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PREPARATION AND CATALYTIC HYDROGENATION OF 1,2,4-OXADIAZOLO [4,5-a] INDOLINES

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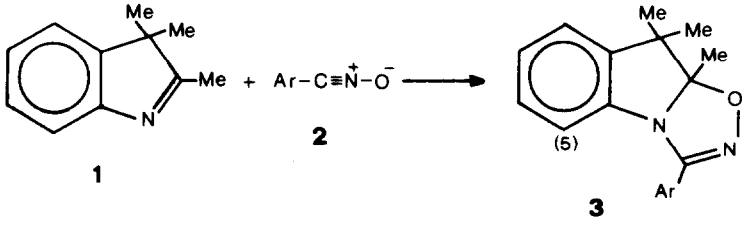
Abstact: 2,3,3-Trimethyl-3H-indole **1** reacts with nitrile oxides **2** to afford 1,2,4-oxadiazolo [4,5-a] indolines **3** in high yields. Catalytic hydrogenation of compounds **3** over Raney nickel results in the cleavage of the oxadiazole ring and gives almost quantitatively products **4** or **5**.

The chemistry of indoles continues to attract considerable interest because of the potential biological activity of many indole derivatives[1]. Especially, the use of mitomycin C as an anticancer chemotherapeutic agent has led to the development of new synthetic methods for pyrrolo[1,2-a]indoles.[2-6]. Previously we obtained from the reactions of nitrile oxides with cycloalkano[b]indoles[7], instead of the expected propellane-type indole derivatives, oxadiazolo[4,5-a] indolines *via* addition of nitrile oxides to the C=N bond of 3-hydroxy-3H-cycloalkano[b]indoles, intermediate oxidation products of cycloalkano[b]indoles. The formation of these adducts was indicative of high dipolarophilicity of the C=N bond of 3H-indoles. Although some types of cycloadditions to 3H-indoles have been used to a rather limited extend for synthetic purposes,[8,9] 1,3-dipolar cycloaddition reactions have not been studied so far to the best of our knowledge. With the aim to utilize these reactions for the synthesis of a-fused indole derivatives, we studied in this paper the reactions of nitrile oxides **2** with the readily available[10] 2,3,3-trimethyl-3H-indole **1**. Also, we investigated the reductive cleavage of the obtained new a-fused-indolines.

RESULTS AND DISCUSSION

The C=N bond of 2,3,3-trimethyl-3H-indole **1** showed very strong dipolarophilic activity in the reactions with nitrile oxides **2**. All the reactions were carried out at room temperature using equimolar amounts of the reactants in chloroform with stable nitrile oxides **2d, e** or in benzene with unstable nitrile oxides **2a-c**, generated *in situ* from the appropriate substituted benzhydroxamoyl chloride with triethylamine, to give 9,9,9a-trimethyl-3-aryl-1,2,4-oxadiazolo [4,5-a] indolines **3** in high yields (83-99%).

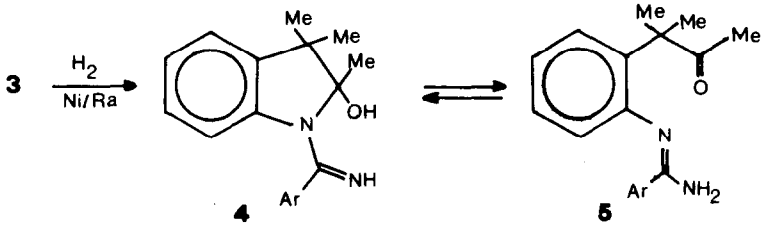


2a, 3a: Ar = C_6H_5
2b, 3b: Ar = 4-ClC_6H_4
2c, 3c: Ar = 2-ClC_6H_4
2d, 3d: Ar = 2,6-$Cl_2C_6H_3$
2e, 3e: Ar = 2,4,6-$Me_3C_6H_2$

