Amidrazones as Acyl Anion Equivalents

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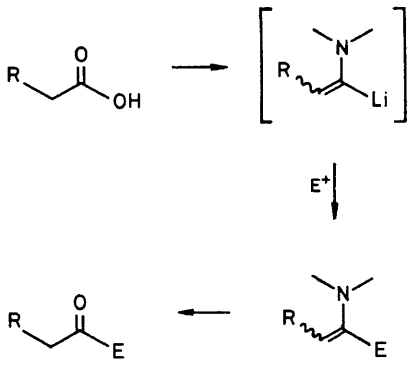
Summary 2,4,6-Tri-isopropyl-benzenesulphonyl-amidrazones on treatment with t-butyl-lithium and after decomposition of the initial dilitho-species yield α-lithioenamines which act as acyl anion equivalents.

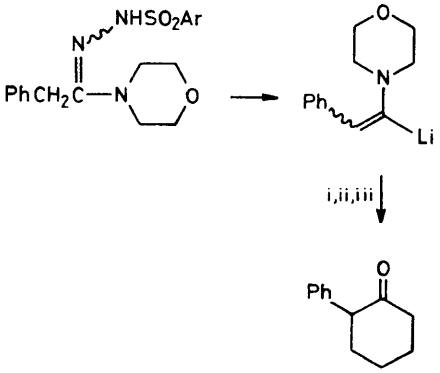
MANY of the large number of acyl anion equivalents described[1] suffer from difficulties related to deblocking conditions or the requirement of inconvenient starting materials, such as aldehydes. We report here a procedure which effectively allows the achievement of the transformation in Scheme 1, starting from the carboxylic acid.



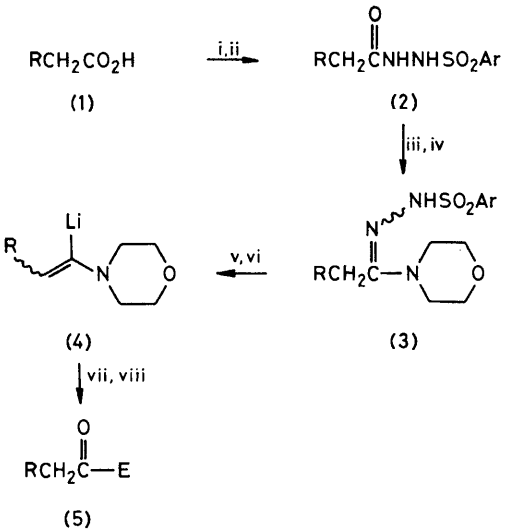
SCHEME 1

This process is based on the Shapiro[2] reaction of an arenesulphonyl-amidrazone readily derivable from a carboxylic acid. The method, described in Scheme 2, involves treatment of the 2,4,6-tri-isopropyl-benzenesulphonyl ('trisyl')[3] amidrazones (**3**) with 2·3 equiv. of t-butyl-lithium at −78 °C, followed by warming to 10 °C for 5 min, giving nitrogen and, presumably, the α-lithioenamine (**4**), which subsequently reacts to give products (**5**). Thus phenylacetone (**5**; R = Ph, E = Me) was obtained (80%) from the corresponding amidrazone and methyl iodide. The yield of methyl β-phenethyl ketone (**5**; R = $PhCH_2$, E = Me) was lower (25%) when derived again from the amidrazone and methyl iodide, however, thus far, these yields are not optimised. The use of carbonyl groups as electrophiles was demonstrated by conversion of the amidrazone from acetic acid (**3**; R = H) into 1-acetyl-1-hydroxycyclohexane (**5**; R = H, E = $(OH)C_6H_{10}$] (60%) by trapping with cyclohexanone. This method is apparently limited to carboxylic acids bearing an α-methylene group since the amidrazone from cyclohexanone carboxylic acid and t-butyl-lithium did not give clean products.

Since the proposed intermediate (**4**) is potentially a bifunctional nucleophile we examined its reaction with a bifunctional electrophile, *i.e.* 1,4-dibromobutane. After initial reaction at −78 to 0 °C the reaction was warmed (60 °C) with an excess of sodium iodide (to effect halogen exchange in the intermediate enamine) and yielded, after hydrolysis with water 2-phenylcyclohexanone (25%), Scheme 3.



SCHEME 3. i, $Br[CH_2]_4Br$, ii, NaI, heat, iii, H_2O.



SCHEME 2. i, $SOCl_2$, ii, $ArSO_2NHNH_2$, iii, PCl_5, iv, morpholine, v, Bu^tLi, −78 °C, THF, vi, warm to 10 °C, 5 min, vii, E^+, viii, H_2O.

The amidrazones are stable crystalline solids (**3**; R = Ph, m.p. 170—171 °C; R = H, m.p. 129—131 °C; R = $PhCH_2$, m.p. 161—163 °C) prepared from the corresponding acid hydrazides by sequential treatment with PCl_5 (CH_2Cl_2) and morpholine.† In a typical run the amidrazone (1 mmol) in tetrahydrofuran (THF) (5 ml) at −78 °C was treated with t-butyl-lithium (2·3 equiv., 30 min) and warmed to 10 °C (5 min) when nitrogen evolution was observed. The reaction mixture was cooled to −78 °C, and the electrophile was added at this point, with subsequent gradual warming to room temperature.

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† All new compounds have satisfactory analytical data.

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[3] R. M. Adlington and A. G. M. Barrett, *J. Chem. Soc., Chem. Commun.*, 1978, 1071.