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Reaction of Tetraethyl α-Phosphonodicarboxylates with Carbonyl Compounds

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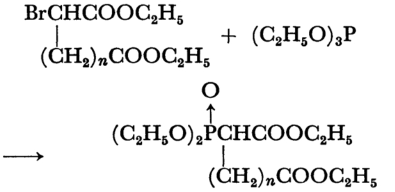
While the reaction of triethyl phosphonoacetate with carbonyl compounds has been well investigated,[1a–c] little attention has been paid to the reaction of tetraethyl α-phosphonodicarboxylates (I) with carbonyl compounds. Wadsworth[2] has reported the reaction of tetraethyl α-phosphonosuccinate with benzaldehyde to give diethyl α-benzylidenesuccinate. On the other hand, a survey of the literature has indicated that a general procedure for preparing diethyl α-alkylidenedicarboxylates (IV) has not yet been reported. Although α-alkylidenesuccinates[3] and glutarates[4] have been prepared by the Stobbe condensation reaction in a single-stage, the preparations of higher α-alkylidenedicarboxylates have dealt almost exclusively with the Reformatskii[5a,b] and Grignard[6] reactions. However, these methods have the disadvantage of low yields.

In connection with the total synthesis of phytol,[7] we have demonstrated that the triethyl phosphonocrotonate anion reacts with carbonyl compounds to give the corresponding α,β-,γ,δ-unsaturated esters. These studies suggest that tetraethyl α-phosphonodicarboxylate anions (II) may also condense with carbonyl compounds to give IV in a single-stage; if so, this reaction would be a more useful method for preparing IV. In the present paper, we have studied the reaction of I with carbonyl compounds in order to develop a new method of preparing IV.

The Michaelis-Arbuzov reactions of diethyl α-bromodicarboxylates with triethyl phosphite were all carried out at 155—160°C; they gave I (n=2, 3,7) in 59—75% yields. These compounds were identified by their elemental analyses and by a study of their infrared spectra. The results are summarized in Table 1.

TABLE 1. REACTION OF DIETHYL α-BROMODICARBOXYLATES WITH TRIETHYL PHOSPHITE



$$\begin{matrix}\mathrm{BrCHCOOC_2H_5}\\ |\\ \mathrm{(CH_2)_nCOOC_2H_5}\end{matrix} + \mathrm{(C_2H_5O)_3P} \longrightarrow \begin{matrix}\mathrm{O}\\ \uparrow\\ \mathrm{(C_2H_5O)_2PCHCOOC_2H_5}\\ |\\ \mathrm{(CH_2)_nCOOC_2H_5}\end{matrix}$$

I n=2, 3, 7

I n	Bp °C/mmHg	Yield %	n_D^{20}	Analysis, % Found C	 H	 Calcd C	 H
2	124/0.2	59	1.4445	47.87	8.15	48.15	7.77
3	150/0.5	75	1.4403	49.33	8.73	49.70	8.04
7	106/0.1	59	1.4479	54.98	8.95	54.81	8.94

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[1] a) H. Takahashi, K. Fujiwara and M. Ohta, This Bulletin, **35**, 1498 (1962). b) B. G. Kovalov, L. A. Yanovskaya and V. F. Kucherov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, **1962**, 1876. c) L. A. Yanovskaya and V. F. Kucherov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1964**, (7) 1341.

[2] W. S. Wadsworth and W. D. Emmons, *J. Am. Chem. Soc.*, **83**, 1733 (1961).

[3] B. Wojcik and H. Adkins, *ibid.*, **56**, 2424 (1934).

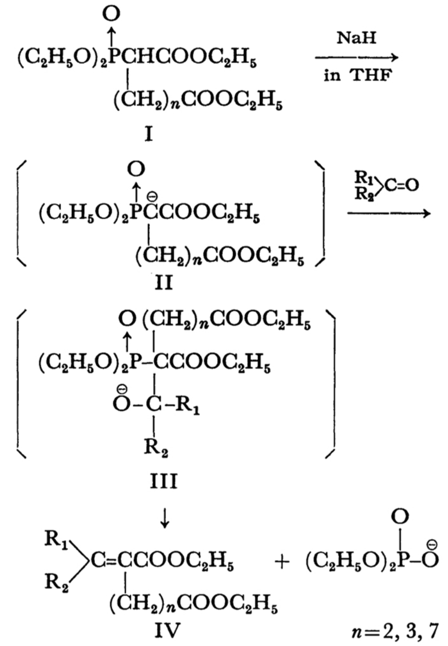
[4] W. H. Puterbaugh, *J. Org. Chem.*, **27**, 4010 (1962).

