Functionalization at C-5 and at the C-6 Methyl Group of 4-Methoxy-6-methyl-2-pyrone (1)

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A new entry to C-5 substituted 4-hydroxy-6-methyl-2-pyrones has been achieved. The best conditions to prepare the monobromo and the dibromo derivatives at C-3 and the C-6 methyl group of the title pyrone have been defined. The synthetic applicability of the phosphonium salts at CH_3-C-6 of both 4-methoxy-6-methyl-2-pyrone, **5**, and dehydroacetic acid, **2**, has also been evaluated.

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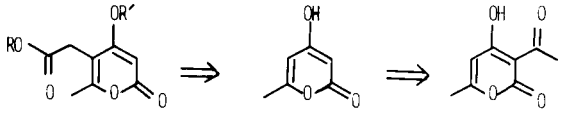
Introduction.

Many important polyketides have the 4-hydroxy(or methoxy)-6-alkyl(or alkenyl)-2-pyrone structure. Some of them also have an alkyl group at C-5, *e.g.*, citreoviridin (3), rosellisin (4), colletopyrone (5), elasnin (6), asteltoxin (7), and aurovertin B (8). Some significant synthetic products, *e.g.*, the Prelog-Djerassi lactone, an intermediate to methymycin (9), and also intermediate products to pederamide (10), although saturated δ-lactones, have still the common feature of an alkyl group at C-5. In the course of synthetic work carried out in our laboratory, we needed substantial amounts of 4-alkoxy-5-alkoxycarbonylmethyl-6-methyl-2-pyrone, **1**, (Scheme 1).

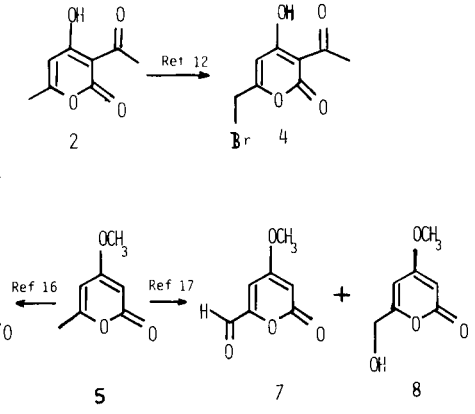
Scheme 1



1 3 2

3-Acetyl-4-hydroxy-6-methyl-2-pyrone, **2**, (dehydroacetic acid) is a convenient starting material for products with a δ-lactone structure since it is commercially readily available. Moreover, its easy deacetylation to 4-hydroxy-6-methyl-2-pyrone, **3**, (triacetic acid lactone) has been described (11). However, to the best of our knowledge, very few reactions at C-5 of either pyrones or their ethers have been reported. The reaction of **2** with bromine under iodine catalysis led to its 5-bromoderivative (12). Also, the reaction of **2** with benzhydryl alcohol with cobalt(II) catalysis produced the 5-benzhydryl derivative (13). The Harris method to enlarge the chain at C-6 produces also minor amounts of 5-alkyl products both on **2** and **3** (14,15). Compound **3** and its ethers are too active at C-3 for any reaction at C-5 to take place. Because of these reasons, we chose a transfer of functionalization from a 6-hydroxymethyl group by a Claisen rearrangement in order to prepare **1**. The oxidation of the C-6 methyl of compound **2** has been reported. The 3-acetyl-6-bromomethyl-4-hydroxy-2-pyrone, **4**, was obtained by Harris, *et al.*, (12). Also, Bloomer and coworkers have described (16) the preparation of 6-bromomethyl-4-methoxy-2-pyrone, **6**, from the methyl ether **5** (Scheme 2). In both cases brominations under radical conditions were required.

