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The Acylation of 2,3-Dimethyl-*bz*-hydroxybenzofurans and the Syntheses of Di- and Tri-methylfuroisoflavones*[1]

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The acylation of 2,3-dimethyl-4-hydroxybenzofuran (1) with acetic acid, phenylacetic acid, 2-methoxyphenylacetic acid or 2,4,5-trimethoxyphenylacetic acid, and polyphosphoric acid gave a mixture of the 5- and 7-acyl compounds (2a, b, c, d, and 3a, c, d respectively). Analogously, the isomeric 2,3-dimethyl-6-hydroxybenzofuran (6) gave the 5-acyl compounds (7a, b, c, d), two (7a, b) of which were also obtained by the Friedel-Crafts acylation of the methyl ether of 6 (9), followed by demethylation. On the other hand, the formation of a dimethylfuran ring on 2,4-dihydroxyphenyl ketones by the action of polyphosphoric acid on their 4-(α-acetylethoxy) derivatives (11a, b, c) also afforded mixtures of the ketones (7a, b, c) and isomeric ketones (2a, b, c). The benzofuranyl ketones (2 and 7) thus obtained were converted to the corresponding 4'',5''-dimethyl-furo[2'',3'':7,8]isoflavones (12b, c, d) and isomeric -furo[3'',2'':6,7]isoflavones (14b, c), and also their 2-methyl derivatives (13b, c, d and isomeric 15b, c), by the general method utilizing ethyl orthoformate, piperidine and pyridine, or acetic anhydride and sodium acetate. The furoisoflavones (12b, c and 13b, c) were also prepared by building up the dimethylfuran ring on 7-hydroxyisoflavones by the action of polyphosphoric acid or sulfuric acid on their 7-(α-acetylethoxy) derivatives (16b, c and 17b, c respectively). The alkaline degradation of these furoisoflavones (12 and 13) also gave the benzofuranyl ketones (2)

Previously, furo[2'',3'':7,8]isoflavones[1,2] and the 4''-methyl derivative[2a] were prepared by building up the furan ring on 7-hydroxyisoflavones, while the 5''-alkyl derivatives[3] and isomeric furo[3'',2'' : 6,7]isoflavones[4] were prepared by the dehydrogenation of the corresponding dihydrofuroisoflavones. The furoisoflavones were also prepared by the pyrone ring formation on hydroxybenzofuranyl ketones.[1-3]

In the present experiments, 2,3-dimethyl-4- and isomeric -6-hydroxy-5-benzofuranyl ketones (2 and 7), which had been prepared by the acylation of the corresponding hydroxy- or methoxybenzofurans (1 and 6 or 9), were converted to furo[2'',3'' : 7,8]isoflavones (12 and 13) and isomeric furo[3'',2'':6,7]isoflavones (14 and 15) respectively by the formation of a pyrone ring on them. Two furoisoflavones (12 and 13) were also prepared by building up the dimethylfuran ring on 7-hydroxyisoflavones; the alkaline degradation of these furoisoflavones also gave the benzofuranyl ketones (2).

Previously, 4-hydroxy- or 4-methoxy-5-benzofuranyl ketones were prepared by the interaction of benzofurancarbonyl chloride with ethyl phenylacetate[2a] or with dibenzylcadmium[5]; also, these ketones as well as the isomeric 6-hydroxy-5-benzofuranyl ketones were prepared by the alkaline degradation of furoisoflavones,[1,4] for the direct acylation of hydroxybenzofurans to give the ketones was not successful. On the other hand, the 2-substituted 6-hydroxy-[6] or 6-methoxy-5-benzofuranyl methyl ketones[7] were obtained by the acetylation of the corresponding benzofurans,

*1 A part of this work was presented at the 20th Annual Meeting of the Chemical Society of Japan, Tokyo, March, 1967.

1) T. Matsumoto, Y. Kawase, M. Nanbu and K. Fukui, This Bulletin, **31**, 688 (1958); K. Fukui and Y. Kawase, *ibid.*, **31**, 693 (1958); Y. Kawase, K. Ogawa, S. Miyoshi and K. Fukui, *ibid.*, **33**, 1240 (1960); K. Fukui, M. Nakayama and M. Hatanaka, *ibid.*, **36**, 872 (1963); K. Fukui, M. Nakayama and K. Okazaki, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **85**, 446 (1964).

2) a) L. R. Row and T. R. Seshadri, *Proc. Indian Acad. Sci.*, **34A**, 187 (1951). b) K. S. Raizada, P. S. Sarin and T. R. Seshadri, *J. Sci. Ind. Research (India)*, **19B**, 76 (1960).

