REGIOSELECTIVE FORMATION OF NOVEL FUNCTIONALIZED 1-AZA-9-OXAFUORENES

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Abstract - A small series of novel 1-aza-9-oxafuorenes have been prepared by regioselective cycloaddition reaction of \( p \)-benzoquinone to the sterically unhindered side of unsymmetrically substituted \( N \)-acyl-1,4-dihydropyridines (1). The stereochemistry of the products is discussed on the basis of X-Ray crystal structure analysis of one starting structure (1a). The formation of pyridine derivatives by possible redox reaction of the adducts was not observed. Rotameric properties of the \( N \)-acyl-1,4-dihydropyridines are demonstrated by \( ^1 \)H and \( ^{13} \)C NMR spectroscopy, thus stabilizing the 1,4-dihydropyridine system towards competing oxidation by the quinone.

Recent investigations in the redox behavior of symmetrically substituted \( NH \) and \( N \)-alkyl-4-phenyl-1,4-dihydropyridines and \( p \)-benzoquinone showed that instead of being oxidized the dihydropyridine derivatives undergo cycloaddition reaction with the quinone to 1-aza-9-oxafuorenes.\(^1\) Steric hindrance based on the pseudoaxial orientation of the phenyl moiety was discussed to prevent the formation of a CT complex between oxidizing quinone and dihydropyridine thus preventing further redox reaction of the compounds.\(^1\) As novel functionalized tricyclic systems, 1-aza-9-oxafuorenes are presently investigated as potential cytostatic agents with DNA intercalating properties.\(^2\) However, with the phenyl substituent of the first reported derivatives\(^1\) standing out of the molecular plane their potential intercalating properties will be low. The current pharmacological interest in these substance class additionally as antiviral agents\(^3\) encouraged to create varied structures following the facile synthetic route of the reported cycloaddion reaction between quinone and 1,4-dihydropyridine. We now report the regioselective formation of 1-aza-9-oxafuorenes using unsymmetrically substituted 1,4-dihydropyridine derivatives. Surprisingly, also the
4-methyl substituted compounds were not oxidized by $p$-benzoquinone. The stereochemistry of the cycloaddition products as well as the certain stability of the $N$-acyl-1,4-dihydropyridines towards competing oxidations are discussed.

**Results and Discussion**

The $N$-acetyl 3-ethoxycarbonyl-1,4-dihydropyridines (1a, b) have been synthesized in two steps: First ethyl nicotinate was $N$-acetylated at low temperatures (-8 °C). Then regioselective arylation or alkylation at 4-position of the pyridinium ring was carried out using Grignard reagents and catalytic amounts of copper(I) iodide.\textsuperscript{4,5} For preparation of corresponding 3-acetyl derivatives (1c, d) the temperature for acetylation was lowered to -15 °C so that no attack of the 3-acetyl group of the pyridine took place. The one-pot synthesis gave the 1,4-dihydropyridines (1a-d) in yields of about 85%.

With two kinds of proton signals for 2-H and 6-H of the dihydropyridine the existence of two rotamers A and B was proved (see **EXPERIMENTAL**). In the $^{13}$C NMR spectrum of selected derivative (1a) corresponding double signals for both C-atoms, C-2 and C-6, were found. While the carbon-atom of the $N$-acyetyl group also gave two signals, the signal of the methyl-C was splitted.

