Substituted 6-Aroyl-2-cyclohexenones from Esters of 3-Phenyl-2-butenoic Acids and Benzylideneacetophenones

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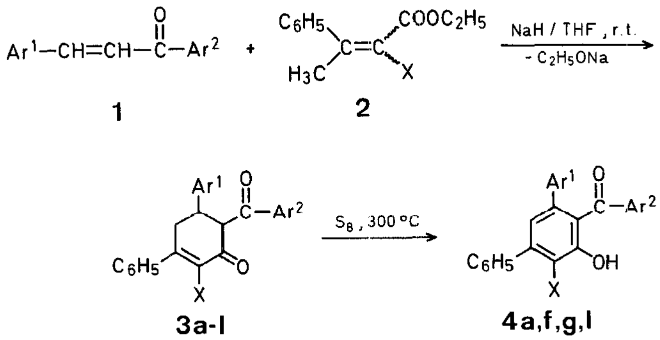
In a number of communications[1-4], it has been shown that, in the presence of a base, the esters of some β-methylated α,β-unsaturated carboxylic acids condense with carbonyl compounds (mainly aromatic aldehydes) in a Stobbe like reaction. This fact, which indicates ability of the mesomeric anions of the starting esters to react as γ-carbanions, prompted us to investigate the behaviour of the same esters under similar conditions toward α,β-unsaturated ketones, esters, and nitriles. We have assumed that in these cases a conjugate addition of the ester anions followed by an intramolecular Claisen condensation could lead to the corresponding substituted 2-cyclohexen-1-ones.



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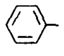
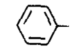
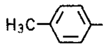
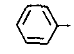
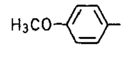
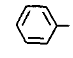
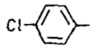
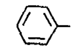
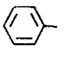
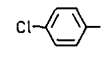
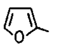
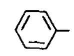
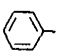
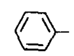
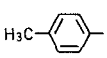
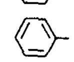
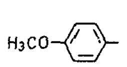
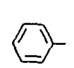
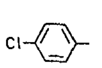
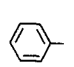
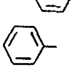
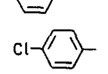
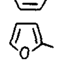
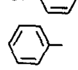
The results of our first experiments, carried out with the ethyl esters of 3-phenyl-2-butenoic and 2-cyano-3-phenyl-2-butenoic acid (**2**, X = H or CN, respectively) and several benzylideneacetophenones (**1**) confirmed this. The expected reaction products: the 6-aroyl-2-cyclohexenones **3**, diastereoisomeric mixtures according T.L.C., were obtained in fairly good yields when the starting substances, dissolved in tetrahydrofuran, were stirred in the presence of sodium hydride for 1 h at room temperature. Refluxing the reaction mixture for the same time did not change substantially the yields. Use of benzene as solvent offered no advantage over the tetrahydrofuran.

All compounds **3** are new. They were identified by their analytical and spectral data as well as on the basis of their dehydrogen-