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4) S. K. Pavanaram, L. R. Row and T. R. Seshadri, *J. Sci. Ind. Research (India)*, **15B**, 495 (1956); S. K. Pavanaram and L. R. Row, *Current Science (India)*, **26**, 145 (1957); K. Fukui and M. Nakayama, *Experientia*, **19**, 621 (1963); *ibid.*, **20**, 668 (1964); K. Fukui, M. Nakayama, A. Tanaka and S. Sasatani, This Bulletin, **38**, 845 (1965); A. S. R. Anjaneyulu, C. S. Krishna and L. R. Row, *Tetrahedron*, **21**, 2677 (1965).

5) Y. Kawase, T. Fujimoto and K. Fukui, This Bulletin, **31**, 691 (1958).

6) J. Oda, H. Fukami and M. Nakajima, *Agr. Biol. Chem.*, **30**, 59 (1966).

7) P. K. Ramachandran, A. T. Tefteller, G. O. Paulson, T. Cheng, C. T. Lin and W. J. Horton, *J. Org. Chem.*, **28**, 398 (1963).

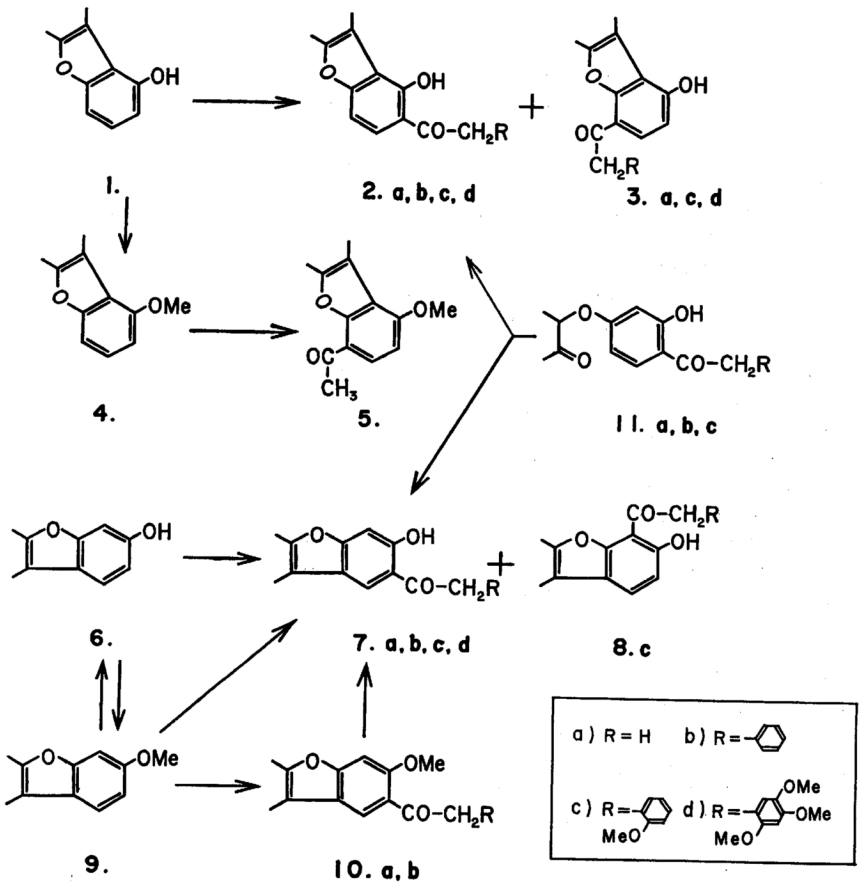

Chart 1

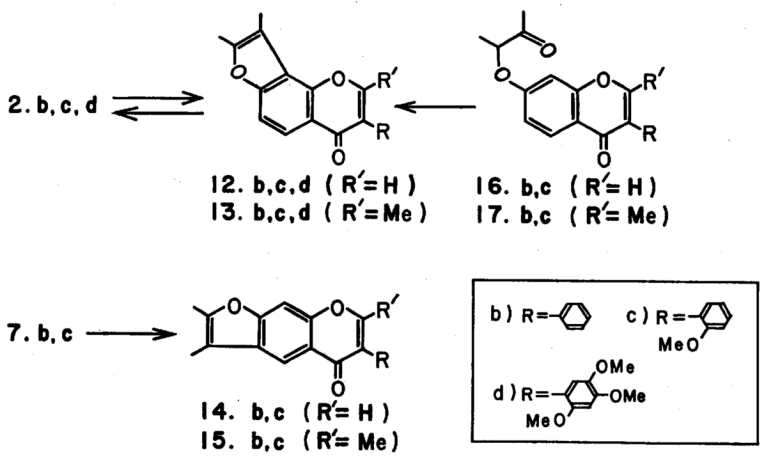

Chart 2

while the acetylation of isomeric 4-methoxy-2-methoxycarbonylbenzofuran afforded the 7-acetyl compound.[7] It has also been reported[8] that the acetylation of 2,3-dimethyl-6-methoxybenzofuran (9) by the Friedel-Crafts reaction gave the 5-acetyl compound (10a), which was then demethylated to the hydroxyketone (7a), while that of isomeric 2,3-dimethyl-4-methoxybenzofuran (4) gave the 7-acetyl compound (5).

