Journal of Organometallic Chemistry 177 (1979) 27—34

THE CARBANIONS OF *S*-ALKANOATE-*O*,*O*-DIALKYL PHOSPHATES· NEW SYNTHONS FOR REACHING α,β-ETHYLENIC ESTERS *

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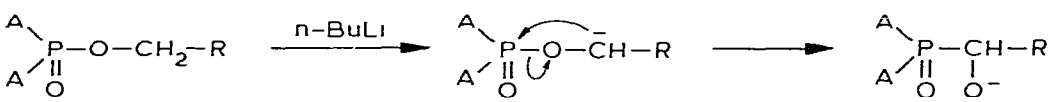
(Received March 28th, 1979)

Summary

The stabilization of phosphorothiolate carbanions has been achieved Condensation of these carbanions with carbonyl derivatives lead to the corresponding α,β-unsaturated esters, a mechanism, via a β-hydroxyphosphorothiolate-β-mercaptophosphate rearrangement, is described These new synthons are compared with the phosphonate analogs (Wittig—Horner's reagent)

Introduction

It has been recently shown that some *O*-benzylic and *O*-allylic phosphoric acid derivatives treated with a strong base produced phosphate carbanions which immediately rearranged into α-hydroxy phosphonate oxanions [1—3]

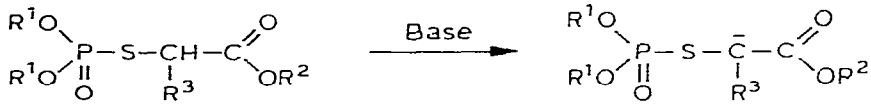


R = phenyl or vinyl
A = RO— or R_2N

N-Benzylic derivatives often react in the same way [4]. Stabilization of these compounds using thiolo esters such as $(R'O)P(O)SCH_2Ph$ and $(R^1O)P(O)$-$SCH_2CH{=}CH_2$ [5], has been tried unsuccessfully

However, stabilization of the carbanionic form of some thiolophosphates seems to be possible through the electron withdrawing mesomeric effect of the carbethoxy group· We have studied the reactivity of carbanions of *S*-alkanoate-*O*,*O*-dialkyl phosphates (I) towards some electrophilic reagents, mainly carbonyl derivatives

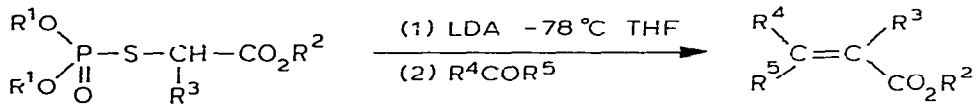
* Dedicated to Professor Henri Normant on the occasion of his 72nd birthday.



(I)

Results

Reaction at −78°C of lithium diisopropyl amide (LDA) in tetrahydrofuran (THF) with *S*-alkanoate-*O*,*O*-dialkyl phosphate (I) and addition of a carbonyl compound at the same temperature leads to the isolation of an α, β-ethylenic ester with a yield of about 50% (Table 1)



(I) (II)

(a) Stereoselectivity, yield

The stereochemistry of the reaction is not well-defined, except for aldehydic substrates which in practice give only the *trans* isomer

In experiment I/1 **, a weak steric hindrance accounts for the formation of a large percentage of *E* isomer. As groups R_4 and R_5 get bulkier, the proportion of *Z* isomer increases (experiment I/3).

On the other hand, the reactivity is quite independent of the alkyl substituents on phosphorus; the same results are obtained (yields, ratio *E*/*Z*) from a diethyl phosphoric ester (experiment I/1) or a diisopropyl phosphoric ester (experiment I/9). These resutls can be compared to those observed in the α,β-ethylenic esters synthesis starting from the Wadsworth and Emmons reagent [6]. The limited yields (about 50%) cannot be explained, in spite of many optimization experiments *. Use of two equivalents of phosphorothiolate/LDA mixture for one carbonyl derivative did not improve the yield The phosphorothiolate could in fact be used both as a nucleophilic reagent and as a desulphurization agent Steric hindrance on the phosphorothiolate carbanion improves the yield in α,β-ethylenic esters (comparison of experiments I/1 and I/8).

