Lactone Cleavage with Triphenylphosphine Dibromide[1a,b]

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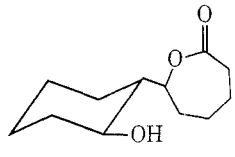
The cleavage of carbon–oxygen bonds with the adduct of triphenylphosphine and bromine (or chlorine) has been known for some time,[2-5] and the stereochemistry and the mechanism of the reaction have been investigated for the conversion of alcohols (e.g., the neopentyl[6] and norbornanol[7,8] systems) to halides.

The early studies of Horner and coworkers[2] established that ketones, aldehydes, and acids, as well as alcohols, could be converted into the corresponding halides by these reagents, and Bestmann and Mott[4] demonstrated that anhydrides followed a similar route; later Anderson and coworkers[9] reported the corresponding cleavage of ethers, and Burton and Koppes[10,11] showed that carboxylic esters and lactones were cleaved to acid halides.

When looking for a mild reagent to convert lactones of the type 1 to the corresponding halides, **2**, we investigated



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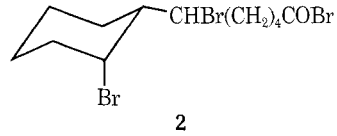
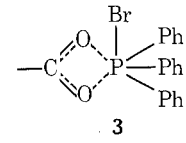


2

the Ph_3PBr_2 ring opening of the series of lactones listed in Table I. The expected products were obtained in every case, though yields were low, usually because of polymerization and tar formation.[12]



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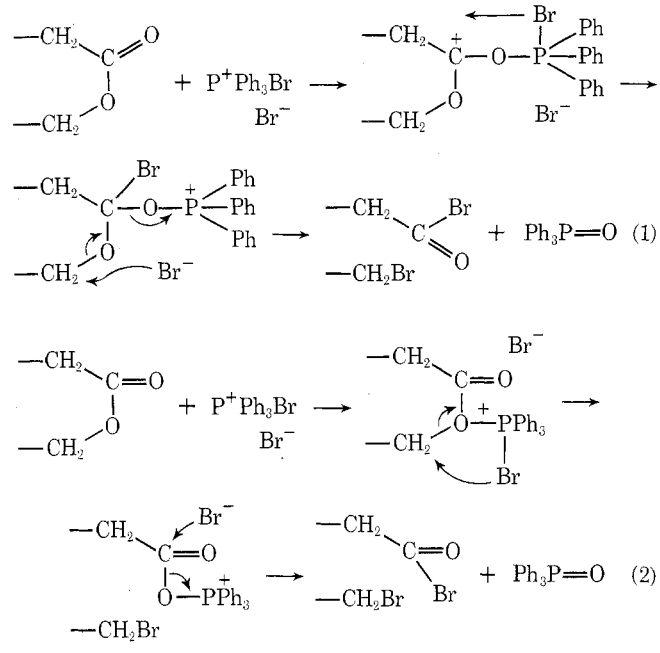
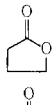
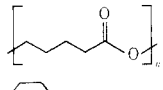


While the reaction of acids, acid anhydrides, esters, and lactones with triphenylphosphine dihalide might be expected to follow the same general mechanistic path as that of the C–O bond cleavage in alcohols, the presence of both a carbonyl and an ester oxygen affords the attacking agent a choice of possible sites (pathways 1 and 2), and, in the case of acids in particular, a transition state, or intermediate, of the form **3** might also be envisioned.

Table I

Lactone	Registry no.	Reaction conditions	Product	Yield, %	Registry no.
	96-48-0	100°, 12 hr	$Br(CH_2)_3COOCH_3$	27	4897-84-1
	504-31-4	110°, 12 hr	$Br(CH_2)_4COOCH_3$	30	5454-83-1
	26499-05-8	82°, 12 hr	$Br(CH_2)_4COOCH_3$	50	
	502-44-3	a. 82°, 12 hr b. 110°, 12 hr	$Br(CH_2)_5COOCH_3$ $Br(CH_2)_5COOCH_3$	34 34	14273-90-6
	539-87-7	110°, 12 hr	$Br(CH_2)_6COOCH_3$	27	54049-24-0

The general procedure was to add the lactone, which was itself prepared from the corresponding ketone by Baeyer–Villiger oxidation with trifluoroperacetic acid, to a preformed suspension of Ph_3PBr_2 in dry acetonitrile. The mixture was then heated for 8–12 hr under nitrogen. Subsequent addition of dry methanol to the mixture converted the acid halide to the methyl ester. The product was purified by chromatography on alumina, followed by distillation, and the identity was established by ir and NMR spectral analysis and elemental analysis.

† Deceased, July 14, 1974.

Experimental Section

General Procedure[13] for the Preparation of the Lactones. ε-Caprolactone. Trifluoroacetic anhydride (27.2 g, 0.13 mol) was added dropwise to an ice-cold suspension of 4.5 ml (0.12 mol) of 90% H_2O_2 in 25 ml of dry, freshly distilled methylene chloride and the mixture was stirred for 30 min. The resulting peroxytrifluoroacetic acid solution was then added dropwise to a vigorously stirred suspension of 30 g of anhydrous Na_2HPO_4 in 100 ml of dry methylene chloride, at 0°, containing 17.6 g (0.18 mol) of cyclohexanone. The mixture was stirred under N_2 for 3–4 hr, after which period water was added, and the aqueous phase was extracted four times with methylene chloride. The combined methylene chloride

extracts were washed twice with 70-ml portions of saturated Na_2CO_3 (aqueous) and dried ($MgSO_4$), and the solvent was removed, leaving a colorless oil, bp 58–59° (0.1 mm) [lit.[14] bp 108° (2.5 mm)] which gave one spot on a thin layer chromatogram, and whose ir and NMR spectra were as expected.

