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Synthesis and Isomerization of 1H-4,4a,5,9b-Tetrahydroindeno-[1,2-b]pyridines

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Abstract Synthesis of 1H-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridines has been accomplished by catalytic hydrogenation of 4H-4a,5-dihydroindenopyridines The isomerization of 1H-4,4a,5,9b-tetrahydroindenopyridines containing an acyl function at C-3 leads to 3H-4,4a,5,9b-tetrahydroindenopyridines in acidic medium

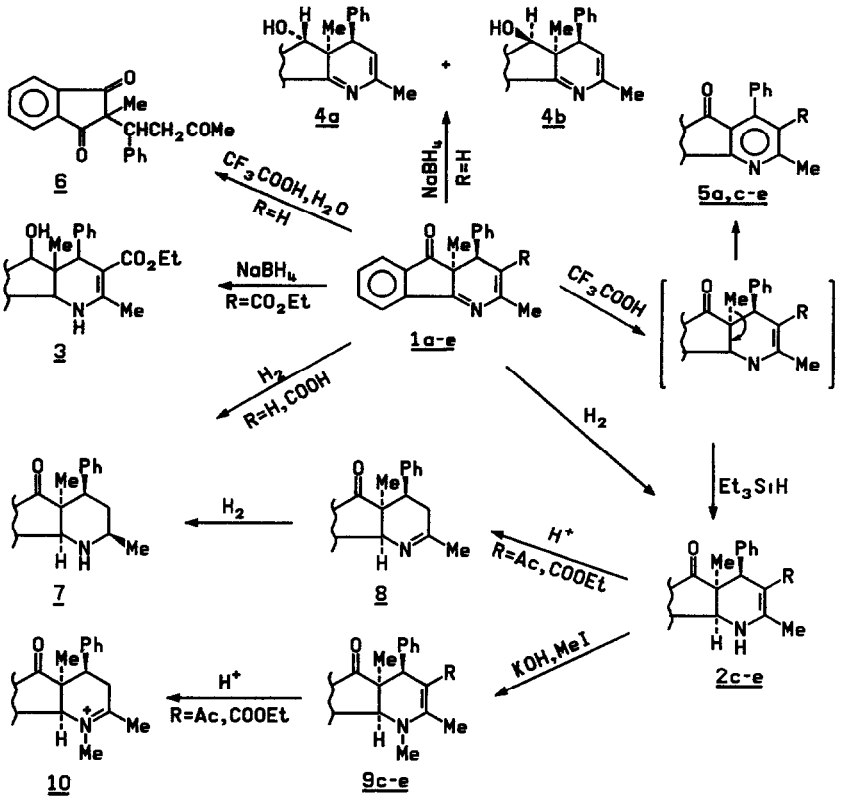
Based on the transformation of dihydrogenated pyridines in acidic medium observed earlier[1-3], a study of similar reactions of 1H-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridine derivatives has been carried out

The synthesis of 1H-4,4a,5,9b-tetrahydroindenopyridine derivatives has been accomplished by reduction of 4H-4a,5-dihydroindeno[1,2-b]pyridines with various reducing agents

The first example of a 1H-4,4a,5,9b-tetrahydroindenopyridine, 3-ethoxycarbonyl-2,4a-dimethyl-5-oxo-4-phenyl-1H-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridine (**2c**), was obtained[4] as a by-product during reduction of 4H-4a,5-dihydroindenopyridine **1b** by sodium borohydride, with 5-hydroxytetrahydroindeno[1,2-b]pyridine **3** as the main product (Scheme 1) Isomeric 5-hydroxy-4H-dihydroindenopyridines **4** with different configuration of the 5-C atom were obtained by reduction of 5-oxo-4a,5-dihydroindenopyridine **1a** with sodium borohydride. The significant upfield chemical shift of the OH proton in the NMR spectrum of isomer **4b** is in agreement with the 1,3-diaxial interaction of this group with the 4-phenyl substituent

The reduction of 4a,5-dihydroindenopyridines **1** with triethylsilane in trifluoroacetic acid does not proceed uniformly The formation of tetrahydroindenopyridines is accompanied by the elimination of the 4a-methyl group followed by aromatization of the dihydropyridine ring and indenopyridine **5** formation Elimination of the methyl group is one of the way of stabilizing the immonium ion formed by protonation of the C=N bond Attempts to reduce the 3-unsubstituted dihydropyridine **1a** with triethylsilane in trifluoroacetic acid were unsuccessful the starting compound was partly converted into pyridine **5**, another part of it during the isolation process (dilution with water) underwent pyridine ring opening (ref [3]) to afford 2-methylindane-1,3-dione derivative **6**

