One-Step Synthesis of Ethyl 3-Cyano-4,6-diaryl-2-hydroxybenzoates

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The base-catalysed condensation of the esters of a variety of 2-butenoic acids with carbonyl compounds leads directly to substituted 2,4-pentadienoic acids[1-4]. However, the possibility to use the same esters for the synthesis of six-membered ring compounds has not received due attention. Recently[5], we reported that, under the action of sodium hydride in tetrahydrofuran at room temperature, ethyl 2-cyano-3-phenyl-2-butenoate **(2a)** reacts with different benzylideneacetophenones giving 3,5-diarylated 6-aroyl-2-cyano-2-cyclohexenones. In our search for further applications of this type of bimolecular cyclisation (a sequence of conjugated addition and intramolecular Claisen condensation), we studied the behaviour of the same ester and its analog – ethyl 3-(4-chlorophenyl)-2-cyano-2-butenoate **(2b)** – towards the ethyl esters of cinnamic, 4-methylcinnamic, and 4-chlorocinnamic acid **(1a–c)**.

Using sodium hydride as deprotonating agent as before, we found that the desired condensation can be realised when benzene instead of tetrahydrofuran is employed as solvent. Moreover, the reaction proceeded better at reflux and when a twofold excess of the ester of the corresponding cinnamic acid **1** was used.

Surprisingly, the products isolated proved to be ethyl 3-cyano-4,6-diaryl-2-hydroxybenzoates **(4a–f)** and not the expected 2-cyano-6-ethoxycarbonyl-2-cyclohexenones **(3a–f)**. A possible explanation of this fact, involving dehydrogenation of **3** under the action of air oxygen, was rejected, however, since the

0039-7881/82/0932-0730 $ 03.00

Table. Ethyl 3-Cyano-4,6-diaryl-2-hydroxybenzoates **(4a-f)**

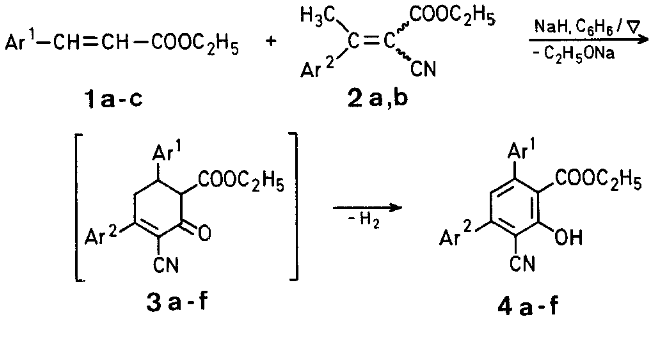
Product **4**	Ar^1	Ar^2	Yield [%]	m.p. [°C] (solvent)	Molecular formula[a, b]	^{1}H-N.M.R. ($CDCl_3$/TMS)[c] δ [ppm]
a	C_6H_5	C_6H_5	52	147-149° (ethanol)	$C_{22}H_{17}NO_3$ (343.4)	0.80 (t, 3H, CH_3); 4.05 (q, 2H, CH_2); 6.92 (s, 1H, H-5); 7.0-8.0 (m, 10H_{arom}); 11.95 (s, 1H, OH)
b	C_6H_5	4-Cl—C_6H_4	36	125-126° (methanol)	$C_{22}H_{16}ClNO_3$ (377.8)	0.77 (t, 3H, CH_3); 4.00 (q, 2H, CH_2); 6.83 (s, 1H, H-5); 7.0-7.5 (m, 9H_{arom}); 12.05 (s, 1H, OH)
c	4-H_3C—C_6H_4	C_6H_5	41	125-127° (methanol)	$C_{23}H_{19}NO_3$ (357.4)	0.82 (t, 3H, $\underline{CH_3}CH_2$); 2.41 (s, 3H, *p*-CH_3); 4.06 (q, 2H, CH_2); 6.92 (s, 1H, H-5); 7.0-7.7 (m, 9H_{arom}); 11.89 (s, 1H, OH)
d	4-H_3C—C_6H_4	4-Cl—C_6H_4	35	148-150° (methanol)	$C_{23}H_{18}ClNO_3$ (391.8)	0.80 (t, 3H, $\underline{CH_3}CH_2$); 2.38 (s, 3H, *p*-CH_3); 4.02 (q, 2H, CH_2); 6.82 (s, 1H, H-5); 6.9-7.6 (m, 8H_{arom}); 11.96 (s, 1H, OH)
e	4-Cl—C_6H_4	C_6H_5	52	150-152° (methanol)	$C_{22}H_{16}ClNO_3$ (377.8)	0.84 (t, 3H, CH_3); 4.08 (q, 2H, CH_2); 6.88 (s, 1H, H-5); 6.9-7.7 (m, 9H_{arom}); 12.01 (s, 1H, OH)
f	4-Cl—C_6H_4	4-Cl—C_6H_4	33	126-128° (methanol)	$C_{22}H_{15}Cl_2NO_3$ (412.3)	0.84 (s, 3H, CH_3); 4.04 (q, 2H, CH_2); 6.79 (s, 1H, H-5); 6.9-7.6 (m, 8H_{arom}); 12.09 (s, 1H, OH)

[a] All products gave satisfactory microanalyses (C ±0.19%; H ±0.28%; N ±0.18%). The analyses were carried out by Mme. L. Pencheva (Sofia University, Laboratory of Elemental Analyses).

[b] I.R. ($CHCl_3$): $\nu = 3400\text{-}3200$ (OH); 2235-2230 (C≡N); 1670-1665 cm^{-1} ($COOC_2H_5$).

[c] Recorded on a Tesla BS-487C spectrometer.

condensation of **1a** and **2a** carried out under argon also led to the aromatic compound **4a**. Therefore, it seems very probable that the sodium hydride itself might serve as dehydrogenating agent, but this assumption requires a more detailed study.



All products **4** are new substances. They were characterised by ^{1}H-N.M.R. and I.R. spectra and microanalyses (Table). Ethyl 2-cyano-3-phenyl-2-butenoate (**2a**; $Ar^2 = C_6H_5$) was prepared according to Ref.[6]. Ethyl 3-(4-chlorophenyl)-2-cyano-2-butenoate (**2b**; Ar^2=4-Cl—C_6H_4) was prepared via the Wittig-Horner reaction[7]; yield: 69%; b.p. 124-128 °C/6 torr; n_D^{22}: 1.5385 (Ref.[8], b.p. 142-145 °C/16 torr; n_D^{19}: 1.5451).

Ethyl 3-Cyano-4,6-diaryl-2-hydroxybenzoates 4; General Procedure:
To a mixture of the ethyl ester of the corresponding cinnamic acid **1** (20 mmol), sodium hydride (0.65 g, 22 mmol), dry benzene (5 ml) and dry ethanol (1-2 drops), a solution of the ethyl 3-aryl-2-cyano-2-butenoate **2** (10 mmol) in benzene (20 ml) is added. The mixture is refluxed for 1 h and quenched after cooling with 10% hydrochloric acid (20 ml). The water layer is extracted with ether (3 x 10 ml) and the combined ether layers are dried with sodium sulfate. The crystals obtained after removing the solvent are purified by recrystallisation from an appropriate solvent (Table).

Received: March 29, 1982

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0039-7881/82/0932-0731 $ 03.00