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METAL-AMMONIA REDUCTION AND REDUCTIVE ALKYLATION OF 2-FUROIC ACID

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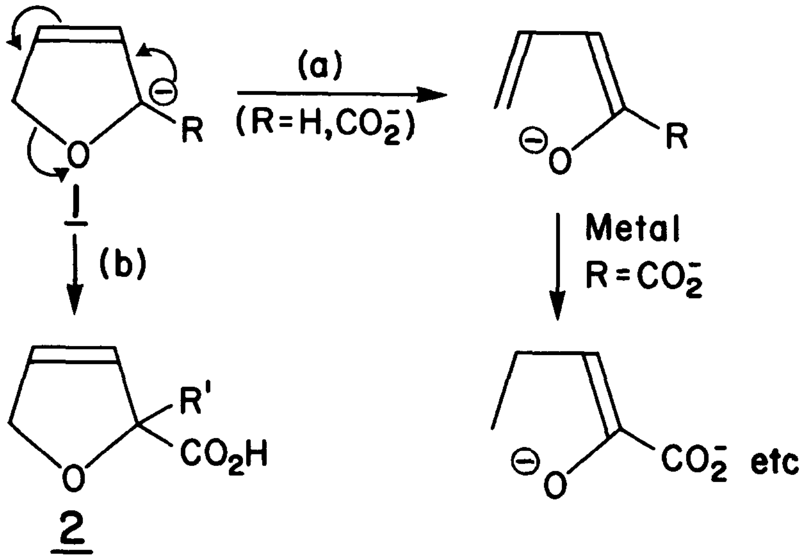
The first alkylations of carbanions derived from carboxylate salts were carried out on crotonic, sorbic, phenylacetic and dihydrobenzoic acids using potassamide in ammonia as base [1] This type of reaction has recently been rediscovered, e g [2,3] It was noted[1] that lead tetraacetate oxidations converted efficiently 1-alkyl-1,4-dihydrobenzoic acids into alkylbenzenes A convenient method of obtaining the requisite anions from benzoic acids is by direct reaction with a metal in ammonia,[3] rather than by the two-stage process initially used [1]

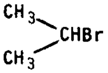
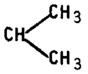
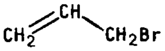
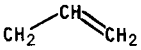
2-Furoic acid with metal and alcohol in ammonia is reported[4] to give mixtures of reduction products, including ring-opened compounds Ring-opening may be due to process (a) below, which is known[5] to occur immediately even at low temperatures with (1, R = H), stabilisation of the carbanion in (1, R = CO_2^-) might be expected to enable this to survive to undergo protonation or alkylation Repetition of the reduction of 2-furoic acid,[4] using lithium and methanol or water as a proton source, confirmed the formation of mixtures containing (2, R' = H) as the main product However, rapid addition of 2-furoic acid to Li (2 5 equivalents) in NH_3 at -78°, followed by NH_4Cl within 3 minutes [process (b)] gave 80% yield of (2, R' = H) in a reasonably pure state It was identified by the p m r spectrum and its cyclohexylamine salt [6] The pure product, recovered from the latter, could be sublimed at 0 5 mm Hg (40-60°) and had m p 50-54° [7]

Addition of an alkyl halide instead of NH_4Cl resulted in conversion of (1, R = CO_2^-) into (2, R' = alkyl) (Table) accompanied by 10-20% of (2, R' = H), readily separated by its higher water solubility The products were purified through the cyclohexylamine salts and structures confirmed by p m r spectra Oxidation of (2, R' = alkyl) with lead tetraacetate in benzene caused loss of CO_2H and formation of 2-alkylfuran

The procedures can be carried out with 3- or 5-methyl-furoic acid, and some applications in terpenoid synthesis will be discussed We are grateful to Professor Miwa for a copy of his paper prior to publication.



Table

Alkyl Halide	Product	Yield*	m p	Cyclohexylamine Salt
	2, R' =			
CH_3I [or $(CH_3)_2SO_4$]	CH_3	75%	41-44°	192-197° (dec)
CH_3CH_2I	CH_2CH_3	75%	liquid	173-176° (dec)
 $(CH_3)_2CHBr$	 $CH(CH_3)_2$	95%	66-67°	179-180° (dec.)
 $CH_2{=}CH{-}CH_2Br$	 $CH_2{-}CH{=}CH_2$	68%	liquid	156-158° (dec)
$PhCH_2Cl$	CH_2Ph	75%	75-76°	183-188° (dec)

* Crude isolated yield No attempt has been made to maximise the yield

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7. Satisfactory analytical results have been obtained for all compounds characterised