Scheme 2



2 4 6 5 7 8

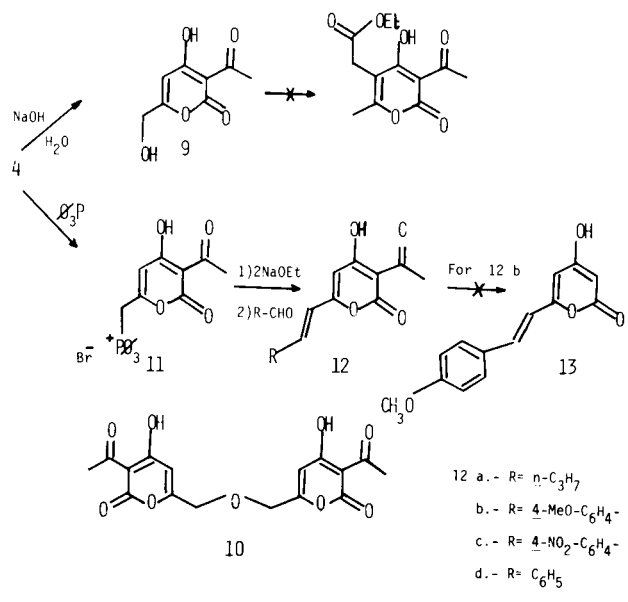
Suzuki *et al.*, used selenium dioxide (17) to oxidize **5** to a mixture of 6-formyl-4-methoxy-2-pyrone, **7**, and 6-hydroxymethyl-4-methoxy-2-pyrone, **8**, (opuntiol), the former being predominant (Scheme 2).

Results.

In our first experiments we found it easier to prepare **4** than **6**, because the synthesis of **6** was not reproduceable. We first converted the bromolactone **4** into 3-acetyl-4-hydroxy-6-hydroxymethyl-2-pyrone, **9**, by treatment with aqueous sodium hydroxide. Slow addition of **4** into a large excess of the alkaline solution was required to avoid the formation of the ether **10**. Unfortunatelly, treatment of **9** with ethyl orthoacetate with propionic acid catalysis gave only a black tar from which no definite products could be characterized (Scheme 3).

The lactone **4** is interesting because several natural products have a modified chain at C-6 of the pyrone nucleus. We have converted **4** into (3-acetyl-4-hydroxy-2-oxo-2*H*-pyran-6-yl)methyltriphenylphosphonium bromide, **11**. Its corresponding ylide, generated with two equivalents of sodium ethoxide, reacted with several aldehydes to afford the corresponding olefins **12a-d** in good yields. One of them is a suitable precursor for yangonin, **18**, a component of the kawa root *(Piper*

Scheme 3

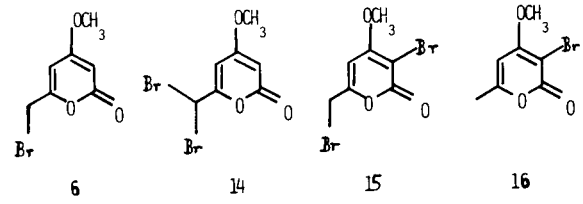


methysticum) (18). Deacylation of **12b** into **13** was not possible by the method of Collie (11) because extensive decomposition took place. Attempted deacetylation of **2** as a model compound under variety of conditions was also unsuccessful.

We then turned to **6** and **8** as precursors of **1**. Unfortunately, compound **5** brominated at C-3 predominantly. Therefore, conditions where radical bromination predominated had to be found. Consequently a broad search was undertaken for the best conditions to prepare all the monobromo and dibromo compounds at C-3 and CH_3-C-6. We have found that high dilution favours the formation of **6** (alkyl bromination) when **5** is refluxed in carbon tetrachloride with NBS, under irradiation, and in the presence of traces of benzoyl peroxide or AIBN. We hypothesize that under the above conditions enough NBS goes into the solution thus favouring the radical process.

Our best conditions to prepare the brominated products of the scheme 4 are collected at the table. The experiment 1 was performed under conditions which are usual in allylic brominations.

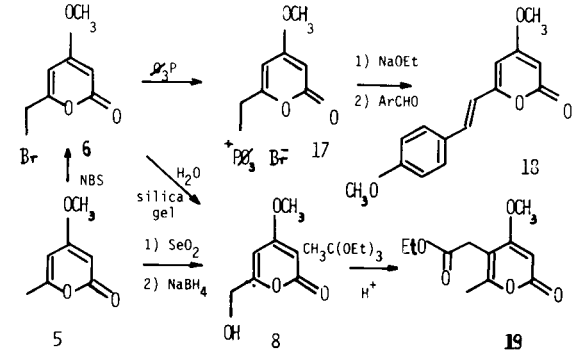
Scheme 4



The predominant reactivity of the C-3 position is evident. The same result was obtained under irradiation (experiment 2). However, when much higher dilution conditions were adopted (experiment 3), product **6** predominated. The ratio solvent/**5** of 23 ml/mmole must be considered as the inferior threshold for a convenient preparation of **6**. On the other hand, higher ratios (experiment 4) have a small influence on the yield of **6**, but significatively **14** took the place of **15** as byproduct when such higher ratios were used.