The influence of a basic medium was also investigated. The use of sodium hydride leads to α, β-ethylenic esters II, but raising the temperature to 30°C favours by-reactions and makes the separation of unsaturated esters II more difficult. Identical results have been observed with bases such as sodium amide and dimsylsodium. ($^{-}CH_2—\underset{\underset{O}{\|}}{S}—CH_3$)

(b) Mechanism

The formation of α,β-ethylenic esters II may be explained by the following stages: oxanion III obtained by condensation of the phosphorothiolate carba-

* The compounds are noted according to their order in Table 1

** Secondary reactions of undefined nature take place

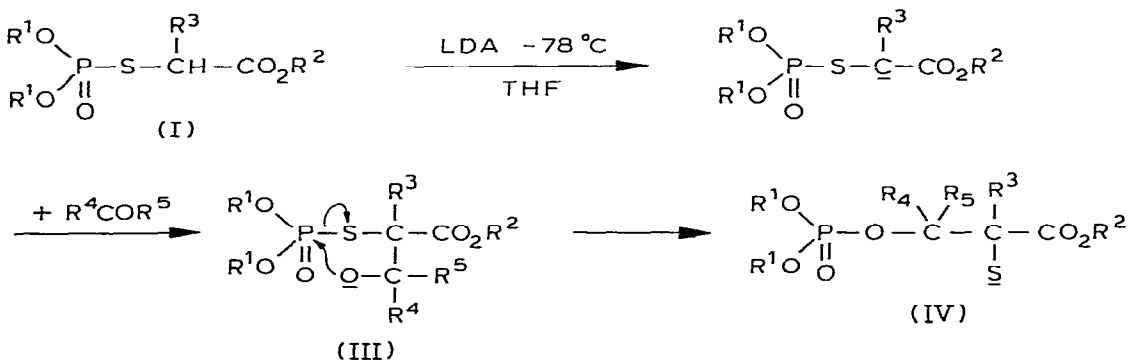
TABLE 1

SYNTHESIS OF α β-UNSATURATED ESTERS II

All products were identified by IR and NMR (^1H and ^{13}C) spectra and comparison with authentic material The *E/Z* ratio was determined by NMR and by GLC analysis

No	R^1	R^2	R^3	R^4	R^5	Yield (%)	*E/Z* ratio	
							E	*Z*
1	C_2H_5	C_2H_5	H	H	$(CH_3)_2CH$	52	95	5
2	C_2H_5	C_2H_5	H	H	C_6H_5	53	95	5
3	C_2H_5	C_2H_5	H	CH_3	C_6H_5	58	60	40
4	C_2H_5	C_2H_5	H	$-CH_2(CH_2)_2CH_2-$		48	—	—
5	C_2H_5	C_2H_5	H	CH_3	C_6H_5	52	58	42
6	C_2H_5	C_2H_5	H	H	$(CH_3)_2CH$	50	96	4
7	C_2H_5	C_2H_5	H	H	$C_6H_5CH=CH-$	52	not determined	
8	C_2H_5	C_2H_5	CH_3	H	$(CH_3)_2CH$	68	52	48
9	i-C_3H_7	C_2H_5	H	H	$(CH_3)_2CH$	51	95	5
10	i-C_3H_7	C_2H_5	H	CH_3	C_6H_5	53	52	48
11	C_2H_5	C_2H_5	CH_3	CH_3	C_6H_5	60	60	40
12	C_2H_5	C_2H_5	H	$-CH_2OCOCH_3$	C_6H_5	68	58	42

nion on the carbonyl compound rearranges to intermediate IV, by means of a transition involving the pentacoordinated phosphorus atom