Scheme 1

The assigned structure of the cycloadducts **3** was supported by their elemental analyses and spectroscopic data (IR, ^{1}H NMR, MS). Concerning the regioselectivity of the reactions it should be mentioned that the cycloadditions at hetero multiple bonds proceed exclusively in the direction in which carbon-hetero bonds are formed[11]. Formation of hetero-hetero bonds is not preferred according to the principle of "maximum gain in σ bond energy"[12]. A characteristic feature supporting the proposed regiochemistry was observed in the ^{1}H NMR spectra of cycloadducts **3**. The H-5 atom is strongly shielded by the 3-aryl substituent and gives a multiplet ranging from δ 6.38-6.60 for **3a** to δ 5.88-6.06 for **3e**. The shielding effect of the 3-aryl group increases in the order C_6H_5~4-ClC_6H_4<2-ClC_6H_4<2,6-$Cl_2C_6H_3$<2,4,6-$Me_3C_6H_2$. This can be explained as follows. When the rotation of the 3-aryl group around the carbon-carbon bond is sterically restricted (**3d**, **3e**) the preferred conformation of the 3-aryl group must be almost perpendicular to the oxadiazole ring. When there is no steric hindrance (**3a**, **3b**), the preferred conformation of the 3-aryl group must be coplanar with the oxadiazole ring because of conjugation with the C=N bond. As it comes out from molecular models the H-5 atom is closer to the shielding region of the 3-aryl moiety in the perpendicular conformation than in the coplanar with the oxadiazole ring.

The fused 1,2,4-oxadiazole ring of compounds **3** is not readily cleaved by acids. Thus no reaction was observed after reflux of a solution of **3a** in methanol containing 20% hydrochloric acid for 6h. On the contrary, reductive cleavage takes place very easily. Hydrogenation of cycloadducts **3** over Raney nickel in methanol solution at room temperature for 1-2h gave almost quantitatively compounds **4** or **5**.

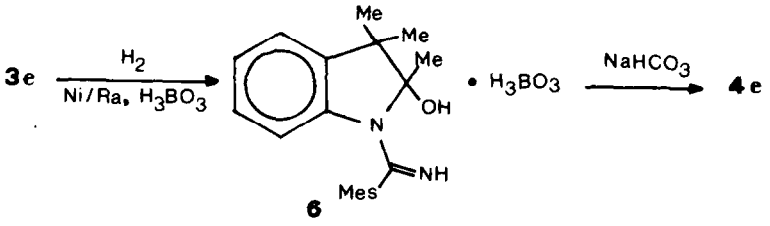


a: Ar = C_6H_5
b: Ar = 4-ClC_6H_4
c: Ar = 2-ClC_6H_4
d: Ar = 2,6-$Cl_2C_6H_3$
e: Ar = 2,4,6-$Me_3C_6H_2$

Scheme 2

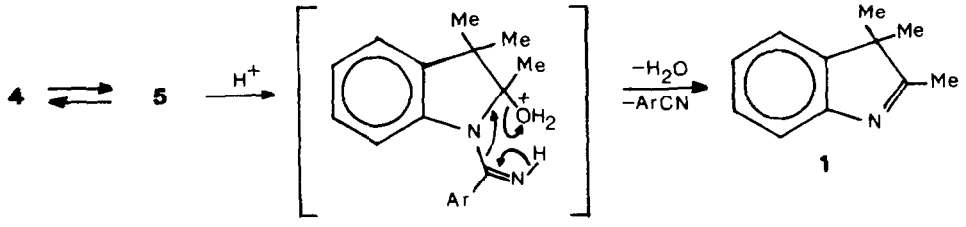
Evidently in all cases the amidines **4** are the initial products formed by breaking of the N-O bond according to the catalytic reduction pathway of 1,2,4-oxadiazoles[13] and especially of the isoxazole heterocycles series[14] Tautomerization of **4**, known for the 2-hydroxy-indolines[15] leads to the opened structure **5**. The site of the tautomeric equilibrium depends on the kind of the aryl group, following almost the same regularity with the shielding effect of the aryl group. Thus, when the aryl is phenyl or 4-chlorophenyl the tautomer **5** is obtained directly as the sole product of the reduction as it was checked by the TLC and ^1H NMR of the crude reaction mixture. When the aryl is 2-chlorophenyl, 2,6-dichlorophenyl or mesityl the crude reaction mixture consists initially of tautomer **4**. However after work up on column chromatography **4c** is tautomerized to **5c**, **4d** is tautomerized only partially to **5d**, whereas **4e** is stable enough and it is obtained unchanged. It seems that when the conjugation of the aryl group with the C=N bond is not sterically hindered structure **5** is more stable than **4** and the equilibrium is moved readily to its direction. When the conjugation is not permitted by steric factors, structure **4** which can be stabilized by intramolecular hydrogen bonds predominates.

