Mercuration of 8-Hydroxyquinoline Phosphates

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Summary: 8-Hydroxyquinoline reacts with phosphorus oxychloride followed by treatment with sodium ethoxide to give ethylquinolinyl phosphate and diquinolinyl phosphate. Mercuration of these products with mercuric acetate, mercuric chloride and mercuric iodide give different monomercurated and dimercurated products. Their proposed structures are confirmed by analytical data IR, UV, and NMR spectra.

Introduction

Several organomercuric quinolin-8 olates were prepared by Bertino et.al. [1] and others [2-4]. These compounds have antifungal and disinfectant activity and are used as pesticides (e.g. in seed dressing for controlling crop diseases [2] and on problems arising from their applications.

Kline et.al. [5] studied the mercuration 8-hydroxyquinoline and some of its metal chelates. The oxine chelates gave 5,7-dimercurated derivatives. No evidence for serious steric hindrance to substitution in the position 7 was observed even in tris chelates. Substitution in the pyridine ring of the oxine ligand did not occur.

It has been reported by Awad et.al. [6] that the mercuration of dialkylbenzylphosphonate with mercuric acetate give benzylacetate and dialkylphosphonyl mercuric acetate. The mercuration of dialkylphenylphosphates in which the good leaving benzyl group is replaced by the more resistant phenoxy group gives alkylacetate [7].

El-Sawi et.al. [8] found that the presence of the NO_2 group in dialkyl p-nitrophenylphosphate facilitate the cleavage of Ar-O-P bond, while the presence of methyl, hydroxyl and naphthyl moiety hindred the cleavage.

In the present investigation, there is much interest in phosphorylation of quinolin-8-olate, and some of its derivatives followed by mercuration with different mercurating agents, such as mercuric acetate, mercuric chloride and mercuric iodide in order to combine the already known biological effect of organophosphorus, organomercuric compounds and to study the effect of quinolinyl moiety on the stability of Ar-O-P bond.

Results and Discussion

Ethyl quinolinylphosphate reacts with mercuric acetate in toluene at its boiling point to give mercuric bis (5,7-acetoxymercuric-quinolinyl) phosphate (I), acetic acid and ethyl acetate. The reaction takes place via electrophilic substitution in the quinolinyl moiety and coordination of mercuric acetate to the highly negative center i.e. the phosphoryl oxygen in the intermediate phosphonium ion with an intramolecular

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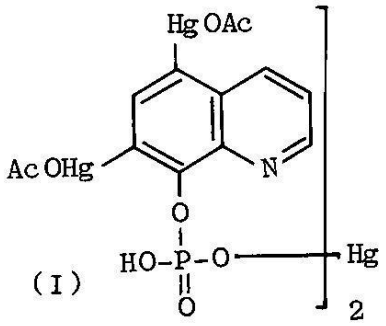
nucleophilic attack of the acetate group occurs on the alkoxy group. The formation of an intermediate phosphonium ion takes plalce via coordination of the formed mercurated product with phosphoryl oxygen of another molecule of mercurated ethylquinolinyl phosphate (formed in the medium).



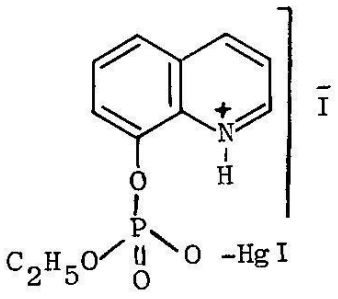
(I)

The IR spectra show the disappearance of the absorption bands of P-O-C aliphatic at 1052 cm^{-1}, 986 cm^{-1}, but it shows the absorption bands which can be attributed to $\nu_{P-O-C(Ar)}$ at 1225,1195 cm^{-1}, ν_{P-O-Hg} at 1360 cm^{-1} and the absorption bands for substituted aromatic.

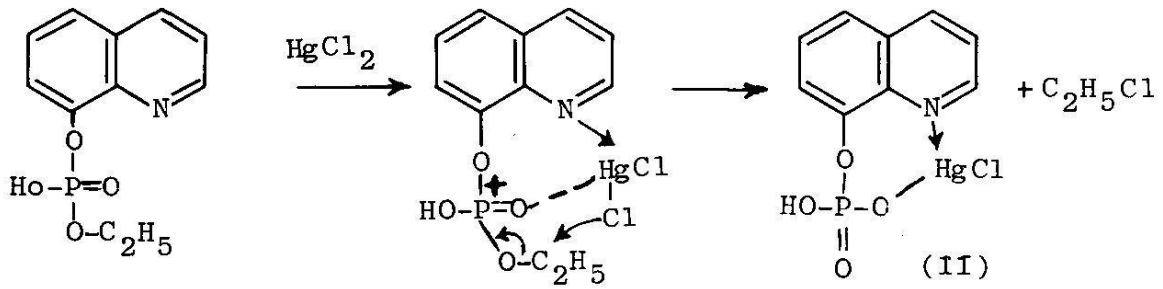
The reaction of ethylquinolinyl phosphate and mercuric chloride (1/1 mole) in toluene at its boiling point gave chloromercuric-quinolinyl phosphate (II). The mechanism of the reaction is proposed in scheme 1.