The dibromo compounds **14** and **15** were the predominant final products in experiments 5, and 6, and 7 when

Scheme 5



Table

Exp.	NBS/**5**	Solvent	ml solvent/ mmoles of **5**	Other conditions	Products (% isolated yield)
1	1.2	Carbon tetrachloride	3.5	Benzoyl peroxide, ref, 17 hours	**16** (86)
2	1.2	Carbon tetrachloride	5.6	Benzoyl peroxide, hν (500 W), ref, 7 hours	**16** (83)
3	1.2	Carbon tetrachloride	23	Benzoyl peroxide, hν (1000 W), ref, 2 hours	**6** (68), **15** (9), **5** (9)
4	1.1	Carbon tetrachloride	35	AIBN, hν (1000 W), ref, 1.5 hours	**6** (63), **14** (14), **5** (22)
5	2.2	Carbon tetrachloride	70	Benzoyl peroxide, hν (1000 W), ref, 1 hour	**14** (81)
6	2.3	Benzene	14	AIBN, hν (500 W), rt, 6 hours	**15** (86)
7	2.2	Carbon tetrachloride	5	Benzoyl peroxide, hν (500 W), ref, 2 hours	**15** (82)

the appropriate NBS/**5** ratios were used. Again, **14** was obtained under high dilution conditions and **15** under lower dilution. The nature of the radical iniciator had no influence on the results.

The bromocompound **6** was converted into (4-methoxy-2-oxo-2*H*-pyran-6-yl)methyltriphenylphosphonium bromide, **17**, (16), (Scheme 5). The ylide of **17** was generated with sodium ethoxide and reacted with 4-methoxybenzaldehyde to afford yangonin, **18**, in 95% yield. The bromide **6** was hydrolized with silica gel and water to yield **8**, as reported for a related case (19). Access to **8** was also achieved by oxidation of **5** with selenium dioxide to yield aldehyde **7**, which was not isolated, but reduced directly with sodium borohydride. Both methods are good enough to prepare **8**. Finally, the hydroxylactone **8** was transformed into 5-ethoxycarbonylmethyl-4-methoxy-6-methyl-2-pyrone, **19**, in 55% yield by the Claisen rearrangement.

EXPERIMENTAL

Infrared and pmr spectra were respectively recorded with a Perkin-Elmer Infracord 720 and a Perkin-Elmer R-12 models. Mass spectra were run with a Hewlett-Packard 5930A spectrometer; only peaks with a m/e value above 20 are indicated unless they correspond to the molecular ion. Irradiations were performed with 500 or 100W bulbs at a distance of about 20 cm. Melting points are uncorrected. The NBS was purchased from Merck (No. 801949) and was dried with phosphorus pentoxide under vacuum before use.

3-Acetyl-6-bromomethyl-4-hydroxy-2-pyrone (**4**).

Compound **4**, mp 114-116° (lit (12), 117-119°), was prepared in 59% yield (after recrystallization from ethanol) by the method described by Harris, *et al.*, (12). The recrystallization liquors were evaporated and the residue recrystallized twice from methylene chloride-hexane to afford a small amount of 3-acetyl-6-dibromomethyl-4-hydroxy-2-pyrone, mp 129-130°; ir (chloroform): 1760, 1650; pmr (deuteriochloroform): 2.7 (s, 3H), 6.13 (s, 1H), 6.42 (s, 1H), 16.9 (s, 1H); ms: 328 (4), 326 (8), 324 (M^+, 4), 247 (50), 245 (50), 167 (23), 153 (100), 111 (50), 100 (23), 69 (38), 43 (96).

3-Acetyl-4-hydroxy-6-hydroxymethyl-2-pyrone (**9**).

