# Isomerisation of 4-aryl-4-methylhex-5-en-2-ones to 5-aryl-4-methylhex-5-en-2-ones by an intramolecular ene-retro ene reaction sequence

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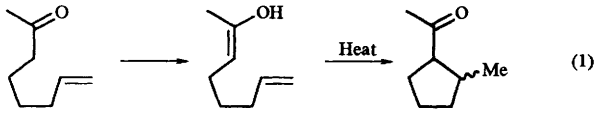
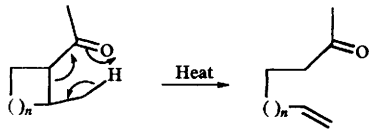
Acid-catalysed thermal rearrangement of 4-aryl-4-methylhex-5-en-2-ones (products of the Claisen rearrangement of β-methylcinnamyl alcohols and 2-methoxypropene) to isomeric 5-aryl-4-methylhex-5-en-2-ones *via* an intramolecular ene reaction of the enol tautomer followed by a retro ene reaction of the resultant acetylcyclopropane is described. Formation of the known diketone **13** *via* the ozonolysis of the rearrangement product **10**, confirmed the structures of the rearranged enones, whereas formation of the enone **15** containing an extra methyl group on the styrene double bond confirmed the proposed mechanism. Finally, the rearrangement has been extended to the formal synthesis of β-cuparenone **20** *via* the enones **22** and **23**.

The reactivity of the carbonyl group in inter- and intramolecular reactions can be regarded in different ways depending on the nature of the reactive centres and the energy sources. In basic or acidic media, the reactions of carbonyl compounds frequently involve an enolate intermediate or the enol tautomer. Another class of intramolecular reactions of the carbonyl group is the thermal reaction of nonconjugated unsaturated carbonyl compounds.[1] Such compounds are able to undergo considerable structural changes, by intramolecular hydrogen displacement leading to ring closure. One such process is the intramolecular variant of the general 'ene' reaction.[2] The most significant example of the thermal behaviour of unsaturated carbonyl compounds is represented[3] by the thermal cyclisation of oct-7-en-2-one, in which four carbon atoms separate the two unsaturated terminals. When heated in a sealed tube or in the vapour phase at around 350 °C, oct-7-en-2-one is converted smoothly and quantitatively into a mixture of *cis*- and *trans*-1-acetyl-2-methylcyclopentanes *via* an ene reaction [eqn. (1)]. From the general considerations of



(1)

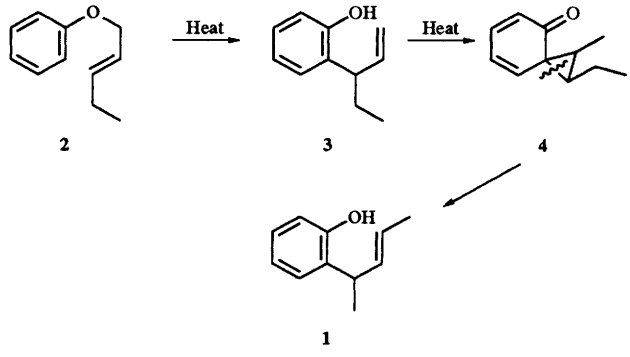
the mechanistic aspects of this reaction, it is expected that the cyclisation of unsaturated carbonyl compounds will occur when the geometry of the system favours a six-electron cyclic process involving the participation of the enol intermediate and the alkenic centre situated in the hydrocarbon. In the case of small ring systems like acylcyclopropanes and acylcyclobutanes, intramolecular hydrogen transfers are also thermally induced leading to a retro ene reaction and a ring-opening occurs preferentially[4] [eqn. (2)]. A combination of these forward and



(2)

$n = 0$ or 1

reverse intramolecular ene reactions was used to explain the formation of abnormal aromatic Claisen rearrangement products,[5] *e.g.* formation of the phenol **1** from the phenyl ether

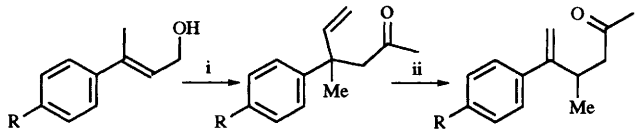



**2** was explained[5d] as proceeding *via* the normal Claisen product **3** and the cyclopropane intermediate **4**. Based on this concept of an intramolecular ene-retro ene reaction sequence, herein we describe[6] a novel acid-catalysed thermal isomerisation of 4-aryl-4-methylhex-5-en-2-ones to 5-aryl-4-methylhex-5-en-2-ones and its extension to a formal synthesis of β-cuparenone.

## Results and discussion

The Claisen rearrangement of the cinnamyl alcohol **5** with 2-methoxypropene in the presence of a catalytic amount of propionic acid in toluene at 180 °C for 36 h, furnished the enone **6**.[7] Thermal activation of the enone **6** in toluene, in the presence of a catalytic amount of propionic acid, in a sealed tube at 250 °C for 48 h generated an inseparable 2:1 mixture of the rearranged enone **7** and the starting enone **6**. The presence of a UV absorption band at $\lambda_{max}$ 239 nm ($\varepsilon$ 6025 $dm^3\ mol^{-1}\ cm^{-1}$) for the mixture indicated the presence of a styrene moiety in the product **7**. The structure of the rearranged enone **7** was established from the $^1H$ NMR spectrum of the product mixture, which exhibited two sets of peaks in the ratio of 2:1 for the enones **7** and **6**. The presence of a close AB quartet centred at $\delta_H$ 7.2 and a typical *gem*-disubstituted olefinic pattern [$\delta_H$ 5.18 (1 H, br s) and 5.0 (1 H, br s)] for the α and *p*-disubstituted styrene moiety, a typical $AMNX_3$ spin pattern [$\delta_H$ 3.1–3.7 (1 H, m), 2.65 (1 H, d of $\frac{1}{2}$ AB q, *J* 16 and 5 Hz), 2.4 (1 H, d of $\frac{1}{2}$ AB q, *J* 16 and 9 Hz) and 1.15 (3 H, d, *J* 7 Hz)] for the $CH_3CHCH_2C{=}O$ moiety, an aromatic methyl (2.39) and an acetyl methyl (2.14) due to the enone **7** (major set) established the structure. The $^{13}C$ NMR spectrum confirmed the structure

