The Reactions of 2-Phenyl-2*H*-1-benzopyrans and 2-Phenyl-4*H*-1-benzopyrans with Lead(IV) Acetate

Kazu KUROSAWA,* Katsutoshi YAMAGUCHI, Yasuyuki NAGATA, and Hisatake OHKI

Department of Chemistry, Faculty of Science, Kumamoto University, Kurokami 2-39-1, Kumamoto 860

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Synopsis. The reactions of 7-methoxy-2-phenyl-2*H*-1-benzopyran and 7-methoxy-2-phenyl-4*H*-1-benzopyran with lead(IV) acetate gave 2-benzoyl-6-methoxybenzofuran and 6-acetoxy-3-methoxy-6-(3-oxo-3-phenyl-1-propenyl)-2,4-cyclohexadien-1-one. The reactions of 7-methoxy-2-(*p*-methoxyphenyl)-2*H*-1-benzopyran and 7-methoxy-2-(*p*-methoxyphenyl)-4*H*-1-benzopyran with lead(IV) acetate also gave the corresponding benzofuran and cyclohexadienone. The reaction pathway is discussed.

As a continuation of the previous reports[1,2] on the oxidations of 2-phenyl-2*H*-1-benzopyrans and 2-phenyl-4*H*-1-benzopyrans with potassium permanganate, which gave flavones in excellent yields, we have now investigated the reactions of these benzopyrans and related compounds with lead(IV) acetate in various organic solvents and with different molar ratios of the oxidant to the substrate.

When 7-methoxy-2-(*p*-methoxyphenyl)-2*H*-1-benzopyran (**1b**) was oxidized with lead(IV) acetate in boiling benzene, two compounds (**5b** and **6b**) were isolated. The NMR spectrum of **5b**, $C_{17}H_{14}O_4$ (mp 149 °C), indicated that the structure is 6-methoxy-2-(*p*-methoxybenzoyl)benzofuran (Fig. 1), which was confirmed by independent synthesis: the reaction of 2-hydroxy-4-methoxybenzaldehyde with 2-bromo-*p*-methoxyacetophenone gave **5b**. The structure of **6b** was confirmed by means of a study of its NMR spectrum to be 6-acetoxy-3-methoxy-6-[3-(*p*-methoxyphenyl)-3-oxo-1-propenyl]-2,4-cyclohexadien-1-one (Fig. 1), in which the configuration of the C=C double bond in the side chain is *trans* (J=16.0 Hz). TLC showed that there were many other products, which, however, could not be purified. Similarly, the reaction of 7-methoxy-2-phenyl-2*H*-1-benzopyran (**1a**) gave the corresponding 2-benzoyl-6-methoxybenzofuran (**5a**) (mp 105—106 °C) and 6-acetoxy-3-methoxy-6-(3-oxo-3-phenyl-1-propenyl)-2,4-cyclohexadien-1-one (**6a**). The reaction of such other 2-phenyl-2*H*-1-benzopyrans as 2-(*p*-methoxyphenyl)-2*H*-1-benzopyran, which has no methoxyl group at the 7-position, resulted in a complex mixture of products and failed to give the corresponding benzofuran and cyclohexadienone. Therefore, it seems that the presence of a methoxyl group at the 7-position of 2-phenyl-2*H*-1-benzopyran is necessary to give the above products. We were particularly interested in the fact that the ring contraction took place to form a benzofuran ring, and so we subsequently studied its reaction pathway.

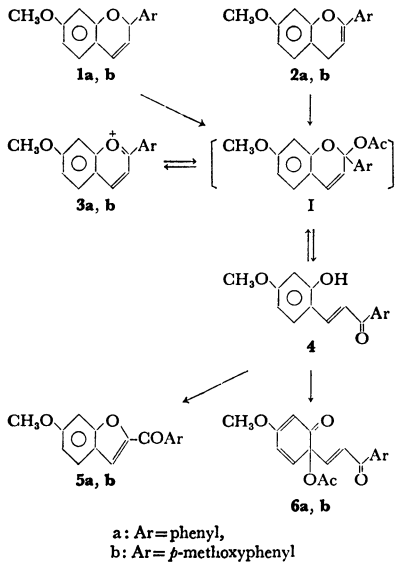

Fig. 1.

