chloric acid (5%, 50 ml.) added and the mixture extracted 3 times with 30 ml. of ether. The extract was dried over sodium sulfate and freed from solvent by aeration. The resulting partially crystallizing sirup was taken up in 80% alcohol, refluxed with 0.5 g. of activated carbon for 30 minutes, filtered, and washed with a small amount of 80% alcohol. The aqueous alcoholic solution was hydrogenated in the presence of palladium–charcoal. After the uptake of hydrogen had ceased, catalyst was filtered; the filtrate was concentrated under reduced pressure, neutralized with barium hydroxide and concentrated under reduced pressure. The crystals obtained upon the addition of ethanol were filtered with suction, washed with ethanol, and dried over phosphorus pentoxide at 100° *in vacuo*, yield 2.6 g. (52.1%).

Anal. Calcd. for $C_2H_5O_4PBa$: C, 9.2; Ba, 52.5. Found: C, 10.3; Ba, 54.0.

The brucine salt of monoethyl phosphate was prepared in the usual manner; softening temperature *ca.* 135–140°, m.p. *ca.* 174–175° dec.

Anal. Calcd. for $C_{48}H_{59}O_{12}N_4P$: N, 6.5. Found: N, 6.54.

Acknowledgment.—We are grateful to Sir A. R. Todd for his interest and encouragement and to Dr. Y. Hirata and Mr. Uritani for their advice.

TOKYO, JAPAN

[CONTRIBUTION FROM THE LABORATORY OF BIOCHEMISTRY, FACULTY OF AGRICULTURE, NAGOYA UNIVERSITY]

Synthesis of Organic Phosphorus Compounds. II. Exhaustive Debenzylation Reactions

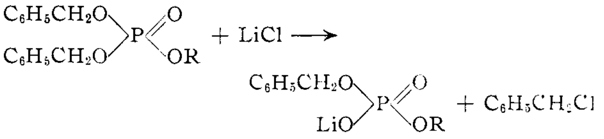
BY MASATERU MIYANO[1]

RECEIVED SEPTEMBER 7, 1954

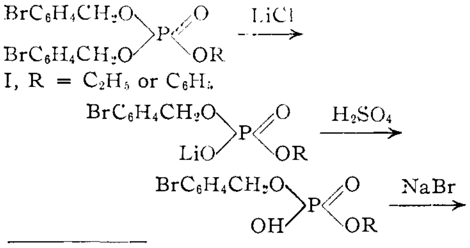
Ethyl phosphate and phenyl phosphate were prepared from di-*p*-bromobenzyl ethyl phosphate (I, R = C_2H_5) and di-*p*-bromobenzyl phenyl phosphate (I, R = C_6H_5), respectively, by the stepwise removal of two *p*-bromobenzyl groups on heating with an inorganic salt in an anhydrous solvent. This reaction "exhaustive debenzylation," a development of the "specific debenzylation" studied by other investigators,[2,3] seems to be a new generally applicable method for the preparation of monoalkyl and monoaryl esters of phosphoric acid. *p*-Chlorobenzyl phosphate and *p*-bromobenzyl phosphate also were prepared by a similar method.

Neutral esters of phosphoric or phosphorous acid, such as tribenzyl phosphate, dibenzyl alkyl phosphate, dibenzyl alkylamidophosphonate and dibenzyl phosphite lose one benzyl group when heated with a strong tertiary amine, amine hydrochloride or better with an inorganic salt in an anhydrous solvent.[2,3]

Lithium chloride in ethoxyethanol is in general the best reagent for this purpose.

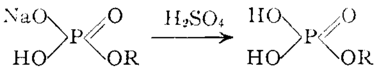


It was suggested that this reaction is applicable only to neutral and not to ionizable esters. However, in this paper is described the removal of *p*-halobenzyl groups from acidic esters (II) as well as neutral esters (I) by heating with lithium chloride or sodium bromide in ethoxyethanol or diethylene glycol. The stepwise splitting off of two *p*-halobenzyl groups, as shown below, is termed exhaustive debenzylation.



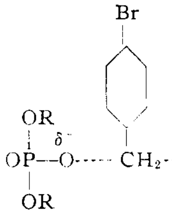
I, R = C_2H_5 or C_6H_5

II, R = C_2H_5 or C_6H_5



These reactions constitute a third method for the preparation of monoalkyl or monoaryl phosphates by the removal of protecting groups; the other methods are hydrolysis and hydrogenolysis. Although the yield obtained by exhaustive debenzylation is somewhat lower than that obtained by hydrogenolysis, this method is useful for cases in which hydrogenolysis is not feasible.

