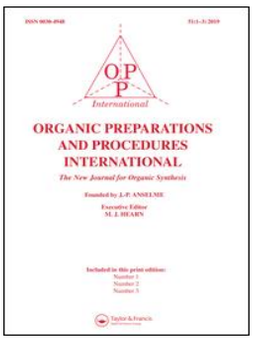

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EXPERIMENTAL PAPER

Ultrasound-Assisted Heterogeneous Oxidation of 1,4-Dihydropyridines

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1,4-Dihydropyridines are of enormous interest to synthetic chemists, in part because of their interesting biological applications. For example, they function as lead molecules for compounds with a wide variety of cardiovascular activities.[1] Oxidation of 1,4-dihydropyridine derivatives has attracted much attention because these compounds are oxidized to the corresponding pyridines by cytochrome p-450 in the liver.[2,3]

Some applications of manganese reagents for the oxidation of Hantzsch 1,4-dihydropyridines have been studied. Researchers have reported oxidation of 3,5-diester 1,4-dihydropyridines by manganese dioxide,[4] manganese triacetate,[5] potassium permanganate in the presence of tungstate sulfuric acid,[6] potassium permanganate in dichloromethane/water,[7] and in acetic acid.[8] Although some of the reported procedures have been successfully implemented for this purpose, a number of them have disadvantages, which include lengthy reaction times, low yields and cumbersome workup. There is thus a need for mild, green, inexpensive, and convenient methods for the oxidation of 1,4-dihydropyridines. In the course of our study of 1,4-dihydropyridines,[9–12] we have investigated the heterogeneous oxidation of 3,5-diacyl or 3,5-diester 1,4-dihydropyridines using $KMnO_4/CuSO_4{\cdot}5H_2O$ under ultrasound irradiation.

In heterogeneous reactions involving solids dispersed in liquids, the reactivity depends upon the available reactive surface area. Ultrasound leads to fragmentation and consequent particle size reduction.[13] In previous investigations, it was reported that, under heterogeneous reaction conditions, permanganate could be used for the oxidation of some compounds.[14–18] The ultrasound effect on the heterogeneous permanganate oxidation of benzyl alcohols and alkyl benzenes was reported.[19] Hence, in our present study, we aimed to investigate oxidation of 1,4-dihydropyridines with potassium permanganate adsorbed on a solid support, such as $CuSO_4{\cdot}5H_2O$, in a nonpolar organic solvent, accelerated by ultrasonic irradiation.

Ten 1,4-dihydropyridines were synthesized to investigate their conversions to the corresponding pyridines with $KMnO_4$ under ultrasonic irradiation (see Scheme 1).

For optimization of the reaction, we used diethyl 2,6-dimethyl-4-phenyl-1,4-dihydropyridine-3,5-dicarboxylate (**1b**) as a representative compound. Several solid supports were used for our heterogeneous oxidation reactions under ultrasonic irradiation (Table 1).

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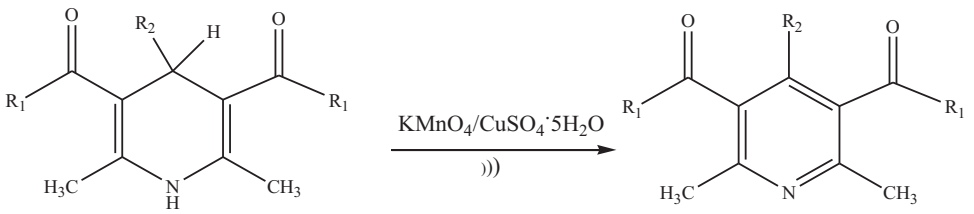

Scheme 1. Heterogeneous oxidative aromatization of 1,4-dihydropyridines.

Table 1. Effect of solid support on the oxidation with potassium permanganate.

Entry	Solid support (g)	$KMnO_4$ (g)	Time (min)	Yield (%)
1	$CuSO_4{\cdot}5H_2O$ (1.25)	1.25	20	94
2	$CuSO_4{\cdot}5H_2O$ (2.5)	1.25	30	92
3	$CuSO_4{\cdot}5H_2O$ (1.25)	0	45	0
4	Silica gel (2.5)	1.25	40	87
5	$BaCl_2{\cdot}2H_2O$ (1.25)	1.25	50	78
6	Al_2O_3 (1.25)	1.25	40	70
7	$MgSO_4{\cdot}7H_2O$ (1.25)	1.25	35	80
8	—————	1.25	70	89

As shown in Table 1, copper (II) sulfate pentahydrate is a more suitable support for this reaction. The oxidant was prepared by grinding equal amounts of potassium permanganate and copper sulfate pentahydrate.