The two tautomers **4** and **5** can be easily distinguished by their IR and ^1H NMR spectral data. Thus in the IR tautomers **5** give the C=O absorption at ν 1700 cm^{-1}, whereas in the ^1H NMR of compounds **4** the H-7 atom is strongly shielded, as in the case of adducts **3**, and gives a multipet ranging from δ 5.73-6.00 **(4c)** to δ 5.15-5.42 **(4e)**. No essensial changes in the mode of the reduction reactions were observed, when they were repeated in the presence of boric acid. Only in the case of the reduction of **3e**, compound **6**, a molecular complex (1:1) of **4e** with boric acid was initially isolated, from which the free **4e** was obtained after reflux with sodium bicarbonate solution.



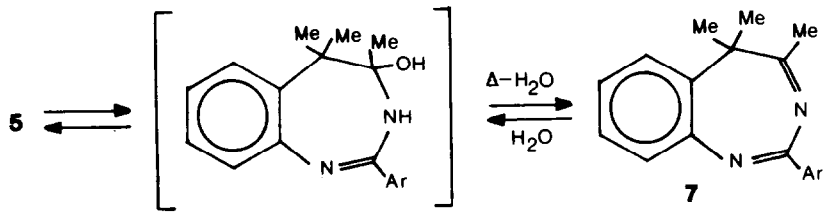
Scheme 3

Attempts to acid catalyzed interconvertion of isomers **4** and **5** (20h reflux with methanol containing 30% hydrochloric acid) led in both cases examined (**4e** and **5a**), to decomposition to the starting 3H-indole **1** and the corresponding nitrile. The decomposition occurs probably through the imino form according to the Scheme 4. It should be mentioned that **4e** is decomposed exclusively according to the Scheme 4, whereas **5a** is decomposed partially to **1** and benzonitrile, isolated from a rather complicated reaction mixture. Under milder reaction conditions (reflux in methanol containing 10% hydrochloric acid) both **4e** and **5a** were stable.



Scheme 4

Of interest is also the thermal behaviour of amidines **4** and **5**. Thus, the amidine **4e** remained essentially unchanged after 5h reflux in toluene, whereas compounds **5a** and **5b** gave through intramolecular Schiff base formation the benzodiazepines **7** as they were identified on the basis of their analytical and spectral data. Benzodiazepines **7** are not very stable and during their purification procedure they are partially converted to the starting amidines **5** (Scheme 5). This reversion of the reaction is not surprising and it can be explained by a covalent hydration of the C=N bond, which is a well known reaction of the nitrogen and especially of the 1,3-dinitrogen heterocycles.[16]



7a: Ar = C_6H_5

7b: Ar = 4-ClC_6H_4

Scheme 5

EXPERIMENTAL

All melting points were uncorrected and were obtained with a Kofler hot-stage apparatus. The IR spectra were obtained with a Perkin-Elmer Model 297 spectrophotometer. The ^1H NMR spectra, reported in δ units were obtained with a Brucker AW-80 spectrometer, with tetramethylsilane as internal standard. The mass spectra were measured with a Hitachi-Perkin-Elmer Model RMU-6L spectrometer, with an ionization energy of 70eV. Elemental analyses were performed with a Perkin-Elmer Model 240-B analyzer. Column chromatography was performed over Merck Kieselgel 60 (particle size 0.063-0.200mm).

Preparation of Starting Materials: 2, 3, 3,-Trimethyl-3H-indole **1** was prepared from isopropyl methyl ketone phenylhydrazone *via* Fischer synthesis.[10] 2, 6-Dichlorobenzonitrile oxide **2d** and mesitonitrile oxide **2e** were prepared according to known procedure[17] from the corresponding aldoximes with N-bromo succinimide and triethylamine. Benzonitrile oxide **2a**, 4-chlorobenzonitrile oxide **2b** and 2-chlorobenzonitrile oxide **2c** were prepared *in situ* with triethylamine from the appropiate substituted benzhydroxamoyl chlorides.[18]

