Heterogeneous catalytic synthesis and structure of 5,5a,10a,11-tetrahydro-10*H*-indeno[1,2-*b*]quinoline

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Hydrogenation of 10*H*-indeno[1,2-*b*]quinoline in benzene in the presence of R_2S_7 (250 °C, p_{H_2} = 140 atm, 4 h) gave 5,5a,10a,11-tetrahydro-10*H*-indeno[1,2-*b*]quinoline, the structure of which was established by mass-, IR, UV, ^{13}C, and ^1H NMR spectra. The *cis* fusion of the indan and tetrahydroquinoline fragments, the axial orientation of the proton at C(5a), and the equatorial orientation of the proton at C(10a) were confirmed by molecular mechanics calculations using the PC MODEL program.

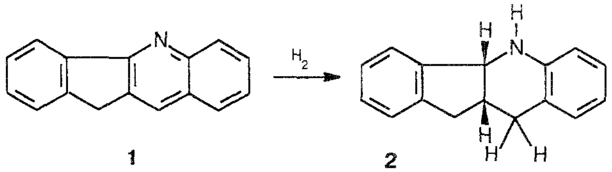
Key words: 10*H*-indeno[1,2-*b*]quinoline, hydrogenation; rhenium heptasulfide; 5,5a,10a,11-tetrahydro-10*H*-indeno[1,2-*b*]quinoline, stereochemistry; molecular mechanics calculations, PC MODEL program.

Compounds possessing a wide spectrum of biological activity have been found in the series of CH-acids with annelated indenyl and azaindenyl groups,[1,2] including some with interferon-inducing[3,4] and anti-tumor[1,2,5] activity. This group of CH-acids includes fluorenes, azafluorenes (indenopyridines), and fused benzoaza(diaza)fluorenes [indenoquinolines (isoquinolines, -quinoxalines)]. The hydrogenated forms of CH-acids and especially their derivatives with piperideine-piperidine groups are also of interest for pharmacology, but only a few examples of derivatives of this type are yet known.[1,2,6]

Taking into account the previously discovered phenomena of selective hydrogenation of nitrogen-containing rings in aryl-containing pyridines,[7] isoquinolines, indolizines,[8] and indenopyridines[6] in the presence of Re_2S_7, it seemed promising to use this catalyst for the synthesis of reduced forms of heterocyclic fragments of benzoaza(diaza)fluorenes.[9,10] In this work we studied the directions of hydrogenation of 10*H*-indeno[1,2-*b*]quinoline (**1**) catalyzed by Re_2S_7.

Under the conditions chosen (250 °C, p_{H_2} = 140 atm, 4 h, benzene as the solvent), the hydrogenation of indenoquinoline (**1**) catalyzed by Re_2S_7 afforded 5,5a,10a,11-tetrahydro-10*H*-indeno[1,2-*b*]quinoline (**2**) in 44 % yield in the form of light-yellow crystals with m.p. 85—90 °C.

According to TLC data, the catalysate contained no starting compound (**1**), hence, the conversion was 100 %. The side products of the catalysis could not be isolated.



1 **2**

The individuality and three-dimensional structure of tetrahydroindenoquinoline (**2**) were established chromatographically, by elemental analysis, by a combination of spectral methods (mass-, IR, electron absorption, ^1H, and ^{13}C NMR), and by molecular mechanics calculations using the PC MODEL program.[11] The molecular mass of compound (**2**) determined by mass spectrometry agrees with its molecular formula. Scheme 1 shows the main routes of fragmentation of compound **2** under electron impact. The intensity of the molecular ion peak is 70 %; the ion with *m/z* 106 has the largest intensity (100 %). The partial loss of aromaticity in compound **2** results in the appearance of ion peaks with *m/z* 217—220, which are due to the hydrogenation of M^+. In addition, the processes of retrodienic decomposition with the cleavage of the N(5)—C(5a) and C(11)—C(10a) bonds are observed and, as a consequence, F-1 ions with *m/z* 116 (20 %) and F-2 ions with *m/z* 105 (28 %), respectively, are formed. The hydrogen atom migrates from the C(5a) position to the nitrogen atom to give the F-3 ion with *m/z* 106, which has an aminotropylium structure. The cleavage of the C(10)—C(10a) and C_{arom}—C(5a) bonds results in the formation of the F-4 ion with *m/z* 90 (6 %) (dehydrotropilium) and the F-5

