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Synthesis of 2-Benzylidene-3(2*H*)-benzofuran-3-ones (Aurones) by Oxidation of 2′-Hydroxychalcones with Mercury(II) Acetate

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Synopsis. The reaction of 2′-hydroxychalcones with mercury(II) acetate in acetic acid gives predominantly 2-benzylidene-3(2*H*)-benzofuran-3-ones (aurones) in 28—62% yield accompanied by flavanones in 5—21% yield.

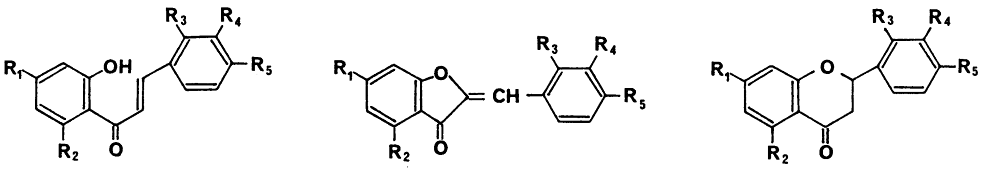
2′-Hydroxychalcones are one of the important intermediates for the synthesis of flavonoids, and afford various products (flavone, flavonol, 3-hydroxyflavanone and aurone) according to the different oxidizing agents.[1] Hydrogen peroxide is the most historical reagent for the oxidation of 2′-hydroxychalcones to flavonols or aurones, but 6′-methoxyl group is necessary for the synthesis of aurones.

On the other hand, the oxidation of 2′-hydroxychalcones with selenium(IV) oxide,[1] palladium(II) lithium chloride,[2] 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ),[3] thallium(III) nitrate trihydride[4] and a combination of nickel chloride, zinc powder and potassium iodide[5] provide only flavones. While, Kurosawa et al.,[6,7] reported that the oxidation of 2′-hydroxychalcones with lead(IV) acetate or manganese(III) acetate in acetic acid gave the aurones as main products, but Ollis et al.,[8] reported that thallium(III) acetate gave the rearranged products. Thus oxidation of 2′-hydroxychalcones with metal acetates afford different products depending on the metal.

This report deals with the synthesis of aurones by the oxidation of 2′-hydroxychalcones with mercury(II) acetate in acetic acid. These results are similar to those of Kurosawa described above but a chalcone (**1c**) having hydroxyl group at 4-position also afforded the product **2c** as a pure crystal. The results are shown in Table 1.

2′-Hydroxychalcones **1a**—**i** were prepared by the usual potassium hydroxide-catalyzed condensation of the corresponding 2′-hydroxyacetophenones and benzaldehyde or its derivatives. The products **1a**—**i** were identified by their physical properties and spectroscopic analyses.

2′-Hydroxychalcones **1** were dehydrogenatively cyclized to the aurones **2** on heating at 90—95 °C for 8 h with two equivalents of mercury(II) acetate in acetic acid. The reaction mixture was separated by the addition of saturated sodium chloride solution followed by extraction with ethyl acetate and column chromatography on silica gel to give aurone **2** accompanied by flavanone **3** produced from acid-catalyzed cyclization of 2′-hydroxychalcone **1**. The aurones **2a**—**i** and flav-



1 **2** **3**

a $R_1=R_2=R_3=R_4=R_5=H$
b $R_1=OMe$, $R_2=R_3=R_4=R_5=H$
c $R_1=R_2=R_3=R_4=H$, $R_5=OH$
d $R_1=R_2=OMe$, $R_3=R_4=R_5=H$
e $R_1=R_2=R_3=OMe$, $R_4=R_5=H$
f $R_1=R_2=R_4=OMe$, $R_3=R_5=H$
g $R_1=R_2=OMe$, $R_3=R_4=H$, $R_5=OCH_2Ph$
h $R_1=R_2=R_3=R_5=OMe$, $R_4=H$
i $R_1=R_2=R_4=OMe$, $R_3=H$, $R_4=OCH_2Ph$

Fig. 1.

Table 1.

