NOVEL SYNTHESIS OF POLYFUNCTIONALIZED 1,4,4a,9a-TETRAHYDRO-1-AZA-9-OXAFLUORENES BY UNEXPECTED CYCLOADDITION OF 4-(4-METHOXYPHENYL)-1,4-DIHYDRO-PYRIDINES AND *p*-BENZOQUINONE

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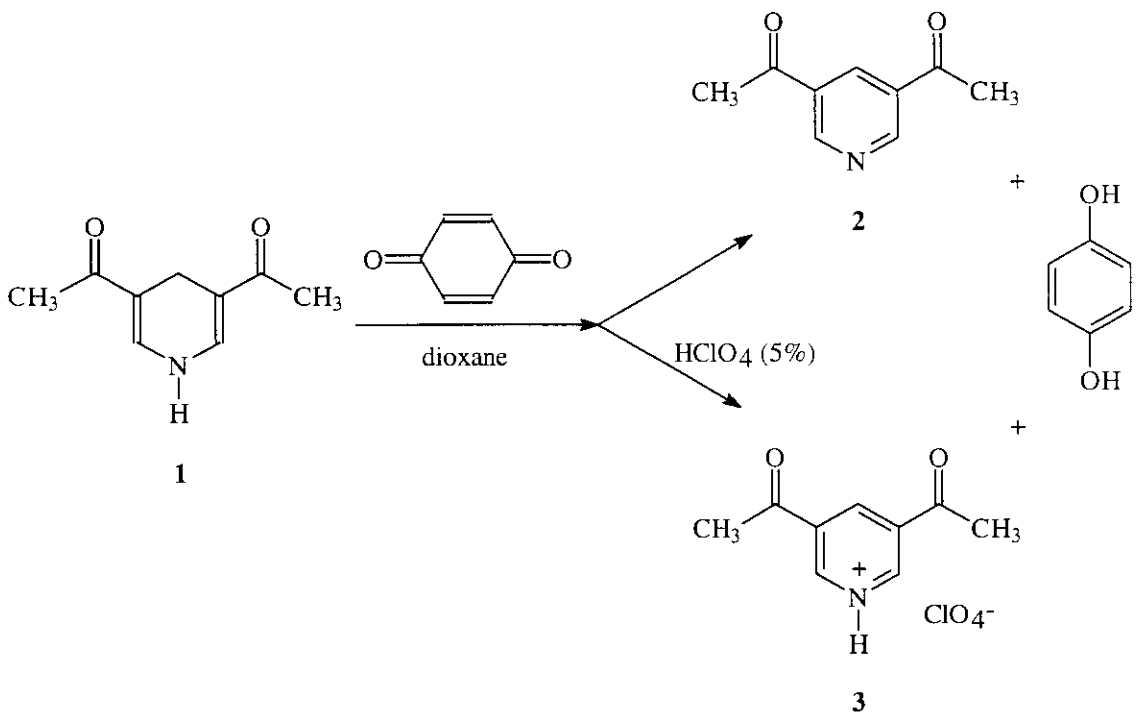
Abstract - A surprising acid-catalysed cycloaddition reaction occurs between 3,5-diacetyl-4-(4-methoxyphenyl)-1,4-dihydropyridine (**4**) and *p*-benzoquinone in dioxane/ $HClO_4$ (5%) yielding novel polyfunctionalized 1,4,4a,9a-tetrahydro-1-aza-9-oxafluorenes (**9**) as exclusive products. On the other hand the corresponding 4-unsubstituted 1,4-dihydropyridine (**1**) is oxidized by *p*-benzoquinone. Novel structures are characterized by standard spectroscopy and, furthermore, confirmed by acetylation. The different reactivity of the 4-substituted and 4-unsubstituted derivatives is dicussed on the basis of semiempirical MNDO calculations and redox potentials.

The structural variety of NADH model compounds meanwhile includes substances with different *N*-alkyl and carboxamide substituents.[1,2] Recent investigations have been taken into the oxidation mechanism of 4-substituted 1,4-dihydropyridines as NAD model compounds.[3,4] We have been interested in the redox behaviour with *p*-benzoquinone of 2,6-unsubstituted 3,5-diacetyl-1,4-dihydropyridines as symmetrically substituted derivatives like 1,2,3,4,5,6,7,8-octahydroacridin-1,8-dione previously investigated by Singh *et al.*[5] as NADH model compound. In the acid-catalysed reaction with *p*-benzoquinone the 4-(4-methoxyphenyl) derivatives (**4**) exclusively undergoe a novel cycloaddition reaction to 1,4,4a,9a-tetrahydro-1-aza-9-oxafluorenes (**9**) without any pyridinium salt being detectible. Thus the unexpected formation of **9** opens a new and attractive synthetic route to functionalized 1-aza-9-oxafluorenes. The later have been reported as pharmacologically interesting agents with a broad antiviral activity.[6]

