# New Method for the Synthesis of 4-Methoxy-6-aryl-2-pyrones; Synthesis and Bromination of 3-Methoxy-5-aryl-(2E,4E)-2,4-pentadienoic Acids

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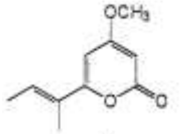
## Abstract:

Synthesis approaches to the 4-methoxy-6-aryl-2-pyrones (11) are described in which the key step is cyclisation of 3-methoxy-4,5-dibromo-5-aryl (2E)-pentenoic acids (9) with triethylamine in benzene followed by oxidation with DDQ. The acids, 3-methoxy-5-aryl-(2E,4E)-2,4-pentadienoic acid (5) are prepared from the reaction of ethyl 3-methoxy-(2E) butenoate (4) with aldehydes in the presence of sodium hydride. Bromination of these acids with bromine gave selectively (9). The stereochemistry of cyclisation reaction are described..

## Introduction:

Compounds containing an 4-methoxy-6-aryl-2-pyrone moiety are widely occurring natural products(1,2), some of which have remarkable activity(3,5). Among them nectriapyrone (1) is one of the major classes of natural antibacterial pyrone isolated from Cyrostroma missouriensis seaver(6). A number of synthetic studied towards these compounds have been reported (7-10). Most of these synthetic effords either skeletal formation of a 1,5-diketone which is then cyclised in acid(11,12) or by condensation of aromativ aldehyde with readily available pyrone e.g. 4-methoxy-6-methyl-2-pyrone (2)(13). This pyrone can also be converted to yield, in which the relevant carbon is activated by the presence of a phosphorance group(14). Treatment with keten leads to the formation of allene. This is the methyl ether of the natural product, tetracetic lactone (3).



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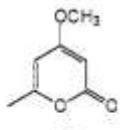

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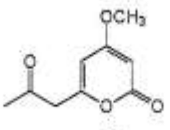

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## Experimental:

All melting points were determined with a Kofler apparatus and uncorrected. IR spectra were recorded on a Perkin-Elmer Model 127 and 237 recording spectrophotometer. $^1$H-NMR spectra were recorded on a Bruker WH 90 DS spectrometer equipped with ASPECT 2000, 32 K computer operated at 22.63 MHz with deuterium internal lock.

**Ethyl (E)-3-methoxy-2-butenoate (4):**

Ethyl acetoacetate (13.0 g, 0.1 mol) is mixed with redistilled trimethyl orthoformate (10.6 g, 0.1 mol) and dry methanol (10 ml). Then concentrated hydrochloric acid (0.05 ml) is added, the mixture is distilled immediately to give (4), yield 14.4 g (~ 100%); b.p. 188-196 °C/1 atm. (Lit.(28) b.p. 188-194 °C/1 atm.

**3-Methoxy-5-aryl-(2E,4E)-2,4-pentadienoic acids (5a-e):**

**General procedure:**

A solution of ethyl (E)-3-methoxy-2-butenoate (4) (28.8 g, 0.2 mol) and the aryl aldehyde (0.2 mol) in dry tetrahydrofuran (150 ml) is added dropwise to the suspension of sodium hydride (50% dispersion in oil, 9.6 g, 0.2 mol) in tetrahydrofuran (150 ml) at 0 °C, stirring is continued for 20 hrs. at room temperature. The mixture is poured into ice (200 g) and acidified with 10% hydrochloric acid and extracted with water (2 × 200 ml) dried with sodium sulfate and evaporated under reduced pressure to give the crude product.

**3-Methoxy-5-phenyl-(2E,4E)-2,4-pentadienoic acid (5a):**

Light yellow crystals (ethanol); m.p. 149-150 °C, 75%, IR (KBr) 1700, 1630, 1625 cm$^{-1}$ for (C=O), (C=C conj.), (ArC=C); $^1$HNMR ($CDCl_3$) δ 3.8 (s, 3H), $OCH_3$), 5.15 (s, 1H, H-2), 7.15 (d, J = 16 Hz, 1 H, H-4), 8.2 (d, J = 16 Hz, 1 H, H-5), 7.8 (A-Bq, 4H, Ar-H).

**3-Methoxy-5-(4-chlorophenyl)-(2E,4E)-2,4-pentadienoic acid (5b):**

White crystals (methanol); m.p. 148-150 °C, 92%, IR (KBr) 1690, 1640, 1590 cm$^{-1}$ for (C=O), (C=C conj.), (ArC=C); $^1$HNMR ($CDCl_3$) δ 3.8 (s, 3H, $OCH_3$), 5.15 (s, 1H, H-2), 7.15 (d, J = 16 Hz, 1 H, H-4), 8.2 (d, J = 16 Hz, 1 H, H-5), 7.8 (A-Bq, 4H, Ar-H).