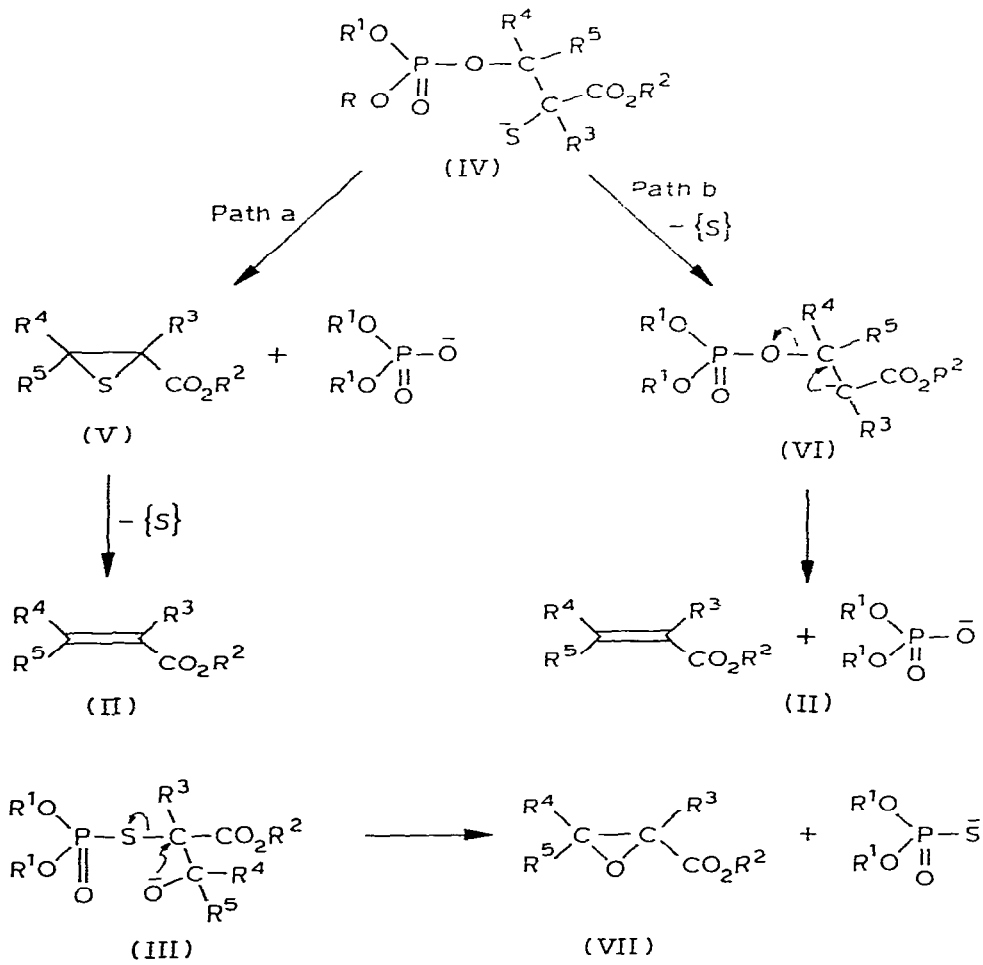


(I) (III) (IV)

The next stage could proceed through a thiirane intermediate (path a) or by a sulphur extrusion mechanism (path b) The phosphate carbanion VI could not be trapped. Addition of carbonyl derivatives to the phosphorothiolate carbanion leading to the unsaturated ester II is very fast even at —78° C. Thus, considering the experimental conditions, path a seems to be the more likely. The dealkylating power of thiolates towards phosphorated esters is already well known [7,8].

The instability of thiiranes V seems to be due to the electron withdrawing effect of the ester group. This sulphur extrusion has been reported frequently [9].

Finally, formation of glycidic esters VII which we never obtained, cannot be considered because the P—S bond is weaker and more sensitive to base hydrolysis than the C—S bond [10].



Synthetic aspects; conclusion

Apart from the reactivity discussed above, the synthetic properties of these phosphorothiolates I are of interest. These compounds are quite similar to the *O*-alkyl *S*-ethoxycarbonyl dithiocarbonates VIII and thiocarbonates IX, whose properties have been described by Tanaka et al [9c,11].

(VIII) (IX)

In addition to the sulphurated compounds VIII and IX giving good yields of unsaturated esters, phosphorothiolates I behave as interesting Wittig—Horner reagents. A greater reactivity of phosphorothiolate anions is observed towards hindered or enolisable ketones. Indeed, at —78° C formation of the olefinic double bond is instantaneous, whereas, in most cases, the reaction mixture

TABLE 2

COMPARED REACTIVITY OF PHOSPHONATES AND PHOSPHOROTHIOLATES TOWARDS KETONES

Phosphorated reagents	Time (h)	Temperature (°C)	Yield (%) of unsaturated esters	
			with $PhCOCH_3$	with $PhCOCH_2OCOCH_3$
$(C_2H_5O)_2P(O)CH_2CO_2C_2H_5$	1	20	~12 (68) [a]	~25 (72) [a]
$(C_2H_5O)_2P(O)SCH_2CO_2C_2H_5$	1	−78	58	68
$(C_2H_5O)_2P(O)CH(CH_3)CO_2C_2H_5$	1	20	~10 (65) [a]	—
$(C_2H_5O)_2P(O)SCH(CH_3)CO_2C_2H_5$	1	−78	60	—

[a] Maximum yield of condensation after refluxing

(phosphonate carbanion/ketone) must be refluxed for several hours in dimethoxy ethane (experimental conditions of Wadsworth—Emmons's reaction) and this difference is even more striking when considering a hindered carbanion (cf. Table 2).