Under acid conditions, 5% of perchloric acid in dioxane, treatment of equimolar mixtures of 1,4-dihydropyridines (1a-d) with $p$-benzoquinone at room temperature yielded one single product monitored by TLC. Within 24 hours the reactions were completed and following preparative TLC led to isolation of 1-aza-9-oxafluorene derivatives (2a-d) (Scheme 2).
The compounds show characterizing IR-absorptions of the N-acetyl group between $\leq 1628 - 1680$ cm$^{-1}$. In comparison to the 1,4-dihydropyridine derivatives (1a, b) the almost unchanged absorptions of the ester carbonyl groups at 1691 cm$^{-1}$ (2a) and 1709 cm$^{-1}$ (2b), respectively, indicated an unchanged vinylogous carbamide ester partial structure in the reaction products, so that an exclusive attack of the $p$-benzoquinone at the enamine side of the dihydropyridine as the sterically unhindered side was suggested. In the $^1$H NMR spectra the 9a-protons with characteristic high field shift between 5.10 and 5.91 ppm appear as doublets, so that the regioselective addition of the quinone at the enamine side of the dihydropyridine was confirmed by coupling of 9a-H to 4a-H with coupling constants $^3J_{9a,4a}$ of about 7.3 Hz. Moreover, the resonances of the 2-protons were found unchanged compared to the dihydropyridines due to the intact carbamide ester structure in 2a-d.

For characterization of the cycloaddition product formation X-Ray crystal structure of one starting 1,4-dihydropyridine (1a) was determined.

![Scheme 2](image-url)
In the molecular structure of \( \text{1a} \) the 4-phenyl substituent shows pseudoaxial orientation as has been reported for the symmetrically substituted 4-phenyl dihydropyridines.\(^6,7\) In consequence, the attack of the \( p \)-benzoquinone will take place from the back side of the dihydropyridine ring thus leading to a Michael addition intermediate that undergoes a following ring closure to the tetrahydropyridine annelated benzofuran product (Scheme 2). In order to decide, whether the ring junction in \( \text{2a-d} \) would be \textit{cis} or \textit{trans} the proton coupling constants of \( 9a\text{-H} \) and \( 4a\text{-H} \) were compared to those of \textit{cis}-orientated \( 4\text{-H} \) and \( 5\text{-H} \) of the \( C_2 \)-symmetric tetrakishomocubane derivative\(^5\) shown in Figure 1 (right). These protons are coupling with a constant of \( ^3J_{4,5} = 9.4 \text{ Hz} \). Furthermore, the \textit{trans}-coupling between \( 4\text{-H} \) and \( 3\text{-H} \) at C-3 with an axially standing phenyl substituent makes \( ^3J_{4,3} = 1.9 \text{ Hz} \). Thus, the ring junction in compounds (\( \text{2a-d} \)) will be \textit{cis} and the coupling of \( 4\text{-H} \) and \( 4\text{-H} \) with \( ^3J_{4a,4} = 1-2 \text{ Hz} \) results from the corresponding pseudoaxial orientation of the phenyl ring as has been shown for the starting 1,4-dihydropyridine (\( \text{1a} \)). Comparing to previous reports of \( N \)-alkyl-1,4-dihydropyridines as NADH or NAD model compounds\(^8,9\) that are being oxidized by quinone derivatives the \( N \)-acyl derivatives (\( \text{1a-d} \)) prove to be stable towards possible competing oxidation by the quinone. However, manganese(IV) oxide treatment in boiling toluene leads to corresponding pyridines (\( \text{3a-d} \)). TLC comparison with the reaction mixture of \( \text{1a-d} \) and \( p \)-benzoquinone showed that no pyridine derivative was formed during the cycloaddition reaction. Obviously, the \( N \)-acyl substituted 1,4-dihydropyridines are stabilized towards quinone oxidation. The stability may result from enhanced conjugation possibilities of the dihydropyridine double bonds with the \( N \)-acyl group. This is supported by the observed rotameric properties of the dihydropyridines that reflect enhanced conjugation over the \( N \)-acyl group.
In summary, the regioselectively controlled cycloaddition reaction between unsymmetrically substituted 1,4-dihydropyridines and \(p\)-benzoquinone leads to novel 1-aza-oxafluorenes that are exclusively yielded by a uniform reaction without possible side products.

**EXPERIMENTAL**

\(^1\)H NMR spectra were recorded with a Varian Gemini-400 and Varian Gemini-500 with tetramethylsilane (TMS) as an internal standard. \(^13\)C NMR spectra were measured with the Varian Gemini-500. Chemical shifts are given on the \(\delta\) scale (ppm). The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, sh = shoulder, spl = splitted. MS was taken with a AMD 402 spectrometer. IR spectra were recorded on a Bruker IFS-28 spectrophotometer. Preparative TLC was carried out with silica gel plates 60F254 with a layer thickness of 1 mm.

