Direct Evidence for an Intermediate Complex in a Nucleophilic Aromatic Substitution

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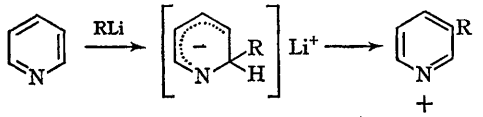
THE nucleophilic substitution of hydride ion in pyridine derivatives by organolithium compounds has been assumed to proceed *via* a two-step addition–elimination process involving the formation of a dihydropyridyl-lithium derivative.[1] Evidence has been presented[1] that the observed products are not formed from pyridyne intermediates, but support for the intervention of a σ-complex (I) in



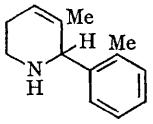
(I)

simple cases has been of an indirect nature. Thus, while Ziegler and Zieser[2] claimed to have isolated the adduct (I) from the reaction of butyl-lithium with pyridine no experimental data in support of this were given. The intermediacy of such a species was assumed from the use of the adduct from pyridine and phenyl-lithium as a reducing agent.[3] The only direct evidence comes from studies with polycyclic compounds. For example, acridine reacts with phenyl-lithium to give an intermediate which, on treatment with water, gives 9,10-dihydro-9-phenylacridine.[4] We now present direct evidence for the intervention of a σ-complex in such a reaction with a simple pyridine derivative.

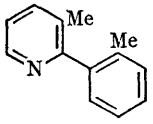
The addition product from *o*-tolyl-lithium and 3-picoline (1 : 1 molar ratio) in boiling ether was treated with oxygen and analyzed by gas chromatography. In addition to the expected products (3-methyl- and 5-methyl-2-*o*-tolylpyridine[5]), a very small amount of 3-methyl-5-*o*-tolylpyridine (identical with authentic synthetic material obtained unambiguously from 3-bromo-5-methylpyridine and 2-methylcyclohexanone) was isolated, together with more substantial quantities of a compound $C_{13}H_{17}N$, whose structure was established as 1,2,5,6-tetrahydro-3-methyl-2-*o*-tolylpyridine (II) on the basis of its n.m.r. and u.v. spectra, and from the fact that it gave 3-methyl-2-*o*-tolylpyridine (III) on oxidation. No 3-methyl-4-*o*-tolylpyridine was detected. If the oxygen treatment was omitted, the amount of (II) formed increased substantially. Compound (II) did not have a u.v. spectrum characteristic of a dihydropyridine. It exhibited a seventeen-proton n.m.r. spectrum, the intensities, positions, and multiplicities of whose lines could be assigned[6] unambiguously to the suggested structure: a 4H singlet at τ 2·98 (C_6H_4), a 1H broad

multiplet at τ 4·35 (·C*H*:C<, C-4 proton), a 1H broad singlet at τ 5·62 (N·C*H*·Ar, C-1 benzylic proton), a 2H multiplet at τ 7·20 (CH_2·N·), a 3H singlet at τ 7·62 (CH_3Ar), a 2H broad multiplet at τ 7·92 (·CH_2·CH:), and a broad 4H singlet at τ 8·61 (NH + :C·CH_3; addition of D_2O reduces this to a 3H singlet at τ 8·58).

The only rational way in which one can conceive of the production of (II) is through the disproportionation of the corresponding dihydro-intermediate

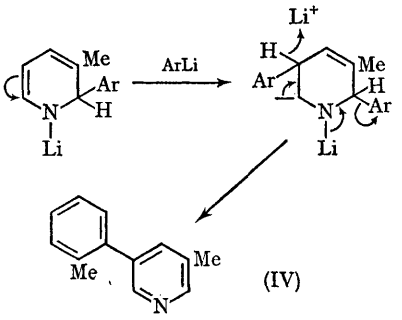


(II)



(III)

which would be expected[7] to give the 3,4-dehydropiperidine derivative. The formation of 3-methyl-5-*o*-tolylpyridine (IV) might be explained on the basis of a modification of the mechanism suggested[1] for the formation of 2,5-diphenylpyridine from pyridine and phenylcalcium iodide[8]:



(IV)

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