Tetrahedron Letters No. 5, pp 413 - 414, 1978. Pergamon Press. Printed in Great Britain.

THE EFFECT OF CROWN ETHERS ON THE REDUCTIVE DIMERIZATION OF SCHIFF BASES

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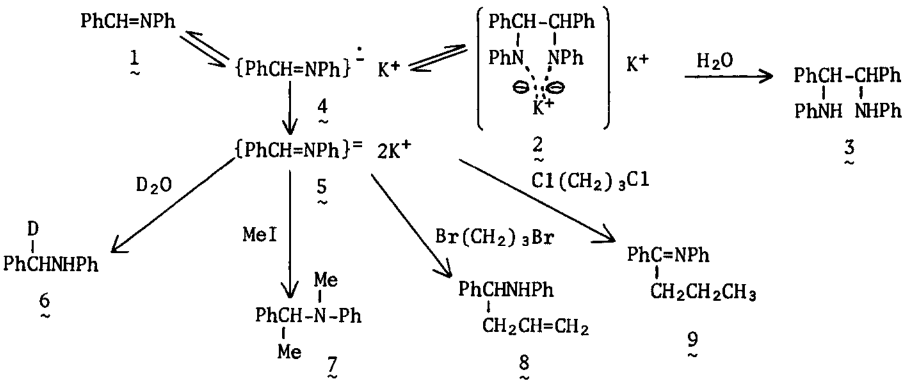
(Received in USA 2 October 1977; received in UK for publication 6 December 1977)

In earlier papers we[1] and others[2] have described the reductive dimerization of Schiff bases such as N-benzalaniline, 1, by alkali metals to dimeric dianions, 2, and demonstrated that the isomerization of the diastereomeric dimeric dianions, 2, is due to an equilibrium with the corresponding radical anion, 4. One interesting feature of the dimerization is that the racemic diastereomer of 2 is greatly favored in the equilibrating system. It has been hypothesized[1b,2] that this is due to contact ion pair formation of two amine anionic centers with one cation. Direct experimental support for this was sought in the use of crown ethers which, it was reasoned, by competitive complexation with the cation would disrupt the association and in some way affect the position of the meso-racemic 2 equilibrating pair. The experimental data presented here shows that crown ethers have a more dramatic effect on the reaction than expected.

Parallel reductions of 1 with potassium in the absence and presence of 18-crown-6[3] were performed and aliquot samples of the reaction mixture withdrawn, quenched and analyzed by nmr. In the absence of crown ether, dimer formation occurred quickly and the isolated 3 was exclusively racemic (no meso-3 being detected). The dimerization was complete in 2 hr and only after 18 hr were detectable amounts of N-benzylaniline formed.

In the presence[4] of 18-crown-6, N-benzylaniline was the only product detected after 2 hr of reaction; dimeric products were observed in the 1 hr sample with rac. 3/meso 3 = 7.5/1. This suggested that, either the radical anion 4 was being protonated, or that the monomeric dianion, 5, was formed. That the latter was the case was established by treatment of 5 with deuterium oxide when N-(α-deuterobenzyl)aniline, 6, was formed (>85% deuteration). Since similar results were obtained after an additional 12 hr storage, 5 is stable in solution for limited periods of time. Alkylation of 5 with methyl iodide produced N-methyl-N-(α-methylbenzyl)aniline[5], 7, showing that both anionic centers of 5 were reactive. It is apparent that the additional stabilization imparted to 4 by solvation of the cation by the crown ether enables 4 to accept a second electron and be reduced further to 5.



Scheme 1. Reductive Dimerization of N-Benzalaniline

Attempts to utilize 5 and prepare pyrrolidine derivatives by alkylation with 1,3-dihalopropanes exposed another feature of these 18-crown-6 promoted reductions. Reaction with 1,3-dibromopropane produced 4-anilino-4-phenyl-1-butene[6,8], 8, in 70% yield rather than the expected pyrrolidine derivative. Evidently alkylation occurred first at the carbon anionic site and the amine anionic site effected rapid dehydrobromination of the pendant bromotrimethylene chain. In contrast, 1,3-dichloropropane produced the anil of n-butyrophenone[8], 9, which was identified by acid hydrolysis and isolation of n-butyrophenone[7] in 75% yield. In this case, the slower dehydrohalogenation of the chlorotrimethylene chain resulted in exposure of 8 to the isomerizing effect of the basic amine anion[9] resulting in the formation of 9.

Successful reductive metalation of organic compounds (without dimerization) occurs with extended conjugated systems. The use of crown ethers enables one to utilize simpler conjugated unsaturated systems than has hitherto been possible and thus expands the potential synthetic utility of this method of generating anionic intermediates. However, the increased basicity of the derived anions introduces complications into their reactions.

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2. J.J. Eisch, D.D. Kaska, and C.J. Peterson, J. Org. Chem., 31, 453 (1966).
3. Prepared and purified according to G.W. Gokel, D.J. Cram, C.L. Liotta, H.P. Harris, and F.L. Cook, J. Org. Chem., 39, 2445 (1974).
4. The standard reduction involved 0.9 g (0.005 m) of N-benzalaniline, 80 ml tetrahydrofuran, excess potassium and, when present, 2.6 g (0.01 m) of 18-crown-6 stirred under nitrogen at 20°. Aliquot samples were withdrawn, quenched in water and the organic products analyzed[1] by nmr.
5. Nmr ($CDCl_3$) 1.44 (d, 3, J=7 Hz, CH-CH_3), 2.10 (s, 3, NCH_3), 5.08 (q, 1, J=7 Hz, CH-CH_3), 6.2-7.4 (m, 10, aromatic H). Attempts to obtain an analytical sample by column chromatography on silica gel resulted in decomposition.
6. Nmr ($CDCl_3$) 2.47 (t, 2, J=7 Hz, $CHCH_2CH=CH_2$), 4.03 (broad s, 1, NH), 4.35 (t, 1, J=7 Hz, $CHCH_2CH=CH_2$), 4.9-5.4 (m, 2, $CH=CH_2$), 5.4-6.3 (m, 1, CH-CH_2), 6.3-7.5 (m, 10, aromatic H); ir (neat) 3420 (NH), 1600, 1500, 1320, 740, 690 cm^{-1}; α-naphthylurethane, mp 133-134°; analysis calc for $C_{27}H_{24}N_2O$, C, 82.16; H, 6.18; N, 7.14; found C, 82.67; H, 6.31; N, 6.96.
7. Spectral data in agreement with that of an authentic sample; 2,4-DNPH derivative, mp 189-190° (reported 191°).
8. Both 8 and 9 are known compounds. H. Gilman, J. Eisch and T. Soddy, J. Amer. Chem. Soc., 79, 1245 (1957); H. Gilman and J. Eisch, ibid., 79, 2150 (1957).
9. Undoubtedly, solvation of the cation by the crown ether increases the basicity of this anion. Marked increases in basicity and nucleophilicity of anions induced by crown ethers have been reported. For eg. see C.L. Liotta and H.P. Harris, J. Amer. Chem. Soc., 96, 2250 (1974) and D.J. Sam and H.E. Simmons, J. Amer. Chem. Soc., 96, 2252 (1974).