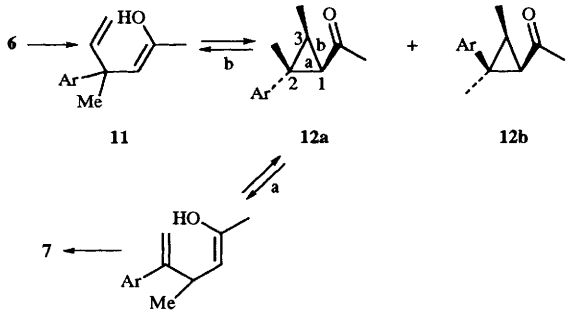
with resonances due to a carbonyl carbon [$\delta_C$ 207.7 (s)], four signals for the 1,4 disubstituted benzene ring [139.1 (s), 137.0 (s), 129.4 (2 C, d) and 126.5 (2 C, d)], a *gem*-disubstituted olefin [153.4 (s) and 110.6 (t)], three methyl carbons [33.4 (q), 30.3 (q) and 21.1 (q)], a methylene α to carbonyl [49.8 (t)] and a methine [33.4 (d)] in addition to the resonances due to the starting enone **6** (minor set). It was observed that the presence of propionic acid accelerated the conversion of the enone **6** into the enone **7**. The same reaction under identical conditions but in the absence of propionic acid furnished only *ca.* 5% of the rearranged enone **7**. In contrast, use of more propionic acid resulted in a considerable amount of decomposition and a very low yield of products was observed.



**5** R = Me, **8** R = H; **6** R = Me, **9** R = H; **7** R = Me, **10** R = H

i, $CH_2$=C(Me)OMe, PhMe, $EtCO_2H$, heat; ii, PhMe, $EtCO_2H$, heat

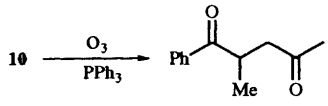
Alternatively, direct reaction of the cinnamyl alcohol **5** in toluene with 2-methoxypropene and a catalytic amount of propionic acid at 230–250 °C in a sealed tube also furnished the same mixture of the enones **6** and **7**. The formation of the enone **7** from the normal Claisen product **6** can be explained as depicted in Scheme 1. Intramolecular ene reaction of the enol tautomer **11** of the enone **6** provides the acetylcyclopropanes **12a** and **12b**. Thermal 1,5-hydrogen transfer (or retro ene reaction) of the acetylcyclopropane **12a**, either from the 2-methyl or 3-methyl to the carbonyl oxygen *via* the cleavage of the corresponding cyclopropane bond [C(1)–C(2) or C(1)–C(3)] furnishes either the rearranged enone **7** or the starting enone **6**, respectively. The other stereoisomer, **12b**, can only revert to the starting enone **6**.



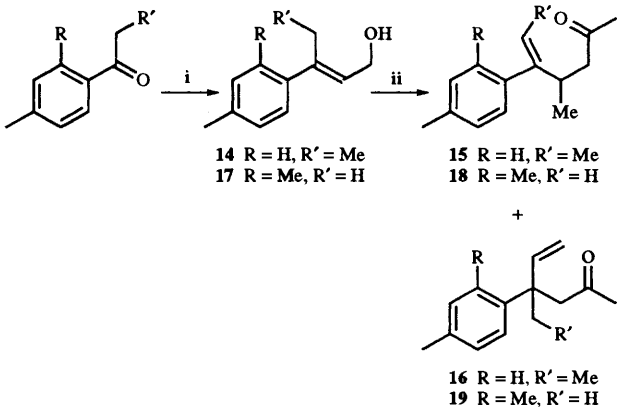
**11** **12a** **12b**

**Scheme 1**

To test the generality of the reaction and also further to establish unambiguously the structure of the rearrangement product **7**, the reaction procedure was carried out with several cinnamyl alcohols. For example, Claisen rearrangement of the alcohol **8**[8] with 2-methoxypropene furnished the enone **9**, which on thermal activation in toluene in the presence of a catalytic amount of propionic acid (sealed tube, 230–240 °C) for 48 h, furnished a 1 : 2 mixture of starting enone **9** and the rearranged enone **10**.[9] Interestingly, the same reaction at elevated temperature (250–270 °C) furnished the rearranged enone **10** with only trace amounts of the enone **9**. Ozonolysis of the enone **10** followed by purification by column chromatography furnished the diketone **13**, which exhibited an $^1$H NMR spectrum identical with that reported in the literature.[10] The formation of the diketone **13**, in turn, confirmed the structure of the enone **10** and, by analogy, that of the enone **7**. To establish the proposed mechanism of the rearrangement, the reaction was carried out starting with the cinnamyl alcohol **14**, as this should, based on the proposed mechanism, result in a methyl group on the styrene double bond. A direct thermal reaction