**3-Methoxy-5-(2,6-dichlorophenyl)-(2E,4E)-2,4-pentadienoic acid (5c):**

White crystals (methanol-benzene); 92%, m.p. 200-201 °C, IR (KBr) 1705, 1610, 1605 cm$^{-1}$ for (C=O), (C=C conj.), (ArC=C); $^1$HNMR ($CDCl_3$) δ 3.8 (s, 3H, $OCH_3$), 5.22 (s, 1H, H-2), 7.27 (d, J = 16 Hz, 1 H, H-4), 8.1 (d, J = 16 Hz, 1 H, H-5), 7.23 (m, 3H, Ar-H).

**3-Methoxy-5-(9-anthracenyl)-(2E,4E)-2,4-pentadienoic acid (5d):**

Yellow crystals (methanol-benzene); m.p. 200 °C Dec., 90%, IR (KBr) 1700, 1670, 1640 cm$^{-1}$ for (C=O), (C=C conj.), (ArC=C); $^1$HNMR ($CDCl_3$) δ 3.95 (s, 3H, $OCH_3$), 5.4 (s, 1H, H-2), 7.8 (d, J = 15 Hz, 1 H, H-4), 8.5 (d, J = 15 Hz, 1 H, H-5), 7.9 (m, 9H, Ar-H).

**3-Methoxy-5-(3-methoxyphenyl)-(2E,4E)-2,4-pentadienoic acid (5e):**

White crystals (methanol); m.p. 158-160 °C, 42%, IR (KBr) 1690, 1610, 1590 cm$^{-1}$ for (C=O), (C=C conj.), (ArC=C); $^1$HNMR ($CDCl_3$) δ 3.82 (s, 3H, $OCH_3$), 5.12 (s, 1H, H-2), 6.86 (d, J = 15 Hz, 1 H, H-4), 7.48 (d, J = 15 Hz, 1 H, H-5), 7.6 (A-Bq, 4H, Ar-H).

**3-Methoxy-4,5-dibromo-5-aryl-2E-pentanoic acid (9a-e):**

To a stirred solution of (5 g, 0.01 mol) in dry carbontetrachloride (50 ml) bromine solution (0.01 mol) was added dropwise, with stirring at 0 °C and the mixture was allowed to stand at room temperature for 12 hours. After the brown colour of bromine had disappeared, the reaction mixture was either filtered and the solids were washed with carbontetrachloride to give the crude products (9), or the reaction mixture was diluted with water (150 ml) and extracted with chloroform (3 × 100 ml), washed with water (100 ml), dried ($Na_2SO_4$) and evaporated to give crude bromocompounds (9), which were purified by crystallization.

**3-Methoxy-(4S,5S)-4,5-dibromo-5-phenyl-2E-pentenoic acid (9a):**

White crystals (chloroform); 64%, m.p. 185-187 °C, IR (KBr) 1675, 1615 $cm^{-1}$ for (C=O), (C=C conj.); $^1$HNMR ($CDCl_3$) δ 3.8 (s, 3H, $OCH_3$), 5.35 (s, 1H, H-2), 5.6 (d, J = 10 Hz, 1 H, H-4), 7.1 (d, J = 10 Hz, 1H, H-5), 7.5 (m, 5H, Ar-H).

**3-Methoxy-5-(4-chlorophenyl)-(4S,5S)-4,5-dibromo-5-phenyl-2E-pentenoic acid (9b):**

White crystals (chloroform); 45%, m.p. 190 °C Dec., IR (KBr) 1670, 1590 $cm^{-1}$ for (C=O), (C=C conj.); $^1$HNMR ($CDCl_3$) δ 3.85 (s, 3H, $OCH_3$), 5.35 (s, 1H, H-2), 5.7 (d, J = 10 Hz, 1 H, H-4), 7.0 (d, J = 10 Hz, 1H, H-5), 7.6-8.1 (A-Bq, 4H, Ar-H).

**3-Methoxy-5-(2,6-dichlorophenyl)-(4S,5S)-4,5-dibromo-2E-pentenoic acid (9c):**

White crystals (chloroform); 76%, m.p. 202-205 °C, IR (KBr) 1665, 1610 $cm^{-1}$ for (C=O), (C=C); $^1$HNMR ($CDCl_3$) δ 3.9 (s, 3H, $OCH_3$), 5.4 (s, 1H, H-2), 6.35 (d, J = 10 Hz, 1 H, H-4), 7.75 (d, J = 10 Hz, 1H, H-5), 7.5 (m, 3H, Ar-H).

