TABLE VI

Expt. no.	Size of column, cm.	Buffer system	HV	HYV	SV	AHYV	Ratio of hypro-allohypro
1	0.9 × 50	Pyridinium acetate	33	9	18	11	49.8:50.2
2	0.9 × 30		20	9	7	10	49.7:50.3
3	0.9 × 20		14	9	2	9	49.9:50.1
4	0.9 × 50	Ammonium acetate	41	10	14	10	46:54

yield from ethyl allylacetaminocyanoacetate), m.p. 245–246° dec., lit. m.p. 247°.[12]

Anal. Calcd. for $C_5H_9NO_3$: C, 45.79; H, 6.92; N, 10.68. Found: C, 45.89; H, 6.83; N, 10.65.

The two AHYV fractions (138 + 132 ml.), processed as above, yielded 2.37 g. Further recrystallization with water–ethanol gave 2.11 g. (32%) of allohydroxy-DL-proline, m.p. 239–240° dec., lit.[12] m.p. 238°.

Anal. Calcd. for $C_5H_9NO_3$: C, 45.79; H, 6.92; N, 10.68. Found: C, 45.70; H, 6.79; N, 10.52.

Separation of Hydroxy-DL-proline and Allohydroxy-DL-proline Obtained from Dichlorovalerolactone.—2,5-Dichloro-4-valerolactone was prepared by the action of sulfuryl chloride on diethyl allylmalonate. The dichlorolactone (13.5 g., 0.08 mole) dissolved in concentrated ammonium hydroxide (200 ml.) was left for 5 days at room temperature. This procedure was found more convenient than the ammonolysis at 100° in a pressure vessel.[12] The solution was evaporated *in vacuo*. The residue on paper chromatography (n-BuOH-AcOH-pyridine-H_2O = 4:1:1:2, v./v.) showed two ninhydrin-positive spots, one belonging to hydroxyproline (R_f 0.23, yellow), and another (R_f 0.16, purple) belonging to an unknown material, *not* proline amide, which disappeared after refluxing for 3 hr. in 100 ml. of 6.0 N hydrochloric acid. After evaporation to dryness the residue was dissolved in water (100 ml.), and the solution was passed through a column (3 × 30 cm.) of Dowex 50W-X8 (100–200 mesh, H^+ form), washed with water, and eluted with 2 N ammonium hydroxide. The ammonia solution was evaporated *in vacuo*, and the residue was made up to a volume of 30 ml. with water.

TABLE VII

Expt. no.	HV[a]	HYV[a]	SV[a]	AHYV[a]
1	177	78	15	81
2	180	81	18	81
3	177	81	15	84

[a] In milliliters.

Each 10 ml. of the above solution was chromatographed as described above. The results obtained are shown in Table VII. The three HYV fractions were pooled and processed as described to yield 4.05 g. of hydroxyproline. Further recrystallization with water–ethanol gave 3.76 g. (35%) of pure hydroxy-DL-proline, m.p. 244–245° dec. By the same synthetic route and separation *via* the copper salts the yield of hydroxy-DL-proline was only 27%.[12]

Anal. Calcd. for $C_5H_9NO_3$: C, 45.79; H, 6.92; N, 10.68. Found: C, 45.77; H, 6.85; N, 10.61.

Similarly, the three portions yielded 2.85 g. of allohydroxyproline. Further recrystallization from water–ethanol gave 2.63 g. (25%), m.p. 238–239° dec. A yield of 27% of allohydroxyproline has been reported *via* the copper salts.[12]

Anal. Calcd. for $C_5H_9NO_3$: C, 45.79; H, 6.92; N, 10.68. Found: C, 45.81; H, 6.88; N, 10.73.

A Novel Method for the Preparation of Acid Anhydrides by Means of *trans*-Dibenzoylethylene and Tertiary Phosphines

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Reactions of *trans*-dibenzoylethylene with tertiary phosphines in the presence of carboxylic acids have been studied. When two equivalents of carboxylic acid were treated with *trans*-dibenzoylethylene and tertiary phosphine, the corresponding acid anhydrides were obtained in good yields, along with dibenzoylethane and phosphine oxide. Similar reactions were further extended to the phosphoric monoesters, and *sym*-pyrophosphates were obtained in good yields. The mechanism of the reaction is discussed.