8) R. Royer, E. Bisagni, A.-M. Laval-Jeantet and J.-P. Marquet, *Bull. Soc. Chim. France*, **1965**, 2607.

In the present experiments, 2,3-dimethyl-4-hydroxybenzofuran[8] (1) was acylated with acetic acid, phenylacetic acid, 2-methoxyphenylacetic acid or 2,4,5-trimethoxyphenylacetic acid, and polyphosphoric acid to give a mixture of the 5- and 7-acyl compounds (2a, b, c, d and 3a, c, d respectively), analogously to the case of 2,3-dihydro-4-hydroxybenzofuran.[9] The 5-acyl compounds (2) were separated from the isomers (3) by the extraction of the latter from the mixture with aqueous sodium hydroxide.

The similar acylation of isomeric 2,3-dimethyl-6-hydroxybenzofuran[8] (6) gave the 5-acyl compounds (7a, b, c, d); 7a and 7b were also prepared by the Friedel-Crafts acylation of methoxybenzofuran (9), followed by demethylation. In the case of the 2-methoxyphenylacetyl derivative (7c), a small amount of an isomeric 7-acyl compound (8c) was also obtained; the structure of this was assigned on the basis of its positive ferric chloride color reaction and the analogous formation of 7-substituted compounds in the acetylation of 6-methoxy-2-methoxycarbonylbenzofuran[7] and in the condensation of 2,3-dimethyl-6-hydroxybenzofuran with ethyl phenylmalonate.[10]

On the other hand, 2,4-dihydroxyphenyl ketones were converted to 4-(α-acetylethoxy)-2-hydroxyphenyl ketones (11a, b, c) by the action of 3-chlorobutanone-2 and potassium carbonate; the subsequent dehydro-cyclization of these ethers (11) by the action of polyphosphoric acid afforded mainly the 6-hydroxy-5-benzofuranyl ketones (7a, b, c), the dimethylfuran ring being formed towards the unhindered 5-position of the ketones, and also gave small amounts of isomeric 4-hydroxy-5-benzofuranyl ketones (2a, b, c). These experiments confirmed the structures of these ketones (2 and 7).

The *o*-hydroxybenzofuranyl ketones (2a, b, c and 7b, c) thus obtained were converted to the corresponding 4'',5''-dimethylfuro[2'',3'':7,8]-isoflavones (12b, c, d) and 4'',5''-dimethylfuro-[3'',2'':6,7]isoflavones (14b, c) by the action of ethyl orthoformate and piperidine in pyridine, and were also converted to 2,4'',5''-trimethylfuro-[2'',3'':7,8]isoflavones (13b, c, d) and 2,4'',5''-trimethylfuro[3'',2'':6,7]isoflavones (15b, c) by the action of acetic anhydride and sodium acetate.

The furo[2'',3'':7,8]isoflavones (12 and 13) were also obtained by building up the dimethylfuran ring on 7-hydroxyisoflavones. 7-Hydroxyisoflavones were converted to 7-(α-acetylethoxy) derivatives (16b, c and 17b,c) by the action of 3-chlorobutanone-2 and potassium carbonate; the subsequent dehydro-cyclization of these ethers with polyphosphoric acid or concentrated sulfuric acid afforded the furoisoflavones (12b, c and 13b, c). In this case, the dimethylfuran ring is formed towards the 8-position of isoflavones, because this position is not as hindered as the 3-position of 4-(α-acetylethoxy)-2-hydroxyphenyl ketones (11), for the one hydroxyl group of the latter is blocked by the formation of the pyrone ring in the former, and because the position is the most reactive site in such electrophilic substitutions as chloromethylation,[11] Mannich reaction,[12] Claisen rearrangement,[3a] Fries rearrengement,[2a] and formylation.[1,2a]

The alkaline degradation of the furo[2'',3'':7,8] isoflavones (12 and 13) also afforded the 4-hydroxy-5-benzofuranyl ketones (2); this method is another route for the preparation of the ketones (2).

