temperature for 20 h with a 1:2 phosphonium salt:sodium hydroxide molar ratio. Considering that the cycloalkyl ester **15** must be a precursor of carboxylic acid **14**, the yield of the latter compound can be optimized.

EXPERIMENTAL

^{1}H-NMR spectra were recorded on a Varian EM 360 spectrometer using deuteriochloroform as solvent and TMS (tetramethylsilane) as internal standard. ^{1}H- and ^{31}P-NMR spectra of compound **9** were recorded on a Bruker AMX300 spectrometer. Uncorrected melting points were measured with a Kofler apparatus. IR spectra were recorded with a Leitz IIIG infrared spectrophotometer. All new compounds were characterized by elemental analysis, NMR and IR spectroscopies.

1-Carboethoxycyclopentyltriphenylphosphonium bromide; **6** *(n = 2)*. A solution of the phosphorane **1** (14.4 g, 41.3 mmol) and 1,4-dibromobutane (4.50 g, 20.64 mmol) in dry benzene, was heated and stirred at reflux under a dry atmosphere for 9 h. The white precipitate (8.29 g) which formed was separated by filtration, washed with benzene and dried at 100°C. Carboethoxycyclopentyltriphenylphosphonium bromide was obtained pure in 37% yield by three successive crystallizations from chloroform-ethyl acetate m.p. 164–166°C dec.; ^{1}H-NMR ($CDCl_3$) δ 1.00 (t, 3H, J = 7 Hz), 1.53–3.27 (m, 8H), 4.12 (q, 2H, J = 7 Hz), 7.40–8.17 (m, 15H); IR (KBr) 2941, 1754, 1428, 1222, 1105 cm^{-1}; Anal. calcd. for $C_{26}BrH_{28}O_2P$: C, 64.60; H, 5.84. Found: C, 64.45; H, 5.85. The combined mother liquors were concentrated under reduced pressure affording 3.4 g (22.5%) of 3-carboethoxy-3-triphenyl phosphoranylidene-2-oxopropanetriphenylphosphonium bromide **9**. m.p. 180–183°C; ^{1}H-NMR ($CDCl_3$) δ 0.57 (t, 3H, J = 7 Hz), 3.67 (q, 2H, J = 7 Hz), 5.37 (d, 2H, J = 12.1 Hz), 7.46–7.82 (m, 30H); ^{31}P-NMR (CDCl3) δ 18.40 (s, C=P), 21.90 (s, CH_2-P$^+$); IR(KBr) 2985, 1653, 1562, 1439, 1105 cm^{-1}; Anal. calc. for $C_{42}BrH_{37}O_3P_2$: C, 68.95; H, 5.10. Found: C, 68.97; H, 4.90. From the residue of the benzene solution was separated 0.7 g of a solid, sparingly soluble in hot ethyl acetate, recrystallization of which afforded 0.3 g (3%) additional product **6** (n = 2). Concentration of the ethyl acetate mother liquor gave 5.1 g (35.5%) of the starting phosphorane **1**.

1-Carboethoxycyclohexyltriphenylphosphonium bromide **6** *(n = 3)*. Following the procedure described above, 14.0 g (40.2 mmol) of the phosphorane **1** reacted with 1,5-dibromopentane (4.76 g, 20 mmol). Recrystallization of the white precipitate (2.7 g) in chloroform-ethyl acetate yielded 1.6 g (11%) of compound **9**. The mother liquor was concentrated under reduced pressure, and the residue, crystallized in chloroform-benzene, yielded 0.2 g of carboethoxymethyltriphenylphosphonium bromide. The filtrate of the reaction mixture was concentrated under reduced pressure. Crystallization of the residue in chloroform-thyl acetate afforded 1.2 g (12%) of 1-carboethoxycyclohexyltriphenylphosphonium bromide. m.p. 169–172°C dec; ^{1}H-NMR ($CDCl_3$) δ 1.07 (t, 3H, J = 7 Hz), 1.27–2.95 (m, 10H), 3.98 (q, 2H, J = 7 Hz), 7.47–8.25 (m, 15H); IR (KBr) 2941, 1709, 1481, 1449, 1099 cm^{-1}; Anal. calc. for $C_{27}BrH_{30}O_2P$: C, 65.20; H, 6.08. Found: C, 65.12; H, 6.07. Concentration of the fraction soluble in ethyl acetate led to the recovery of 6.3 g (45%) of unreacted phosphorane **1**.

