# SYNTHESIS OF 4-R-2,2-DIMETHYL-1,2-DIHYDROBENZO[f]ISOQUINOLINES AND (2,2-DIMETHYL-1,2-DIHYDROBENZO[f]ISOQUINOLYLIDENE-4)ACETIC ACID DERIVATIVES

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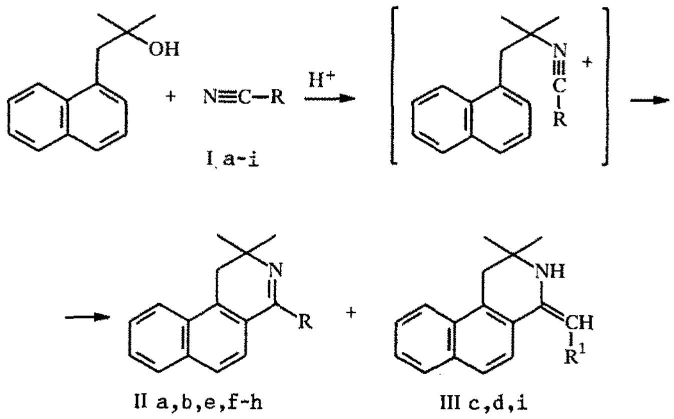
*4-R-2,2-dimethyl-1,2-dihydrobenzo[f]isoquinolines and (2,2-dimethyl-1,2-dihydrobenzo[f]isoquinolylidene-4)acetic acid derivatives have been prepared by Ritter reactions of substituted acetonitriles with 2-methyl-1-(1-naphthyl)propan-2-ol.*

Benzoisoquinolines, particularly benzo[f]isoquinolines, have been studied relatively little [1]. We have used the Ritter reaction [2] for the synthesis of 4-R-2,2-dimethyl-1,2-dihydrobenzo[f]isoquinolines (II).



I, II a R = H, b R = Me, c R = $CH_2COOEt$, d R = $CH_2CONH_2$, e R = $CH_2Ph$,
f R = $CH_2C_6H_3(OMe)_2$-3,4, g R = SMe, h R = $SC_6H_4NH_2$-*p*, i R = $CH_2CN$;
III c $R^1$ = COOEt, d $R^1$ = $CONH_2$, i $R^1$ = CN

One might expect *a priori* two possible products resulting from stabilization of the intermediate carbimmonium cation, namely, at the β- or peri-positions. The PMR spectrum of compound IIb contains two characteristic doublets for the H-5 and H-6 protons (7.61 and 7.75 ppm, respectively), which would not be present in the PMR spectrum of a cyclization product resulting from attack at the periposition. The PMR spectra of compounds IIa, b, e, f indicate that these exist in their azomethine forms, while compounds IIIc, d, i exist in their corresponding enamine forms, due to the presence of electron-donating substituents in the side chains attached to the C-4 atom in the latter compounds. Compounds IIa, g, h also exist as azomethine structures but are not capable of tautomeric conversion [3].

We should note here that when R = $NEt_2$, p-$NO_2C_6H_4$, p-$NH_2C_6H_4$, and p-$CH_3OC_6H_4$ cyclization does not take place. This can be explained based on the fact that under the conditions of the Ritter reaction protonation occurs at either the amino

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TABLE 1. Physical Characteristics of Compounds IIa,b,e-h and IIIc,d,i

| Compound | Empirical formula | $T_{mp}$ °C | PMR spectra (δ, ppm) |  |  |  | Yield, % |
|---|---|---|---|---|---|---|---|
|  |  |  | 6H, s, $Me_2$ | 2H, s, $(C_1)$ | 6H, m, arom | Other protons |  |
| IIa | $C_{13}H_{11}N$ | 190...192 | 1,53 | 3,66 | 7,10...8,46 | — | 80 |
| IIb | $C_{14}H_{13}N$ | 53...55 | 1,67 | 2,90 | 7,10...8,17 | 2,33 (3H, t, Me) | 89 |
| IIIc* | $C_{17}H_{16}NO_2$ | 299...301 | 1,23 | 3,10 | 6,96...8,20 | 1,23 (3H, t, Me ethvl<br>4,07 (2H, $CH_2$ ethyl<br>8,87 (1H, s, NH) | 87 |
| IIId | $C_{15}H_{13}N_2O$ | 90...92 | 1,30 | 3,10 | 7,1...8,1 | 5,06 (1H, s, CH);<br>5,06 (2H, s, $NH_2$);<br>9,43 (1H, s, NH) | 93 |
| IIe* | $C_{20}H_{17}N$ | 251...253 | 1,67 | 3,33 | 6,90...8,17** | 4,77 (2H, s, $CH_2$) | 90 |
| IIf | $C_{22}H_{22}NO_2$ | 124...126 | 1,67 | 3,37 | 6,53...7,80** | 3,66 (3H, s, OMe-*m*);<br>3,80 (3H, s, OMe-*p*);<br>4,77 (2H, s, $CH_2$) | 81 |
| IIg | $C_{14}H_{13}NS$ | 85...86 | 1,17 | 3,00 | 7,10...7,97 | 2,33 (3H, s, Me) | 85 |
| IIh | $C_{19}H_{16}N_2S$ | 170...172 | 1,06 | 2,90 | 6,50...8,07 | 4,8 (2H, s, $NH_2$) | 73 |
| IIIi | $C_{15}H_{11}N_2$ | 206...208 | 1,30 | 3,00 | 7,10...8,30 | 5,9 (1H, CH);<br>8,8 (1H, s, NH) | 83 |

*Identified in the form of its hydrochloride.

**For compound IIe the integrated intensity is IIH, m, $H_{arom}$; for compound IIf, 9H, m, $H_{arom}$.

group nitrogen atom or the methoxy group oxygen atom, leading to a sharp increase in the electronegativity of radical R and, as a result, to a reduction of the nucleophilic nature of the nitrile group.

## EXPERIMENTAL

PMR spectra were recorded on an RYa-2310 (60 MHz) spectrometer using $CDCl_3$ as solvent and HMDS as internal standard. High resolution PMR spectra were measured on a Bruker WM-250 spectrometer. Compound purity was checked by TLC on Silufol-254 plates which were visualized using a chloranil solution.

**Compounds IIa,b,e-h and IIIc,d,i (Table 1).** To 50 ml conc. $H_2SO_4$ was added dropwise with stirring at 10°C a solution of a mixture of 0.1 mole 2-methyl-1-(1-naphthyl)propanol and 0.1 mole of the appropriate nitrile in 50 ml benzene, and the reaction mixture was then heated for 5 min in a boiling water bath; the mixture was cooled, diluted with 150 ml water, and the organic layer was separated to leave the aqueous phase, which was washed with 100 ml benzene and treated with aqueous ammonia to a neutral reaction point. The resulting crystals which formed were removed by filtration and recrystallized to give the pure products. In the case of compounds IIe and IIIc after ammonia workup the organic phase was separated by extraction with ether and was then dried over $MgSO_4$; hydrogen chloride gas was bubbled through the resulting ether solution to generate the corresponding hydrochlorides, which were also purified by recrystallization. The PMR spectra of compounds IIe and IIIc were taken after conversion of their hydrochlorides to the free base forms.

## LITERATURE CITED

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