In the infrared spectra, the di- (12b, c, d and 14b, c) and tri-methylfuroisoflavones (13,b c, d and 15b, c) exhibit an absorption at about 1655—1640 cm^{-1} (ν_{CO}), much as the furoisoflavones without dimethyl groups have an absorption at about 1650—1634 cm^{-1}.[1,4,9]

In the ultraviolet spectra, the furo[2'',3'':7,8]-isoflavones (12b, c and 13b, c) have two bands, a strong band, I, at about 247—255 mμ and a weak band, II, at about 313—320 mμ, while the isomeric furo[3'',2'':6,7]isoflavones (14b, c and 15b, c) have corresponding bands at about 248—254 mμ and at 330—338 mμ respectively. These data show that the band II of furoisoflavones with a linearly-fused furan ring is at a wavelength longer by 17—18 mμ than is that of the isomers with an angularly-fused furan ring, but the band I is at almost the same wavelength. These figures are comparable to those of furoisoflavones without dimethyl groups[1,4,9]; this proves that the introduction of dimethyl groups to the furan ring of furoisoflavones causes a bathochromical shift of 10—13 mμ in the band II and one of 2—7 mμ in the band I.

Experimental*2

The Preparation of Benzofuranyl Ketones. *a) By the Acylation of 2,3-Dimethyl-hydroxybenzofurans (1 and 6) with Carboxylic Acid and PPA.**3 A mixture of 2,3-dimethyl-4-hydroxybenzofuran[13] (1) (5 g), acetic acid (2.2 g, 1.2 mol equivalents), and PPA (n=1.5, 125 g) was heated at 90°C for 1 hr with stirring. The cooled mixture was then poured into ice water and extracted with ether. The ethereal solution was washed with

9) Y. Kawase, M. Nanbu and H. Yanagihara, This Bulletin, **41**, 1201 (1968).
10) J.-P. Lechartier, P. Demerseman, A. Cheutin and R. Royer, *Bull. Soc. Chim. France*, **1966**, 1716.
11) Y. Kawase, M. Nakayama and S. Matsutani, This Bulletin, **35**, 1367 (1962).
12) P. Da Re and L. Verlicchi, *Ann. Chim. (Rome)*, **50**, 1273 (1960).
*2 All melting points are uncorrected; the IR spectra were measured in the form of KBr disks, and the UV spectra were measured in ethanol. The detailed data are summarized in the tables and figures.
*3 Polyphosphoric acid.
13) E. Bisagni and R. Royer, *Bull. Soc. Chim. France*, **1962**, 925.

Table 1. The preparation of benzofuranyl ketones

Starting compound	Reagent[a]	Procedure,[b] temp.×hr	Produced ketone (yield, %)
1	Acetic acid	A, 90°×1	2a(25)+3a(6)
1	PAA	A, 100°×1	2b(52)
1	2-Methoxy-PAA	A, 80°×1	2c(37)+3c(5)
1	2,4,5-Trimethoxy-PAA	A, 85°×0.5	2d(30)+3d(6)
6	Acetic acid	A, 100°×1	7a(28)
6	PAA	A, 100°×1	7b(20)
6	2-Methoxy-PAA	A, 80°×1	7c(10)+8c(1)
6	2,4,5-Trimethoxy-PAA	A, 80°×2	7d(20.5)
9	Acetyl chloride	B, {Room×2, Reflux×1	7a(43)
9	Phenylacetyl chloride	B, {Room×2, Reflux×10′	7b(41)
9	Phenylacetyl chloride	B, Room×2	10b(74)
10b		C, Reflux×10′	7b(56)+10b(20)
c)	Chlorobutanone	D	2a(d)+7a(9)
e)	Chlorobutanone	D	2b(d)+7b(6)
f)	Chlorobutanone	D	2c(6)+7c(d)
12b	50% KOH	E, Reflux×3	2c(75.5)
13b	50% KOH	E, Reflux×3	2b(96)
13c	50% KOH	E, Reflux×3	2c(83.5)

a) PAA: Phenylacetic acid. b) A: Polyphosphoric acid (n=1.5), B: Friedel-Crafts reaction in benzene, C: Aluminum chloride in benzene, D: Reflux with potassium carbonate in acetone then cyclization by polyphosphoric acid, E: In ethanol. c) 2,4-Dihydroxyphenyl methyl ketone. d) A small amount. e) 2,4-Dihydroxyphenyl benzyl ketone. f) 2,4-Dihydroxyphenyl 2-methoxybenzyl ketone.

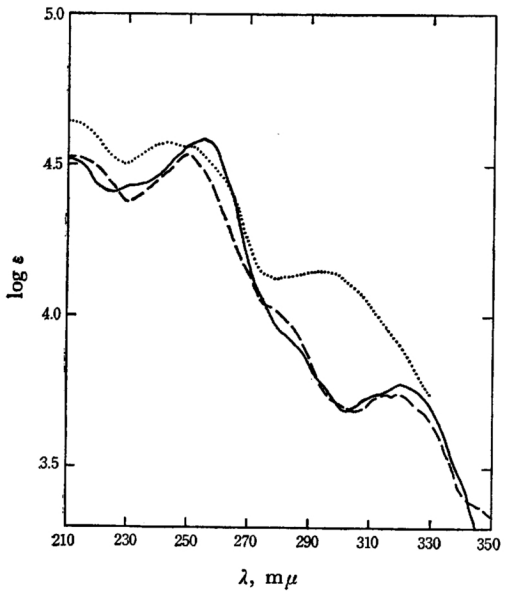

Fig. 1. The UV spectra of furoisoflavones:
—— 12b, ---- 12c and ····· 12d.

