unsaturated acyl residues can be expected to be stable. β,β,β-trichloroethylchloroformate (**1**)[10] was allowed to react with ethanolamine in a suspension of dioxane containing magnesium oxide to give the syrupy N-(β,β,β-trichloroethoxycarbonyl)ethanolamine (**2**) in 90–95% yield. Treatment of **2** with excess phosphorus oxychloride in benzene afforded the dichloride **3**. Hydrolysis of **3** gave N-β,β,β-trichloroethoxycarbonyl-2-aminoethylphosphoric acid (**4**), which was isolated as the dicyclohexylamine salt. The purified dicyclohexylamine salt of **4** was converted into the free acid by stirring a solution of the salt with Amberlite IR-120 (H^+) ion-exchange resin.

The synthesis of O-(1,2-dilinoleoyl-*sn*-glycero-3-phosphoryl)ethanolamine (**7**), *i.e.*, 1,2-dilinoleoyl-3-*sn*-phosphatidylethanolamine,[11] is an example of the use of the intermediate **3**. *sn*-Glycerol 1,2-dilinoleate (**5**)[1] was allowed to react in chloroform with a benzene solution of **3** with pyridine as the acid acceptor. The derived diacylglycerophosphate ester chloride **6** was treated without further purification with zinc in 95% acetic acid. Thin layer chromatography of the crude phosphatidylethanolamine **7** showed one ninhydrin positive material and some trace phosphate-containing impurities.[12] Filtration of the crude product through DEAE-cellulose in the acetate form[13] provided 1,2-dilinoleoyl-3-*sn*-phosphatidylethanolamine. The phosphatide was hydrolyzed with boron trifluoride–methanol, and glpc analysis of the derived methyl esters indicated about 98% methyl linoleate.

Experimental Section[14]

N-(β,β,β-Trichloroethoxycarbonyl)ethanolamine (2).—A solution of 100 g (0.47 mol) of β,β,β-trichloroethylchloroformate[10] in 50 ml of dioxane was added at 0° to a mixture of 36.7 g (0.6 mol) of ethanolamine, 40 g of MgO, 125 ml of dioxane, and 125 ml of H_2O. The suspension was warmed to room temperature and stirred for an additional 16 hr. Ether (500 ml) was added, the inorganics were filtered, and the filtrate was washed with dilute HCl, brine, 5% NaHCO, and brine again. After being dried (Na_2SO_4), the solvent was evaporated to yield 112 g of the colorless syrup **2**. An analytical specimen was prepared by chromatography over Florisil, using 1:1 Et_2O–petroleum ether as the eluent: infrared absorption at 3.04, 5.83 and 8.01 μ.

Anal. Calcd for $C_5H_8Cl_3NO_3$: C, 25.39; H, 3.41; Cl, 44.98. Found: C, 25.56; H, 3.55; Cl, 44.48.

The 3,5-dinitrobenzoate derivative of **2** had mp 86–87° after crystallization from acetone–H_2O.

Anal. Calcd for $C_{12}H_{10}Cl_3N_3O_8$: C, 33.47; H, 2.34; N, 9.76. Found: C, 33.37; H, 2.20; N, 9.54.

Dichloro(N-β,β,β-trichloroethoxycarbonyl-2-aminoethyl)phosphate (3).—A solution of 41 g (0.174 mol) of **2** in 100 ml of dry C_6H_6 was added dropwise under N_2 over 4 hr to a cooled, stirred solution of 60 ml (0.64 mol) of freshly distilled $POCl_3$ in 250 ml of dry C_6H_6. After being stirred for 16 hr at room temperature, the reaction mixture was concentrated at H_2O aspirator pressure at 40°. Then the residue was azeotroped with dry C_6H_6 several times and finally concentrated at 1 mm to give about 55 g of crude **3**. The product was dissolved in dry C_6H_6, diluted to volume in a 100-ml volumetric flask, and stored at 0° under N_2. Under these conditions, the compound is stable for several months. Attempted molecular distillation at high vacuum did not give an analytically pure sample of **3**; the material readily polymerized in the distilling flask.

Dicyclohexylammonium Salt of N-β,β,β-Trichloroethoxycarbonyl-2-aminoethylphosphoric Acid (4).—A solution of 5 g of crude **3**, 50 ml of 50% aqueous dioxane, and 100 ml of 0.1 *N* KCl was stirred at room temperature for 2 hr. Solid NaCl was added, and the mixture was extracted several times with EtOAc. The EtOAc extracts were washed with H_2O, dried (Na_2SO_4), and concentrated to a colorless oil. Acetone (150 ml) was added, and the solution was treated with cyclohexylamine until basic. After being cooled, the white solid was filtered to give 5.8 g (80%) of the dicyclohexylammonium salt of **4**, mp 201–203°. Several recrystallizations from a mixture of EtOH–cyclohexylamine–H_2O (90:10:1) gave an analytical sample, mp 204–205°.

