A Convenient Conversion of 3-Acetyl-4-aryl-4-butanolides to 3-Acetyl-4-aryl-3-butenoic Acids

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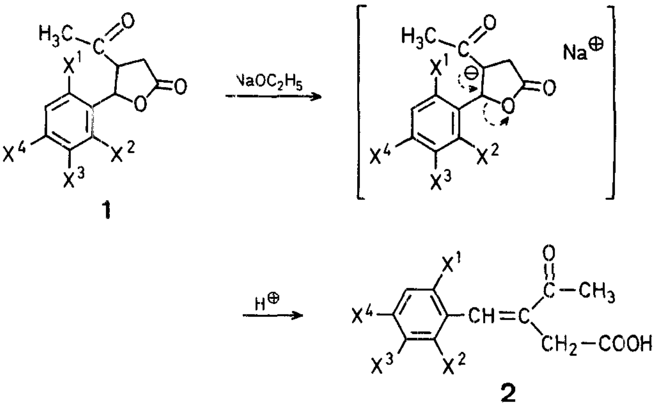
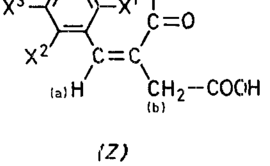
In a previous paper[1], we described the synthesis and pharmacological effects of 3-acetyl-4-(3′,4′-dimethoxyphenyl)-4-butanolide (**1**, $X^1=X^2=H$, $X^3=X^4=OCH_3$). We now report a simple, high yield conversion of butanolides (**1**) into 3-acetyl-4-aryl-3-butenoic acids (**2**). These compounds were previously obtained in poor yields by condensation of levulinic acid with aromatic aldehydes[2,3,4,5].

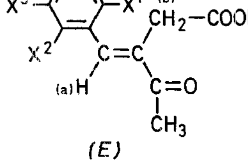
By use of this new procedure, 3-acetyl-4-aryl-3-butenoic acids (**2**) can be prepared in a high selectivity. The conversion was performed by treating 3-acetyl-4-aryl-4-butanolides (**1**) with a stoichiometric amount of sodium ethoxide in absolute ethanol at room temperature for 20 hours. The dark color obtained by the reaction mixture gives evidence for carbanion formation, suggesting the following reaction pathway.



This mechanism is in good agreement with that proposed by Cignarella et al.[6] for the formation of 3-aroyl-3-butenoic acids from 4-aroyl-2-(3*H*)-dihydrofuranones.

The 3-butenoic acids **2** can exist as (*Z*)- or (*E*)-isomers. The formation of a single isomer was evidenced by thin layer chromatographic and ^{1}H-N.M.R. spectroscopic analysis. However, identification of the isomer present using the value of the chemical shift of the H(a) proton or the size of the $^4J_{H(a),H(b)}$ coupling constant was not possible.


(*Z*)


(*E*)

Thus, we had to make use of the intramolecular nuclear Overhauser effect[7,8,9]. Irradiation of the H(b) methylene protons may influence H(a) signal in two different ways according to molecular geometry: in (*Z*)-isomers, the H(a) signal intensity should be increased by up to 50%, while in (*E*)-isomers no significant variation should occur. In our ethylenic acids **2**, no variation in the H(a) signal intensity has been observed by irradiation of H(b) protons: so these compounds must be (*E*)-isomers.

Yields and physical constants of the 3-acetyl-4-aryl 3-butenoic acids (**2**) are summarized in the Table. As it can be observed,

Table. 3-Acetyl-4-aryl-3-butenoic Acids **2a-h**

Product No.	X^1	X^2	X^3	X^4	Yield [%]	m.p. [°C]	Molecular formula[a] or Lit. m.p.	I.R. (KBr) ν [cm^{-1}]	^{1}H-N.M.R. (DMSO-d_6/TMS) δ [ppm]
2a	H	H	H	H	85	125–126°	125° [2,4]	1710, 1660	2.4 (s, 3H); 3.35 (s, 2H); 7.4 (s, 5H); 7.75 (s, 1H)
2b	H	H	H	Cl	94	152–153°	$C_{12}H_{11}ClO_3$ (238.7)	1700, 1650	2.5 (s, 3H); 3.4 (s, 2H); 7.5 (m, 4H); 7.9 (s, 1H)
2c	H	H	H	NO_2	89	176–178°	85° [4]	1700, 1650	2.5 (s, 3H); 3.4 (s, 2H); 7.9 (s, 1H); 8.1 (m, 4H)
2d	H	H	H	OCH_3	83	139–140°	58° [4]	1710, 1620	2.4 (s, 3H); 3.4 (s, 2H); 3.8 (s, 3H, OCH_3); 7.3 (m, 4H); 7.7 (s, 1H)
2e	H	H	Cl	H	92	137–139°	$C_{12}H_{11}ClO_3$ (238.7)	1700, 1650	2.4 (s, 3H); 3.2 (s, 2H); 7.4 (m, 4H); 7.8 (s, 1H)
2f	H	H	NO_2	H	90	172–175°	$C_{12}H_{11}NO_5$ (249.2)	1700, 1660	2.7 (s, 3H); 3.6 (s, 2H); 8.1 (m, 4H); 8.5 (s, 1H)
2g	Cl	H	H	H	87	99–100°	$C_{12}H_{11}ClO_3$ (238.7)	1700, 1665	2.5 (s, 3H); 3.2 (s, 2H); 7.5 (m, 4H); 7.7 (s, 1H)
2h	Cl	Cl	H	H	91	145–146°	$C_{12}H_{10}Cl_2O_3$ (273.1)	1710, 1680	2.1 (s, 3H); 3.4 (s, 2H); 6.2 (s, 1H); 7.3 (m, 3H)

[a] Satisfactory microanalyses obtained: C ±0.26, H ±0.06, N ±0.02, Cl ±0.23.

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we find dramatic discrepancies in melting points of compounds **2c** and **2d** with regard to the literature values. We think that compounds described by the authors[4] were not definite species, but mixtures of α-, β-, and δ-condensation products of levulinic acid with the corresponding aldehydes. Furthermore no spectroscopic data were indicated.

In comparison to previous methods[2,3,4,5], the new procedure described in this paper is mild, regiospecific, and stereoselective, leading to the expected products in excellent yields.

3-Acetyl-4-aryl-3-butenoic Acids 2a–h; General Procedure:
The 3-acetyl-4-aryl 4-butanolide[1] **1** (0.01 mol) is added to a stirred solution of sodium (0.23 g, 0.01 mol) in absolute ethanol (30 ml). A deep coloration appears immediately. Stirring is continued for 20 h at room temperature. Then the solvent is removed in vacuo. The residual sodium salt is dissolved in water (20 ml) and the solution is acidified to pH 1 with dilute hydrochloric acid. An oily precipitate is formed which soon crystallizes. The product is collected by filtration, washed with water, dried, and recrystallized from ethanol.

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