Table 1. 6-Aroyl-2-cyclohexenones **3**

Product[a] 3	Ar¹	Ar²	X	Yield [%]	m.p. [°C] (solvent)	Molecular formula[b,c]	¹H-N.M.R. (CDCl₃ or DMSO-d_6/TMS)[d] δ [ppm]
a			H	54	171–174° (benzene)	$C_{25}H_{20}O_2$ (352.4)	3.2 (m, 2H, CH_2); 4.2 (m, 1H, H-5); 4.90 (d, 1H, H-6, $J_{5,6}$ = 11.2 Hz); 6.59 (s, 1H, H-2); 7.0–8.0 (m, 15 H_{arom})
b			H	31	138–143° (ethanol)	$C_{26}H_{22}O_2$ (366.5)	2.23 (s, 3H, CH_3); 3.1 (m, 2H, CH_2); 4.1 (m, 1H, H-5); 4.88 (d, 1H, H-6, $J_{5,6}$ = 11.8 Hz); 6.57 (s, 1H, H-2); 6.9–8.1 (m, 14 H_{arom})
c			H	40	141–143° (ethanol)	$C_{26}H_{22}O_3$ (382.5)	3.1 (m, 2H, CH_2); 3.70 (s, 3H, OCH_3); 4.1 (m, 1H, H-5); 4.83 (d, 1H, H-6, $J_{5,6}$ = 11.5 Hz); 6.4–8.1 (m, 14 H_{arom} and H-2)
d			H	35	157–164° (ethanol)	$C_{25}H_{19}ClO_2$ (386.9)	3.1 (m, 2H, CH_2); 4.1 (m, 1H, H-5); 4.84 (d, 1H, H-6, $J_{5,6}$ = 12.2 Hz); 6.55 (s, 1H, H-2); 7.0–7.9 (m, 14 H_{arom})
e			H	36	149–155° (ethanol)	$C_{25}H_{19}ClO_2$ (386.9)	3.2 (m, 2H, CH_2); 4.1 (m, 1H, H-5); 4.92 (d, 1H, H-6, $J_{5,6}$ = 12.5 Hz); 6.60 (s, 1H, H-2); 7.0–7.9 (m, 14 H_{arom})
f			H	40	154–160° (ethyl acetate)	$C_{23}H_{18}O_3$ (342.4)	3.3 (m, 2H, CH_2); 4.2 (m, 1H, H-5); 4.85 (d, 1H, H-6, $J_{5,6}$ = 9.9 Hz); 6.1 (m, 2H, β-furyl); 6.50 (s, 1H, H-2); 7.0–8.2 (m, 11 H_{arom})
g			–CN	63	207–208° (benzene)	$C_{26}H_{19}NO_2$ (377.5)	3.5 (m, 2H, CH_2); 4.3 (m, 1H, H-5); 5.96 (d, 1H, H-6, $J_{5,6}$ = 12.3 Hz); 7.2–8.4 (m, 15 H_{arom})
h			–CN	60	197–203° (ethyl acetate)	$C_{27}H_{21}NO_2$ (391.5)	2.45 (s, 3H, CH_3); 3.5 (m, 2H, CH_2); 4.3 (m, 1H, H-5); 5.91 (d, 1H, H-6, $J_{5,6}$ = 13.4 Hz); 7.1–8.3 (m, 14 H_{arom})
i			–CN	58	201–206° (benzene)	$C_{27}H_{21}NO_3$ (407.5)	3.5 (m, 2H, CH_2); 3.86 (s, 3H, OCH_3); 4.3 (m, 1H, H-5); 5.85 (d, 1H, H-6, $J_{5,6}$ = 13.5 Hz); 6.8–8.3 (m, 14 H_{arom})
j			–CN	49	214–217° (ethyl acetate)	$C_{26}H_{18}ClNO_2$ (411.9)	3.6 (m, 2H, CH_2); 4.4 (m, 1H, H-5); 5.94 (d, 1H, H-6, $J_{5,6}$ = 13.6 Hz); 7.3–8.3 (m, 14 H_{arom})
k			–CN	45	208–210° (ethyl acetate)	$C_{26}H_{18}ClNO_2$ (411.9)	4.0 (m, 1H, H-5); 5.72 (d, 1H, H-6, $J_{5,6}$ = 13.2 Hz); 7.0–8.1 (m, 14 H_{arom})
l			–CN	37	176–194° (ethyl acetate)	$C_{24}H_{17}NO_3$ (367.4)	3.6 (m, 2H, CH_2); 4.5 (m, 1H, H-5); 5.70 (d, 1H, H-6, $J_{5,6}$ = 11.8 Hz); 6.5 (m, 2H, β-furyl); 7.6–8.4 (m, 11 H_{arom}).

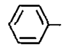
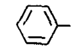
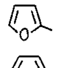
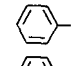
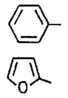
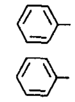
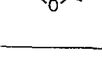
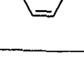
[a] T.L.C. showed mixtures of diastereoisomers.