A preparative method (quantitative yield) for the synthesis of 5-oxo-1H-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridines **2** with electron accepting groups in 3 position involves the catalytic hydrogenation (Raney Ni or Pd/C catalysts) of the appropriate 4H-4a,5-dihydroindenopyridines **1** Under the same reaction conditions 3-unsubstituted dihydroindenopyridine **1a** affords 5-oxo-1H-2,3,4,4a,5,9b-hexahydroindenopyridine **7** in quantitative yield The formation of hexahydro derivative **7** resulting from the hydrogenation of 3-carboxylic acid **1b** can be explained by the prior decarboxylation of the acid Hydrogenation of 3H-4,4a,5,9b-tetrahydroindenopyridine **8** obtained via isomerization and decarboxylat-



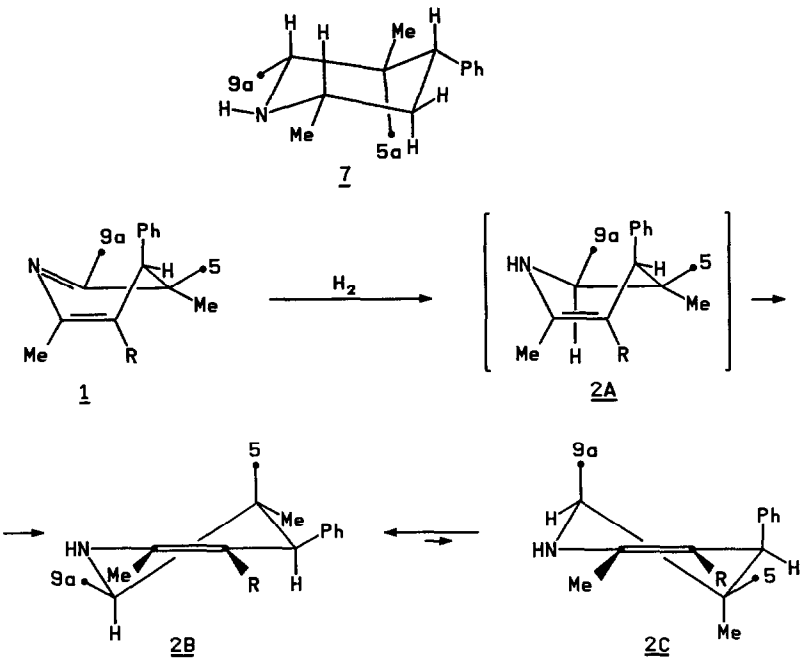
Scheme 1. **1, 2, 5, 9** R = H (a), COOH (b), COOEt (c), Ac (d), CN (e)

tion of 1H-4,4a,5,9b-tetrahydroindenopyridines **2c,d** also yields the same hexahydroindenopyridine isomer **7**

Hydrogenation of N = C_{9b} bond in dihydroindenopyridine **1** proceeds stereoselectively to give only one diastereomer of tetrahydroindenopyridine **2**

According to X-ray analysis[4] the dihydropyridine ring in 4H-4a,5-dihydroindenopyridine adopts a distorted boat-like conformation with 4-Ph and 4a-CH_3 substituents oriented axially The transition of compound **1** to the configuration with equatorial orientation of these substituents is impossible due to twisting of the five-membered ring. Hydrogenation of dihydroindenopyridines **1** does not affect the 4-C and 4a-C atoms, consequently, their reduced derivatives **2** maintain the same configuration, where 4-Ph and 4a-CH_3 substituents are *aa* or *ee* oriented For the conclusion as to substituent location at 9b-C a spectrum of hexahydroindenopyridine **7** resulting from **2→8→7** reactions without change in the configuration at 9b has been analyzed. The pyridine ring of **7** exists in a stable chair-like conformation characteristic of saturated six-membered rings (Scheme 2) The large spin-spin coupling constants of 3-H_a and 4-H (J = 13 0 Hz) as well as 2-H (J = 10 2 Hz) indicate the axial location of the last atom Consequently, the 2-CH_3 and 4-Ph groups are in the equatorial position 4a-CH_3 group and 9a-C atom have the same orientation, whereas 9b-H and 5-C atoms are located axially The inversional chair-like conformation is unfavourable due to diaxial interaction Thus, it can be concluded that the 4a-CH_3 group and 9b-H atom of tetrahydroindenopyridine **2** are in the *cis*-orientation

