BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 1498—1501 (1973)

The Reactions of 2-Hydroxybenzophenones with Lead Tetraacetate and Manganic Acetate

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(Received August 11, 1972)

2-Hydroxy-4-methoxy- and 2-hydroxy-4,4′-dimethoxybenzophenones were oxidized to dimeric compounds with lead tetraacetate and with manganic acetate. 2-Hydroxy-2′,4,4′-trimethoxy- and 2-hydroxy-3′,4,4′-trimethoxybenzophenones were oxidized to substituted xanthones. The structures of the products were determined by NMR and mass spectra, and were confirmed by syntheses.

In the reaction of phenolic compounds with lead tetraacetate, it was demonstrated that oxidative cyclization took place in 2′-hydroxychalcones[1,2] and in the Schiff base from *o*-aminophenols,[3] giving rise to aurones and benzoxazols respectively. We investigated the reactions of 2-hydroxybenzophenones with lead tetraacetate and with manganic acetate in the hope that they could be oxidized to xanthones; it was found that trisubstituted 2-hydroxybenzophenones did give xanthones and that mono- and di-substituted 2-hydroxybenzophenones give dimeric products.

When 2-hydroxy-4-methoxybenzophenone (Ia) and 2-hydroxy-4,4′-dimethoxybenzophenone (Ib) were treated with lead tetraacetate and with manganic acetate respectively, several products (II, III, IV, and VI) were isolated after separation by column chromatography and preparative tlc. They are listed in Table 1.

Product (IIb) has a higher melting point (232—234 °C), and its mass spectrum showed the molecular ion at *m*/*e* 514, corresponding to a molecular formula of $C_{30}H_{28}O_8$. This indicates that IIb is a dimeric compound. The IR and UV spectra of IIb were very similar to those of Ia and Ib (Table 2). The NMR spectra (60 MHz) of IIa, IIb, their acetates (Ac-IIa and Ac-IIb), and a methyl ether (Me-IIb) showed two singlets in the aromatic region, indicating the presence of *para*-related protons. This reveals that the newly-formed bond is located at the C_5-position in IIb. The chemical shifts of the protons and other protons on phenyl and *p*-methoxyphenyl groups were well correlated in these compounds (Table 3). These spectral data showed that IIb is 5,5′-bis(*p*-methoxybenzoyl)-4,4′-dihydroxy-2,2′-dimethoxybiphenyl. The structure of IIa was also determined to be 5,5′-dibenzoyl-4,4′-dihydroxy-2,2′-dimethoxybiphenyl.

The IIIb product, $C_{15}H_{14}O_5$ (mp 164—165 °C), was obtained only when lead tetraacetate was used in the

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TABLE 1. REACTION OF 2-HYDROXYBENZOPHENONES WITH $Pb(OAc)_4$ AND $Mn(OAc)_3$ IN AcOH

Compound	Reagent	Reaction conditions			Recovery of I (%)	Product (%)				
		Molar ratio	Time(hr)	Temp. (°C)						
Ia[4]	$Mn(OAc)_3$	1 : 4	5	100	Ia(40)	IIa(7)		IVa(10)		VIa(16)
Ia	$Pb(OAc)_4$	1 : 2	5	100	Ia(15)	IIa(15)	IIIa(3.3)			VIa(36)
Ib[5]	$Mn(OAc)_3$	1 : 4	5	100	Ib(18)	IIb(11)		IVb(3.7)		VIb(18)
Ib	$Pb(OAc)_4$	1 : 2	5	100	Ib(6)	IIb(21)	IIIb(1)			VIb(32)
Ic	$Mn(OAc)_3$	1 : 4	$4\frac{2}{3}$	100	Ic(4)				Vc(24)[6]	VIc(10)[7]
Ic	$Pb(OAc)_4$	1 : 2	3	100	Ic(12)				Vc(2)	VIc(14)
Id	$Mn(OAc)_3$	1 : 4	5	100					Vd(42)	VId(9)[8]
Id	$Pb(OAc)_4$	1 : 2	5	100					Vd(30)	VId(10)

