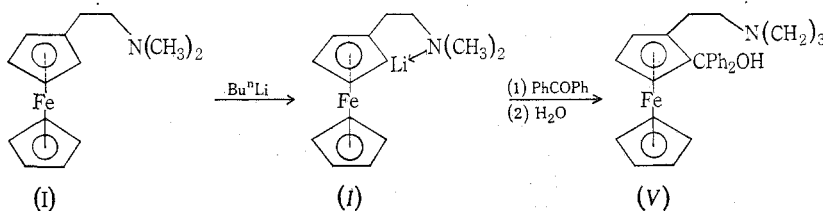


COMPARATIVE BEHAVIOUR UPON LITHIATION OF DIMETHYLAMINOETHYLFERROCENE AND β -PHENETHYLDIMETHYLAMINE*

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We recently reported¹ that dimethylaminoethylferrocene (I) can be metalated by *n*-butyllithium, that the lithium atom evidently enters the 2-position of the molecule to produce lithio-intermediate (I), and that synthesis of a variety of condensation products with electrophilic molecules can be carried out. Scheme 1 outlines this procedure for the condensation of the lithiated amine (I), namely (I), with benzophenone.



Scheme 1

This 2-position lithiation of (I) was particularly interesting in that the lithiation of β -phenethyldimethylamine (II) which should have formed the analogous lithio-intermediate (II) apparently failed to produce any condensation product.² In contrast, 2-position lithiation had been exhibited in the case of both dimethylamino-methylferrocene (III) (lithio-intermediate (III))³ and benzyldimethylamine (IV) (lithio-intermediate (IV))⁴ with good yields of condensation products being reported from each.

We have now found conditions (cf. Table 1) that apparently maximize the yield of lithio-intermediate (I); condensations with electrophilic reagents under these conditions give product yields which compare favourably with those from lithiation

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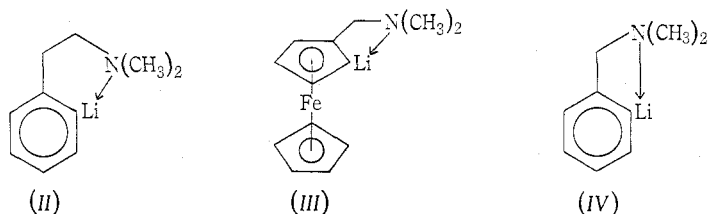
¹ Slocum, D. W., Jennings, C. A., Engelmann, T. R., Rockett, B. W., and Hauser, C. R., Abstr. 154th Meeting Am. chem. Soc., Chicago, Illinois, Sept. 1967, p. S148.

² Vaulx, R. L., Jones, F. N., and Hauser, C. R., *J. org. Chem.*, 1965, **30**, 58.

³ Slocum, D. W., Rockett, B. W., and Hauser, C. R., *J. Am. chem. Soc.*, 1965, **87**, 1241.

⁴ Jones, F. N., Zinn, M. F., and Hauser, C. R., *J. org. Chem.*, 1963, **28**, 663; Jones, F. N., Vaulx, R. L., and Hauser, C. R., *J. org. Chem.*, 1963, **28**, 3461.

of (III)³ and (IV).⁴ In addition, a re-examination of the lithiation of (II) has been undertaken. Our results show that 2-lithiation of this molecule (lithio-intermediate (II)) does take place, but that only small yields of condensation products may be obtained.



A time study of the lithiation of (I) as determined by its condensation product with benzophenone is recorded in Table 1; maximum yield of the condensation product, 2-(α,α -diphenylhydroxymethyl)dimethylaminoethylferrocene (V), was found after a metalation period of 2 hr. That for (III) was reported to be after a period of 1 hr.³ The usual analytical, i.e., and n.m.r. criteria for the structure of the molecule were satisfactorily met.

TABLE 1
METALATION OF DIMETHYLAMINOETHYLFERROCENE (I) WITH *n*-BUTYL-LITHIUM; CONDENSATION WITH BENZOPHENONE
Condensation period 4 hr at room temperature. Lithiation was effected in ether-hexane at room temperature

Mole Ratio Amine (I)/Bu ⁿ Li	Lithiation Period (hr)	Yield (%) Carbinolamine (V)
1 : 1.5	1	36
1 : 1.5	2	68
1 : 1.5	10	32
1 : 1.5	20	13
1 : 3.0	20	45

We have also found that amine (II) can be successfully 2-metalated (maximum yield benzophenone condensation product was 6.8% after 11 hr). While this work was in progress, Narasimhan and Ranade⁵ published a parallel study of the metalation of amine (II) and reported the isolation of product from the condensation of lithio-intermediate (II) with benzaldehyde and benzophenone. Their results and ours agree to the point that 2-condensation can be brought about. Interestingly, our results are in direct contrast to those observed for the lithiation of (IV),⁴ where good yields of condensation products were obtained after metalation periods of 20–30 hr.

That the extent of 2-metalation of (II) differs so markedly from that of (I) deserves some comment. An explanation of this difference may lie in the relative acidities of the ring protons and the methylene protons α to the ring in the respective

⁵ Narasimhan, N. S., and Ranade, A. C., *Tetrahedron Lett.*, 1966, 603.

amines. Lithiation of (II) apparently involves a competing E_2 reaction which results in the formation of styrene and thence polystyrene. No comparable material was found among the products of the lithiation of (I) and condensation with benzophenone. We, therefore, conclude that the methylene protons α to the benzene system are much more acidic than those α to the ferrocene system. A recent study has shown the ferrocene system as a substituent to be electron donating.⁶

Lastly, we would also like to point out that there is an accompanying difference in the acidity of the ring protons in the two aromatic systems. The known ability of n-butyllithium to lithiate the ferrocene molecule itself, whereas benzene is unaffected by n-butyllithium, illustrates the greater acidity of ferrocene ring protons.

Detailing and perfection of these metalation and rearrangement techniques should prove invaluable in the synthesis of several types of substituted β -phenethylamines and their ferrocene analogues, the former a class of compounds known for their hallucinogenic and adrenergic properties.

⁶ Nesmeyanov, A. N., Perevalova, E. G., Gubin, S. P., Grandberg, K. I., and Kozlovsky, A. G., *Tetrahedron Lett.*, 1966, 2381.