Addition of hydrogen to the N = C_{9b} bond changes the pyridine ring conformation The boat-like pyridine ring formed initially is energetically disadvantageous due to the repulsion of the eclipsed groups



Scheme 2

The conformational transfiguration of the pyridine ring results in the formation of a flattened chair-like conformation characteristic of 1,2,3,4-tetrahydropyridines[5] The conversion of **2B** to **2C** is unfavourable due to the diaxial interaction of the 4-Ph substituent and the indane moiety (atom 9a-C) Therefore the obtained 1H-tetrahydroindenopyridines exist exclusively as a single conformer as revealed by their NMR spectra

1H-Tetrahydroindenopyridines **2** undergo alkylation with methyl iodide in aprotic medium in the presence of alkali agent to produce N-methyl derivatives **9** (Scheme 1)

Tetrahydroindenopyridines **2c,d** and **9c,d** possessing an acyl function at 3-C undergo isomerization in acidic medium (0 4 M HCl in 80 % ethanol) This process is accompanied by the elimination of the substituent as the corresponding acid Isomerization of N-unsubstituted derivatives **2c,d** results in 3H-4,4a,5,9b-tetrahydroindenopyridine **8**, whereas N-methyl derivatives **9c,d** with acid form 1-methyl-4,4a,5,9b-tetrahydroindenopyridinium cation, isolated as perchlorate **10** Elimination of the 3-substituent in the form of acid was demonstrated during isomerization of derivative **2d**, when the presence of acetic acid in the reaction medium was proved by GLC

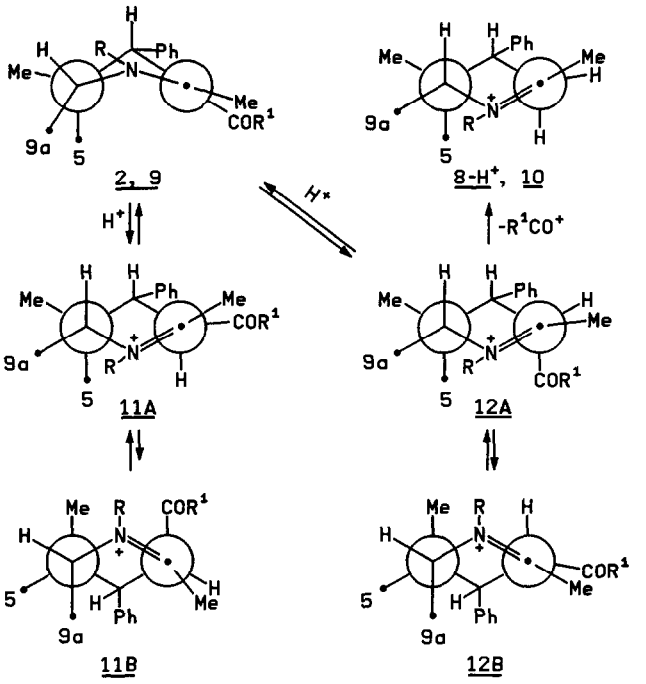
In contrast to the above compounds, 3-cyano derivatives **2e** and **9e** remain unchanged under these conditions (also when the concentration of acid reaches 1 5 M/l) and can be quantitatively recovered from the reaction mixture

Interaction of tetrahydroindenopyridines **2** and **9** with acid can be interpreted by regarding the chain of atoms $N\text{-}C_2 = C_3$ as an enamine system Protonation at any of the three basic centres (N, O or β-C) of the enaminocarbonyl fragment $N\text{-}C = C\text{-}CO$ can take place

The existence of C-protonated **9c** in CD_3CN solution in the presence of CF_3COOH was confirmed by NMR spectra The singlet of the 4-H proton transforms to a doublet after protonation and the new 3-H proton can be observed as a doublet at 3 54 ppm The signals of the $N\text{-}CH_3$ group and 9b-H are strongly (0 44 and 0 97 ppm) shifted downfield due to the presence of a positively charged nitrogen atom The

spin-spin coupling constant (J = 12 9 Hz) between 3-H and 4-H indicates their *trans*-orientation The same is observed in the case of compound **2c** (see Experimental section)