**13**



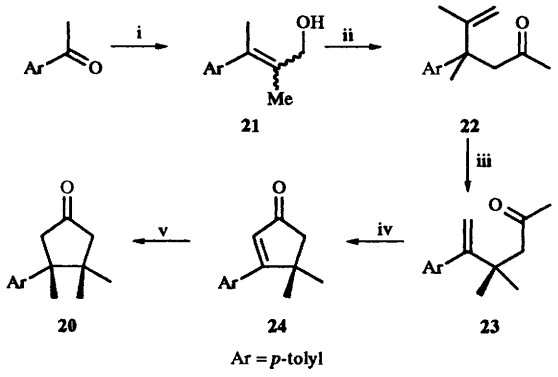
**14** R = H, R′ = Me; **17** R = Me, R′ = H; **15** R = H, R′ = Me; **18** R = Me, R′ = H; **16** R = H, R′ = Me; **19** R = Me, R′ = H

i, (a) NaH, $(EtO)_2P(O)CH_2CO_2Et$, THF, reflux; (b) $LiAlH_4$, $Et_2O$, −70 °C; ii, $CH_2$=C(Me)OMe, $EtCO_2H$, PhMe, heat

was carried out starting from the cinnamyl alcohol **14**. Thus, thermal activation of the cinnamyl alcohol **14**, obtained in two steps from 4-methylpropiophenone, with 2-methoxypropene and a catalytic amount of propionic acid in toluene at 200–210 °C for 48 h furnished directly the rearranged enone **15** accompanied by a minor amount (*ca.* 6%) of the normal Claisen product, the enone **16**. The structure of the enone **15** was deduced from its spectral data. The $^1$H NMR spectrum exhibited signals at $\delta_H$ 5.51 (q, olefinic H) and 1.46 (d, olefinic Me), confirming the presence of a trisubstituted olefin. The stereochemistry of the double bond was assigned as *E*, based on the chemical shift of the methyl on the styrene.[11] The formation of the rearranged enone **15** containing a methyl group on the styrene double bond, unambiguously established the proposed mechanism of the rearrangement. Interestingly, Claisen rearrangement of the cinnamyl alcohol **17**, obtained from 2,4-dimethylacetophenone, with 2-methoxypropene and a catalytic amount of propionic acid in toluene (sealed tube, 190–200 °C), resulted in the rearranged enone **18**, with only traces of the normal Claisen product **19**. Quite expectedly, preparation of the normal Claisen rearrangement products, the enones **16** and **19**, *via* the mercuric acetate-catalysed reaction of the cinnamyl alcohols **14** and **17** and 2-methoxypropene, followed by thermal activation of the enones **16** and **19** in toluene at 250 °C in the presence of a catalytic amount of propionic acid furnished the rearranged enones **15** and **18**, respectively, with only a trace amount (by NMR) of the starting enones **16** and **19**. The preferential formation of the rearranged products **15** and **18** in thermal reactions indicates the influence of the product stability on this conversion. Finally, the intramolecular ene-retro ene reaction sequence has been extended to the synthesis of β-cuparenone **20**.

The bicyclic aromatic sesquiterpene β-cuparenone, **20**, was first isolated[12] from the ketonic fraction of the essential oil Mayur pankhi (*Thuja orientalis* L). The cuparenoids present an

interesting synthetic challenge owing to the steric congestion, due to the presence of two vicinal quaternary carbon atoms on a cyclopentane ring. Synthesis of β-cuparenone starting from 4-methylacetophenone is depicted in Scheme 2. Thus, Wittig–




**Scheme 2** *Reagents and conditions*: i, (a) NaH, $(EtO)_2P(O)CH(Me)CO_2Et$, THF, reflux, 14 h, 62%; (b) $LiAlH_4$, $Et_2O$, −70 °C, 2 h, 89%; ii, $CH_2{=}C(Me)OMe$, $EtCO_2H$, PhMe, 180 °C, 48 h, 62%; iii, PhMe, $EtCO_2H$, 240–260 °C, 48 h, 77%, 5:1 ratio of **23** and **22**; iv, (a) $O_3$, $CH_2Cl_2$–MeOH, −50 °C; (b) $PPh_3$, −50 °C–room temp., 14 h, 62%; (c) MeOH, aq. NaOH, reflux, 4 h, 81%; v, ref. 15

Horner–Emmons reaction of 4-methylacetophenone with triethyl α-phosphonopropionate using sodium hydride as base in refluxing THF, followed by reduction of the resultant cinnamate with $LiAlH_4$ generated the requisite cinnamyl alcohol **21**.[13] Claisen rearrangement of the cinnamyl alcohol **21** with 2-methoxypropene in the presence of a catalytic amount of propionic acid furnished the enone **22** (2,4-DNP derivative mp 152–53 °C). Propionic acid-catalysed thermal rearrangement of the enone **22** at 240–260 °C for 48 h furnished, in 77% yield, a 5:1 mixture of the rearranged enone **23** (2,4-DNP derivative mp 138–39 °C) and the starting enone **22**. Ozonolysis of the enone mixture followed by purification by column chromatography furnished the diketone precursor to **24**. Base-catalysed intramolecular aldol condensation of the diketone produced the cyclopentenone **24**, an immediate precursor to β-cuparenone **20**, which exhibited spectral data identical with those reported in the literature.[14]

In conclusion, rearrangement of γ,δ-unsaturated ketones to isomeric enones *via* an intramolecular ene-retro ene reaction sequence, and its extension to the formal synthesis of β-cuparenone has been achieved. The structures of the products, as well as the mechanism of the rearrangement have been unambiguously established. The formation of the same products directly from the thermal reaction of the corresponding cinnamyl alcohols with 2-methoxypropene and propionic acid points to the versatility of the method as well as the necessity to exercise care in assigning the structures of the normal Claisen products in related reactions.

