A Novel, General Method for the Synthesis of 2-Methyl-Substituted and 2-Unsubstituted Methyl 5-Aryl-2,4-pentadienoates[1]

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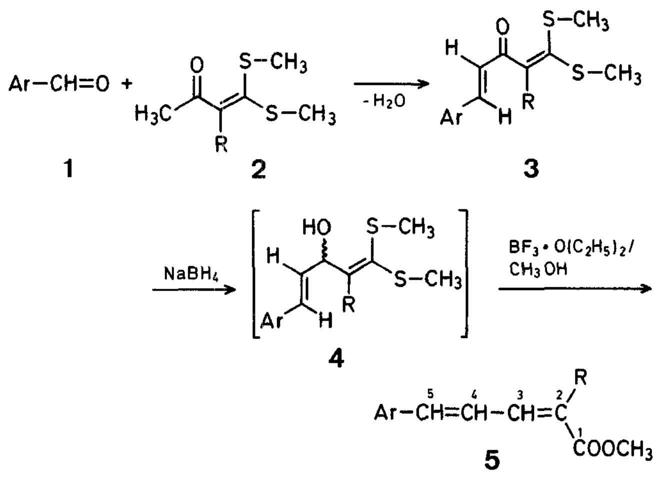
5-Aryl-2,4-pentadienoic acids and their amides are known to exhibit a wide range of biological activities[2-5], similar to abscisic acids[6-9], which enable plants to endure water deprivation. The most commonly used methods to prepare these compounds involve (a) the condensation of cinnamaldehyde with maleic acids followed by decarboxylation of the intermediates[2,10,11], (b) Reformatsky reaction between substituted benzaldehydes and the corresponding γ-halocrotonates[2,11], (c) Wittig reaction between benzaldehydes and phosphonium salts of γ-halocrotonates[2,11-16].

The first two methods suffer from poor yields and undesirable side products. The Wittig reaction is the most widely used method for the preparation of 5-aryl-2,4-pentadienoic esters. A few other methods are described in the literature[17-20]. We report a facile, novel method for the synthesis of methyl 5-aryl-2,4-pentadienoates directly from the ketoketene dithioacetal **3**, which is obtained by the condensation of arylaldehydes **1** and ketoketene dithioacetals **2**.

When the thioacetal **3a** was refluxed with sodium borohydride in ethanol for 2 h, the corresponding carbinol **4a** was obtained in nearly quantitative yield. The carbinol was found



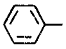
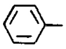
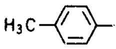
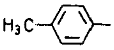
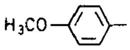
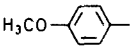
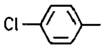
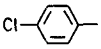
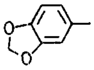
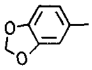
3-5	Ar	R	3-5	Ar	R
a		H	f		CH_3
b		H	g		CH_3
c		H	h		CH_3
d		H	i		CH_3
e		H	j		CH_3

Table. Compounds **5a-j** prepared

Product	Reflux time [h]	Yield [%][a]	m.p. [°C]	Molecular formula[b] or Lit. m.p. [°C]	I.R. (KBr) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]	M.S. *m/e* (M^+)
5a	18	75	69-70°	71°[11]	1720 (C=O); 1630 (C=C)	3.48 (s, 3H, OCH_3); 5.85 (d, *J* = 15 Hz, 1H, H-2); 6.80 (br. d, *J* = 6 Hz, 2H, H-4, H-5); 7.2-7.6 (m, 5H_{arom} + H-3)	188
5b	12	72	98-99°	100°[11]	1718 (C=O); 1628 (C=C)	2.30 (s, 3H, CH_3); 3.70 (s, 3H, OCH_3); 5.88 (d, *J* = 15 Hz, 1H, H-2); 6.75 (br. d, *J* = 6 Hz, 2H, H-4, H-5); 7.0-7.6 (m, 5H_{arom} + H-3)	202
5c	14	69	125-126°	126°[11]	1720 (C=O); 1630 (C=C)	3.71 (s, 3H, OCH_3); 3.78 (s, 3H, OCH_3); 5.88 (d, *J* = 15 Hz, H-2); 6.7-7.0 (m, 2H_{arom} + H-4 + H-5); 7.2-7.6 (m, 2H_{arom} + H-3)	218
5d	15	71	129-131°	132°[11]	1712 (C=O); 1630 (C=C)	3.72 (s, 3H, OCH_3); 5.95 (d, *J* = 15 Hz, 1H, H-2); 6.80 (br. d, *J* = 6 Hz, 2H, H-4, H-5); 7.2-7.6 (m, 4H_{arom} + H-3)	224, 222
5e	10	55	148-149°	146°[26]	1715 (C=O); 1620 (C=C)	3.60 (s, 3H, OCH_3); 5.87 (d, *J* = 15 Hz, 1H, H-2); 5.91 (s, 2H, CH_2); 6.5-7.3 (m, 3H_{arom} + H-3 + H-4 + H-5)	232
5f	14	78	85-86°	86-87°[16]	1720 (C=O); 1628 (C=C)	2.01 (d, *J* = 1.5 Hz, 3H, CH_3); 3.72 (s, 3H, OCH_3); 6.8-7.1 (m, 3H_{olefin}); 7.1-7.4 (m, 5H_{arom})	202
5g	16	71	viscous semi-solid	$C_{14}H_{16}O_2$ (216.1)	1720 (C=O); 1610 (C=C)[c]	2.30 (d, *J* = 1.5 Hz, 3H, CH_3); 2.38 (s, 3H, CH_3); 3.72 (s, 3H, OCH_3); 6.7-7.9 (m, 4H_{arom} + 3H_{olefin})	216
5h	11	68	67°	$C_{14}H_{16}O_3$ (232.1)	1715 (C=O); 1600 (C=C)	2.00 (d, *J* = 1.5 Hz, 3H, CH_3); 3.72 (s, 3H, OCH_3); 3.79 (s, 3H, OCH_3); 6.7-7.5 (m, 4H_{arom} + 3H_{olefin})	232
5i	13	78	101-102°	$C_{13}H_{13}ClO_2$ (236.6)	1708 (C=O); 1630 (C=C)	2.02 (d, *J* = 1.5 Hz, 3H, CH_3); 3.75 (s, 3H, OCH_3); 6.7-7.1 (m, 3H_{olefin}); 7.1-7.5 (4H_{arom})	238, 236
5j	11	70	110-112°	$C_{14}H_{14}O_4$ (246.1)	1700 (C=O); 1610 (C=C)	2.01 (d, *J* = 1.5 Hz, 3H, CH_3); 3.75 (s, 3H, OCH_3); 5.91 (s, 2H, CH_2); 6.7-7.4 (m, 3H_{arom} + 3H_{olefin})	246