Results and Discussion

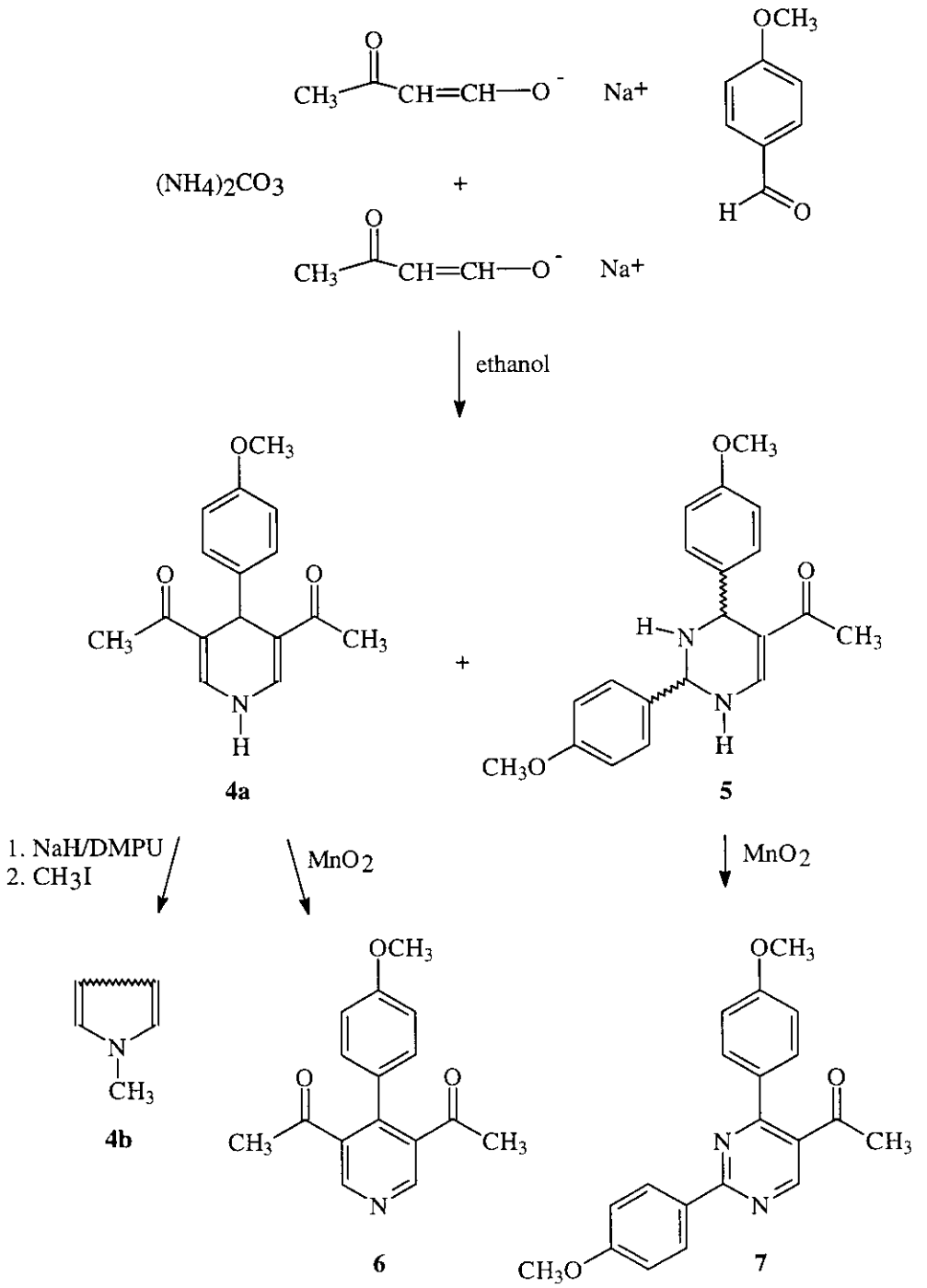
On treatment with equimolar amounts of *p*-benzoquinone 3,5-diacetyl-1,4-dihydropyridine (**1**)[7] was completely oxidized to 3,5-diacetylpyridine (**2**)[7] in dioxane at room temperature (90%) without any other detectible product as was monitored by TLC. Under acid conditions, which have been reported as favourable for oxidizing NADH model compounds by quinones,[5] in dioxane/$HClO_4$ (5%) oxidation proceeds more quickly with no more starting **1** detectible by TLC after 6 hours at room temperature. The formed precipitate was filtered off and recrystallized from chloroform/acetone/toluene. It proved to be 3,5-diacetylpyridinium perchlorate (**3**) with a yield of 95%.