Product **4** (1.2 g, 4.8 mmoles) was dissolved in 35 ml of aqueous sodium hydroxide (200 mg, 5.0 mmoles). This solution was slowly added in 2.5 hours over a second solution of sodium hydroxide (3.0 g, 75 mmoles) in 60 ml of water kept at 50° under magnetic stirring. The mixture was then acidified with concentrated hydrochloric acid and the formed precipitate was extracted three times with 100 ml portions of chloroform. The organic solution was dried and evaporated. The residue was recrystallized from chloroform-hexane to give **9**, mp 131-133°, in 67% yield; ir (potassium bromide): 3500, 1730, 1640; pmr (deuteriochloroform): 2.7 (s, 3H), 2.3-2.7 (broad s, 1H), 4.5 (s, 2H), 6.3 (broad s, 1H), 16.8 (s, 1H); ms: 184 (M^+,55), 153 (100), 111 (33), 69 (20), 43 (23).

Anal. Calcd. for $C_8H_8O_5$: C, 52.18; H, 4.38. Found: C, 52.14; H, 4.18.

Bis(3-acetyl-4-hydroxy-2-oxo-2*H*-pyran-6-yl)methyl Ether (**10**).

The lactone **4** (1.5 g, 6.0 mmoles) was slowly added into a magnetically stirred solution of sodium hydroxide (800 mg, 20 mmoles) in 40 ml of water. The mixture was stirred at room temperature for 14 hours and then acidified with concentrated hydrochloric acid. The appeared precipitate was centrifugated and recrystallized from dimethylformamide to yield **10**, mp 254-255° in 86% yield; ir (potassium bromide): 1730, 1650; pmr (trifluoroacetic acid): 2.38 (s, 3H), 4.12 (s, 2H), 6.12 (s, 1H); ms: 350 (M^+,40), 168 (48), 153 (100), 111 (20), 44 (21), 43 (23).

Anal. Calcd. for $C_{16}H_{14}O_9$: C, 54.86; H, 4.03. Found: C, 54.59; H, 4.01.

(3-Acetyl-4-hydroxy-2-oxo-2H-pyran-6-yl)methyltriphenylphosphonium Bromide (**11**).

Triphenylphosphine (8.0 g, 30.5 mmoles) in anhydrous benzene (25 ml) was slowly added under argon to a solution of the bromolactone **4** (6.83 g, 27.6 mmoles) in the same solvent (75 ml). The mixture was refluxed for 15 hours. The appeared brown precipitate was filtered off and dried to yield 95% of crude **11**. Recrystallization from ethanol gave 9.15 g (65%) of pure **11**, mp 194-198° dec, as a cream coloured solid; ir (chloroform): 1745 (broad), 1640, 1620 (shoulder); pmr (deuteriochloroform): 2.57 (s, 3H), 5.97 (d, 2H, J = 16 Hz), 7.04 (d, 1H, J = 4 Hz), 7.90 (m, 15H); ms: 429 (0.5), 428 (2), 427 (1.5), 82 (91), 80 (100).

3-Acetyl-4-hydroxy-6-((*E*)-4-methoxystyryl)pyran-2-one (**12b**).

A solution of sodium ethoxide (from sodium (280 mg, 12.2 mmoles), ethanol (10 ml) and dimethylformamide (5 ml)) was added in 20 minutes at 0° and under magnetic stirring into a solution of **11** (3.0 g, 5.9 mmoles) in dimethylformamide (30 ml). The mixture was kept at room temperature for 0.5 hours, after which 4-methoxybenzaldehyde (800 mg, 6.5 mmoles) in dimethylformamide (7 ml) was added. The solution was left for 16 hours under stirring and finally poured into water. On acidification with aqueous hydrochloric acid, an orange precipitate appeared. It was filtered and dried to afford a practically quantitative yield of **12b**. It was recrystallized from methylene chloride-hexane to yield pure **12b**, mp 190-192°; ir (potassium bromide): 1740, 1720, 1600, 970; pmr (deuteriochloroform): 2.80 (s, 3H), 3.95 (s, 3H), 6.10 (s, 1H), 6.55 (d, 1H, J = 16 Hz), 7.10 (d, 2H, J = 9 Hz), 7.60 (d, 2H, J = 9 Hz), 7.70 (d, 1H, J = 16 Hz); ms: 286 (M^+, 94), 268 (41), 201 (35), 185 (74), 175 (61), 174 (81), 161 (100), 159 (29), 145 (21), 144 (23), 133 (47), 131 (26), 121 (38), 115 (53), 103 (26), 89 (32), 67 (33), 59 (45), 43 (89).