**3-Methoxy-5-(9-anthracenyl)-(4S,5S)-4,5-dibromo-2E-pentenoic acid (9d):**

Yellow crystals (chloroform); 77%, m.p. 159-160 °C, IR (KBr) 1680, 1610 $cm^{-1}$ for (C=O), (C=C); $^1$HNMR ($CDCl_3$) δ 3.9 (s, 3H, $OCH_3$), 5.4 (s, 1H, H-2), 6.35 (d, J = 10 Hz, 1 H, H-4), 7.7 (d, J = 10 Hz, 1H, H-5), 7.8 (m, 9H, Ar-H).

**3-Methoxy-5-(4-methoxyphenyl)-4,5-dibromo-2E-pentenoic acid (9e); (Mixture of 4S, 5S and 4S, 5R):**

White ppt, 74%, IR (KBr) 1710, 1580 $cm^{-1}$ for (C=O), (C=C); $^1$HNMR (4S,5S) ($CDCl_3$) δ 3.6 (s, 3H, $OCH_3$), 4.5 (s, 1H, H-2), 5.6 (d, J = 10 Hz, 1 H, H-4), 5.8 (d, J = 10 Hz, 1H, H-5), 7.5 (A-Bq, 4H, Ar-H). $^1$HNMR (4S,5S) ($CDCl_3$) δ 3.85 (s, 3H, $OCH_3$), 4.8 (s, 1H, H-2), 5.95 (d, J = 8 Hz, 1 H, H-4), 6.2 (d, J = 8 Hz, H-5), 7.4 (A-Bq, 4H, Ar-H).

**4-Methoxy-6-aryl-pyrones (11a-e):**

**General procedure: (from bromoacid 9):**

To a stirred solution of triethylamine and dry benzene (50 ml, 1:6 portions) bromo acid (9) (1 g) was added rapidly followed by further stirring at room temperature for 18 hrs. (monitored by TLC). The reaction mixture was filtered and the residue washed with benzene. The combined filtrate was concentrated under vacuum to give crude pyrones lla-e which were purified either by crystallization or by passing through silica gel column using chloroform as eluent.

**4-Methoxy-6-phenyl-2-pyrone (11a):**

White crystals (benzene), 90%, m.p. 126-128 °C, IR (KBr), 1730, 1650, 1570 $cm^{-1}$ for (C=O lactone), (C=C); $^1$HNMR ($CDCl_3$) δ 3.95 (s, 3H, $OCH_3$), 5.8 (d, J = 1.5 Hz, 1H, H-3), 6.95 (d, J = 1.5 Hz, 1 H, H-5), 7.5-7.9 (m, 5H, Ar-H).

**4-Methoxy-6-(4-chlorophenyl)-2-pyrone (11b):**

White crystals (benzene), 70%, m.p. 129-130 °C, IR (KBr), 1730, 1645, 1570 $cm^{-1}$ for (C=O lactone), (C=C); $^1$HNMR ($CDCl_3$) δ 3.95 (s, 3H, $OCH_3$), 5.8 (d, J = 1.5 Hz, 1H, H-3), 7.0 (d, J = 1.5 Hz, 1 H, H-5), 7.8 (A-Bq, 4H, Ar-H).

**4-Methoxy-6-(3,4-dichlorophenyl)-2-pyrone (11c):**

White crystals (benzene), 70%, m.p. 175 °C Dec., IR (KBr), 1735, 1640, 1570 $cm^{-1}$ for (C=O lactone), (C=C); $^1$HNMR ($CDCl_3$) δ 3.45 (s, 3H, $OCH_3$), 5.85 (d, J = 1.5 Hz, 1H, H-3), 7.1 (d, J = 1.5 Hz, 1 H, H-5), 7.9 (m, 3H, Ar-H).

**4-Methoxy-6-(9-anthracenyl)-2-pyrone (11d):**

Yellow crystals (benzene), 87%, m.p. 220 °C Dec., IR (KBr), 1735, 1650 $cm^{-1}$ for (C=O lactone), (C=C); $^1$HNMR ($CDCl_3$) δ 3.9 (s, 3H, $OCH_3$), 6.0 (d, J = 1.5 Hz, 1H, H-3), 7.2 (d, J = 1.5 Hz, 1 H, H-5), 7.9 (m, 9H, Ar-H).

**4-Methoxy-6-(4-methoxy phenyl)-2-pyrone (11e):**

White crystals (benzene), 48%, m.p. 145-146 °C, IR (KBr), 1740, 1640, 1570 $cm^{-1}$ for (C=O lactone), (C=C); $^1$HNMR ($CDCl_3$) δ 3.8 (s, 3H, $OCH_3$), 5.5 (d, J = 1.5 Hz, 1H, H-3), 6.3 (d, J = 1.5 Hz, 1 H, H-5), 6.9 (A-Bq, 4H, Ar-H), 3.7 (s, 3H, Ar-$OCH_3$).

