Stabilized Enamine Anions

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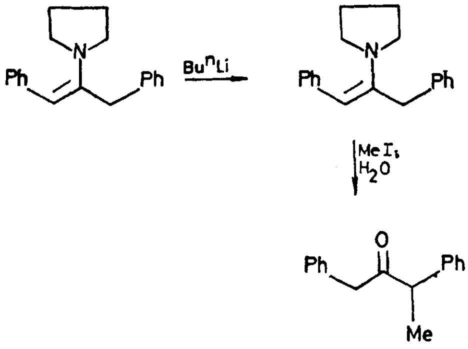
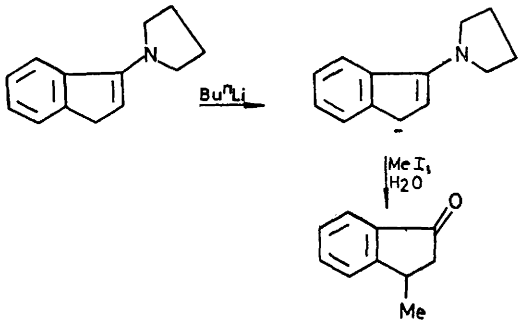
Summary Enamines of several ketones having phenyl groups at the α or β positions have been deprotonated to give allylic anions which are reactive nucleophiles; treatment of these intermediates with methyl iodide has led to high yields of methylated ketones.

The depressed acidity of protons allylic to electron-rich olefins can be enhanced by adjacent anion-stabilizing groups such as carbonyl. Thus monoenamines[1] of 1,3-dicarbonyl compounds have recently been deprotonated and used as nucleophiles.[2] We report here that suitably placed phenyl groups may also confer such acidity in enamines and that the anions resulting from treatment with strong bases[3] can be alkylated under mild conditions to give high yields of alkylated ketones after hydrolysis.

The noteworthy characteristics of this procedure are: (i) because enamines are not susceptible to nucleophilic attack, self-condensation analogous to that common during formation of enolates is not encountered; (ii) the anions produced are highly reactive; (iii) because of negligible proton exchange between anion and neutral product, monoalkylation is easily achieved; (iv) these anions have a much higher charge density on carbon than do neutral enamines, therefore *N*-alkylation is negligible; (v) in certain instances alkylation can be achieved at the position β to the original carbonyl group.





The pyrrolidine enamine of indan-2-one[4a] in tetrahydrofuran was treated under nitrogen at *ca.* −65° with n-butyl-lithium in hexane. Proton removal was complete in about 10 min as judged by measurement of the volume of gas evolved. The anion was quenched at −65° with methyl iodide and after 5 min the mixture was hydrolysed

TABLE

Methylation of anions from pyrrolidine enamines

Ketone	Base	Temp. (°)	Product	Yield (%)
Indan-2-one	$\mathrm{Bu^nLi}$	*ca.* −65	1-Methylindan-2-one	82
1,3-Diphenylacetone	$\mathrm{Bu^nLi}$	0	2-Methyl-1,3-diphenylacetone	85
1,3-Diphenylacetone	$\mathrm{LiNPr^i_2}$	45—50	2-Methyl-1,3-diphenylacetone	96
Indan-1-one	$\mathrm{Bu^nLi}$	*ca.* −65	3-Methylindan-1-one[a]	85
Indan-1-one	$\mathrm{Bu^nLi}$[b]	0—65	3,3-Dimethylindan-1-one[c]	96
3,4-Diphenylcyclopentenone	$\mathrm{Bu^nLi}$	*ca.* −40	2-Methyl-3,4-diphenylcyclopent-2-en-1-one	70

[a] Ref. 5. [b] In two portions, the second equiv. added after the first equiv. of methyl iodide. [c] Ref. 6.

with aqueous HCl, worked-up as usual, and distilled to provide 82% of 1-methylindan-2-one[4a] of high purity, no attempt having been made to maximize the yield. By contrast, in a study of the normal alkylation of several enamines (including the pyrrolidine enamine) of indan-2-one,[4a] the best yield achieved was 40%. Base-catalysed alkylations with unsubstituted indanones commonly fail entirely or give extremely low yields, due to the aforementioned self-condensation, which is acute in these compounds.[4]

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[3] This process is to be distinguished from the α-deprotonation of imines described by G. Stork and S. R. Dowd, *J. Amer. Chem. Soc.*, **1963**, **85**, 2178.

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