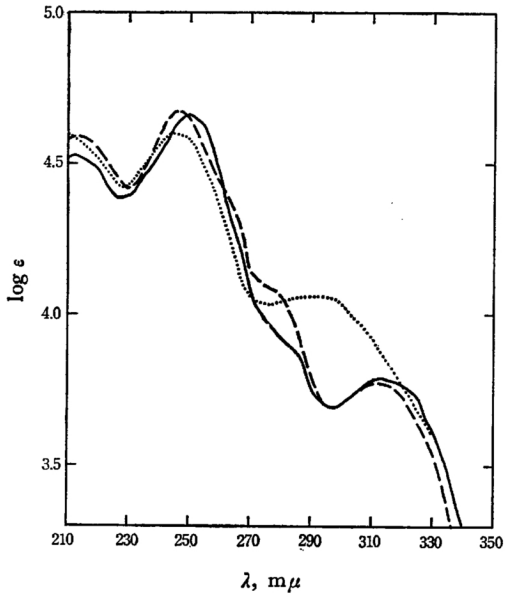

Fig. 2. The UV spectra of furoisoflavones:
—— 13b, ---- 13c and ····· 13d.

aqueous sodium carbonate and then extracted with aqueous sodium hydroxide. The product obtained from the ethereal solution was recrystallized from ethanol to give 2,3-dimethyl-4-hydroxy-5-benzofuranyl methyl ketone (2a), which had a positive ferric chloride color reaction in ethanol. The alkaline solution was acidified, and the crystalline product formed was collected and recrystallized from ethanol to give the isomeric 2,3-dimethyl-4-hydroxy-7-benzofuranyl methyl ketone (3a), which had a negative ferric chloride color reaction in ethanol.

Similarly, the 2,3-dimethyl-4-hydroxy-5-benzofuranyl

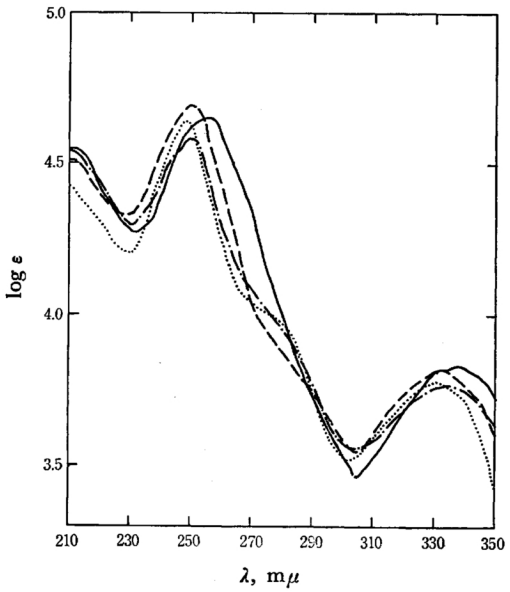

Fig. 3. The UV spectra of furoisoflavones: —— 14b, —·—· 14c, ---- 15b and ····· 15c.

benzyl ketones (2b), the 2,3-dimethyl-4-hydroxy-5-benzofuranyl 2-methoxybenzyl ketones (2c), the 2,3-dimethyl-4-hydroxy-5-benzofuranyl 2,4,5-trimethoxybenzyl ketone (2d), the isomeric 2,3-dimethyl-4-hydroxy-7-benzofuranyl 2-methoxybenzyl ketone (3c), and the 2,3-dimethyl-4-hydroxy-7-benzofuranyl 2,4,5-trimethoxybenzyl ketone (3d) were obtained by this procedure.