The physical features of ultrasound irradiation enhance the kinetics and yield of permanganate oxidation.[20] In order to compare the effects of ultrasound and mechanical mixing, 1 mmol of **1b**, 2.5.g oxidant, and 20 cc CH_2Cl_2 at room temperature was irradiated under ultrasound irradiation or stirred without ultrasound (Table 2). The results indicated that ultrasonic irradiation leads to a shorter reaction time. In addition, oxidation of **1b** yields **2b** with retention of the substituent in position 4.

The results of oxidation of 1,4-dihydropyridines by $KMnO_4/CuSO_4{\cdot}5H_2O$ in CH_2Cl_2 under ultrasonic irradiation are summarized in Table 3.

As can be seen in Table 3, oxidation of **1a-1j** yielded **2a-2j** with retention of the substituent in position 4. Compounds **1a** and **1f,** with no substituent in position 4 of the dihydropyridine ring, converted to the corresponding pyridine in a shorter time than other 3,5-diester and 3,5-diacetyl 1,4-dihydropyridines. However, oxidation of 3,5-diacetyl 1,4-dihydropyridines was slower than 3,5-diester 1,4-dihydropyridines under the same conditions.

Furthermore, the efficiency of $KMnO_4/CuSO_4{\cdot}5H_2O$ under ultrasonic irradiation has been compared with other reagents used in the oxidative aromatization (Table 4). Most of these methods are used only for oxidation of 3,5-diester 1,4-dihydropyridines. The results of this study have now revealed that $KMnO_4/CuSO_4{\cdot}5H_2O$ under ultrasonic irradiation is an efficient, inexpensive, and safe reagent for the oxidation of 3,5-diacetyl and 3,5-diester 1,4-dihydropyridine derivatives with retention of the substituent in position 4.

Experimental section

All Hantzsch 1,4-dihydropyridines were synthesized according to the known procedures.[26–28] All products' specifications were determined, and their physical and spectroscopic data were compared with those of authentic samples. Melting points were

Table 2. The effect of ultrasound on the heterogeneous oxidation of 1,4-dihydropyridines with $KMnO_4/CuSO_4{\cdot}5H_2O$.

Condition	stirring	)))
Time	72 h	20 min
yield (%)	90	94

Table 3. Heterogeneous oxidative aromatization of some 1,4-dihydropyridines using $KMnO_4/CuSO_4{\cdot}5H_2O$ under ultrasonic irradiation.

Comp.	R_1	R_2	yield (%)[a]	Time (min)
1a	OC_2H_5	H	90	15
1b	OC_2H_5	C_6H_5	94	20
1c	OC_2H_5	4-ClC_6H_4	91	35
1d	OC_2H_5	3-$NO_2C_6H_4$	92	25
1e	OC_2H_5	4-$OCH_3C_6H_4$	97	30
1f	CH_3	H	90	18
1g	CH_3	C_6H_5	95	23
1h	CH_3	4-ClC_6H_4	90	42
1i	CH_3	3-$NO_2C_6H_4$	90	30
1j	CH_3	4-$OCH_3C_6H_4$	96	32

[a]Isolated yield.

determined on a Barnstead Electrothermal apparatus and were uncorrected; literature values are provided in parentheses, and the literature reference is supplied. IR spectra were recorded on Shimadzu IR-470 spectrometer, ^{1}HNMR data were obtained using a Brüker 300 MHz spectrometer in $CDCl_3$. Ultraviolet (UV) spectra were measured on an Agilent 8453 spectrometer. Elemental analyses were performed using a Perkin–Elmer 2400 Series II CHNS/O analyzer.

General procedure for preparation of oxidant

The oxidant was prepared by simply grinding equal weights of potassium permanganate and copper sulfate pentahydrate with a mortar and pestle until homogeneous.