**4-Methoxy-6-aryl-pyrones (11e-g):**

**General procedure: (Oxidation of dihydropyrone 12 with DDQ):**

In 100 ml three-necked flask fitted with a condenser (calcium chloride tube) and stirring bas was placed a mixture of (12, 0.01 mole) and 2,3-dichloro-5,6-dicyanoquinone (DDQ, 0.01 mole) in 50 ml of dry benzene. The red solution was refluxed for 18 hrs during which the reaction turned yellow with the formation of a tan precipitate. The reaction mixture was cooled, filtered and the filtrate was chromatographed on aluminum oxide (benzene:chloroform; 1:4 then 1:1) to give compounds (11e-g).

**4-Methoxy-6-(4-methoxy phenyl)-2-pyrone (11e):**

Under the condition described above, (12e) gave 86% of (11e). For physical and spectral properties see above.

**4-Methoxy-6-(3,4-methylene dioxyphenyl)-2-pyrone (11f):**

Under the condition described above, (12f) gave 91% of (11f), white crystals (benzene); m.p. 138-140 °C, Lit. m.p. (139-140)[28]; IR (KBr), 1740, 1690, 1630 $cm^{-1}$ for (C=O lactone), (C=C); $^1$HNMR ($CDCl_3$) δ 3.8 (s, 3H, $OCH_3$), 5.45 (d, J = 1.5 Hz, 1H, H-3), 5.45 (d, J = 1.5 Hz, 1 H, H-5), 7.5 (d, J = 16 Hz, H-8), 7.3 (m, 5H, Ar-H).

**4-Methoxy-6-(trans-2-phyenethenyl)-2-pyrone (11g):**

Under the condition described above, (12g) gave 89% of (11g), white crystals (benzene); m.p. 138-140 °C, Lit. m.p. (139-140)[28]; IR (KBr), 1740, 1690, 1630 for $cm^{-1}$ (C=O lactone), (C=C); $^1$HNMR ($CDCl_3$) δ 3.8 (s, 3H, $OCH_3$), 5.45 (d, J = 1.5 Hz, 1H, H-3), 5.45 (d, J = 1.5 Hz, 1 H, H-5), 6.5 (d, J = 16 Hz, H-7), 7.3 (m, 5H, Ar-H).

**4-Methoxy-6,6-diphenyl-5,6-dihydro-2H-pyran-2-one (18):**

Ethyl 4-bromo-(E)-3-methoxy-2-butenoate (4; $CH_3CH_2Br$; 2.24 g, 10 mmoles) admixed with benzophenone (10 mmole) in 50 ml of dry benzene. This was slowly added to 1.5 g of industrial zinc. After initial heating, the mixture was refluxed for 3 hrs. It was then allowed to cool to room temperature. The entire mixture was introduced in a thin stream into a 10% hydrochloric acid solution (100 ml), and then extracted with ethyl acetate (3 × 150 ml). The combined organic layers were washed with water (2 × 100 ml), 5% sodium bicarbonate (2 × 100 ml) and water (2 × 100 ml). Drying ($Na_2SO_4$) and concentration in vacuum afford (18, 75%) as needled; m.p. 139-140 °C, IR (KBr) 1735, 1640, 1580 $\text{cm}^{-1}$ for (C=O lactone), (C=C); $^1$HNMR ($CDCl_3$) δ 3.2( s, 2H, H-5), (s, 3H, $OCH_3$), 5.1 (s, 1H, H-3), 7.2 (m, 10H, Ar-H).

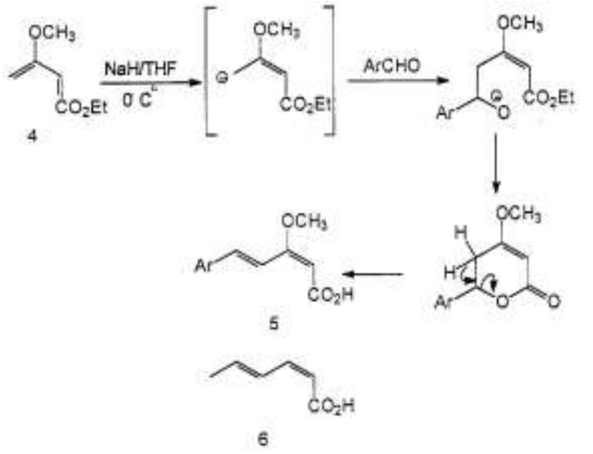
**4-Methoxy-6-aryl-5,6-dihydro-2H-pyran-2-ones (12a-i):**
These compounds were prepared under the conditions described for compound (18). Compound (12a-i) are all known compounds(7,22).