As mentioned above, the pyridine ring of tetrahydroindenopyridine adopts a chair-like conformation, the N-C_2 = C_3-C_4 atoms being coplanar, with 4-CH_3 and 4-Ph substituents oriented equatorially (form **2B**) Protonation of this conformer is possible on either side Depending on the direction of proton attack, two C-protonated forms with different 3-C configurations can occur and the formation of two corresponding 3H-tetrahydroindenopyridinium isomers (**11** and **12**) takes place (Scheme 3)



Scheme 3 R^1 = Me, OEt

It is known that the 3H-tetrahydropyridine ring[6], its N-protonated derivatives[7] as well as N-alkyl-3H-tetrahydropyridinium salts[8,9] exist in a flattened chair-like conformation, although the envelope conformation with a 4-C or 5-C atoms out of the plane has been found for the latter compounds[10-12] Consequently, it can be assumed that the conformation of the pyridine ring of tetrahydroindenopyridine is a flattened chair-like containing C_{9b}-N = C_2-C_3 atoms in the plane Protonation of conformer **2A** on 4-Ph substituent side affords 3H-tetrahydroindenopyridine **11A** The axial orientation of the 3-H and 4-H protons is established by NMR spectroscopy, other 3-H isomers are undetected The conformational transition of **11A** conformer to **11B** conformer is energetically unfavourable due to the steric repulsion of the 4-Ph substituent and the indane moiety in **11B** Evidently, this shifts the conformational equilibrium completely to favour isomer **11A**

Protonation of **2A** conformer on the 4-H atom side affords a sterically hindered 3H-tetrahydro isomer **12A** where the 3- and 5-carbonyl function are oriented diaxially The conformer **12B** where the 4-phenyl substituent and the indane moiety are in 1,3-diaxial interaction is also sterically hindered Consequently, both sterically strained conformers of the 3H-isomer **12** can be stabilized by elimination of the R-CO group

In neutral medium the pyridine ring of 3H-tetrahydroindenopyridine **8** is comparatively flat, the coupling constants (J_{34} = 6 4 and 5 1 Hz) being almost equal providing evidence for this fact The appearance of a positive charge in the ring (protonation of **8** or occurrence of N-methyl-3H-tetrahydroindenopyridinium **10**) transforms the pyridine ring to more chair-like conformation, where one of the pseudo-axially oriented 3-H atoms transforms into axially oriented (J_{3a4} = 9 8 Hz, J_{3e4} = 4.0 Hz) This axially oriented C-H bond eclipses the p_Z-orbital of 2-C atom and compensates the charge in the ring In the elimination products **8** and **10** 4-Ph and 4a-CH_3 substituents are orientated equatorially An analogous situation is observed for the C-protonated form **11A.**

EXPERIMENTAL

NMR spectra were recorded on the Bruker WH-90 apparatus Chemical shifts are expressed in ppm relative to tetramethylsilane used as internal standard IR spectra were recorded with PE 580 B spectrometer Mass spectra were determined on the MS-50 mass spectrometer (70 eV) by means of the direct introduction of a substance The FAB mass spectra were obtained on the MS-50 mass spectrometer with the Ion Tech Ltd ion source Ionizing agent - argon, accelerating voltage 8 keV, matrix - thioglycerol

Reduction of 4a-methyl-5-oxo-4H-4a,5-dihydroindeno[1,2-b]pyridines **1**

A Catalytic hydrogenation In a "Parr" hydrogenation apparatus dihydroindenopyridine[13] **1** (10 mmol) was shaken with catalyst (0 2 g 2 % Pd/C or 0 5 g Raney Ni) in isopropanol (100 ml) during 5-8 h under pressure (2-4 atm) at 60° The catalyst was separated and washed with hot solvent The filtrate was evaporated and the residue recrystallised from methanol The yield is quantitative Reduction of **1a** and **1b** gives hexahydroindenopyridine **7** under the similar conditions

3-Ethoxycarbonyl-2,4a-dimethyl-5-oxo-4-phenyl-1H-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridine, (**2c**), m p 211-213° PMR (DMSO-D_6) 0 99 (3H, t, J = 7 0 Hz, $OCH_2C\underline{H}_3$), 1 34(3H,s,4a-CH_3), 2 44(3H,s, 2-CH_3), 3 80(2H,q, J = 7 0 Hz, $OC\underline{H}_2CH_3$), 3 86(1H,s,4-H), 4 60(1H,d, J = 3 8 Hz, 9b-H), 6 40-6 73(5H,m,4-Ph), 6 80-7 18(2H,m) and 7 38-7 67(2H,m) arom protons, 7 84(1H,d,NH) IR 3330(NH), 1720(5-CO), 1638, 1602, 1525 cm^{-1} MS m/z(%) 361 (28)$[M]^+$, 288(100)$[M-CO_2C_2H_5]^+$

