

Synthesis of New Phthalimidines and 3,4-Dihydroisocarbostyrils: New Method involving an Unusual Cyclohydration¹

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RECENTLY, *N*-methylbenzamide² and *N*-methyl-*o*-toluamide³ were converted by *n*-butyl-lithium in tetrahydrofuran-hexane into dilithio-amides (I) and (IV), respectively; this was evidenced by condensations at the *ortho*- and 2-methyl-positions with electrophilic compounds such as benzophenone to form (II) and (V), which were cyclized to give lactones (III) and (VI), respectively.

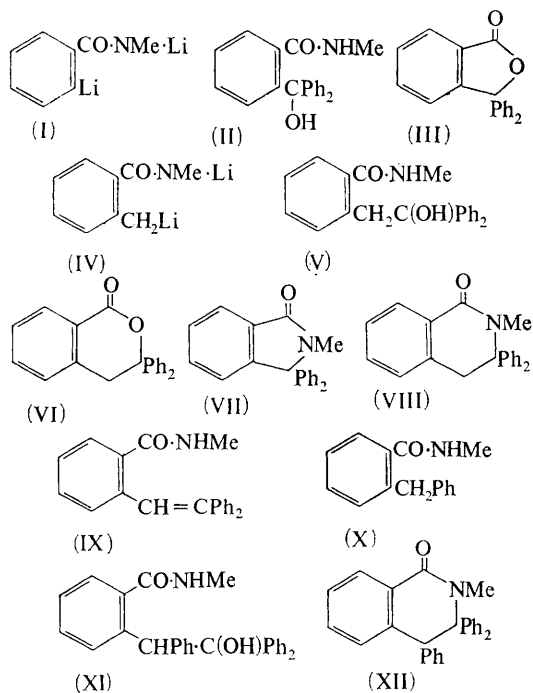
We now report that alcohol-amides (II) and (V) undergo cyclodehydration with cold, concentrated sulphuric acid to afford phthalimidine (VII) and 3,4-dihydroisocarbostyril (VIII), respectively. In the latter reaction, none of the possible linear dehydration product (IX) was isolated. The five-membered cyclic amide (VII) readily formed an isolable sulphuric acid salt, whereas the six-membered cyclic amide (VIII) did not.

Similarly, *N*-methyl-2-benzylbenzamide (X) was condensed through its dilithioamide with benzophenone to form alcohol-amide (XI) which was cyclized with sulphuric acid to give 3,4-dihydroisocarbostyril (XII). None of the corresponding linear dehydrated derivative was isolated.

The structures of the products were established by analyses and i.r. and n.m.r. spectra. The pure products were obtained readily in good yields (55–80%).

The cyclodehydrations of the alcohol-amides (V) and (XI) are of special interest, since an intermediate diphenylmethyl type carbonium ion

might have been expected to undergo linear dehydration.



These reactions furnish convenient methods for the synthesis of the substituted phthalimidines and 3,4-dihydroisocarbostyrils. Further work is in progress on similar reactions with various ketones (or aldehydes) and on the corresponding series of reactions of the *N*-phenylamides. Also, studies are contemplated on the factors governing cyclodehydration *versus* cyclodeamination of alcohol-amides of type (II), and cyclodehydration

versus linear dehydration or cyclodeamination of alcohol-amides of types (V) and (XI).

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