[b] All products gave satisfactory microanalyses (C ± 0.28%, H ± 0.29%, N ± 0.28%); analyses were performed by Mme L. Pencheva (Sofia University, Laboratory of Elemental Analyses).

[c] I.R. ($CHCl_3$): ν = 2240–2235 (conj. C≡N); 1700–1685 (conj. C=O); 1685–1655 cm⁻¹ (exocyclic C=O).

[d] Recorded on a Tesla BS-487 C spectrometer; solvents: $CDCl_3$ for **3a–f**, DMSO-d_6 for **3g–l**.

Table 2. 2-Hydroxybenzophenones **4**

4	Ar¹	Ar²	X	Yield [%]	m.p. [°C] (solvent)	Molecular formula[a]	¹H-N.M.R. ($CDCl_3$/TMS)[b] δ [ppm]
a			H	62	157–159°[c] (benzene/hexane)	$C_{25}H_{18}O_2$ (350.4)	6.8–7.9 (m, 17 H_{arom}); 9.88 (s, 1H, OH)
f			H	12	169–171° (ethanol)	$C_{23}H_{16}O_3$ (340.4)	6.0–6.4 (m, 2H, β-furyl); 7.0–7.9 (m, 13 H_{arom}); 9.65 (s, 1H, OH)
g			–CN	52	160–162° (ethanol)	$C_{26}H_{17}NO_2$ (375.4)	6.8–7.9 (m, 16 H_{arom}); 10.55 (s, 1H, OH)
l			–CN	18	160–162° (ethanol)	$C_{24}H_{15}NO_3$ (365.4)	6.1–6.6 (m, 2H, β-furyl); 7.1–7.9 (m, 12 H_{arom}); 10.10 (s, 1H, OH)

[a] Satisfactory microanalyses (C ± 0.28%; H ± 0.30%; N ± 0.22%).

[b] I.R. ($CHCl_3$): ν = 3400–3300 (OH); 2235–2230 (C≡N); 1630–1625 cm⁻¹ (C=O).

[c] Ref.[5], m.p. 158–160°C.

ation products. Thus, upon heating with sulfur, the 2-cyclohexenones **3a, f, g, l** were converted to the corresponding 2-hydroxybenzophenones **4**, of which only **4a** was previously described in the literature.

6-Aroyl-2-cyclohexenones 3; General Procedure:

To a mixture of the benzylideneacetophenone **1** (10 mmol), sodium hydride (0.65 g, 27 mmol), dry tetrahydrofuran (5 ml), and dry ethanol (1–2 drops), a solution of the corresponding ester (10 mmol) in tetrahydrofuran (20 ml) is added. The mixture is stirred for 1 h at room temperature, quenched with water (10 ml), and acidified with 1:1 hydrochloric acid (10 ml). The water layer is extracted with chloroform (3 × 3 ml). The combined chloroform solutions are dried with sodium sulfate. After evaporation of the solvent, the residue is stirred with a small volume of ether. The crystals so formed are isolated and purified by recrystallisation from an appropriate solvent (Table 1).

Dehydrogenation of 3; General Procedure:

A mixture of **3** (3 mmol) and sulfur (0.96 g, 3.7 mmol) is melted and then heated at 300–320 °C until no more hydrogen sulfide is evolved. After cooling, the residue is dissolved in glacial acetic acid (2 ml). The crystals formed after cooling of the solution are purified by recrystallisation (for the solvent used see Table 2).

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[1] E. Smissman, A. Voldeng, *J. Org. Chem.* **29**, 3161 (1964).

[2] Y. Anghelova, C. Ivanov, *Chem. Ber.* **106**, 2643 (1973).

[3] Y. Anghelova, *Synthesis* **1974**, 343.

[4] J. Martelli, D. Danion, R. Carrié, *Tetrahedron* **30**, 3063 (1974).

[5] T. Harris, C. Harris, *J. Org. Chem.* **32**, 970 (1967).