Anal. Calcd. for $C_{16}H_{14}O_5$: C, 67.13; H, 4.93. Found: C, 67.26; H, 4.88.

The following compounds were prepared in a similar manner.

3-Acetyl-4-hydroxy-6-((*E*)-1-penten-1-yl)pyran-2-one (**12a**).

This compound had bp 140-160° (oven temperature)/0.3 mm Hg; mp 79-82°; ir (chloroform): 1740, 1725, 965; pmr (deuteriochloroform): 0.8-2.5 (m, 7H), 2.65 (s, 3H), 5.9 (s, 1H), 6.05 (d, 1H, J = 15 Hz), 7.0 (dt, 1H, J = 15 and 8 Hz), ms: 222 (M^+, 8), 69 (37), 67 (20), 55 (42), 53 (25), 43 (100), 41 (56). No correct elemental analysis could be obtained from this compound.

3-Acetyl-4-hydroxy-6-((*E*)-4-nitrostyryl)pyran-2-one (**12c**).

This compound had mp 241-245° dec (from acetic acid; ir (potassium bromide): 1750, 1725, 1525, 1355, 970; ms: 301 (M^+, 6), 97 (20), 69 (72), 57 (32), 55 (42), 43 (100).

Anal. Calcd. for $C_{15}H_{11}NO_6$: C, 59.80; H, 3.68; N, 4.65. Found: C, 59.97; H, 3.66; N, 4.72.

3-Acetyl-4-hydroxy-6-(*E*)-styrylpyran-2-one (**12d**).

This compound had mp 197-199° (from acetone); ir (chloroform): 1740, 1720, 960; pmr (deuteriochloroform): 2.77 (s, 3H), 6.25 (s, 1H), 6.80 (d, 1H, J = 17 Hz), 7.70 (m, 5H), 7.90 (d, 1H, J = 17 Hz); ms: 256 (M^+, 70), 238 (60), 213 (20), 211 (22), 173 (25), 171 (40), 170 (26), 155 (90), 145 (42), 144 (67), 131 (100), 128 (55), 127 (41), 115 (40), 103 (65), 77 (53), 69 (40), 43 (51).

Anal. Calcd. for $C_{15}H_{12}O_4$: C, 70.30; H, 4.72. Found: C, 70.43; H, 4.70.

3-Bromo-4-methoxy-6-methyl-2-pyrone (**16**). Experiment 1 (Table).

4-Methoxy-6-methyl-2-pyrone (**5**), (18), (1.0 g, 7.1 mmoles) and NBS (1.5 g, 8.4 mmoles) were refluxed in anhydrous carbon tetrachloride (25 ml) for 17 hours in the presence of a catalytic amount of benzoyl peroxide. The solvent was evaporated and the residue was partitioned between chloroform and 10% aqueous sodium hydroxide. The organic layer was washed, dried and evaporated to afford a solid which upon recrystallization in methylene chloride gave **16** in 86% yield, mp 154-155° (lit (12), 155-156°). Product **16** was also prepared under the conditions described for experiment 2 (See table).

The following products were prepared in a similar manner (See Table).

6-Bromomethyl-4-methoxy-2-pyrone (**6**).

This compound was obtained as indicated for experiment 3. Column chromatography of the reaction mixture gave the following products: the starting material, **5**, (eluted with hexane-ether (45/55)), the bromolactone **6**, mp 93-95° (from methylene chloride-pentane) (lit (16), 93-95°) (eluted with hexane-ether (2/3)), and the dibromolactone **15** (see below for description, eluted with hexane (3/7)).

6-Dibromomethyl-4-methoxy-2-pyrone (**14**).

This compound was obtained as indicated for experiment 5. This lactone was purified by passing through a silica gel column with hexane-ether as eluent. It had mp 155-157° (from methylene chloride-pentane); ir (potassium bromide): 1710, 1640; pmr (deuteriochloroform): 3.8 (s, 3H), 5.43 (d, 1H, J = 2 Hz), 6.1 (s, 1H), 6.2 (d, 1H, J = 2 Hz); ms: 300 (3), 298 (6), 296 (M^+, 3), 219 (33), 217 (33), 125 (100), 69 (70), 59 (33).