TABLE 2. IR AND UV SPECTRAL DATA FOR BENZOPHENONES, BIPHENYLS AND XANTHONES

Compound	Mp (°C)	νOH	νCO	$\nu OCOCH_3$	λ_{max} (nm) (ε)			
			(cm^{-1})					
Ia	64	3000	1620			244(10700)	290(15000)	329(9600)
Ib	117—118	3000	1620				294(16700)	332(13600)
Ic	104—105	3000	1620		233(15000)		285(16000)	333(12700)
Id	135—136	3000	1623		237(17200)		290(15100)	336(16000)
Ie	136—137[b]	3100	1615		240(s)(8760)	253(s)(6750)	288(11400)	344(11400)
If	147—148	3100	1620		233(s)(15600)	249(s)(13100)	288(13100)	365(11500)
IIIa	182—183	3565	1640			255(15200)	292(9900)	370(7700)
IIIb	164—165	3565	1639			256(10600)	296(13100)	370(8350)
IIa	199—200	3000	1620			254(31300)	289(24600)	345(12500)
IIb	232—234	3000	1620		226(30200)	260(35000)	296(36800)	350(20000)
Ac-IIa	219—220		1655	1762		254(40000)	284(s)(23100)	
Ac-IIb	190—191		1648	1760		256(s)(27200)	292(41700)	
Me-IIb	190—191		1649			259(31800)	288(41200)	
IVa	217—218		1670 1630 1618			251(37100)	285(18500)	331(10300)
IVb	207—208		1680 1665 1640 1620			244(30600)	292(34800)	331(18100)
Vc	182—183		1648		243(44100)	269(10800)	313(23900)	320(26200)
Vd	216—217		1643		246(35300)	267(11400)	313(20600)	342(s)(10300)

reaction; it was isolated from the mother liquor of IIb. The IR spectrum of IIIb was quite similar to those of IIa and IIb except that an absorption due to a hydroxyl group appeared at 3565 cm^{-1}. Its NMR spectrum showed two singlets in the aromatic region, again indicating the presence of *para*-related protons: the rest of the spectrum was very close to that of IIb. Thus, the structure of IIIb was determined to be 2-(*p*-methoxy) benzoyl-5-methoxyhydroquinone; this was finally confirmed by synthesis. The reaction of 2-methoxyhydroquinone[9] and anisic acid, with boron-trifluoride as a catalyst, gave IIIb. IIIa was also prepared in a similar way.

The IVb product, $C_{30}H_{24}O_9$ (analysis and mass spectrum) (mp 207—208 °C), showed complicated carbonyl absorptions (1620—1680 cm^{-1}) in the IR spectrum, indicating the presence of quinone carbonyls. The NMR spectrum of IVb (60 MHz) exhibited four methoxy groups (at δ 3.76, 3.85, 3.88, and 3.91), three protons (at δ 6.02 (s), 6.40 (s), and 7.38 (s)), two *para*-substituted phenyl groups (at δ 6.83 (d, 2H), 7.78 (d, 2H), 7.00 (d, 2H), and 7.52 (d, 2H)), and a proton at a lower field corresponding to a hydroxyl proton. These spectral data showed that a bond formation took place at the phenyl group having the hydroxyl group. This leads to two possible structures; *p*-quinone (IVb) and *o*-quinone (IVb′). Considering that the singlet appeared at δ 6.02, the *p*-quinone structure (IVb) is favored; IVb′ must be oxidized further to a symmetrical biquinone which was not found in the reaction mixture. The IVb was determined to be 3-(4′-hydroxy-2′-methoxy-5′-*p*-methoxybenzoyl) phenyl-2-methoxy-5-(*p*-methoxy)benzoylbenzoquinone. Similarly, the structure of IVa was also determined to be 5-benzoyl-3-

