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Preliminary communication

1,2 Rearrangement in the reactions of lithium with β-(2- and 4-pyridyl)ethyl chlorides

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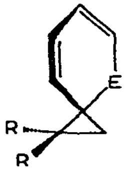
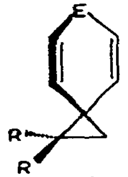
In recent years 2,2,2-triphenylethyl- and 2,2-diphenylpropyl-alkali metallics have been shown to undergo 1,2 phenyl shifts[1-4]. These rearrangements are thought to proceed via an intramolecular[5], anionic[4] process involving a cyclic intermediate or a transition state[6] of the type Ia.



(I)

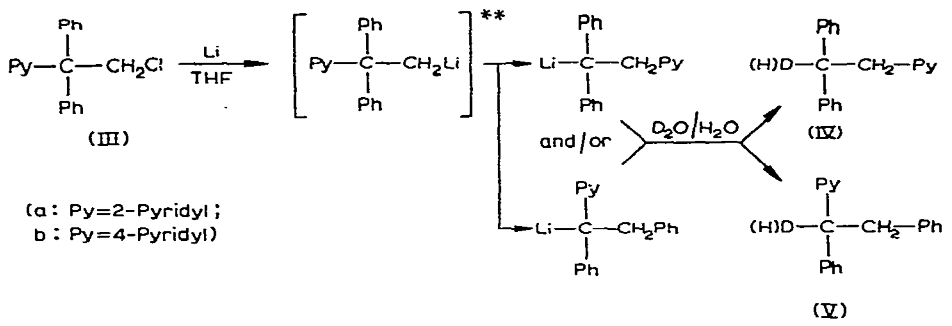


(II)

(a: $E = CH^-$, $R = C_6H_5$;
b: $E = N^-$, $R = C_6H_5$;
c: $E = N{-}CH_3$, $R = CH_3$;
d: $E = N{-}CH_3$, $R = C_6H_5$)

Relatively little work has been done on the migratory aptitudes of different aromatic groups. The limited number of competitive migrations studied, one showing phenyl favored over *p*-tolyl[4], the other showing *p*-biphenylyl favored over *m*-biphenylyl[6], tends to support the suggestion of molecular orbital calculations[7], that in an anionic, cyclic rearrangement electron-withdrawing substituents on a phenyl group would enhance its migratory aptitude.

In order to put this hypothesis of an anionic rearrangement to the test and to search for evidence bearing on the existence of I as an intermediate, we have studied the migratory aptitudes of aromatic heterocyclic groups in competition with phenyl groups. For our first study we have selected the 2-pyridyl- and 4-pyridyl-ethyl systems. In light of the electron-withdrawing nature of the pyridine ring, the following sequence of migratory aptitudes was expected: 2-pyridyl > 4-pyridyl > phenyl. Further, we entertained the hope that in the pyridyl groups the anionic charge, largely situated on a nitrogen atom, might be adequately stabilized to permit the detection of the spiro intermediate, e.g., Ib. Failing to trap Ib we hoped to prepare a suitable model system of the putative spiro intermediate. The compounds, 2-(2-chloro-1,1-diphenylethyl)pyridine (IIIa, m.p. 81–82°) and 4-(2-chloro-1,1-diphenylethyl)pyridine (IIIb, m.p. 127–129°), were prepared and then treated individually with lithium in tetrahydrofuran (Scheme 1). After 3h at 0° the 2-pyridyl system on hydrolysis gave as the only detectable rearrangement product, compound IVa. The identity of this product was established by comparison with authentic

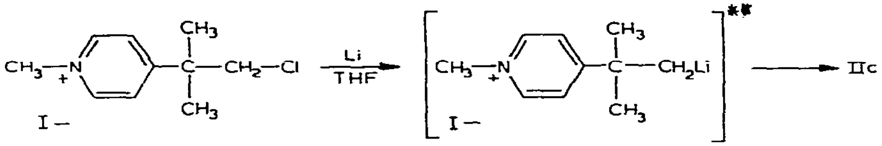


Scheme 1

samples of the possible rearrangement products. Already after 1h at –60°, hydrolysis of the reaction mixture gave some of compound IVa, showing that migration in the 2-pyridylethyl case occurred at a temperature where the 2,2,2-triphenylethyl system did not rearrange[2]★. Work-up of the rearrangement mixture with D_2O introduced a deuteron on the carbon attached to the two phenyl rings.