Preparation of Indolines **3**: In the reactions of **1** with the stable nitrile oxides **2d** and **2e**, a solution of **1** (1mmol) and **2** (1mmol) in chloroform was allowed to stay at room temperature until the disappearance of the starting nitrile oxide, as it was monitored by TLC (11-23 days). After evaporation of the solvent the product **3** was separated from the reaction mixture by column chromatography on silica gel, using a mixture of hexane/ethyl acetate (15:1) as eluant. In the reactions of **1** with the unstable nitrile oxides **2a, 2b, 2c** a benzene solution of **1** (1mmol) and the appropriate substituted benzhydroxamoyl chloride (1mmol) and triethylamine (1.5mmol) was kept at room temperature for 1 day. After the filtration of the precipitated triethylamine hydrochloride and evaporation of the solvent, the residue was chromatographed on a silica gel column, using hexane/ethyl acetate (15:1) as eluant. All products **3a-e** were further purified by recrystallization from dichloromethane/hexane mixtures or diethylether.

9, 9, 9a-Trimethyl-3-phenyl-1, 2, 4-oxadiazolo [4,5-a] indoline **3a**: Yield 98%. M.p.105-108 °C. IR(Nujol) cm^{-1}: 1600 (C=N). ^1H NMR ($CDCl_3$), δ: 1.30 (3H, s), 1.45(3H,s), 1.53 (3H,s), 6.38-6.60 (1H, m), 6.72-7.22 (3H, m), 7.33-7.56 (3H, m), 7.80-8.03 (2H, m). MS, m/z: 278 (M^+, 27), 263 (1), 235 (9), 221 (100), 175 (5), 160 (75), 144 (12), 132 (76), 103 (30), 43 (60). Anal. calcd for $C_{18}H_{18}N_2O$ (278.34): C, 77.67; H,6.52; N, 10.07. Found: C, 77.38; H,6.28; N, 10.19.

9, 9, 9a-Trimethyl-3-(4'-chlorophenyl)-1, 2, 4-oxadiazolo [4,5-a] indoline **3b**: Yield 99%. M.p.102-104 °C. IR(Nujol), cm^{-1}: 1595 (C=N). ^1H NMR ($CDCl_3$), δ: 1.32 (3H,s), 1.47 (3H.s), 1.54 (3H,s), 6.37-6.60

(1H, m), 6.88-7.60 (5H, m), 7.88 (2H,d,j=10Hz). MS, m/z: 314/312 (M^+, 37), 299/297 (1), 271/269 (10), 257/255 (97), 175 (7), 169 (100), 144 (83), 139/137 (61), 132 (90), 43 (60). Anal.calcd for $C_{18}H_{17}ClN_2O$ (312.79): C, 69.11; H, 5.48; N, 8.96. Found: C, 69.33; H, 5.62; N, 9.10.

9, 9, 9a-Trimethyl-3-(2'-chlorophenyl)-1, 2, 4-oxadiazolo [4,5-a] indoline **3c** :Yield 88%. M.p.87-89 °C. IR(Nujol), cm^{-1}: 1595 (C=N). ^1H NMR ($CDCl_3$), δ: 1.38 (3H,s), 1.43 (3H,s), 1.63 (3H,s), 6.12-6.35 (1H, m), 6.87-7.75 (7H, m). MS, m/z: 314/312 (M^+, 8), 299/297 (1), 271/269 (3), 257/255 (33), 175 (4), 160 (56), 144 (44), 139/137 (31), 132 (39), 43 (100). Anal.calcd for $C_{18}H_{17}ClN_2O$ (312.79): C, 69.11; H, 5.48; N, 8.96. Found: C, 69.16; H, 5.87; N, 9.10.

9, 9, 9a-Trimethyl-3-(2', 6'-dichlorophenyl)-1, 2, 4-oxadiazolo [4,5-a] indoline **3d**: Yield 83%. M.p.144-148 °C. IR(Nujol), cm^{-1}: 1605 (C=N). ^1H NMR ($CDCl_3$), δ: 1.40 (6H,s), 1.67 (3H,s), 5.97-6.16(1H, m), 6.78-7.15(3H, m), 7.20-7.49 (3H, m). MS, m/z: 350/348/346 (M^+, 9), 335/333/331 (1), 307/305/303 (5), 293/291/289 (30), 175 (14), 175/173/171 (8), 160 (100), 144 (8), 132 (71), 43 (45). Anal.calcd for $C_{18}H_{16}Cl_2N_2O$ (347.24): C, 62.26; H, 4.65; N, 8.07. Found: C, 62.13; H, 4.87; N, 8.27.

