Synthesis and Reaction of 6-Substituted 3-Methoxycarbonyl-4-methylthio-2*H*-pyran-2-one Derivatives

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Reaction of aryl and styryl methyl ketones **1a-m** with dimethyl bis(methylthio)methylenemalonate (**2**) in the presence of potassium hydroxide in dimethyl sulfoxide gave the corresponding methyl 6-aryl- and 6-styryl-4-methylthio-2-oxo-2*H*-pyran-3-carboxylates **3a-m**.

6-Aryl derivatives **3a-d,g** were treated with sodium methoxide in methanol to give the corresponding 6-aryl-4-methoxy-2*H*-pyran-2-ones **8a-d** and **9**. Phenylcoumalin (**7a**) and paracotoin (**7b**) were synthesized by the desulfurization of 6-aryl-4-methylthio-2*H*-pyran-2-ones **4a,b**. Similarly, anibine (**8e**) was also synthesized from **3g**.

Treatment of **3** with hydrogen peroxide or 3-chloroperoxybenzoic acid gave the corresponding 4-methylsulfiny-2*H*-pyran-2-ones **10a-f** in good yields. Displacement reactions of **10a-f** with nucleophilic reagents are also described.

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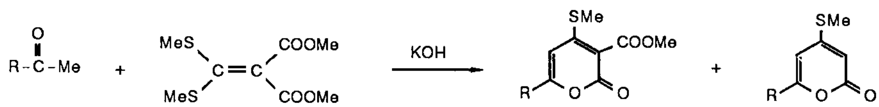
Ketene dithioacetals appropriately functionalized (cyano, methoxycarbonyl, sulfonyl, nitro, acyl, *etc.*,) are versatile reagents which have been extensively utilised in heterocyclic synthesis [1-8]. As part of our expanding studies on ketene dithioacetals, we now wish to report the synthesis of naturally occurring 2*H*-pyran-2-ones and related derivatives using dimethyl bis(methylthio)methylenemalonate (**2**) [9].

A number of 4-hydroxy-2*H*-pyran-2-ones and their methyl ethers have been isolated from natural sources [2,3, 10-20]. We have recently described a convenient method for the preparation of 6-aryl or 6-styryl-4-methylthio-2-oxo-2*H*-pyran-3-carbonitriles by the reaction of various methyl ketones with ketene dithioacetal, methyl 2-cyano-2,3-bis-(methylthio)acrylate [2]. The methylthio group at the 4-position on the pyrone ring in these compounds is highly reactive with nucleophiles, such as amines or active methylene compounds, to give the corresponding 4-substituted 2*H*-pyran-2-ones. These compounds also react with methoxide anion to give 4-methoxy-2-oxo-2*H*-pyran-3-carbonitrile, which can be regarded as useful intermediates for the preparation of natural products. However, we were un-

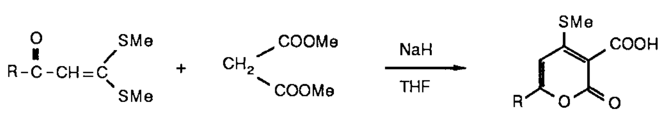
Chart 1



1a-m **2** **3a-m** **4b-d**

1,3a R = C_6H_5
b R = *p*-MeO-C_6H_4
c R = 3,4-$(MeO)_2$-C_6H_3
d R = 3,4-O-CH_2-O-C_6H_3
e R = 3,4,5-$(MeO)_3$-C_6H_2
f R = *p*-Br-C_6H_4
g R = 3-pyridyl
h, R = 2-pyridyl
i, R = 1-methylpyrrol-2-yl
j, R = 2-thienyl
k, R = 2-furyl
l, R = *p*-MeO-styryl
m, R = 3,4-O-CH_2-O-styryl

4b, R = *p*-MeO-C_6H_4
c, R = 3,4-$(MeO)_2$-C_6H_3
d, R = 3,4-O-CH_2-C_6H_3



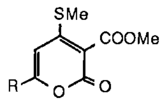
5a-c **6a - c**

5a, R = C_6H_5
b, R = *p*-MeO-C_6H_5
c, R = *p*-Br-C_6H_5

6a, R = C_6H_5
b, R = *p*-MeO-C_6H_5
c, R = *p*-Br-C_6H_5

Table I

6-Substituted 3-Methoxycarbonyl-4-methylthio-2*H*-pyran-2-ones



No.	R	Yield (%)	mp (°C)	Recryst. Solvent	Appearance	Formula	Analysis (%) Calcd./Found C	H	N	S
3a	C_6H_5	32	186	C_6H_6	pale yellow needles	$C_{14}H_{12}O_4S$	60.86 60.73	4.38 4.41		11.60 11.76
b	*p*-MeO-C_6H_4	39	181	MeOH-C_6H_6	yellow needles	$C_{15}H_{14}O_5S$	58.81 58.77	4.61 4.81		10.47 10.11
c	3,4-$(MeO)_2$-C_6H_3	23	170	MeOH	yellow needles	$C_{16}H_{16}O_6S$	57.13 57.11	4.79 4.81		9.53 9.47
d	3,4-O-CH_2-O-C_6H_3	37	234	MeOH-C_6H_6	greenish yellow needles	$C_{15}H_{12}O_6S$	56.25 56.09	3.78 3.77		10.01 9.94
e	3,4,5-$(MeO)_3$-C_6H_2	41	159	MeOH-C_6H_6	yellow needles	$C_{17}H_{18}O_7S$	55.73 55.73	4.95 5.01		8.75 8.76
f	*p*-Br-C_6H_4	59	229	MeOH-C_6H_6	yellow needles	$C_{14}H_{11}BrO_4S$	47.32 47.42	3.10 3.00		9.02 9.15
g	3-pyridyl	34	193	MeOH-C_6H_6	pale yellow needles	$C_{13}H_{11}NO_4S$	56.31 56.20	4.00 4.00	5.05 5.06	11.56 11.64
h	2-pyridyl	48	194	MeOH-C_6H_6	pale yellow needles	$C_{13}H_{11}NO_4S$	56.31 56.30	4.00 3.99	5.05 5.01	11.56 11.32
i	1-methylpyrrol-2-yl	7	170	MeOH	yellow needles	$C_{13}H_{13}NO_4S$	59.12 59.11	4.69 4.72	5.01 4.96	11.48 11.45
j	2-thienyl	42	181	MeOH	yellow needles	$C_{11}H_{10}O_4S_2$	51.05 51.18	3.57 3.57		22.71 22.80
k	2-furyl	25	187	MeOH	yellow needles	$C_{12}H_{10}O_5S$	54.13 53.90	3.79 3.79		12.10 12.05
l	*p*-MeO-styryl	15	189	MeOH-C_6H_6	yellow needles	$C_{17}H_{16}O_5S$	61.43 61.21	4.85 4.93		9.65 9.86
m	3,4-O-CH_2-O-styryl	17	184	MeOH-C_6H_6	yellow amorphous	$C_{17}H_{14}O_6S$	58.96 58.65	4.08 4.08		9.24 9.07

	IR ν (potassium bromide) cm^{-1}	UV (ethanol) λ max nm (log ε)		NMR δ (ppm)
3a	1700 (C=O) 1680 (C=O)	238 (4.05), 254 (4.24), 329 (4.24), 360 (4.18)	T	2.78 (3H, s, SCH_3), 4.13 (3H, s, OCH_3), 7.40 (1H, s, 5-H), 7.59-7.772 (3H, m, 3', 4', 5'-H), 7.95-8.04 (2H, m, 2',6'-H)
b	1720 (C=O) 1675 (C=O)	243 (4.22), 258 (4.08), 342 (4.26), 386 (4.41)	T	2.79 (3H, s, SCH_3), 4.04 (3H, s, OCH_3), 4.19 (3H, s, OCH_3), 7.23 (2H, d, J = 10 Hz, 3',5'-H), 7.41 (1H, s, 5-H), 8.11 (2H, d, J = 10 Hz, 2',6'-H)
c	1722 (C=O) 1672 (C=O)	237 (4.22), 246 (4.20), 389 (4.40)	C	2.55 (3H, s, SCH_3), 3.92 (3H, s, OCH_3), 3.95 (6H, s, OCH_3), 6.67 (1H, s, 5-H), 6.94 (1H, d, J = 9 Hz, 5'-H), 7.39 (1H, d, J = 1.5 Hz, 2'-H), 7.48 (1H, dd, J = 1.5, 9 Hz, 6'-H)
d	1720 (C=O) 1672 (C=O)	239 (4.22), 389 (4.36)	T	2.76 (3H, s, SCH_3), 4.14 (3H, s, OCH_3), 6.11 (2H, s, O-CH_2-O), 6.99 (1H, d, J = 9 Hz, 5'-H), 7.27 (1H, s, 5-H), 7.42 (1H, d, J = 2 Hz, 2'-H), 7.66 (1H, dd, J = 2, 9 Hz, 6'-H)
e	1720 (C=O) 1690 (C=O)	254 (4.14, shoulder), 380 (4.33)	C	2.56 (3H, s, SCH_3), 3.93 (12H, s, OCH_3), 6.64 (1H, s, 5-H), 7.25 (2H, s, 2',6'-H)
f	1705 (C=O)	245 (3.82), 338 (4.08)	D	2.65 (3H, s, SCH_3), 3.78 (3H, s, OCH_3), 7.12 (1H, s, 5-H), 7.72 (2H, d, J = 9 Hz, 3',5'-H), 7.95 (2H, d, J = 9 Hz, 2',6'-H)

