Synthesis of *N*-Substituted 3-Hydroxy-2-methyl-4-pyridones and -pyridonimines

M. Färber, H. Osiander and T. Severin*

Institut für Pharmazie und Lebensmittelchemie, Universität München,
Sophienstrasse 10, D-80333 München, Germany

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Carbohydrates with 1,4 glycosidic bonds like maltose, lactose, dextrin or starch react with primary amines as well as amino acids or proteins to give *i.e.* 3-hydroxy-2-methyl-4-pyridones **5** and 3-hydroxy-2-methyl-4-pyridonimines **7**. A generally applicable synthesis of compounds of this type is described. The pyridones **5** and pyridonimines **7** are strongly complexing agents. Molybdenum-derivatives, for instance, are suitable as fairly stable oxidation catalysts.

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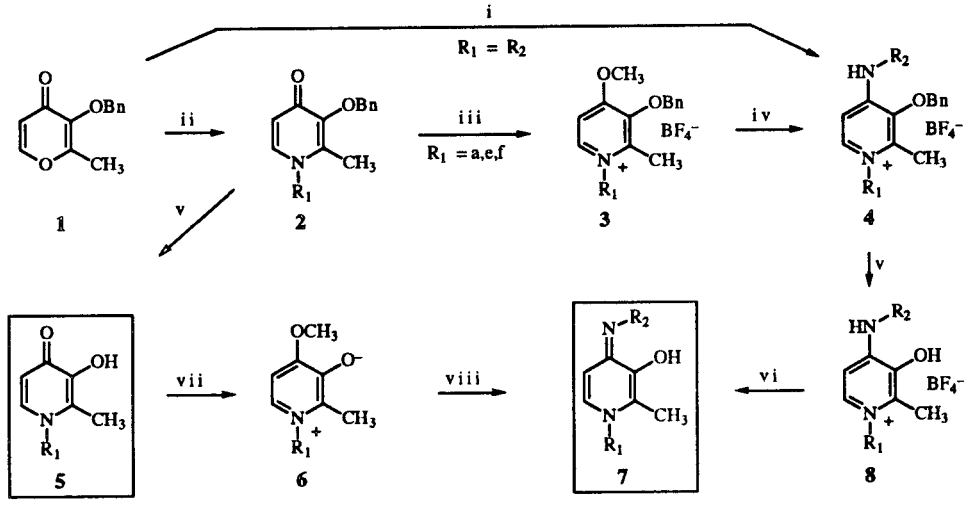
Reactions of reducing sugars with primary or secondary amines generally lead to mixtures of substances showing a great variety of different structures. When maltose or lactose are heated with primary amines in neutral aqueous solution besides other compounds 3-hydroxy-2-methyl-4-pyridones **5** are formed [1]. The same substances are obtained from oligo- or polysaccharides with 1,4-glycosidic bonds like starch and dextrins [2]. The pyridones **5** are strongly complexing agents for 3-valent metal ions like iron and aluminium, and such compounds have been proposed for the treatment of iron overload [3] and other diseases of iron unbalance [4]. *N*-Aryl substituted 3-hydroxypyridones were successfully employed for the separation of several metal ions [5]. Recently we have shown that besides the hydroxypyridones **5** hydroxypyridonimines of general structure **7** can be isolated from maltose or lactose/amine reaction mixtures [6].

In heated foods sugars react with the amino groups of lysine side chains of proteins [6]. Until now it is unknown whether lysine derived hydroxypyridones are resorbed in the human body and whether they are toxic or not.

In this communication we describe the synthesis and some metal complexes of the 2-hydroxy-3-methyl-4-pyridones and 3-hydroxy-2-methylpyridonimines.

