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THE MERCURATION OF PHOSPHONATE ESTERS

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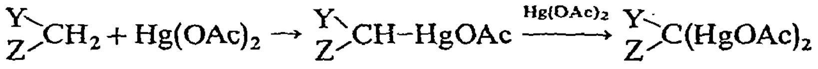
SUMMARY

The reactions of $[(EtO)_2(O)P]_2CH_2$, $(EtO)_2(O)PCH_2CO_2Et$, $(EtO)_2(O)PCH_2CN$ and $[(EtO)_2(O)P]_2CHCl$ with mercuric acetate in refluxing THF gave $[(EtO)_2(O)P]_2C(HgOAc)_2$, $(EtO)_2(O)PC(CO_2Et)(HgOAc)_2$, $(EtO)_2(O)PC(CN)(HgOAc)_2$ and $[(EtO)_2(O)P]_2CClHgOAc$, respectively. Redistribution reactions were used to prepare $[(EtO)_2(O)P]_2C(HgX)_2$ (X=Cl, Br or Ph). The C–Hg bonds of tetraethyl bis(acetoxymercuri)methylenediphosphonate were cleaved by chlorine to give $[(EtO)_2(O)P]_2CCl_2 \cdot HgCl_2$ and by hydrogen sulfide in ethanol to give $[(EtO)_2(O)P]_2CH_2$.

INTRODUCTION

In earlier work, we have prepared some mercury-containing organophosphorus esters[1,2]. In one preparation, the direct mercuration of $HC(N_2)P(O)(OMe)_2$ to give $[(MeO)_2P(O)C(N_2)]_2Hg$ was achieved[2]. This suggested that the mercuration of other suitably activated phosphonic acid esters should be possible.

The mercuration of active hydrogen compounds (eqn. 1) has been known for



$$\overset{Y}{\underset{Z}{>}}CH_2 + Hg(OAc)_2 \rightarrow \overset{Y}{\underset{Z}{>}}CH{-}HgOAc \xrightarrow{Hg(OAc)_2} \overset{Y}{\underset{Z}{>}}C(HgOAc)_2 \qquad (1)$$

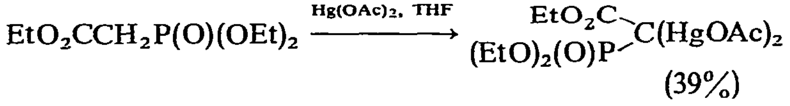
$Y, Z = CO_2R, CO_2R; CO_2R, CN; CO_2R, COR'; CO_2R, NO_2$

some time[3]. Recently, Russian workers[4] have extended such reactions to include β-disulfones ($Y=Z=ArSO_2$). We report here concerning the successful mercuration of phosphonate esters.

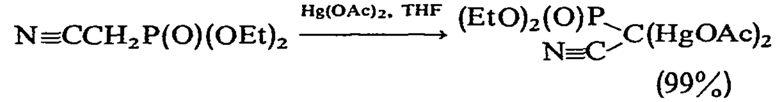
RESULTS AND DISCUSSION

The reaction of tetraethyl methylenediphosphonate, $(EtO)_2P(O)CH_2P(O)(OEt)_2$, with two equivalents of mercuric acetate in THF at reflux gave the expected $[(EtO)_2P(O)]_2C(HgOAc)_2$ in 95% yield. An attempt to prepare the monomercurated product by using the reactants in 1/1 molar ratio resulted in isolation of the dimercurated product and unconverted phosphonate ester. It would seem that the latter is less reactive toward mercuric acetate than is the mono-mercurated compound,

$[(EtO)_2P(O)]_2CHHgOAc$. The reaction of triethyl phosphonoacetate with mercuric acetate (1/2 molar ratio) also gave a dimercurated product (eqn. 2), and the same behavior was observed with diethyl cyanomethylphosphonate (eqn. 3). The action of mercuric acetate on diethyl chloromethylenediphosphonate gave $[(EtO)_2P(O)]_2CClHgOAc$ in 55% yield. However, attempted aliphatic mercuration of dimethyl benzylphosphonate was not successful.



$$\mathrm{EtO_2CCH_2P(O)(OEt)_2} \xrightarrow{\mathrm{Hg(OAc)_2,\ THF}} \mathrm{(EtO)_2(O)P(EtO_2C)C(HgOAc)_2} \quad (39\%) \tag{2}$$



$$\mathrm{N{\equiv}CCH_2P(O)(OEt)_2} \xrightarrow{\mathrm{Hg(OAc)_2,\ THF}} \mathrm{(EtO)_2(O)P(N{\equiv}C)C(HgOAc)_2} \quad (99\%) \tag{3}$$

Other suitably activated organophosphorus compounds such as $(RO)_2P(O)CH_2P(O)(OR)_2$, $(RO)_2P(O)CH_2C(O)R'$, $R_2P(O)CH_2CO_2R'$, etc., most probably are capable of being mercurated with mercuric acetate in THF under these conditions.