3-Acetyl-2,4a-dimethyl-5-oxo-4-phenyl-1H-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridine ,(**2d**), m p 220-222° PMR ($CDCl_3$) 1 52(3H,s,4a-CH_3), 1 97(3H,s,$COCH_3$), 2 38(3H,s,2-CH_3), 3 88(1H,s,4-H), 4 57(1H,d,J = 4,0 Hz,9b-H), 5 15(1H,d,NH), 6 71(5H,s,4-Ph), 7 06(2H,m) and 7 40(2H,m) arom protons IR 3270(NH), 1725(5-CO), 1632, 1612, 1530 cm^{-1} MS m/z(%) 331 (18)$[M]^+$, 288(100)$[M-COCH_3]^+$

3-Cyano-2,4a-dimethyl-5-oxo-4-phenyl-1H-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridine ,(**2e**), m p 299-301° PMR (DMSO-D_6) 1 43(3H,s,4a-CH_3), 2 33(3H,s,2-CH_3), 3 38(1H,s,4-H), 4 63(1H,d,J = 4 4 Hz, 9b-H), 6 53(2H,m) and 6 73(3H,m,4-Ph), 6 84-7 20(2H,m) and 7 52(2H,m) arom protons, 8 10(1H,d,NH) IR 3295(NH), 2138(CN), 1723(5-CO), 1621, 1612, 1550 cm^{-1} MS m/z(%) 314(56)$[M]^+$, 144(100) [2-methylinden-2-one-1]$^+$

B Reduction with triethylsilane Triethylsilane (0 32 ml, 2 mmol) was added to a solution of dihydroindenopyridine **1c-e** (2 mmol) in 6 ml trifluoroacetic acid and the mixture was stirred for 4 h Then it was diluted with water (30 ml) and extracted with ethyl acetate (2x20 ml, **1c,d**) or chloroform (**1e**) The organic phase was washed with water (up to pH 7), dried and evaporated The product obtained from **1c,d** was recrystallized from methanol to give tetrahydroindenopyridines **2c** (61 %) and **2d** (58 %) Derivative **2e** was isolated chromatographically (silica gel L 40/100, plates 30x40 cm, eluent - chloroform hexane acetone 7 9 1) The first yellow zone gave indenopyridine **1e** (31%) and the second zone (UV absorption) - tetrahydroindenopyridine **2e** (68%) After separation of **2c** and **2d**, additional amounts can be obtained by preparative chromatography, along with indenopyridines **5c,d**[14]

3-Cyano-2-methyl-5-oxo-4-phenylindenopyridine, (**5d**), m p 209-211° PMR ($CDCl_3$) 2 91 (3H,s,2-CH_3), 7 46-7 77(8H,m) and 7 96(1H,m) arom protons MS m/z(%) 296(100)[M]

The reduction of **1a** was carried out similarly The reaction mixture was extracted with ethyl acetate Chromatographic isolation (eluent - hexane acetone 3 1) yields indenopyridine **5a** (7%, m p 115°)[15] and indane-1,3-dione **6** (55 %, m p 110°) PMR ($CDCl_3$) 1 33(3H,s,2'-CH_3), 2 03(3H,s,$COCH_3$), 3 23 (2H,m, ^2J = 18 7Hz, ^3J = 3 0 Hz, ^3J = 3 3 Hz, CH_2), 3 77(d, ^3J = 3 3 Hz) and 3 84(d, ^3J = 3 0 Hz, CH), 6.98(5H,m,Ph), 7 61-7 87(4H,m,H of indanedione).

