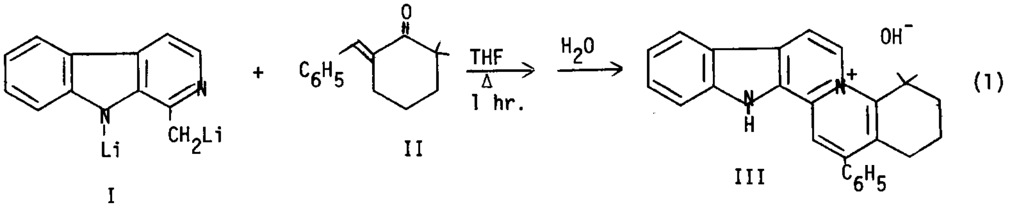
Tetrahedron Letters No. 41, pp 3583 - 3584, 1975. Pergamon Press. Printed in Great Britain.

NEW BASE-CATALYZED PREPARATION OF CERTAIN QUINOLIZINIUM SALTS

Edwin M. Kaiser* and Philip L.A. Knutson
Department of Chemistry, University of Missouri-Columbia,
Columbia, Missouri 65201, USA

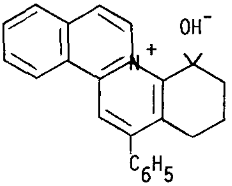
(Received in USA 15th July, 1975; received in UK for publication 1st September, 1975)

As part of a continuing study of the chemistry of lithiomethylated nitrogenous heterocycles,[1] a new remarkably facile synthesis of certain quinolizinium salts has been found. The one-pot reactions consisting of a conjugate addition of such carbanions with α,β-unsaturated ketones followed by spontaneous in situ oxidative cyclizations are illustrated by the reaction of dilithioharman (I) with cyclohexanone II to afford indoloquinolizinium salt III[2] (49%)(eq. 1). To our knowledge, such cyclizations are the first ones effected by basic rather than acidic reagents.[3]

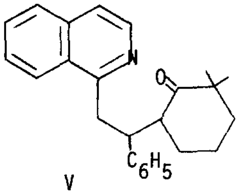


Similarly, 1-lithiomethylisoquinoline has been reacted with II in the presence of excess lithium diisopropylamide to afford benzoquinolizinium salt IV[2] (40-45%). Interestingly, this latter reaction in the absence of excess base fails to give cyclized product; instead, only the open-chain product V[2] is obtained (86%). These results suggest that the cyclization might proceed via a process illustrated by VI where a new α-methyl carbanion is formed which indirectly attacks the carbonyl (or the corresponding enolate anion) as shown. Loss of a "hydride" and dehydration of the alcohol or lithioalkoxide would complete the process.

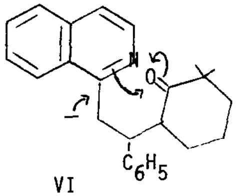
In contrast, reaction of 2-lithiomethylquinoline with II gives the open-chain product VII[2] which, to date, has resisted cyclization to VIII. Perhaps such a cyclization is precluded in this case by peri-hydrogen interaction since it is nearly impossible to make a space-filling model of VIII.



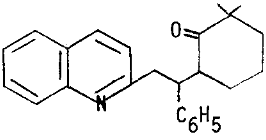
IV



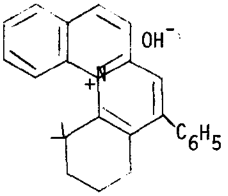
V



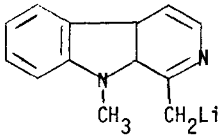
VI



VII



VIII



IX

At first glance, the above conjugate additions appear to be similar to the previously reported reaction of lithio-N-methylharman (IX) with isopropoxymethylene cyclohexanone to give sempervirine methochloride.[4] However, this sequence involved a 1,2-addition to the ketone followed by an acid-catalyzed cyclization.

An active study is in progress to assess the types of lithiomethylated heterocycles and α,β-unsaturated carbonyl compounds that will undergo such condensations and oxidative cyclizations.

Acknowledgement: This work, supported by grant 1 R01 GM21500-01 from the National Institute of General Medical Sciences, National Institutes of Health, is acknowledged with thanks.

References

1. Previous paper: E.M. Kaiser and W.R. Thomas, J. Org. Chem., 39, 2659 (1974).
2. These compounds exhibited correct ir and nmr spectra and satisfactory elemental analysis (±0.3%).
3. For example, see "Ring Index," A.M. Patterson, American Chemical Society, Washington, D.C., 1960, Chapter XI, p. 1046.
4. R.B. Woodward and W.M. McLamore, J. Amer. Chem. Soc., 71, 379 (1949).