Chalcone			Aurone				Flavanone			
No.	Mp (lit) θ_m/°C	Ref.	No.	Yield %	Mp (lit) θ_m/°C	Ref.	No.	Yield %	Mp (lit) θ_m/°C	Ref.
1a	86—8 (88—9)	9	**2a**	51	108—9 (108)	15	**3a**	6	75—6 (75—6)	21
1b	108—9 (107—8)	10	**2b**	40	147—8 (145—6)	16	**3b**	21	86—7 (89)	22
1c	158—9 (162)	11	**2c**	28	238—9 (242)	17	**3c**	9	186—7 (186—7)	11
1d	89—90 (91)	12	**2d**	62	152—3 (151—2)	18	**3d**	5	168—9 (152—3)	23
1e	113—4 (106—8)	13	**2e**	42	220—1 (214—6)	19	**3e**	11	130 (124—5)	24
1f	96.5—7 (—)	—	**2f**	54	194—5 (190—1)	19	**3f**	7	102—3 (—)	—
1g	163—4 (—)	—	**2g**	62	205—6 (197)	20	**3g**	10	168—9 (—)	—
1h	171—3 (128)	14	**2h**	55	215—7 (211—7)	19	**3h**	12	165—6 (167—8)	25
1i	123—4 (—)	—	**2i**	31	191—2 (—)	—	**3i**	14	128 (—)	—

anones **3a—i** were identified by their physical properties and spectroscopic analyses.

Experimental

The melting points were determined on a Yanaco micromelting point apparatus and are uncorrected. The IR spectra were taken on a Hitachi 270-30 infrared spectrophotometer. The ultraviolet spectra were determined by a Shimadzu UV-210 digital spectro-photometer. The ^{1}H NMR spectra were recorded on a JEOL FX 90Q spectrometer. Chemical shifts are given on the δ (ppm) scale with tetramethylsilane as an internal standard (s, singlet; d, doublet; t, triplet; m, multiplet). The MS were taken on a Shimadzu LKB-9000 and a JEOL JNM-PM-60 spectrometer by the direct inlet method; ionization voltage 70 eV.

Preparation of Chalcones. A solution of an equimolar amount of 2′-hydroxychalcone and benzaldehyde in a small volume of ethanol was treated with 10% ethanolic potassium hydroxide with stirring at 35—40 °C for 12 h. The reaction mixture was poured into ice-water and acidified with dilute hydrochloric acid. The resulting precipitate was collected by filtration and washed with water. The crude product was purified by column chromatography on silica gel and recrystallized from ethanol. **1f**: IR (KBr) 1635 and 1584 cm^{-1}. UV (C_2H_5OH) 250 (log ε 4.04) and 345 nm (4.30). ^{1}H NMR ($CDCl_3$) δ=3.84 (3H, s, OCH_3), 3.85 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 5.96 (1H, d, J=2.2 Hz, H-3′), 6.10 (1H, d, J=2.2 Hz, H-5′), 6.80—7.30 (4H, m, H-2, 4, 5 and 6), and 7.80 (2H, d, J=4.4 Hz, H-α and β). MS m/z (rel intensity 314 (M$^+$; 96), 297 (20), 286 (17), 207 (100), and 180 (29). High MS Found: m/z 314.1145, Calcd for $C_{18}H_{18}O_5$: M, 314.1152. **1g**: IR (KBr) 1632, 1622, and 1581 cm^{-1}. UV (C_2H_5OH) 250 (log ε 4.10) and 365 nm (4.54). ^{1}H NMR ($CDCl_3$) δ=3.83 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 5.11 (2H, s, $-C\underline{H}_2Ph$), 5.93 (1H, d, J=2.2 Hz, H-3′), 6.01 (1H, d, J=2.2 Hz, H-5′), 6.96 (2H, d, J=8.8 Hz, H-3 and 5), 7.39 (5H, s, PhH), 7.52 (2H, d, J=8.8 Hz, H-2 and 6), and 7.78 (2H, s, H-α and β). MS m/z (rel intensity) 390 (M$^+$; 22), 271 (18), 181 (22), and 91 (100). High MS Found: m/z 390.1489, Calcd for $C_{24}H_{22}O_5$: M, 390.1466. **1i**: IR (KBr) 1629 and 1581 cm^{-1}. UV (C_2H_5OH) 245 (log ε 4.00) and 371 nm (4.50). ^{1}H NMR ($CDCl_3$) δ=3.82 (6H, s, 2× OCH_3), 3.93 (3H, s, OCH_3), 5.20 (2H, s, $-C\underline{H}_2Ph$), 5.92 (1H, d, J=2.2 Hz, H-3′), 6.10 (1H, d, J=2.2 Hz, H-5′), 6.90 (1H, d, J=8.4 Hz, H-2 or 3), 7.15 (1H, d, J=2.2 Hz, H-6), 7.40 (6H, m, PhH and H-2 or 3), and 7.68 (2H, s, H-α and β). MS m/z (rel intensity) 420 (M$^+$; 34), 181 (42), 180 (31), and 91 (100). High MS Found: m/z 420.1563, Calcd for $C_{25}H_{24}O_6$: M, 420.1571.