It has recently been reported that the various carboxylic acids, phosphoric acids, and sulfonic acid were converted into the corresponding acid anhydrides in the course of oxidation–reduction reactions between diphenylmercury and tri-n-butylphosphine.[1]

$$(C_6H_5)_2Hg + 2RCO_2H + (n\text{-}C_4H_9)_3P \longrightarrow Hg + 2C_6H_6 + (RCO)_2O + (n\text{-}C_4H_9)_3P{=}O$$

In the present study, it was found that *trans*-dibenzoylethylene can be employed as a hydrogen acceptor in place of the diphenylmercury mentioned in the above experiments. When tri-n-butylphosphine was added to an anhydrous benzene solution of *trans*-dibenzoylethylene at room temperature, it assumed a red color with evolution of heat. After standing for 10 min., it was added to an anhydrous benzene solution of two equivalents of propionic acid and the mixture was refluxed for 2 hr.; propionic anhydride was obtained in 78% yield along with dibenzoylethane (77%) and tri-n-butylphosphine oxide (84%). Similar reaction was observed in the cases of the other carboxylic acids (see Table I).

$$C_6H_5COCH{=}CHCOC_6H_5 + (n\text{-}C_4H_9)_3P + 2RCO_2H \longrightarrow C_6H_5COCH_2CH_2COC_6H_5 + (n\text{-}C_4H_9)_3P{=}O + (RCO)_2O$$

Triphenylphosphine was likewise successfully used as an oxygen acceptor and propionic anhydride was obtained in 70% yield under the same condition.

The most probable pathway of this reaction may be sketched in the following manner. Initially, tri-n-butylphosphine reacts with *trans*-dibenzoylethylene to form an adduct (I),[2] which in turn is transformed into "phosphonium carboxylate" (II) in the presence of car-

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(1) T. Mukaiyama, I. Kuwajima, and Z. Suzuki, *J. Org. Chem.*, **28**, 2024 (1963).

(2) Horner, *et al.*, reported that *trans*- and *cis*-dibenzoylethylene react with triethylphosphine to form an adduct similar to I in 95% and 65% yields, respectively: L. Horner and K. Klupfel, *Ann.*, **591**, 69 (1955).

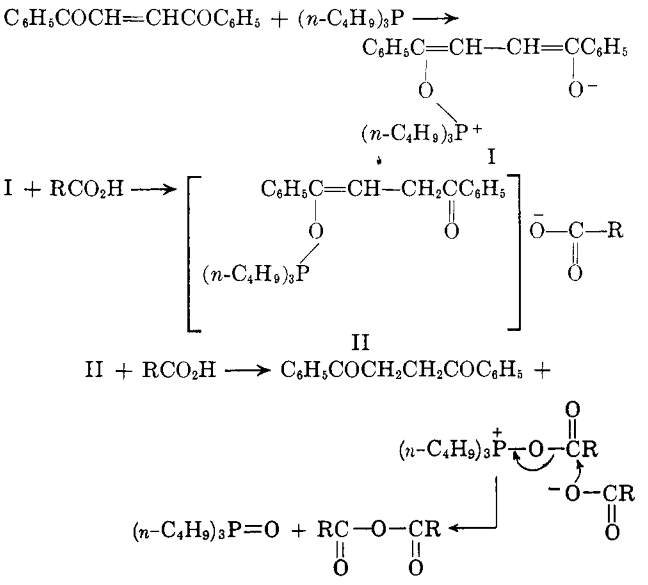
TABLE I

THE REACTIONS OF TRI-*n*-BUTYLPHOSPHINE WITH *trans*-DIBENZOYLETHYLENE IN THE PRESENCE OF CARBOXYLIC ACIDS

Carboxylic acid	Yield, %: Anhydride (m.p. or b.p., °C.)	Dibenzoylethane	$(n\text{-}C_4H_9)_3P{=}O$
Propionic	78 (66–68° at 18 mm.)	77	84
n-Butyric	77 (85–86° at 18 mm.)	76	79
Isobutyric	81 (74–76° at 18 mm.)	77	83
Benzoic	52[a]	49	
Phthalic	63 (130–131°, m.p.)	45	58
Succinic	82 (117–119°, m.p.)	89	87

[a] Since benzoic anhydride could not be separated from tri-*n*-butylphosphine oxide by fractional distillation, the yield was determined from the weight of the corresponding anilide derived from the anhydride. [b] The reactions were carried out in anhydrous benzene for 2 hr. at reflux.

boxylic acid. The "phosphonium carboxylate" (II) thus formed may react with the other carboxylic acid to yield the corresponding acid anhydride, dibenzoylethane, and tri-*n*-butylphosphine oxide.[3,4]



Further extension of this reaction to phosphoric monoesters was examined. When phenyl dihydrogen phosphate was used in place of carboxylic acid, a reaction could not be observed and the starting materials were recovered almost quantitatively. This may be due to poor nucleophilicity of the phosphate anion and the reaction is stopped in the step of phosphonium phosphate. Based on these results, tertiary ammonium phenyl hydrogen phosphate was used in the above experiment in order to increase its nucleophilicity. While the triethylammonium salt gave *sym*-diphenyl pyrophosphate, the pyridinium salt did not.