General procedure for oxidation of 1,4-dyhdropyridines using potassium permanganate, supported on copper (II) sulfate pentahydrate, under ultrasonic irradiation

The 1,4-dihydropyridine (1.0 mmol) in CH_2Cl_2 (20 cc) and the oxidant (2.5 g) were irradiated in a glass reactor fitted to an ultrasonic horn (20 kHz, 400W) at room temperature. The progress of the reaction was followed by TLC (silica gel, petroleum ether:ethyl acetate 3:1) . In the next step when the reaction had completed, the reaction mixture was filtered and the residue was washed with CH_2Cl_2. Then the residue was allowed to dry and recrystallized using petroleum ether/ethyl acetate (4:1). The structures of the products were confirmed by spectroscopy, elemental analysis and comparison with authentic samples, which were prepared by methods in the literature.[4,5,28–32]

Diethyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1a)

M.p.: 170-172 °C (172-174 °C)[33]; UV-Vis (Methanol, nm): λ (log ε)=372 (3.84), 230 (4.18); FT- IR (KBr, cm^{-1}): 1696 (C = O), 3346 (N-H); ^{1}H NMR (300 MHz, $CDCl_3$,

Table 4. Oxidative aromatization of 1,4-dihydropyridines with $KMnO_4/CuSO_4{\cdot}5H_2O$ under ultrasonic irradiation.

Reagent	Conditions	Yield (%)	Time[ref.]
$KMnO_4/CuSO_4{\cdot}5H_2O$	)))/ CH_2Cl_2 / r.t.	90-97	15-42 min[This work]
MnO_2	CH_2Cl_2 / 20 °C	81-94	5-200 min[4]
$KMnO_4$ / Montrnorillonite	))) /CH_2Cl_2, H_2O / r.t.	>80	150-300 s[7]
$KMnO_4$	CH_3CO_2H / heat	34-80	5 h[8]
TSA[a]/$KMnO_4$	CH_2Cl_2 / r.t.	90-97	7-40 min[6]
Mn $(OAc)_3$	CH_3CO_2H / r.t.	91-98	20-90 min[5]
Na_2SO4 / TBHP[b]	EtOAC / air./ r.t.	73-96	2-6 h[21]
poly(4-vinylpyridinium nitrate) / silica sulfuric acid	CH_2Cl_2 / r.t.	79-98	0.5-9 h[22]
I_2	))) / CH_3CN	94-98	5-45 min[23]
$CuBr_2$	EtOAC, CH_3Cl / reflux	71-99	40-120 min[24]
SVA[c]–H_2O_2	CH_3CN / H_2O_2	50-97	9-90 min[25]

[a]Tungstate sulfuric acid.
[b]*tert*-Butylhydroperoxide.
[c]Silica vanadic acid.

ppm): $\delta = 1.28$ (t, J = 6.5 Hz, 6H, $CO_2CH_2\mathbf{CH_3}$), 2.19 (s, 6H, 2 and 6-CH_3), 3.26 (s, 2H, 4-H) , 4.16 (q, J = 6.5 Hz, 4H, $CO_2\mathbf{CH_2}CH_3$), 5.45 (br. s, 1H, NH).

Anal. Calcd for $C_{13}H_{19}NO_4$: C, 61.64; H, 7.56; N, 5.53. Found: C, 61.58; H, 7.61; N, 5.50.

Diethyl-2,6-dimethyl 4-phenyl–1,4-dihydropyridine-3,5-dicarboxylate (1b)

M.p.: 161-164 °C (160-162 °C)[33]; UV-Vis (Methanol, nm): λ (log ε)=355 (3.93), 238 (4.33); FT- IR (KBr, cm^{-1}): 1690 (C=O), 3343 (N-H); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 1.23$ (t, J = 6 Hz, 6H, $CO_2CH_2\mathbf{CH_3}$), 2.31 (s, 6H, 2 and 6-CH_3), 4.09 (q, J = 6 Hz, 4H, $CO_2\mathbf{CH_2}CH_3$), 5.00 (s, 1H, 4-H), 6.05 (brd s, 1H, NH), 7.24 (m, 5H, C_6H_5).

Anal. Calcd for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.04; N, 4.25. Found: C, 69.28; H, 7.03; N, 4.24.

Diethyl-4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1c)

M.p.: 145-147 °C (150 °C)[34]; UV-Vis (Methanol, nm): λ (log ε)=355 (3.90), 238 (4.36); FT- IR (KBr, cm^{-1}): 1696(C=O), 3359 (N-H); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 1.21$ (t, J = 7. 2 Hz, 6H, $CO_2CH_2\mathbf{CH_3}$), 2.31 (s, 6H, 2 and 6-CH_3), 4.11 (q, J = 7. 2 Hz, 4H, $CO_2\mathbf{CH_2}CH_3$), 4.96 (s, 1H, 4-H), 5.80 (brd s, 1H, NH), 7.19 (m, 4H, C_6H_4Cl).

