mixture with ice and concd. hydrochloric acid, the aluminum complex and the free 4-acylphenol precipitated together. The complex was separated from the 4-acylphenol by treating the mixture with aqueous sodium hydroxide. The complex was decomposed with cold concd. sulfuric acid, and the free 2-acylphenol precipitated upon dilution with water. The aqueous filtrate gave a positive test for the aluminum ion. Upon treating the free 2-acylphenol with alcoholic tetramminenickel (II) chloride solution, a yellow solution resulted. Evaporation of most of the alcohol resulted in the precipitation of the stable nickel chelate, which was pale yellow. There was a striking resemblance of this chelate to that of the known nickel chelate of *o*-hydroxyacetophenone.[3] Treatment of this chelate with cold concd. sulfuric acid released the original 2-acylphenol upon dilution with water. The aqueous filtrate gave a positive test for the nickel ion.

Anal. Calcd. for $(C_{13}H_8O_4N)_2Ni$: Ni, 10.81. Found: Ni, 10.82.

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Condensation of Triethyl Phosphonoacetate with Aromatic Aldehydes

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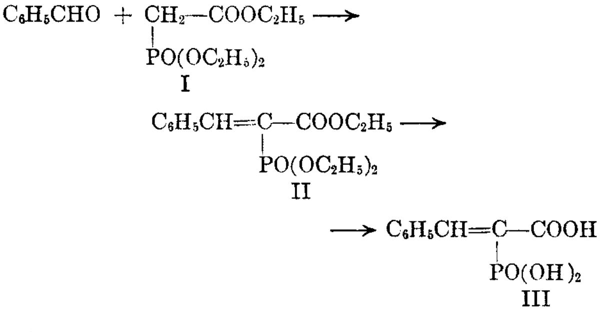
Our interest was attracted by a communication in which benzaldehyde and triethyl phosphonoacetate (I), on heating at 160–170° with acetic anhydride was reported to give triethylbenzylidenephosphonoacetate (II) yielding on acid hydrolysis what was claimed to be the benzylidene phosphonoacetic acid (III).[1]



$$C_6H_5CHO + \underset{PO(OC_2H_5)_2}{\underset{|}{CH_2}}-COOC_2H_5 \longrightarrow$$

I

$$C_6H_5CH{=}\underset{PO(OC_2H_5)_2}{\underset{|}{C}}-COOC_2H_5 \longrightarrow$$

II

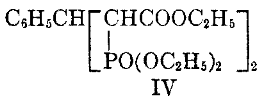
$$\longrightarrow C_6H_5CH{=}\underset{PO(OH)_2}{\underset{|}{C}}-COOH$$

III

In view of the instability of the arylidenemalonic acids, which lose carbon dioxide rather easily both under acidic and basic conditions, the preparation of benzylidene phosphonoacetic acid by acid hydrolysis of the corresponding triester was somewhat surprising, and as no experimental details or analysis of the final product are given in Pudovik and Lebedeva's paper, we decided to re-investigate this reaction.

Under the conditions of the Russian authors, which are essentially those of the Perkin reaction, we obtained about 12% of a product, which gave on hydrolysis cinnamic acid, while 83–85% of the aldehyde could be recovered unchanged. The physical constants of the primary condensation product obtained by us, as well as its carbon-hydrogen analysis were in reasonable agreement with that obtained by the Russian authors, although the yield was very much smaller than claimed by them. On the other hand, we were unable to obtain by the hydrolysis of the triester any other product but cinnamic acid (which was identified by melting point, mixed melting point, analysis, and melting point of its bromophenacyl bromide derivative), although widely varied concentrations of both hydrochloric acid and potassium hydroxide were employed in various experiments. Indeed, the acid obtained by Pudovik and Lebedeva was stated by them to have a melting point of 132°, which is practically identical with that of cinnamic acid, and we believe that it actually was cinnamic acid. As no analysis is given in their paper, it may well be that this was identified as benzylidenephosphonoacetic solely on the assumption that hydrolysis of the triester must give the corresponding tribasic acid, without the occurrence of any further reaction.

