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Preliminary communication

1,4-Addition of allylmagnesium chloride to 2-methylquinoline via 1,2-addition and subsequent rearrangement

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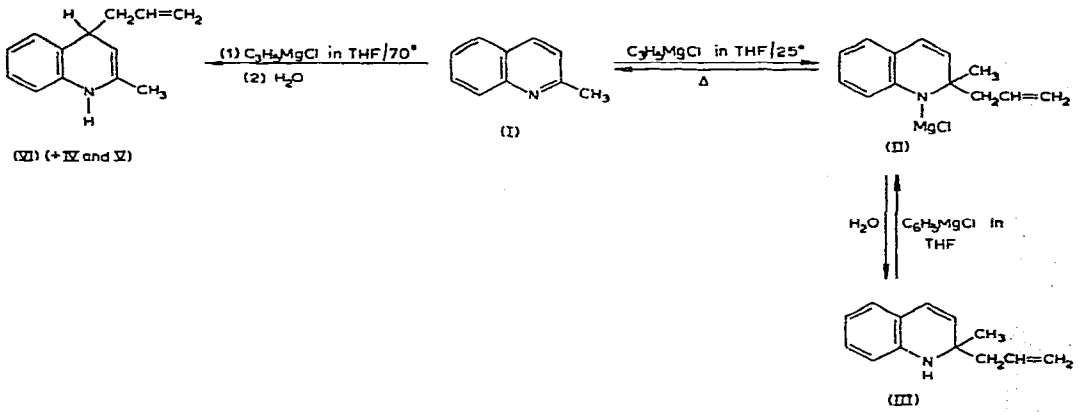
A recent claim that phenyllithium adds in a 1,4-manner to the quinoline system and that the resulting adduct slowly rearranges to the 1,2-adduct[1] has been disproved by us[2] through an NMR and infrared spectral re-examination of the purported 1,4-adducts. Use of 2-deuterated quinolines and refined spectral resolution were decisive in showing that the adducts were actually of the 1,2-type★. In the course of further research directed toward the discovery of novel rearrangements[4] and isomerizations[5] in heterocyclic systems, we have now uncovered a genuine organometallic rearrangement unprecedented in the quinoline system. Thus, treatment of 2-methylquinoline (I) with three equivalents of allylmagnesium chloride in tetrahydrofuran solution at room temperature led, upon hydrolysis, to a 94% yield of 2-allyl-2-methyl-1,2-dihydroquinoline★★ (III) (analytical data: NMR (TMS, δ): 1.17 s, CH_3; 2.18 center of d (7 Hz), CH_2; 3.58 broad s, NH; 4.85–6.0 m, $CH{=}CH_2$ and C_3H and 6.1–7.1 m, 5H; infrared (neat, cm^{-1}) 3425 (sh) NH; 1655 (sh) C=C; 1625 (sh) arom.C=C; 1590 conjug. C=C; and 915 and 995 $CH{=}CH_2$). When the reaction was conducted over extended periods at the reflux temperature, very little III was detected upon hydrolysis. Under these conditions, the principal products were 4-allyl-2-methyl-quinoline (IV) and its 1,2-dihydro (V) and 1,4-dihydro (VI) derivatives in a total yield of 75% (analytical data: NMR (TMS, δ) 1.10 center of d (6 Hz) CH_3 of V; 2.20 s CH_3 of VI; 3.60 s CH_3 of IV; 4.8–6.0 m $CH{=}CH_2$; and 6.0–8.2 arom. CH; infrared (neat, cm^{-1}) 3300–3400 (broad) NH; 1645 (sh) C=C; 1625 (sh) arom. C=C; 1590 conj. C=C; and 915 and 995, $CH{=}CH_2$).

The structure proof of the mixture of IV, V and VI was achieved by catalytic hydrogenation of the allyl groups (10% Pd/C in EtOH). Treatment of the reduction product with ethanolic picric acid yielded the picrate (VIII) of the unknown 2-methyl-4-n-propyl-

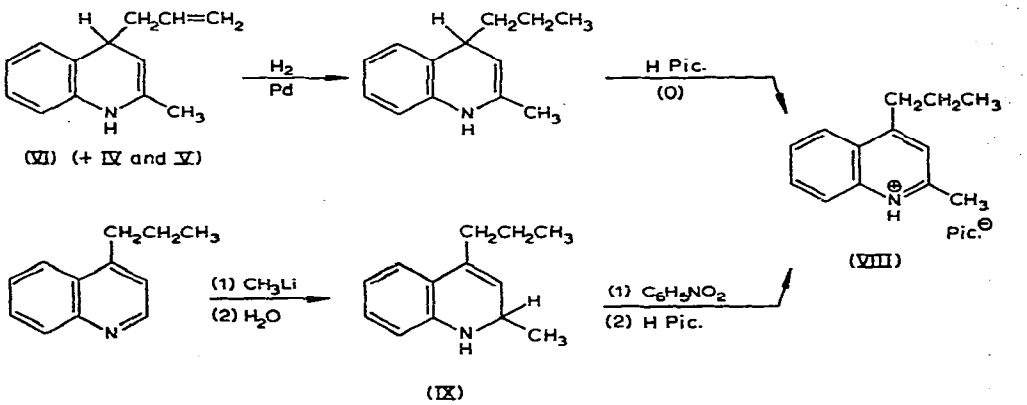
★In a recent communication, an NMR study contemporaneous with ours, employing model 1,2- and 1,4-dihydroquinolines, also raised objection to the claim of these Japanese workers (ref. 3).