Anal. Calcd for $C_{19}H_{22}ClNO_4$: C, 62.72; H, 6.09; N, 3.85. Found: C, 62.68; H, 6.10; N, 3.88.

Diethyl-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (1d)

M.p.: 163-165 °C (163 °C)[34]°C; UV-Vis (Methanol, nm): λ (log ε)=354 (3.81), 236 (4.43); FT- IR (KBr, cm^{-1}):1706 (C=O), 3345 (N-H); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 1.25$ (t, J = 7. 0 Hz, 6H, $CO_2CH_2\mathbf{CH_3}$), 2.34 (s, 6H, 2 and 6-CH_3), 4.11 (q, J = 7. 0 Hz, 4H, $CO_2\mathbf{CH_2}CH_3$), 5.01 (s, 1H, 4-H) , 5.85 (brd s, 1H, NH), 7.20 (m, 4H, $C_6H_4NO_2$).

Anal. Calcd for $C_{19}H_{22}N_2O_6$: C, 60.95; H, 5.92; N, 7.48. Found: C, 60.98; H, 5.93; N, 7.44.

Diethyl-4-(4-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1e)

M.p.: 160-162 °C (160 °C)[34]°C; UV-Vis (Methanol, nm): λ (log ε)=354 (3.92), 222 (4.34); FT- IR (KBr, cm^{-1}): 1690(C=O), 3343 (N-H); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 1.15(t, J = 7. 1 Hz; 6H, $CO_2CH_2\mathbf{CH_3}$), 2.24 (s, 6H, 2 and 6-CH_3), 3.68 (s, 3H, 4'-OCH_3), 4.01 (q, J = 7. 1, 4H, $CO_2\mathbf{CH_2}CH_3$), 4.85 (s, 1H, 4-H), 5.64 (brd s, 1H, NH), 7.12 (d.d, J = 6.3. 0 and 4.1 Hz, 4H, $C_6H_4OCH_3$).

Anal. Calcd for $C_{20}H_{25}NO_5$: C, 66.84; H, 7.01; N, 3.90. Found: C, 66.85; H, 7.03; N, 3.87.

3,5-Diacetyl-2,6- dimethyl-1,4-dihydropyridine (1f)

M.p.: 213-214 °C (213-215 °C)[33]°C; UV-Vis (Methanol, nm): λ (log ε)=407 (3.88), 251 (4.05); FT- IR (KBr, cm^{-1}): 1671 (C=O), 3392 (N-H); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 2.20 (s, 6H, 2 and 6-CH_3), 2.24 (s, 6H, 3-and 5-$COCH_3$), 5.30(s, 1H, NH), 4.37 (s, 2H, 4-H).

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.39; H, 7.83; N, 7.24.

Diacetyl-2,6-dimethyl-4-phenyl-1,4-dihydropyridine (1g)

M.p.: 184-186 °C (185-186 °C)[28]; UV-Vis (Methanol, nm): λ (log ε) = 382 (3.89), 255 (4.16); FT- IR (KBr, cm^{-1}): 1670 (C=O), 3321 (N-H); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 2.19 (s, 6H, 2 and 6-CH_3), 2.23 (s, 6H, 3-and 5-$COCH_3$), 5.03 (s, 1H, 4-H), 6.52 (s, 1H, NH), 7.15 (m, 5H, C_6H_5).

Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.83; H, 7.09; N, 5.21.

Diacetyl-4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine (1h)

M.p.: 140-142 °C (140-141 °C)[28]; UV-Vis (Methanol, nm): λ (log ε) = 378 (3.29), 254 (3.67); FT- IR (KBr, cm^{-1}): 1652(C=O), 3262 (N-H); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 2.13 (s, 6H, 2-and 6-CH_3), 2.26 (s, 6H, 3-and 5-$COCH_3$), 5.13 (s, 1H, 4-H), 6.52 (s, 1H, NH), 7.18 (s, 4H, C_6H_4Cl).

Anal. Calcd for $C_{17}H_{18}ClNO_2$: C, 67.21; H, 5.97; N, 4.61. Found: C, 67.21; H, 5.98, N, 4.60.