Anal. Calcd. for $C_7H_6Br_2O_3$: C, 28.22; H, 2.03. Found: C, 28.10; H, 2.03.

3-Bromo-6-bromomethyl-4-methoxy-2-pyrone (**15**).

This compound was obtained as indicated for experiment 7. The dibromolactone **15** had mp 162-164° (from methylene chloride-pentane); ir (potassium bromide): 1690, 1630; pmr (deuteriochloroform): 4.05 (s, 3H), 4.2 (s, 2H), 6.42 (s, 1H); ms: 300 (12), 298 (24), 296 (M^+,12), 219 (50), 217 (50), 191 (62), 189 (62), 163 (25), 161 (25), 149 (40), 147 (40), 95 (30), 93 (30), 82 (22), 81 (26), 80 (22), 79 (30), 69 (25), 67 (42), 66 (25), 65 (20), 59 (70), 53 (100), 51 (30), 50 (22), 42 (60).

Anal. Calcd. for $C_7H_6Br_2O_3$: C, 28.22; H, 2.03. Found: C, 28.47; H, 2.06.

(4-Methoxy-2-oxo-2*H*-pyran-6-yl)methyltriphenylphosphonium Bromide (**17**).

Triphenylphosphine (650 mg, 2.4 mmoles) in anhydrous benzene (15 ml) was slowly added to the bromolactone **6** (500 mg, 2.2 mmoles) dissolved in the same solvent (25 ml). The mixture was refluxed under nitrogen for 16 hours. The phosphonium salt **17** was separated by filtration (92% yield). It had mp 223-225 (from ethanol) (lit (16), 224-226°). Alternatively, **17** can be prepared from bromination mixtures enriched in **6**.

4-Methoxy-6-((*E*)-4-methoxystyryl)pyran-2-one, (Yangonin) (**18**).

The phosphonium salt **17** (481 mg, 1.0 mmole) was dissolved in dimethylformamide (10 ml) and the solution was cooled in an ice-water bath. A solution (3 ml) of sodium ethoxide (from 23 mg of sodium (1.0 mmoles)) was then slowly added under magnetic stirring. Finally, 4-methoxybenzaldehyde (150 mg, 1.1 mmoles) in dimethylformamide (3 ml) was added. The mixture was stirred at room temperature for 16 hours, after which it was poured into ice-water and the resulting mixture acidified with 6*N* hydrochloric acid. The precipitated yangonin (95%) was filtered off and exhibited mp 154-155° (from methanol) (lit (18), 155-157°).

6-Hydroxymethyl-4-methoxy-2-pyrone (**8**).

From **6**.

Compound **6** (330 mg, 1.5 mmoles) was dissolved in chloroform, then silica gel was added (15 g) and the solvent evaporated. Water (30 ml) was added and the mixture was then refluxed with magnetic stirring for 18 hours. After cooling at room temperature, three extractions were performed with portions of chloroform-ethyl acetate (1/1) (50 ml each). The organic solution was dried and evaporated to yield 195 mg (83%) of the hydroxypyrone **8**, mp 178-181° (from methanol) (lit (17), 180-181°).

From **5** *via* **7**.

The pyrone **5** (10 g, 71 mmoles) and selenium dioxide (40 g, 0.36 moles) were refluxed in anhydrous dioxane (500 ml) for 24 hours. The precipitate was filtered and the solution evaporated to afford the crude aldehyde **7** contaminated with selenium compounds. This residue was dissolved in absolute ethanol (300 ml) and the solution was cooled in an ice-water bath and treated under stirring with sodium borohydride (3.12 g, 82 mmoles) which was portionwise added until the *p*H was permanently basic. The mixture was kept two additional hours at room temperature, then acidified with ethanolic hydrochloric acid and filtered. The solution was evaporated to yield a residue which upon recrystallization in methanol gave the hydroxylactone **8** (2.1 g). The mother liquor from the recrystallization was evaporated and the new residue passed through a silica gel column to afford 3.8 g of **8** (eluted with methylene chloride-methanol (1/1)).