It has been shown previously that maltol reacts with primary amines under rather drastic conditions to give 3-hydroxypyridones **5**, but the yields were moderate or low [7]. On the other hand the pyridones **5** can be obtained in high yield as pure substances when 3-*O*-benzylmaltol is heated with primary amines followed by catalytic hydrogenation of the 3-*O*-benzylpyridones **2** [8]. In a similar reaction sequence *N*-aryl- and *N*-heteroaryl substituted 3-hydroxypyridones of general structure **5** have been synthesized starting with 3-*O*-methylmaltol and fi-

Scheme 1



Bn = $-CH_2-$ (phenyl)

i 1.) $(CH_3)_3O^+BF_4^-$, CH_2Cl_2, 5 h, rt; 2.) R–NH_2, overnight.
ii R_1-NH_2, (C_2H_5OH/H_2O), 8-10 h.
iii $(CH_3)_3O^+BF_4^-$, CH_2Cl_2, 5 h, rt.
iv CH_2Cl_2, R_2-NH_2, 3 h rt, 3 h Δ.
v Pd/C, H_2, CH_3OH/C_2H_5OH, rt, overnight.
vi 2N-NaOH/CH_3OH, rt, overnight, CH_2Cl_2-extraction.
vii 1.) $(CH_3)_3O^+BF_4^-$, CH_2Cl_2, 5 h, rt; 2.) 2,2,6,6-tetramethylpiperidine, water-extraction.
viii R_2-NH_2, 120°, 7 h.

nally cleavage of the *O*-methyl ether-bond with 48% aqueous hydrobromic acid [9].

Synthesis of the pyridonimines **7** has been achieved by different routes as shown in Scheme 1.

Table 1

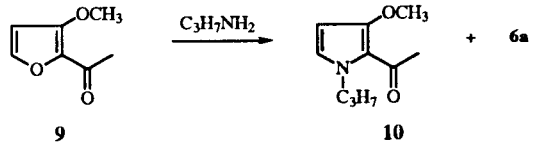
No. 2, 5, (3, 6)	R_1 =
a	$-C_3H_7$
b	$-(CH_2)_3OH$
c	$-(CH_2)_2N(C_2H_5)_2$
d	$-CH_2COOH$
e	$-(CH_2)_2-C_6H_5$
f	$-C_6H_5$
g	$-C_6H_4-OH$
h	$-C_6H_4-COOC_2H_5$

Methylation of **2** with trimethyloxonium tetrafluoroborate leads to the pyridinium salts **3** which react with primary amines at room temperature or under heating to give the 4-aminopyridinium salts **4** generally in high yield. The diphenyl derivative **4d** may be synthesized by methylation of **1** and subsequent treatment with aniline at room temperature. The pyridinium salts **4** described here are obtained as crystalline compounds which are easily purified by recrystallization. Debenzylation is performed by hydrogenation with palladium on carbon as catalyst. The pyridonimines **7** can be extracted with dichloromethane from aqueous solutions of compounds **8** after addition of a base. If necessary the products can be purified by chromatography on silica gel.

Methylation of the pyridones **5** with oxonium salts results in the formation of the pyridinium betaines **6**, which when heated with primary amines react to give the pyridonimines **7** as main products. The betaines **6** are far less reactive when compared with the pyridinium salts **3**.

Finally the pyridinium betaines **6** have been synthesized following the pathway observed for the degradation of maltose and lactose: when isomaltol methyl ether **9** is heated with a primary amine, a mixture of **6** and **10** is obtained which is easily separated by extraction of **10** from the aqueous solution with an organic solvent.

Scheme 2



9 **10**

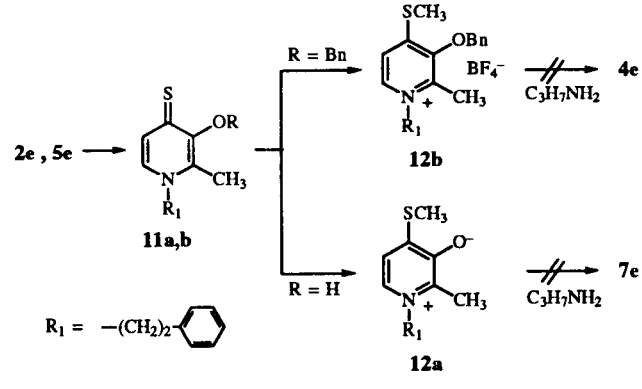
Transformation of **2e** and **5e** into the corresponding thiopyridones **11a,b** could be achieved by standard procedures as described in the literature [10,11]. Contrary to our expectation the mercaptopyridinium compounds