3-Carboethoxy-3-triphenylphosphoranylidene-2-oxopropanetriphenylphosphonium bromide **9**. a) A mixture of carboethoxymethyltriphenylphosphorane **1** (1.0 g, 2.87 mmol) and carboethoxymethyltriphenylphosphonium bromide **5** (1.23 g, 2.87 mmol) in 2.5 ml of dry benzene was heated and stirred at reflux for 17 h. The white precipitate which formed was separated by filtration, washed with benzene and dried at 100°C. Recrystallization in chloroform-ethyl acetate gave 0.96 g (46%) of compound **9**. Its properties are described above.

b) Phosphorane **1** (1.0 g, 2.87 mmol) and the phosphonium salt **5** (1.42 g, 3.30 mmol) were dissolved in 2.5 ml of *N,N*-dimethylformamide. The resulting solution was heated at 90°C for 20 h. The solvent was evaporated under high vacuum, and the residue was washed with hot benzene and dried at 100°C. This material was recrystallized from water giving 1.2 g (57%) of pure compound **9**.

Ethyl 2,4-bis(triphenylphosphoranylidene)-3-oxobutanoate **10**. Compound **9** (4.8 g, 6.56 mmol) was added to 150 ml of a 10% solution of sodium carbonate which was then kept at 40–50°C for 20 h. The resulting mixture was filtered, the solid was dissolved in chloroform and recrystallized in chloroform-ethyl acetate to yield 2.8 g (65.6%) of compound **10**. mp. 191–197°C dec; ^{1}H-NMR ($CDCl_3$) δ 0.52 (t, 3H, J = 7 Hz), 3.67 (q, 2H, J = 7 Hz), 5.02 (d, 1H, J = 30 Hz), 7.0–8.1 (m, 30H). IR (KBr) 1587, 1439 cm^{-1}. Anal. calc. for $C_{42}H_{36}O_3P_2$: C, 77.53; H, 5.58; found: C, 77.72; H, 5.58. Concentration of the mother liquor afforded 0.3 g (6.2%) of starting compound **9**.

Hydrolysis of compound **10**. Compound **10** was added to a solution of 10% aqueous sodium carbonate, and the reaction mixture was heated under reflux for 2 h. The suspension was filtered to obtain 1.1 g of a solid. ^{1}H-NMR of this material showed that it was a mixture of triphenylphosphine oxide and ethanoyl carboethoxymethylenetriphenyl phosphorane (**11**). Recrystallization in ethyl acetate afforded the acyl phosphorane **11** in 88% yield.[8] m.p. 169–171°C; ^{1}H-NMR ($CDCl_3$) δ 0.63 (t, 3H, J = 7 Hz), 2.46 (s, 3H), 3.73 (q, 2H, J = 7 Hz), 7.48 (m, 15H); IR (KBr) 1640, 1540 cm^{-1}.

Wittig reaction of compound **10** *with benzaldehyde*. Benzaldehyde (0.16 g, 1.65 mmol) was added to a heated solution of phosphorane **10** (1.0 g, 1.54 mmol) in dry benzene (40 ml) and the mixture was heated under reflux for 20 h. The solvent was evaporated under vacuum giving a residue (1.1 g of viscous oil) which solidified when stirred with petroleum ether. ^{1}H-NMR analysis of the solid obtained (0.8 g) revealed a mixture of 48% of cinnamoylcarboethoxymethylene triphenylphosphorane (**12**)[8] and triphenylphosphine oxide (52%). This material was recrystallized in ethyl acetate to give 0.31 g (42%) of phosphorane **12**. m.p. 118–120°C; ^{1}H-NMR ($CDCl_3$) δ 0.70 (t, 3H, J = 7 Hz), 3.80 (q, 2H, J = 7 Hz), 7.20–8.53 (m, 22H); IR (KBr) 1670, 1680 cm^{-1}.

Reaction of compound **10** *with ethyl chloroformate*. Ethyl chloroformate (0.25 ml, 3.1 mmol) was added to a heated solution of phosphorane **10** (2.0 g, 3.07 mmol) in dry benzene (80 ml). The reaction mixture was heated and stirred at reflux for 8 h. The white precipitate (0.3 g, 13%) which formed was separated by filtration and identified as compound **9**. From the residue of the benzene filtrate was separated 0.04 g (1.78%) additional compound **9**, sparingly soluble in hot ethyl acetate.