## Experimental

UV and IR spectra were recorded on Shimadzu UV-190 and Hitachi 270–50 and Perkin-Elmer spectrophotometers respectively. ε Values are given in $dm^3\ mol^{-1}\ cm^{-1}$. $^1H$ (90, 200, 270 MHz) and $^{13}C$ (22.5, 67.5 MHz) NMR spectra in $CDCl_3$ were recorded on JEOL FX-90Q, Brucker ACF-200 and WH-270 spectrometers. δ Values quoted are relative to tetramethylsilane and *J* values are in Hz. In the $^{13}C$ NMR spectra off-resonance multiplicities, when recorded, are given in parentheses. Low and high resolution mass measurements were carried out with a JEOL JMS-DX 303 GC–MS instrument using direct inlet mode. Relative intensities of the ions are given in parentheses. Melting points are not corrected. Ozonolysis was carried out using a Penwalt Wallace and Tierman ozonator. Acme's silica gel (100–200 mesh) was used for column chromatography. Dry THF was obtained by distilling over sodium benzophenone ketyl. All the high temperature reactions were carried out using a heating jacket. All the cinnamyl alcohols were prepared from the corresponding acetophenones *via* the Wittig–Horner–Emmons reaction followed by $LiAlH_4$ reduction of the resultant cinnamates. All the products were purified by column chromatography and unless otherwise specified all the spectral data are for the chromatographically pure (> 97%) compounds.

### 4-Methyl-5-(*p*-tolyl)hex-5-en-2-one 7

A solution of the enone **6**[7] (202 mg, 1 mmol) and a catalytic amount of propionic acid (5–10 $mm^3$) in toluene (1 $cm^3$) were placed in a sealed tube under nitrogen and heated to 230–250 °C for 48 h. The reaction mixture was cooled, poured into water (10 $cm^3$) and extracted with benzene (10 $cm^3$ × 3). The combined extracts were washed with saturated aqueous $NaHCO_3$ (10 $cm^3$), and brine and dried ($Na_2SO_4$) and evaporated. Purification of the residue on a silica gel (4 g) column using ethyl acetate–hexane (1:20) as eluent gave a 1:2 mixture of the starting enone **6** and the rearranged enone **7** (137 mg, 68%) as a yellow oil; $\lambda_{max}$(MeOH)/nm 239 (ε 6025); $\nu_{max}/cm^{-1}$ 1720 (C=O); $\delta_H$(90 MHz) for the starting enone **6** (minor set)[7] 7.2 (4 H, m, ArH), 6.16 (1 H, dd, *J* 18 and 10.8, C*H*=$CH_2$), 5.17 (1 H, d, *J* 10.8) and 5.06 (1 H, d, *J* 18, CH=C$H_2$), 2.9 (2 H, close AB q, *J* 16, $CH_2C$=O), 2.36 (3 H, s, $ArCH_3$), 1.94 (3 H, s, $CH_3C$=O) and 1.56 (3 H, s, *tert*-$CH_3$); for the rearranged enone **7** (major set) 7.24 (4 H, 2 × AB q, *J* 7.5, ArH), 5.18 (1 H, br s) and 5.03 (1 H, br s) (C=$CH_2$), 3.1–3.7 (1 H, m, allylic), 2.65 (1 H, d of ½ AB q, *J* 16 and 5) and 2.4 (1 H, d of ½ AB q, *J* 16 and 9) ($CH_2$–C=O), 2.39 (3 H, s, $ArCH_3$), 2.14 (3 H, s, $CH_3C$=O) and 1.15 (3 H, d, *J* 7, CHC$H_3$); $\delta_C$(22.5 MHz) for the starting enone **6** (minor set)[7] 207.6 (s, C=O), 146.2 (d, *C*H=$CH_2$), 143.2 (s), 135.8 (s), 129.0 (2 C, d) and 126.3 (2 C, d) (ArC), 112.1 (t, C=$CH_2$), 54.2 (t, *C*$H_2$–C=O), 43.2 (s, C-4), 32.0 (q, *C*$H_3$–C=O), 25.4 (q, *tert*-$CH_3$) and 21.1 (q, $ArCH_3$); for the rearranged enone **7** (major set) 207.7 (s, C=O), 153.4 (s, *C*=$CH_2$), 139.1 (s), 137.0 (s), 129.4 (2 C, d) and 126.5 (2 C, d) (ArC), 110.6 (t, C=$CH_2$), 49.8 (t, *C*$H_2$C=O), 33.4 (d, allylic), 30.3 (q, *C*$H_3$C=O), 21.1 (q, $ArCH_3$) and 19.8 (q, CH*C*$H_3$) (Found: $M^+$, 202.1377. $C_{14}H_{18}O$ requires *M*, 202.1358).