The synthetic interest of these new synthons must be found in the limited scope of the Wittig—Horner reaction The Wadsworth—Emmons reaction is limited by steric hindrance when hindered ketones are used for condensation. the formation of betaine intermediates is reduced and so is the obtainment of olefins The phosphorothiolate carbanions, however, avoid this difficult stage since they only need a hydrolysis reaction of the phosphorothiolate function (breaking of the P—S bond and not of the P—C bond)

Experimental

The structures of all products obtained were established by the usual analytical techniques (microanalyses, IR and NMR spectra, GLC analysis) and by comparison with authentic samples obtained by the Wadsworth—Emmons reactions [12]

The IR spectra were taken on a Perkin—Elmer model type 297 spectrometer The ^1H NMR spectra were recorded on a Jeol C 60 HL model, using 30% solutions in $CDCl_3$ and TMS as internal standard. The ^{13}C NMR spectra were measured on a Jeol FX 60 spectrometer.

The results of elemental analysis are satisfactory and are not given The GLC analyses were recorded on a Girdel, model 75 FD-1 with a column (1 50 m) filled with SE-30 (10%) on Chromosorb W (80—100 mesh)

Phosphorothiolates III. general procedure

These compounds are obtained according to Schrader's method [13] with dialkyl phosphites, sulphur and α-halogen esters (see Table 3)

α,β-Unsaturated esters IV typical procedure

To a stirred solution of 0.01 mol of phosphorothiolate III in 20 ml of anhydrous THF is added, at −78°C, 0.01 mol of lithium diisopropylamide (LDA) The reaction mixture is stirred at −78°C for approximately 30 min. Then 0 011

TABLE 3

PHYSICAL AND SPECTRAL DATA FOR THE PHOSPHOROTHIOLATES III

Products	B p (°C)/torr	Yield (%)	IR (film) ∂_{max} (cm^{-1})	^1H NMR ($CDCl_3$) δ (ppm), J (Hz)
$(CH_3CH_2O)_2P(O)SCH_2CO_2CH_2CH_3$ a b c d e	82/0 02	92	1715(C=O), 1248(P=O) 1220(C–O–C), 1105(P–O–C)	1 30 (H_a, H_e, td), 4 08 (H_b, H_d, qd with $J(P–H_b)$ = 7 3 = $J(H_aH_b)$), 3 48 (H_c, d with $J(P–H_c)$ = 14 8)
$(CH_3CH_2O)_2P(O)SCH_2CO_2CH_3$ a b c d	87/0 03	95	1720(C=O), 1250(P=O) 1196(C–O–C), 1035(P–O–C)	1 41 (H_a, t), 4 22 (H_b, q with $J(P–H_b)$ = 7 12 = $J(H_a–H_b)$), 3 62 (H_c, d with $J(P–H_c)$ = 15), 3 78 (H_d, s)
$(CH_3CH_2O)_2P(O)SCH(CH_3)CO_2CH_2CH_3$ a b c d e f	98/0 02	90	1720(C=O), 1246(P=O) 1200(C–O–C), 1028(P–O–C)	1 42 (H_a, H_d, H_f in broadened peak) 4 18 (H_b, H_c, H_e in broadened peak)
$\{(CH_3)_2CHO\}_2P(O)SCH_2CO_2CH_3$ a b c d	95/0 02	85	1730(C=O), 1252(P=O) 1225(C–O–C), 1065(P–O–C)	1 42 (H_a, d with $J(H_aH_b)$ = 7 2 = $J(P–H_b)$ 4 81 (H_b, m), 3 64 (H_c, d with $J(P–H_c)$ = 15) 3 79 (H_d, s)