Anal. Calcd for $C_{17}H_{35}Cl_3N_3O_6P \cdot 0.5H_2O$: C, 38.98; H, 6.93; N, 8.02; H_2O, 1.72. Found: C, 38.58; H, 6.97; N, 7.69; H_2O, 1.60.[15]

N-β,β,β-Trichloroethoxycarbonyl-2-aminoethylphosphoric Acid (4).—The cyclohexylammonium salt of **4** (1 g) was dissolved in Me_2CO (100 ml) and H_2O and stirred with 10 ml of Amberlite IR-120 (H^+) for 1 hr. The resin was filtered and washed with $CHCl_3$, and the filtrate was concentrated to a viscous syrup. Chromatography on silicic acid with 9:2 $CHCl_3$–MeOH gave pure **4**, a colorless, viscous syrup.

Anal. Calcd for $C_5H_9Cl_3NO_6P$: C, 19.13; H, 2.87; N, 4.43; Cl, 33.61; P, 9.79. Found: C, 19.38; H, 3.11; N, 4.23; Cl, 33.45; P, 9.52.

1,2-Dilinoleoyl-3-*sn*-phosphatidylethanolamine (7).—A solution of 4.0 g (0.00644 mol) of **5**[1] in 35 ml of dry $CHCl_3$ and 3 ml of dry pyridine was added to an ice-cold solution of 4.1 g (0.0116 mol) of **3** in 10 ml of C_6H_6. The addition took about 70 min and, after being stirred 1 hr at 0°, the solution was stirred at room temperature under N_2 for 18 hr longer. Ether (700 ml) was added, and the mixture was washed with H_2O, dilute HCl, brine, 5% $NaHCO_3$, and brine again. The Et_2O layer was evaporated without drying to give the creamy **6**. Tlc showed one major spot which was phosphate positive. This material was dissolved in HOAc (50 ml) and Et_2O (25 ml) and 20 g of activated zinc[16] were added. Then the suspension was stirred at 25° for 16 hr. After being diluted with Et_2O (600 ml), the zinc and inorganics were filtered, and the filtrate was washed with four 200-ml portions of H_2O, then with 5% $NaHCO_3$ (the addition of brine retards emulsification), and finally with brine. Evaporation of the dried (Na_2SO_4) solvent gave 5.8 g of a yellow oil which contained one ninhydrin-positive material and some lesser amounts of phosphate-positive products. Chromatography on 400 g of DEAE-cellulose in the acetate form[13] gave 1.2 g of homogeneous **7** and an additional 0.8 g containing trace impurities (42% yield over-all): $[\alpha]^{25}D$ +6.2° (*c* 1, $CHCl_3$) {lit.[11] $[\alpha]D$ +5.8° (*c* 5, $CHCl_3$)}; R_f 0.67, using the solvent system 65:25:4, $CHCl_3$–MeOH–H_2O, on 0.25-mm silica gel G plates.

Anal. Calcd for $C_{41}H_{74}NO_8P$: C, 66.55; H, 10.08; N, 1.89. Found: C, 66.51; H, 9.94; N, 1.75.

Registry No.—**2**, 20708-12-7; **2** (3,5-dinitrobenzoate derivative), 20708-13-8; **4**, 20728-37-4; **4** (dicyclohexylammonium salt), 20708-11-6; **7**, 20707-71-5.

(10) Aldrich Chemical Co.

(11) E. Baer and J. Blackwell [*Biochemistry*, **3**, 975 (1964)] prepared this compound by acylation of the barium salt of L-α-glycerylphosphoryl-2′-hydroxyethylphthalimide followed by hydrazinolysis.

(12) J. C. Dittmer and R. L. Lester, *J. Lipid Res.*, **5**, 126 (1964).

(13) G. Rouser, G. Kritchevsky, D. Heller, and E. Lieber, *J. Amer. Oil Chemists Soc.*, **40**, 425 (1963).

(14) Elemental analyses and optical rotations were obtained by Miss Margaret Carroll and Mr. Walter Hamill with their staffs, respectively, of the Smith Kline and French Physical and Analytical Chemistry Section.

(15) Thermal gravitational analysis performed on a Du Pont 950 thermogravimetric analyzer.

(16) E. Baer and D. Buchnea, *J Biol. Chem.*, **230**, 447 (1958).