**General Procedure for the Preparation of 1-Acetyldihydropyridines**

1.0 g (6.62 mmol) of ethyl nicotinate or 0.8 g (6.62 mmol) of 3-acetylpyridine were solved in 60 mL of anhydrous THF. After addition of copper(I) iodide 0.06 g (0.33 mmol) the solution was cooled down to -8 °C for preparation of \(1a, b\) and to -15 °C for preparation of \(1c, d\). Then 0.52 g (6.62 mmol) of acetyl chloride were added dropwise to the solution. The reaction mixture was stirred for 15 min at the low temperatures, Then 6.6 mL (6.6 mmol) of a 1 M solution of phenylmagnesium chloride or methylmagnesium chloride were added. Stirring was continued for 15 min and for additional 30 min at rt. Then 36 mL of an aqueous solution of ammonium chloride (20%, 7.2 g, 134.6 mmol) were added, followed by the extraction with ether (3 x 150 mL). The ether phase was then washed with 36 mL of a 20% solution mixture (1/1) of ammonia/ammonium chloride (3.6 g, 67.3 mmol), 36 mL of water, 36 mL of 10% hydrochloric acid (2 x), 36 mL of water and 36 mL of a saturated solution of sodium chloride. The ether phase was dried over sodium sulfate. After filtration the ether was removed under vacuum leaving yellow oils of \(1a, 1b\) and \(1d\) and a yellow powder of \(1d\).

**Ethyl 1-Acetyl-1,4-dihydro-4-phenylpyridine-3-carboxylate (1a)**

Colorless needles from methanol, mp 55-57 °C (1.35 g, 75%). IR (KBr): 1693 (COOCH\(_2\)CH\(_3\)), 1680 (NCOCH\(_3\)) cm\(^{-1}\). MS m/z: 271 (M\(^+\)). \(^1\)H NMR (CDCl\(_3\)): 8.37 (br s, 1 H, 2-H, \(1a, b\)), 7.80 (br s, 1 H, 2-H, \(1a, b\)), 7.30-7.16 (m, 11 H, aromat. H, \(1a, b\)), 6.60 (br "s", 1 H, 6-H, \(1a, b\)), 5.24 (br m, 2 H, 5-H, \(1a, b\)), 4.47 (d, \(3J_{4,5} = 4.3\) Hz, 2 H, 4-H, \(1a, b\)), 4.05 (q, \(3J = 7.2\) Hz, 4 H, COOCH\(_2\)CH\(_3\), \(1a, b\)), 2.37 (br s, 6 H, NCOCH\(_3\), \(1a, b\)), 1.14 (t, \(3J = 7.2\) Hz, 6 H, COOCH\(_2\)CH\(_3\), \(1a, b\)). \(^13\)C NMR (CDCl\(_3\)): 166.98, 166.63 (COCH\(_3\), \(1a, b\)), 166.64 (COOCH\(_2\)CH\(_3\), \(1a, b\)), 144.66 (C1´, \(1a, b\)), 132.13 (C2, \(1a, b\)), 130.03 (C2, \(1a, b\)), 128.55 (C3´, C5´, \(1a, b\)), 128.12 (C4´, \(1a, b\)), 126.91 (C2´, C6´, \(1a, b\)), 121.05 (C6, \(1a, b\)), 119.28 (C6, \(1a, b\)), 113.55 (C5, \(1a, b\)), 113.52 (C3, \(1a, b\)), 60.49 (CH\(_2\)CH\(_3\), \(1a, b\)), 39.18 (C4, \(1a, b\)), 21.33 (spl, COCH\(_3\), \(1a, b\)), 13.93 (CH\(_2\)CH\(_3\), \(1a, b\)). Anal. Calcd for C\(_{16}\)H\(_{17}\)NO\(_3\): C, 70.83; H, 6.32; N 5.16. Found: C, 70.96; H 6.40; N 5.09.

