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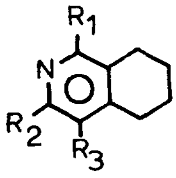
# AMIDE CATALYSED FACILE ISOMERIZATION OF 5,6-DIHYDROISOQUINOLINES: SYNTHESIS OF STABLE 1,2-DIHYDROISOQUINOLINES.

T.R. KASTURI* AND LALITHA KRISHNAN
Department of Organic Chemistry, Indian Institute of Science,
Bangalore-560012, India.

Summary: Stable 1,2-dihydroisoquinolines have been synthesized by an amide catalysed novel isomerization reaction of 5,6-dihydroisoquinolines.

Cyclohexa-1,4-dienes react with $KNH_2$ in liq.$NH_3$ losing a hydride ion to yield benzenes.[1] $KNH_2$ in $NH_3$ also causes disproportionation of cyclohexa-1,3-diene to benzene and cyclohexene.[2] In this note, we wish to report an unusual intramolecular disproportionation of substituted 5,6-dihydroisoquinolines with $KNH_2$ in liq.$NH_3$ yielding stable 1,2-dihydroisoquinolines.

The 5,6-dihydroisoquinoline derivatives[3] (4a-j) were synthesized from the corresponding tetrahydro-derivatives (1a-j) via the respective ketones (2a-j) and alcohols (3a-j).[4] Treatment of (4a) in dry THF with freshly prepared $KNH_2$ in liq.$NH_3$ ($-33^{o}C$, $N_2$ atmosphere), gave, after usual workup and purification (TLC, Hexane:EtOAc 3:1), two compounds: The more polar component (60%) mp. 132-135°C (benzene:hexane) UV:$\lambda_{max}$ 262 ($\varepsilon$, 11,000) and 312 nm (9000), IR$\nu_{max}$ (nujol): 3800-3400 br(NH) and 2230 $cm^{-1}$ (conj. $-C\equiv N$), analysed for $C_{13}H_{14}N_2O$ ($M^+$ 214). On the basis of the PMR spectrum ($CDCl_3$): $\delta$ 1.4 (m, 6H $2CH_3$), 4.3-4.5 (m, 2H $-OC\underline{H}_2CH_3$), 4.6-4.7 (m, 1H $NC\underline{H}$), 4.9 (bs, 1H $D_2O$ exchangeable, $-N\underline{H}$) and 6.9-7.3 (m, 4H ar-H) and spin decoupling (Irradiation of the methyl signals resulted in the collapse of the 4.6-4.7 multiplet to a broad triplet and the 4.3-4.5 multiplet to a quartet[5]), the 1,2-dihydroisoquinoline structure (5a) could be assigned to this product. The less polar component (20%) was shown to be the earlier reported (6a).[4] Similar reactions of (4b-e) yielded the corresponding 1,2-dihydroisoquinolines (5b-e) and the isoquinolines (6b-e). Only (5e) could not be isolated in a pure state due to its instability However, its presence was inferred from the PMR multiplet at 4.7$\delta$ characteristic of the C-1 proton of 1,2-dihydroisoquinolines.[6,7] The probable mechanism of formation of (5a-d) could be as shown in the chart. Examples of such 1,2-dihydroisoquinolines wherein the N-atom is secondary are very few.[6,8] Extending the reaction to the compounds (4f-h) resulted in each case, in the formation of only the aromatized compounds (6f-h) and the amines (6i-j) but no 1,2-dihydroisoquinolines. The reaction thus appears to be a general one for 1-substituted (aryl, alkyl) or unsubstituted 5,6-dihydroisoquinolines.



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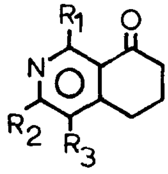

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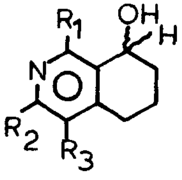

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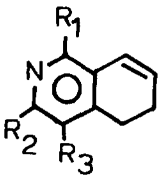

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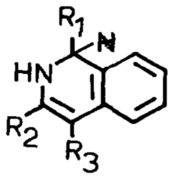

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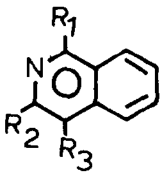

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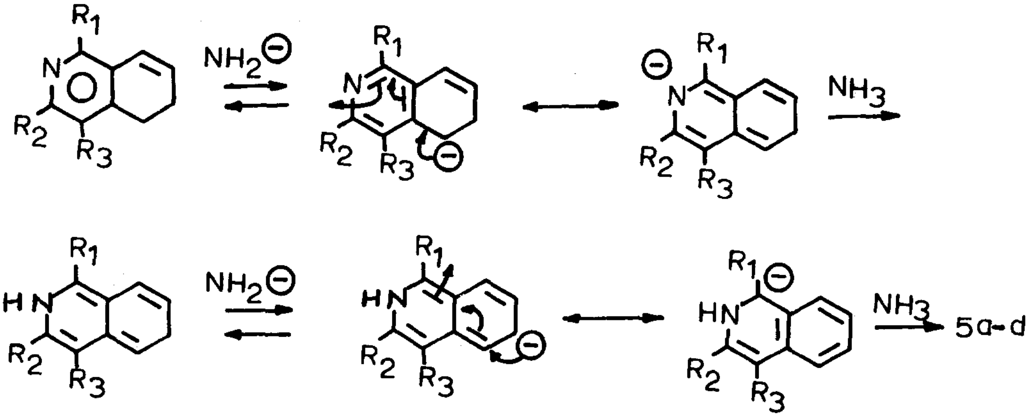
a: $R_1=CH_3$, $R_2=OCH_2CH_3$, $R_3=CN$; b: $R_1=CH_2CH_3$, $R_2=OCH_3$, $R_3=CN$;

c: $R_1=C_6H_5$, $R_2=OCH_3$, $R_3=CN$; d: $R_1=CH_2CH_3$, $R_2=OCH_3$, $R_3=H$;

e: $R_1=H$, $R_2=OCH_3$, $R_3=CN$; f: $R_1=R_2=OCH_3$, $R_3=CN$;

g: $R_1=R_2=OCH_2CH_3$, $R_3=CN$; h: $R_1=OCH_2CH_3$, $R_2=OCH_3$, $R_3=CN$;

i: $R_1=NH_2$, $R_2=OCH_3$, $R_3=CN$; j: $R_1=NH_2$, $R_2=OCH_2CH_3$, $R_3=CN$.



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