The IR spectra shows absorption bands at 1285 cm^{-1}, 1330 cm^{-1}, 1225-1200 cm^{-1} which can be attributed to $\nu_{P=O}$, ν_{P-OHg}, $\nu_{P-O-C(Ar)}$ and the absorption bands which assigned to aromatic protons also ν_{OH} at 2700-2500 cm^{-1}. The uv spectra shows a blue shift if compared with the starting material, from 375-365 nm. This can be attributed to the coordination between mercury and quinolinyl nitrogen. The NMR spectra shows signals at δ 9.3 ppm, δ 8.2 ppm, δ 7.7 ppm which can be attributed to aromatic protons, whereas the signals for aliphatic protons disappeared. Signals for OH proton was shifted towards lower field from δ 9.8 ppm. to δ 12.4 ppm. This is attributed to the formation of the electron attracting P-O-Hg group and its deshielding effect.

Mercuration of ethylquinolinyl phosphate with mercuric iodide in boiling toluene gave ethyl, mercuriiodide, quinolinyl phosphate hydroiodide (III).



(III)



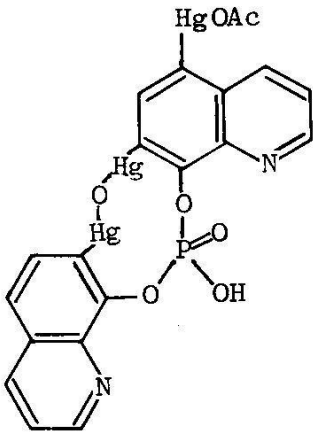
(II)

Scheme 1

The IR spectra shows the absence of the absorption bands for the OH group whereas the absorption bands for P-O-C_2H_5, P-O-C(Ar) and P-O-Hg are present at 1052 cm^{-1}; 1225, 1194 cm^{-1}; and 1360 cm^{-1}. UV spectrum shows the absence of transitions at 311, 322, 375 nm as compared with the starting material according to $n-\pi^*$ transition of the lone pair of electrons on the nitrogen atom due to the formation of $\overset{+}{N}$-H. The NMR spectra show the absence of the OH proton and the preence of $-CH_2CH_3$ protons which confirms the suggested structure.

Mercuration reactions of diquinolinyl phosphate with mercuric acetate, mercuric chloride and mercuric iodide gave rise to polymercurated, monomercurated, and mercuri bis (monomercurated) compounds (IX-VII) respectively.

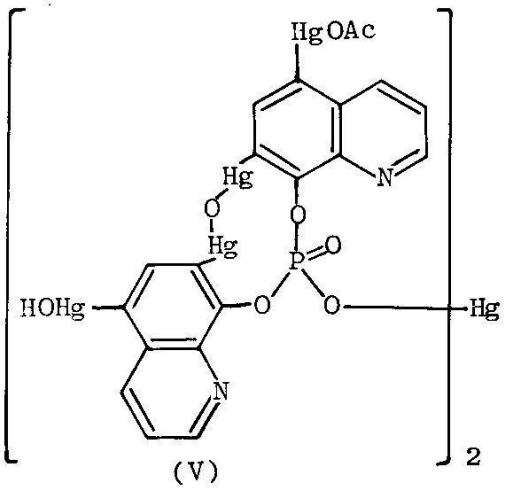
The reaction mechanism can be interpreted if the primary electrophilic substitution is considered to take place at the 5,7 and 7 positions followed by elimination of acid anhydride from 7 and 7 acetoxy mercury with the formation of Hg-O-Hg linkage for compound (IV).



(IV)

The IR spectrum shows absorption bands at 1300-1250 cm^{-1}, 1195 cm^{-1}, 3640-3200 cm^{-1} which can be attributed to $\nu_{P=O}$, $\nu_{P-O-C(Ar)}$, ν_{OH} also the absorption bands for substituted aromatic. The NMR spectrum shows signals attributed only to $-CH_3$ protons at 7, 7.6, 8.2, 8.8 ppm. and signal at 11.12 ppm. for -OH proton.

For compound (V) obtained from the same reaction mercury replaced 2H atoms from the OH group of two molecules with the formation of the bis-form.



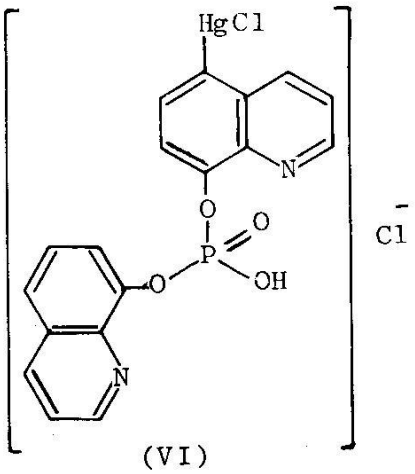
(V)

The IR spectrum shows an absorption band at 1360 cm^{-1} which can be attributed to P-O-Hg. All IR, NMR, mass spectrum and elemental analysis confirmed the proposed structure.