Since $-S_2$ substitution reactions are generally accelerated by a +I substituent or a −E substituent,[4] *para*-substituted bromine which has both a +I and a −E effect should accelerate $-S_2$ reaction. This was borne out by our finding[5] that the alkaline hydrolysis (which is believed to follow as $-S_2$ mechanism (X = OH)) of *p*-halobenzyl groups proceeded more easily than that of benzyl groups. If debenzylation reactions also proceed by a $-S_2$ mechanism (X = Cl or Br), the *p*-bromobenzyl group would be expected to be removed more easily than the unsubstituted benzyl group, although the latter still may undergo exhaustive debenzylation.



Di-*p*-bromobenzyl phosphate (IVa) and di-*p*-chlorobenzyl phosphate (IVb) were prepared in

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[1] Department of Agricultural Chemistry, Tokyo University.

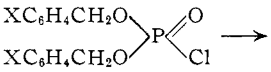
[2] J. Baddiley, V. M. Clark, J. J. Michalski and A. R. Todd, *J. Chem. Soc.*, 815 (1949).

[3] V. M. Clark and A. R. Todd, *ibid.*, 2023 (1950); (b) 2030 (1950).

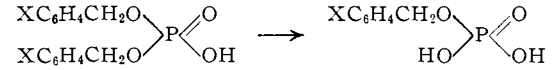
[4] M. J. S. Dewar, "The Electronic Theory of Organic Chemistry," Oxford University Press, London, 1949, pp. 71–72.

[5] M. Miyano and S. Funahashi, THIS JOURNAL, **77**, 3522 (1955).

good yield by the solvolysis of the corresponding chlorophosphonates (IIIa, b) with aqueous acetone.[6] Our attempt to synthesize IVb from *p*-chlorobenzyl alcohol and phosphorus oxychloride failed, as *p*-chlorobenzyl chloride was obtained in a quantitative yield. The *p*-halobenzyl phosphates (V) were prepared by the reaction of IV with lithium chloride.



IIIa, X = Br; b, X = Cl



IVa, X = Br; b, X = Cl   Va, X = Br; b, X = Cl

p-Chlorobenzyl phosphate, which has a structure similar to *p*-chlorophenoxyacetic acid, accelerated germination of the sesame root at 10^{-5}–10^{-7} *M* and exerted an inhibitory effect at higher concentration (by Miss H. Yamada).

When di-*p*-bromobenzyl phosphate was heated with N-methylmorpholine, it was partially debenzylated to mono-*p*-bromobenzyl phosphate.

Acknowledgment.—The author thanks Mr. and Mrs. Ishii, Mrs. K. Satô, Misses M. Suzuki and I. Isobe who performed microanalyses in this and previous works.

Experimental[7]

***p*-Bromobenzyl Ethyl Phosphate** (II, R = C_2H_5).—Di-*p*-bromobenzyl chlorophosphonate[6] (prepared from 24 g. of the phosphite) in benzene (100 ml.) was added gradually to an ice-cold mixture of ethanol (7.5 ml.) and pyridine (30 ml.). After standing for 3 hours at room temperature, the mixture was washed with dilute hydrochloric acid, water and aqueous potassium carbonate solution. It was dried with potassium carbonate and concentrated under vacuum to give a sirup (di-*p*-bromobenzyl ethyl phosphate (I, R = C_2H_5)) which crystallized partially on standing at room temperature. This semi-crystalline sirup dissolved in ethoxyethanol (100 ml.) containing lithium chloride (5.0 g.) was heated at 107° for 2.5 hours. Aqueous potassium carbonate was added to the cooled solution and the mixture extracted with chloroform, acidified with sulfuric acid, and extracted with ether. The ethereal extract was dried over phosphorus pentoxide *in vacuo* for 24 hours; yield 19.2 g. This material (R_f: A, 0.96; C, 0.88) which was essentially *p*-bromobenzyl ethyl phosphate containing a small amount of unidentified phosphate (R_f: A, 0.77; C, 0.73) was used in next reaction without further purification. It was identified as the crystalline cyclohexylamine salt which was prepared in the usual manner and recrystallized from water; m.p. 164–166°.

Anal. Calcd. for $C_{19}H_{25}O_4NPBr$: N, 3.55. Found: N, 3.5.