Using different reaction techniques and basic catalysts, we were able to obtain much better yields of the triethylbenzylidenephosphonoacetate. (See Table I.) Incidentally, by careful fractionation of the reaction product obtained in the ethanol-piperidine mixture, an additional substance could be obtained, which gave the correct analysis for benzylidene bis(triethyl phosphonoacetate) IV, i.e., the condensation product of one mole of benzaldehyde with two moles of triethyl phosphonoacetate. This product, too, gave cinnamic acid on hydrolysis, and its formation is analogous to the formation of a similar condensation product from two moles of ethyl nitroacetate and one mole of benzaldehyde.[2]



$$C_6H_5CH\left[\begin{array}{l}CHCOOC_2H_5\\ |\\ PO(OC_2H_5)_2\end{array}\right]_2$$

IV

In similar experiments, with *p*-nitrobenzaldehyde and triethyl phosphonoacetate in ethanol as solvent and piperidine as the catalyst, very high yields (83%) of ethyl *p*-nitrocinnamate were obtained. No phosphorus-containing product could be isolated from the reaction mixture.

The relative strength of carbon-carbon and carbon-phosphorus bonds. The strength of carbon-carbon and carbon-phosphorus bonds, other things being equal, is of about the same order.[3]

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(1) A. N. Pudovik and N. M. Lebedeva, *Doklady Akad. Nauk S.S.S.R.*, **90**, 799 (1953) [*Chem. Abstr.*, **50**, 2429^d (1956)], names the final product (III) erroneously benzylidene phosphonic acid instead of benzylidene phosphonoacetic acid, as in the Russian text.

(2) A. D. Dornow and G. Wiehler, *Ann.* **578**, 117 (1952).

(3) For a review of recent literature see P. C. Crofts, *Quart. Rev.* **12**, 341 (1958), and papers quoted there.

TABLE I

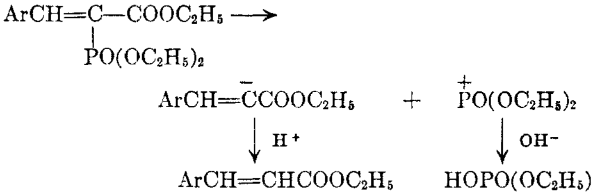
REACTION OF BENZALDEHYDE (BzH) WITH TRIETHYL PHOSPHONOACETATE (TPA)

No.	BzH, mole	TPA, mole	Solvent, Ml.	Catalyst	Temp.	Hr. Heating	Yield, %, of Cinnamic Acid
1.[a]	0.0312	0.0312	50 ml. acetic anhydride	—	160–170	5.5	12
2.[b]	0.0623	0.03	50 ml. ethanol	0.4 g. piperidine	Reflux	5	40
3.[c]	0.0312	0.0312	25 ml. pyridine	0.4 g. piperidine	100	19	22
4.[d]	0.070	0.062	25 ml. benzene	0.002 mole piperidine + 0.001 mole acetic acid	Reflux	44	70

[a] Hydrolysis of condensate by KOH/C_2H_5OH, 84% of the aldehyde recovered. [b] Fraction collected at 140–160°/1 mm: *benzylidenebis TPA* (IV), 10%. Hydrolysis of residue either by HCl or by KOH/C_2H_5OH. Longer heating of reaction mixture resulted in lower yields. [c] Fraction 140–160°/15 mm. hydrolyzed by KOH/C_2H_5OH. [d] Removal of water by azeotropic distillation. Fraction 160–170°/0.02 mm., redist. 140°/0.01 mm., 70% triester; 67% cinnamic acid (after hydrolysis).

In the present case, the question arises, as to why it is that after the hydrolysis of the triester, the elimination of the phosphonic acid group should be so much preferred against the elimination of the carboxyl group. Furthermore, in the case of the reaction between *p*-nitrobenzaldehyde and triethyl phosphonoacetate, the phosphonate group is eliminated already under the mild conditions of the condensation reaction, resulting in ethyl *p*-nitrocinnamate as the first product which can be isolated.

As the nitro group in the *para*-position of the aromatic group can hardly be responsible for any steric acceleration of the elimination, we believe that its effect is mainly the stabilization, by charge distribution, of the intermediate carbanion formed in the elimination. Owing to the rather small partial double-bond character of the phosphorus-oxygen bond,[3] its stabilizing effect will be much smaller than that of the carbonyl group in a dienic system C=C—C=O and therefore the elimination of the phosphonate group will be favored:



$$\underset{\displaystyle\mathrm{PO(OC_2H_5)_2}}{\mathrm{ArCH{=}C{-}COOC_2H_5}} \longrightarrow$$

$$\begin{array}{ccc} \mathrm{ArCH{=}\overset{-}{C}COOC_2H_5} & + & \mathrm{\overset{+}{P}O(OC_2H_5)_2} \\ \downarrow \mathrm{H^+} & & \downarrow \mathrm{OH^-} \\ \mathrm{ArCH{=}CHCOOC_2H_5} & & \mathrm{HOPO(OC_2H_5)_2} \end{array}$$

This effect seems to be strong enough to make the elimination of the phosphonate group possible under the mild conditions of the piperidine containing ethanol solvent with Ar = *p*-nitrophenyl, whereas in the case of Ar=phenyl, a strong base such as potassium hydroxide, is required.