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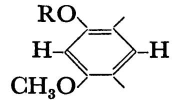
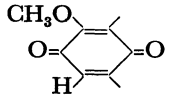
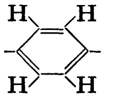
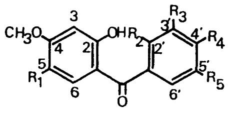
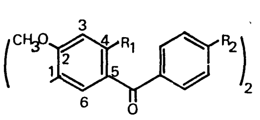
Table 3. NMR spectral data for benzophenones and biphenyls(δ value at 60 MHz)

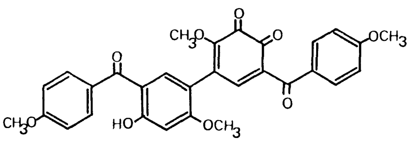
Compound						Ph	CH_3O	$OCOCH_3$	OH
IIa	6.52(2)	7.39(2)				7.2—7.3(10)	3.82 (6)		
IIb	6.52(2)	7.46(2)		7.64(4)	6.90(4)		3.85(12)		
Me-IIb	6.55(2)	7.28(2)		7.79(4)	6.86(4)		3.78 (6) 3.83(12)		
Ac-IIa	6.64(2)	7.48(2)				7.3—7.9(10)	3.84 (6)	2.04(6)	
Ac-IIb	6.73(2)	7.42(2)		7.75(4)	6.88(4)		3.83 (6) 3.86 (6)	2.08(6)	
IIIa	6.58(1)	7.13(1)				7.4—7.8 (5)	3.96 (3)		5.25(1)
IIIb	6.53(1)	7.14(1)		7.66(2)	6.96(2)		3.88 (3) 3.96 (3)		5.26(1)
IVa	6.41(1)	7.33(1)	6.02(1)			7.1—8.1(10)	3.69 (3) 3.83 (3)		
IVb	6.40(1)	7.38(1)	6.02(1)	7.52(2) 7.78(2)	7.00(2) 6.83(2)		3.76 (3) 3.85 (3) 3.88 (3) 3.91 (3)		



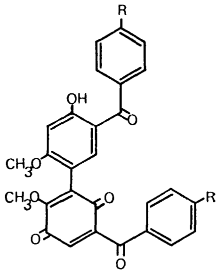
Ia $R_1=R_2=R_3=R_4=R_5=H$
Ib $R_1=R_2=R_3=R_5=H$, $R_4=OCH_3$
Ic $R_1=R_3=R_5=H$, $R_2=R_4=OCH_3$
Id $R_1=R_2=R_3=H$, $R_4=R_5=OCH_3$
Ie $R_1=R_3=R_5=H$, $R_2=OH$, $R_4=OCH_3$
If $R_1=R_3=H$, $R_2=OH$, $R_4=R_5=OCH_3$
IIIa $R_1=OH$, $R_2=R_3=R_4=R_5=H$
IIIb $R_1=OH$, $R_2=R_3=R_5=H$, $R_4=OCH_3$



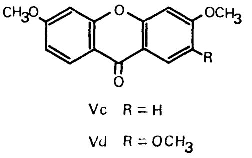
IIa $R_2=H$, $R_1=OH$
IIb $R_1=OH$, $R_2=OCH_3$
Ac-IIa $R_2=H$, $R_1=OAc$
Ac-IIb $R_1=OAc$, $R_2=OCH_3$
Me-IIb $R_1=R_2=OCH_3$



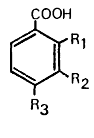
IVb'



IVa R = H
IVb R = OCH_3



Vc R = H
Vd R = OCH_3



VIa $R_1=R_2=R_3=H$
VIb $R_1=R_2=H$, $R_3=OCH_3$
VIc $R_2=H$, $R_1=R_3=OCH_3$
VId $R_1=H$, $R_2=R_3=OCH_3$

(5′-benzoyl-4′-hydroxy-2′-methoxy) phenyl-2-methoxybenzoquinone. Benzoic acid (VIa) and anisic acid (VIb) were obtained from the reaction mixtures of Ia and Ib respectively, and were identified with authentic samples by studying their IR spectra.

