Phenyl Migration during Reaction of Neophyl Chloride with Lithium

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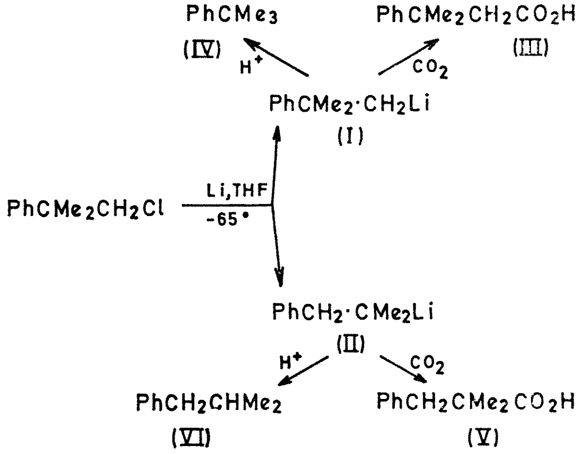
Summary Reaction of 1-chloro-2-methyl-2-phenylpropane with lithium in tetrahydrofuran at −65° gives 2-methyl-2-phenylpropyl-lithium containing some 1,1-dimethyl-2-phenylethyl-lithium.

WHILE thermal rearrangements of organolithium compounds, especially those containing phenyl or like groups, are known,[1] it is normally assumed that reaction of lithium with alkyl halides gives rise at low temperature to organolithium compounds of unrearranged carbon skeleton. Significant deviations from this simple rule would place limitations on the utility of organolithium reagents in synthesis. Neophylmagnesium chloride from the reaction of neophyl chloride (1-chloro-2-methyl-2-phenylpropane) with magnesium is said not to be contaminated with isomers or to be only immaterially so, while in contrast the hydrocarbons produced as by-products in the synthesis of this Grignard reagent contain a significant amount of compounds with the phenyl group shifted to a new position.[2]

We now report that in the reaction of neophyl chloride with lithium the organolithium product itself contains a significant amount of rearranged material. This product is prepared in yields up to 80% from neophyl chloride and lithium metal (0·05% Na, maximum) by first initiating the reaction with *ca.* 5% of the chloride and a small portion of methyl iodide at −10° for 1 hr. and then reaction at −65° for some 4 hr. in tetrahydrofuran under a nitrogen atmosphere with stirring by a Morton high-speed apparatus.[3] Carbonation of the reaction mixture and analysis of the acids (as methyl esters) and neutral materials by g.l.c. gave in a typical run 71% of 3-methyl-3-phenylbutanoic acid (III), 3·3% 2,2-dimethyl-3-phenylpropanoic acid (V), 6·4% t-butylbenzene (IV), 2·9% of isobutylbenzene (VI), and 13% of unreacted neophyl chloride. The presence of isobutylbenzene in the hydrocarbon product was further confirmed by n.m.r. analysis. The average proportion of the acid of rearranged structure (V) in the mixture of acids from five such runs was 5·3 ± 0·5%. In a preparation in which neophyl chloride was added to lithium over a period of 30 min. and a portion carbonated immediately, the proportion of (V) was 6·4%; after 4 hr. at −70° this proportion decreased to 5·5% and after an additional 4 hr. to 3·9%. An increase in reaction temperature from −65° to −40° for 2 hr. decreased the proportion of (V) a similar amount but had little effect on the yield of (III). An increase in temperature to 4° for 4 hr. resulted in a negligible yield of (V) and a greatly reduced yield of (III) with approximately correponding increases in yields of hydrocarbons (VI) and (IV), respectively.† Thus isobutylbenzene seems to arise by protonation of 1,1-dimethyl-2-phenylethyl-lithium (II) and t-butylbenzene similarly from 2-methyl-2-phenylpropyllithium (I); the chief source of such protons appears to be the solvent tetrahydrofuran. The data indicate that the rearranged organolithium compound (II) is formed along with the expected compound (I) during the reaction of neophyl chloride with lithium and that (II) is not a subsequent product formed by rearrangement of (I), although such rearrangements involving 1,2-shift of phenyl are known[1] in cases in which the rearranged product is thermodynamically more stable than the unrearranged product.



According to g.l.c. analysis, the starting neophyl chloride was free from isomeric impurities; in particular it was demonstrated that the chloride related to (II), *i.e.*, 2-chloro-2-methyl-1-phenylpropane, was present (if at all) in an amount of less than 0·5%. Moreover reduction of the starting chloride with sodium in refluxing dioxan–t-pentyl alcohol gave t-butylbenzene containing less than 1·2% of isobutylbenzene. It is, therefore, very unlikely that the rearrangement products could arise from impurities in the starting halide. Since in most experiments *ca.* 5% of neophyl chloride was added during the initiation stage at −10°, it was conceivable that most of the rearrangement products could have been formed at this temperature. This possibility was disproved by a preparation run at −10° for 1 hr., which gave a 0·9% yield of rearranged acid (V), 5·7% of isobutylbenzene, and mostly unrearranged acid (III). The possibility that the methyl iodide used in initiating the reaction might be responsible for the rearrangement was also disproved by experiments in which the methyl iodide was omitted without changing the results (save for somewhat more unreacted neophyl chloride than usual in the products). Finally the possibility that neophyl chloride could have been isomerized under the reaction conditions to 2-chloro-2-methyl-1-phenylpropane was disproved by blank experiments. The evidence, therefore, appears good that rearrangement occurred during the reaction of neophyl chloride with lithium metal itself.

We suggest that the present results are to be explained on the basis that neophyl chloride reacts with lithium metal by a one-electron transfer process to give neophyl radical which in part is free enough from the metal to undergo the known[4] 1,2-migration of phenyl; reduction of the radicals with lithium then gives the organolithium products (I) and (II). A similar explanation has been advanced to account for the rearranged hydrocarbons formed during reaction of neophyl chloride with magnesium[2] and for racemization (but no rearrangement of phenyl) during reaction of optically active 1-halogeno-1-methyl-2,2-diphenylcyclopropane with magnesium and lithium. We believe that the present case constitutes the most convincing evidence available that the preparation of organolithium compounds through reaction of metallic lithium with primary alkyl chlorides proceeds, at least in part, by way of free radicals.

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† Low yields of several incompletely identified acids were also obtained, including *o*-t-butylbenzoic acid.

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[4] For a review of free-radical rearrangements, see C. Walling in "Molecular Rearrangements," ed. P. de Mayo, Part 1, Interscience, New York, 1963, ch. 7.

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