### 4-Methyl-4-phenylhex-5-en-2-one 9

A solution of the cinnamyl alcohol **8**[8] (296 mg, 2 mmol), 2-methoxypropene (1 $cm^3$, 10 mmol) and a catalytic amount of propionic acid in toluene (2 $cm^3$) were placed in a sealed tube under nitrogen and heated to 160 °C for 48 h. Work-up as described in the previous experiment and purification of the residue on a silica gel (8 g) column using ethyl acetate–hexane (1:20) as eluent gave the enone **9** (259 mg, 69%) as a pale yellow oil; $\nu_{max}/cm^{-1}$ 1722 (C=O), 915; $\delta_H$(90 MHz) 7.1–7.5 (5 H, m, ArH), 6.12 (1 H, dd, *J* 18 and 10.8, C*H*=$CH_2$), 5.12 (1 H, d, *J* 10.8) and 5.02 (1 H, d, *J* 18) (CH=C$H_2$), 2.88 (2 H, close AB q, *J* 18, $CH_2C$=O), 1.88 (3 H, s, $CH_3C$=O) and 1.51 (3 H, s, *tert*-$CH_3$); $\delta_C$(22.5 MHz) 206.5 (s, C=O), 145.7 (2 C, d and s), 127.9 (2 C, d), 126.0 (2 C, d), 111.8 (t, CH=C$H_2$), 53.5 (t, *C*$H_2$C=O), 43.1 (s, C-4), 31.5 (q, *C*$H_3$C=O) and 25.0 (q, *tert*-$CH_3$); *m/z* 188 ($M^+$, 7%), 173 (11), 145 (33), 131 (100), 115 (14), 105 (13) and 91 (42) (Found: $M^+$, 188.1213. $C_{13}H_{16}O$ requires *M*, 188.1201).

### 4-Methyl-5-phenylhex-5-en-2-one 10

Thermal reaction of the enone **9** (200 mg, 1.06 mmol) and a catalytic amount of propionic acid in toluene (2 $cm^3$) in a sealed tube at 250–270 °C for 48 h and work-up were performed as described for the enone **7**. Purification of the residue on a silica

gel (4 g) column using ethyl acetate–hexane (1:20) as eluent gave the rearranged enone **10** (140 mg, 70%) containing a trace amount of the starting enone **9** as a pale yellow oil;[9] $\delta_H$(90 MHz) 7.1–7.5 (5 H, m, aromatic), 5.2 (1 H, s) and 5.04 (1 H, s) (C=C$H_2$), 3.08–3.44 (1 H, m, allylic H), 2.66 (1 H, d of $\frac{1}{2}$ AB q, *J* 17 and 5) and 2.38 (1 H, d of $\frac{1}{2}$ AB q, *J* 17 and 9) (C$H_2$C=O), 2.12 (3 H, s, C$H_3$C=O) and 1.13 (3 H, d, *J* 7.2, CHC$H_3$); $\delta_C$(22.5 MHz) 207.1 (s, C=O), 153.4 (s, *C*=CH$_2$), 141.8 (s), 128.1 (2 C, d), 127.3 (d) and 126.4 (2 C, d) (ArC), 110.9 (t, C=*C*H$_2$), 49.5 (t, *C*H$_2$C=O), 33.2 (d, allylic C), 30.1 (q, *C*H$_3$–C=O) and 19.6 (q, CH*C*H$_3$).

**2-Methyl-1-phenylpentane-1,4-dione 13**

A stream of ozone in oxygen was purged through a magnetically stirred, cold (−70 °C), methanol–methylene dichloride (1:5; 10 cm$^3$) solution of the enone **10** (38 mg, 0.2 mmol) until the blue colour persisted. Excess of ozone was flushed off with oxygen and triphenylphosphine (105 mg, 0.4 mmol) was added. The solution was allowed to warm up to room temperature and stirred for 2 h. Evaporation of the solvent under reduced pressure followed by purification of the residue on a silica gel (3 g) column using ethyl acetate–hexane (1:20) as eluent gave the dione **13** (31 mg, 80%) as a colourless oil which exhibited a $^1$H NMR spectrum similar to that reported in the literature;[10] $\nu_{max}$/cm$^{-1}$ 1719 (C=O), 1683 (ArC=O) and 1610, 1510; $\delta_H$(200 MHz) 7.99 (2 H, *d*, *J* 7.4) and 7.50 (3 H, m) (ArH), 3.97 (1 H, m, CH–C=O), 3.17 (1 H, d of $\frac{1}{2}$ AB q, *J* 18.5 and 8.5) and 2.55 (1 H, d of $\frac{1}{2}$ AB q, *J* 18.5 and 5.0) (C$H_2$–C=O), 2.16 (3 H, s, C$H_3$C=O) and 1.2 (3 H, d, *J* 7.2, CHC$H_3$) [lit.,[10] $\delta_H$(60 MHz) 7.2–8.0 (5 H, m), 3.9 (1 H, m), 3.13 (1 H, dd), 2.46 (1 H, dd), 2.15 (3 H, s) and 1.23 (3 H, d)].

**3-(*p*-Tolyl)pent-2-en-1-ol 14**

**Wittig–Horner–Emmons reaction**. To a magnetically stirred suspension of sodium hydride, (50% dispersion in oil; 750 mg, 15 mmol) in dry THF (15 cm$^3$) was added dropwise, a solution of triethyl phosphonoacetate (3 cm$^3$, 15 mmol) in dry THF (5 cm$^3$) and stirred at room temperature for 30 min. A solution of ethyl *p*-tolyl ketone (1.48 g, 10 mmol) in dry THF (5 cm$^3$) was added dropwise to the reaction mixture which was then stirred at room temperature for 16 h. After this it was poured into water (30 cm$^3$) and extracted with ether (3 × 30 cm$^3$). The combined extracts were washed with brine, dried ($Na_2SO_4$) and evaporated. The residue was purified on a silica gel (10 g) column using ethyl acetate–hexane (1:20) as eluent to give ethyl 3-(*p*-tolyl)pent-2-enoate (1.33 g, 61%) as a pale yellow oil; $\nu_{max}$/cm$^{-1}$ 1716 and 1626; $\delta_H$(90 MHz) 7.35 and 7.15 (4 H, 2 × AB q, *J* 8.2, ArH), 6.0 (1 H, br s, olefinic H), 4.18 (2 H, q, *J* 7.2, OC*H*$_2$CH$_3$), 3.1 (2 H, q, *J* 7.2, 4-H), 2.38 (3 H, s, ArCH$_3$), 1.32 (3 H, t, OCH$_2$C*H*$_3$) and 1.09 (3 H, s, 5-H); *m*/*z* 218 (M$^+$, 90%), 173 (72), 172 (100), 157 (40), 145 (25), 143 (26), 129 (47), 128 (37), 115 (48), 105 (27) and 91 (25) (Found; M$^+$, 218.1303. $C_{14}H_{18}O_2$ requires *M*, 218.1307).