Scheme 1

The 4-(4-methoxyphenyl)-1,4-dihyropyridine (**4a**) was prepared by cyclocondensation reaction of 4-methoxybenzaldehyde, the sodium salt of hydroxymethylenacetone[8] and ammonium carbonate in boiling ethanol following the method of Paleček and Kuthan.[9] However, the formation of two products was monitored by TLC. The main product turned out to be the desired 1,4-dihydropyridine (**4a**). The other one could be identified as 1,2,3,4-tetrahydropyrimidine (**5**), preliminarily characterized by standard spectroscopy as well as by oxidation to corresponding pyrimidine (**7**) with manganese(IV) oxide in boiling toluene.

The *N*-methyl derivative (**4b**) was achieved by methylation of **4a** in dimethylpropyleneurea (DMPU) *via* the 1,4-dihydropyridine anion formed by treatment with a 1.5-fold excess of sodium hydride. With equimolar amounts of methyl iodide at room temperature the *N*-methylation succeeded selectively without any acetyl group attack.



Scheme 2

Surprisingly equimolar mixtures of both **4a** and **4b** with *p*-benzoquinone in dioxane remained unchanged, at room temperature and under heating. Even the addition of an excess of *p*-benzoquinone did not result in the expected oxidation of **4**.

On treatment with perchloric acid in dioxane (5%) at room temperature novel substances were yielded. However, their first analysis by MS spectrometry indicated the formation of adducts of 1,4-dihydroypyridine and *p*-benzoquinone. Further characterization by IR and ^{1}H NMR spectrometry suggested the structures (**9a**) and (**9b**) as cycloaddition products. Additionally, these have been confirmed by the *O*- and *N*-acetylation to **10a** and **b**, respectively (see Scheme 3).

While the *N*-H derivative (**9a**), *e. g*, has two carbonyl bands with ν = 1711 and 1606 cm^{-1} in IR spectrum, its *N*-acetyl derivative (**10a**) shows additional carbonyl absorptions at 1762 and 1636 cm^{-1}. The ^{1}H NMR spectrum of **9a** shows characteristic singlets at 4.76 (4-H) and 6.31 (9a-H) ppm. The doublet of 2-H at 7.49 ppm (J = 7 Hz) coupling with the 1-*N*H at 7.87 ppm appears as a singlet after D_2O-exchange.

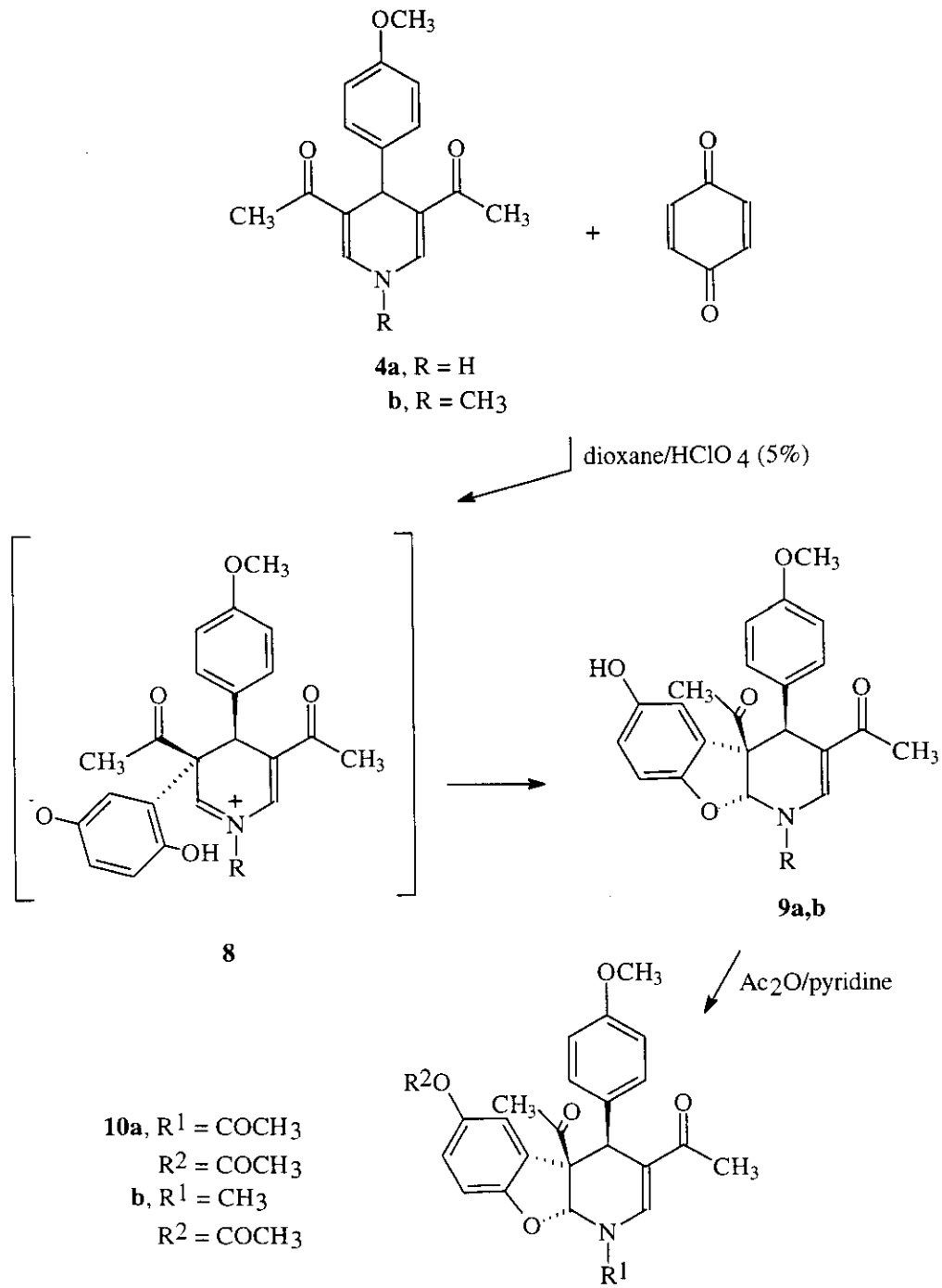
Even the *N*H-derivate (**4a**) exclusively yielded the 1,4,4a,9a-tetrahydro-1-aza-9-oxafluorene (**9a**) without any detectible pyridine base (**6**) as proved by TLC in comparison with oxidized **4a**, which was achieved by reaction with manganese(IV) oxide.