**4-Methoxy-5-benzylidene-2(5H)-furanone (21):**
A mixture of 18 (28 g, 0.01 mole), N-bromosuccinimide (1.78 g, 0.1 mole) and benzoylperoxide (50 mg) in dry carbontetrachloride (100 ml) was refluxed for 3 hrs. under UV light. The reaction mixture was cooled and filtered. Solvent was removed by concentration under vacuum and the residue was dissolved in 100 ml of 10% methanolic potassium hydroxide solution and the mixture was refluxed for 0.5 hr. The mixture was cooled and extracted with dichloromethane (3 × 100 ml), dried ($MgSO_4$) and evaporated in vacuo. Column chromatography of the residue with hexane-ethyl acetate mixture (1:4) gave (21, 1.4 g, 50%) as a white crystals; m.p. 120-123 °C; I.R. (KBr) 1780, 1650, 1590 $\text{cm}^{-1}$ for (C=O lactone), (C=C); $^1$HNMR ($CDCl_3$) δ 3.35 (s, 3H, $OCH_3$), 5.15 (s, 1H, H-3), 7.2 (s, 10H, Ar-H).

## Results And Discussion:

**Synthesis of 3-methoxy-5-aryl-(2E,4E)-3,4-pentadienoic acid (5):**
Recently we developed(15,16) the synthesis of 3-methoxy-5-aryl-(2E,4E)-2,4-pentadienoic acids (5) from the condensation of ethyl 3-methoxy-(2E)-butenoate (4) in tetrahydrofurane 0 °C with aromatic aldehydes and ketones. As a continuation of our previous studies(17) and an extension of this work, we were interested in the synthesis of 4-methoxy-6-aryl-2-pyrone from dienoic acids.

Thus the requisite dienoic acids (5a-e) was synthesized as follows (Scheme 1).



a: Ar = $C_6H_5$
b: Ar = 4-Cl.$C_6H_4$
c: Ar = 2,6-$Cl_2$.$C_6H_3$
d: Ar = 9-anthracenyl
e: Ar = 4-$CH_3O$.$C_6H_4$

**Scheme (1)**

**Attempted cyclisation of pentadienoic acid (5):**
We thought it might be interesting to use these acids as synthone for 2-pyrones either by direct cyclisation with strong acids such as polyphosphoric acid (PPA)(18) or indirect cyclisation by bromination of the dienoic acid(19). Effectively the acids (5) could be used as a precursor in this synthesis.

With this consideration in mind, we examined the lactonisation of (5) by strong acids. With a large number of attempted cyclodehydration we failed to separate the expected product and polymeric material was formed. Conversion of the usually all-trans acid (2E,4E) to the (2E,4Z) acid is apparently a necessary perquisite(18) and it seems probable that these reagents either attack the carbonyl group producing highly polarized donor-acceptor co-ordination complex or protonate the ethylene linkage(20) which lead to different products. Thus the direct lactonisation of these acids are unsuccessful.

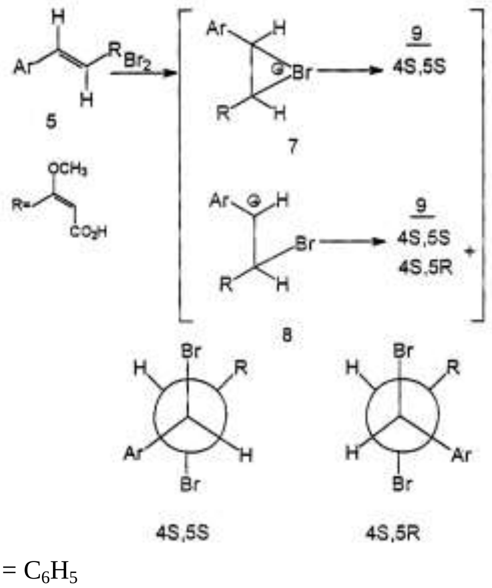
Kuhn(19) have confirmed the inhibitory action of the synthetic δ-hexenolacton prepared by treatment with water of the dibromohexoic acid formed by addition of hydrogenbromide to sorbic acid (6). Thus the lactonisation of the dibromo acid was investigated.

When the dienoic acid (5a) was treated with excess of bromine the 4,5-dibromo-5-phenyl-2E-pentenoic acid (9a) was only formed by 1,2-addition of bromine molecule to the more nucleophilic character $C_4$-$C_5$ double bond of the acid. This product can be easily interpreted if we assumed that the addition pass through the cyclic bromination ion (7), since the second step is an $SN^2$ process which must occur from the backside to give the more stable isomer (4S,5S) (Scheme 2). Other type of mechanism carbonium ion of the type B, should give a racemic mixture (4S,5S and 4S,5R).

The $^1$HNMR spectrum of the products (9a) (Table 1) exhibited one vinyl proton at δ 5.35 for H-2 and two doublets at δ 5.6 and 7.1 (J:10 Hz) for H-4 and H-5 respectively.

