Michael Reactions of the Anions generated by the Metal–Ammonia Reduction of Benzoic Acids

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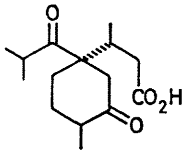
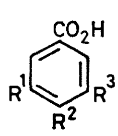
Summary A novel method for the construction of carbon–carbon bonds is described in which anions obtained by the metal–ammonia reduction of benzoic acid and its derivatives undergo ready Michael reaction with methyl crotonate to give the addition products.

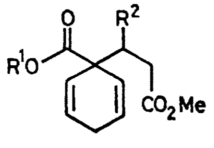
The discovery that lithium enolates generated by the metal–ammonia reduction of αβ-unsaturated ketones and related compounds could be alkylated,[1] carboxylated,[1] or added to αβ-unsaturated systems[2,3] (Michael reaction) has extended the synthetic utility of this reduction process for the construction of carbon–carbon bonds in complex molecules. We have earlier described[4] a total synthesis of acoric acid (**1**), isolated from *Acorus calamus*[5] based on a similar approach, involving the regiospecific generation of the enolate from α-acetoxy ketones and subsequent Michael addition. Our original plan of the synthesis of acoric acid (**1**) was to construct a carbon–carbon bond at the α-position of αβ-unsaturated ketones, by trapping the enolates obtained by the metal–ammonia reduction of the unsaturated ketone, and allowing them to react with methyl vinyl ketone and methyl acrylate. This failed however.[5] We now describe a novel and general method involving Michael addition to anions generated by the metal–ammonia reduction of benzoic acids, Birch reduction and reductive alkylations of benzoic[6] and naphthoic acids[7] having been well established.



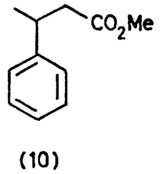
(1)



(2) $R^1 = R^2 = R^3 = H$
(3) $R^1 = R^3 = H; R^2 = OMe$
(4) $R^1 = R^2 = R^3 = OMe$
(5) $R^1 = R^3 = H; R^2 = Me$



(6) $R^1 = R^2 = H$
(7) $R^1 = H; R^2 = Me$
(8) $R^1 = R^2 = Me$
(9) $R^1 = Me; R^2 = H$



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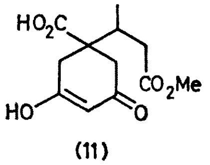

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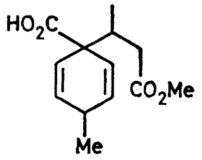

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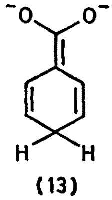

(13)

Reduction of benzoic acid (**2**) with lithium (4 equiv.) in liquid ammonia† followed by quenching of the mixture with methyl crotonate afforded the acid (**7**) in 70% yield, which was purified and characterised as its dimethyl ester (**8**), b.p. 142 °C at 7 mmHg; ν_{max} 1740 cm^{-1}; δ 0·8 (d, *J* 6 Hz, 3H), 1·6 and 2·6 (m, 5H), 3·5 (s, 3H, OMe), 3·65 (s, 3H, OMe), and 5·8 (brs, 2H, vinyl-H). The acid (**7**) readily undergoes oxidative decarboxylation on standing to give the aromatic compound (**10**). Reduction of benzoic acid (**2**) with lithium in ammonia, followed by the addition of methyl acrylate, afforded the acid (**6**) which was esterified with diazomethane to give the diester (**9**) in 65% yield.

Similar results were obtained in the lithium–ammonia reduction of the acids (**3**), (**4**), and (**5**) followed by reaction with methyl crotonate affording compounds (**7**), (**11**), and (**12**) respectively in good yield which were characterised‡ as their methyl esters.

These results clearly demonstrate that the anion (**13**) resulting from the reduction of aromatic acids can be readily trapped and subjected to Michael reaction with unsaturated esters. Attempted reaction of the anion (**13**) with methyl vinyl ketone failed, presumably owing to the polymerisation of methyl vinyl ketone in ammonia.

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† Reductive Michael reactions were carried out at −78 °C in redistilled ammonia.

‡ All the new compounds gave satisfactory analytical and spectral data.

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