The steric course of the condensation reaction. In most cases the crude ethyl *p*-nitrocinnamate obtained from the condensation melted at about 80–85° and even after one or two recrystallizations it still melted on rapid heating at 86–87° and on slow heating at 137–138°. Only after three or four recrystallizations did the ester melt both on rapid and on slow heating at 138°. We believe that the interpretation of these results must be that *p*-nitrobenzaldehyde with triethyl phosphonoacetate gives a primary condensation product in which the larger phosphonate group occupies the *trans*-position in reference to the aryl group, giving, on elimination of the phosphonate group, the unstable *cis*-ethyl *p*-nitrocinnamate (not described in the literature), which later isomerizes to the known *trans*-ester (high melting isomer, m.p. 138[4]).

Molecular models support this conclusion, as do also measurements of the C=C stretching frequency of II, which was found to be at 1625 cm.$^{-1}$. The C=C stretching frequency of diethylbenzylidene malonate is at 1650 cm^{-1}. If compound II were more hindered sterically than diethylbenzylidene malonate, it would be expected to give a higher wave number.[5]

EXPERIMENTAL

Materials used. Ethanol, benzene, pyridine, and piperidine were pure commercial products. Benzaldehyde was redistilled immediately before use. *p*-Nitrobenzaldehyde was recrystallized before use (m.p. 107°). Triethyl phosphonoacetate was prepared from diethyl phosphite[6] and ethyl chloroacetate, using a well dispersed suspension of sodium in xylene (instead of in hexane[7]).

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(4) E. Bergmann, S. Berkovic, and R. Ikan, *J. Chem. Soc.*, 402 (1936); E. Bergmann, *et al.*, *J. Am. Chem. Soc.*, **78** 6037 (1956).

(5) A less hindered compound, ethylbenzylidene cyanoacetate, gave the same stretching frequency at 1615 cm.$^{-1}$. Measurements of various similar compounds with different substituents in the aryl group showed that polar effects are relatively small and do not interfere with the above conclusion. (Y. Zabicky, personal communication.)

(6) H. McCombie, B. C. Saunders, G. J. Stacey, *J. Chem. Soc.*, 380 (1945).

(7) G. M. Kosolapoff, *J. Am. Chem. Soc.*, **68**, 1103 (1946).

Experiments with benzaldehyde are summarized in Table I. The *triethylbenzylidene phosphonoacetate* obtained in experiment No. 4, b.p. 140°/0.01 mm., $n_D^{20} = 1.520$–1.524, had the correct analysis.

Anal. Calcd. for $C_{15}H_{21}O_5P$: C, 57.7; H, 6.77. Found: C, 57.2; H, 7.1.

The cinnamic acid obtained from all experiments was identified by melting point and mixed melting point of the substance itself and by its *p*-bromophenacyl bromide derivative, m.p. 147.[8]

The substance obtained in experiment No. 2 had the correct analysis for *benzylidenebis(triethyl)phosphonoacetate*), $C_6H_5CH[CH(COOC_2H_5)PO(OC_2H_5)_2]_2$, IV.

Anal. Calcd. for $C_{23}H_{38}O_{10}P_2$: C, 51.57; H, 7.09. Found: C, 51.67; H. 6.85.

No attempt was made to establish the structure of this compound, but its analysis and the fact that it gave cinnamic acid on hydrolysis are strong evidence for its constitution.

The reaction of p-nitrobenzaldehyde with triethyl phosphonoacetate. In a representative experiment, 6 g. (0.0398 mole) of *p*-nitrobenzaldehyde and 5.5 g. (0.0246 mole) of triethyl phosphonoacetate were refluxed for 5 hr. in 60 ml. of pure ethanol containing 0.4 g. of piperidine. After removal of most of the solvent *in vacuo*, the residue solidified and melted at 80–85°. After one recrystallization from dilute ethanol, the substance melted at 86–87° (fast heating) and 90–91° (slow heating). After the second recrystallization the substance melted at 86° (fast heating) and at 138° (slow heating). After the third recrystallization the melting point was 138°, both on fast and slow heating.

The *cis*-ethyl *p*-nitrocinnamate is not described in the literature; the *trans*-ester melts at 138°.[4]

Anal. Calcd. for $C_{11}H_{11}O_4N$: C, 59.8; H, 4.98; N, 6.34. Found: C, 60.2; H, 5.4; N, 6.3.