Table I (continued)

	IR ν (potassium bromide) cm^{-1}	UV (ethanol) λ max nm (log ε)		NMR δ (ppm)
g	1750 (C=O) 1688 (C=O)	246 (4.20), 325 (4.23)	D	2.67 (3H, s, SCH_3), 3.77 (3H, s, OCH_3), 7.22 (1H, s, 5-H), 7.59 (1H, dd, J = 5, 8 Hz, 5'-H), 8.36 (1H, dd, J = 1.5, 8 Hz, 4'-H), 8.78 (1H, dd, J = 2, 8 Hz, 6'-H), 9.24 (1H, d, J = 1.5 Hz, 2'-H)
h	1727 (C=O) 1678 (C=O)	223 (3.96), 247 (4.25), 328 (4.24)	D	2.64 (3H, s, SCH_3), 3.81 (3H, s, OCH_3), 7.51 (1H, s, 5-H), 7.56-7.66 (1H, m, 4'-H), 7.98-8.08 (2H, m, 3',5'-H), 8.76-8.86 (1H, m, 6'-H)
i	1720 (C=O) 1668 (C=O)	232 (3.93), 263 (4.04), 338 (4.04), 396 (4.47)	D	2.58 (3H, s, SCH_3), 3.74 (3H, s, N-CH_3), 3.89 (3H, s, OCH_3), 6.16-6.24 (1H, m, 4'-H), 6.68 (1H, s, 5-H), 7.05 (1H, dd, J = 2, 4 Hz, 3 -H), 7.16-7.22 (1H, m, 5'-H)
j	1715 (C=O) 1685 (C=O)	234 (4.00), 275 (4.15), 390 (4.32)	C	2.54 (3H, s, SCH_3), 3.91 (3H, s, OCH_3), 6.58 (1H, s, 5-H), 7.15 (1H, dd, J = 3.7, 4.8 Hz, 4'-H), 7.57 (1H, dd, J = 0.9, 4.8 Hz, 3'-H), 7.72 (1H, dd, J = 0.9, 3.7 Hz, 5'-H)
k	1730 (C=O) 1680 (C=O)	228 (3.90), 260 (4.18), 345 (4.23) 365 (4.31)	C	2.55 (3H, s, SCH_3), 3.92 (3H, s, OCH_3), 6.62 (1H, dd, J = 1.8, 3.5 Hz, 4'-H), 6.70 (1H, s, 5-H), 7.18 (1H, bd, J = 3.5 Hz, 3'-H), 7.58 (1H, dd, J = 0.8, 1.8 Hz, 5'-H)
l	1725 (C=O) 1675 (C=O)	245 (4.28), 276 (4.08), 416 (4.38)	C	2.49 (3H, s, SCH_3), 3.85 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 6.22 (1H, s, 5-H), 6.49 (1H, d, J = 16 Hz, C=C-H), 6.91 (2H, d, J = 8.8 Hz, 2',6'-H), 7.49 (2H, d, J = 8.8 Hz, 3',5'-H), 7.66 (1H, d, J = 16 Hz, C=C-H)
m	1725 (C=O) 1675 (C=O)	245 (4.25), 270 (4.12), 418 (4.32)	D	2.53 (3H, s, SCH_3), 3.75 (3H, s, OCH_3), 6.08 (2H, s, O-CH_2-O), 6.68 (1H, s, 5-H), 6.96 (1H, d, J = 8 Hz, 6'-H), 6.96 (1H, d, J = 16 Hz, C=C-H), 7.22 (1H, d, J = 8 Hz, 5'-H), 7.34 (1H, s, 2 -H), 7.42 (1H, d, J = 16 Hz, C=C-H)

T, Trifluoroacetic acid. C, Deuteriochloroform. D, DMSO-d_6.

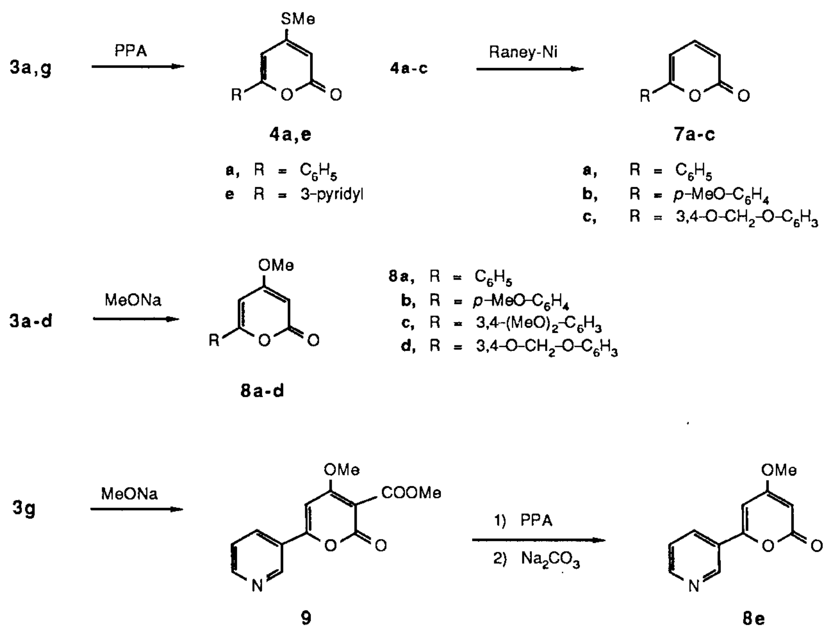
able to obtain the decyanation products from those 3-cyano compounds. Recently, the decarboxylation of ethyl 2-oxo-2*H*-pyran-3-carboxylate derivatives, which are prepared by the reaction of dimethyl ethoxymethylenemalonate with active methylene compounds, has been reported [20]. We attempted the alternative preparation of 6-aryl-4-methylthio-2*H*-pyran-2-one derivatives, substituted with ester groups at the 3-position on the pyrone ring, using ketene dithioacetal, **2**. Methyl 6-aryl-4-methylthio-2-oxo-2*H*-pyran-3-carboxylates **3a-k** were synthesized from various acetyl compounds (**1a**, acetophenone; **b**, *p*-methoxyacetophenone, **c**, 3,4-dimethoxyacetophenone; **d**, 3,4-dimethylenedioxyacetophenone; **e**, 3,4,5-trimethoxyacetophenone; **f**, *p*-bromoacetophenone; **g**, 3-acetylpyridine; **h**, 2-acetylpyridine; **i**, 1-methyl-2-acetylpyrrole; **j**, 2-acetylthiophene; **k**, 2-acetylfuran; **l**, *p*-methoxybenzalacetone; **m**, 3,4-methylenedioxybenzalacetone) and **2** in the presence of powdered potassium hydroxide as a base in dimethyl sulfoxide (DMSO) gave the corresponding 2*H*-pyran-2-one derivatives **3a-m** in yields shown in Table I. When compounds **1b,c**, or **d** was allowed to react with **2** under the same conditions, the products deesterified, 6-aryl-4-methylthio-2*H*-pyran-2-ones **4b-d**, which appeared from the filtrate on standing, were simultaneously obtained in low yield.

Next, we attempted alternatively the application of α-oxoketene dithioacetals to the synthesis of 2*H*-pyran-2-one derivatives. These α-oxoketene dithioacetals **5a-c** have been shown to be versatile synthons for heterocyclic compounds by Junjappa, *et al.* [21-24]. α-Oxoketene dithioacetals **5a-c** reacted with dimethyl malonate in the presence of sodium hydride in tetrahydrofuran (THF) to give 6-aryl-4-methylthio-2-oxo-2*H*-pyran-3-carboxylic acids **6a-c**. These products were formed by displacement of the methylthio group on the ketene dithioacetal followed by cyclization and saponification when the reaction mixture was taken-up in water.