C Reduction of dihydroindenopyridine **1a** *with sodium borohydride.* To a solution of dihydroindenopyridine (1 0 g, 3 46 mmol) in acetonitrile (50 ml) and methanol (5 ml) during one hour $NaBH_4$ (0 18 g, 4 7 mmol) was added with stirring The stirring was continued for 1h, then 200 ml of water was added and the mixture was extracted with chloroform (3x40 ml) The chloroform was washed with water, dried and evaporated The residue was fractionated chromatographically as described above, eluent - chloroform hexane acetone 9 7 1 The first yellow zone gave unchanged dihydroindenopyridine **1** (70%), the second zone (UV absorption) yielded 5-hydroxy derivative **4a**, the third zone (UV absorption) - 5-hydroxy derivative **4b**

5-Hydroxydihydroindenopyridine, **4a** isomer, m p 193-195° PMR ($CDCl_3$) 1 21(3H,s,4a-CH_3), 1 97* (1H,br s,5-OH), 2 19(3H,m,2-CH_3), 3.53(1H,m, J_{34} = 6 2 Hz, $J_{4H\text{-}CH_3}$ = 1 4 Hz, 4-H), 4 60(1H,s,5-H), 5 42(1H,m J_{34} = 6 2 Hz, $J_{3H\text{-}CH_3}$ = 1 3 Hz, 3-H), 7 11(5H,m,4-Ph), 7 39(3H,m) and 7 83(1H,m) protons at C_6-C_9, $J_{5H\text{-}OH}$ < 0,8 Hz MS m/z (%) 9(37)$[M]^+$, 272(60)$[M\text{-}OH]^+$, 258(30)$[M\text{-}Ph]^+$, 144(32) IR 1655, 1598 cm^{-1}

5-Hydroxydihydroindenopyridine, **4b** isomer, m p 128-130° PMR ($CDCl_3$) 0 55* (1H,d,$J_{5H\text{-}OH}$ = = 10 5 Hz,5-OH), 1 21(3H,s,4a-CH_3), 2 14(3H,m,2-CH_3), 3 44(1H,m, J_{34} = 6 3 Hz, $J_{4H\text{-}CH_3}$ = 0 9 Hz, 4-H), 5 05(1H,d, J = 10 5 Hz, 5-H), 5 43(1H,m, J_{34} = 6 3 Hz, $J_{3H\text{-}CH_3}$ = 1 4 Hz, 3-H), 7 09(5H,s,4-Ph), 7 47(3H,m) and 7.96(2H,m) protons at C_6-C_9 MS m/z(%) 289 (66)$[M]^+$, 288(87), 274 (84)$[M\text{-}CH_3]^+$, 145(61), 144(100) IR 1648, 1595 cm^{-1}.

2,4a-Dimethyl-5-oxo-4-phenyl-1H-2,3,4,4a,5,9b-hexahydroindeno[1,2-b]pyridine (**7**) was obtained by hydrogenation of 3H-4,4a,5,9b-tetrahydroindenopyridine **8** or 4H-4a,5-dihydroindenopyridines **1a,b** (catalyst Raney Ni, solvent isopropanol) according to A method The yield of product 7 is quantitative, m p 114-116° (hexane) PMR (WH-360, $CDCl_3$) 1 08 (3H,d, $J_{2H\text{-}CH_3}$ = 6 1 Hz,2-CH_3), 1 17(3H,s,4a-CH_3), 1 37(1H,br s,NH), 1.55 (1H,m, J_{23a} = 10 2 Hz, J_{3a4} = 13 0 Hz, J_{3a3e} = 13 0 Hz,3-H_a), 1 82(1H,m, J_{3e4} = 3 0 Hz, J_{23e} = 3 0 Hz, J_{3a3e} = 13 0 Hz,3-H_e), 2 93(1H,dd, J_{3a4} = 13 0 Hz, J_{3e4} = 3 0 Hz,4-H), 3 05(1H,m, J_{23a} = 10 2 Hz, J_{23e} = 3 0 Hz, $J_{2H\text{-}CH_3}$ = 6 1 Hz, 2-H), 4 14(1H,s,9b-H), 7 22-7 44(6H,m) and 7 56-7 69(3H,m) arom protons, J_{19b} < 1 0 Hz, J_{12} < 1 0 Hz IR 3355(NH), 1708(5-CO) cm^{-1} MS m/z (%) 291(72)$[M]^+$, 276(100) $[M\text{-}CH_3]^+$, 144(68)[2-methylinden-2-one-1]$^+$, 132(72) Found C 81 91, H 7 36, N 4 61% $C_{20}H_{21}NO$ Calc C 82 44, H 7 26, N 4 81%

1,2,4a-Trimethyl-5-oxo-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridines **9** 1H-Tetrahydroindenopyridine **2** (5 mmol) was dissolved in 30 ml abs DMFA and 2 8 g of powdered KOH was added and stirred for 40 min Then 1 0 ml of methyl iodide was added and stirred for 40 min After the addition of methyl iodide (0 5 ml) the mixture was continued to be stirred for another 1 5 h The reaction mixture was poured into 250 ml of water, the obtained precipitate was filtered off and recrystallized from methanol