Ethyl Phosphate.—A solution of crude *p*-bromobenzyl ethyl phosphate (18.4 g.) and sodium bromide (2.0 g.) in diethylene glycol (150 ml.) was heated at 120–135° for 3 hours. The cooled solution was diluted with water (500 ml.), extracted with ether (90 ml.) and passed through a column of Amberlite IR-120 (2 × 40 cm.). The combined filtrate and washings (about 1 l.) was neutralized with barium hydroxide (phenolphthalein), and concentrated under reduced pressure. Upon the addition of ethanol to the concentrate, crystals separated which were filtered, washed with 95% ethanol, and dried over phosphorus pentoxide under vacuum; yield 5.25 g. (yield based on di-*p*-bromobenzyl phosphite).

Anal. Calcd. for $C_2H_5O_4PBa$: Ba, 52.5. Found: Ba, 53.5.

The barium salt was converted to the diammonium salt with ammonium sulfate. The diammonium ethyl phosphate which was chromatographed showed the same R_f value as an authentic specimen: A, 0.51; B, two spots 0.66 and 0.24 corresponding to the free acid and the mono-ammonium salt, respectively; C, 0.72.

The diisothiouronium salt was prepared in the usual manner and recrystallized from water; m.p. 135°.

Anal. Calcd. for $C_{18}H_{27}N_4S_2O_4P$: N, 12.2. Found: N, 11.9.

The barium salt was treated with dilute sulfuric acid, and then with ethanolic brucine; the brucine salt was recrystallized twice from hot water; m.p. 174–175°.

Anal. Calcd. for $C_{48}H_{59}O_{12}N_4P$: N, 6.1. Found: N, 6.1.

Di-*p*-bromobenzyl Phenyl Phosphate (I, R = C_6H_5).—Di-*p*-bromobenzyl chlorophosphonate (from 32.8 g. of phosphite) in 200 ml. of benzene was added in one portion to sodium phenoxide (8.8 g.) and the mixture vigorously shaken for 30 minutes. The mixture was washed with dilute hydrochloric acid, water and aqueous potassium carbonate solution; dried with calcium chloride; and concentrated under reduced pressure. Light petroleum was added to opalescence, cyclohexane (2 ml.) was added and the solution set aside in a refrigerator. The crystalline mass was filtered with suction, and washed with light petroleum; yield 17.4 g., m.p. 62–64°; additional material was obtained from the mother liquor by concentration and cooling; combined yield 27.5 g. (71%). This was recrystallized from cyclohexane-light petroleum; m.p. 71–72°.

Anal. Calcd. for $C_{20}H_{17}O_4Br_2P$: C, 46.9; H, 3.35. Found: C, 46.7; H, 3.3.

***p*-Bromobenzyl Phenyl Hydrogen Phosphate** (II, R = C_6H_5).—Crude di-*p*-bromobenzyl phenyl phosphate (11 g.) and lithium chloride (2.1 g.) were dissolved in ethoxyethanol (50 ml.) and heated at 100° for two hours. The mixture was diluted with water, extracted with ether, acidified with sulfuric acid and extracted with chloroform. The chloroform extract was dried with sodium bromide and concentrated to a thick sirup. This was dissolved in ethanol and excess cyclohexylamine added. The clear ethanolic solution was concentrated under reduced pressure and water was added. The separated cyclohexylamine salt was filtered with suction and washed with water; 8.55 g. (90%), m.p. 192–193°; R_f value of free acid: A, 0.86; C, 0.93.

Anal. Calcd. for $C_{19}H_{25}O_4NPBr$: C, 51.6; H, 5.7; N, 3.2. Found: C, 51.9; H, 5.7; N, 3.3.

Phenyl Phosphate.—(A) The crude dicyclohexylamine salt of *p*-bromobenzyl phenyl phosphate (m.p. 183–188°) suspended in dilute sulfuric acid (10 ml.), was extracted with chloroform (30 ml.). The organic layer was dried with calcium chloride and concentrated to a thick sirup. Sodium bromide (1.2 g.) and ethoxyethanol (30 ml.) were added, and the clear solution was heated for 50 minutes at 100° and for an additional one hour at 130°. The cooled solution was diluted with water (50 ml.), extracted with chloroform, acidified with sulfuric acid, and extracted with ether. The ethereal extract was concentrated to a small volume. Excess cyclohexylamine and acetone (40 ml.) were added and the solid was filtered with suction and dried; 0.81 g. (46%), m.p. 208–209°. Recrystallization from aqueous ethanol gave a compound which had the same m.p., mixed m.p. (214–215° cor.), and R_f values as authentic sample (B) prepared as described below.

