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# TRI-IONIZATION OF PHENYLACETAMIDE BY n-BUTYLLITHIUM. DECOMPOSITION TO FORM LITHIOPHENYLACETONITRILE.*

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Phenylacetamide (I) has previously been shown to undergo primary ionization of an amido hydrogen and secondary ionization of an α-hydrogen with two molecular equivalents of sodium amide in liquid ammonia to form disodio salt I'', which was alkylated at the α-carbon with alkyl halides to give II (1).

$C_6H_5\overset{Na}{C}HCONHNa$

I''

$C_6H_5\overset{R}{C}HCONH_2$

II

We have now found that phenylacetamide undergoes not only such di-ionization with two molecular equivalents of n-butyllithium in tetrahydrofuran (THF)-hexane to form dilithioamide I'', but also tri-ionization with another equivalent of this reagent to give trilithioamide I''', which eliminates lithium oxide even at 0° to afford lithiophenylacetonitrile III' (Scheme I).

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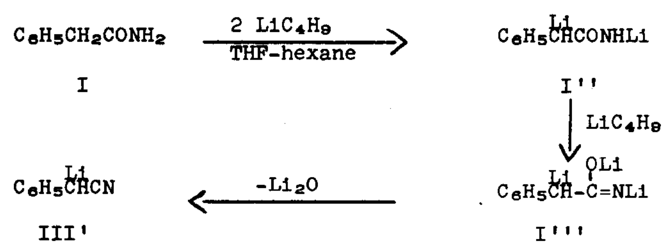
Scheme I



That the intermediate dilithioamide I'' is stable was shown by its preparation by means of two molecular equivalents of the reagent, and alkylation with n-butyl bromide at room temperature to afford α-derivative II (R = n-$C_4H_9$) in 87% yield without a trace of phenylacetonitrile being detected. Therefore, the nitrile must have arisen in the experiment with three equivalents of the reagent through decomposition of trilithioamide I'''.

That the tertiary ionization involved the second amido hydrogen rather than the second α-hydrogen (see Scheme I) was supported by the observation that, whereas dianion I'' undergoes preferential alkylation (1) or benzoylation (2) at the α-carbon, the trilithioamide I''' underwent N-benzoylation with benzoyl chloride at -80° to form the N-benzoyl derivative IV in 37% yield; although this yield is not high, it is much better than that (3%) obtained on benzoylating monolithiophenylacetamide under similar conditions. Moreover, deuteration of the dilithioamide I'' and trilithioamide I''' afforded $ID_2$ and $ID_3$, respectively. Mass spectra and n.m.r. determinations on $ID_2$ and $ID_3$ showed them to contain 0.9-0.922 benzyl deuteriums per molecule; the mass spectra also contained fragments with two and three deuteriums per molecule, respectively. Part of the deuterium on the nitrogen, however, might have been acquired by exchange of the protium with deuterium by means of lithium deuteroxide and deuterium oxide.

$C_6H_5CH_2CONHCOC_6H_5$ IV

$C_6H_5CHDCONHD$ ID$_2$

$C_6H_5CHDCOND_2$ ID$_3$

That the decomposition of the trilithioamide I''' afforded lithionitrile III' rather than the free phenylacetonitrile (see Scheme I) was shown by deuteration and *n*-butylation of the reaction mixtures to form corresponding derivatives of the nitrile.

The trilithiation of phenylacetamide was strongly exothermic. Unless externally cooled, the reaction mixture became sufficiently hot to reflux the solvent to afford lithionitrile III' and, on acidification, phenylacetonitrile in 78% yield within a few minutes. Even when the reaction mixture was maintained at -5°, the yield was 33%.

In contrast to *n*-butyllithium, three molecular equivalents o lithium amide or potassium amide in liquid ammonia or THF (refluxed one hour) failed to convert phenylacetamide to phenylacetonitrile, and most of the starting phenylacetamide was recovered. Evidently, the amide ion is not a sufficiently strong base to effect tertiary ionization of dianion I''.

Further work is in progress on such novel tri-ionizations of phenylacetamide and certain other related amides by means of *n*-butyllithium.

## References

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