**Table 1**: $^1$HNMR data for compounds 5a and 91

| Compound | (5a) (2E,4E) | (9a) (4S,5S) |
|---|---|---|
| Proton H-2 | 5.16, s, 1H | 5.35, s, IH |
| H-4 | 7.17, d (J = 15 Hz), 1H | 5.6, d (J = 10 Hz), 1H |
| H-5 | 8.03, d (J = 15 Hz), 1H | 7.1, d (J = 10 Hz), 1H |
| $OCH_3$ | 3.74, s, 3H | 3.8, s, 3H |



a: Ar = $C_6H_5$
b: Ar = 4-Cl.$C_6H_4$
c: Ar = 2,6-$Cl_2$.$C_6H_3$
d: Ar = 9-anthracenyl
e: Ar = 4-$CH_3O$.$C_6H_4$

**Scheme (2)**

It is worth noting that in this reaction the nature of the substituent on the aromatic ring of the acid (5) plays a role not only in the rate of the reaction but also in the ratio of the products formed (9). Two types of acids bearing electron withdrawing (5b and 5c) and electron-donating (5e) groups were prepared and subjected to this reaction. It has been found that bromination of compounds (5b-d) gave only one isomer (4S,5S)-9b-d while 5e gave a mixture of products (4S,5S and 4S,5R)-9e in the ratio 4:1 (Table 2).

**Table 2**: $^1$HNMR data for compounds 5e and 9e compound (*)

| | (5e) | (9e) | |
|---|---|---|---|
| Proton | (2E,4E) | (4S,5S) | (4S,5R) |
| Proton H-2 | 5.1, s, 1H | 4.5, s, 1H | 4.8, s, IH |
| H-4 | 7.1, d (J = 16 Hz), 1H | 5.6, d (J = 10 Hz), 1H | 5.95, d (J = 8 Hz), 1H |
| H-5 | 7.95, d (J= 16 Hz), 1H | 8.5, d (J = 10 Hz), 1H | 6.2, d (J = 8 Hz), 1H |
| $OCH_3$ | 3.82, s, 3H | 3.6, s, 3H | 3.85, s, 3H |

(*) Diastereoisomer rations were calculated from the integrated $^1$HNMR signals of the enomeric protons. $^J$4S,5S > $^J$4S,5R.

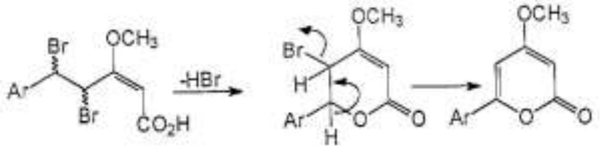
The formation of the mixture of 9e must be via a step-wise addition process and through the carbonium ion intermediate of the type (8), in which the second step is the same as the second step of the $SN^1$ mechanism. The exclusive formation of 4S,5S isomer (9b-d) can be explained, again, by cyclic brominium ion intermediate (7).

It is worth noting that the bromination of the dienoic acids having 5-aryl (5a and 5d) or phenyl containing deactivating group (5b and 5e) affords only one isomer, (4S,5S) through the cyclic bromonium ion intermediate (7) whereas the presence of activating moiety on the phenyl group of the acid (5e) will shift the mechanism of bromination to pass through the classical carbonium ion intermediate (8) (Scheme 2).

### Synthesis of 4-methoxy-6-aryl-2-pyrone (11):

### A: Cyclisation of 3-methoxy-4,5-bromo-5-aryl-2E-pentenoic acid (9):

At an early stage on our investigation, we found it attractive to think that the dibromo acids (9a-e) could yield 4-methoxy-6-aryl-2-pyrone (11) by reaction with organic base. The reaction envisaged is shown in Scheme 3. This reaction would be expected to be concerted initiated be elimination of hydrogen bromide molecule to give the dihydropyrone (10) as intermediate followed by another elimination of hydrogen bromide to give 4-methoxy-6-aryl-2-pyrone (11a-e). With these considerations in mind, we treated the corresponding dibromo acids (9a-e) with triethylamine in benzene as expected, compounds (11a-e) were formed, taking formed, taking ca. 18 hrs. for near-completion, in a good yield.