X-Ray Diffraction Analysis of \(1a\): A colourless crystal C\(_{16}\)H\(_{17}\)NO\(_3\) (from methanol), crystal size 0.38 x
0.29 x 0.23 mm, was measured at a temperature of 220 (2) K by using a Stoe-IPDS Diffractometer with Mo-K$_\alpha$ radiation ($\lambda$ = 0.71073 Å) and a graphite monochromator. 9186 Reflexions were collected in the range 5.06$^\circ$ ≤ 2$\Theta$ ≤ 51.82$^\circ$; h,k,l range from –13, -9, -18 to 14, 9, 20. Crystal system: Monoclinic, space group $P2_1/c$, Z = 4, $a$ = 11.5025(15) Å, $b$ = 7.4994(14) Å, $c$ = 16.326(2) Å, $\beta$ = 99.593(16)$^\circ$; $V$ = 1388.6(4) Å$^3$; $D_x$ = 1.298 g cm$^-3$; $\mu$ = 0.090 mm$^-1$. The structure was solved by direct methods (SHELXS-97$^{10}$) using 2586 independent reflections. Structure refinement: Full matrix least-squares methods on $F^2$ using SHELXL-97$^1$, all the non-hydrogen atoms with anisotropic displacement parameters. All hydrogen atoms were taken from a difference fourier synthesis and isotropically refined. The refinement converged to a final $wR_2 = 0.1285$ for 2586 unique reflections and $R_1$ = 0.0470 for 1923 observed reflections [$I_0 > 2.0\Phi(I_0)$] and 249 refined parameters.

**Ethyl 1-Acetyl-1,4-dihydro-4-methylpyridine-3-carboxylate (1b)**

Yellow oil (1.12 g, 81%). IR (CHCl$_3$): 1694 (COOCH$_2$CH$_3$), 1672 (NCOCH$_3$) cm$^-1$. MS $m/z$: 209 (M$^+$). $^1$H NMR (CDCl$_3$): 8.14 (br s, 1 H, 2-H, A), 7.61 (br s, 1 H, 2-H, A), 7.06 (br d, $^3$J$_{6,5}$ = 6.4 Hz, 1 H, 6-H, A), 6.49 (d, $^3$J$_{6,5}$ = 9.8 Hz, 1 H, 6-H, B), 5.14 (br m, 2 H, 5-H, A, B), 4.19 (q, $^3$J = 7.0 Hz, 4 H, COOCH$_2$CH$_3$, A, B), 3.30 (dq, $^3$J$_{4,5}$ = 3.99 Hz, $^3$J = 6.84 Hz, 2 H, 4-H, A, B), 2.12 (s, 6 H, NCOCH$_3$, A, B), 1.27 (t, $^3$J = 7.0 Hz, 6 H, COOCH$_2$CH$_3$, A, B), 1.13 (d, $^3$J = 6.84 Hz, 6 H, C4-CH$_3$, A, B). For elemental analysis of the pyridine-picrate (3b) see below.

**1,3-Diacetyl-1,4-dihydro-4-phenylpyridine (1c)**

Yellow powder, mp 122-126 $^\circ$C from methanol (1.40 g, 88%). IR (KBr): 1704 (COCH$_3$), 1671 (NCOCH$_3$). MS $m/z$: 241 (M$^+$). $^1$H NMR (CDCl$_3$): 8.33 (br s, 1 H, 2-H, B), 7.34-7.15 (m, 12 H, aromat. H, A, B, 2-H, 6-H, A), 6.60 (br "s", 1 H, 6-H, B), 5.32-5.26 (br m, 2 H, 5-H, A, B), 4.58 (d, $^3$J$_{4,5}$ = 3.78 Hz, 2 H, 4-H, A, B), 2.34 (s, 6 H, COCH$_3$, A, B), 2.27 (s, 6 H, NCOCH$_3$, A, B). Anal. Calcd for C$_{15}$H$_{15}$NO$_2$: C, 74.69; H, 6.22; N, 5.81. Found: C, 74.38, H, 6.24, N, 5.73.