The relative stereochemistry of asymmetric C-4 and C-9a could be determined by NOESY of **10b** with an observed NOE between 9a-H and 2´-and 6´-H of the 4-(4-methoxyphenyl) substituent, proving an axial orientation for 9a-H and the 4-(4-methoxyphenyl) substituent. Due to energetic reasons the ring junctions of the dihydrofurane ring will be *cis* as was found in the X-ray crystal structure of structurally closely related 4(*SR*),4a(*RS*),9a(*RS*)-3,4a-dimethoxycarbonyl-1,4,4a,9a-tetrahydro-6-hydroxy-4-(4-methoxyphenyl)-1,8-dimethylbenzo[4,5]dihydrofuro[2,3-*b*]pyridine as the corresponding cycloaddition product of methyl-*p*-benzoquinone and 3,5-diethoxycarbonyl-4-(4-methoxyphenyl)-1-methyl-1,4-dihydropyridine with a corresponding axial orientation of 9a-H and the 4-(4-methoxyphenyl) substituent.[10]

The formation of **9** may proceed *via* the postulated adduct (**8**) given by the Michael additon of nucleophlic C-3 of the 1,4-dihydropyridine at C-2 of *p*-benzoquinone which takes place *trans* to the 4-aryl moiety due to sterical reasons as the 4-(4-methoxyphenyl) substituent shows an axial orientation bisecting the 1,4-dihydropyridine plane which was reported for corresponding 3,5-dialkoxycarbonly derivatives.[11] The addition reaction is completed by the following nucleophilic OH-attack at C-2 of the dihydropyridine ring *trans* to the 4-aryl moiety, leading to the *cis* fused ring junctions. Thus, in the first step, the reaction follows the "Nenitzescu-reaction" of enaminone and *p*-benzoquinone leading to indoles.[12]

In order to investigate the different reaction behaviour of 4-(4-methoxyphenyl) substituted 3,5-diacetyl-1,4-dihydropyridines (**4a,b**) and the corresponding 4-unsubstituted derivative (**1**) semiempirical MNDO-calculations have been made. They prove C-3/5 of all three derivatives to be soft nucleophilic centers with low charge density and high orbital coefficients (c), respectively (see Table 1). The LUMO energy of *p*-

charge density and high orbital coefficients (c), respectively (see Table 1). The LUMO energy of *p*-benzoquinone was calculated with -1.51 eV. With a HOMO-LUMO energy difference between the 1,4-dihydropyridines and *p*-benzoquinone of less than 7.5 eV the soft-soft interaction[13] makes a primarily orbital controlled reaction between 1,4-dihydropyridines and *p*-benzoquinone possible.



Scheme 3

Table 1. Semiempirical MNDO calculations with MOPAC 6.0

	charge/*N*	charge/O	charge/C-3	E/HOMO-1	c/*N*	c/C-3
1	-0.315	-0.292	-0.250	-8.78 eV	0.499	0.488
4a	-0.264	-0.290	-0.226	-8.97 eV	0.487	0.480
4b	-0.337	-0.287	-0.244	-8.71 eV	0.528	0.490

Thus the observed formation of 1,4,4a,9a-tetrahydro-1-aza-9-oxafluorenes (**9a,b**) *via* the postulated adduct (**8**) may be explained. However, as **1** with a comparable calculated reactivity towards *p*-benzoquinone gives no cycloaddition product, further investigations had to be undertaken to explain the different reaction behaviour.