Diacetyl-2,6-dimethyl-4-(3-nitrophenyl)–1,4-dihydropyridine (1i)

M.p.: 211-213 °C (210-211 °C)[28]; UV-Vis (Methanol, nm): λ (log ε)=378 (3.33), 253 (3.88); FT- IR (KBr, cm^{-1}): 1628 (C=O), 3297 (N-H); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 2.20 (s, 6H, 2-and 6-CH_3), 2.30 (s, 6H, 3-and 5-$COCH_3$), 5.22 (s, 1H, 4-H), 6.15 (s, 1H, NH), 7.95 (m, 5H, $C_6H_4NO_2$).

Anal. Calcd for $C_{17}H_{18}N_2O_4$: C, 64.96; H, 5.77; N, 8.91. Found: C, 65.00; H, 5.75; N, 8.90.

Diacetyl-4-(4-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine (1j)

M.p.: 174-175 °C (175-176 °C)[28]; UV-Vis (Methanol, nm): λ (log ε)=353 (3.76), 223 (4.28); FT- IR (KBr, cm^{-1}): 1668 (C=O), 3343 (N-H); ^{1}H NMR (300 MHz, $CDCl_3$,

ppm): $\delta = 2.18$ (s, 6H, 2-and 6-CH_3), 2.23 (s, 6H, 3-and 5-$COCH_3$), 4.96 (s, 1H, 4-H), 6.13 (s, 1H, NH), 7.08ppm (dd, 4H, $C_6H_4CH_3$).

Anal. Calcd for $C_{18}H_{21}NO_3$: C, 72.22; H, 7.07; N, 4.68. Found: C, 72.20; H, 7.08; N, 4.67.

Diethyl-2,6-dimethylpyridine-3,5-dicarboxylate (2a)

M.p.: 67-69 °C (69-71 °C)[33]; UV-Vis (Methanol, nm): λ (log ε) = 273 (3.52); FT-IR (KBr, cm^{-1}): 1717 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 1.40$ (t, J = 7.0 Hz, 6H, $CO_2CH_2\mathbf{CH_3}$), 2.84 (s, 6H, 2 and 6-CH_3), 4.38 (q, J = 7.0 Hz, 4H, $CO_2\mathbf{CH_2}CH_3$), 8.67 (s, 1H, 4-H) .

Anal. Calcd for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57. Found: C, 62.11; H, 6.82; N, 5.59.

Diethyl-2,6-dimethyl-4-phenylpyridine-3,5-dicarboxylate (2b)

M.p.: 64-65 °C (63-65 °C)[33]; UV-Vis (Methanol, nm): λ (log ε) = 236 (3.75); FT-IR (KBr, cm^{-1}): 1726 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 0.86$ (t, J = 6.5 Hz, 6H, $CO_2CH_2\mathbf{CH_3}$), 2.58 (s, 6H, 2 and 6-CH_3), 3.97 (q, J = 6.5 Hz, 4H, $CO_2\mathbf{CH_2}CH_3$), 7.28 (m, 5H, C_6H_5).

Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.75; H, 6.48; N, 4.28.

Diethyl-4-(4-chlorophenyl)-2,6-dimethylpyridine-3,5-dicarboxylate (2c)

M.p.: 65-67 °C (63-65 °C)[35]; UV-Vis (Methanol, nm): λ (log ε) = 212 (4.47); FT-IR (KBr, cm^{-1}): 1716 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 0.96$ (t, J = 7.1 Hz, 6H, $CO_2CH_2\mathbf{CH_3}$), 2.61 (s, 6H, 2 and 6-CH_3), 4.03 (q, J = 7.1 Hz, 4H, $CO_2\mathbf{CH_2}CH_3$), 7.25 (m, 4H, C_6H_4Cl).

Anal. Calcd for $C_{19}H_{20}ClNO_4$: C, 63.07; H, 5.57; N, 3.87. Found: C, 63.04; H, 5.59; N, 3.90.

Diethyl-2,6-dimethyl-4-(3-nitrophenyl) pyridine-3,5-dicarboxylate (2d)

M.p.: 62-64 °C (62-64 °C)[36]; UV-Vis (Methanol, nm): λ (log ε) = 257 (4.75); FT-IR (KBr, cm^{-1}): 1722 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 1.01$ (t, J = 7.0 Hz, 6H, $CO_2CH_2\mathbf{CH_3}$), 2.68 (s, 6H, 2 and 6-CH_3), 4.06 (q, J = 7.0 Hz, 4H, $CO_2\mathbf{CH_2}CH_3$), 7.25 (m, 4H, $C_6H_4NO_2$)) .