9 10 11

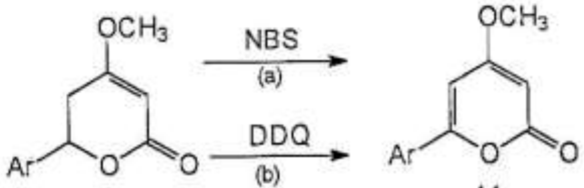
a: Ar = $C_6H_5$
b: Ar = 4-Cl.$C_6H_4$
c: Ar = 2,6-$Cl_2$.$C_6H_3$
d: Ar = 9-anthracenyl
e: Ar = 4-$CH_3O$.$C_6H_4$

**Scheme (3)**

### B: Oxidation of 4-methoxy-6-aryl-5,6-dihydro-2H-pyran-2-one (12):

We have previously described the synthetic routes to piper-oloids (13)$^{(17)}$ and related compounds and have revised some structures proposed for them in the early literature$^{(21)}$. In the course of our work with dihydro-2H-pyran-2-ones$^{(7,22)}$, some new examples of which are reported, the most interesting reactions we uncovered were either their oxidation to the corresponding pyrones (12) or their ring contraction to butenoloids$^{(23)}$. We now provide details of the investigation of these reactions.

The dihydropyrones (12a-i) were prepared by Reformatsky reaction of ethyl 4-bromo-3-methoxy-2-butenoate with various aldehydes$^{(7,22,25)}$. It is known that the generation of conjugated double bond in the $\alpha,\beta$-unsaturated carbonyl compounds could be achieved either by allylic bromination followed by dehydrobromination (path a) or by oxidation with quinone compounds e.g. DDQ (path b) (Scheme 4).

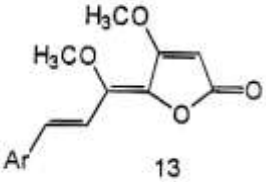


12 11

a: Ar = $C_6H_5$ b: Ar = 4-Cl.$C_6H_4$
c: Ar = 2,6-$Cl_2$.$C_6H_3$ d: Ar = 9-anthracenyl
e: Ar = 4-$CH_3O$.$C_6H_4$ f: Ar = 3,4-($OCH_2O$).$C_6H_3$
g: Ar = CH=CH.CH.$C_6H_5$ h: Ar = $\beta$-naphthyl
i: Ar = 3,4.$(OCH_3)_2$.$C_6H_3$

**Scheme (4)**

Abramson and Wormser$^{(24)}$ found that the bromination of 5,6-dihydropyrones with NBS gave a variety of products. Recently$^{(25)}$ we reported this reaction with compounds (12a-i) by using one or two mole equivalents of NBS. HPLC-studies of the reaction mixture by using one mole of NBS, after three hours reflux, revealed the presence of four types of compounds$^{(25)}$, while the two mole equivalents of NBS led to the formation of 4-methoxy-5-bromo-6-aryl-2-pyrone (14).



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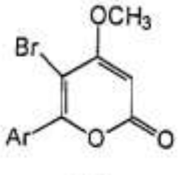

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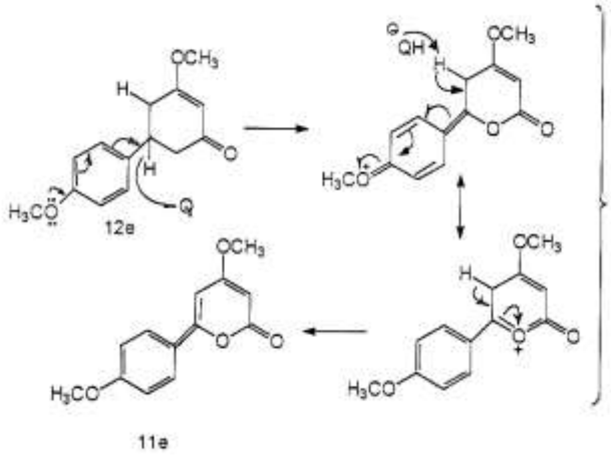
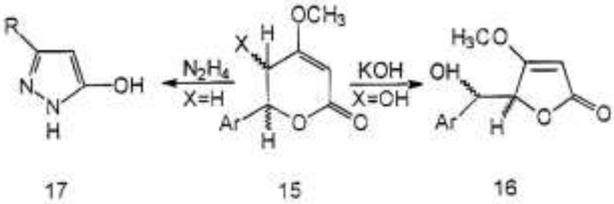
We therefore turned our attention to the synthesis of compound (11) through the oxidation of (12) with DDQ. Compounds (12a-i) differ by only the nature of the substituent on the benzene ring i.e. activating group e.g. 12d-i and deactivating group e.g. 12b,d. from a comparison of their oxidation with DDQ it was clear that the participation of the substituent on the benzene ring is necessary for oxidation. Thus the lone pair of electrons on the oxygen atom in the substituent in compound 12e and i should provide a considerable driving force for hydride ion abstraction and this will increase the rate of oxidation. This oxidation failed; recoverey of starting material was almost quantitative. With compounds like 12a-d and h. This failed may be attributed to the electronic effect of the substituents on the ring (Scheme 5).