On hydrolysis the substance yielded *trans-p*-nitrocinnamic acid, m.p. 285° dec., showing no depression with an authentic sample.

Attempted reaction of benzophenone with triethyl phosphonoacetate. Using the same conditions as in the above experiment, over 85% of the benzophenone was recovered unchanged and no other product could be isolated from the reaction mixture.

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[8] J. Reid, *J. Am. Chem. Soc.*, **42**, 1055 (1920).

Substituted γ-Lactones. V.[1] Synthesis of Certain α,β-Disubstituted γ-Lactones. A Route to Lignans of the α, β-Dibenzylbutyrolactone Class

Hans Zimmer, Johannes Rothe,[2] and James M. Holbert

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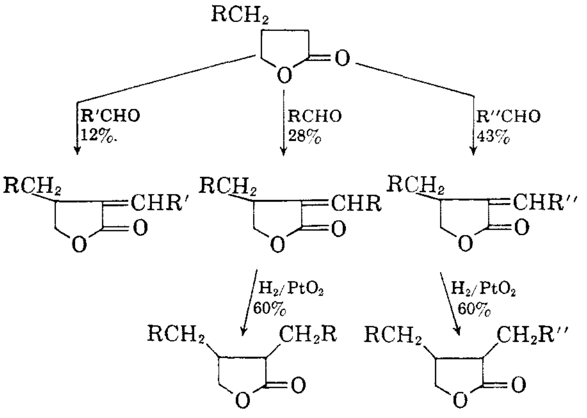
In our investigations dealing with substituted γ-lactones[3a–c] we became interested in the synthesis of α,β-disubstituted γ-butyrolactones, especially α,β-unsymmetrically substituted γ-butyrolactones. This type of butyrolactones occurs in nature as a class of lignans.[4,5] These are compounds which, at least formally, could be derived from substituted *n*-propylbenzenes which are dimerized by joining the β-carbon atoms of the side chain. Haworth and Woodcock[6] gave a synthesis of such a compound, namely, matairesinol (I), and its dimethylether (II).

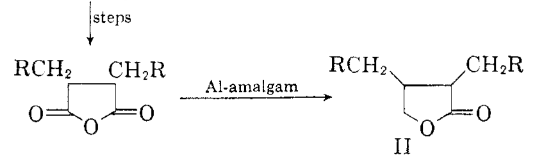
In paper III[3a] of this series we described a method which is generally applicable for the synthesis of β-benzyl-γ-butyrolactones. In paper I[3b] of this series we showed that γ-butyrolactone condenses with a large variety of aldehydes to yield α-benzylidene-γ-butyrolactones. A combination of these two methods resulted in a convenient procedure for synthesizing symmetrically and unsymmetrically α,β-disubstituted γ-butyrolactones. We tested this method in the synthesis of II as a member of a natural occurring lignan and in the synthesis of α-(4-dimethylaminobenzyl)-β-(3,4-dimethoxybenzyl)-γ-butyrolactone as an example for an α,β-unsymmetrically substituted γ-butyrolactone.

The following chart illustrates the route of the syntheses.



R = 3,4-dimethoxyphenyl
R′ = 3,4-dioxymethylenephenyl
R″ = 4-dimethylaminophenyl

2 RCHO + diethyl succinate (Route by Haworth *et al.*[6])



II

II was converted into a dinitro derivative. II and its dinitro derivative synthesized by this route were identical in melting points and infrared spectra with II and dinitro-II prepared by Haworth's method. Both compounds gave no depressions when mixed melting points were determined.

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[1] Paper IV of this series, Hans Zimmer, J. Rothe, and Dolores Gracian, *J. Org. Chem.*, in press.

[2] Chattanooga Medicine Company Post-doctorate Research Fellow, 1956–1958. Recipient of a Fulbright Travel Grant.

[3] (a) J. Rothe and Hans Zimmer, *J. Org. Chem.*, **24**, 586 (1959); (b) Hans Zimmer and J. Rothe, *J. Org. Chem.*, **24**, 28 (1959); (c) Hans Zimmer and J. Rothe, *J. Org. Chem.*, **24**, 100 (1959).

[4] R. D. Haworth, *Nature*, **147**, 225 (1941).

[5] W. M. Hearon and W. S. MacGregor, *Chem. Rev.*, **55**, 957 (1955).

[6] R. D. Haworth and D. Woodcock, *J. Chem. Soc.*, **1939**, 154.