**LiAlH$_4$ reduction**. To a cold (−40 °C), magnetically stirred suspension of LiAlH$_4$ (380 mg, 10 mmol) in dry ether (6 cm$^3$) was added a solution of the cinnamate (1.09 g, 5 mmol) obtained above in dry ether (5 cm$^3$). The reaction mixture was allowed to warm to room temperature over 3 h after which the excess of LiAlH$_4$ was decomposed by careful addition of wet ether followed by water (10 cm$^3$) and 10% aqueous $H_2SO_4$ (3.5 cm$^3$). The mixture was extracted with ether (3 × 25 cm$^3$) and the combined extracts were washed with saturated aqueous NaHCO$_3$ (20 cm$^3$) and brine, dried ($Na_2SO_4$) and evaporated. Purification of the product on a silica gel (7 g) column using ethyl acetate–hexane (1:4) as eluent, gave the cinnamyl alcohol **14** (720 mg, 82%) as a colourless oil; $\nu_{max}$/cm$^{-1}$ 3334, 1647 and 1515; $\delta_H$(90 MHz) 7.0–7.4 (4 H, m, ArH), 5.8 (1 H, t, *J* 7.2, olefinic H), 4.33 (2 H, d, *J* 7.2, C$H_2$OH), 2.55 (2 H, q, *J* 7.2, 4-H), 2.4 (1 H, s, OH), 2.36 (3 H, s, ArCH$_3$) and 0.98 (3 H, t, *J* 7.2, 5-H); *m*/*z* 176 (M$^+$, 10%), 159 (22), 149 (100), 119 (60), 105 (35) and 91 (40).

**4-Methyl-5-(*p*-tolyl)hept-5-en-2-one 15 and 4-ethyl-4-(*p*-tolyl)hex-5-en-2-one 16**

A solution of the cinnamyl alcohol **14** (352 mg, 2 mmol), 2-methoxypropene (1 cm$^3$, 10 mmol) and a catalytic amount of propionic acid in toluene (3 cm$^3$) were placed in a sealed tube under nitrogen and heated to 200–210 °C for 48 h. Work-up followed by purification of the residue on a silica gel (8 g) column using ethyl acetate–hexane (1:20) as eluent furnished a 9:1 mixture of rearranged enone **15** and the normal Claisen product **16** (285 mg, 66%) as a colourless oil; $\nu_{max}$/cm$^{-1}$ 1719 (C=O) and 1515; $\delta_H$(90 MHz) for the major enone **15** 7.15 and 6.95 (4 H, 2 × AB q, *J* 8), 5.51 (1 H, q, *J* 7.2, olefinic H), 2.96 (1 H, m, allylic H), 2.55 (1 H, d of $\frac{1}{2}$ AB q, *J* 16 and 6) and 2.35 (1 H, m) (CH$_2$–C=O), 2.36 (3 H, s, ArCH$_3$), 2.08 (3 H, s, CH$_3$C=O), 1.46 (3 H, d, *J* 7.2, olefinic CH$_3$) and 1.03 (3 H, d, *J* 7.2, CHC$H_3$); for the Claisen product, enone **16** 6.0 (dd, *J* 18 and 10.8, C*H*=CH$_2$), 5.18 (1 H, d, *J* 10.8) and 5.04 (1 H, d, *J* 18), (CH=C$H_2$), 2.86 (2 H, s, CH$_2$C=O), 2.34 (3 H, s, ArCH$_3$), 1.82 (3 H, s, CH$_3$C=O) and 0.76 (3 H, t, *J* 7.2, CH$_2$C$H_3$); $\delta_C$(22.5 MHz) for the major enone **15**, 206.8 (s, C=O), 145.3 (s, *C*=CHMe), 136.8 (s), 135.4 (s) and 128.4 (4 C, d) (aromatic C), 119.5 (d, C=*C*HMe), 49.1 (t, *C*H$_2$C=O), 36.8 (d, allylic C), 29.6 (q, *C*H$_3$C=O), 20.6 (q, ArCH$_3$), 19.3 (q, CH*C*H$_3$) and 14.2 (q, olefinic CH$_3$); for the Claisen product, enone **16** 144.3, 141.3, 135.0, 126.5, 112.5, 49.7, 46.5, 31.4 and 8.2; *m*/*z* 216 (M$^+$, 74%), 173 (100), 159 (50), 158 (77), 145 (45), 143 (59), 131 (85), 115 (20) and 105 (20) (Found; M$^+$, 216.1495. $C_{15}H_{20}O$ requires *M*, 216.1514).