[5] a) W. Treibs and G. Leichssenring, *Chem. Ber.*, **84**, 52 (1951). b) R. Gelin and S. Gelin, *Compt. Rend.*, **255**, 1400 (1962).

[6] R. Mayer and W. Treivs, *Chem. Ber.*, **87**, 349 (1954).

[7] K. Sato, S. Mizuno and M. Hirayama, *J. Org. Chem.*, **32**, 177 (1967).

When phosphonate anions II ($n=2,3,7$), prepared by adding I to a slurry of sodium hydride in dry tetrahydrofuran (THF), were treated with carbonyl compounds, the corresponding α-alkylidenedicarboxylates, IV ($n=2,3,7$), were obtained in 10—86% yields. Phosphonate anions, II, reacted exothermically with benzaldehyde even at low temperatures to give the corresponding α-benzylidenedicarboxylates (IVa) ($n=2,3,7$) in good yields. Similarly, the reactions of II with aldehydes, such as propionaldehyde and p-toluoxyacetaldehyde, were carried out smoothly to give the corresponding α-propylidene- (IVb) and α-(p-toluoxyethylidene)-dicarboxylates (IVc) ($n=2,3,7$) in good yields. In contrast, the reaction with acetone resulted in a low yield of diethyl α-isopropylidenedicarboxylates (IVd) ($n=2,3,7$), and acetophenone failed to react with II at all. The results are summarized in Table 2.



IVa $R_1=C_6H_5$, $R_2=H$
IVb $R_1=CH_3CH_2$, $R_2=H$
IVc $R_1=p\text{-}CH_3C_6H_4OCH_2$, $R_2=H$
IVd $R_1=CH_3$, $R_2=CH_3$
IVe $R_1=C_6H_5$, $R_2=CH_3$

Recently Yanovskaya and her co-workers[1c)] reported that triethyl phosphonoacetate did not react with diisopropyl ketone or di-t-butyl ketone, and that the reaction of triethyl phosphonoacetate with methyl t-butyl ketone gave ethyl 3,4,4-trimethyl-2-pentenoate in a poor yield. In explaining their data and also the results summarized in Table 2, the mechanism suggested by Wadsworth[2)] can be applied to the behavior of carbonyl compounds toward II; such an application indicates that II is less reactive to ketones, which can find it difficult to take the intermediate III because of the steric hindrance, than to aldehydes, which can readily take III. The products IV ($n=2,3,7$) were confirmed by their elemental analyses and by a study of their infrared spectra, which showed two ester carbonyl absorptions of the α,β-unsaturated ester carbonyl group and the normal ester carbonyl group, in addition to the double-bond absorption.

In comparison with the Reformatskii reaction, the reaction using phosphonate anions, II, proceeds smoothly under mild conditions and, especially in the case of the reactions with aldehydes, gives the products in good yields. Therefore, the reaction is a useful method of preparing IV.

TABLE 2. REACTION OF TETRAETHYL α-PHOSPHONODICARBOXYLATES (I) WITH CARBONYL COMPOUNDS

I, n	Aldehydes or ketones		Reaction condition		Product	Yield, %
	R_1	R_2	Temp., °C	Time, hr		
2	C_6H_5	H	0—5	3	IVa	84
	CH_3CH_2	H	0—5	2	IVb	53
	p-$CH_3C_6H_4OCH_2$	H	−25—−20	1	IVc	70
	CH_3	CH_3	−10—5	15	IVd	21
	C_6H_5	CH_3	−10—room temp.	15	IVe	0
3	C_6H_5	H	0—5	3	IVa	86
	CH_3CH_2	H	0—5	3	IVb	54
	p-$CH_3C_6H_4OCH_2$	H	−20—−15	2	IVc	77
	CH_3	CH_3	−10—5	15	IVd	10
	C_6H_5	CH_3	−10—room temp.	15	IVe	0
7	C_6H_5	H	0—5	3	IVa	79
	CH_3CH_2	H	0—5	3	IVb	56
	p-$CH_3C_6H_4OCH_2$	H	−20—−15	2	IVc	61
	CH_3	CH_3	−10—5	15	IVd	35
	C_6H_5	CH_3	−10—room temp.	15	IVe	0

Experimental[8)]

Materials. The triethyl phosphite was prepared by the procedure described by Ford-Moor and Perry.[9)] The diethyl α-bromodicarboxylates were obtained by the method of Teichmann[10)] in 30—40% yields.