It was found that the reactions of 2-phenyl-4*H*-1-benzopyrans (**2a** and **2b**) with lead(IV) acetate in benzene also gave the benzofurans (**5a** and **5b**) and the cyclohexadienones (**6a** and **6b**) in yields similar to those in the reactions of **1a** and **1b** (Entries 3, 4, 9, and 10). When the reaction of **2b** was conducted in chloroform, the yields were practically the same as those in benzene (Entry 11). In acetic acid, however, the yield of **5b** decreased, whereas the yield of **6b** increased, and a characteristic fluorescence of flavylium ion was observed. This may suggest that either the flavylium ion (**3**) or 2-acetoxy-2-phenyl-2*H*-1-benzopyran (I) could be a reaction intermediate. Thus, the oxidation of **3b** was carried out under various reaction conditions. As has been mentioned above, the yield of **5b** in the reaction of **2b** in acetic acid was lower than in any other solvent, but the reactions of **3a** and **3b** in acetic acid containing two equivalents of potassium acetate gave **5a** and **5b** in improved yields (Entries 6 and 14—16). This indicates that I is a more adequate reaction intermediate. It is well known that the hydrolysis of the flavylium ion (**3**) gives an equilibrium mixture of 2-hydroxy-2-phenyl-2*H*-1-benzopyran and (*Z*)- and (*E*)-2-hydroxychalcone;[3] in fact, the treatment of **3b** with acetic acid containing potassium acetate did give (*E*)-2-hydroxy-4,4'-dimethoxychalcone (**4**). The reaction of **4** with lead(IV) acetate gave **5b** and **6b**. It has been reported that the reaction of *o*-substituted phenols with lead(IV) acetate gave 6-acetoxy-2,4-cyclohexadienones[4] and that the reaction of phenols with a double bond in the side chain with this reagent gave a cyclized compound, as has been shown in the cases of 2'-hydroxychalcones,[5] 2-hydroxystilbene,[6] 3-(*o*-hydroxyphenyl)-coumarin,[7] and 2'-hydroxyisoflavone.[8] Thus, it may be concluded that the reaction pathway of this interesting ring-contraction is as is shown in Fig. 1. **1** and **2** are oxidized by lead(IV) acetate to give I. Isomerization between **1** and **2** is not likely to occur under the present reaction conditions, as both **1b** and **2b** were recovered unchanged on heating in benzene.

Table 1. Reactions of 2-phenyl-2*H*-1-benzopyrans (**1**), 2-phenyl-4*H*-1-benzopyrans (**2**), flavylium perchlorates (**3**), and 2-hydroxy-4,4′-dimethoxychalcone (**4**) with lead (IV) acetate

Entry	Substrate	Reaction conditions: Molar ratio of substrate and oxidant	Reaction conditions: Solvent[a]	Reaction conditions: Temp[b] °C	Product (yield[c]/%): 5	Product (yield[c]/%): 6
1	**1a**	1 : 2	B	reflux	10	7
2	**1a**	1 : 3	B	reflux	12	18
3	**2a**	1 : 2	B	reflux	11	11
4	**2a**	1 ; 3	B	reflux	12	15
5	**3a**	1 : 2	A	100	3	28
6	**3a**	1 : 2	A, K	100	3	43
7	**1b**	1 : 2	B	reflux	11	13
8	**1b**	1 : 3	B	reflux	9	8
9	**2b**	1 : 2	B	reflux	9	8
10	**2b**	1 : 3	B	reflux	8	10
11	**2b**	1 : 3	C	reflux	9	10
12	**2b**	1 : 3	A	100	3	14
13	**3b**	1 : 2	A	100	4	35
14	**3b**	1 : 1.5	A, K	100	5	34
15	**3b**	1 : 2	A, K	100	7	44
16	**3b**	1 : 2.5	A, K	100	7	42
17	**4**	1 : 2	A	100	7	14
18	**4**	1 : 2	C	reflux	9	9

a) A: acetic acid, B: benzene, C: chloroform, and K: potassium acetate (2 mmol). b) Heating was continued for 30 min. c) Isolated yield, based on the amount of the substrate used.

I can also be formed by the addition of the acetate ion to **3**. I then becomes a mixture of (*Z*)- and (*E*)-chalcones, the latter being oxidized to give **5** and **6**.

Experimental

All the ^{1}H-NMR spectra were recorded for the deuteriochloroform solution with a Hitachi R-24 NMR spectrometer, with TMS as the internal standard. The IR spectra were recorded for the chloroform solution with a JASCO IRA-1 spectrometer, while the UV spectra were recorded for the methanol solution on a Hitachi EPS-3T UV spectrophotometer. The melting points were determined on a Yanagimoto hot-stage and are uncorrected.

Materials. 7-Methoxy-2-phenyl-2*H*-1-benzopyran (**1a**),[1] 7-methoxy-2-(*p*-methoxyphenyl)-2*H*-1-benzopyran (**1b**),[9] 7-methoxy-2-phenyl-4*H*-1-benzopyran (**2a**),[2] 7-methoxy-2-(*p*-methoxyphenyl)-4*H*-1-benzopyran (**2b**),[10] 7-methoxyflavylium perchlorate (**3a**),[11] 4′,7-dimethoxyflavylium perchlorate (**3b**),[12] and (*E*)-2-hydroxy-4,4′-dimethoxychalcone (**4**)[13] were prepared by the literature methods.

*Oxidations of 2-Phenyl-2*H*-1-benzopyrans (**1a** and **1b**), 2-Phenyl-4*H*-1-benzopyrans (**2a** and **2b**), Flavylium Perchlorates (**3a** and **3b**), and (E)-2-Hydroxy-4,4′-dimethoxychalcone (**4**).* To a mixture of a substrate (1 mmol) and a solvent (20 ml), lead(IV) acetate[14] (1.5—3 mmol) was added, after which the mixture was heated for 30 min. The reaction mixture was filtered (in the case of a reaction using acetic acid as the solvent, the acetic acid was removed *in vacuo* and the residue was extracted with chloroform), and the filtarte was concentrated and chromatographed on TLC, with chloroform as the developing solvent. **5a** and **5b** were further purified by recrystallization.