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Scheme 1

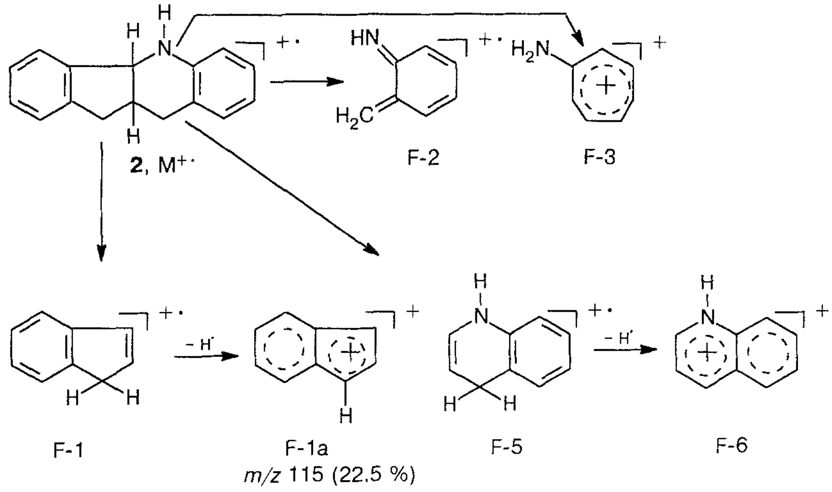

Table 1. IR (in KBr pellets) and UV (EtOH) spectral data of indenoquinoline **1** and tetrahydroindenoquinoline **2**

Compound	IR/cm^{-1}								UV, λ_{max}/nm(log ε)		
	Valence vibrations, ν					Deformation vibrations, δ			Absorption bands		
	N—H	=C—H	—C—H	C=N	C=C	C—H(N—H)	C—N	=C—H	β	ρ	α
1	—	3075 av	2940 w 2860 w	1635 av	1620 w 1585 sh 1570 s 1555 av 1530 av *1510 s	1470 av	—	780 v.s 740 v.s	214 (4.51) 224 (4.28)	264 (4.43)	314 (3.94) 323 (3.97) 330 (4.12) 337 (4.03) 349 (4.23) 354sh (3.83)
2	3399 av	3075 av 3050 w 3025 w	2950 av 2930 av 2903 av *2840 av	—	1615 av 1595 av 1520 sh	1465 av 1440 av (1495 v.s)	1267 v.s	760 v.s 745 v.s	211 (4.49)	251 3.96 272 sh (3.54)	300 (3.97) 335 sh (2.64) 344 (2.69)

* The center of the doublet.

ion with *m/z* 131 (7 %), which undergoes dehydrogenation to afford the stable quinolinium cation F-6 with *m/z* 130 (14 %).

The IR spectral data for the crystalline samples of compounds **1** and **2** and the UV spectral data for their ethanolic solutions are given in Table 1. A narrow intense absorption band corresponding to the stretching vibrations of the N—H bond and an intense absorption band at 1495 cm^{-1}, which may result from the deformation vibrations of this bond, are observed in the IR spectrum of compound **2**. These bands are absent in the spectrum of the starting compound **1**. The existence of the very intense δ(C—N) band at 1267 cm^{-1} in the IR spectrum of compound **2** also confirms the hydrogenation of the starting compound **1** at the pyridine ring.

The absorption regions of β-, ρ-, and α-bands in the UV spectrum of compound **2** are typical of stilbene-type conjugated benzene rings; the α-band is noticeably shifted hypsochromically and its vibrational structure is smoothed as compared with the position and shape of the similar band in the spectrum of the starting compound **1**.

The ^{13}C NMR spectrum of compound **2** contains signals of four aliphatic carbon atoms at 30.2 (C(10a)), 36.8 (C(10)), 37.1 (C(11)) and 59.2 ppm (C(5a)). The aromatic region contains signals of eight protonated carbon atoms at 113.3—128.8 ppm and signals of four quaternary carbon atoms, namely, three signals at 141.5—146.3 ppm and one at 123.7 ppm.

The ^{1}H NMR spectrum of compound **2** was interpreted by comparing it with the spectrum of the starting compound **1** (Table 2). The position, multiplicity, integral intensity, and coupling constants of the signals of the aliphatic protons observed in the spectrum of compound **2** completely confirm the proposed direction of the hydrogenation of indenoquinoline **1**.

The Stewart—Brygleb molecular models show that in the case of *trans* fusion the H(5a) and H(10a) protons have axial orientation, while the C(4a), N(5), C(11), and C(11a) atoms are coplanar. As a result, the nitrogen-containing ring is strained. In the case of *cis* fusion this ring has a boat-like conformation and the system is less strained, although some distortion of the

Table 2. NMR spectral data (400 MHz, $CDCl_3$, $SiMe_4$ as the internal standard) of compounds **1** and **2**