Mercury(II) Acetate Oxidation of Chalcones. A solution of chalcone (**1**) (5 mol dm^{-3}) and mercury(II) acetate (10 mol dm^{-3}) in 100 cm^3 of acetic acid was heated at 90—95 °C for 8 h. After removal of the acetic acid in vacuo, the resulting solid was treated with saturated sodium chloride solution and then extracted with ethyl acetate. The ethyl acetate layer was separated and evaporated. The residue was dissolved in a small amount of a mixture of benzene-ethyl acetate (6/1 volume ratio) and separated by silica-gel column chromatography with a mixture of benzene-ethyl acetate (6/1 volume ratio) as eluant. Aurones **2** were obtained as the first fraction and flavanones **3** were obtained as the second fraction. **2i**: IR (KBr) 1692, 1673, 1614, and 1595 cm^{-1}. UV (C_2H_5OH) 252 (log ε 3.68), 265 (sh, 3.62), 380 (sh, 4.08), and 395 nm (4.15). ^{1}H NMR ($CDCl_3$) δ=3.93 (3H, s, OCH_3), 3.95 (6H, s, 2×OCH_3), 5.24 (2H, s, $-C\underline{H}_2Ph$), 6.12 (1H, d, J=1.8 Hz, H-5), 6.29 (1H, d, J=1.8 Hz, H-7), 6.68 (1H, s, H-10), 6.93 (1H, d, J=8.4 Hz, H-5′), and 7.45 (7H, m, PhH, H-2′ and 6′). MS m/z (rel intensity) 418 (M$^+$; 42), 327 (41), 299 (14), 181 (31), and 91 (100). High MS Found: m/z 418.1406, Calcd for $C_{25}H_{22}O_6$: M, 418.1414. **3f**: IR (KBr)1674, 1608, and 1566 cm^{-1}. UV (C_2H_5OH) 282 (log ε 4.29) and 310 nm (sh, 3.67). ^{1}H NMR ($CDCl_3$) δ=2.91 (2H, m, H-3), 3.85 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 5.38 (1H, d,d, J=15.6 and 4.0 Hz, H-2), 6.11 (1H, d, J=2.4 Hz, H-6), 6.19 (1H, d, J=2.4 Hz, H-8), and 6.97 (4H, m, H-2′, 3′, 4′, and 6′). MS m/z (rel intensity) 314 (M$^+$; 55), 207 (29), and 180 (100). High MS Found: m/z 314.1168, Calcd for $C_{18}H_{18}O_5$: M, 314.1153. **3g**: IR (KBr) 1680, 1608, and 1569 cm^{-1}. UV (C_2H_5OH) 282 (log ε 3.93) and 310 nm (sh, 3.14). ^{1}H NMR ($CDCl_3$) δ=2.39 (2H, m, H-2), 3.18 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 5.08 (2H, s, $-C\underline{H}_2Ph$), 5.34 (1H, d,d, J=13.3 and 4.0 Hz, H-2), 6.08 (1H, d, J=2.4 Hz, H-6), 6.13 (1H, d, J=2.4 Hz, H-8), 7.00 (2H, d, J=9.8 Hz, H-3′ and 5′), 7.38 (2H, d, J=9.8 Hz, H-2′ and 6′), and 7.39 (5H, s, PhH). MS m/z (rel intensity) 390 (M$^+$; 22), 299 (8), and 91 (100). High MS Found: m/z 390.1491, Calcd for $C_{22}H_{22}O_5$: M, 390.1476, **3i**: IR (KBr) 1674, 1608, and 1572 cm^{-1}. UV (C_2H_5OH) 283 (log ε 4.29) and 311 nm (sh, 3.68). ^{1}H NMR ($CDCl_3$) δ=2.27 (2H, m, H-3), 3.81 (3H, s, OCH_3), 3.89 (6H, s, 2×OCH_3), 5.16 (2H, s, $-C\underline{H}_2Ph$), 5.28 (1H, d,d, J=16.0 and 4.0 Hz, H-2), 6.09 (1H, d, J=2.2 Hz, H-6), 6.12 (1H, d, J=2.2 Hz, H-8), 6.95 (3H, m, H-2′, 3′, and 6′), and 7.38 (5H, m, PhH). MS m/z (rel intensity) 420 (M$^+$; 43), 181 (45), 105 (45), and 91 (100). High MS Found: m/z 420.1559, Calcd for $C_{25}H_{24}O_6$: M, 420.1576.