Although the behavior of the 2-pyridylethyl system accorded with expectations based on an anionic rearrangement, the 2,2-diphenyl-2-(4-pyridyl)ethyl chloride gave, surprisingly, only compound Vb, together with material of higher molecular weight. This conclusion again was substantiated by comparing the product with authentic samples of IVb and Vb by means of NMR and TLC. Thus, the observed migratory tendencies, 2-pyridyl > phenyl > 4-pyridyl, are not consistent with the operation of a simple 1,2-carbanionic rearrangement in every case.

As to the presence of a spiro intermediate of type I, we attempted to trap such a substance during the rearrangement of IIIa by methylating on nitrogen with methyl iodide, but no product corresponding to Id could be isolated. However, preparation of 1,1,6-trimethyl-6-azaspiro[2.5]octa-4,7-diene (IIc) as a model compound for a possible rearrangement intermediate was achieved, as shown in Scheme 2. Because this substance was labile even under nitrogen at room temperature, complete purification could not be



Scheme 2

achieved and NMR and IR spectroscopic techniques were employed for its identification. Characteristic peaks (δ, ppm) in the NMR were at 5.80 (δ, J = 8Hz) for α-protons 4.05 (δ, J = 8Hz) for the β-protons and 2.79 (s) for the N-methyl protons. These resonances are similar to those found for 1,4,4-trimethyl-1,4-dihydropyridine by Kosower[8]. In general, the

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★Also, in contrast with the triphenylethyl system, almost all of IIIa had undergone rearrangement after 4 h at –60°.

★★Of course, the nature of the intermediates in these reactions, whether they are organolithium compounds or free radicals, is the point at issue. The bracketed reagents rest upon the moot assumption of a carbanionic rearrangement.

IR spectrum of compound IIc resembled that of Kosower's compound. Specifically, characteristic bands for 1,4-dihydropyridines between 1662–1668 cm^{-1} were also present in our compound. Other peaks in the NMR of IIc were at 0.99 (s) for the methyl groups on the cyclopropyl ring and 0.19 (s) for the cyclopropyl hydrogens. The integrated intensities of these peaks were also consistent with the proposed structure. The existence of this model spiro compound, though short-lived, suggests that cyclic systems may be intermediates, rather than transition states, in these rearrangements[★].

Since the above results did not give the migratory aptitudes expected for anionic processes, we have examined the rearrangement for the possible involvement of a radical process. Monitoring the rearrangement of compound IIIa by ESR spectroscopy, after removal of the excess lithium metal by filtration, revealed a broad (30 gauss), strong signal. A similar signal was also observed when the 2,2,2-triphenylethyl chloride–lithium metal system[2] was examined by means of ESR spectroscopy. These findings now prompt us to re-examine by instrumental techniques some of these so-called carbanionic rearrangements for the possible importance of radical processes[★★]. This work is in progress.

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[★] In a study contemporaneous to ours, on the behavior of 2-(4-pyridyl)-2-methyl-propylmagnesium chloride toward ethyl chloroformate, Cooper and Fraenkel[10] detected by NMR a spirocyclopropyl derivative of type II, where R = CH_3 and E = $NCOOC_2H_5$.

[★★] Free radicals have been implicated in the reaction of neophyl chloride with lithium, on the basis of ca. 5% rearranged organolithium compound, although the rearrangement 2,2,2-triarylethyl chloride system is still thought to occur carbanionically[9].