Compound	δ (multiplicity, integral intensity, assignment, coupling constant, *J*/Hz)
1	3.88 (s, 2 H, CH_2); 7.48—7.75 (m, 6 H, H(1), H(2), H(3), H(7), H(8), H(9)); 8.01 (s, 1 H, H(11)); 8.23 (d, 1 H, H(6), $J_{6,7}$ = 8.4); 8.35 (d, 1 H, H(4), $J_{4,3}$ = 7.2)
2	2.4 (dd, 1 H, H(10), $J_{10,10'}$ = 16.5, $J_{10,10a}$ = 10.3); 2.76 (m, 3 H, H(10a), H(11), H(11'); 3.09 (dd, 1 H, H(10'), $J_{10',10a}$ = 7.4); 4.03 (br.s, 1 H, 5-NH); 4.78 (d, 1 H, H(5a), $J_{5a,10a}$ = 6.5); 6.5—7.3 (m, 8 H, arom. protons)

C(4a)—N(5)—C(5a) and C(11a)—C(11)—C(10a) bond angles is observed which, in turn, creates complications for the determination of the actual space orientation of the protons at the C(5a)—C(10a) bond using molecular models of compound **2**. According to the data from these models, the H(5a) proton has the equatorial configuration and the H(10a) proton has the pseudo-equatorial configuration. On the other hand, the data from the Stewart—Brygleb models unambiguously indicate the *cis*-configuration of these protons in the case of *cis* fusion of the indene and tetrahydroquinoline fragments. The most probable conformers of this stereoisomer are conformer **A**, with axial orientation of the H(5a) proton and equatorial orientation of the H(10a) proton, and conformer **B**, with the opposite orientation of these protons. In order to establish the conformation of compound **2**, we calculated the **A** and **B** conformers by the molecular mechanics method using the PC MODEL program, which also makes it possible to calculate the values of the vicinal coupling constants[11] (Table 3). The

Table 3. Parameters of the *cis-trans* forms of the possible isomers of 5,5a,10a,11-tetrahydro-10*H*-indeno[1,2-*b*]quinoline **2** calculated by molecular mechanics methods using the PC MODEL program

Isomer (connection)	*J*/Hz*	Angle /deg	ΔH^0_{293} /kcal mol^{-1}
A (*cis*)	$^3J_{5a(a),10a(e)}$ = 5.53 (J^1)	38	22.9
	$^3J_{10,10a(e)}$ = 11.35 (J^4)	161	
	$^3J_{10',10a(e)}$ = 6.94 (J^5)	37	
	$^3J_{11(a),10a(e)}$ = 4.98 (J^2)	47	
	$^3J_{11'(e),10a(e)}$ = 1.68 (J^3)	71	
B (*cis*)	$^3J_{5a(e),10a(a)}$ = 6.30 (J^1)	37	24.3
	$^3J_{10,10a(a)}$ = 7.17 (J^4)	34	
	$^3J_{10',10a(a)}$ = 0.98 (J^5)	89	
	$^3J_{11(a),10a(a)}$ = 12.08 (J^2)	170	
	$^3J_{11'(e),10a(a)}$ = 4.51 (J^3)	51	
C (*trans*)	$^3J_{5a(a),10a(a)}$ = 10.74 (J^1)	170	25.14
	$^3J_{10,10a(a)}$ = 11.81 (J^4)	166	
	$^3J_{10',10a(a)}$ = 6.25 (J^5)	41	
	$^3J_{11(a),10a(a)}$ = 12.35 (J^2)	177	
	$^3J_{11'(e),10a(a)}$ = 3.44 (J^3)	58	

* The numbers of the calculated vicinal coupling constants shown in Fig. 1 are indicated in parentheses.