3-Ethoxycarbonyl-1,2,4a-trimethyl-5-oxo-4-phenyl-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridine, (**9c**), m p 132-134° PMR ($CDCl_3$) 0 98(3H,t, J = 7 0 Hz, $OCH_2\underline{CH_3}$), 1 48(3H,s,4a-CH_3), 2 74(3H,s,2-CH_3), 3 54(3H,s,NCH_3), 3 89(2H,q, J = 7 0 Hz, $OC\underline{H_2}CH_3$), 4 05(1H,s,4-H), 4 41(1H,s,9b-H), 6 61(5H,m,4-Ph), 7 01(2H,m) and 7 41(2H,m) protons at C_6-C_9 IR 1721 (5-CO), 1645, 1610, 1573 cm^{-1}

3-Acetyl-1,2,4a-trimethyl-5-oxo-4-phenyl-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridine, (**9d**), m p 161-163°. PMR ($CDCl_3$) 1 49(3H,s,4a-CH_3), 1 91(3H,s,$COCH_3$), 2 71(3H,s,2-CH_3), 3 54(3H,s,NCH_3), 3 78(1H,s,4-H), 4 40(1H,s,9b-H), 6 63(5H,m,4-Ph), 6 98(2H,m) and 7 33 (2H,m) protons at C_6-C_9 IR 1721(5-CO), 1638, 1611, 1535 cm^{-1}

*Easily exchanged for deuterium in D_2O

3-Cyano-1,2,4a-trimethyl-5-oxo-4-phenyl-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridine, (**9e**), m p 214-215° PMR ($CDCl_3$)· 1.53(3H,s,4a-CH_3), 2 46(3H,s,2-CH_3), 3.51(4H,br.s, NCH_3 and 4-H), 4.42(1H,s, 9b-H), 6 53(2H,m) and 6.71(3H,m,4-Ph), 6 99(2H,m) and 7.40(2H,m) protons at C_6-C_9. IR: 2182(CN), 1722(5-CO), 1605 cm^{-1}

Isomerization of 1H-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridines **2c,d** A mixture of tetrahydroindenopyridine **2a** (1 81 g, 5 mmol), ethanol (100 ml), water (20 ml) and conc HCl (4 5 ml, 50 mmol) was refluxed for 4 h, then the mixture was diluted with 500 ml of water and neutralised with sodium hydroxide (5 7 g NaOH, 20 ml water) The colourless solid was filtered off and identified as **8** (94 %), m p 111-113° (hexane)

The same product **8** (92 %) was obtained from **2d** using the technique described above

2,4-Dimethyl-5-oxo-4-phenyl-3H-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridine, (**8**), PMR ($CDCl_3$) 1 39 (3H,s,4a-CH_3), 2 10(3H,m, $J_{3H_a\text{-}CH_3}$ = 0 9 Hz, $J_{3H_e\text{-}CH_3}$ = 1 6 Hz, 2-CH_3), 2 40(2H,m, ^2J = 16 6 Hz, J_{3a4} = 6 4 Hz, J_{3e4} = 5 1 Hz, $J_{3H_a\text{-}CH_3}$ = 0 9 Hz, $J_{3H_e\text{-}CH_3}$ = 1 6 Hz, 3-H_a and 3-H_e), 3 06(1H,m, J_{3a4} = 6 4 Hz, J_{3e4} = 5 1 Hz,4-H), 4 93(1H,s,9b-H), 6.97(5H,m,4-Ph), 7 24-7 86(4H,m) protons at C_6-C_9, PMR ($CDCl_3$ + CF_3COOH) 2 64(3H,s,2-CH_3) 3 03(1H,dd, ^2J = 18 0 Hz, J_{3a4} = 9 8 Hz,3-H_a), 3 13(1H,dd, ^2J = 18 0 Hz, J_{3e4} = 4 0 Hz,3-H_e), 3 34(1H,dd, J_{3a4} = 9 8 Hz, J_{3e4} = 4 0 Hz,4-H) MS m/z(%) 289(100)$[M]^{+\cdot}$, 274(39)$[M\text{-}CH_3]^+$, 198(15), 184(10), 144(17), 128(27), 115(30) IR (film) 1728(5-CO), 1672, 1610, 1500 cm^{-1} Found C 77 97, H 6 85, N 4 29 % $C_{20}H_{19}NO\,H_2O$ Calc C 78 14, H 6 88, N 4 56 %