Phenylcoumalin (**7a**) [25,26] and paracotoin (**7b**) [27,28] have no methoxy group on the 4-position of the pyrone ring. This problem is resolved by the desulfurization of the methylthio group in compounds **4**. We tried to synthesize phenylcoumalin and paracotoin. The deesterified products, 6-aryl-4-methylthio-2*H*-pyran-2-ones **4a,e** were easily prepared by the treatment of **83a,g** with polyphosphoric acid (PPA) at 100°. Finally, the desulfurization of **4a-c** was easily effected with Raney-nickel to afford the desired compounds, 6-aryl-2*H*-pyran-2-ones **7a-e** in 42, 45, and 49% yields, respectively.

Some 6-aryl-4-methoxy-2*H*-pyran-2-ones are known as natural products such as 4-methoxyphenylcoumarin (**8a**)

Chart 2



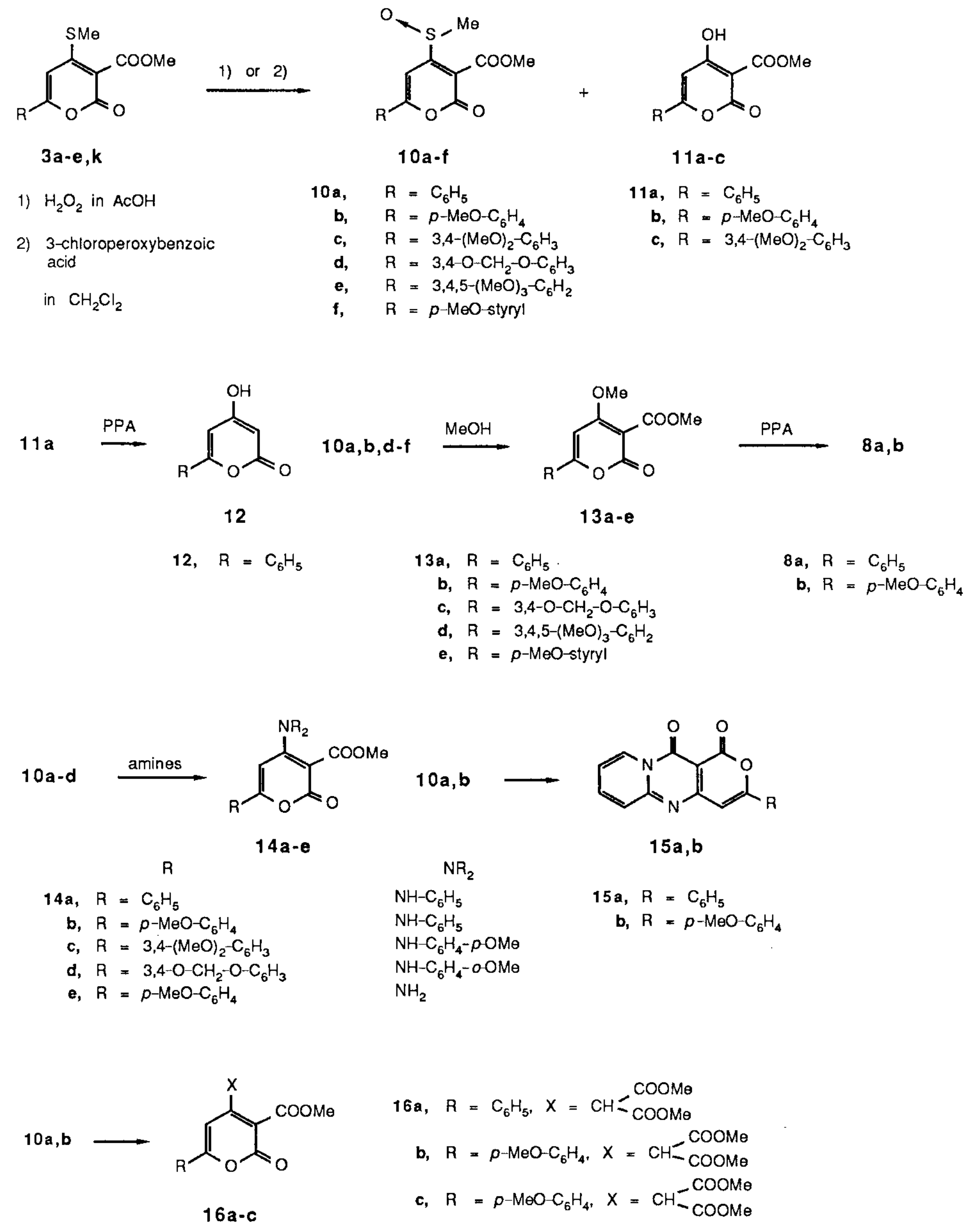
[28], methoxyparacotoin (**8d**) [27], anibine (**8e**) [27], *etc.* It has been reported that the methylthio group in 4-methylthio-oxo-2*H*-pyran-3-carbonitrile undergoes displacement readily with nucleophilic reagents such as amines, active methylene compounds, or methoxide anion [2]. Treatment of **3a-d** with sodium methoxide in methanol afforded the corresponding 4-methoxy derivatives **8a-d** which underwent displacement of methoxide anion followed by deesterification. When **3g** was treated with sodium methoxide in methanol, 4-methoxy-6-(3-pyridyl)-2-oxo-2*H*-pyran-3-carboxylate (**9**) was obtained in 67% yield. The treatment of **9** with PPA at 100° for 5 hours afforded anibine, 4-methxoy-6-(3-pyridyl)-2*H*-pyran-2-one (**8e**) as colorless needles, mp 176°, in 86% yield [29].

However, displacement of the methylthio group in compounds **3** with amines or active methylene compounds was not successful. In order to obtain the various 4-substituted 2*H*-pyran-2-one derivatives, activation of the methylthio group is necessary. It is known that nucleophilic displacement of alkylsulfinyl and alkylsulfonyl groups occurs more rapidly than the corresponding displacement of alkylthio groups [30]. Treatment of **3a** with 30% hydrogen peroxide in acetic acid gave the sulfinyl derivative **10a** and the hydroxy derivative **11a** in 84% and 9% yields, respectively. It is assumed that the 4-hydroxy compound **11a** was produced from 4-methylsulfonyl compound which has the high reactivity to nucleophiles. Compound **11a** also prepared by the hydrolysis of **10a** with water in acetic acid at 100° for 5 hours. Compound **11a** was treated with PPA at 100° to give 4-hydroxy-6-phenyl-2*H*-pyran-2-one (**12**) in good yield, which is a key intermediate for the synthesis of Hyprenone-A [19]. Compound **10a** was also prepared by oxidation of **3a** with 3-chloroperoxybenzoic acid in dichloromethane in 92% yield. Compounds **10b-f** were also obtained in a manner similar to the above described method. The 4-methylsulfinyl group on **10** was smoothly displaced with methoxide anion to give 4-methoxy derivatives **13a-e**, which were readily converted to **8a** and **b**.

Displacement reaction of **3** with nucleophilic reagents such as amines or active methylene compounds was unsuccessful. However, **10** was smoothly reacted with amines (aniline, *p*-methoxyaniline, *o*-methoxyaniline, ammonia) or active methylene compounds (dimethyl malonate, methyl cyanoacetate) to give the corresponding displacement products **14a-e** and **16a-c** in good yields. When compounds **10a,b** reacted with 2-aminopyridine, 2-phenylpyrano-[3,4-*d*]pyrido[1,2-*a*]pyrimidine derivatives **15a,b** were obtained in 86 and 67% yields, respectively.

The displacement reaction of **2** with acetyl compounds is an efficient method for the preparation of 4-methylthio-2*H*-pyran-2-one derivatives. These 2*H*-pyran-2-ones are valuable intermediates in the preparation of 4-substituted 2*H*-pyran-2-ones since they have an active methylthio group against the various nucleophiles.

Chart 3



EXPERIMENTAL

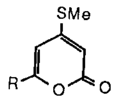
All melting points were determined in a capillary tube and are uncorrected. Infrared (ir) spectra were recorded in potassium bromide pellets on a JASCO IRA-2 spectrometer, ultraviolet (uv) absorption spectra were determined on a Hitachi EP-S2 spectrometer in 95% ethanol, and nuclear magnetic resonance (nmr) spectra were obtained with a JNM-PS-100 (100 MHz) and JNM-FX-90 (90 MHz) spectrometers with tetramethylsilane as an internal standard. Mass (ms) spectra were recorded on a JEOL JMS-01SG and JMS-DX303 spectrometers.

General method for the Preparation of Methyl 4-Methylthio-2-oxo-2*H*-pyran-3-carboxylates **3a-m**.