The Reaction of β-Keto Esters with 1,3-Diketones

L. L. WOODS

Texas Southern University, Houston, Texas 77004

Received January 14, 1969

The reaction of β-keto esters with 5,5-dimethyl-1,3-cyclohexanedione and 1,3-indanedione in trifluoroacetic acid (TFA) shows an interesting contrast of the action

TABLE I

4-PYRONES FROM β-KETO ESTERS FROM 1,3-DIKETONES

No.	β-Keto ester used	Mp, °C	Yield, %	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
				5,5 Dimethyl-1,3-cyclohexanedione(methone)						
1	Ethyl acetoacetate	207–208	84	$C_{12}H_{14}O_3$	69.88	6.84		69.69	7.06	
2	Ethyl *p*-nitrobenzoylacetate	203–204	96	$C_{17}H_{15}NO_5$	65.17	4.82	4.47	64.90	4.64	4.19
3	Ethyl benzoylacetate	123–125	52	$C_{17}H_{16}O_3$	76.10	6.01		75.94	6.08	
				1,3-Indanedione						
4	Ethyl acetoacetate	129	95	$C_{13}H_8O_3$	73.58	3.80		73.70	3.94	
5	Ethyl benzoylacetate	209–210	91	$C_{18}H_{10}O_3$	78.82	3.67		78.57	3.90	
6	Ethyl *p*-nitrobenzoylacetate	179–181	99	$C_{18}H_9NO_5$	67.71	2.84	4.38	67.43	2.59	4.17
7	Dimethyl acetone dicarboxylate	129–131	81	$C_{13}H_8O_3$	73.58	3.80		73.85	4.04	

1 = 7,8-Dihydro-2,7,7-trimethyl-4H-1-benzopyran-4,5(6H)-dione
2 = 7,8-Dihydro-7,7-dimethyl-2-(4-nitrophenyl)-4H-1-benzopyran-4,5(6H)-dione
3 = 7,8-Dihydro-7,7-dimethyl-2-phenyl-4H-1-benzopyran-4,5(6H)-dione
4 = 2-Methylindeno[1,2-*b*]pyran-4,5-dione
5 = 2-Phenylindeno[1,2-*b*]pyran-4,5-dione
6 = 2-(4-Nitrophenyl)indeno[1,2-*b*]pyran-4,5-dione
7 = 2-Methylindeno[1,2-*b*]pyran-4,5-dione

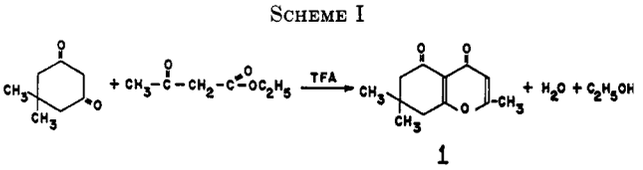
of the same reagents and catalyst with resorcinol and substituted resorcinols.

It has been shown that resorcinols, which under certain conditions have a 1,3-diketo structure, always react with β-keto esters *ortho* to one hydroxyl and *para* to the other, rather than at the position between the two hydroxyls, and that the product is always a coumarin.[1]

The two cyclic 1,3-diketones selected for this study react with β-diketones at the position between the two keto groups simply because it is either the only position having an active methylene group, as in 1,3-indanedione, or the only position having a single active methylene group available, as in 5,5-dimethyl-1,3-cyclohexanedione, because positions 4 and 6 are effectively covered and sterically hindered by the two methyl groups at position 5.

The chief product from 1,3-dimethyl-1,3-cyclohexanedione is a 4-pyrone, and the general course of the reaction may be considered to be the same as given in Scheme I for compound **1**. However, the difficulty in

SCHEME I

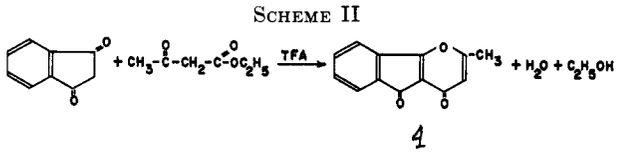


1

purification of compounds **1–3** appears to indicate that an appreciable amount of the product is 2-pyrone, which is removed along with occluded trifluoroacetic acid by the sodium bicarbonate treatment described in the Experimental Section.

No such difficulty, was encountered in the reaction of 1,3-indanedione with β-keto esters and Scheme II,

SCHEME II



4

giving the visualized reaction for compound **4**, may be considered to be a faithful representation of the general reaction for compounds **4–7**.

Hydrolysis and decarboxylation of compound **7** takes place during the course of the reaction and is the same as **4** by melting point, mixture melting point, and analysis.