Further, the acylation of isomeric 2,3-dimethyl-6-hydroxybenzofuran[13] (6) by this procedure gave the 2,3-dimethyl-6-hydroxy-5-benzofuranyl methyl ketone (7a), the 2,3-dimethyl-6-hydroxy-5-benzofuranyl benzyl ketone (7b), the 2,3-dimethyl-6-hydroxy-5-benzofuranyl 2-methoxybenzyl ketone (7c), and the 2,3-dimethyl-6-hydroxy-5-benzofuranyl 2,4,5-trimethoxybenzyl ketone (7d). The ketone 7a has a mp of 121—123°C (from ethanol) (lit.[8] mp 122°C) and ν_{max}: 1650 cm^{-1} (CO). In the case of the ketone 7c, a small amount of the isomeric 2,3-dimethyl-6-hydroxy-7-benzofuranyl 2-methoxybenzyl ketone (8c) was also obtained.

b) By the Acylation of 2,3-Dimethyl-6-methoxybenzofuran (9), Followed by Demethylation. i) Methoxy-ketone 10b: Powdered anhydrous aluminum chloride (2 g) was added to a solution of 9[13] (2.6 g) and phenylacetyl chloride (2.4 g) in benzene (15 ml); the mixture was stirred at room temperature for 2 hr and then poured into ice water and extracted with benzene. The benzene was distilled off, and the residual product was recrystallized from ethanol to give the 2,3-dimethyl-6-methoxy-5-benzofuranyl benzyl ketone (10b), which had a negative ferric chloride color reaction in ethanol.

ii) Demethylation: Amixture of 10b (1.5 g), benzene (10 ml), and aluminum chloride (1 g) was refluxed for 10 min. The cooled mixture was poured into ice water and extracted with benzene. The benzene was distilled off, and the residue was recrystallized from ethanol to give the ketone 7b, which had a positive ferric chloride color reaction in ethanol. Some 10b was recovered from the mother solution.

c) By the Acylation of 9 in One Step. Aluminum chloride (3.1 g) was added to a solution of 9 (2.6 g) and phenylacetyl chloride (2.4 g) in benzene (15 ml); the mixture was stirred at room temperature for 2 hr and then refluxed for 10 min. The cooled mixture was treated much as has been described above to give the ketone 7b.

The ketone 7a was also prepared by this procedure.

d) By the Furan-ring Formation on 2,4-Dihydroxyphenyl Ketones through 4-(α-Acetylethoxy)-2-hydroxyphenyl Ketones (11). A mixture of the 2,4-dihydroxyphenyl methyl ketone (6.8 g), 3-chlorobutanone-2 (5.2 g), anhydrous potassium carbonate (15 g), potassium iodide (0.5 g), and acetone (60 ml) was refluxed for 7 hr. The cooled mixture was treated with water and extracted with ether. The ethereal layer was washed with aqueous sodium hydroxide, and then the ether was distilled off. The residual product was distilled to give the 4-(α-acetylethoxy)-2-hydroxyphenyl methyl ketone (11a); bp 148—153°C/2.5 mmHg, 5.9 g (59%). In the case of 11a, the analytical sample was recrystallized from petroleum ether.

A mixture of this crude ether 11a (1.5 g) and PPA

TABLE 2. THE PREPARATION OF 7-(α-ACETYLETHOXY)- AND FUROISOFLAVONES

Compd.	Starting compound[a]	Procedure[b] temp.×hr	Yield %
	7-(α-Acetylethoxy)isoflavones		
16b	7-Hydroxy-IF	A, (A), Reflux×5	51
16c	7-Hydroxy-2'-methoxy-IF	A, (A), (KI), Reflux×8	49
17b	7-Hydroxy-2-methyl-IF	A, (M), Reflux×5	91
17c	7-Hydroxy-2'-methoxy-2-methyl-IF	A, (M), (KI), Reflux×6	62.5
	Furoisoflavones		
12b	16b	B, 100°×1	33
12b	16b	C, 30°×1.5	43
12b	2b	D, Reflux×8	c)
12c	16c	B, 100°×2	c)
12c	2c	D, Reflux×8	19.5
12d	2d	D, Reflux×8	63
13b	17b	B, 100°×2	70
13b	17b	C, 30°×1.5	80
13c	2c	E, Reflux×12	46
13c	17c	B, 100°×2	62.5
13c	2c	E, Reflux×12	46.5
13d	2d	E, Reflux×12	75
14b	7b	D, Reflux×8	58
14c	7c	D, Reflux×8	58
15b	7b	E, Reflux×12	18.5
15c	7c	E, Reflux×12	46

a) IF: Isoflavone. b) A: Chlorobutanone and potassium carbonate in acetone (A) or methyl ethyl ketone (M) with or without the addition of potassium iodide (KI), B: Polyphosphoric acid (n=2.5), C: Concentrated sulfuric acid, D: Ethyl orthoformate, piperidine and pyridine, E: Acetic anhydride and sodium acetate. c) A small amount.