TABLE 4

PHYSICAL AND SPECTRA DATA FOR THE UNSATURATED ESTERS IV

Product [a]	B p (°C)/torr	Yield (%)	n_D^t	IR (film) ∂_{max} (cm^{-1})	^1H NMR ($CDCl_3$) δ (ppm), J (Hz)
1	62–64/15	52	1 43055/21	1620(C=C), 1725(C=O)	1 14 ($(CH_3)_2C$, d with J(H–H) = 6 2), 1 34 (CH_3–C, t), 2 43 (CH isopropyl, m), 4 15 (CH_2, q), 5 71 (CO–CH, d), 6 92 (CO–C=CH, dd with J(H–H) = 16 8)
2	92/0 05	53	1 5496/20	1635(C=C), 1575(C_6H_5), 1708(C=O)	1 35 (CH_3, t), 4 28 (CH_2, q), 6 46 (CO–CH, d with J(H–H) = 16 9), 7 58 (CO–C=CH, t), 7 43(C_6H_5, broadened peak)
3	80/0 02	58	1 5297/20	1623(C=C), 1592(C_6H_5, 1710(C=O)	*cis* 1 12 (CH_3(ester), t), 2 24 (CH_3–C=C, s), 4 03 (CH_2, q), 5 95 (CH=C, broadened s), 7 37 (C_6H_5, m) *trans* 1 35 (CH_3(ester), t), 2 63 (CH_3–C=C,s), 4 26 (CH_2, q), 6 18 (CH=C, broadened s), 7 37 (C_6H_5, m)
4	98/15	48	1 4479/20	1645(C=C), 1705(C=O)	1 32 (CH_3(ester), t), 1 78 (CH_2, m), 2 51 (CH_2, m) 4 11 (CH_2(ester), q) 5 86 (CH=C, broadened s)
5	68/0 03	52	1 5401/20	1626(C–C), 1572(C_6H_5), 1718(C=O)	*cis* 2 21 (CH_3, d), 3 62 (CH_3–CO, s), 5 93 (CH, d with J(H–CH_3) = 1 8), 7 32 (C_6H_5, m) *trans* 2 65 (CH_3, d), 3 81 (CH_3–CO, s), 6 18 (d with J(H–CH_3) = 0 96) 7 32 (C_6H_5, m)
6	49/15	50	1 43155/19	1645(C=C), 1728(C=O)	1 12 ($(CH_3)_2C$, d with J = 7 8), 2 42 (CH–C, m), 3 73 (CH_3(ester), s), 5 70 (CH=C, d with J(H–H) = 15 6), 6 87 (C=CH–CH, dd with J(H–H) = 7 2)
7	F = 70°C	52	—	1620(C=C), 1586(C_6H_5), 1702(C=O)	3 78 (CH_3, s), 5 81 (CH=C, d with J = 15 2), 6 73 (C=C–CH=, m), 7 32 (C_6H_5 and CH=C–, m)
8	96–98/15	68	1 43650/22	1645(C=C), 1710(C=O)	*cis* 0 82 ($(CH_3)_2C$, d), 1 25 (CH_3(ester) t), 1 83 (CH_3, s), 4 16 (CH_2, q) 5 63 (CH, d with J(H–H) = 9 8) *trans* 1 08 ($(CH_3)_2C$, d), 1 25 (CH_3(ester), t), 1 90 (CH_3, s), 4 16 (CH_2, q), 5 52 (CH, d with J(H–H) = 11 2)
11	83/0 02	60	1 5199/20	1700(C=O), 1625(C=C), 1596(C_6H_5)	*cis* 0 83 (CH_3(ester), t), 1 84 (CH_3, s), 2 13 (CH_3, s), 3 88 (CH_2, q), 7 32 (C_6H_5, broadened peak) *trans* 1 39 (CH_3(ester), t), 1 84 (CH_3, s), 2 32 (CH_3, s), 4 29 (CH_2, q), 7 32 (C_6H_5, broadened peak)
12	122/0 02	68	1.5223/17	1700–1750(C=O), 1630 (C=C), 1600 and 1580 (C_6H_5)	*cis* 1 02 (CH_3(ester), t), 2 16 (CH_3CO, s), 4 02 (CH_2CO, q), 4 76 (CH_2–O, d), 6 01 (CH, broadened s), 7 31 (C_6H_5, broadened peak) *trans* 1 31 (CH_3(ester), t), 2 06 (CH_3CO, s), 4 13 (CH_2CO, q), 5 56 (CH_2–O, d), 6 12 (CH, broadened s), 7 31 (C_6H_5, broadened peak)

[a] See Table 1

mol of the carbonyl derivative is added The agitation and temperature are maintained for 30 min at —78° C. Then, the mixture is allowed to warm to room temperature and is hydrolysed with 50 ml of water The aqueous solution is extracted with diethyl ether The organic phases are combined and dried over sodium sulphate. The organic solvent is removed under reduced pressure to give an oil which is distilled in vacuo. (see Table 4)

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