9, 9, 9a-Trimethyl-3-mesityl-1, 2, 4-oxadiazolo [4,5-a] indoline **3e**: Yield 95%. M.p.97-100 °C. IR(Nujol), cm^{-1}: 1590 (C=N). ^1H NMR ($CDCl_3$), δ: 1.39 (6H,s), 1.63 (3H,s), 1.98 (3H,s), 2.29(3H, s), 2.43 (3H, s), 5.88-6.06 (1H, m), 6.78-7.30 (5H, m). MS, m/z: 320 (M^+, 45), 305 (4), 277 (30), 263 (55), 175 (10), 160 (75), 159 (48), 145 (78), 144 (68), 132 (90), 130 (100), 43 (22). Anal.calcd for $C_{21}H_{24}N_2O$ (320.42): C, 78.72; H, 7.55; N, 8.74. Found: C, 78.62; H, 7.59; N, 8.61.

General Procedure for the Reduction of Indolines **3**: To a solution of indoline **3** (1mmol) in methanol (15ml) a catalytic amount (a spatula tip, estimated 20mg) of W-2 Raney nickel was added. A ballon, filled with hydrogen was addapted to the reaction flask by means of a three-way stopcock. After repeated evacuations and flushings with hydrogen gas, the reaction mixture was stirred under hydrogen atmosphere for 1-2 h at room temperature. Nickel was separated by careful filtration through Celite and washed several times with methanol and dichloromethane. The combined filtrate and washings were concentrated under *vacuo* and the residue was disolved in dichloromethane and dried over sodium sulfate. After filtration and evaporation of the solvent the crude reaction mixture was checked by ^1H NMR and was subjected to column chromatography using mixtures of hexane with increasing amounts of ethyl acetate from 25% to 100% as eluant. From the colum either pure compounds **4** or **5**, or mixtures of **4** and **5** were isolated.

Reduction of **3a**. The ^1H NMR spectrum of the crude reaction mixture showed N-[o-(1', 1'-dimethyl-2'-oxo-propyl)-phenyl]-benzamidine **5a** as the sole reaction product. Column chromatography afforded **5a** as an oil in 82% yield: IR (neat), cm^{-1}: 3450, 3350(NH_2), 1690(C=0), 1625 (C=N). ^1H NMR ($CDCl_3$), δ: 1.38 (6H,s), 2.01 (3H, s),5.05 (2H, br s), 6.74-7.94 (9H, m). MS, m/z: 280 (M^+, 29), 265(10), 237 (67), 220 (53), 159 (15), 144 (37), 104 (55), 103 (97), 43 (100), m* = 250.8, 204.2. Anal.calcd for $C_{18}H_{20}N_2O$ (280.36): C, 77.11; H, 7.19; N, 9.99. Found: C, 76.89; H, 6.99; N, 9.71.

Reduction of **3b**. The ^1H NMR spectrum of the crude reaction mixture showed N-[o-(1', 1'-dimethyl-2'-oxo-propyl)-phenyl]-4-chlorobenzamidine **5b** as the sole reaction product. After column chromatography **5b** was isolated in 76% yield: M.p 104-114 °C (from diethyl ether/hexane). IR (Nujol), cm^{-1}: 3450, 3350(NH_2), 1700(C=0), 1625 (C=N). ^1H NMR ($CDCl_3$), δ: 1.33(6H,s), 1.95 (3H, s),5.03 (2H, br s), 6.83-7.90 (8H, m). MS, m/z: 316/314 (M^+, 40), 301/299(11), 273/271 (100), 256/254 (39), 159 (12), 144 (11), 140/138 (32), 43 (28), m* = 284.7, 238.0. Anal.calcd for $C_{18}H_{19}ClN_2O$ (314.80): C, 68.67 H, 6.08; N, 8.90 Found: C, 68.61; H, 6.16 N, 8.78.