TABLE 3. THE PHYSICAL CONSTANTS AND ANALYSES OF NEW COMPOUNDS

Compd.	Mp°C (solvent)[a]	ν_{OH}^{KBr} cm^{-1}	ν_{CO}^{KBr} cm^{-1}	Formula	Found C%	Found H%	Calcd C%	Calcd H%
			Benzofuranyl Ketones					
2a	58.5—60(E)		1630	$C_{12}H_{12}O_3$	70.26	5.99	70.57	5.92
2b	116—117(E)		1635	$C_{18}H_{16}O_3$	76.53	5.78	77.12	5.75
2c	108—109.5(E)		1640	$C_{19}H_{18}O_4$	73.13	5.66	73.53	5.85
2d	152—153.5(E)		1630	$C_{21}H_{22}O_6$	67.93	5.77	68.09	5.99
3a	206—208(E)	3050	1630	$C_{12}H_{12}O_3$	70.10	5.83	70.57	5.92
3c	222—223(E)	3250	1640	$C_{19}H_{18}O_4$	73.61	5.99	73.53	5.85
3d	221—222(E)	3530 3150	1665	$C_{21}H_{22}O_6 \cdot H_2O$	65.09	6.17	64.93	6.23
7b	167—168(E)		1635	$C_{18}H_{16}O_3$	76.83	5.81	77.12	5.75
7c	122—123(E)		1645	$C_{19}H_{18}O_4$	73.86	5.96	73.53	5.85
7d	140.5—144.5(E)		1648	$C_{21}H_{22}O_6$	68.18	6.13	68.09	5.99
8c	142—145(E)		1640	$C_{19}H_{18}O_4$	73.18	5.75	73.53	5.85
10b	98—98.5(E)		1675	$C_{19}H_{18}O_3$	77.49	6.17	77.53	6.16
			Aryloxybutanones					
11a	56—57(P)		1720 1645	$C_{12}H_{14}O_4$	64.80	6.67	64.85	6.35
16b	113.5—114.5(A)		1710 1620	$C_{19}H_{16}O_4$	74.13	5.05	74.01	5.23
16c	138—138.5(A)		1710 1640	$C_{20}H_{18}O_5$	70.90	5.33	70.99	5.36
17b	114—115(A)		1700 1630	$C_{20}H_{18}O_4$	74.68	5.45	74.52	5.63
17c	121—123(A)		1715 1645	$C_{21}H_{20}O_5$	71.66	5.78	71.58	5.72
			Furoisoflavones					
12b	155—156(E)		1640[b]	$C_{19}H_{14}O_3$	78.50	4.43	78.68	4.85
12c	161—163(E)		1650[b]	$C_{20}H_{16}O_4$	74.62	5.20	74.99	5.03
12d	205—206(E)		1645	$C_{22}H_{20}O_6$	69.51	5.65	69.46	5.30
13b	164—165(E)		1640[b]	$C_{20}H_{16}O_3$	79.16	5.21	78.93	5.30
13c	182—183(E)		1640[b]	$C_{21}H_{18}O_4$	75.15	5.27	75.43	5.43
13d	209—209.5(E)		1640	$C_{23}H_{22}O_6$	70.10	5.72	70.04	5.62
14b	187.5—188.5(A)		1650	$C_{19}H_{14}O_3$	78.91	4.98	78.60	4.85
14c	197—198(A)		1655	$C_{20}H_{16}O_4$	74.73	5.17	74.99	5.03
15b	194—196(E)		1647	$C_{20}H_{16}O_3$	79.22	5.46	78.93	5.30
15c	181—182(A)		1645	$C_{21}H_{18}O_4$	75.42	5.22	75.43	5.43

a) A: Ethyl acetate, E: Ethanol, P: Petroleum ether. b) These of homologous compounds are: furo-(2'',3'':7,8)isoflavone, 1640; 2'-methoxy-, 1650; 2-methyl, 1635; 2'-methoxy-2-methyl-, 1640.

(n=1.5, 40 g) was heated at 80°C for 1 hr with stirring. The cooled mixture was poured into ice water and then extracted with ether. The ethereal layer was washed with aqueous sodium carbonate, and the ether was distilled off. The residual product was crystallized to give the ketone 7a. A small amount of the isomeric ketone 2a was also obtained from the mother solution of the crystallization of 7a.

Similarly, the ketone 7b and a small amount of isomeric 2b were also obtained by this procedure through the 4-(α-acetylethoxy)-2-hydroxyphenyl benzyl ketone (11b); bp 180—220°C/4 mmHg (yield 76%), ν_{max}: 1720 and 1620 cm^{-1} (CO). The ketone 2c and the isomeric 7c were also obtained through the 4-(α-acetylethoxy)-2-hydroxyphenyl 2-methoxybenzyl ketone (11c); bp 200—250°C/10 mmHg (yield 79%).

e) By the Alkaline Degradation of Furoisoflavones. A mixture of the furoisoflavone, 12b (1.1 g), 50% aqueous potassium hydroxide (5 g), and ethanol (60 m*l*) was refluxed for 3 hr, and then most of the ethanol was distilled off. The residue was diluted with water and acidified. The crystalline product formed was collected and recrystallized from ethanol to give the ketone 2b.