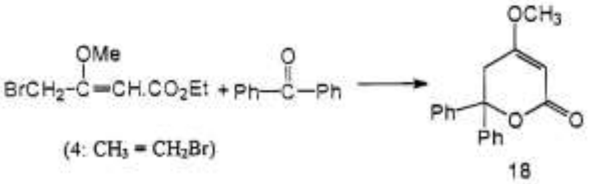
**Scheme (5)**

**Ring contraction of 5,6-dihydro-2-pyrone:**

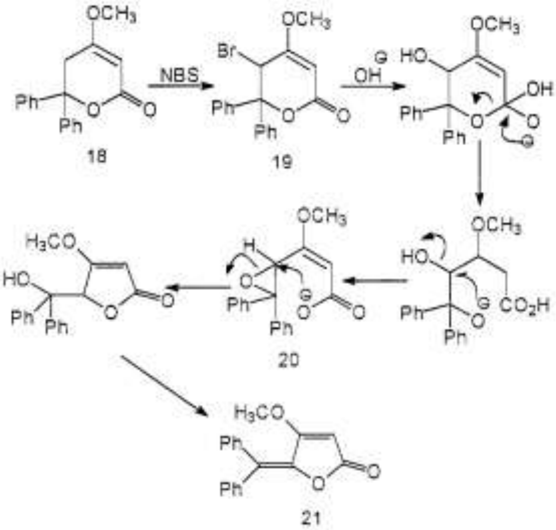
We have previously described two general routes to the synthesis of 2(5H)-furanones and have revised some structures proposed for them in the early literature (17). Further it seemed possible the 2(5H)-furanone (16) could arise from the ring contraction of 5-hydroxydihydropyrone (15)(23,26), since we found that the later compounds with hydrazine gave the corresponding pyrazoles (17)(27).



As an analogy for the intervention of the 5-hydroxypyrone (15) as an intermediate in the formation of butenoloide (16) we investigated the bromination of 4-methoxy-6,6-diphenyl-5,5-dihydro-2H-pyrone (18). This compound was prepared from the reaction of ethyl-4-bromo-3-methoxy-2-butenoate (4; $CH_3$=$CH_2Br$) with benzophenone by Reformatsky-like reaction.



When (18) was treated with 1.1 mole equiv. of NBS in carbon tetrachloride it gave 4-methoxy-5-bromo-6,6-diphenyl-5,6-dihydro-2-pyrone (19). Attempts to isolate this intermediate was unsuccessful. This 5-bromopyrone (19) was converted into 5-benzyl-indene-4-methoxy-2(5H)-furanone (21) by potassium hydroxide in methanol. A possible mechanism for the formation of compound (21) is given in Scheme (6) and is based on our earlier work(23,26).



**Scheme (6)**

The anion (20) formed by ring opening of pyrone moiety attacks the epoxide group of the same molecule at C-5 and would give the observed butenoloide (21) by elimination of water. The differences between the pyrone (18) and butenoloide (20) are emphasized (Table 3).

**Table (3)**: Characterization of compounds (18) and (20)

| Compound | (18) | (20) |
|---|---|---|
| m.p. (°C) | 138-140 | 120-123 |
| ν $cm^{-1}$ (KBr) | 1735 (C=O lactone) | 1765 (C=O lactone) |
| δ-H, DMSO-$d_6$ | | |
| H-3 | 5.1, S 1H | 5.15, S, 1H |
| H-5 | 3.2, S, 2H | - - - |
| $OCH_3$ | 3.6, S, 3H | 3.35, S, 3H |
| Ar-H | 7.2, m, 10H | 7.2, S, 10H |

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# طريقة جديدة لتحضير ٤-مثيل-٦-اريل-بايرون؛ تحضير وبرومة ٣-ميثوكسي-٥-اريل (2E-4E)-حامض البنتاداينويك

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## الملخص:

تم تحضير مركبات ٤-ميثوكسي-٦-اريل-٢-بايرون (١١)، حيث ان حولقة مركبات ٣-ميثوكسي-٤،٥-ثنائي برومو-٥-اريل (2E) حوامض البنتينويك (٩) هي الخطوة المحددة للتفاعل باستخدام ثلاثي اثيل امين المذاب في البنزين، يعقبها خطوة الاكسدة باستخدام ٢،٣-ثنائي كلورو-٥،٦-ثنائي سيانو كوينون (DDQ) . ٣-ميثوكسي-٥-اريل-(2E,4E)-٢،٤-حامض البنتينويك حضر من تفاعل ٣-ميثوكسي (2E) بيوتينوات الاثيل (٤) مع الالديهايد بوجود هيدروكسيد الصوديوم. تفاعل البروم مع هذه الحوامض يعطي انتقائيا المركب (٩). وضحت الكيمياء الفراغية لتفاعلات الحولقة اعلاه.