The tetraethyl methylenediphosphonate-derived product was converted to the bis-halomercuri compounds, $[(EtO)_2(O)P]_2C(HgX)_2$ ($X=Cl$, Br), by reaction with the appropriate mercuric halide in excess in THF solution. A reaction with diphenylmercury also resulted in redistribution (eqn. 4).

$$[(EtO)_2(O)P]_2C(HgCl)_2 + 2\ Ph_2Hg \rightarrow [(EtO)_2(O)P]_2C(HgPh)_2 + 2\ PhHgCl \tag{4}$$

Mercury–carbon bond cleavage reactions of such mercurated phosphonate esters also were investigated briefly. The chlorination of $[(EtO)_2(O)P]_2C(HgCl)_2$ in carbon tetrachloride resulted in C–Hg fission. The chlorinolysis product was isolated as its crystalline mercuric chloride adduct, $[(EtO)_2(O)P]_2CCl_2 \cdot HgCl_2$. The action of hydrogen sulfide on the bis-chloromercuri diphosphonate ester resulted in reduction (eqn. 5).

$$[(EtO)_2(O)P]_2C(HgCl)_2 + 2\ H_2S \xrightarrow{EtOH} [(EtO)_2(O)P]_2CH_2 + 2\ HgS + 2\ HOAc \tag{5}$$

EXPERIMENTAL

General comments

The mercuration reactions were carried out in three-necked flasks of the appropriate volume equipped with a reflux condenser topped with a nitrogen inlet tube and a magnetic or mechanical stirring assembly under an atmosphere of prepurified nitrogen. IR spectra were obtained using a Perkin Elmer 457A IR spectrophotometer, NMR spectra using a Varian Associates T60 spectrometer. Chemical shifts are reported in δ units, ppm downfield from internal tetramethylsilane. THF was dried by distillation from lithium aluminum hydride.

The new compounds prepared in this study, their melting points, their spectroscopic properties and their analyses are collected in Table 1.

Mercuration of phosphonate esters

These reactions were carried out on a 5–10 mmol scale. The phosphonate

TABLE 1

MERCURATED PHOSPHONATE ESTERS

Compound	*M.p. (°C)*	*Analysis found (calcd.) (%)*	
		C	H
$[(EtO)_2(O)P]_2C(HgOAc)_2$[a]	236–237 (dec.)	19.26 (19.39)	3.28 (3.25)
$[(EtO)_2(O)P]_2C(HgCl)_2$	252–253 (dec.)	14.40 (14.25)	2.69[c] (2.66)
$[(EtO)_2(O)P]_2C(HgBr)_2$	233–235 (dec.)	12.76 (12.76)	2.40 (2.38)
$[(EtO)_2(O)P]_2C(HgPh)_2$	136.5–137.5	29.50 (29.97)	3.77 (3.59)
$[(EtO)_2(O)P]_2C\begin{smallmatrix}\nearrow Cl\\ \searrow HgOAc\end{smallmatrix}$	146.5–147.0	22.50 (22.73)	3.95[d] (3.99)
$(EtO)_2(O)P\underset{CO_2Et}{\underset{\vert}{C}}(HgOAc)_2$[b]	173–174	19.37 (19.44)	2.90 (2.86)
$(EtO)_2(O)P\underset{CN}{\underset{\vert}{C}}(HgOAc)_2$	263–265 (dec.) (without melting)	17.22 (17.29)	2.41 (2.32)

[a] NMR (in $CDCl_3$): 1.33 (t, *J* 7 Hz, 12H, $OCH_2C\underline{H}_3$), 2.03 [s, 6H, $OC(O)C\underline{H}_3$], 4.20 (quintet, *J* 7 Hz, 8H, $OC\underline{H}_2CH_3$). [b] NMR (in D_2O): 1.2 [t, *J* 7 Hz, 3H, $C\underline{H}_3CH_2OC(O)$], 1.3 (t, *J* 7 Hz, 6H, $POCH_2C\underline{H}_3$), 2.05 [s, 6H, $C\underline{H}_3C(O)$], 4.2 (quintet, 6H, all CH_2). [c] Cl found 9.02, calcd. 9.35%. [d] Cl found 5.89, calcd. 6.10%.

ester and 2 molar equivalents of mercuric acetate in well-dried THF (50 ml for a 5 mmol reaction) were stirred and heated at reflux for 20–26 h. In the case of $(EtO)_2(O)PCH_2CN$, $(EtO)_2(O)PCH_2CO_2Et$ and $(EtO)_2(O)PCHClP(O)(OEt)_2$, a homogeneous reaction mixture resulted which was evaporated at reduced pressure. The solid residue was washed with several portions of ether and recrystallized, the products from the first two from absolute ethanol, the product from the chloromethylenediphosphonate ester from dichloromethane/hexane. The dimercuration product from tetraethyl methylenediphosphonate precipitated during the course of the reflux period and was filtered and recrystallized from absolute ethanol.

