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A GENERAL METHOD FOR THE ALKALINE CLEAVAGE OF ENOLISABLE KETONES

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Abstract: An efficient method is described for the cleavage of enolisable aryl methyl and aryl ethyl ketones using an excess of KOH in DMF at an elevated temperature. It presents a general hydrolytic method yielding aromatic carboxylic acids, and is complementary to the widely used oxidative methods for ketone cleavage. © 1999 Elsevier Science Ltd. All rights reserved.

Besides the Haller–Bauer reaction, a method widely used for the alkaline cleavage of carbon-carbon bonds of non-enolisable ketones,¹⁻³ there is practically no data on the cleavage of enolisable ketones in the literature. This is because the reaction proceeds with either poor or no conversion of the starting ketones, even with sodium amide.^{1,4} Moreover, with bis- and polychloroacetophenones the aromatic ring is cleaved, giving reasonable yields of halogenated benzenes.⁵ Other enolisable ketones require heating for prolonged periods at high temperatures with either neat KOH, KOH in water or in paraffin oil, to undergo cleavage.⁶ For cyclobutafuranone derivatives, cleavage was preceded by an aldol-type dimerisation to a ketol.⁷

We report a mild and efficient alkaline cleavage of methyl- and ethyl aryl ketones.⁸ After treating the ketones with an excess of KOH in DMF at 65–68 °C, TLC revealed that more than 80% of the starting material has been consumed within 3 to 6 hours. To ensure complete conversion, however, heating was continued for a further 12 hours. In all test cases (Tables 1 and 2) the bond between the alkyl chain and the carbonyl group had been cleaved exclusively, irrespective of the substituents on the aromatic ring. The procedure was tested using a variety of ketones containing phenyl, naphthalene, and phenanthrene rings with a variety of substituents, and with either a methyl or an ethyl group as the alkyl side chain. The corresponding aryl carboxylic acids were isolated in reasonable yields. The resultant acids were isolated and characterized in the form of free acids or as benzyl esters.

We consider the above transformation to be a general method, complementary to methods of oxidative cleavage of ketones, namely the haloform reaction and the Baeyer-Villiger oxidation, and an extension of the Haller-Bauer reaction. A detailed investigation with the aim to find the scope and limitations of the method and to elucidate the mechanism of the above transformation is in progress.

Table 1. The cleavage of aryl-methyl ketones

Ar	yield ^c	Ar	yield ^c
	64% ⁹		51% ¹¹
	60% ⁹		67% ¹²
	47% ¹⁰		36% ¹³
	61% ¹⁰		58% ¹⁴
	84% ¹⁰		71% ¹⁵

Table 2. The cleavage of aryl-ethyl ketones

Ar	yield ^c
	63% ¹⁶
	67% ¹⁷

a: KOH/DMF, 65-68 °C, 12 h.
 b: 1. KOH/DMF 2. PhCH₂Br.
 c: isolated yield.

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- Benzyl 6-methoxy-2-naphthoate: m.p. 102-3 °C; Anal. Calcd for C₁₉H₁₆O₃: C, 78.06; H, 5.52; Found: C, 77.98; H, 5.54. ¹H NMR δ: 3.94 (3H,s); 5.41 (2H,s); 7.15 (1H,d, J= 2.6); 7.19 (1H, dd, J= 2.6 and 8.9); 7.39 (3H, m); 7.49 (2H, m); 7.75 (1H, d, J= 8.7); 7.83 (1H, d, J= 8.9); 8.06 (1H,dd, J= 1.8 and 8.7); 8.56 (1H, d, J= 1.8).
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