Reduction of **3c**. The ^1H NMR spectrum of the crude reaction mixture showed 1-(α-imino-2'-chlorobenzyl)-2-hydroxy-2, 3, 3-trimethyl-indoline **4c** as the sole reaction product. ^1H NMR ($CDCl_3$), δ: 1.35 (6H, s), 1.76 (3H, s), 5.73-6.00 (1H, m), 6.63-7.79 (9H, m). Treatment of the reaction

mixture on column chromatography gave N-[o-(1', 1'-dimethyl-2'-oxo-propyl)-phenyl]-2-chlorobenzamidine **5c** in 60%, as an oil: IR (neat), cm-1: 3460, 3350 (NH_2), 1700 (C=0), 1635 (C=N). ^1H NMR ($CDCl_3$), δ: 1.35 (6H, s), 2.00 (3H, s), 4.93 (2H, br s), 6.75-7.84 (8H, m). MS, m/z: 316/314 (M^+, 28), 301/299 (16), 273/271 (81), 256/254 (20), 237 (100), 159 (41), 144 (44), 139/137 (28), 43 (60). Anal.calcd for $C_{18}H_{19}ClN_2O$ (314.80): C, 68.67; H, 6.08; N, 8.90. Found: C, 68.81; H, 6.06; N, 8.89.

Reduction of **3d**. The 1H NMR of the crude reaction mixture showed 1-(α-imino-2', 6'-dichlorobenzyl)-2-hydroxy- 2, 3, 3-trimethyl-indoline **4d** as the sole reaction product. ^1H NMR ($CDCl_3$), δ: 1.31 (6H, s), 1.71 (3H, s), 5.59-5.92 (1H, m), 6.56-7.78 (8H, m). Treatment of the reaction mixture on column gave in 80% yield a mixture of **4d** and **5d** in a ratio 10:1, as it was shown by ^1H NMR. Attempts to separate the mixture components by repeated chromatographies were unsucessful. The presence of the **5d** in the mixture was indicated by the additional signals at δ 1.88 (s) and 4.81-5,21 (br s) in the ^1H NMR spectrum as well as by the absorptions at 3470, 3320, and 1700cm^{-1} in the IR spectrum. MS, m/z: 352/350/348 (M^+, 5), 337/335/333 (15), 315/313 (14), 309/307/305 (54), 292/290/288 (3), 176/174/172 (14), 159 (6), 144 (8), 43 (100). Anal. calcd for $C_{18}H_{18}Cl_2N_2O$ (349.25): C, 61.90; H, 5.19; N, 8.02. Found: C, 61.69; H, 5.18; N, 7.99.

Reduction of **3e**. The reduction of **3e** afforded as sole product 1-(α-imino-2', 4', 6'-trimethylbenzyl)-2-hydroxy-2, 3, 3-trimethyl-indoline **4e** as it was shown by ^1H NMR spectrum. Treatment of the reaction mixture on column gave unchanged **4e** in 92% yield. Efforts to crystallize the oily reaction product using a variety of solvents were unsuccessful. After a long period of staying, **4e** was solidified, m.p 65-75 °C. IR (Nujol), cm^{-1}: 3340 (OH, NH), 1610 (C=N). ^1H NMR ($CDCl_3$), δ: 1.27 (6H, s), 1.65 (3H, s), 2.16 (6H, s), 2.33 (3H, s), 5.15-5.42 (1H, m), 6.48-7.27 (7H, m). MS, m/z: 322 (M^+, 29), 307 (71), 279 (100), 263 (7), 159 (16), 146 (32), 144 (21), 43 (56). Anal.calcd for $C_{21}H_{26}N_2O$ (322.43): C, 78.22; H, 8.13; N, 8.69. Found: C, 78.43; H, 8.18; N, 8.48.

Reduction of Indolines **3** in the Presence of Boric Acid. Indoline **3** (1mmol), with W-2 Raney nickel (ca 20mg) and boric acid (5mmol) were stirred in methanol/water (5:1,15ml) as described above and the same work up was followed. In addition the dichloromethane solution of the reaction mixture was washed with water to remove boric acid, before drying. The formed products were the same with those obtained from the reactions without the boric acid, with the exception of the reduction of **3e**, which gave in 91% yield 1-(α-imino-2', 4', 6'-trimethylbenzyl)-2-hydroxy-2, 3, 3-trimethyl-indoline. boric acid complex **6**: M.p. 218 °C (dec.), (from diethyl ether/hexane). IR (Nujol), cm^{-1}: 3350 (OH, NH), 1580 (C=N). ^1H NMR ($CDCl_3$), δ: 1.18 (3H, s), 1.34 (3H, s), 1.60 (3H, s), 2.06 (3H, s), 2.23 (3H, s), 2.30 (3H.s), 5.35-5.58 (1H, m), 6.59-7.26 (5H, m). Anal. calcd for $C_{21}H_{26}N_2O.H_3BO_3$ (384.25): C, 65.64; H, 7.60; N, 7.28. Found: C, 65.48; H, 7.46; N, 7.35.