Tetraethyl α-Phosphonoadipate (I, $n=3$). Typical Procedure for a Tetraethyl α-Phosphonodicarboxylates (I). A mixture of diethyl α-bromoadipate (26.4 g, 0.094 mol) and triethyl phosphite (20 g, 0.12 mol) was heated with stirring for 5 hr at 150—160°C. The distillation gave a 74.8% yield of (I, $n=3$), bp 150°C/0.5 mmHg, n_D^{20} 1.4403.

Found: C, 49.33; H, 8.73%. Calcd for $C_{14}H_{27}O_7P$: C, 49.70; H, 8.04%.

The Reaction of Tetraethyl α-Phosphonoadipate with Benzaldehyde. Typical Procedure for the Reaction of Tetraethyl α-Phosphonodicarboxylates with Carbonyl Compounds. Tetraethyl α-phosphonoadipate (15 g, 0.044 mol) was added, drop by drop at 0—5°C, to a slurry of 50% sodium hydride (2.4 g, 0.05 mol) in 100 m*l* of dry THF. After the addition, the mixture was stirred for 2 hr until the evolution of hydrogen gas had ceased. Benzaldehyde (4.7 g, 0.044 mol) was then added to the mixture at the same temperature, and the mixture was stirred for 3 more hr. The excess THF having been evaporated, the mixture was taken up in an excess of water, neutralized, and extracted with ether. The ether layer, after being dried over calcium chloride and evaporated, gave a liquid residue. The residue was then distilled, giving 11.1 g of a clear liquid, bp 150°C/0.22 mmHg (lit.[5a)] 169°C/1.5 mmHg), 86% yield n_D^{20} 1.5170. The infrared spectrum of the product contained bands at 1620 cm^{-1} (C=C), 1730, and 1705 cm^{-1} (C=O).

Found: C, 70.39; H, 7.98%. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64%.

Table 3. Physical constants and analytical characteristics of products

Compound		Bp °C/mmHg	n_D^{20}	IR cm^{-1}			Analyses, %			
				C=O	C=O (conju.)	C=C	Found		Calcd	
							C	H	C	H
$n=2$	IIIa	126/0.2	1.5231	1735	1710	1630	69.40	7.63	69.55	7.30
	IIIb	80/0.2	1.4510	1740	1710	1650	62.98	8.85	63.14	8.83
	IIIc	155/0.2	1.5072	1735	1710	1650	67.25	7.84	67.38	7.55
	IIId	81/0.4	1.4496	1740	1715	1630	63.34	9.04	63.14	8.83
$n=3$	IIIa	150/0.2	1.5170	1730	1705	1630	70.39	7.98	70.32	7.64
	IIIb	95/0.4	1.4493	1730	1705	1635	64.33	9.45	64.44	9.15
	IIIc	156/0.2	1.4950	1730	1710	1645	68.08	8.14	68.24	7.84
	IIId	94—94.5/0.3	1.4486	1735	1710	1635	64.17	9.26	64.44	9.15
$n=7$	IIIa	161/0.15	1.5029	1740	1715	1635	72.80	8.73	73.30	8.94
	IIIb	125/0.3	1.4564	1740	1715	1635	68.32	10.13	68.42	10.13
	IIIc	188/0.2	1.4976	1735	1710	1650	70.09	9.06	69.81	9.05
	IIId	137/0.2	1.4592	1735	1710	1635	68.46	10.39	68.42	10.13

[8)] All boiling points are uncorrected. Infrared spectra were recorded on a Hitachi Model EPI-S2 spectrophotometer. Gas chromatographic analyses were carried out on a Shimadzu Model GC-1C chromatograph.

[9)] A. H. Ford-Moor, "Organic Syntheses," Coll. Vol. IV, p. 955 (1963).

[10)] B. Teichmann, *Z. Chem.*, **5**(1), 18 (1965).