A mixture of 10 mmoles of acetyl compounds **1** (**a**, acetophenone; **b**, *p*-methoxyacetophenone; **c**, 3,4-dimethoxyacetophenone; **d**, 3,4-methylenedioxyacetophenone; **e**, 3,4,5-trimethoxyacetophenone; **f**, *p*-bromoacetophenone; **g**, 3-acetylpyridine; **h**, 2-acetylpyridine; **i**, 1-methyl-2-acetalpyrrole; **j** 2-acetylthiophene; **k**, 2-acetylfuran; **l**, *p*-methoxybenzalacetone; **m**, 3,4-methylenedioxybenzalacetone), 10 mmoles of dimethyl bis(methylthio)methylenemalonate (**2**), 40 mmoles of powdered potassium hydroxide, and 50 ml of DMSO was stirred at room temperature for 3-5 hours. The reaction mixture was poured into 300 ml of ice-water and the whole was stirred at room temperature for 4-5 hours. The yellow precipitate that appeared were collected by filtration, washed with water, and recrystallized from benzene + methanol to give the corresponding 4-methylthio-2-oxo-2*H*-pyran-3-carboxylates **3a-m**. The above filtrate was acidified with 10% hydrochloric acid, and the mixture was allowed to stand for 48 hours. The precipitate that appeared was collected by filtration, washed with water and recrystallized from methanol to give the corresponding 4-methylthio-2*H*-pyran-2-ones **4b-d** (see Table I). The spectral data and elemental analysis are listed in Tables I and II.

Table II

6-Substituted 4-Methylthio-2*H*-pyran-2-one



No.	R	Yield (%)	mp (°C)	Recryst. Solvent	Appearance	Formula	Analysis (%) Calcd./Found C	H	S
4a	C_6H_5	80	135	MeOH	colorless needles	$C_{12}H_{10}O_2S$	66.03 65.93	4.62 4.62	14.69 14.74
b	*p*-MeO-C_6H_4	33 [a]	61	MeOH	colorless needles	$C_{13}H_{12}O_3S$	62.89 62.72	4.87 4.82	12.91 12.92
c	3,4-(MeO)$_2$-C_6H_3	8 [a]	146	MeOH	colorless needles	$C_{14}H_{14}O_4S$	60.42 60.43	5.07 5.01	11.52 11.59
d	3,4-O-CH_2-O-C_6H_3	15 [a]	242	MeOH-C_6H_6	colorless needles	$C_{13}H_{10}O_4S$	59.53 59.39	3.84 3.76	12.22 12.30
e	3-pyridyl	91	182	MeOH	colorless needles	$C_{11}H_9NO_2S$	60.27 60.33	4.14 4.19	14.62 14.52

[a] These yields were obtained by the reaction of **1b-d** with **2**.

No.	MS m/z (M^+)	IR ν (potassium bromide) cm^{-1}	UV (ethanol) λ max nm (log ε)		NMR δ (ppm)
4a	218	1725 (C=O)	233 (4.07), 251 (4.27), 299 (4.22)	C	2.48 (3H, s, SCH_3), 5.90 (1H, d, J = 1.5 Hz, 3 -H), 6.52 (1H, d, J = 1.5 Hz, 5-H), 7.42-7.52 (3H, m, 3', 4', 5'-H), 7.71-7.86 (2H, m, 2',6'-H)
b	248	1722 (C=O)	234 (4.14), 262 (4.20), 301 (4.22), 348 (4.24)	C	2.43 (3H, s, SCH_3), 3.79 (3H, s, OCH_3), 5.82 (1H, d, J = 1 Hz, 3-H), 6.37 (1H, d, J = 1 Hz, 5-H), 6.89 (2H, d, J = 9 Hz, 2',6'-H), 7.71 (2H, d, J = 9 Hz, 3',5'-H)
c	278	1735 (C=O)	240 (4.23), 260 (4.22), 302 (4.13), 357 (4.27)	C	2.46 (3H, s, SCH_3), 3.92 (3H, s, OCH_3), 3.94 (3H, s, OCH_3), 5.94 (1H, d, J = 1.5 Hz, 3-H), 6.42 (1H, d, J = 1.5 Hz, 5-H), 6.94 (1H, d, J = 9 Hz, 5'-H), 7.33 (1H, d, J = 1.5 Hz, 2'-H), 7.22 (1H, dd, J = 1.5, 9 Hz, 6'-H)
d	262	1730 (C=O)	236 (4.40), 260 (4.29), 303 (4.17), 356 (4.33)	T	2.59 (3H, s, SCH_3), 6.04 (2H, s, O-CH_2-O), 6.36 (1H, d, J = 1 Hz, 3-H), 6.93 (1H, d, J = 8.5 Hz, 5'-H), 6.94 (1H, d, J = 1 Hz, 5-H), 7.31 (1H, d, J = 2 Hz, 2'-H), 7.48 (1H, dd, J = 2, 8.5 Hz, 6'-H)
e	219	1730 (C=O)	240 (4.22), 253 (4.29), 300 (4.28)	C	2.50 (3H, s, SCH_3), 5.95 (1H, d, J = 1.5 Hz, 3-H), 6.57 (1H, d, J = 1.5 Hz, 5-H), 7.49 (1H, dd, J = 4.8, 8 Hz, 5'-H), 8.16 (1H, m, 4'-H), 8.68 (1H, dd, J = 1.5, 4.8 Hz, 6'-H), 9.02 (1H, d, J = 1.9 Hz, 2'-H)

C, Deuteriochloroform. T, Trifluoroacetic acid.

4-Methylthio-6-phenyl-2-oxo-2*H*-pyran-3-carboxylic Acid (**6a**).

To a suspension of 0.72 g (50%, 15 mmoles) of sodium hydride in mineral oil in 100 ml of absolute tetrahydrofuran, 0.26 g (20 mmoles) of dimethyl malonate was added portionwise at room temperature and then 10 mmoles of **5a** was added. The mixture was stirred at room temperature for 30 minutes and refluxed for 2 hours. After evaporation of the solvent, the residue was dissolved in 200 ml of cold water and acidified with 10% hydrochloric acid. The precipitate was collected by filtration and recrystallized from methanol + benzene to give pale yellow needles, mp 248°, in 34% yield, ir (potassium bromide): ν max cm^{-1} 1725, 1690 (C=O); uv (ethanol): λ max nm (log ε) 239 (4.02), 258 (4.19), 350 (4.17); ^{1}H nmr (deuteriochloroform): δ 2.61 (3H, s, SMe), 6.99 (1H, s, 5-H), 7.51-7.63 (3H, m, 3',4',5'-H), 7.85-7.97 (2H, m, 2',6'-H), 12.93 (1H, bs, OH).

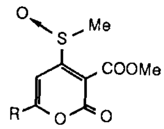
Anal. Calcd. for $C_{13}H_{10}O_4S$: C, 58.53; H, 3.83; S, 12.22. Found: C, 58.41; H, 3.88; S, 12.35.

6-(*p*-Methoxyphenyl)-4-methylthio-2-oxo-2*H*-pyran-3-carboxylic Acid (**6b**).

This compound was synthesized from **5b** in 26% yield in a manner similar to that used for the preparation of **6a**. An analytical sample was recrystallized from methanol + benzene to give greenish yellow prisms, mp 218°; ir (potassium bromide): ν max cm^{-1} 1725, 1645 (C=O); uv (ethanol): λ max nm (log ε) 245 (4.12), 265 (4.15), 380 (4.31); ^{1}H nmr (deuteriochloroform): δ 2.59 (3H, s, SMe), 3.91 (3H, s, OMe), 6.87 (1H, s, 5-H), 7.02 (2H, d, J = 9.0 Hz, 3', 5'-H), 7.87 (2H, d, J = 9.0 Hz, 2', 6'-H), 12.95 (1H,

Table III

6-Substituted 3-Methoxycarbonyl-4-methylsulfinyl-2*H*-pyran-2-ones



No.	R	Yield (%)	mp (°C)	Recryst. Solvent	Appearance	Formula	Analysis (%) Calcd./Found C	H	S
10a	C_6H_5	84 (92) [a]	163	MeOH	yellow needles	$C_{14}H_{12}O_5S$	57.52 57.30	4.14 4.21	10.97 10.59
b	*p*-MeO-C_6H_4	78 (92) [a]	207	MeOH	yellow needles	$C_{15}H_{14}O_6S$	55.89 55.92	4.38 4.39	9.95 9.94
c	3,4-(MeO)$_2$-C_6H_3	57 (91) [a]	222	MeOH	yellow needles	$C_{16}H_{16}O_7S$	54.54 54.32	4.58 4.61	9.10 8.94
d	3,4-O-CH_2-O-C_6H_3	96	219	MeOH-C_6H_6	orange needles	$C_{15}H_{12}O_7S$	53.57 53.44	3.60 3.61	9.53 9.33
e	3,4,5-(MeO)$_3$-C_6H_2	89	202	MeOH	orange needles	$C_{17}H_{18}O_8S$	53.40 53.17	4.73 4.78	8.39 8.25
f	*p*-MeO-styryl	88	218	MeOH-C_6H_6	orange leaflets	$C_{17}H_{16}O_6S$	68.61 58.91	4.63 4.60	9.20 9.15

[a] These yields were obtained by the oxidation of **10a**, **b**, and **c** with 3-chloroperoxybenzoic acid.