Similarly, the ketones 2b and 2c were obtained from the furoisoflavones 13b and 13c respectively.

The Preparation of Furoisoflavones. *a) By the Furan-ring Formation on 7-Hydroxyisoflavones through 7-(α-Acetylethoxy)isoflavones (16). i) The Preparation of 16*: A mixture of 7-hydroxyisoflavone (10 g), 3-chlorobutanone-2 (4.5 g), anhydrous potassium carbonate (17 g), and acetone (150 m*l*) was refluxed for 5 hr. The cooled mixture was filtered, the solvent was distilled off, and the residue was treated with water and then heated for a while on a water-bath. The precipitates

TABLE 4. THE UV SPECTRA OF FUROISOFLAVONES

Compd.	λ_{max}^{EtOH} mμ[a] (log ε)
12b[b]	214[s](4.51), 255(4.59), 320(3.78)
12c[b]	215[s](4.52), 249(4.51), 280[s](4.01), 318(3.75)
12d	213[s](4.64), 243(4.58), 252[s](4.56), 295(4.15)
13b[b]	212(4.53), 251(4.66), 285[s](3.88), 314(3.79)
13c[b]	213(4.59), 247(4.68), 280[s](4.06), 313(3.79)
13b	245(4.60), 292(4.06)
14b	213[s](4.55), 254(4.66), 338(3.83)
14c	212[s](4.54), 250(4.58), 335(3.77)
15b	212[s](4.51), 250(4.69), 332(3.82)
15c	248(4.64), 280[s](3.97), 330(3.78)

a) [s]: Shoulder. b) λ_{max} of homologous compounds are: furo(2'',3'':7,8)isoflavone, 253(4.50), 310(3.86); 2'-methoxy-, 220[s](4.31), 305(3.70); 2-methyl-, 247(4.46), 304(3.76); 2'-methoxy-2-methyl, 240(4.62), 275[s](4.02), 303(3.72).

formed on cooling were collected and recrystallized to give 7-(α-acetylethoxy)-isoflavone (16b).

ii) The Dehydro-cyclization of 16 by PPA: A mixture of 16b (1.3 g) and PPA (n=2.5, 30 g) was poured into ice water; the crystalline product thus formed was collected and recrystallized from ethanol to give 4'',5''-dimethylfuro[2'',3'':7,8]isoflavone (12b).

iii) The Dehydro-cyclization of 16 by Sulfuric Acid: The isoflavone 16b (2 g) was gradually added to concentrated sulfuric acid (20 g) at about 30°C; the mixture was allowed to stand at that temperature for 1.5 hr, and then poured into ice water. The crystalline product thus formed was recrystallized from ethanol to give 12b.

Similarly, 4'',5''-dimethyl-2'-methoxyfuro[2'',3'':7,8]isoflavone (12c), 2,4'',5''-trimethylfuro[2'',3'':7,8]isoflavone (13b), and 2'-methoxy-2,4'',5''-trimethylfuro-[2'',3'':7,8]isoflavone (13c) were also prepared by this procedure through 7-(α-acetylethoxy)-2-methylisoflavone (17b) and its 2'-methoxy derivative (17c).

b) By the Action of Ethyl Orthoformate on the Benzofuranyl Ketones. A mixture of the ketone 2b (0.2 g), ethyl orthoformate (2 g), piperidine (1 drop) and pyridine (8 ml) was refluxed for 8 hr. Dilute hydrochloric acid was added to the cooled mixture, and the crystalline product formed was collected and recrystallized from ethanol to give 12b.

Similarly, 12c and 4'',5''-dimethyl-2',4',5'-trimethoxyfuro[2'',3'':7,8]isoflavone (12d) as well as the isomeric 4'',5''-dimethylfuro[3'',2'':6,7]isoflavone (14b) and 4'',5''-dimethyl-2'-methoxyfuro[3'',2'':6,7]isoflavone (14c) were also prepared by this procedure.

c) By the Action of Acetic Anhydride and Sodium Acetate on the Benzofuranyl Ketones. A mixture of the ketone 2b (0.2 g), sodium acetate (2 g), and acetic anhydride (10 ml) was refluxed for 12 hr, and then the cooled mixture was poured into ice water and left overnight. The crystalline product formed was collected and recrystallized from ethanol to give 13b.

Similarly, 13c and 2',4',5'-trimethoxy-2,4'',5''-trimethylfuro[2'',3'':7,8]isoflavone (13d), as well as the isomeric 2,4'',5''-trimethylfuro[3'',2'':6,7]isoflavone (15b) and 2'-methoxy-2,4'',5''-trimethylfuro-[3'',2'':6,7]isoflavone (15c), were also prepared by this procedure.

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