*2-Benzoyl-6-methoxybenzofuran (**5a**)*: Mp 105—106 °C (MeOH); IR 1640 cm^{-1} (C=O); UV λ_{max} (log ε) 236^{sh} (3.99), 259 (4.00), and 345 nm (4.34); NMR δ=3.87 (3H, s, OCH_3), 6.8—7.1 (2H, m, $H_{(5)}$ and $H_{(7)}$), 7.4—7.7 (5H, m), and 7.9—8.1 (2H, m, $H_{(2')}$ and $H_{(6')}$). Found: C, 75.96; H, 4.81%. Calcd for $C_{16}H_{12}O_3$; C, 76.18; H, 4.80%.

*6-Methoxy-2-(p-methoxybenzoyl)benzofuran (**5b**)*: Mp 149 °C (MeOH); IR 1645 cm^{-1} (C=O); UV λ_{max} (log ε) 228^{sh} (4.23), 259^{sh} (3.81), 307^{sh} (4.07), and 347 nm (4.33); NMR δ=3.89 (6H, s, 2×OCH_3), 6.8—7.2 (4H, m, $H_{(3')}$, $H_{(5)}$, $H_{(5')}$, and $H_{(7)}$), 7.45 (1H, s, $H_{(3)}$), 7.57 (1H, d, J=8.5 Hz, $H_{(4)}$), and 8.08 (2H, m, $H_{(2')}$ and $H_{(6')}$). Found: C, 72.33; H, 5.01%. Calcd for $C_{17}H_{14}O_4$; C, 72.33; H, 5.00%.

*6-Acetoxy-3-methoxy-6-(3-oxo-3-phenyl-1-propenyl)-2,4-cyclohexadien-1-one (**6a**)*: Mp 116—117 °C; IR 1680 and 1758 cm^{-1} (OAc); UV λ_{max} (log ε) 260 (3.93) and 308^{sh} nm (3.72); NMR δ=2.21 (3H, s, OAc), 3.82 (3H, s, OCH_3), 5.59 (1H, t, J=1.5 Hz, $H_{(2)}$), 6.26 (2H, d, J=1.5 Hz, $H_{(4)}$ and $H_{(5)}$), 6.67 (1H, d, J=17.6 Hz, $H_{(1')}$), 7.37 (1H, d, J=17.6 Hz, $H_{(2')}$), 7.3—7.7 (3H, m) and 7.8—8.0 (2H, m); MS *m/e* 312.0941 (calcd for $C_{18}H_{16}O_5$; 312.0998), 284, 270, 202, 165, 160, 152, 111, and 105.

*6-Acetoxy-3-methoxy-6-[3-(p-methoxyphenyl)-3-oxo-1-propenyl]-2,4-cyclohexadien-1-one (**6b**)*: Liquid; IR 1680 (C=O) and 1760 cm^{-1} (OAc); UV λ_{max} (log ε) 225 (4.26) and 295 nm (4.19); NMR δ=2.21 (3H, s, OAc), 3.81 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 5.61 (1H, t, J=1.5 Hz, $H_{(2)}$), 6.27 (2H, d, J=1.5 Hz, $H_{(4)}$ and $H_{(5)}$), 6.65 (1H, d, J=16.0 Hz, $H_{(2')}$), 7.01 (2H, m, $H_{(3'')}$ and $H_{(5'')}$), 7.37 (1H, d, J=16.0 Hz, $H_{(1')}$), and 8.04 (2H, m, $H_{(2'')}$ and $H_{(6'')}$); MS *m/e* 342.1088 (calcd for $C_{19}H_{18}O_6$; 342.1103), 314, 300, 282, 190, 165, 161, 111, 135, and 92.

*Preparation of 6-Methoxy-2-(p-methoxybenzoyl)benzofuran (**5b**).* To a hot, ethanolic solution (20 ml) of 2-hydroxy-4-methoxybenzaldehyde (456 mg) and potassium hydroxide (168 mg), we added 2-bromo-*p*-methoxyacetophenone (689 mg), after which the reaction mixture was heated under reflux for 2 h. The reaction mixture was then acidified with dilute hydrochloric acid, and the precipitates were collected. The subsequent recrystallization of the crude product from ethanol gave colorless needles (375 mg, 44%); mp 149 °C.

*Treatment of 4′,7-Dimethoxyflavylium Perchlorate (**3b**) with Potassium Acetate in Acetic Acid.* **3b** (367 mg) was heated in acetic acid (10 ml) containing potassium acetate (200 mg) for 5 min. The reaction mixture was then diluted with water (60 ml), and the precipitates were collected by filtration to give **4** (240 mg, 85%), found to be identical with an authentic sample in all respects.

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