When 2-hydroxy-2′,4,4′-trimethoxybenzophenone (Ic) and 2-hydroxy-3′,4,4′-trimethoxybenzophenone (Id) were oxidized with lead tetraacetate or with manganic acetate, Vc and Vd respectively were obtained as the products. The mass spectrum of Vc showed the molecular ion at *m/e* 256, corresponding to a molecular formula of $C_{15}H_{12}O_4$; this indicated that an intramolecular coupling between the hydroxyl group and the C_2'-position in Ic took place and that the methanol was removed from Ic. Vc was found to be 3,6-dimethoxyxanthone; it was identical with that prepared from Ie.[6] The structure of Vd was similarly determined to be 2,3,6-trimethoxyxanthone. This was also identified by independent synthesis from If.

2,4-Dimethoxybenzoic acid (VIc) and 3,4-dimethoxybenzoic acid (VId) were isolated from reaction mixtures of Ic and Id respectively. They were identified with authentic samples by a comparison by their IR spectra and also by the vpc of their methyl esters. Thus, the reaction takes place as expected in the cases of Ic and Id, but the reaction with Ia and Ib are not so simple.

The formation of the dimeric products (IIa, IIb, IVa, and IVb) may suggest a free radical mechanism,[10–12] but an ionic mechanism cannot be ruled out, for a phenoxylium cation has been known to convert to a dimeric product with phenol:[13]

$$\mathrm{ArOH} + \mathrm{ArO}^+ \longrightarrow \text{dimeric product} + \mathrm{H}^+$$

Both paths are equally probable, and no conclusive evidence to differentiate these two paths in the present situation is available at this time.

Although only four of the benzophenones were examined so far, this reaction was shown to be an useful method in synthesizing xanthones from 2-hydroxybenzophenones.

Experimental

NMR spectra were recorded for deuteriochloroform solutions with a Hitachi NMR spectrometer model R-20B with

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TABLE 4. ANALYSES OF NEW COMPOUNDS

Compound	Molecular formula	Found		Calcd	
		C%	H%	C%	H%
Ic	$C_{16}H_{16}O_5$	66.72	5.65	66.66	5.59
Id	$C_{16}H_{16}O_5$	66.54	5.65	66.66	5.59
If	$C_{16}H_{16}O_6$	63.33	5.43	63.15	5.30
IIa	$C_{28}H_{22}O_6$	74.02	5.01	74.00	4.88
IIb	$C_{30}H_{26}O_8$	69.81	5.07	70.03	5.09
Ac-IIa	$C_{32}H_{28}O_8$	71.42	4.96	71.10	5.22
Ac-IIb	$C_{34}H_{30}O_{10}$	68.35	5.06	68.22	5.05
Me-IIb	$C_{32}H_{30}O_8$	70.68	5.57	70.83	5.57
IIIa	$C_{14}H_{12}O_4$	68.75	5.15	68.84	4.95
IIIb	$C_{15}H_{14}O_5 \cdot \frac{1}{6}C_6H_6$	67.01	5.29	66.89	5.26
IVa	$C_{28}H_{20}O_7$	72.51	4.38	71.79	4.30
IVb	$C_{30}H_{24}O_9$	68.42	4.57	68.18	4.58
Vd	$C_{16}H_{14}O_5$	67.05	5.08	67.12	4.93

tetramethylsilane as an internal standard; IR spectra were recorded for chloroform solutions with a JASCO DS 403G grating spectrometer; UV spectra were obtained for methanol solutions with a Hitachi EPS-3T spectrophotometer; mass spectra were recorded with a Hitachi mass spectrometer, RMU-6L; vpc were recorded with a Shimadzu GC-1C using polyethyleneglycol-succinate at 200 °C. Preparative and analytical tlc were carried out with Wakogel B10. Melting points were determined with a Yanagimoto micro-melting-point apparatus and uncorrected.