**1,3-Diacetyl-1,4-dihydro-4-methylpyridine (1d)**

Yellow oil (1.0 g, 84%). IR (CHCl$_3$): 1704 (COCH$_3$), 1659 (NCOCH$_3$) cm$^-1$. MS $m/z$: 179 (M$^+$). $^1$H NMR (CDCl$_3$): 8.12 (br s, 1 H, 2-H, B), 7.50 (br s, 1 H, 2-H, A), 7.07 (br "s", 1 H, 6-H, A), 6.49 (br "s", 1 H, 6-H, B), 5.16 (br m, 2 H, 5-H, A, B), 3.39 (dq, $^3$J$_{4,5}$ = 5.08 Hz, $^3$J = 6.84 Hz, 2 H, 4-H, A, B), 2.31 (s, 6 H, COCH$_3$, A, B), 2.27 (s, 6 H, NCOCH$_3$, A, B), 1.07 (d, $^3$J = 6.84 Hz, 6 H, C4-CH$_3$, A, B). For elemental analysis of the pyridine-picrate (3d) see below.

**General Procedure for the Preparation of 1-Aza-9-oxafluorenes**

A mixture of 1 g (3.7 mmol) of 1a or 0.77 g (3.7 mmol) of 1b, 0.89 g (3.7 mmol) of 1c or 0.66 g (3.7 mmol) of 1d with 0.4 g (3.7 mmol) of $p$-benzoquinone was solved in a minimum volume of dioxane/HClO$_4$ (5%). The mixture was stirred at rt for 24 h and then poured into ice-water. Extraction with ether (3 x 150 mL) followed and the organic phase was dried over sodium sulfate. After filtration ether was removed in vacum leaving a brownish oil. Preparative TLC of the oil in chloroform / ethyl acetate /
methanol (85/15/2) led to compounds (2a-d).

**Ethyl 4(SR),4a(RS),9a(RS)-1-Acetyl-6-hydroxy-4-phenyl-1,4,4a,9a-tetrahydrobenzo[4,5]furo[2,3-b]-pyridine-3-carboxylate (2a)**

Yellow oil (0.77 g, 55%). IR (CHCl₃): 3374 (OH), 1691 (COOCH₂CH₃), 1640 (NCOCH₃). MS m/z: 379 (M⁺). ¹H NMR (CDCl₃): 8.40 (br s, 1 H, 2-H), 7.35-7.19 (m, 5 H, aromat. H), 6.73 (d, ⁴J₅,₇ = 1.4 Hz, 1 H, 5-H), 6.66 (d, ³J₈,₇ = 8.5 Hz, 1 H, 8-H), 6.61 (dd, ⁴J₇,₅ = 1.4 Hz, 1 H, 7-H), 6.13 (br "s", 1 H, 9a-H), 5.10 (s, 1 H, OH, exchangeable), 4.32 (d, ³J₄,₄a = 2.5 Hz, 1 H, 4-H), 4.21 (dd, ³J₄a,₉a = 7.5 Hz, ³J₄a,₄ = 2.5 Hz, 1 H, 4a-H), 4.08 (q, ³J = 7.5 Hz, 2 H, COOCH₂CH₃), 2.42 (s, 3 H, NCOCH₃). Anal. Calcd for C₂₂H₂₁NO₅: C, 69.65; H, 5.58; N, 3.69. Found: C, 69.66; H, 5.46; N, 3.62.