A nuclear magnetic resonance study of compound **1** by the author and by an experienced spectroscopist[2] failed to show decisive results as to whether the compound was a 2-pyrone or a 4-pyrone. This indecision was resolved by preparing bis-2,4-dinitrophenylhydrazones from compounds **1** and **4** labeled as **1A** and **4A**, respectively. No structures other than those proposed in Schemes I and II would form such substances.

Table I records the essential data on the **1–7** series. Compounds **4–7** are powerful fluorescers.

Experimental Section[3]

Preparation of Members of 1–7 Series.—A mixture consisting of 0.1 mol of the 1,3-diketone, 0.1 mol of β-keto ester, and 40 ml of trifluoroacetic acid was refluxed for 24 hr in the case of the **1–3** compounds; however, in the case of the **4–7** compounds, the refluxing period was dropped to 2 hr because the product began to precipitate out of solution.

Upon the termination of the reflux period, each of the mixtures was poured into 400 ml of water. All of the compounds quickly crystallized except compounds **1** and **3**. In these two cases, the oils were separated from the water-diluted solutions and let into about 500 ml of a saturated solution of sodium bicarbonate in a 1000-ml beaker. Neutralization of the occluded acid in this manner permits the product to crystallize. All compounds were then filtered and the precipitates were dried in air.

Compounds **1–3** were purified three times by taking them up in boiling heptane followed by chilling. Compounds **4–7** were purified by extracting small powdered samples with boiling ethyl acetate and filtering. The precipitate was discarded and the compound was recovered by precipitating with heptane and chilling. The precipitate was again purified by repeating the process. Extreme care was taken on the second precipitation to use no more ethyl acetate than required to redissolve the compounds, and 10–20 times that volume of heptane was used.

(1) L. L. Woods and John Sapp, *J. Org. Chem.*, **27**, 3703 (1962).

(2) Sadtler Research Laboratories, Philadelphia, Pa. 19104.

(3) All analyses were performed by Dr. Carl Tiedcke, 705 George St., Teaneck, N. J. Melting points were taken on a Fisher–Johns melting point block.

An integrated nmr of compound I gave chemical shifts δ 1.10, 1.66, 2.20–2.80, 3.35, and 5.50, interpreted as 6, 2, 4, 0.4, and 0.6 protons, respectively.

2,4-Dinitrophenylhydrazones of Compounds 1 and 4.—Two grams each of compound 1 and 2,4-dinitrophenylhydrazine and 2 ml of concentrated hydrochloric acid were gently heated at 70–80° for 10 min in 70 ml of absolute ethanol. Compound 4 was treated in a similar manner. The cooled solutions wre filtered and the filtrates were discarded. The air-dried precipitates were extracted with two successive 50-ml portions of boiling ethanol. The precipitates were again dried in air. The melting points of the hydrazones 1A and 4A were 205–207° and 248–249°, respectively.

Anal. Calcd for $C_{24}H_{22}N_8O_9$ (1A): N, 19.10. Found: N, 19.23. Calcd for $C_{25}H_{16}N_8O_9$ (4A): N, 16.66. Found: N, 16.49.

Registry No.—1, 20452-84-0; 1A, 20452-85-1; 2, 20452-86-2; 3, 20452-87-3; 4, 20452-88-4; 4A, 20452-89-5; 5, 20452-90-8; 6, 20452-91-9.

Acknowledgment.—The author acknowledges with thanks the financial support for this project by the Robert A. Welch Foundation and thanks Dr. Kurt Leoning of the Chemical Abstracts Service for his assistance in the naming of the compounds.

Bond Fission in the Hydrolysis of 2,4-Dinitrophenyl Phosphate[1]

C. A. BUNTON AND J. M. HELLYER

Department of Chemistry, University of California at Santa Barbara, Santa Barbara, California 93106

Received January 27, 1970

The hydrolyses of 2,4- and 2,6-dinitrophenyl phosphate differ from those of most simple monophosphates in that the dianion, rather than the monoanion, is the most reactive species.[2,3]

It is assumed that the dianion generates phenoxide and metaphosphate ions, and the inorganic phosphate

$$ArO\,PO_3^{2-} \xrightarrow[}{\text{slow}} ArO^- + PO_3^- \xrightarrow[\text{fast}]{H_2{}^{18}O} H_2PO^{18}O_3^-$$

should therefore have 25% of the abundance of the water. Experiments in mixed aqueous organic solvents show that the phosphorus–oxygen bond is broken, as required by this mechanism. The aim of the present work was to confirm the phosphorus–oxygen bond fission for hydrolysis of the dianion in water, and in addition to determine the position of bond fission for hydrolysis at high pH, where part of the reaction involves attack of hydroxide ion upon the dianion.[3] (The over-all reaction rate is increased approximately sixfold by 1 *M* potassium hydroxide; however sodium and potassium chloride have marked salt effects on the spontaneous hydrolysis of the dianion, and, assuming that the potassium chloride and hydroxide exert similar salt effects, approximately half the reaction in 1 *M* hydroxide ion will involve attack of this reagent and the rest will be a salt-assisted spontaneous hydrolysis of the dianion.)