[a] Yield of pure isolated product.

[b] Satisfactory microanalyses obtained: C ±0.31, H ±0.33.

[c] Neat film.

to be unstable. So, without isolation, it was subjected to methanolysis in the presence of boron trifluoride etherate. The corresponding 5-phenyl-2,4-pentadienoic ester **5a** was obtained in 75% yield.

Similarly, the dienoic esters **5b–e** were gained in 55–72% overall yields. The ketoketene dithioacetals **3f–j** obtained by the condensation of **1** and the methyl-substituted **2** also underwent facile reduction and methanolysis under identical conditions to give the corresponding 2-methyl esters **5f–j** in 50–78% overall yields.

The stereochemical assignments of the esters **5a–e** were made by ^{1}H-N.M.R. spectra, which showed them to be (2-*E*,4-*Z*)-isomers[21]. Hydrolysis of the ester **5a** yielded an acid (m.p. 165–166 °C), which was earlier assigned the (2-*E*,4-*E*)-stereochemistry, but was later shown to be the (2-*E*,4-*Z*)-isomer by ^{1}H-N.M.R. spectra[22,23]. The melting point, I.R., and ^{1}H-N.M.R. spectral data of the 2-methyl ester **5f** and the corresponding acid were similar to the reported values for the (2-*E*,4-*E*)-isomer[16,24]. The 2-methyl esters **5g–j** were similarly assigned the (2-*E*,4-*E*)-geometry. Hydrolysis of the ester **5f** yielded an acid (m.p. 162–163 °C) which is identical to the reported (2-*E*,4-*E*)-acid[16,24].

Thus, the present method is highly stereoselective and provides a simple route to **5** from easily available starting materials in good yields.

The starting arylidene *S*,*S*-acetals **3a–j** were prepared according to the reported procedure[25].

5-Aryl-2,5-pentadienoic Esters (5); General Procedure:

To a well-stirred suspension of **3** (0.02 mol) in absolute ethanol (70 ml) an excess of sodium borohydride (2.5 g, 0.07 mol) is added and the mixture is heated under reflux for 2 h. The cooled reaction mixture is poured into water (150 ml) and the solution is extracted with chloroform (2 × 100 ml). The extract is washed twice with brine (100 ml), dried with sodium sulfate, and evaporated under vacuum to give the carbinols **4** in nearly quantitative yields as undistillable, viscous liquids, which showed strong absorption between 3100-3500 cm^{-1} (ν_{OH}) in their I.R. spectra.

To the crude carbinol **4** (0.02 mol), boron trifluoride etherate (15 ml) is added and the mixture is stirred at room temperature for 5 min. It is then diluted with absolute methanol (50 ml) and the solution is refluxed for 12–24 h (Table). The cooled reaction mixture is poured into water (250 ml) and the solution is extracted with chloroform (2 × 100 ml). The extracts are washed successively with saturated sodium hydrogen carbonate solution (200 ml), brine (100 ml), and water (100 ml), dried with sodium sulfate, and evaporated to give the crude esters **5a–j** which are further purified by passing through a short column of silica gel using hexane as eluent (Table).

Hydrolysis of the Esters 5a and 5f:

A solution of ester **5a** or **5f** (0.016 mol) and sodium hydroxide (1.40 g, 0.035 mol) in methanol (15 ml) is refluxed for 3 h. The precipitated sodium salts of the corresponding acids are filtered, washed with ether, and dried in vacuum. They are then dissolved in water (35 ml) and acidified with concentrated hydrochloric acid (0.5 ml), filtered, washed with water, and dried. Recrystallisation from dilute ethanol yields the 5-phenylpentadienoic acid; m.p. 165–166 °C (Lit.[14], m.p. 165 °C).

The ester **5e** similarly gives 5-phenyl-2-methylpentadienoic acid; m.p. 162–163 °C (Lit.[16], m.p. 164–165 °C).

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