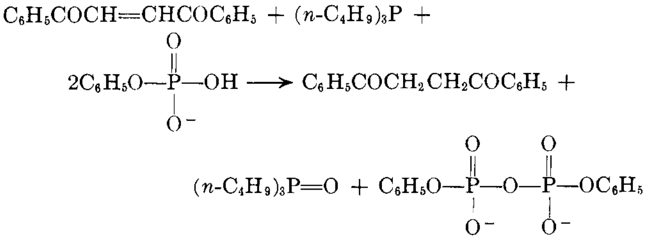


TABLE II

THE REACTIONS OF TRI-*n*-BUTYLPHOSPHINE WITH *trans*-DIBENZOYLETHYLENE IN THE PRESENCE OF PHOSPHORIC MONOESTERS[a]

$\mathrm{RO{-}\overset{O}{\overset{\Vert}{P}}(OH)_2}$	Yield, %: Pyrophosphate (R_f value)	Dibenzoylethane	$(n\text{-}C_4H_9)_3P{=}O$
R = C_6H_5	82 (0.80)	75	
R = *p*-$CH_3C_6H_5$	84 (0.82)	80	

[a] The reactions were carried out in anhydrous benzene. When acetonitrile was used as solvent, a reaction was not observed and the starting materials were recovered.

Experimental

Materials.—*trans*-Dibenzoylethylene (m.p. 109–110°) was prepared by the method of Lutz.[5]

Reaction of Propionic Acid with *trans*-Dibenzoylethylene and Tri-*n*-butylphosphine.—Tri-*n*-butylphosphine (3.00 g., 0.015 mole) was added dropwise to *trans*-dibenzoylethylene (3.54 g., 0.015 mole) in 20 ml. of anhydrous benzene. It turned red with evolution of heat. After 10-min. standing, it was mixed with propionic acid (2.22 g., 0.03 mole) and refluxed for 2 hr. Then the reaction mixture was concentrated and the separated dibenzoylethane, 2.74 g. (77%), m.p. 142–144°, was filtered off. Its filtrate was distilled *in vacuo*, giving propionic anhydride, 1.52 g. (78%), b.p. 66–68° (18 mm.), and tri-*n*-butylphosphine oxide, 2.74 g. (84%), b.p. 133–135° (0.8 mm.).

By a similar procedure, the other carboxylic anhydrides were obtained.

Reaction of Benzoic Acid with *trans*-Dibenzoylethylene and Tri-*n*-butylphosphine.—Benzoic acid (2.44 g., 0.02 mole) reacted with tri-*n*-butylphosphine (2.00 g., 0.01 mole) and *trans*-dibenzoylethylene (2.36 g., 0.01 mole) under the same condition as described above. Then the reaction mixture was concentrated and dibenzoylethane, 1.17 g. (49%), m.p. 140–143°, was filtered off. The filtrate was dissolved in 30 ml. of ether and it was treated with cold aqueous sodium bicarbonate solution. From the ether layer, benzanilide, 1.03 g. (52%), m.p. and m.m.p. 159–161°, was obtained by treatment with aniline (0.93 g., 0.01 mole). From the aqueous layer, benzoic acid, 0.89 g. (36%), m.p. and m.m.p. 118–120°, was isolated by the acidification with dilute hydrochloric acid.

Reaction of Triethylammonium Phenyl Hydrogen Phosphate with *trans*-Dibenzoylethylene and Tri-*n*-butylphosphine.—Tri-*n*-butylphosphine (1.00 g., 0.005 mole) and *trans*-dibenzoylethylene (1.18 g., 0.005 mole) were treated as described above. The resulting solution was added to 20 ml. of an anhydrous benzene solution of phenyl dihydrogen phosphate (1.74 g., 0.01 mole) and triethylamine (0.51 g., 0.01 mole). It was refluxed for 2 hr. Then the reaction mixture was concentrated and dibenzoylethane, 0.90 g., (75%), m.p. 142–144°, was filtered off. A solution of barium chloride ($BaCl_2 \cdot 2H_2O$, 2.30 g.) in 10 ml. of water and pyridine (3 ml.) was added to the cold reaction mixture and allowed to stand in a refrigerator for about 30 min. The white precipitate was washed twice with acetone, dried, and then washed with 30 ml. of water thoroughly. The undissolved precipitate was filtered and dried *in vacuo* over phosphorus pentoxide at room temperature; 2.00 g. (80%) of barium diphenyl pyrophosphate was obtained, R_f 0.80 (1-propanol–concentrated ammonia–water, 6:3:1).

By the same procedure barium di-*p*-tolyl pyrophosphate was obtained.

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(3) S. Tripett, *J. Chem. Soc.*, 2337 (1962).

(4) I. J. Borowitz and R. Virkhaus, *J. Am. Chem. Soc.*, **85**, 2185 (1963).

(5) R. E. Lutz, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons. Inc., New York, N. Y., 1955, p. 248.