Careful concentration of the ethyl acetate soluble fraction led to the recovery of 0.81 g (36%) unreacted phosphorane **10** and 0.2 g (10%) of diethyl 2,4-bis(triphenylphosphoranylidene)-3-ketoglutarate (**13**); m.p. 200–203°C; ^{1}H-NMR δ 0.87 (t, 6H, J = 8 Hz), 3.9 (q, 4H, J = 8 Hz), 7.17–8.00 (m, 30H); IR (KBr) 3077, 1639, 1488, 1439, 1105 cm^{-1}. Anal. calc. for $C_{45}H_{40}O_5P_2$: C, 74.78%; H, 5.58%; found: C, 74.93%; H, 5.88%.

The same reaction under transylidation conditions in dry benzene at reflux for 20 h did not show any improvement in yield (11%).

Hydrolysis of 1-carboethoxycyclopentyltriphenylphosphonium bromide (**6**, n = 2). a) Using a catalytic quantity of sodium hydroxide. To a solution of compound **6** (7.0 g, 14.48 mmol) in 80 ml of hot water, was added 2 N aqueous sodium hydroxide (2 ml). The solution was heated under reflux for 10 h, and then cooled to separate the starting compound (**6**, n = 2) as a white solid. The aqueous solution was extracted with ether, and the ether extracts were dried and partially evaporated to obtain triphenylphosphine oxide (0.46 g) as a precipitate. The residue obtained after evaporation of the ethereal solution under vacuum was shown by ^{1}H-NMR analysis to be a mixture of triphenylphosphine oxide and ethyl cyclopentanecarboxylate in a 26:74 ratio. This corresponds to a 44% yield of triphenylphosphine oxide and 26% of ester.

b) Using 1:1 sodium hydroxide:phosphonium salt molar ratio. Phosphonium salt **6** (6.0 g, 12.4 mmol) dissolved in 70 ml of hot water was allowed to react with 40 ml of sodium hydroxide solution (0.5 g, 12.5 mmol). The solution was refluxed for 20 hours, after which the pH was neutral. The solution was cooled to precipitate triphenylphosphine oxide (1.7 g), which was filtered off, and the aqueous filtrate was extracted with ether. Partial concentration of the extracts afforded a supplementary precipitate of triphenylphosphine oxide (0.7 g) which was filtered off. The filtrate was evaporated under vacuum to afford a residue (0.7 g) which was shown by ^{1}H-NMR to be a mixture of cyclopentanecarboxylic acid and ethyl cyclopentanecarboxylate in a 14:86 ratio.

The original aqueous solution was extracted with chloroform and the extracts were dried and evaporated under vacuum to afford the starting phosphonium salt (**6**, n = 2). The aqueous layer was made acid with dilute hydrochloric acid and extracted with ether. Evaporation under vacuum of this extract yielded cyclopentanecarboxylic acid (0.24 g).

The total calculated yields were: triphenylphosphine oxide 82%, cyclopentanecarboxylic acid 26.64% and ethyl cyclopentanecarboxylate 41.2%.

c) Using 2:1 sodium hydroxide:phosphonium salt **6** molar ratio. With the same technique described above the phosphonium salt **6** (6 g, 12.4 mmol) dissolved in hot water (100 ml) was allowed to react with sodium hydroxide (1.2 g in 20 ml of water). The solution was heated under reflux for 20 h to

obtain triphenylphosphine oxide (3.9 g, 96.8%) as a precipitate and a mixture of ethyl cyclopentanecarboxylate (18.5%) and cyclopentanecarboxylic acid (64.7%).

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REFERENCES

1. I. Gosney and A. G. Rowley in "Organophosphorus Reagents in Organic Synthesis," J. I. G. Cadogan, ed., Academic Press, New York, (1979).
2. H. J. Bestmann and H. Schulz, *Chem. Ber.*, **95,** 292 (1962).
3. P. L. Fuchs, *J. Am. Chem. Soc.*, **96,** 1607 (1974).
4. P. J. Murphy and J. Brennan, *Chem. Soc. Rev.*, **17,** 1 (1988).
5. V. Subramanyan, E. H. Silver and A. H. Soloway, *J. Org. Chem.*, **41,** 1272 (1976).
6. A. P. Vistewaal, F. L. Jonkers and A. Vandergen, *J. Org. Chem.*, **43,** 3306 (1978).
7. M. Le Corre, *Bull. Soc. Chim. Fr.*, 2005 (1974).
8. P. A. Chopard, R. J. Searle and F. H. Devitt, *J. Org. Chem.*, **30,** 1015 (1965).