The overall yield of **8** was 53%, mp 178-181°.

5-Ethoxycarbonylmethyl-4-methoxy-6-methyl-2-pyrone (**19**).

The hydroxylactone **8** (2.3 g, 14.7 mmoles), freshly distilled ethyl orthoacetate (20 g, 0.123 moles) and propionic acid (150 mg) were placed in a round bottom flask fitted to a Claisen distillation head. The flask, containing also a magnetic bar for stirring, was inmersed in an oil bath at 175-180°. Ethanol was distilled off over a period of 8 hours during which some more propionic acid was added. The inner temperature, just above the liquid surface was 138-142°. The course of the reaction was monitored by tlc. The remaining ethyl orthoacetate was distilled off at water pump pressure. More propionic acid (100 mg) was added to the residue and the mixture was heated at 170° for 15 minutes under magnetic stirring and finally evaporated *in vacuo*. The residue was chromatographed with ether elution through a silica gel column to yield the pyrone **19** (1.83 g, 55%). Some starting material, **8** (0.3 g, 13%) was also eluted later. Product **19** had mp 91-93° (from methylene chloride-pentane); ir (potassium bromide): 1730, 1700, 1640; pmr (deuteriochloroform): 1.27 (t, 3H, J = 8 Hz), 2.22 (s, 3H), 3.33 (s, 2H), 3.77 (s, 3H), 4.1 (q, 2H, J = 8 Hz), 5.4 (s, 1H); ms: 226 (M^+, 10), 156 (31), 153 (58), 125 (100), 69 (33), 43 (21).

Anal. Calcd. for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24. Found: C, 58.32; H, 6.20.

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REFERENCES AND NOTES

(1) Part of this work was presented at the 8th International Congress of Heterocyclic Chemistry, held Graz (Austria) in August 1981.

(2) To whom the correspondence should be addressed.

(3) N. Sakabe, T. Goto and Y. Hirata, *Tetrahedron Letters*, 1825 (1964).

(4) M. S. R. Nair, *Phytochemistry*, **15**, 1090 (1976).

(5) M. Gohbara, S-B. Hyeon, A. Suzuki, and S. Tamure, *Agric. Biol. Chem.*, **40**, 1453 (1976).

(6) S. Omura, A, Nakagawa and H. Ohno, *J. Am. Chem. Soc.*, **101**, 4386 (1979).

(7) G. J. Kruger, P. S. Steyn, R. Vleggaar and C. J. Rabie, *J. Chem. Soc. Chem Commun.*, 441 (1979).

(8) P. S. Steyn, R. Vleggaar and P. L. Wessels, *ibid.*, 1041 (1979).

(9) P. A. Grieco, Y. Ohfune, Y. Yokoyama and W. Owens *J. Am. Chem. Soc.*, **101**, 4749 (1979).

(10) M. A. Adams. A. J. Duggan, J. Smolanoff and J. Meinwald, *ibid.*, **101**, 5364 (1979).

(11) J. N. Collie, *J. Chem Soc.*, **59**, 607 (1891).

(12) T. M. Harris, C. M. Harris and C. K. Brush, *J. Org. Chem.*, **35**, 1329 (1970).

(13) J. Marquet and M. Moreno-Mañas, *Chem. Letters*, 173 (1981).

(14) M. P. Wachter and T. M. Harris, Tetrahedron, **26**, 1685 (1970); T. M. Harris, C. M. Harris and M. P. Wachter, *ibid.*, **24**, 6897 (1968).

(15) R. Bacardit and M. Moreno-Mañas, *Chem. Letters*, 5 (1982).

(16) J. L. Bloomer, S. Munir, H. Zaidi, J. T. Strupczewski, C. S. Brosz and L. A. Gudzyk, *J. Org. Chem.*, **39**, 3615 (1974).

(17) E. Suzuki, R. Hamajima and S. Inoue, Synthesis, 192 (1975).

(18) J. D. Bu'Lock and H. G. Smith, *J. Chem. Soc.*, 502 (1960).

(19) O. Caputo, L. Cattel and F. Viola, *Farmaco, Ed. Sci.*, **34**, 869 (1979).