The kind of protonation of the three compounds was expected to be the same according to the calculations. In fact, all three compounds undergo *N*-protonation as was shown by ^{1}H NMR spectrometry in dioxane-d_8 and dioxane-d_8/$HClO_4$ with a shift of the 2-H/6-H signals from 7.2 to 8.0 ppm due to *N*-protonation. However, *O*-protonation with a resulting C-2-*N* double bond in the mesomeric equilibrium would have brought a higher shift to about 9.3 ppm compared with the chemical shift of corresponding protons in 3,5-diacetylpyridine (**2**) or its perchlorate (**3**), respectively.

Finally, potentiometric measurements of the redox potentials have been made in acetic acid (30 mL) by titration of 25 mg of **4a**, **4b**, **1** and *p*-hydroquinone, respectively, with 0.1 N potassium dichromate solution. The resulting redox potentials at $\tau = 0.5$ (vs Ag/AgCl electrode) of **4a** and **b** with 0.605 and 0.618 V were higher than the determined redox potential of *p*-benzoquinone with 0.530 V. Consequently, an acid-catalyzed oxidation of **4a** and **b** by *p*-benzoquinone is unlikely. However, redox potential of **1** with 0.510 V makes less than the one of *p*-benzoquinone, so that an oxidation reaction is possible. Nevertheless, the merely slight potential differences suggest that moreover stereochemical features may influence the different reaction behaviour. Due to the axially orientated 4-(4-methoxyphenyl) substituent the formation of charge transfer (CT) complexes between both reactants which proceeds the redox reaction may be sterically hindered in the case of compounds (**4a**) and (**4b**). In compound (**1**) with no sterical hindrance the formation of a CT complex may proceed, although CT complex formation is not detectible by UV absorbance at longer wavelenghts. This may be explained by the following prompt redox reaction as was previously reported by Singh *et al.* for corresponding redox reactions especially in acid media.[5]

In summary, 3,5-diacetyl-1,4-dihydropyridine (**1**) with a lower redox potential is oxidizied by *p*-benzoquinone, whereas the corresponding 4-(4-methoxyphenyl) derivatives (**4**) with higher redox potentials, however, prove to be stable towards *p*-benzoquinone oxidation. They undergo an unexpected cycloaddition reaction with *p*-benzoquinone to novel 1,4,4a,9a-tetrahydro-1-aza-9-oxafluorenes (**9**).

EXPERIMENTAL

^{1}H-NMR spectra were recorded with a Bruker AC-200 F spectrometer with tetramethylsilane (TMS) as an internal standard. Chemical shifts are given on the δ scale (ppm). The following abbreviations are used: s = singlet, d = doublet, dd = double doublet and m = multiplet. MS was taken with a Finnigan 3500 spectrometer. IR spectra were recorded on a Perkin-Elmer 881 spectrophotometer.

3,5-Diacetylpyridine (2)

3,5-Diacteyl-1,4-dihydropyridine (**1**)[7] (0.20 g, 1.2 mmol) was stirred with an equimolar amount of *p*-benzoquinone (0.13 g, 1.2 mmol) in 100 mL of dioxane at rt. After 8 h the solution was evaporated to dryness and the remaining oil was dissolved in toluene from which *p*-hydroquinone crystallized (0.10 g, 75 %). The mother liquid was evaporated to dryness again and the residual oil dissolved in petroleum ether from which **2** crystallized in white needles (0.18 g, 90%), mp 71-72 °C (lit.,[7] 72 °C).

3,5-Diacetylpyridinum perchlorate (3)

3,5-Diacteyl-1,4-dihydropyridine (**1**) (0.20 g, 1.2 mmol) was stirred with an equimolar amount of *p*-benzoquinone (0.13 g, 1.2 mmol) in 100 mL of dioxane/$HClO_4$ (5%) for 6 h at rt. The precipitate was filtered off and recrystallized from chloroform/acetone under the dropwise addition of toluene in white needles, mp 108-109 °C (0.30 g, 95%). IR (KBr): 1705 (CO) cm^{-1}. MS *m/z*: 163 (M^+ - base), 148 (M^+-CH_3). ^{1}H NMR (DMSO-d_6): 9.31 (br s, 2 H, 2-H, 6-H), 8.66 (br t, $J_{2,6/4}$ = 2 Hz, 1 H, 4-H), 7.78 (br s, exchangeable, 1 H, N^+H), 2.70 (s, 6 H, $COCH_3$). *Anal.* Calcd for $C_9H_9NO_2$ x $HClO_4$: C, 41.00; H, 3.82; N, 5.31. Found: C, 40.79; H, 3.77; N 5.21.