**3-(2,4-Dimethylphenyl)but-2-en-1-ol 17**

The Wittig–Horner–Emmons reaction of 2,4-dimethylphenyl methyl ketone (1.48 g, 10 mmol) with triethyl phosphonoacetate (3 cm$^3$, 15 mmol) and NaH (50% suspension in oil; 750 mg, 15 mmol) for 16 h, followed by purification of the product on a silica gel (10 g) column using ethyl acetate–hexane (1:20) as eluent gave ethyl 3-(2,4-dimethylphenyl)but-2-enoate (1.26 g, 58%) as a pale yellow oil; $\nu_{max}$/cm$^{-1}$ 1719 and 1641; $\delta_H$(90 MHz) 6.98 (3 H, br s, aromatic), 5.74 (1 H, q, *J* 1.8, olefinic H), 4.22 (2 H, q, *J* 7.2, OCH$_2$C$H_3$), 2.45 (3 H, d, *J* 1.8, olefinic CH$_3$), 2.34 (3 H, ArCH$_3$), 2.3 (3 H, s, ArCH$_3$) and 1.34 (3 H, t, *J* 7.2, OCH$_2$C$H_3$); *m*/*z* 218 (M$^+$, 32%), 203 (16), 173 (100), 145 (20), 144 (30), 129 (28), 128 (20), 115 (13) and 105 (11) (Found: M$^+$, 218.1332. $C_{14}H_{18}O_2$ requires *M*, 218.1307). LiAlH$_4$ reduction (380 mg, 10 mmol) of the cinnamate (1.09 g, 5 mmol) obtained above in dry ether (5 cm$^3$) and purification of the product on a silica gel (10 g) column using ethyl acetate–hexane (1:4) as eluent gave the cinnamyl alcohol **17** (704 mg, 80%) as a colourless oil; $\nu_{max}$/cm$^{-1}$ 3310 (OH), 1614; $\delta_H$(90 MHz) 6.98 (3 H, s, aromatic H), 5.5 (1 H, q of t, *J* 7.2 and 1.0, olefinic H), 4.31 (2 H, d, *J* 7.2, C$H_2$OH), 2.34 (3 H, s, ArCH$_3$), 2.28 (3 H, s, ArCH$_3$), 1.96 (3 H, br s, olefinic CH$_3$) and 1.4 (1 H, br s, OH); $\delta_C$(67.5 MHz) 142.0, 139.6, 136.5, 134.5, 131.0, 128.1 (2 C) and 126.4 (aromatic and olefinic H), 59.7 (CH$_2$OH), 21.0, 19.7 and 18.4 (3 × CH$_3$); *m*/*z* 176 (M$^+$, 70%), 161 (84), 158 (55), 143 (100), 133 (59), 128 (35), 115 (27), 105 (23), 91 (34) and 55 (35) (Found: M$^+$, 176.1208. $C_{12}H_{16}O$ requires *M*, 176.1201).

**5-(2,4-Dimethylphenyl)-4-methylhex-5-en-2-one 18**

Thermal reaction of the cinnamyl alcohol **17** (352 mg, 2 mmol) with 2-methoxypropene (1 cm$^3$, 10 mmol) and a catalytic amount of propionic acid in toluene (3 cm$^3$) in a sealed tube at 190–200 °C for 48 h and work-up were performed as described

for the enone **15**. Purification of the residue on a silica gel (10 g) column using ethyl acetate–hexane (1:20) as eluent gave the enone **18** (290 mg, 67%) containing trace amounts of the normal Claisen product **19** as a colourless oil; $\nu_{max}/cm^{-1}$ 3082, 1719 (C=O), 903 and 1635; $\delta_H$(90 MHz) 6.94 (3 H, br s, aromatic H), 5.12 (1 H, br s) and 4.87 (1 H, br s) (C=$CH_2$), 2.36–3.1 (1 H, m, allylic H), 2.66 (1 H, d of $\frac{1}{2}$ AB q, *J* 16 and 5) and 2.3 (1 H, m) ($CH_2$C=O), 2.3 (3 H, s, $ArCH_3$), 2.24 (3 H, s, $ArCH_3$), 2.1 (3 H, s, $CH_3$C=O) and 1.07 (3 H, d, *J* 6.6, CHC$H_3$); $\delta_C$(22.5 MHz) 206.6 (s, C=O), 153.2 (s, *C*=$CH_2$), 139.4 (s), 136.0 (s), 134.4 (s), 130.6 (d), 128.3 (d) and 125.7 (d) (aromatic C), 111.9 (t, C=*C*$H_2$), 48.7 (t, *C*$H_2$C=O), 35.2 (d, allylic C), 29.8 (q, *C*$H_3$C=O), 20.6 (q), 19.5 (q) and 18.6 (q) (3 × $CH_3$); *m/z* 216 ($M^+$, 25), 173 (100), 159 (17), 158 (22), 143 (17), 131 (20) and 119 (11) (Found: $M^+$, 216.1533. $C_{15}H_{20}O$ requires *M*, 216.1514).