Isomerization of 1-methyl-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridines **9c,d.** 3 1 ml 57 % $HClO_4$ (26 mmol) was added to a solution of 1-methyl derivative **9c** (1 0 g, 2 67 mmol) in 30 ml ethanol The reaction mixture was refluxed for 3 h, cooled, diluted with 300 ml of ethyl ether and left overnight The crystalline solid precipitate was filtered off and washed with ether The yield of salt **10** is 1 03 g (97 %)

Tetrahydroindenopyridine **9d** gives **10** in 89 % yield under the similar conditions

1,2,4a-Trimethyl-5-oxo-4-phenyl-3H-4,4a,5,9b-tetrahydroindeno[1,2-b]pyridinium perchlorate, (**10**), m p 204-205° (ethanol) PMR ($CDCl_3$) 1 53 (3H,s,4a-CH_3), 2 68(3H,s,2-CH_3), 3 04(2H,m, ^2J = 18 6 Hz, J_{3a4} = 12 0 Hz, J_{3e4} = 4 2 Hz,3-H_a and 3-H_e), 3 88(1H,dd, J_{3e4} = 4 2 Hz, J_{3a4} = 12 0 Hz, 4-H), 4 09(3H,s,NCH_3), 5 42(1H,s,9b-H), 7 09(2H,m) and 7 33(3H,m,4-Ph), 7 82 (4H,m, protons at C_6-C_9) MS (FAB) m/z 304 $[C_{21}H_{22}NO]^+$ IR 1718 (5-CO), 1668, 1608 cm^{-1} Found C 62 52, H 5 46, N 3 45 $C_{21}H_{22}NO\,ClO_4$ Calc C 62 45, H 5 49, N 3 47%

The protonation of tetrahydroindeno[1,2-b]pyridines **2c** *and* **9c** Compound **2c**, PMR (CD_3CN) 2 46(3H,s,2-CH_3), 3 92(2H,m, ^3J = 7 2 Hz, ^2J = 1 4 Hz, $OC\underline{H}_2CH_3$), 3 98(1H,s,4-H), 4 68(1H,d, J_{19b} = 4 8 Hz,9b-H), 6 17(1H,d,J = 4 8 Hz,NH) PMR (CD_3CN + CF_3COOH) 2 52(3H,m,$J_{3H\text{-}CH_3}$ = 1 6 Hz, $J_{9bH\ CH_3}$ = 1 4 Hz, 2-CH_3), 3 64(1H,d, J_{34} = 11 2 Hz,4-H), 3 97(2H,q, J = 7 1 Hz,$OC\underline{H}_2CH_3$), 4 02 (1H,m, J_{34} = 11 2 Hz, $J_{3H\text{-}CH_3}$ = 1 6 Hz,3-H), 5 41(1H,q, $J_{9bH\text{-}CH_3}$ = 1 4Hz,9b-H) Compound **9c**, PMR (CD_3CN) 2 69(3H,s,2-CH_3), 3 55(3H,s,NCH_3), 3 84(2H,m, ^3J = 7 0 Hz, ^2J = 3 5 Hz, $OC\underline{H}_2CH_3$), 3 97(1H,s,4-H), 4 56(1H,s,9b-H) PMR (CD_3CN + CF_3COOH) 2 51(3H,s,2-CH_3), 3 54(1H,d, J_{34} = 12 9 Hz,4-H), 3 81(1H,d, J_{34} = 12 9 Hz,3-H), 3.88(2H,m, ^3J = 7 0 Hz, ^2J = 1 1 Hz, $OC\underline{H}_2CH_3$), 3 99(3H,s,NCH_3), 5 53(1H,s,9b-H)

Determination of acetic acid during isomerization of **2d** Tetrahydroindenopyridine **2d** solution (0 95 g, 2 87 mmol) in ethanol (5 ml) together with conc HCl (0 23 ml, 28 mmol) and water (1 ml) was heated in a sealed ampoule for 1 h at 70° Acetic acid was determined by GLC (2m column, ø 3 mm, stationary phase "Porapac Q 50/80", carrier gas - helium, p = 1 5 atm, 230°, flame ionization detector, external standard) The reaction mixture contains acetic acid (8 3 mg/ml) and ethyl acetate (1 7 mg/ml)

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