# A Facile and Convenient Synthesis of Methyl 7-Aryl-2,4,6-heptatrienoates[1]

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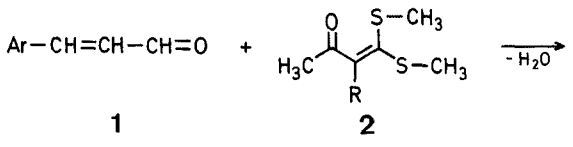
We have recently reported[2] an efficient and highly stereoselective synthesis of methyl 5-aryl-2,4-pentadienoates by reduction of cinnamoylketene dithioacetals with sodium borohydride, followed by methanolysis of the resultant 3-hydroxyketene dithioacetals in the presence of boron trifluoride etherate. We have now successfully extended this method to the synthesis of methyl 7-aryl-2,4,6-heptatrienoates (**5**) and their 2-methyl derivatives.

The previously unreported starting materials **3a–h** were obtained in high yields by the known[3] condensation of cinnamaldehydes (**1**) with acylketene *S,S*-dimethyl acetals (**2**). Compounds **3** were reduced with sodium borohydride in boiling ethanol to give the hydroxy-substituted ketene *S,S*-acetals **4** which, without purification, were subjected to the reaction with methanol in the presence of boron trifluoride etherate to give the desired methyl 2,4,6-heptatrienoates **5** in 58–74% overall yields.



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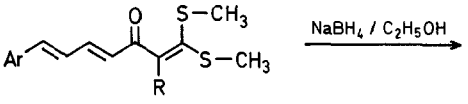

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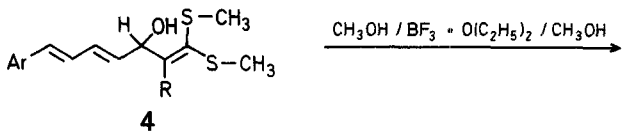

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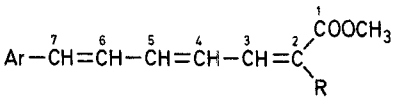

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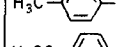
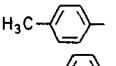
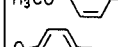
| 3-5 | Ar | R | 3-5 | Ar | R |
|---|---|---|---|---|---|
| a |  | H | e |  | $CH_3$ |
| b |  | H | f |  | $CH_3$ |
| c |  | H | g |  | $CH_3$ |
| d |  | H | h |  | $CH_3$ |

Previous methods for the preparation of compounds **5** employ one of the variants of aldol condensation using cinnamaldehyde and either crotonate ester (or its methyl analogs)[4], bromocrotonates (Reformatsky)[5], or the corresponding phosphonium salts (Wittig Reaction)[6]. The esters **5** or the corresponding acids have also been obtained by condensation of 5-arylpentadienals with either malonic acid (Knoevenegal reaction)[7], bromoacetate (Reformatsky)[8,9], or the appropriate Wittig reagent[10]. However, these alkadienals