**4,5-Dimethyl-4-(*p*-tolyl)hex-5-en-2-one 22**

Claisen rearrangement of the cinnamyl alcohol **21**[13] (200 mg, 1.14 mmol) with 2-methoxypropene (1 $cm^3$, 10 mmol) and a catalytic amount of propionic acid in toluene (2 $cm^3$) in a sealed tube at 180 °C for 48 h as described for the enone **9** and purification of the residue on a silica gel (10 g) column using ethyl acetate–hexane (1:20) as eluent gave *the enone* **22** (150 mg, 61%) as a colourless oil; $\nu_{max}/cm^{-1}$ 1710 (C=O), 1641, 1515 and 894; $\delta_H$(90 MHz) 7.12 (4 H, s, aromatic H), 4.95 (2 H, s, C=$CH_2$), 3.05 and 2.8 (2 H, AB q, *J* 13, $CH_2$C=O), 2.32 (3 H, s, $ArCH_3$), 1.82 (3 H, s, $CH_3$C=O) and 1.55 (6 H, s, 2 × $CH_3$); $\delta_C$(67.5 MHz), 208.5 (C=O), 151.6 (*C*=$CH_2$), 143.4, 136.4, 129.6 (2 C) and 127.0 (2 C) (aromatic C), 111.1 (C=*C*$H_2$), 53.8 (*C*$H_2$C=O), 46.7 (C-4), 32.5 (*C*$H_3$C=O), 25.0, 21.4 and 20.7 (3 × $CH_3$); *m/z* 216 ($M^+$, 15%), 159 (100), 158 (85), 143 (30), 115 (20), 105 (20) and 91 (20) (Found: $M^+$, 216.1521. $C_{15}H_{20}O$ requires *M*, 216.1514). 2,4-DNP derivative mp 152–153 °C (Found: C, 63.45; H, 6.1; N, 13.9. $C_{21}H_{24}N_4O_4$ requires C, 63.62; H, 6.10; N, 14.13%).

**4,4-Dimethyl-5-(*p*-tolyl)hex-5-en-2-one 23**

Thermal reaction of the enone **22** (200 mg, 1 mmol) in toluene (4 $cm^3$) in the presence of a catalytic amount of propionic acid in a sealed tube at 240–260 °C for 48 h and work-up was performed as described for the enone **7**. Purification on a silica gel (5 g) column using ethyl acetate–hexane (1:20) as eluent gave a 1:5 mixture of the starting enone **22** and *the rearranged enone* **23** (155 mg, 77%) as a colourless oil. Spectral data for the rearranged enone **23**: $\nu_{max}/cm^{-1}$ 1719 (C=O), 1608, 1515 and 900; $\delta_H$(90 MHz) 7.05 (4 H, s, aromatic H), 5.16 (1 H, d, *J* 1.5) and 4.84 (1 H, d, *J* 1.5) (C=$CH_2$), 2.5 (2 H, s, $CH_2$C=O), 2.34 (3 H, s, $ArCH_3$), 2.05 (3 H, s, $CH_3$C=O) and 1.24 (6 H, s, 2 × $CH_3$); $\delta_C$(22.5 MHz), 207.2 (s, C=O), 157.1 (s, *C*=$CH_2$), 139.9 (s), 136.0 (s), 129.0 (2 C, d) and 128.0 (2 C, d) (aromatic C), 113.0 (C=*C*$H_2$), 53.5 (t, *C*$H_2$C=O), 38.5 (s, C-4), 32.0 (q, *C*$H_3$C=O), 28.0 (2 C, q, 2 × $CH_3$) and 20.9 (q, $ArCH_3$); *m/z* 216 ($M^+$, 40%), 201 (30), 159 (100), 143 (40), 133 (40), 117 (50), 105 (35) and 91 (20) (Found: $M^+$, 216.1511. $C_{15}H_{20}O$ requires *M*, 216.1514). 2,4-DNP derivative mp 138–139 °C (Found: C, 63.6; H, 6.2; N, 14.2. $C_{21}H_{24}N_4O_4$ requires C, 63.62; H, 6.10; N, 14.13%).

**4,4-Dimethyl-3-(*p*-tolyl)cyclopent-2-enone 24**

Ozonation of the 1:5 mixture of the enones **22** and **23** (45 mg, 0.21 mmol) in 1:5 methanol–methylene dichloride (10 $cm^3$) and reduction of the ozonide with triphenylphosphine (157 mg, 0.6 mmol) as described for the dione **13** followed by careful purification on a silica gel (4 g) column using ethyl acetate–hexane (1:15) as eluent gave 2,2-dimethyl-1-(*p*-tolyl)pentane-1,4-dione (35 mg, *ca.* 90%) containing a small amount of the dione derived from the enone **22**, as a colourless oil;[14,15] $\nu_{max}/cm^{-1}$ 1713 (C=O) and 1677 (ArC=O); $\delta_H$(90 MHz) 7.45 and 7.15 (4 H, 2 × AB q, *J* 8, aromatic H), 2.92 (2 H, s, $CH_2$C=O), 2.38 (3 H, s, $ArCH_3$), 2.08 (3 H, s, $CH_3$C=O) and 1.38 (6 H, s, 2 × $CH_3$).

To a solution of the diketone (23 mg, 0.12 mmol) obtained above in methanol (1 $cm^3$) was added 1 mol $dm^{-3}$ aqueous NaOH (1 $cm^3$) and the reaction mixture was refluxed for 4 h. It was then cooled, poured into water (5 $cm^3$) and extracted with methylene dichloride (2 × 5 $cm^3$). The combined extracts were washed with brine, dried ($Na_2SO_4$) and evaporated and purification of the residue on a silica gel (4 g) column using ethyl acetate–hexane (1:20) as eluent gave the cyclopentenone **24** (17 mg, 81%) as an oil;[14,15] $\nu_{max}/cm^{-1}$ 1727, 1700 and 820; $\delta_H$(90 MHz) 7.45 and 7.25 (4 H, 2 × AB q, *J* 8, aromatic H), 6.18 (1 H, s, olefinic H), 2.46 (2 H, s, $CH_2$C=O), 2.40 (3 H, s, $ArCH_3$) and 1.43 (6 H, s, 2 × $CH_3$) [lit.,[14] $\delta_H$($CCl_4$) 7.4 (4 H, $A_2B_2$, *J* 8), 6.2 (1 H, s), 2.46 (2 H, s), 2.4 (3 H, s) and 1.43 (6 H, s)].

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