Materials. Lead tetraacetate and manganic acetate were prepared according to the references.[14,15]

2-Hydroxybenzophenones. 2-Hydroxybenzophenones (Ib, Ic, and Id) were prepared from 3-methoxyphenol and corresponding benzoic acids with boron trifluoride as catalyst and purified by recrystallization from ethanol. Ia was obtained from partial methylation of 2,4-dihydroxybenzophenone[4] which was prepared by the reaction of resorcinol and benzoic acid. If was prepared by the reaction of 3,4-dimethoxyphenol[16] (500 mg) and 2-hydroxy-4-methoxybenzoic acid[17] (450 mg) with phosphorus oxychloride (3.5 ml) and fused zinc chloride (1.5 g) heating at 65—70 °C for 1 hr and separated on silica gel (20 g) eluting with benzene, followed by recrystallization from ethanol. IIIa and IIIb were prepared by the reaction of 2-methoxyhydroquinone[9] (10 mmol), and benzoic acid (10 mmol) and anisic acid (10 mmol), respectively, with boron trifluoride etherate (20 ml), heating at 100 °C for 30—45 min. This gave IIa (5%) and IIIb (26%), respectively.

Reaction of Lead Tetraacetate with 2-Hydroxybenzophenones (Ia—d). 2-Hydroxybenzophenone (10 mmol) and lead tetraacetate (20 mmol) were dissolved in acetic acid (100 ml) and heated at 100 °C for 5 hr. After removal of the acetic acid, the resulting viscous liquid was treated with 2N sulfuric acid and then extracted with chloroform (100 ml). The chloroform layer was washed with aqueous sodium bicarbonate and saturated sodium chloride solution. The chloroform solution was evaporated and the residue was separated on silica gel (100 g). The column was eluted with benzene and then chloroform. From benzene fraction, II, III, and V were obtained after recrystallization from benzene or ethanol. The chloroform fraction was concentrated and again separated on tlc effected with chloroform, but this failed to give any crystalline compound. After acidification of the sodium bicarbonate solution, VI was obtained.

Reaction of Manganic Acetate with 2-Hydroxybenzophenones (Ia—d). 2-Hydroxybenzophenone (10 mmol) and manganic acetate (40 mmol) was dissolved into acetic acid (100 ml) containing acetic anhydride (1.0 ml). The mixture was heated at 100 °C until the colour of the manganic acetate disappeared. It usually took 5 hr. After removal of the acetic acid and acetic anhydride, the remaining viscous liquid was treated with 2N sulfuric acid (100 ml) and then extracted with chloroform. Working up in the same way as in the above, products II, IV, V, and VI were obtained.

Acetylation of II. IIa (100 mg) and IIb (100 mg), respectively, were treated with acetic anhydride (0.5 ml) in pyridine (1 ml) at room temperature overnight. The reaction mixture was poured into iced water and the precipitates were collected. After recrystallization from ethanol Ac-IIa (89 mg, 75%) and Ac-IIb (106 mg, 91%) were obtained.

Methylation of IIb. IIb (50 mg) was treated with dimethylsulfate (128 mg) in acetone (10 ml) containing anhydrous potassium carbonate (283 mg) under reflux for 4 hr. After removal of the acetone, the residue was triturated with water and the precipitates were collected. The crude product was recrystallized from ethanol to give a methyl ether (Me-IIb) (42 mg, 80%).

2,3,6-Trimethoxyxanthone (Vd). 2,2′-Dihydroxy-4,4′,5-trimethoxybenzophenone (If) (100 mg) was heated in water in a sieled tube at 230—240 °C for an hr. The crude product was collected and recrystallized from a mixture of chloroform and ethanol. This gave Vd (64 mg, 68%).

Authors wish to thank Dr. Shinzaburo Hishida and the staff of Hitachi Co., Ltd. at Katsuta for measuring NMR and mass spectra.

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