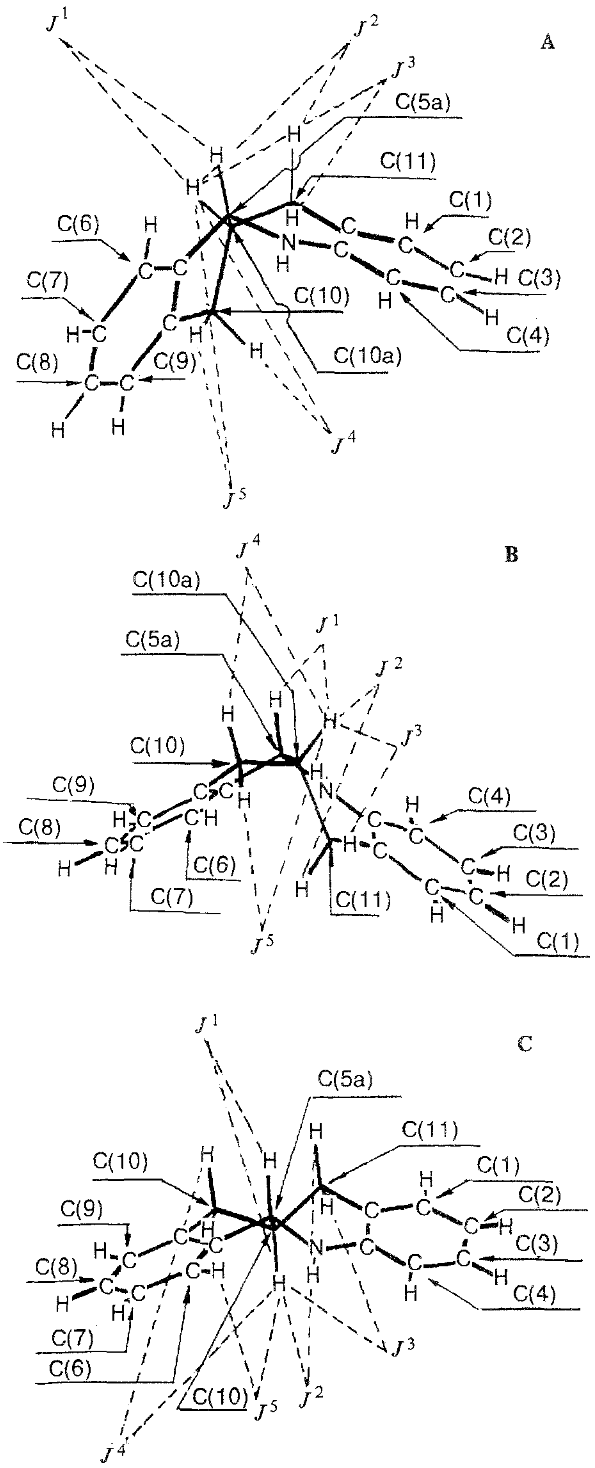

Fig. 1. Computer images of conformers **A**, **B**, and **C** of compound **2** (calculated values of coupling constants J^1—J^5 are given in Table 3).

comparison of the experimental coupling constant, $J_{5a,10a}$ = 6.5 Hz, with the calculated value shows that the *trans* isomer with axial orientation of the H(5a) and H(10a) protons, whose coupling constant should be ~11 Hz, can be excluded from consideration when one discusses the various ways of linking the indene and tetrahydroquinoline fragments in compound **2**. Of the two *cis*-forms of this compound, the coincidence of the experimental and calculated values of the coupling constants for the H(10a) proton with that of the H(10) and H(10′) protons is observed only for conformer **A**. This makes it possible to assign the structure of *cis*-conformer **A**, which has the minimum heat of formation of the possible stereoisomers (Table 3), to the crystal sample of compound **2** obtained by us. The computer-created images of the structures of conformers **A**, **B**, and **C** are given at Fig. 1.

Thus, the formation of a new heterocyclic system, 5,5a,10a,11-tetrahydro-10*H*-indeno[1,2-*b*]quinoline **2**, by hydrogenation of 10*H*-indeno[1,2-*b*]quinoline **1** catalyzed by rhenium heptasulfide confirms the efficiency of the latter as a catalyst for selective hydrogenation of nitrogen-containing rings in polynuclear heterocyclic compounds.

Experimental

IR spectra were recorded on a UR-20 instrument in KBr pellets. UV spectra were obtained on a Specord UV-vis spectrophotometer in EtOH. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX-400 spectrometer (400 MHz, relative to $SiMe_4$) in $CDCl_3$. EI mass spectra were obtained on a Kratos MS 25RF mass spectrometer (70eV).

10*H*-indeno[1,2-*b*]quinoline (1) was prepared by dehydrogenation of a mixture of 2-*o*-tolylquinoline and the corresponding 1,2-dihydroderivative using the K-16 catalyst according to the known procedures. [9,10]

5,5a,10a,11-tetrahydro-10*H*-indeno[1,2-*b*]quinoline (2). The hydrogenation was carried out in a steel autoclave (0.15 L) with a glass lining. The autoclave was charged with 1 g of indenoquinoline **1**, 0.1 g (10 % weight of the starting compound) of Re_2S_7, and 15 mL of benzene. The autoclave was purged with nitrogen and hydrogen. Hydrogenation was carried out for 4 h at a hydrogen pressure of 140 atm and 250 °C. Then the autoclave was cooled to room temperature, and the catalyst was filtered off and washed with benzene and acetone. The solvent was distilled off and the oil-like residue (1.02 g, R_f = 0.81 (ether-hexane, 3 : 1)) was crystallized from hexane to give 0.45 g (44 %) of tetrahydro-derivative **2** as light yellow crystals, m.p. 85—90 °C (hexane), R_f = 0.85 (ether-hexane, 1 : 1, Alufol). MS, *m/z*: 221 [M$^+$]. Found (%): C, 86.60; H, 6.53; N, 6.53. $C_{16}H_{15}N$. Calculated (%): C, 86.88; H, 6.79; N, 6.33.

The residue of the catalysate (0.4 g, R_f = 0.83 (ether-hexane, 1 : 1, Alufol)) remaining after isolation of the crystal sample of **2** is an oily product whose structure was not determined.

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