3,5-Diacetyl-4-(4-methoxyphenyl)-1,4-dihydropyridine (4a)

A mixture of 5 g (47 mmol) of the sodium salt of hydroxymethylenacetone,[8] 2.9 g (37 mmol) of ammonium carbonate in 30 mL of water and 3.3 g (24 mmol) of 4-methoxybenzaldehyde dissolved in 25 mL of ethanol was stirred at rt for 1 h and then heated at 85 °C for additional 5 h. After that the solution was extracted with chloroform (3 x 150 mL), the combined extracts were dried over sodium sulphate and evaporated. The crude reaction product partly dissolved in a mixture of ethyl acetate/ethanol/petroleum ether/acetone/chloroform. The insoluble residue consisted of pure **4a** as yellow powder, mp 214-216 °C (2.1 g, 32%). IR (KBr): 3321 (*N*H), 1628 (CO) cm^{-1}. MS *m/z*: 271 (M^+). ^{1}H NMR (DMSO-d_6): 9.43 (t, $J_{1/2,6}$ = 5 Hz, 1 H, exchangeable, *N*H), 7.52 (d, $J_{1/2.6}$ = 5 Hz, after D_2O-exchange s, 2 H, 2-H, 6-H), 7.03-6.72 (m, 4 H, aromat. *H*), 4.89 (s, 1 H, 4-H), 3.66 (s, 3 H, OCH_3), 2.12 (s, 6 H, $COCH_3$). *Anal.* Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N 5.20. Found: C, 70.90; H, 6.46; N 4.84.

3,5-Diacetyl-4-(4-methoxyphenyl)-1-methyl-1,4-dihydroypridine (4b)

1.0 g (3.7 mmol) of **4a** dissolved in 3 mL of dimethylpropyleneurea (DMPU) were treated with 80% sodium hydride suspension in oil (7 g, 5.6 mmol). After stirring for 1 h at rt 0.53 g (3.7 mmol) of methyl iodide were added. Having stirred for additional 2 h at rt the excess of sodium hydride was hydrolysed with portions of

water. Left standing overnight the separated, semisolid product was filtered off and recrystallized from toluene in yellow crystals, mp 172-174 °C, (0.25 g, 24%). IR (KBr): 1630 (CO) cm^{-1}. MS *m/z*: 285 (M^+). ^1H NMR ($CDCl_3$) 7.09 (s, 2 H, 2-H, 6-H), 7.25-6.76 (m, 4 H, aromat. H), 5.09 (s, 1 H, 4-H), 3.74 (s, 3 H, OCH_3), 3.34 (s, 3 H, *N*-CH_3), 2.15 (s, 6 H, $COCH_3$). *Anal.* Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.90. Found: C, 71.59; H, 6.70; N, 4.91.

5-Acetyl-1,2,3,4-tetrahydro-2,4-bis(4-methoxyphenyl)pyrimidine (5)

The solution of the crude reaction product of **4a** was evaporated and the residue dissolved in chloroform. The insoluble material turned out to be pure **5** as yellow powder, mp 238-239 °C (0.08 g, 6%). IR (KBr): 3212 (*N*H), 1609 (CO) cm^{-1}. MS *m/z*: 338 (M^+). ^1H NMR (DMSO-d_6): 7.74 (d, $J_{1/6}$ = 7 Hz, after D_2O exchange s, 1 H, 6-H), 7.63 (d, $J_{1/6}$ = 7 Hz, 1 H, exchangeable, *N*-1-H), 7.28-6.82 (m, 8 H, aromat. H), 4.83 (d, $J_{2/3}$ = 3 Hz, after D_2O exchange s, 1 H, 2-H), 4.52 (d, $J_{3/4}$ = 11 Hz, after D_2O exchange s, 1 H, 4-H), 3.75, 3.73 (s, 6 H, OCH_3), 2.92 (dd, $J_{3/4}$=11 Hz, $J_{2/3}$ = 3 Hz, 1 H, exchangeable, *N*-3-H), 2.09 (s, 3 H, $COCH_3$). *Anal.* Calcd for $C_{20}H_{22}N_2O_3$: C, 70.99; H, 6.66; N, 8.23. Found: C, 71.07; H, 6.67; N, 8.03.

3,5-Diacetyl-4-(4-methoxyphenyl)pyridine (6)

3,5-Diacetyl-4-(4-methoxyphenyl)-1,4-dihydropyridine (**4a**) (0.3 g, 1.1 mmol) was heated with 0.6 g (6.9 mmol) manganese(IV) oxide in boiling toluene (100 mL) for 10 h. After that the oxidizing reagent was filtered off of the solution which was dried over sodium sulphate and evaporated. The residual oil was dissolved in petroleum ether from which **6** crystallized in white needles, mp 97-98 °C (0.12 g, 40%). IR (KBr): 1685 (CO) cm^{-1}. MS *m/z*: 269 (M^+). ^1H NMR ($CDCl_3$): 8.74 (s, 2 H, 2-H, 6-H), 7.27-6.98 (m, 4 H, aromat. H), 3.88 (s, 3 H, OCH_3), 1.96 (s, 6 H, $COCH_3$). *Anal.* Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.57; H, 5.66; N, 5.11.