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References

1) J. B. Harborne, T. J. Mabry, and H. Mabry, "The Flavonoids," Chapman and Hall, London (1975).

2) A. Kasahara, T. Izumi, and M. Oshima, *Bull. Chem. Soc. Jpn.*, **47**, 2526 (1974).

3) T. Tanaka, K. Iwashima, and S. Matsuura, *Yakugaku Zasshi*, **104**, 1306 (1984).

4) M. Meyer-Dayan, B. Bodo, C. Deschamps-Vallent, and D. Molho, *Tetrahedron Lett.*, **1978**, 3359.

5) S. M. Ali, J. Iqbal, and M. Liyas, *J. Chem. Res. (S)*, **1984**, 236.

6) K. Kurosawa, *Bull. Chem. Soc. Jpn.*, **42**, 1456 (1969).

7) K. Kurosawa and J. Higuchi, *Bull. Chem. Soc. Jpn.*, **45**, 1132 (1972).

8) W. D. Ollis, K. L. Ormand, and I. O. Sutherland, *J. Chem. Soc. C*, **1970**, 119.

9) J. Buckingham, "Dictionary of Organic Compounds," Chapman and Hall, London (1982), p. 3220.

10) S. Matsueda, K. Sannohe, and Y. Saito, *Bull. Chem. Soc. Jpn.*, **36**, 1528 (1963).

11) T. A. Geissman and R. O. Clinton, *J. Am. Chem. Soc.*, **68**, 697 (1946).

12) R. Haensel, G. Ranft, and R. Baehr, *Z. Naturforch*, **18b(5)**, 370 (1963).

13) J. Buckingham, "Dictionary of Organic Compounds," Chapman and Hall, London (1982), p. 3227.

14) "Beilstein's Handbuch der Organishen Chemie," Vol. 8, p. 543.

15) W. Feuerstein and St. von Kostanecki, *Ber.*, **31**, 1759 (1898).

16) S. K. Grover, V. N. Gupta, A. C. Jain, and T. R. Seshadri, *J. Sci Ind. Res. (Indian)*, **19B**, 258 (1960).

17) "Beilstein's Handbuch der Organishen Chemie," Vol. 10, p. 61.

18) R. N. Goel, V. B. Mahesh, and T. R. Seshadri, *Proc. Indian Acad. Sci., Sect. A*, **47**, 184 (1958).

19) V. D. Vittorio, *Rent. Ist. Super Sanita*, **21**, 418 (1958).

20) F. Lor and G. Agnes and N. Mihaly, *Acta Chem. (Budapest)*, **53**, 311 (1968).

21) H. Ryan and G. Cruess-Callaghan, *Proc. R. Ir. Acad.*, **39**, 124 (1919).

22) J. Shinoda, *Yakugaku Zasshi,* **48**, 214 (1928).

23) M. Hasegawa and T. Shirato, *J. Am. Chem. Soc.*, **79**, 450 (1975).

24) "Beilstein's Handbuch der Organischen Chemie," Vol. 18, p. 395.

25) "Beilstein's Handbuch der Organischen Chemie," Vol. 10, p. 209.