Mercuration reaction with mercuric chloride proceeds by electrophilic substitution in position 5 with the formation of quinolinyl nitrogen hydrochloride (VI). The UV spectrum shows no $n-\pi^*$ transition (due to protonation of quinolinyl nitrogen).

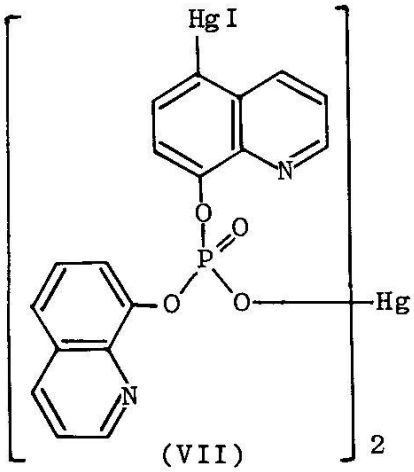
Table 1

Reagents	Products	m.p.°C & yield	Recrys from	Analysis				
				C%	H%	N%	Hg%	
1-Ethyl Qu.Ph.(3)		280		F. 18.0	0.93	2.1	59.8	
a-with $Hg(OAc)_2$	$C_{26}H_{22}N_2O_6P_2Hg_5$(I)	95%	AcOH	C 18.5	1.30	1.86	59.59	
b-"" $HgCl_2$	$C_9H_7NO_4OHgCl$(II)	180-1 93%		F. 24.0 C. 23.5	1.63 1.52	2.93 3.04	43.45 43.60	
c-"" HgI_2	$C_{11}H_{11}NO_4PHgI.HI$(III)	140-2 96%	EtOH	F. 17.8 C. 18.6	1.53 1.83	2.1 1.97	28.60 28.34	1% 35.8 35.8
2-Diqu.Phos (4)								
a-With $Hg(OAc)_2$	$C_{20}H_{13}N_2O_7OHg_3$(IV)	289-90 70%	AcOH	F. 22.7 C. 23.3	1.31 1.26	2.66 2.72	58.02 58.6	
	$C_{40}H_{24}N_4O_{16}P_2Hg_9$(V)		above Toluene	F. 17.6	0.75	2.21	67.65	
		300° 27.6%	pet.ether	C. 17.8	0.88	2.08	67.28	
b-with $HgCl_2$	$C_{18}H_{13}N_2O_4PHgCl_2.H_2O$(VI)	225-7 97.8%	EtOH	F. 33.8 C. 33.6	2.51 2.33	4.45 4.36	31.19 31.26	
c-With HgI_2	$C_{36}H_{22}N_4O_8P_2Hg_3I_2$(VII)	149-50 98.5%	Toluene	F. 22.3 C. 22.9	1.8 1.5	2.82 2.63	27.61 28.24	1% 35.3 35.7



(VI)

In the case of mercuration with HgI_2 compound (VII) is obtained due to electrophilic substitution in position 5 and formation of mercuri-bis (5-iodo-mercuri-diquinolinyl phosphate).



(VII)

Experimental

Preparation of ethylquinolinyl phosphate and diquinolinyl-phosphate:

0.1 mole phosphorus oxychloride was added to 0.1 mole 8-hydroxyquinoline dropwise with stirring at 130°C. The reaction mixture was treated with ethyl alcohol whereby the yellowish-white precipitate(1) was obtained by filteration in 27.5% yield, m.p. 284-5°C. Ether was added to the filtrate to obtain a white precipitate which was filtered, dried and recrystallised from ethyl alcohol and ether to give product (2) 36% yield, its m.p.249-250°C.

The products were treated with sodium ethoxide (1:2 molar ratio) in an ice bath whereby sodium chloride was deposited. The reaction mixture was treated with ether and filtered.The etherial layer washed several times with water and dried over anhydrous sodium sulphate, filtered and evaporated. Product (1) give yellow crystals (3). Recrystallised from ethyl alcohol in 93.2% yield m.p. 237-238°C.(Found:C, 51.98; H, 4.62; N, 5.70. $C_{11}H_{12}NO_4P$ calcd.: C,52.17; H, 4.74; N, 5.53%).

Reactions of ethylquinolinyl phosphate and diquinolinyl phosphate with mercuric salts.

General Procedure

1/1 molar ratio of the reactants in 50 ml toluene was stirred at room temperature. 10 ml Acetic acid was added to the reaction mixture, then boiled for 4 hours whereby the solution became clear followed by precipitation of crystalline product during heating, filtered, dried and recrystallised from the suitable solvent.

Addition of ether to the filterate in case of the reaction with mercuric acetate gave (V).

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