**Table 1.** 1,1-Bis[methylthio]-3-oxo-7-aryl-1,4,6-heptatrienes (**3**) prepared

| 3 | Yield [%] | m.p. [°C] | Molecular Formula[a] | M.S. *m/e* ($M^+$) | I.R. (KBr) ν [$cm^{-1}$] | $^1$H-N.M.R. ($CDCl_3$/$TMS_{int}$) δ [ppm] |
|---|---|---|---|---|---|---|
| **a** | 76 | 94° | $C_{15}H_{14}OS_2$ (274.3) | 274 | 1638, 1595 | 2.33 (s, $SCH_3$); 2.38 (s, 3H, $SCH_3$); 6.15 (d, 2H, *J* = 15 Hz); 6.61–7.48 (m, $8H_{arom+olefin}$) |
| **b** | 81 | 124–125° | $C_{16}H_{16}OS_2$ (288.3) | 288 | 1635, 1580 | 2.11 (s, 3H, $CH_3$); 2.28 (s, 3H, $SCH_3$); 2.35 (s, 3H, $SCH_3$); 6.31 (d, 2H, *J* = 15 Hz); 6.8–7.4 (m, $7H_{arom+olefin}$) |
| **c** | 82 | 127–130° | $C_{16}H_{16}O_2S_2$ (304.3) | 304 | 1648, 1590 | 2.52 (s, 6H, $SCH_3$); 3.78 (s, 3H, Ar—$OCH_3$); 6.23–7.56 (m, $9H_{arom+olefin}$) |
| **d** | 80 | 134° | $C_{16}H_{14}O_3S_2$ (318.3) | 318 | 1650, 1592 | 2.21 (s, 3H, $SCH_3$); 2.32 (s, 3H, $SCH_3$); 5.88 (s, 2H, O—$CH_2$—O); 6.24 (d, 2H, *J* = 15 Hz); 6.58–7.26 (m, $6H_{arom+olefin}$) |
| **e** | 73 | 106–107° | $C_{16}H_{16}OS_2$ (288.3) | 288 | 1648, 1595 | 2.09 (s, 3H, $CH_3$); 2.21 (s, 3H, $SCH_3$); 2.32 (s, 3H, $SCH_3$); 6.31 (d, 2H, *J* = 15 Hz); 6.78–7.49 (m, $7H_{arom+olefin}$) |
| **f** | 77 | 138–141° | $C_{17}H_{18}OS_2$ (302.3) | 302 | 1648, 1618 | 2.09 (s, 3H, $CH_3$); 2.11 (s, 3H, Ar—$CH_3$); 2.22 (s, 3H, $SCH_3$); 2.31 (s, 3H, $SCH_3$); 6.26 (d, 2H, *J* = 15 Hz); 6.69–7.41 (m, $6H_{arom+olefin}$) |
| **g** | 79 | 92–93° | $C_{17}H_{18}O_2S_2$ (318.3) | 318 | 1645, 1590 | 2.12 (s, 3H, $CH_3$); 2.21 (s, 3H, $SCH_3$); 2.35 (s, 3H, $SCH_3$); 3.81 (s, 3H, $ArOCH_3$); 6.31 (d, 2H, *J* = 15 Hz); 6.61–7.59 (m, $6H_{arom+olefin}$) |
| **h** | 77 | 103–105° | $C_{17}H_{16}O_3S_2$ (332.3) | 332 | 1642, 1595 | 2.13 (s, 3H, $CH_3$); 2.21 (s, 3H, $SCH_3$); 2.32 (s, 3H, $SCH_3$); 5.89 (s, 2H, O—$CH_2$—O); 6.25 (d, 2H, *J* = 15 Hz); 6.59–7.26 (m, $5H_{arom+olefin}$) |

[a] The microanalyses showed the following maximum deviations from the calculated values: C ± 0.33; H ± 0.24.

**Table 2.** Methyl 7-Aryl-2,4,6-heptatrienoates (**5**) prepared

| 5 | Yield[a] [%] | m.p. [°C] | Molecular Formula[b] or m.p. [°C] reported | M.S. ($M^+$) *m/e* | I.R. (KBr) ν [$cm^{-1}$] | $^1$H-N.M.R. ($CDCl_3$/$TMS_{int}$) δ [ppm] |
|---|---|---|---|---|---|---|
| **a** | 61 | 111–113° | 112°[5] | | 1715 (ester); 1610 | 3.68 (s, 3H, $OCH_3$); 5.85 (d, 1H, *J* = 15 Hz, 2-H); 6.35–6.85 (m, $3H_{olefin}$); 7.11–7.62 (m, $7H_{arom+olefin}$) |
| **b** | 62 | 131–132° | $C_{15}H_{16}O_2$ (228.3) | 228 | 1716 (ester); 1600 | 2.32 (s, 3H, $CH_3$); 3.71 (s, 3H, $OCH_3$); 5.85 (d, 1H, *J* = 15 Hz, 2-H); 6.15–6.88 (m, $3H_{olefin}$); 6.95–7.52 (m, $6H_{arom+olefin}$) |
| **c** | 58 | 164–165° | 167–168°[7] | | 1716 (ester); 1600 | 3.70 (s, 3H, $OCH_3$); 3.78 (s, 3H, Ar—$OCH_3$); 5.80 (d, 1H, *J* = 15 Hz, 2-H); 6.52–6.95 (m, $5H_{arom+olefin}$); 7.10–7.55 (m, $4H_{arom+olefin}$) |
| **d** | 68 | 172–173° | 174°[5] | | 1718 (ester); 1600 | 3.70 (s, 3H, $OCH_3$); 5.65–6.10 (m, 3H, O—$CH_2$—O + 2-H); 6.15–7.00 (m, $8H_{arom+olefin}$) |
| **e** | 71 | 107–108° | 108°[6] | | 1698 (ester); 1600 | 1.95 (s, 3H, 2-$CH_3$); 3.68 (s, 3H, $OCH_3$); 6.25–6.82 (m, $4H_{olefin}$); 6.95–7.52 (m, $6H_{arom+olefin}$) |
| **f** | 68 | 101–102° | $C_{16}H_{18}O_2$ (242.3) | 242 | 1697 (ester); 1592 | 1.97 (s, 3H, 2-$CH_3$); 2.32 (s, 3H, Ar-$CH_3$); 3.71 (s, 3H, $OCH_3$); 6.35–6.82 (m, $4H_{olefin}$); 6.92–7.45 (m, $5H_{arom+olefin}$) |
| **g** | 72 | 95–96° | $C_{16}H_{18}O_3$ (258.3) | 258 | 1698 (ester); 1596 | 1.98 (s, 3H, 2-$CH_3$); 3.71 (s, 3H, $OCH_3$); 3.79 (s, 3H, Ar-$OCH_3$); 6.35–7.00 (m, $6H_{arom+olefin}$); 7.10–7.55 $3H_{arom+olefin}$) |
| **h** | 74 | 123° | $C_{16}H_{16}O_4$ (272.3) | 272 | 1698 (ester); 1595 | 1.92 (s, 3H, 2-$CH_3$); 3.71 (s, 3H, $OCH_3$); 5.90 (s, 2H, O—$CH_2$—O); 6.21–6.95 (m, $7H_{arom+olefin}$); 7.05–7.35 (m, $1H_{olefin}$) |