Transformation of **6** to **4e**. A suspension of **6** (0.1mmol) in a saturated solution of sodium bicarbonate (5ml) was refluxed for 30min. After cooling the reaction mixture was extracted with dichloromethane. The organic layer was dried over sodium sulfate and after evaporation of the solvent compound **4e** was isolated in 95% yield.

Treatment of **4e** with Hydrochloric Acid. A solution of **4e** (0.3mmol) in methanol containing 30% hydrochloric acid (34%) was heated to reflux for 25h. Then the reaction mixture was diluted with water and extracted with diethyl ether. The organic layer was dried, evaporated and the residue was purified by column chromatography (silica gel, hexane/ethyl acetate 10:1) to give mesitonitrile in 80% yield. The aqueous layer was neutralized with sodium bicarbonate solution, extracted with diethyl ether and the organic layer after drying and evaporation of the solvent was chromatographed on column (silica gel, hexane/ethyl acetate 1:1) to give in order of elution: a) indole **1** in 80% yield b) unreacted **4e** in 20% yield.

Treatment of **5a** with Hydrochloric Acid. A solution of **5a** (0.5mmol) in methanol containing 30% hydrochloric acid (34%) was heated to reflux. After 25 h reflux no unreacted **5a** was detected

and a complicated reaction mixture resulted, as it was checked by TLC. Following the above described procedure for the decomposition of **4e**, benzonitrile and 3H-indole **1** were isolated in 20% yield.

Thermal Transformation of **5** to **7**. A solution of **5** in toluene was refluxed for 5h. Toluene was removed *in vacuo* and the residue was subjected to column chromatography (silica gel, hexane/ethyl acetate 4:1) to give in order of elution compound **7**, unreacted **5** and 3H-indole **1**.

2-Phenyl-4, 5, 5-trimethyl-5H-1, 3-benzodiazepine **7a**: Yield 61%. M.p. 122-126 °C, (from ethanol). IR (Nujol), cm^{-1}: 1625 (C=N). ^1H NMR ($CDCl_3$), δ: 0.83 (3H, s), 1.83 (3H, s), 2.14 (3H, s), 7.06-7.77 (7H, m), 8.09-8.33 (2H, m). MS, m/z: 262 (M^+, 23), 221 (100), 206 (49), 144 (15), 103 (45), 91 (38), m*=192.0. Anal.calcd for $C_{18}H_{18}N_2$ (262.34): C, 82.40; H, 6.92; N, 10.68. Found: C, 82.38; H, 6.92; N,10.48.

2-(4'-chlorophenyl)-4, 5, 5-trimethyl-5H-1, 3-benzodiazepine **7b**: Yield 52%. M.p. 108-110 °C, (from ethanol). IR (Nujol), cm^{-1}: 1625 (C=N). ^1H NMR ($CDCl_3$), δ: 0.82 (3H, s), 1.84 (3H, s), 2.14 (3H, s), 7.14-7.74 (6H, m), 8.13 (2H, d, j=10Hz). MS, m/z: 298/296 (M^+, 65), 257/255 (100), 242/240 (79), 144 (43), 139/137 (47), 103 (69), 91 (80), m*=225.9. Anal.calcd for $C_{18}H_{17}ClN_2$ (296.79): C, 72.84; H, 5.77; N, 9.44. Found: C, 72.73; H, 5.81; N, 9.49.

Hydration of **7a** to **5a**. A solution of **7a** (1mmol) in dichloromethane (5ml) was absorbed on silica gel (5g) and it was kept at room temperature for 2 days. Then the silica gel was extracted with dichloromethane/methanol 10:1 and the solvents were evaporated. ^1H NMR and TLC of the residue showed that it contained no **7a**, consisted mainly from **5a** and 3H-indole **1**.

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