Tetraethyl bis(chloromercuri)methylenediphosphonate

A solution of 4.03 g (5.0 mmol) of tetraethyl bis(acetoxymercuri)methylenediphosphonate and 8.15 g (30 mmol) of mercuric chloride in 175 ml of THF (just sufficient to dissolve all solids at reflux) was heated at reflux under nitrogen for 26 h. The solution was evaporated at reduced pressure and the residue was extracted with three 100 ml portions of cold water. The remaining solid was dissolved in 300 ml of hot ethanol and this solution was filtered through Celite, concentrated to 250 ml and refrigerated. White needles, 2.57 g, m.p. 252–253° (dec.), were obtained. Concentration of the mother liquor to 50 ml gave another 0.15 g of needles, m.p. 249–250° (dec.), for a total yield of 72%.

When copper(II) chloride was used in place of mercuric chloride in a similar reaction carried out in ethanol solution for 43 h at reflux, $[(EtO)_2(O)P]_2C(HgCl)_2$ was obtained in 62% yield.

Tetraethyl bis(bromomercuri)methylenediphosphonate

A solution of 4.03 g (5.0 mmol) of tetraethyl bis(acetoxymercuri)methylenediphosphonate and 9.0 g (25 mmol) of mercuric bromide in 150 ml of dry THF was heated at reflux under nitrogen for 17 h. The solution was evaporated at reduced pressure and the residue was taken up in 100 ml of hot absolute ethanol, filtered and cooled. The white powder which precipitated (3.1 g, 73% yield) was recrystallized from 45 ml of ethanol.

Tetraethyl bis(phenylmercuri)methylenediphosphonate

A solution of 2.24 g (2.96 mmol) of tetraethyl bis(chloromercuri)methylenediphosphonate and 2.10 g (5.92 mmol) of diphenylmercury in 150 ml of absolute ethanol was stirred and heated at reflux under nitrogen for 65 h. The reaction mixture was cooled and filtered to remove 1.744 g (94%) of phenylmercuric chloride, m.p. 251–253°. The filtrate was evaporated at reduced pressure and the residue recrystallized from 50 ml of 9/1 hexane/dichloromethane. A second crop was obtained upon concentrating the mother liquor to half its volume, to give a total of 1.492 g (60%) of the product. Further crops were oily and were discarded.

Chlorinolysis of tetraethyl bis(chloromercuri)methylenediphosphonate

A suspension of 1.90 g (2.51 mmol) of $[(EtO)_2(O)P]_2C(HgCl)_2$ in 25 ml of carbon tetrachloride in flask sealed with a no-air stopper, at 0°, was treated with a solution of ca. 2.5 mmol of chlorine in about 2 ml of CCl_4. The mixture was stirred at 0° for 3 h and for 30 min at room temperature, after which time the yellow chlorine color had been discharged. The precipitate which resulted was filtered to give 1.535 g, melting range 175° to 210°, a mixture of mercuric chloride and starting material. Recrystallization from 60 ml of absolute ethanol gave 979 mg of pure starting material m.p. 245–247° (dec.). Evaporation of the filtrate left 518 mg of a white solid whose recrystallization from dichloromethane/hexane gave 226 mg of white needles, m.p. 104–104.5°. Analysis for C, H and Cl suggested the composition $[(EtO)_2(O)P]_2$-$CCl_2 \cdot HgCl_2$. (Found: C, 17.21; H, 3.29; Cl, 22.47. $C_9H_{20}Cl_4HgO_6P_2$ calcd.: C, 17.19; H, 3.21; Cl, 22.56%.) IR (Nujol mull): 1615 w, 1250 s, 1155 m, 1085 (sh), 1020 s, 950 (sh), 880 m, 780 (sh), 760 w and 725 w cm^{-1}.

Hydrogen sulfide reduction of tetraethyl bis(acetoxymercuri)methylenediphosphonate

A solution of 1.611 g (2.0 mmol) of the title compound in 30 ml of absolute ethanol was stirred in a 100 ml flask equipped with a condenser with a $CaSO_4$ drying tube and an immersed gas inlet tube at room temperature while a slow stream of hydrogen sulfide (Matheson) was bubbled in for 30 min. An immediate reaction occurred, as evidenced by the formation of a heavy, black precipitate of mercuric sulfide. The mixture was stirred for 30 min and then was filtered through Celite (Filter-cel grade). The filtrate was evaporated at reduced pressure to leave a yellow oil having the odor of acetic acid. Further heating of the oil at 0.03 mmHg for 2 h to remove acetic acid left 332 mg (58%) of $[(EtO)_2(O)P]_2CH_2$ contaminated with a small amount of acetic acid (by IR).

Preparation of phosphonate esters

$(EtO)_2(O)PCH_2CN$ and $(EtO)_2(O)PCH_2CO_2Et$ were purchased from the

Aldrich Chemical Co. Tetraethyl methylenediphosphonate was prepared by the method of Schwarzenbach and Zurc[5]. Tetraethyl chloromethylenediphosphonate was prepared[6] by hydrolysis of $[(EtO)_2(O)P]_2CClLi$.

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