5-Acetyl-2,4-bis(4-methoxyphenyl)pyrimidine (7)

5-Acetyl-1,2,3,4-tetrahydro-2,4-bis(4-methoxyphenyl)pyrimidine (**5**) (0.3 g, 0.9 mmol) was heated with 0.6 g (6.9 mmol) manganese(IV) oxide in boiling toluene (100 mL) for 14 h. After that the oxidizing reagent was filtered off of the solution which was dried over sodium sulphate and evaporated. The residual oil was dissolved in ether from which **7** crystallized as white powder, mp 159-160 °C (0.1 g, 33%). IR (KBr): 1675 (CO) cm^{-1}. MS *m/z*: 334 (M^+), 319 (M^+-CH_3). ^1H NMR ($CDCl_3$): 8.85 (s, 1 H, 6-H), 8.56-6.98 (m, 8 H, aromat. H), 3.90 (s, 6 H, OCH_3), 2.19 (s, 3 H, $COCH_3$). *Anal.* Calcd for $C_{20}H_{18}N_2O_3$: C, 71.84; H, 5.42; N, 8.37. Found: C, 71.60; H, 5.23; N, 8.15.

4(*SR*),4a(*RS*),9a(*RS*)-3,4a-Diacetyl-1,4,4a,9a-tetrahydro-6-hydroxy-4-(4-methoxyphenyl)benzo-[4,5]dihydrofuro[2,3-*b*]pyridine (9a)

3,5-Diacetyl-4-(4-methoxyphenyl)-1,4-dihydropyridine (**4a**) (0.5 g, 1.8 mmol) and 0.19 g (1.8 mmol) of *p*-benzoquinone were stirred at rt in dioxane/(5%) $HClO_4$ (100 mL) for 48 h. After that the solution was evaporated and the residual oil dissolved in isopropyl alcohol from which **9a** crystallized as brownish powder

(0.55 g). It was recrystallized from toluene, mp 190-192 °C (0.5 g, 75%). IR (KBr): 3374 (OH), 3308 (NH), 1707 (C-4a-$COCH_3$), 1608 (C-3-$COCH_3$) cm^{-1}. MS *m/z*: 379 (M^+), 336 (M^+-$COCH_3$). ^1H NMR (DMSO-d_6): 9.14 (s, 1 H, exchangeable, OH), 7.87 (d, $J_{1/2}$ = 7 Hz, 1 H, exchangeable, *N*H), 7.49 (d, $J_{1/2}$ = 7 Hz, after D_2O exchange s, 1 H, 2-H), 7.20-7.16 (m, 2 H, 2´-H, 6´-H), 6.92 (d, $J_{5/7}$ = 2 Hz, 1 H, 5-H), 6.79-6.75 (m, 2 H, 3´-H, 5´-H), 6.65 (d, $J_{7/8}$ = 9 Hz, 1 H, 8-H), 6.58 (dd, $J_{7/8}$ = 9 Hz, $J_{5/7}$ = 2 Hz, 1 H, 7-H), 6.31 (s, 1 H, 9a-H), 4.76 (s, 1 H, 4-H), 3.69 (s, 3 H, OCH_3), 2.00 (s, 3 H, C-3-$COCH_3$), 1.90 (s, 3 H, C-4a-$COCH_3$). *Anal.* Calcd for $C_{22}H_{21}NO_5$: C, 69.65; H, 5.58; N, 3.69. Found: C, 69.12; H, 5.17; N, 3.48.

4(*SR*),4a(*RS*),9a(*RS*)-3,4a-Diacetyl-1,4,4a,9a-tetrahydro-6-hydroxy-4-(4-methoxyphenyl)-1-methylbenzo[4,5]dihydrofuro[2,3-*b*]pyridine (9b)

3,5-Diacetyl-4-(4-methoxyphenyl)-1-methyl-1,4-dihydroypridine (**4b**) (0.5 g, 1.8 mmol) and and 0.19 g (1.8 mmol) of *p*-benzoquinone were stirred at rt in dioxane/5% $HClO_4$ (100 mL) for 48 h. After that the solution was evaporated and the remaining brownish powder (0.7 g) of **9b** was recrystallized from toluene, mp 243-245 °C (0.56 g, 80%). IR (KBr): 3394 (OH), 1708 (C-4a-$COCH_3$), 1607 (C-3-$COCH_3$) cm^{-1}. MS *m/z*: 393 (M^+), 350 (M^+-$COCH_3$). ^1H NMR (DMSO-d_6): 9.17 (s, 1 H, exchangeable, OH), 7.57 (s, 1 H, 2-H), 7.18-7.13 (m, 2 H, 2´-H, 6´-H), 6.93 (d, $J_{5/7}$ = 2 Hz, 1 H, 5-H), 6.79-6.75 (m, 2 H, 3´-H, 5´-H), 6.70 (d, $J_{7/8}$ = 9 Hz, 1 H, 8-H), 6.58 (dd, $J_{7/8}$ = 9 Hz, $J_{5/7}$ = 2 Hz, 1 H, 7-H), 6.18 (s, 1 H, 9a-H), 4.77 (s, 1 H, 4-H), 3.70 (s, 3 H, OCH_3), 3.17 (s, 3 H, *N*-CH_3), 1.99 (s, 3 H, C-3-$COCH_3$), 1.92 (s, 3 H, C-4a-$COCH_3$). *Anal.* Calcd for $C_{23}H_{23}NO_5$: C, 70.21; H, 5.89; N, 3.55. Found: C, 70.35; H, 6.15; N, 3.81.