**Ethyl 4(RS),4a(RS),9a(RS)-1-Acetyl-6-hydroxy-4-methyl-1,4,4a,9a-tetrahydrobenzo[4,5]furo[2,3-b]-pyridine-3-carboxylate (2b)**

Brownish powder, mp > 360 °C from ether (0.76 g, 65%). IR (KBr): 3375 (OH), 1709 (COOCH₂CH₃), 1680 (NCOCH₃). MS m/z: 317 (M⁺). ¹H NMR (CDCl₃): 8.15 (br s, 1 H, 2-H), 6.61-6.57 (m, 3 H, 5-H, 8-H, 7-H), 5.91 (br "s", 1 H, 9a-H), 4.19 (s, 1 H, OH, exchangeable), 4.13 (q, ³J = 7.0 Hz, 2 H, COOCH₂CH₃), 3.93 ("d", ³J₄₆,₉a = 7.8 Hz, 1 H, 4a-H), 4.32 (q, ³J = 6.4 Hz, 1 H, 4-H), 2.43 (br s, 3 H, NCOCH₃), 1.23 (d, ³J = 6.4 Hz, 3 H, C₄-CH₃), 1.22 (t, ³J = 7.0 Hz, 3 H, COOCH₂CH₃). Anal. Calcd for C₁₇H₁₉NO₅: C, 64.35; H, 5.99; N, 4.42. Found: C, 64.32; H, 5.67; N, 4.43.

**4(SR),4a(RS),9a(RS)-1,3-Diacetyl-6-hydroxy-4-phenyl-1,4,4a,9a-tetrahydrobenzo[4,5]furo[2,3-b]-pyridine (2c)**

Yellow crystals, mp 135-139 °C from ether (0.14 g, 88%). IR (KBr): 3247 (OH), 1710 (COCH₃), 1660 (NCOCH₃). MS m/z: 349 (M⁺). ¹H NMR (CDCl₃): 8.96 (br s, 1 H, 2-H), 7.31-7.29 (m, 5 H, aromat. H), 6.66 (d, ⁴J₅,₇ = 2.57 Hz, 1 H, 5-H), 6.59 (d, ³J₈,₇ = 9.52 Hz, 1 H, 8-H), 6.51 (dd, ³J₇,₈ = 9.52 Hz, ⁴J₇,₅ = 2.57 Hz, 1 H, 7-H), 5.65 (d, ³J₉₆,₄₆ = 7.32 Hz, 1 H, 9a-H), 4.34 ("s", 1 H, 4-H), 3.88 ("d", ³J₄₆,₉a = 7.32 Hz, 1 H, 4a-H), 2.10 (s, 3 H, COCH₃), 1.98 (s, 3 H, NCOCH₃). Anal. Calcd for C₂₁H₁₉NO₄: C, 72.21; H, 5.44; N, 4.01. Found: C, 72.52; H, 5.68; N, 4.21.

**4(RS),4a(RS),9a(RS)-1,3-Diacetyl-6-hydroxy-4-methyl-1,4,4a,9a-tetrahydrobenzo[4,5]furo[2,3-b]-pyridine (2d)**

Brownish powder, mp 249-252 °C from ether (0.80 g, 75%). IR (KBr): 3257 (OH), 1710 (COCH₃), 1628 (NCOCH₃). MS m/z: 287 (M⁺). ¹H NMR (CDCl₃): 7.66 (s, 1 H, 2-H), 6.64 (d, ³J₈,₇ = 8.4 Hz, 1 H, 8-H), 6.62 (d, ⁴J₅,₇ = 1.56 Hz, 1 H, 5-H), 6.59 (dd, ³J₇,₈ = 8.4 Hz, ⁴J₇,₅ = 1.56 Hz, 1 H, 7-H), 5.74 (d, ³J₉₆,₄₆ = 7.23 Hz, 1 H, 9a-H), 4.22 (br s, 1 H, OH, exchangeable), 3.71 ("d", ³J₄₆,₉a = 7.23 Hz, 1 H, 4a-H), 3.43 ("q", spl, ³J = 6.05 Hz, ³J₄₆ < 1 Hz, 1 H, 4-H), 2.72 (s, 3 H, COCH₃), 2.43 (br s, 3 H, NCOCH₃), 1.65 (d, ³J = 6.05 Hz, 3 H, C₄-CH₃). Anal. Calcd for C₁₆H₁₇NO₄: C, 66.88; H, 5.96; N, 4.88. Found: C, 66.87; H, 5.82; N, 4.82.
General Procedure for the Oxidation to Pyridines (3a-d)

1 g (3.7 mmol) of 1a, 0.77 g (3.7 mmol) of 1b, 0.89 g (3.7 mmol) of 1c and 0.66 g (3.7 mmol) of 1d were stirred in boiling toluene (100 mL) with a 10-fold molar excess (3.22 g, 37 mmol) of manganese(II) oxide for 72 h. Then the oxidizing reagent was filtered off and the solvent was removed in vacuum, leaving the pyridine derivatives as brownish oils (3a-d).