★★Satisfactory elemental analyses for C, H and N were obtained for III and VIII.



quinoline (VII)*. An authentic sample of VII was synthesized in an unambiguous fashion from the known 4-n-propylquinoline[6] by treatment with methyllithium and subsequent oxidation of the resulting 1,2-dihydro adduct IX with nitrobenzene. The picrate of this authentic VII** and that isolated from the hydrogenation of the foregoing Grignard product were shown to be identical by NMR, mass and infrared spectral comparisons and by a mixture melting point.

From the foregoing results, it is clear that allylmagnesium chloride adds to 2-methylquinoline in the expected[7] 1,2-fashion and that the allyl group subsequently rearranges to the 4-position. However, whether this rearrangement involved an intramolecular, Cope pathway or a 1,2-elimination of allylmagnesium chloride and a subsequent



*The filtrate from the isolation of the picrate yielded, after basification with sodium hydroxide, an oil that by NMR, mass and infrared spectral measurements was shown to be 1,2,3,4-tetrahydro derivatives of VII, presumably formed by disproportionation of V and VI.

**Satisfactorily elemental analysis for C, H and N were obtained.

1,4-re-addition, remained to be determined. Therefore, to test for the reversibility of the 1,2-addition, the magnesium chloride salt of 2-allyl-2-methyl-1,2-dihydroquinoline (II) was generated in THF solution in an independent manner, namely by treating a pure sample of III with a four-fold excess of phenylmagnesium chloride in THF solution. The immediate formation of a dark green solution signaled the generation of II. Hydrolysis after 24 h at 25° gave a 60% yield of quinaldine (I) and 40% of III; after an additional 24 h at reflux the yield of quinaldine rose to ca. 75% and the amount of remaining III was under 5%. At the same time 25% of the 1,4-addition product VI was now formed. The ready dissociation of II, even at 25°, and its nearly complete dissociation at 70° where VI begins to form are not in accord with the intramolecular, Cope pathway, in which II would be the key intermediate. Therefore, there is little doubt that the rearrangement of III into VI involves the 1,2-elimination of allylmagnesium chloride from II and its 1,4-addition to quinaldine. Accordingly, this interplay of 1,2- and 1,4-additions to the quinoline nucleus represents a case of competitive kinetic and thermodynamic controls of reaction. The recent observation that 1-methyl-1,2-dihydroquinoline is isomerized into 1-methyl-1,4-dihydroquinoline by potassium t-butoxide in dimethyl sulfoxide solution[8] supports the conclusion that III is the kinetically favored and VI the thermodynamically favored product.

Although the observation of reversible additions of organometallic reagents to various functional groups is not novel, the ease with which the allyl Grignard reagent adds in a reversible 1,2-fashion to quinaldine is, to our knowledge, unprecedented. Moreover, this attainment in high yield of either the 1,2-addition or the 1,4-addition of a given organometallic reagent to an α,β-unsaturated carbonyl-like linkage appears to be without parallel. The synthetic and mechanistic implications of these findings are receiving our further attention.

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REFERENCES

1 Y. Otsuji, K. Yutani and E. Imoto, *Bull. Chem. Soc. Japan*, 44 (1971) 520.
2 J.J. Eisch and D.R. Comfort, *J. Organometal. Chem.*, 38 (1972) 209.
3 C.E. Crawforth, O. Meth-Cohn and C.A. Russell, *Chem. Commun.*, (1972) 259.
4 J.J. Eisch and C.A. Kovacs, *J. Organometal. Chem.*, 25 (1970) C 33.
5 J.J. Eisch and D.A. Russo, *J. Organometal. Chem.*, 14 (1968) P 13.
6 A.E. Chichibabin, *Bull. Soc. Chim. France*, [5] 3 (1936) 1607.
7 H. Gilman, J.J. Eisch and T.S. Soddy, *J. Amer. Chem. Soc.*, 81 (1959) 4000.
8 R.M. Coates and E.F. Johnson, *J. Amer. Chem. Soc.*, 93 (1972) 4016.