	IR (potassium bromide) ν max cm^{-1}	UV (ethanol) λ max nm (log ϵ)	NMR (deuteriochloroform) δ
10a	1745 (C=O) 1680 (C=O)	257 (3.98), 380 (4.23)	2.97 (3H, s, $SOCH_3$), 3.96 (3H, s, OCH_3), 7.49-7.60 (3H, m, 3′, 4′, 5′-H), 7.67 (1H, s, 5-H), 7.97-8.08 (2H, m, 2′, 6′-H)
b	1730 (C=O) 1675 (C=O)	256 (3.93), 412 (4.39)	2.96 (3H, s, $SOCH_3$), 3.90 (3H, s, OCH_3), 3.95 (3H, s, OCH_3), 7.00 7.00 (2H, d, J = 9.1 Hz, 3′, 5′-H), 7.57 (1H, s, 5-H), 8.00 (2H, d, J = 9.1 Hz, 2′, 6′-H)
c	1735 (C=O) 1670 (C=O)	265 (3.99), 424 (4.39)	2.97 (3H, s, $SOCH_3$), 3.96 (3H, s, OCH_3), 3.98 (3H, s, OCH_3), 6.96 (1H, d, J = 8.6 Hz, 5′-H), 7.44 (1H, d, J = 2.2 Hz, 2′-H), 7.58 (1H, s, 5-H), 7.70 (1H, dd, J = 2.2, 8.6 Hz, 6′-H)
d	1735 (C=O) 1670 (C=O)	265 (3.88), 420 (4.36)	2.96 (3H, s, $SOCH_3$), 3.95 (3H, s, OCH_3), 6.09 (2H, s, O-CH_2-O), 6.92 (1H, d, J = 8.4 Hz, 5′-H), 7.45 (1H, d, J = 1.8 Hz, 2′-H), 7.53 (1H, s, 5-H), 7.64 (1H, dd, J = 1.8, 8.4 Hz, 6′-H)
e	1750 (C=O) 1670 (C=O)	266 (3.74), 410 (4.31)	2.98 (3H, s, $SOCH_3$), 3.95 (9H, s, OCH_3 × 3), 3.96 (3H, s, OCH_3), 7.20 (2H, s, 2′, 6′-H), 7.58 (1H, s, 5-H)
f	1740 (C=O) 1680 (C=O)	292 (4.15), 450 (4.54)	2.94 (3H, s, $SOCH_3$), 3.86 (3H, s, OCH_3), 3.94 (3H, s, OCH_3), 6.65 (1H, d, J = 15.8 Hz, ethenyl-H), 6.94 (2H, d, J = 8.8 Hz, 2′, 6′-H), 2′, 6′-H), 7.12 (1H, s, 5-H), 7.73 (1H, d, J = 15.8 Hz, ethenyl-H)

bs, OH).

Anal. Calcd. for $C_{14}H_{12}O_5S$: C, 59.47; H, 4.28; S, 11.34. Found: C, 59.45; H, 4.27; S, 11.28.

6-(*p*-Bromophenyl)-4-methylthio-2-oxo-2*H*-pyran-3-carboxylic Acid (**6c**).

This compound was synthesized from **5c** in 44% yield in a manner similar to that used for the preparation of **6a**. An analytical sample was recrystallized from methanol to give yellow needles, mp 231°; ir (potassium bromide): ν max cm^{-1} 1722, 1655 (C=O); uv (ethanol): λ max nm (log ϵ) 243 (3.97), 263 (4.23), 352 (4.25); ^{1}H nmr (deuteriodimethylsulfoxide): δ 2.66 (3H, s, SMe), 7.25 (1H, s, 5-H), 7.82 (2H, d, J = 9.0 Hz, 2′, 6′-H), 8.04 (2H, d, J = 9.0 Hz, 3′, 5′-H).

Anal. Calcd. for $C_{13}H_9BrO_4S$: C, 45.77; H, 2.66; S, 9.40. Found: C, 45.34; H, 2.63; S, 9.50.

Deesterification of **3a** or **e** with Polyphosphoric Acid (PPA).

A mixture of 10 mmoles of **3a** or **e** and 20 g of PPA was heated at 100° for 5-6 hours. The reaction mixture was poured into 300 ml of ice-water, and the whole was stirred at room temperature for 1-2 hours. In the case of **3e**, an aqueous solution of the reaction mixture was neutralized with sodium carbonate. The precipitate was collected by filtration, washed with water and recrystallized from methanol to give pale yellow crystals (**4a** and **e**). The spectral data and elemental analysis are listed in Table II.

6-Phenyl-2*H*-pyran-2-one (Phenylcoumalin) (**7a**).

A suspension of 10 mmoles of **4a** and 10 ml of Raney-nickel prepared by the W-2 method in 50 ml of ethanol was refluxed for 10 hours. After removal of Raney-nickel and the evaporation of the ethanol. The residue was recrystallized from hexane to give **7a** as colorless needles, mp 68° (lit [26] mp 68°), in 42% yield; ^{1}H nmr (deuteriochloroform): δ 6.29 (1H, d, J = 9.5 Hz, 3-H), 6.68 (1H, d, J = 7.0 Hz, 5-H), 7.38-7.54 (4H, m, 4-H, 3', 4', 5'-H), 7.80-7.92 (2H, m, 2', 6'-H).

6-*p*-Methoxyphenyl-2*H*-pyran-2-one (**7b**).

This compound was synthesized from **4b** in 45% yield in a manner similar to that described for the preparation of **7a**. A crude product was recrystallized from methanol to give colorless needles, mp 98° (lit [31] mp 101°); ^{1}H nmr (deuteriochloroform): δ 3.85 (3H, s, OMe), 6.20 (1H, d, J = 9.5 Hz, 3-H), 5.94 (1H, d, J = 6.7 Hz, 5-H), 6.94 (2H, d, J = 9.5 Hz, 2', 6'-H), 7.42 (1H, d, J = 6.7, 9.5 Hz, 4-H), 7.80 (2H, d, J = 9.5 Hz, 3', 5'-H).

6-(3,4-Methylenedioxyphenyl)-2*H*-pyran-2-one (Paracotoin) (**7c**).

This compound was synthesized from **4c** in 49% yield in a manner similar to that described for the preparation of **7a**. A crude product was recrystallized from methanol to give colorless needles, mp 150° (lit [27] mp 151°]; ^{1}H nmr (trifluoroacetic acid): δ 6.03 (2H, s, O-CH$_2$-O), 6.58 (1H, d, J = 9.0 Hz, 3-H), 6.92 (1H, d, J = 9.0 Hz, 5'-H), 6.99 (1H, d, J = 7 Hz, 5-H), 7.32 (1H, d, J = 2.0 Hz, 2'-H), 7.49 (1H, dd, J = 2.0, 9.0 Hz, 6'-H), 7.88 (1H, dd, J = 7.0, 9.0 Hz, 4-H).

4-Methoxy-6-phenyl-2*H*-pyran-2-one (4-Methoxyphenylcoumalin) (**8a**).

Sodium methoxide (10 mmoles) was added to a solution of 20 mmoles of **3a** in 100 ml of methanol, and the mixture was refluxed on a water bath for 5 hours, followed by evaporation down to 20 ml. This concentrate was poured into 200 ml of water. The precipitate was collected by filtration and recrystallized from hexane-benzene to give colorless needles, mp 136° (lit [28] mp 130°), in 24% yield; ir (potassium bromide): ν max cm^{-1} 1710, 1640 (C=O); uv (ethanol): λ max nm (log ε) 221 (4.25), 236 (4.21), 317 (4.16); ^{1}H nmr (deuteriochloroform): δ 3.86 (3H, s, OMe), 5.54 (1H, d, J = 2.0 Hz, 3-H), 6.44 (1H, d, J = 2.0 Hz, 5-H), 7.44-7.55 (3H, m, 3', 4', 5'-H), 7.76-7.90 (2H, m, 2', 6'-H).

4-Methoxy-6-(*p*-methoxyphenyl)-2*H*-pyran-2-one (**8b**).