Ethyl 4-Phenylnicotinate (3a)

Yellow oil (0.67 g, 80%). IR (CHCl₃): 1724 (COOCH₂CH₃) cm⁻¹. MS m/z: 227 (M⁺). ¹H NMR (CDCl₃): 8.91 (s, 1 H, 2-H), 8.77 (d, 3J₆,₅ = 3.9 Hz, 1 H, 6-H), 7.42-7.29 (m, 6 H, aromat. H, 5-H), 4.14 (q, 3J = 7.03 Hz, 2 H, COOCH₂CH₃), 1.14 (t, 3J = 7.03 Hz, 3 H, COOCH₂CH₃). Anal. Calcd for C₂₀H₁₆N₄O₉ (picrate, mp 126-129 °C from ethanol): C, 52.63; H, 3.53; N, 12.28. Found: C, 52.95; H, 3.51; N, 12.14.

Ethyl 4-Methylnicotinate (3b)

Yellow oil (0.54 g, 88%). IR (CHCl₃): 1723 (COOCH₂CH₃) cm⁻¹. MS m/z: 165 (M⁺). ¹H NMR (CDCl₃): 9.06 (s, 1 H, 2-H), 8.54 (br "s", 1 H, 6-H), 7.17 (d, 3J₅,₆ = 4.69 Hz, 1 H, 5-H), 4.37 (q, 3J = 7.0 Hz, 2 H, COOCH₂CH₃), 2.60 (s, 3 H, C₄-CH₃), 1.39 (t, 3J = 7.0 Hz, 3 H, COOCH₂CH₃). Anal. Calcd for C₁₅H₁₄N₄O₉ x 0.5 H₂O (picrate, mp 128-134 °C from ethanol/water): C, 44.67; H, 3.75; N, 13.89. Found: C, 44.88; H, 3.82; N, 13.51.

3-Acetyl-4-phenylpyridine (3c)

Yellow oil (0.61 g, 83 %). IR (CHCl₃): 1692 (COCH₃) cm⁻¹. MS m/z: 197 (M⁺). ¹H NMR (CDCl₃): 8.80 (br "s", 2 H, 2-H, 6-H), 7.49-7.33 (m, 6 H, aromat. H, 5-H), 2.06 (s, 3 H, COCH₃). Anal. Calcd for C₁₉H₁₄N₄O₈ (picrate, mp 145-148 °C from ethanol): C, 53.52; H, 3.29; N, 13.15. Found: C, 53.38; H, 3.46; N, 12.81.

3-Acetyl-4-methylpyridine (3d)

Yellow oil (0.58 g, 79 %). IR (CHCl₃): 1692 (COCH₃) cm⁻¹. MS m/z: 135 (M⁺). ¹H NMR (CDCl₃): 8.91 (s, 1 H, 2-H), 8.77 (d, 3J₆,₅ = 7.81 Hz, 1 H, 6-H), 7.48 (d, 3J₅,₆ = 7.81 Hz, 1 H, 5-H), 2.56 (s, 3 H, COCH₃). Anal. Calcd for C₁₄H₁₂N₄O₈ (picrate, mp 137-140 °C from ethanol): C, 46.16; H, 3.32; N, 15.39. Found: C, 45.76; H, 3.32; N, 14.98.

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REFERENCES

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12. The brownish or yellow colors of compounds (2b-c) may be explained by the formation of intermolecular charge-transfer complexes between the hydroquinone partial structures on one hand and the nitrogen atoms of the enaminone partial structure that adopt positive charges in the system of conjugated double bonds on the other hand.