4(*SR*),4a(*RS*),9a(*RS*)-6-Acetoxy-1,3,4a-triacetyl-1,4,4a,9a-tetrahydro-4-(4-methoxyphenyl)benzo-[4,5]dihydrofuro[2,3-*b*]pyridine (10a)

4(*SR*),4a(*RS*),9a(*RS*)-3,4a-Diacetyl-1,4,4a,9a-tetrahydro-6-hydroxy-4-(4-methoxyphenyl)benzo-[4,5]dihydrofuro[2,3-*b*]pyridine **(9a)** (0.3 g, 0.8 mmol) was dissolved in 100 mL of acetic anhydride. After addition of 10 drops of pyridine the solution was stirred for 2 h at rt and then evaporated. The residue was taken up in warm cyclohexane from which **10a** crystallized as white powder, mp 255-256 °C (0.19 g, 50%). IR (KBr): 1762 (C-6-CH_3COO), 1711 (C-4a-CH_3CO), 1636 (*N*-$COCH_3$), 1609 (C-3-CH_3CO) cm^{-1}. MS *m/z*: 463 (M^+). ^1H NMR ($CDCl_3$): 8.21 (s, 1 H, 2-H), 7.17 (d, $J_{5/7}$ = 2 Hz, 1 H, 5-H), 7.09-7.05 (m, 2 H, 2´-H, 6´-H), 6.95 (dd, $J_{7/8}$ = 9 Hz, $J_{5/7}$ = 2 Hz, 1 H, 7-H), 6.81 (d, $J_{7/8}$ = 9 Hz, 1 H, 8-H), 6.79 (s, 1 H, 9a-H), 6.79-6.75 (m, 2 H, 3´-H, 5´-H), 4.98 (s, 1 H, 4-H), 3.75 (s, 3 H, OCH_3), 2.66 (br s, 3 H, *N*-$COCH_3$), 2.29 (s, 3 H, C-6-CH_3COO), 2.18 (s, 3 H, C-3-CH_3CO), 2.13 (s, 3 H, C-4a-CH_3CO). *Anal.* Calcd for $C_{26}H_{25}NO_7$: C, 67.38; H, 5.43; N, 3.02. Found: C, 67.03; H, 5.26; N, 2.79.

4(*SR*),4a(*RS*),9a(*RS*)-6-Acetoxy-3,4a-diacetyl-1,4,4a,9a-tetrahydro-4-(4-methoxyphenyl)-1-methylbenzo[4,5]dihydrofuro[2,3-*b*]pyridine (10b)

4(*SR*),4a(*RS*),9a(*RS*)-3,4a-Diacetyl-1,4,4a,9a-tetrahydro-6-hydroxy-4-(4-methoxyphenyl)-1-methylbenzo[4,5]dihydrofuro[2,3-*b*]pyridine (**9b**) (0.24 g, 0.6 mmol) was dissolved in 20 mL of acetic

anhydride. After addition of 10 drops of pyridine the solution was stirred for 2 h at rt and then evaporated. The remaining oil was dissolved in toluene from which **10b** crystallized in white needles, mp 196-198 °C (0.21 g, 80%). IR (KBr): 1759 (C-6-CH_3COO), 1706 (C-4a-CH_3CO), 1605 (C-3-CH_3CO) cm^{-1}. MS *m/z*: 435 (M^+), 392 (M^+-$COCH_3$). ^1H NMR ($CDCl_3$): 7.50 (s, 1 H, 2-H), 7.23-7.13 (m, 3 H, 5-H, 2´-H, 6´-H), 6.93 (dd, $J_{7/8}$ = 9 Hz, $J_{5/7}$ = 2 Hz, 1 H, 7-H), 6.82 (d, $J_{7/8}$ = 9 Hz, 1 H, 8-H), 6.79-6.73 (m, 2 H, 3´-H, 5´-H), 6.36 (s, 3 H, 9a-H), 4.87 (s, 1 H, 4-H), 3.75 (s, 3 H, OCH_3), 3.20 (s, 3 H, *N*-CH_3), 2.28 (s, 3 H, C-6-CH_3COO), 2.06 (s, 3 H, C-3-CH_3CO), 2.01 (s, 3 H, C-4a-CH_3CO). *Anal.* Calcd for $C_{25}H_{25}NO_6$: C, 68.95; H, 5.79; N, 3.21. Found: C, 69.12; H, 5.88; N, 3.05.

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