This compound was synthesized from **3b** in 74% yield in a manner similar to that used for the preparation of **8a**. An analytical sample was recrystallized from methanol to give colorless needles, mp 153°; ir (potassium bromide): ν max cm^{-1} 1725 (C=O); uv (ethanol): λ max nm (log ε) 253 (3.96), 330 (4.27); ^{1}H nmr (deuteriochloroform): δ 3.85 (6H, s, OMe), 5.49 (1H, d, J = 2.0 Hz, 3-H), 6.32 (1H, d, J = 2.0 Hz, 5-H), 6.97 (2H, d, J = 9.0 Hz, 2', 6'-H), 7.81 (2H, d, J = 9.0 Hz, 3', 5'-H).

Anal. Calcd. for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21. Found: C, 67.02; H, 5.23.

4-Methoxy-6-(3,4-dimethoxyphenyl)-2*H*-pyran-2-one (**8c**).

This compound was synthesized from **3c** in 69% yield in a manner similar to that used for the preparation of **8a**. An analytical sample was recrystallized from methanol to give colorless needles, mp 174°; ir (potassium bromide): ν max cm^{-1} 1730 (C=O); uv (ethanol): λ max nm (log ε) 338 (4.32); ^{1}H nmr (trifluoroacetic acid): δ 4.03 (3H, s, OMe), 4.05 (3H, s, OMe), 4.08 (3H, s, OMe), 6.09 (1H, d, J = 1.5 Hz, 3-H), 6.86 (1H, d, J = 1.5 Hz, 5-H), 7.13 (1H, d, J = 8.0 Hz, 5'-H), 7.57 (1H, d, J = 1.0 Hz, 2'-H), 7.62 (1H, dd, J = 1.0, 8.0 Hz, 6'-H).

Anal. Calcd. for $C_{14}H_{14}O_5$: C, 64.12; H, 5.38. Found: C, 63.88; H, 5.45.

4-Methoxy-6-(3,4-methylenedioxyphenyl)-2*H*-pyran-2-one(methoxyparacotoin) (**8d**).

This compound was synthesized from **3d** in 74% yield in a manner similar to that used for the preparation of **8a**. The crude product was recrystallized from methanol to give colorless needles, mp 224° (lit [27] mp 224°); ir (potassium bromide): ν max cm^{-1} 1720 (C=O); uv (ethanol): λ max nm (log ε) 340 (3.96); ^{1}H nmr (deuteriodimethylsulfoxide): δ 3.85 (3H, s, OMe), 5.61 (1H, d, J = 2.0 Hz, 3-H), 6.11 (2H, s, O-CH$_2$-O), 6.75 (1H, d, J = 2.0 Hz, 5-H), 7.01 (1H, d, J = 9.0 Hz, 5'-H), 7.37-7.49 (2H, m, 2', 6'-H).

Methyl 4-Methoxy-6-(3-pyridyl)-2-oxo-2*H*-pyran-3-carboxylate (**9**).

This compound was synthesized from **3g** in 67% yield in a manner similar to that used for the preparation of **8a-d**. An analytical sample was recrystallized from methanol to give colorless needles, mp 242°; ir (potassium bromide): ν max cm^{-1} 1763, 1713 (C=O); uv (ethanol); λ max nm (log ε) 233 (4.35), 266 (3.80), 338 (4.23); ^{1}H nmr (deuteriochloroform): δ 3.91 (3H, s, OMe), 4.09 (3H, s, OMe), 6.77 (1H, s, 5-H), 7.50 (1H, dd, J = 5.0, 8.0 Hz, 5'-H), 8.25 (1H, bd, J = 8.0 Hz, 4'-H), 8.75 (1H, dd, J = 2.0, 5.0 Hz, 6'-H), 9.13 (1H, d, J = 1.5 Hz, 2'-H).

Anal. Calcd. for $C_{13}H_{13}NO_5$: C, 59.77; H, 4.24; N, 5.36. Found: C, 59.72; H, 4.23; N, 5.32.

4-Methoxy-6-(3-pyridyl)-2*H*-pyran-2-one (Anibine) (**8e**).

A mixture of 10 mmoles of **9** and 19 g of PPA was heated at 100° for 3 hours. The reaction mixture was poured into 100 ml of ice-water and neutralized with sodium carbonate. The precipitate was collected by filtration, washed with water, and recrystallized from methanol to give colorless needles, mp 176° (lit [27] mp 176°) in 86% yield.

Methyl 6-Aryl-4-methylsulfinyl-2-oxo-2*H*-pyran-3-carboxylates **10a-f**.

Method a.

A solution of 10 mmoles of **3a-e** and 10 ml of 30% hydrogen peroxide in 150 ml of acetic acid was heated at 40-50° for 1 hour. The reaction mixture was poured into 700 ml of ice-water, and the precipitate that appeared was collected by filtration. The products were recrystallized from methanol + benzene to give **10a-f** as yellow or orange crystals (Table III). The above filtrate was allowed to stand for a day. The precipitate that appeared was collected by filtration and was recrystallized from methanol to give **10a-c**. The yields of **11a**, **b** and **c** were 11, 7, and 6%, respectively.

Method b.

A solution of 1.73 g (10 mmoles) of 3-chloroperoxybenzoic acid in 15 ml of dichloromethane was added dropwise during 10 minutes to a solution of 100 mmoles of **3a-e** in 30 ml of dichloromethane, and the reaction mixture was stirred at room temperature for 3 hours. The dichloromethane was removed under reduced pressure to give a yellow solid. This solid was washed with methanol for removal of 3-chlorobenzoic acid to yield the corresponding 3-methylsulfinyl compounds **10a-f**. The spectral data and elemental analysis of **10a-f** are listed in Table III.

Table III

Methyl 4-Hydroxy-2-oxo-6-phenyl-2*H*-pyran-2-one (**11a**).

A solution of 5 mmoles of **10a** and 2 ml of water in 30 ml of acetic acid was heated at 100° for 10 hours. The reaction mixture was poured into 200 ml of ice-wtaer. The precipitate that appeared was collected by filtration and recrystallized from methanol to give tan plates, mp 125°, in 73% yield; ir (potassium bromide): ν max cm^{-1} 3450 (OH), 1740, 1640 (C=O); uv (ethanol): λ max nm (log ε) 218 (4.30), 237 (4.21), 280 (3.86), 326 (4.13); ^{1}H nmr (deuteriochloroform): δ 4.00 (3H, s, OMe), 6.58 (1H, s, 5-H), 7.46-7.56 (3H, m, 3', 5'-H), 7.83-7.94 (2H, m, 2', 6'-H), 13.89 (1H, s, OH).

Anal. Calcd. for $C_{14}H_{12}O_6$: C, 60.87; H, 4.38. Found: C, 60.65; H, 4.40.

Methyl 4-Hydroxy-6-(*p*-methoxyphenyl)-2-oxo-2*H*-pyran-3-carboxylate (**11b**).

This compound was synthesized from **10b** in a manner similar to that described for the preparation of **11a**. An analytical sample was recrystallized from methanol to give tan needles, mp 187°, in 68% yield; ir (potassium bromide): ν max cm^{-1} 3450 (OH), 1740, 1650 (C=O); uv (ethanol): λ max nm (log ε) 222 (4.41), 247 (4.21), 324 (4.34); ^{1}H nmr (deuteriochloroform): δ 3.88 (3H, s, OMe), 3.99 (3H, s, OMe), 6.47 (1H, s, 5-H), 6.97 (2H, d, J = 9.1 Hz, 3', 5'-H), 7.84 (1H, d, J = 9.1 Hz, 2', 6'-H), 13.85 (1H, s, OH).

Anal. Calcd. for $C_{14}H_{12}O_6$: C, 60.87; H, 4.38. Found: C, 60.65; H, 4.40.

Methyl 4-Hydroxy-6-(3,4-dimethoxyphenyl)-2-oxo-2*H*-pyran-3-carboxylate (**11c**).

This compound was synthesized from **10d** in a manner similar to that used for the preparation of **11a**. An analytical sample was recrystallized from methanol to give tan needles, mp 202°; ir (potassium bromide): ν max nm^{-1} 3450 (OH), 1740, 1620 (C=O); uv (ethanol): λ max nm (log ε) 225 (4.41), 288 (3.89), 335 (4.25); ^{1}H nmr (deuteriochloroform): δ 3.95 (3H, s, OMe), 3.96 (3H, s, OMe), 4.00 (3H, s, OMe), 6.48 (1H, s, 5-H), 6.93 (1H, d, J = 8.6 Hz, 5'-H), 7.34 (1H, d, J = 2.2 Hz, 2'-H), 7.51 (1H, dd, J = 2.2, 8.6 Hz, 6'-H).

Anal. Calcd. for $C_{15}H_{14}O_7$: C, 58.83; H, 4.61. Found: C, 58.56; H, 4.60.