(B) Phenyl dichlorophosphinate (77 g.) was added dropwise to a stirred solution of potassium carbonate (102 g. in

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[6] IVa and b were obtained in poor yield when the corresponding phosphites were oxidized with carbon tetrachloride in the presence of sodium hydroxide due to the hydrolysis of the *p*-halobenzyl groups; ref. 5.

[7] Melting points are not corrected unless otherwise indicated. Paper chromatography was carried out by the ascending method on filter paper pretreated with dilute hydrochloric acid followed by distilled water. Untreated paper gave R_f values which were not clear due to severe tailing. Hanes–Isherwood[8] spray reagent was used. The percentage composition of solvents was A: isopropyl alcohol 40, isobutyl alcohol 20, concentrated ammonia 1, water 39[9]; B: acetic acid 10, butanol 40, water 50[10]; and C: methanol 60, concentrated ammonia 10, water 30.[11]

[8] C. S. Hanes and F. A. Isherwood, *Nature*, **169**, 1107 (1949).

[9] J. P. Ebel, *Bull. soc. biol. chim.*, **34**, 330 (1952).

[10] J. Baddiley and E. M. Thain, *J. Chem. Soc.*, 803 (1952).

[11] R. S. Bandurski and B. Axelrod, *J. Biol. Chem.*, **193**, 405 (1953).

TABLE I

Phosphate	Yield, %	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
p-Bromobenzyl[a] ammonium	97.2[b]	217[c]	$C_7H_{11}NO_4PBr$	29.6	28.9	3.9	3.8	4.9	5.3
p-Bromobenzyl dibrucine		134–135	$C_{53}H_{60}O_{12}N_4PBr$					5.3	5.3
p-Chlorobenzyl[d] ammonium	94.0	210[c]	$C_7H_{11}NO_4PCl$	35.5	35.5	4.6	4.6	5.85	5.9
p-Chlorobenzyl[e]		126–127	$C_7H_8O_4PCl$	37.8	37.1	3.6	3.8	4.9	5.3
p-Chlorobenzyl[f] dibrucine		137–137	$C_{53}H_{60}O_{12}N_4PCl$					5.5	5.5

[a] Contaminated with a small amount of the diammonium salt. [b] Crude material calculated as monoammonium salt. [c] Corrected. [d] R_f values: A, 0.76; B, 0.91; C, 0.80. [e] Calcd. Cl, 15.9; found Cl, 15.8. [f] Hygroscopic.

200 ml. of water) at 50–60°. Stirring was continued until all the oily substance had disappeared. The solution was then cooled, strongly acidified with sulfuric acid and extracted with ether. The ethereal extract was dried with sodium bromide, concentrated to a thick sirup and taken up in absolute ethanol. Concentrated aqueous ammonia was added. After cooling the diammonium salt was filtered and washed with ethanol; yield 60.5 g., m.p. 164–169° dec.; R_f value: A, 0.76; C, 0.73.

Anal. Calcd. for $C_6H_{13}N_2O_4P$: N, 13.4. Found: N, 13.2.

The diammonium salt was dissolved in a minimum amount of water, acidified with sulfuric acid, and extracted with ether. Excess aqueous cyclohexylamine was added to the concentrated ether extract and the separated dicyclohexylamine salt was filtered with suction and recrystallized from hot water; m.p. 214–215° (cor.).

Di-*p*-halobenzyl Hydrogen Phosphate (IVa, b).—Di-*p*-halobenzyl phosphite[12] was suspended in carbon tetrachloride (50 ml.), and sulfuryl chloride (1.7 ml.) was added to the cooled solution (about 15°) with shaking. The clear solution was allowed to stand for 30 minutes at room temperature, and then concentrated *in vacuo*. Acetone (100 ml.) and water (100 ml.) was added in one portion. After 3 hours, water (100 ml.) was added gradually and crystals separated. Almost all the acetone was removed under reduced pressure and the resultant crystals were filtered with suction. IVa was obtained as long needles, m.p. 156° reported[1] 155–156°); R_f: A, 0.97; B, 0.88. The crude IVb (m.p. 134°, yield 82.2%) upon recrystallization from aqueous ethanol gave the same m.p. (136°) as an authentic specimen; R_f: A, 0.95; B, 0.91; C, 0.87.

