GENERAL METHOD FOR THE SYNTHESIS OF 9-(2,2,2-TRIFLUOROETHYL)-1,2,3,4,4a,9a-HEXAHYDRO-γ-CARBOLINES

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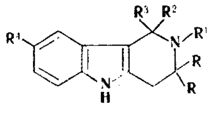
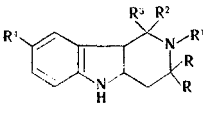
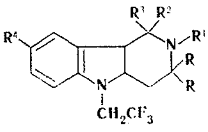
We have established that when alkali metal borohydrides are added gradually to solutions of 1,2,3,4-tetrahydro-γ-carbolines (I-VIII) in trifluoroacetic acid, the double bond of the indole ring is reduced to give indolines (IX-XIV) and the indoline nitrogen atom undergoes 2,2,2-trifluoroethylation to give 9-(2,2,2-trifluoroethyl)-1,2,3,4,4a,9a-hexahydro-γ-carbolines (XV-XX) in 70-90% yields.

The structures of the compounds of the IX-XX type were confirmed by the UV spectra (for example, the spectra of IX and XV and ordinary indolines are similar to one another), the IR spectra (for example, the spectrum of IX contains a ν_{NH} band at 3400 cm^{-1}, whereas the spectrum of XV does not contain this band), the PMR spectra (for example, the spectra of IX and X contain a multiplet of a 9a-H proton at $\delta \sim 3.7$ ppm; quartets with $J \sim 10$ Hz from the signals of NCH_2CF_3 protons are observed at 3.5 ppm in the spectra of XV-XVII because of spin-spin coupling with three magnetically equivalent ^{19}F nuclei with spin $1/2$; a multiplet from the 9a-H proton is observed at ~3.3 ppm, and the number of aromatic protons does not change during the reaction), and the mass spectra (for example, the molecular ions of XV-XVIII are found at m/e 284, 304, 288, and 286, respectively). The course of the reduction and alkylation was monitored by gas-liquid chromatography (GLC) and thin-layer chromatography (TLC) in the case of I, II, and V, and it was established that initially (1-2 moles of borohydride) the double bond undergoes reduction to give indolines IX-XI, after which (5-6 moles of borohydride) the compounds undergo trifluoroethylation to give XV, XVI, and XIX, respectively. Compounds of the IX-XIV type can be obtained in 60-80% yields in sufficiently pure form in the case of appropriate monitoring of the reaction. Compound IX was converted to XV in ~90% yield with excess $NaBH_4$. This procedure was used to obtain the following compounds [melting points of the base and (or) hydrochloride or dihydrochloride given]: IX · 2HCl, 274-286; X · 2HCl, 245-246; XI · 2HCl, 242-244; XII, 66-67.5; XII · 2HCl, 242-244; XIII, 101-102; XIII · 2HCl, 246-247; XIV · 2HCl, 225-226; XV, 84-85; XV · HCl, 225-227; XVI, 94.5-96; XVI · HCl, 234-236; XVII, 52-53.5; XVII · HCl, 230-232; XVIII · HCl, 232-233.5; XIX · HCl, 256-257; XX · HCl, 265-266. Compounds XII, XIII, and XV-XVII were crystallized from petroleum ether, and the hydrochlorides or dihydrochlorides of IX-XIX were crystallized from alcohol. All of the compounds gave satisfactory results in the case of elementary analysis and were configurationally homogeneous (evidently with cis-fused rings). The reductive cleavage of the piperidine ring that is observed in the case of the action of zinc in hydrochloric acid [1] does not occur under these conditions in the case of polyalky-


I-VIII


IX-XIV


XV-XX

I, IX, XV $R=R^2=R^3=H$, $R^1=R^4=CH_3$; II, X, XVI $R=R^2=R^3=H$, $R^1=CH_3$, $R^4=Cl$; III, XVII $R=R^2=R^3=H$, $R^1=CH_3$, $R^4=F$; IV, XVIII $R=R^2=R^3=H$, $R^1=CH_3$, $R^4=OH$; V, XI, XIX $R=R^2=R^3=CH_3$, $R^1=R^4=H$; VI, XII, XX $R=R^2=R^3=R^4=CH_3$, $R^1=H$; VII, XIII $R=CH_3$, $R^1=R^2=R^4=H$; $R^3=C_6H_5$; VIII, XIV $R=CH_3$, $R^1=R^2=R^3=R^4=H$.

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lated tetrahydro-γ-carbolines (form example, V-VIII). Trifluoroethylation was either not observed or occurred to a very small extent (in one case up to 7%) [2] in the reaction of borohydrides with indoles and indolines in CF_3COOH.

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ANOMALOUS REACTION OF 1-ETHYL(BENZYL)-3-METHYL-2-BENZOPYRYLIUM SALTS WITH DIMETHYLAMINE

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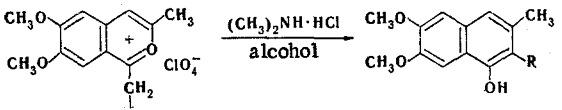
It is known that 2-benzopyrylium salts [1] react with secondary amines to give aromatic amine derivatives.

We have observed that heating of 1-ethyl(benzyl)-3-alkyl-2-benzopyrylium salts (I) for 2 h with a twofold excess of dimethylamine hydrochloride in alcohol gives substituted naphthols (II) in considerably higher yields (70-83%) than in the case of alkaline recyclization [2] (~40%).



I a-d II a-d

I, II a $R = CH_3$; b $R = 3,4\text{-}(OCH_3)_2C_6H_3$; c $R = 2\text{-}Br\text{-}4,5\text{-}(OCH_3)_2C_6H_2$; d $R = 2\text{-}I\text{-}4,5\text{-}(OCH_3)_2C_6H_2$

Naphthols IIa-d were isolated in the form of colorless crystals after dilution of the reaction mixtures with water. Naphthol IIa, with mp 149° (from benzene), was obtained in 70% yield. PMR spectrum (CF_3COOH, 60°C): s, 1.88 (3H); 1.95 (3H); 3.63 (6H); m, 6.70-7.10 ppm (3H). Compound IIb, with mp 177° (from alcohol) (mp 177° [2]), was obtained in 83% yield. Naphthol IIc, with mp 162° (from methanol), was obtained in 80% yield. Naphthol IId, with mp 171° (from methanol), was obtained in 83% yield.

The results of analysis for C, H, Br, and I of all of the compounds obtained were in agreement with the calculated values. The IR spectra contained characteristic absorption bands at 3480-3520, 1610-1620, and 1580-1589 cm^{-1}.

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