4-Hydroxy-6-phenyl-2*H*-pyran-2-one (**12**).

A mixture of 1.23 g (5 mmoles) of **11a** and 10 g of PPA was heated at 100° for 4 hours. The reaction mixture was poured into 100 ml of ice-water. The precipitate that appeared was collected by filtration and recrystallized from methanol to give a colorless powder, mp 257° (lit [32] mp 254-256°), in 92% yield; ^{1}H nmr (deuteriochloroform + deuteriodimethylsulfoxide): δ 3.00 (1H, bs, OH), 5.56 (1H, d, J = 1.8 Hz, 3-H), 6.48 (1H, d, J = 1.8 Hz, 5-H), 7.35-7.49 (3H, m, phenyl-H), 7.70-7.86 (2H, m, phenyl-H).

Methyl 4-Methoxy-6-phenyl-2-oxo-2*H*-pyran-3-carboxylate (**13a**).

A solution of 0.58 g (2 mmoles) of **10a** in 200 ml of methanol was refluxed for 15 hours. After removal of the solvent, the residue was recrystallized from methanol to give pale yellow needles, mp 126°, in 81% yield; ir (potassium bromide): ν max cm^{-1} 1735, 1672 (C=O); uv (ethanol): λ max nm (log ε) 224 (4.17), 240 (4.05), 270 (3.64), 340 (4.22); ^{1}H nmr (deuteriochloroform): δ 3.89 (3H, s, OMe), 4.05 (3H, s, OMe), 7.41-7.57 (3H, m, 3', 4', 5'-H), 7.81-7.92 (2H, m, 2', 6'-H).

Anal. Calcd. for $C_{14}H_{12}O_5$: C, 64.61; H, 4.65. Found: C, 64.28; H, 4.69.

Methyl 4-Methoxy-6-(*p*-methoxyphenyl)-2-oxo-2*H*-pyran-3-carboxylate (**13b**).

This compound was synthesized from **10b** in 78% yield in a manner similar to that used for the preparation of **13a**. An analytical sample was recrystallized from methanol to give yellow leaflets, mp 165°; ir (potassium bromide): ν max cm^{-1} 1725, 1675 (C=O); uv (ethanol): λ max nm (log ε) 236 (4.16), 255 (3.76, shoulder), 280 (3.67), 360 (4.35); ^{1}H nmr (deuteriochloroform): δ 3.87 (3H, s, OMe), 3.88 (3H, s, OMe), 4.04 (3H, s, OMe), 6.53 (1H, s, 5-H), 6.97 (2H, d, J = 9.1 Hz, 3', 5'-H), 7.82 (2H, d, J = 9.1 Hz, 2', 6'-H).

Anal. Calcd. for $C_{15}H_{14}O_6$: C, 62.07; H, 4.86. Found: C, 61.88; H, 4.85.

Methyl 4-Methoxy-6-(3,4-methylenedioxyphenyl)-2-oxo-2*H*-pyran-3-carboxylate (**13c**).

This compound was synthesized from **10d** in 67% yield in a manner similar to that used for the preparation of **13a**. An analytical sample was recrystallized from methanol to give pale yellow needles, mp 195°; ir (potassium bromide): ν max cm^{-1} 1735, 1675 (C=O); uv (ethanol): λ max nm (log ε) 226 (4.26), 288 (3.30), 370 (4.31); ^{1}H nmr (deuteriochloroform): δ 3.89 (3H, s, OMe), 4.03 (3H, s, OMe), 6.06 (2H, s, O-CH_2-O), 6.49 (1H, s, 5-H), 6.89 (1H, d, J = 8.4 Hz, 5'-H), 7.29 (1H, d, J = 1.6 Hz, 2'-H), 7.45 (1H, dd, J = 1.6 Hz, 8.4 Hz, 6'-H).

Anal. Calcd. for $C_{16}H_{16}O_7$: C, 60.00; H, 5.04. Found: C, 59.75; H, 5.11.

Methyl 4-Methoxy-6-(3,4,5-trimethoxyphenyl)-2-oxo-2*H*-pyran-3-carboxylate (**13d**).

This compound was synthesized from **10e** in 88% yield in a manner similar to that used for the preparation of **13a**. An analytical sample was recrystallized from methanol to give pale yellow needles, mp 154°; ir (potassium bromide): ν cm^{-1} 1740, 1680 (C=O); uv (ethanol): λ max nm (log ε), 217 (4.61), 348 (4.36); ^{1}H nmr (deuteriochloroform): δ 3.89 (3H, s, OMe), 3.92 (3H, s, OMe), 3.93 (6H, s, 2 × OMe), 4.06 (3H, s, OMe), 6.53 (1H, s, 5-H), 7.03 (2H, s, 2', 6'-H).

Anal. Cacld. for $C_{17}H_{18}O_8$: C, 58.29; H, 5.18. Found: C, 58.35; H, 5.20.

Methyl 4-Methoxy-6-(*p*-methoxystyryl)-2-oxo-2*H*-pyran-3-carboxylate (**13e**).

This compound was synthesized from **10f** in 66% yield in a manner similar to that described for the preparation of **13a**. An analytical sample was recrystallized from methanol + benzene to give yellow needles, mp 208°; ir (potassium bromide): ν max cm^{-1} 1730, 1670 (C=O); uv (ethanol): λ max nm (log ε) 220 (4.31), 238 (4.26), 388 (4.57); ^{1}H nmr (deuteriochloroform): δ 3.85 (3H, s, OMe), 3.88 (3H, s, OMe), 3.98 (3H, s, OMe), 6.04 (1H, s, 5-H), 6.49 (2H, d, J = 15.8 Hz, ethenyl-H), 6.92 (2H, d, J = 8.8 Hz, 3', 5'-H), 7.48 (2H, d, J = 8.8 Hz, 2', 6'-H), 7.62 (1H, d, J = 15.8 Hz, ethenyl-H).

Anal. Calcd. for $C_{17}H_{16}O_6$: C, 64.55; H, 5.10. Found: C, 64.33; H, 5.08.

Deesterification of **13a,b** with PPA.

A mixture of 10 mmoles of **13a** or **13b** and 10 g of PPA was heated at 100° for 5 hours. The reaction mixture was poured into 100 ml of ice-water, and the whole was stirred at room temperature for 1 hour. The precipitate was collected by filtration, washed with water, and recrystallized from methanol to give the corresponding 6-substituted 4-methoxy-2*H*-pyran-2-one **8a,b** in 91 and 67% yields, respectively.

Methyl 4-Anilino-2-oxo-6-phenyl-2*H*-pyran-3-carboxylate (**14a**).

A mixture of 2 mmoles of aniline and 1 mmole of **10a** was heated for 1 hour at 100°. The reaction mixture crystallized was washed with methanol and the product was recrystallized from methanol to give pale yellow plates, mp 190°, in 85% yield; ir (potassium bromide): ν max cm^{-1} 1720, 1630 (C=O); uv (ethanol): λ max nm (log ε) 223 (4.23), 247 (4.24), 325 (4.25); ^{1}H nmr (deuteriochloroform): δ 3.95 (3H, s, OMe), 6.50 (1H, s, 5-H), 7.20-7.81 (10H, m, phenyl-H), 11.59 (1H, bs, NH).

Anal. Calcd. for $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36. Found: C, 71.14; H, 4.76; N, 4.15.

Methyl 4-Anilino-6-(*p*-methoxyphenyl)-2-oxo-2*H*-pyran-3-carboxylate (**14b**).

This compound was synthesized from **10b** and aniline in 88% yield in a manner similar to that used for the preparation of **14a**. An analytical sample was recrystallized from methanol to give pale yellow needles, mp 177°; ir (potassium bromide): ν max cm^{-1} 3010 (NH), 1715, 1625 (C=O); uv (ethanol): λ max nm (log ε) 231 (4.42), 345 (4.48); ^{1}H nmr (deuteriochloroform): δ 3.84 (3H, s, OMe), 3.94 (3H, s, OMe), 6.40 (1H, s, 5-H), 6.89 (2H, d, J = 9.0 Hz, 3', 5'-H), 7.20-7.48 (5H, m, phenyl-H), 7.67 (2H, J = 9.0 Hz, 2', 6'-H), 11.43 (1H, bs, NH).

Anal. Calcd. for $C_{20}H_{17}NO_5$: C, 68.37; H, 4.88; N, 3.99. Found: C, 68.29; H, 4.93; N, 3.69.

Methyl 4-(*p*-Methoxyanilino)-6-(3,4-dimethoxyphenyl)-oxo-2*H*-pyran-3-carboxylate (**14c**).