Inorganic phosphate was isolated after complete hydrolysis in ^{18}O-enriched water and its excess isotopic abundance, N, was determined. The results (Table I) show that hydrolysis of the dianion, at pH 6.0, introduces one oxygen of the water into inorganic phosphate, as expected.

TABLE I
BOND FISSION IN THE HYDROLYSIS OF 2,4-DINITROPHENYL PHOSPHATE[a]

Reagent	N_{H_2O}[b]	N_P[b]	% N_P/N_{H_2O}
pH 6.0[c]	0.80	0.21	26
pH 6.0[c]	0.78	0.18	23
1 *M* KOH	1.37	0.31	23
1 *M* KOH	1.37	0.33	24
1 *M* KOH	0.73	0.19	26

[a] At 25.0° unless specified. [b] Atom per cent excess above normal. [c] At 45.0° with acetate buffer; the pH was readjusted during the reaction.

The dianion with alkoxide ion in methanol or ethanol gives both phenol and phenolic ether, showing that phosphorus- and aryl–oxy fission are occurring.[3] In water we find predominantly phosphorus–oxygen fission (Table I). The spontaneous hydrolysis of the dianion makes some contribution to the over-all reaction, even with 1 *M* hydroxide ion, but not enough to account for all the phosphorus–oxygen fission, and therefore the hydroxide ion is attacking the phosphorus atom, although attack upon the aryl group is important with alkoxide ion in alcohol.[3] For nucleophilic attack upon 2,4-dinitrophenyl tosylate it was found that the more polarizable reagents tended to attack the aryl group preferentially,[4] but amines have been shown to attack the phosphorus atom of 2,4-dinitrophenyl phosphate.[5] These changes in the site of attack with changes in reagent accord with Pearson's classification of "hard" and "soft" reagents.[6]

However there was some nucleophilic attack upon the aryl group in the reaction between the bis-2,4-dinitrophenyl phosphate monoanion and hydroxide ion.[7] In this system two aryl groups are available for attack, and the spontaneous hydrolysis makes little contribution to the over-all reaction in alkali. These results provide other examples of phosphorylation by anions of phosphate esters.[3,5,7] Phosphorylations of one anion by another have been considered as models for degradations of several biologically important phosphates.[8]

Experimental Section

Materials.—2,4-Dinitrophenyl phosphate was prepared and isolated as its cyclohexylamine salt, mp 145° (lit.[3] mp 147°). The water was distilled from $KMnO_4$ (twice) and its isotopic abundance was determined by equilibration with CO_2 which was analyzed mass spectrometrically.

Reaction Conditions.—The following conditions are typical. The aryl phosphate (1 g), as its cyclohexylamine salt, was dis-

(1) (a) Abstracted from the thesis of J. M. Hellyer, submitted in partial fulfillment of the requirements of the Doctor of Philosophy degree of the University of California at Santa Barbara. (b) Support of this work by the National Institute of Arthritis and Metabolic Diseases of the U. S. Public Health Service is gratefully acknowledged.

(2) A. J. Kirby and A. G. Varvoglis, *J. Amer. Chem. Soc.*, **89**, 415 (1967).

(3) C. A. Bunton, E. J. Fendler, and J. H. Fendler, *ibid.*, **89**, 1221 (1967).

(4) J. F. Bunnett and J. Y. Bassett, *ibid.*, **81**, 2014 (1959).

(5) A. J. Kirby and A. G. Varvoglis, *J. Chem. Soc., Phys. Org.*, 135 (1968).

(6) R. G. Pearson, *J. Amer. Chem. Soc.*, **85**, 3533 (1963).

(7) C. A. Bunton and S. J. Farber, *J. Org. Chem.*, **34**, 767 (1969).

(8) J. R. Cox and O. B. Ramsay, *Chem. Rev.*, **64**, 343 (1964); J. R. Cox and J. P. Cleveland, in the Symposium on Naturally Occurring Phosphate Esters, Newcastle, The Chemical Society, London, 1967; D. G. Oakenfull, D. I. Richardson, and D. A. Usher, *J. Amer. Chem. Soc.*, **89**, 5491 (1967).