***p*-Halobenzyl Dihydrogen Phosphate (Va, b).**—The crude IVb (2.0 g.) was dissolved in 25 ml. of ethoxyethanol (saturated with lithium chloride); IVa (2.0 g.) was dissolved in 20 ml. of ethoxyethanol (saturated with lithium chloride). The solution was heated for 1.5 hours at 120°,[13] acidified with sulfuric acid and extracted with ether. The ether was removed from the extract, and ethanol (50 ml.) and concentrated ammonia (5 ml.) added. The separated monoammonium salt was filtered with suction, washed with ethanol, and dried over phosphorus pentoxide *in vacuo*. The analytical results are reported in Table I.

N-Methylmorpholine on Di-*p*-bromobenzyl Phosphate.—Di-*p*-bromobenzyl phosphate (0.6 g.) in N-methylmorpholine (1 ml.) was heated at 105° for 3 hours; the mixture was acidified with dilute sulfuric acid and extracted with ether. The ethereal extract was concentrated under reduced pressure, and chromatographed. A small spot of the starting material (R_f: A, 0.97) and a small but distinct spot of mono-*p*-bromobenzyl phosphate (R_f: A, 0.79) were identified.

Reaction of *p*-Chlorobenzyl Alcohol and Phosphorus Oxychloride.—A mixture of *p*-chlorobenzyl alcohol (22.7 g., 1 mole) and pyridine (12.6 g., 1 mole) was added dropwise to a stirred solution of phosphorus oxychloride (24.4 g., 1 mole) in ether (10 ml.) at about 10°; stirring was continued for 20 minutes after the addition was complete. The reaction mixture was washed with dilute sulfuric acid (40 ml.), dried with calcium chloride, and concentrated under reduced pressure; 23.1 g. (90%), m.p. and mixed m.p. with authentic *p*-chlorobenzyl chloride 28°.

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(12) Bromobenzyl compound, 8.2 g.; chlorobenzyl, 6.4 g.

(13) After a few minutes heating the fine white needles of the lithium salt of the starting material, which began to separate, disappeared and a yellow amorphous solid was deposited. Heating of IVb to 100° for 2 hours resulted in a poor yield of the desired product.

ANJÔ, AICHI-KEN, JAPAN

[CONTRIBUTION FROM THE CHEMICAL RESEARCH LABORATORIES, THE LUBRIZOL CORPORATION]

The Preparation and Reactions of Diphenylphosphinous Chloride

BY CARL STUEBE, W. M. LESUER AND G. R. NORMAN

RECEIVED NOVEMBER 23, 1954

A new preparation of diphenylphosphinous chloride, based on the reduction of diphenylphosphoranetrioic trichloride with elemental phosphorus, is described. Certain esters of the diphenylphosphinate and phosphinite type, as well as phosphines and their oxidation products, derived from diphenylphosphinous chloride are reported.

The preparation of diphenylphosphinous chloride has been a subject of investigation in several laboratories.[1] The best methods developed previously are outlined in the following reactions. Yields of the desired product are relatively low in all cases.

$$C_6H_5PCl_2 + (C_6H_5)_2Hg \longrightarrow (C_6H_5)_2PCl + C_6H_5HgCl^{1a} \quad (1)$$

$$C_6H_6H + PCl_3 \xrightarrow{AlCl_3} (C_6H_5)_2PCl + C_6H_5PCl_2 + HCl^{1b} \quad (2)$$

$$(C_6H_5)_3PCl_2 \xrightarrow{\text{distn.}} (C_6H_5)_2PCl + C_6H_5Cl^{1c} \quad (3)$$

In reaction (2) above the diphenylphosphinous chloride was not isolated, but was used directly in the formation of an ester, following breakdown of the aluminum chloride complex.

A new method has been developed for the preparation of diphenylphosphinous chloride in good yield, utilizing the readily available diphenylphosphinodithioic acid as a starting material. The preparation of diphenylphosphinodithioic acid from the reaction of phosphorus pentasulfide and benzene in the presence of aluminum trichloride has been reported recently.[2] Dried crude diphenylphosphinodithioic acid obtained after hydrolysis of the reac-

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(1) (a) F. G. Mann and I. T. Millar, *J. Chem. Soc.*, 4453 (1952); (b) G. M. Kosolapoff and W. F. Huber, THIS JOURNAL, **69**, 2020 (1947); (c) A. Michaelis and H. Soden, *Ann.*, **229**, 303 (1885).

(2) W. A. Higgins, P. W. Vogel and W. G. Craig, THIS JOURNAL, **77**, 1864 (1955).