This compound was synthesized from **10c** and *p*-methoxyaniline in 92% yield in a manner similar to that used for the preparation of **14a**. An analytical sample was recrystallized from methanol to give pale yellow needles, mp 191°; ir (potassium bromide): ν max cm^{-1} 3200 (NH), 1715, 1660 (C=O); uv (ethanol): λ max nm (log ε) 235 (4.50), 354 (4.46); ^{1}H nmr (deuteriochloroform): δ 3.86 (3H, s, OMe), 3.90 (3H, s, OMe), 3.91 (3H, s, OMe), 3.94 (3H, s, OMe), 6.31 (1H, s, 5-H), 6.78-7.28 (8H, m, phenyl-H), 11.39 (1H, s, NH).

Anal. Calcd. for $C_{22}H_{21}NO_7$: C, 64.23; H, 5.14; N, 3.40. Found: C, 64.25; H, 5.13; N, 3.16.

Methyl 4-(*o*-Methoxyanilino)-6-(3,4-methylenedioxyphenyl)-2-oxo-2*H*-pyran-3-carboxylate (**14d**).

This compound was synthesized from **10d** and *o*-methoxyaniline in 80% yield in a manner similar to that used for the preparation of **14a**. An analytical sample was recrystallized from methanol to give pale yellow prisms, mp 213°; ir (potassium bromide): ν max cm^{-1} 3150 (NH), 1730, 1650 (C=O); uv (ethanol): λ max nm (log ε) 218 (4.60), 352 (4.52); ^{1}H nmr (deuteriochloroform): δ 3.87 (3H, s, OMe), 3.94 (3H, s, OMe), 6.01 (2H, s, O-CH$_2$-O), 6.34 (1H, s, 5-H), 6.81 (1H, d, J = 8.6 Hz, 5'-H), 6.91-8.42 (6H, m, phenyl-H), 11.35 (1H, bs, NH).

Anal. Calcd. for $C_{21}H_{17}NO_7$: C, 63.80; H, 4.33; N, 3.54. Found: C, 63.87; H, 4.36; N, 3.22.

Methyl 4-Amino-6-(*p*-methoxyphenyl)-2-oxo-2*H*-pyran-3-carboxylate (**14e**).

A mixture of 5 ml of 28% ammonia and **10a** (1 mmole) was heated for 1 hour at 100°. The precipitate was collected by filtration and recrystallized from methanol to give yellow leaflets, mp 269°, in 70% yield; ir (potassium bromide): ν max cm^{-1} 3390, 3240 (NH), 1680 (C=O); uv (ethanol): λ max nm (log ε) 224 (4.54), 335 (4.44); nmr (deuteriochloroform + deuteriodimethylsulfoxide, 2:1): δ 3.79 (3H, s, OMe), 3.86 (3H, s, OMe), 6.53 (1H, s, 5-H), 6.99 (2H, d, J = 9.0 Hz, 3', 5'-H), 7.74 (2H, d, J = 9.0 Hz, 2', 6'-H), 8.10 (1H, bs, NH), 8.84 (1H, bs, NH).

Anal. Calcd. for $C_{14}H_{13}NO_5$: C, 61.09; H, 4.76; N, 5.09. Found: C, 60.94; H, 4.77; N, 5.14.

2-Phenylpyrano[3,4-*d*]pyrido[1,2-*a*]pyrimidine-4,5(4*H*,5*H*)-dione (**15a**).

A mixture of 1 mmole of **10a** and 1 mmole of 2-aminopyridine was heated 2 hours at 100°. The resulting red solid was washed with methanol, and recrystallized from methanol-benzene to give pale yellow crystals, mp 286°, in 86% yield; ir (potassium bromide): ν max nm^{-1} 1750, 1665 (C=O); uv (ethanol): λ max nm (log ε) 218 (4.28), 304 (4.45), 347 (4.35), 367 (4.37); ms: m/z 290 (M$^+$); ^{1}H nmr (deuteriochloroform): δ 6.91 (1H, s, 1-H), 7.24 (1H, near t, 8-H), 7.42-7.56 (3H, m, 3', 4', 5'-H), 8.64 (1H, near d, J = 8.0 Hz, 10-H), 8.83-7.04 (3H, m, 9, 2', 6'-H), 9.18 (1H, near d, J = 8.0 Hz, 7'-H).

Anal. Calcd. for $C_{17}H_{10}N_2O_3$: C, 70.34; H, 3.47; N, 9.65. Found: C, 70.31; H, 4.41; N, 9.19.

2-(*p*-Methoxyphenyl)pyrano[3,4-*d*]pyrido[1,2-*a*]pyrimidine-4,5(4*H*,5*H*)-dione (**15b**).

This compound was also synthesized from **10b** in a manner similar to that described for the preparation of **15a**. An analytical sample was recrystallized from methanol + benzene to give pale yellow needles, mp 308°, in 82% yield; ir (potassium bromide): ν max cm^{-1} 1765, 1670 (C=O); uv (ethanol): λ max nm (log ε) 225 (4.25), 320 (4.49), 360 (shoulder, 4.52), 380 (shoulder, 4.58), 388 (4.60); ms: m/z 320 (M$^+$); ^{1}H nmr (deuteriochloroform + deuteriodimethylsulfoxide, 2:1): δ 3.88 (3H, s, OMe), 6.80 (1H, s, 1-H), 6.99 (2H, d, J = 9.0 Hz, 3', 5'-H), 7.11-7.29 (1H, m, 8-H), 7.60 (1H, bd, J = 8.0 Hz, 10-H), 7.90 (2H, d, J = 9.0 Hz, 2', 6'-H), 9.14 (1H, bd, J = 8.0 Hz, 7-H).

Anal. Calcd. for $C_{18}H_{12}N_2O_4$: C, 67.50; H, 5.78; N, 8.75. Found: C, 67.29; H, 3.67; N, 8.63.

Reaction of **10a,b** with Active Methylene Compounds.

An active methylene compound (dimethyl malonate or methyl cyanoacetate) (20 mmoles) and 30 mmoles of potassium carbonate was added with stirring to a solution of 10 mmoles of **10a** or **10b** in 50 ml of DMSO at room temperature, and the mixture was stirred at the same temperature for 3 hours. The reaction mixture turned reddish-brown. This mixture was poured into 200 ml of ice-water, and the whole was acidified with 10% hydrochloric acid. The precipitate was collected by filtration, washed with water, and recrystallized from methanol to give the corresponding products **16a-c**.

Compound **16a**.

This compound was obtained in a yield of 88%, pale yellow needles, mp 121°; ir (potassium bromide): ν max cm^{-1} 1750, 1730, 1710, 1660 (C=O); uv (ethanol): λ max nm (log ε) 253 (4.26), 352 (4.27); ^{1}H nmr (deuteriochloroform): δ 3.82 (6H, s, 2 × OMe), 3.94 (3H, s, OMe), 5.17 (1H, s, -CH-), 6.91 (1H, s, 5-H), 7.40-7.52 (3H, m, phenyl-H), 7.81-7.92 (2H, m, phenyl-H).

Anal. Calcd. for $C_{18}H_{16}O_8$: C, 60.00; H, 4.48. Found: C, 60.01; H, 4.46.

Compound **16b**.

This compound was obtained in a yield of 90%, yellow needles, mp 121°; ir (potassium bromide): ν max cm^{-1} 1760, 1750, 1710, 1620 (C=O); uv (ethanol): λ max nm (log ε) 264 (4.06), 380 (4.37); ^{1}H nmr (deuteriochloroform): δ 3.82 (6H, s, 2 × OMe), 3.87 (3H, s, OMe), 3.93 (3H, s, OMe), 5.21 (1H, s, -CH-), 6.79 (1H, s, 5-H), 6.96 (2H, d, J = 9.0 Hz, phenyl-H), 7.82 (2H, d, J = 9.0 Hz, phenyl-H).

Anal. Calcd. for $C_{19}H_{18}O_9$: C, 58.46; H, 4.65. Found: C, 58.37; H, 4.56.

Compound **16c**.

This compound was obtained in a yield of 74%, pale yellow needles, mp 215°; ir (potassium bromide): ν max cm^{-1} 1755, 1650, 1630 (C=O); uv (ethanol): λ max nm 274, 340; (ethanol): λ min nm 244, 307; ^{1}H nmr (deuteriochloroform): δ 3.88 (3H, s, OMe), 4.12 (3H, s, OMe), 4.19 (3H, s, OMe), 6.99 (2H, d, J = 9.0 Hz, phenyl-H), 7.83 (1H, s, 5-H), 7.86 (2H, d, J = 9.0 Hz, phenyl-H), 14.51 (1H, bs, -CH-).

Anal. Calcd. for $C_{18}H_{15}NO_7$: C, 60.51; H, 4.23; N, 3.92. Found: C, 60.19; H, 4.27; N, 3.67.

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