Anal. Calcd for $C_{19}H_{20}N_2O_6$: C, 61.28; H, 5.41; N, 7.52. Found: C, 61.24; H, 5.43; N, 7.52.

Diethyl-4-(4-methoxyphenyl)-2,6-dimethylpyridine-3,5-dicarboxylate (2e)

M.p.: 53-56 °C (49-52 °C)[36]; UV-Vis (Methanol, nm): λ (log ε) = 243 (4.96); FT-IR (KBr, cm^{-1}): 1697 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 0.99$ (t, J = 7.1 Hz,

6H, $CO_2CH_2\mathbf{CH_3}$), 2.63 (s, 6H, 2 and 6-CH_3), 3.95 (s, 3H, 4′-OCH_3),4.05 (q, J = 7.1 Hz, 4H, $CO_2\mathbf{CH_2}CH_3$), 7.30 (m, 4H, $C_6H_4OCH_3$)) .

Anal. Calcd for $C_{20}H_{23}NO_5$: C, 67.21; H, 6.49; N, 3.92. Found: C, 67.22; H, 6.48; N, 3.95.

3,5-Diacetyl-2,6-dimethylpyridine (2f)

M.p.: 66-67 °C (65-67 °C)[33]; UV-Vis (Methanol, nm): λ (log ε) = 246 (4.14); FT-IR (KBr, cm^{-1}): 1681 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 2.62 (s, 6H, 2-and 6-CH_3), 2.77 (s, 6H, 3-and 5-$COCH_3$), 4.30 (s, 1H, 4-H)).

Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.07; H, 6.85; N, 7.34.

Diacetyl-2,6-dimethyl-4-phenylpyridine (2g)

M.p.: 186-188 °C (185-186 °C)[28]; UV-Vis (Methanol, nm): λ (log ε) = 258 (4.28); FT-IR (KBr, cm^{-1}): 1699 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ = 2.19 (s, 6H, 2-and 6-CH_3), 2.44 (s, 6H, 3-and 5-$COCH_3$), 7.36 (m, 5H, C_6H_5)) .

Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.37; H, 6.41; N, 5.24.

3,5-Diacetyl-4-(4-chlorophenyl)-2,6-dimethylpyridine (2h)

M.p.: 172-174 °C (174-175 °C)[28]; UV-Vis (Methanol, nm): λ (log ε) = 275 (4.39); FT-IR (KBr, cm^{-1}): 1704 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ = 1.86 (s, 6H, 2-and 6-CH_3), 2.43 (s, 6H, 3-and 5-$COCH_3$), 7.22 (m, 4H, C_6H_4Cl)) ;

Anal. Calcd for $C_{17}H_{16}ClNO_2$: C, 67.66; H, 5.34; N, 4.64. Found: C, 67.62; H, 5.37; N, 4.65.

3,5-Diacetyl-2,6-dimethyl-4-(3-nitrophenyl)pyridine (2i)

M.p.: 124-126 °C (126-127 °C)[28]; UV-Vis (Methanol, nm): λ (log ε) = 257 (4.73); FT-IR (KBr, cm^{-1}): 1696 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ = 2.18 (s, 6H, 2-and 6-CH_3), 2.58 (s, 6H, 3-and 5-$COCH_3$), 7.65 (m, 4H, $C_3H_4NO_2$).

Anal. Calcd for $C_{17}H_{16}N_2O_4$: C, 65.38; H, 5.16; N, 8.97. Found: C, 65.40; H, 5.17; N, 8.97.

3,5-Diacetyl-4-(4-methoxyphenyl)-2,6-dimethylpyridine (2j)

M.p.: 165-166 °C (164-165 °C)[28]; UV-Vis (Methanol, nm): λ (log ε) = 239 (4.42); FT-IR (KBr, cm^{-1}): 1696 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ = 1.88 (s, 6H, 2-and 6-CH_3), 2.48 (s, 6H, 3-and 5- $COCH_3$), 3.83(s, 3H, 4-OCH_3), 7.04 (m, 4H, $C_6H_4OCH_3$).

Anal. Calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.68; H, 6.45; N, 4.76.

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