[a] Yield of isolated pure product.

[b] The microanalyses showed the following maximum deviations from the calculated values: C ± 0.31; H ± 0.21.

are difficult to prepare[10] and the yields are usually low in these reactions. Compound **5a** has also been prepared by Michael addition of allylidenetriphenylphosphoranes to β-chloroacrylates followed by elimination of chloride ion and deprotonation to give a stabilized yield which reacts *in situ* with benzaldehyde to afford **5a** in good yield[11,12].

The present alternative method for the preparation of compounds **5** is simple to perform, uses easily available starting materials, and affords good yields. The keteoketene *S,S*-acetals **2** can be considered as synthetic equivalents of crotonic esters (or their 2-methyl derivatives) which are transformed into the 2-alkenoic ester moiety via reduction of the carbonyl group, the conversion **3** → **5** as a whole representing a 1,3-carbonyl transposition[13].

In all reactions, only one stereoisomer of **5** was obtained as is evident from the sharp melting points and the highly resolved methoxy (and methyl) signals in the $^1$H-N.M.R. spectra of **5**. However, it was not possible to make definite stereochemical assignments, since most of the olefinic protons in the $^1$H-N.M.R. spectra of **5** were merged with the aromatic proton signals.

**1,1-Bis[methylthio]-3-oxo-7-aryl-1,4,6-heptatrienes (Acylketene *S,S*-Acetals 3); General Procedure (cf. Ref.[3]):**
To a well stirred and ice cold mixture of cinnamaldehyde (**1**; 0,03 mol) and ketene *S,S*-acetal **2** (0.03 mol) in 95% ethanol (30 ml) sodium ethoxide (0.06 mol) in ethanol (15 ml) is added slowly (5 min) and stirring is continued at room temperature for 3 h. The mixture is then diluted with water (100 ml), when the acylketene *S,S*-acetal **3** separates out as a yellow solid which is further purified by recrystallization from methanol.

**Methyl 7-Aryl-2,4,6-heptatrienoates (5); General Procedure:**
To a well stirred suspension of the ketene *S,S*-acetal **3** (0.02 mol) in absolute ethanol (100 ml), excess sodium borohydride (2.5 g, 0.07 mol) is added and the mixture is refluxed for 2 h. The cooled mixture is then poured onto crushed ice (150 g) and extracted with chloroform (2 × 150 ml). The chloroform extract is washed with saturated salt solution (2 × 100 ml), dried with sodium sulphate, and evaporated under vacuum to give the crude carbinol **4** in nearly quantitative yields as an undistillable thick viscous liquid. The crude carbinol is dissolved in absolute methanol (100 ml) and boron trifluoride etherate (10 ml) is added with stirring. The mixture is then refluxed for 20–24 h (**5a–d**) or 8–10 h (**5e–h**). The cooled mixture is poured into water (250 ml) and extracted with chloroform (2 m 100 ml). The chloroform extract is washed with saturated sodium hydrogen carbonate solution (2 × 100 ml) and with water (2 × 100 ml), dried with sodium sulphate, and evaporated to give the crude esters **5a–h**, which are further purified by passing through a silica gel column, using hexane as eluent.

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[1] Part XXXIV of the series. For Part XXIII, see: L. W. Singh, A. K. Gupta, H. Ila, H. Junjappa, *Synthesis* **1984**, 516.
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