General Procedure for Triphenylphosphine Dibromide Cleavage of Lactones. To 52.4 g (0.2 mol) of triphenylphosphine in 200 ml of dry, freshly distilled acetonitrile under N_2 was added dropwise 32 g (0.2 mol) of bromine. The mixture was stirred at 0° throughout the addition, and the stirring was continued for 30 min thereafter. The lactone (22.8 g, 0.2 mol) in acetonitrile was then added dropwise, and the mixture was stirred under reflux for 10 hr, during which time it changed color to dark brown. After cooling, 20 ml of anhydrous methanol was added and the stirring was continued for a further 30 min. Removal of the solvent left a dark, viscous residue, which was dissolved in ether–benzene. This solution was washed several times with water and then dried ($MgSO_4$). The solvents were removed, and the dark residue thus produced was passed through a 14 × 2 in. dry alumina column, benzene being used as eluent. Examination of the column under uv light allowed identification of the fluorescent $Ph_3P{=}O$ band. The faster moving bromomethyl ester band appeared lower down, and methylene chloride extraction of the bottom section of the column gave a relatively pure sample of the expected ester, which was then distilled. A thin layer chromatogram showed one spot. Anal. Calcd for $Br(CH_2)_5COOCH_3$: C, 40.19; H, 6.22. Found: C, 39.91; H, 6.02. Ir 1730 cm^{-1} (ester C=O); NMR ($CDCl_3$) δ 1.8 [m, 6, $-(CH_2-)_3$], 2.3 (t, 2, $-CH_2COOCH_3$), 3.4 (t, 2, $-CH_2Br$), 3.7 (s, 3, ester CH_3). This is consistent with literature reports [Sadtler NMR spectrum no. 4566M and ir spectrum no. 32825 for $Br(CH_2)_4COOEt$].

Registry No.—Triphenylphosphine dibromide, 1034-39-5.

References and Notes

(1) (a) Taken in part from the Ph.D. Dissertation submitted by H.N.A. to the University of Kansas, Feb 1973. (b) This work was supported by a Training Grant (GM 1341) and a Research Grant (NS 9399), National Institutes of Health.
(2) L. Horner, H. Oediger, and H. Hoffmann, *Justus Liebigs Ann. Chem.*, **626**, 26 (1959).
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(10) D. J. Burton, University of Iowa, private communication, 1970.
(11) D. J. Burton and W. M. Koppes, *J. Chem. Soc., Chem. Commun.*, 425 (1973).
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(13) E. E. Smissman and J. R. J. Sorenson, *J. Pharm. Sci.*, **54**, 324 (1965).
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Reaction of Phenanthrenequinone with Ammonium Acetate

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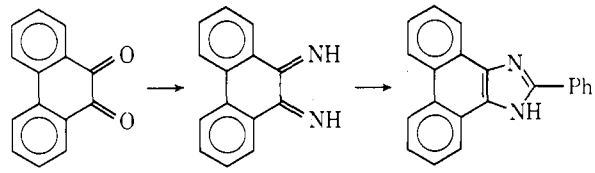
One of the synthetic methods available for the preparation of 2-aryl-1*H*-phenanthro[9,10-*d*]imidazoles is the condensation of phenanthrenequinones with an aromatic aldehyde in the presence of excess ammonium acetate in glacial acetic acid. This reaction has been suggested to proceed via diimine **1**, which condenses with the aldehyde forming a labile adduct that yields imidazole **2** after a facile proton shift and ring closure. From the condensation of phenanthrenequinone and ammonium acetate, Day et al.[2,3] isolated a base-soluble compound which was considered to be the intermediate **1**; it was indicated that this product was converted to **2** by reaction with benzaldehyde in base.



1 **2**

In a reexamination of this reaction, we found that condensation of the quinone, ammonium acetate, and benzaldehyde indeed leads to the imidazole **2**. We also obtained a crystalline product, apparently the same as that described by Day et al., from the reaction of the quinone with ammonium acetate. This substance, however, did not furnish **2** on treatment with benzaldehyde.

The quinone–ammonium acetate product was base soluble; acidification caused the compound to reprecipitate unchanged (under these conditions, hydrolysis of **1** would be expected). The uv, ir, NMR, and high-resolution mass spectra together with the chemical transformations shown in Scheme I leave little doubt that the compound is correctly formulated as 2′-(1*H*-phenanthro[9,10-*d*]imidazol-2-yl)-2-biphenylcarboxylic acid (**4**). Acid **4** could be dimethylated with methyl iodide in alkaline DMSO solution or in refluxing acetone and potassium carbonate to yield the *N*-methyl methyl ester **5**. Vacuum sublimation of **4** or reaction with acetyl chloride gave the dehydration product **6**. On refluxing in ethanolic hydrochloric acid, **6** was converted to the ester **7**. Structure **4** was further substantiated by independent synthesis. Condensation reactions aimed at the formation of aromatic phenanthroimidazoles (cf. **2**) showed much improved yields when the quinone, aromatic aldehyde, and ammonium acetate were allowed to react in DMSO instead of the glacial acetic acid employed pre-

Scheme I