Table 2

No. 4, 7, 8	R_1 =	R_2 =
a	H_7C_3-	$-C_3H_7$
b	H_7C_3-	$-(CH_2)_2N(C_2H_5)_2$
c	$-C_6H_5$	$-C_3H_7$
d	$-C_6H_5$	$-C_6H_5$
e	$-(CH_2)_2-C_6H_5$	$-C_3H_7$
f	"	$-(CH_2)_3OH$
g	"	$-(CH_2)_2NHCOCH_3$

12a,b did not react with primary amines to give substitution products **4e** and **7e** in appreciable amounts.

Scheme 3



The 3-hydroxypyridonimines **7** readily form complex compounds with several metal ions. Analytically pure substances have been obtained with copper and molybdenum by reaction of **7a,d** or **e** with the metal acetylacetonates. For comparison some previously unknown iron, molybdenum, vanadium, manganese and copper complexes of the 3-hydroxypyridones **5a** and **5e** have been prepared. The great variety of amines which can be introduced into the pyridone-nucleus or the pyranone-nucleus respectively enables the construction of metal complexes with different properties.

In preliminary experiments we have shown that metal complexes of 3-hydroxypyridones and 3-hydroxypyridonimines are suitable as catalysts for oxidation reactions. For example when a benzene solution of cyclooctene or

Scheme 4

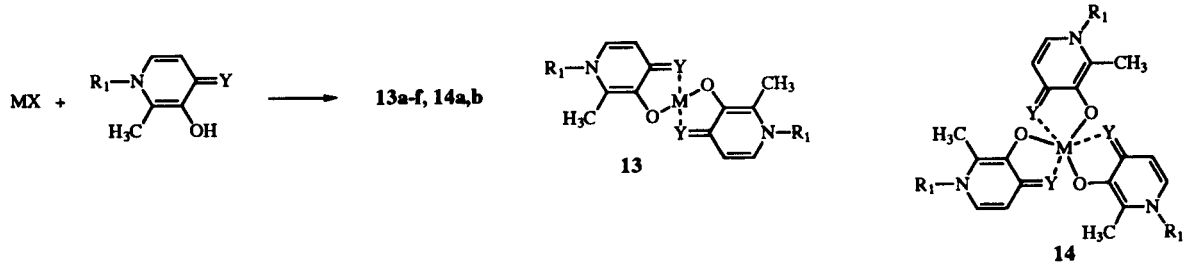
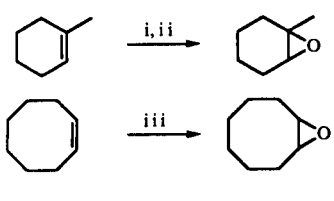


Table 3

No. 13	MX	Y=	R_1 =	M
a	$Cu(II)Cl_2$ $x(H_2O)_2$	O	$-C_3H_7$	Cu
b	VO (acac)$_2$	O	$-C_3H_7$	V=O
c	MoO_2 (acac)$_2$	N(C_3H_7)	$-C_3H_7$	O=Mo=O
d	"	O	$-C_2H_4$- 	"
e	"	N(C_3H_7)	$-C_2H_4$- 	"
f	Cu (acac)$_2$	N- 	- 	Cu
No. 14				
a	$FeCl_3$ $Mn[III]$ (ac)$_3$ $x(H_2O)_2$	O	$-C_2H_4$- 	Fe
b		O	$-C_3H_7$	Mn

1-methylcyclohexene is treated with *tert*-butyl peroxide in the presence of catalytic amounts of the molybdenum-compounds **13d** or **13c** the epoxy-derivatives are formed in nearly quantitative yield. Epoxidation of 1-methyl-1-cyclohexene was also performed by oxygen and an aldehyde using **14a** as catalyst.

Scheme 5



i) *tert*-BuOOH, **13c**, benzene, 22 h, 80°C.

ii) O_2, isobutyraldehyde, **14a**, 1,2-dichloroethane, 60°C, 22 h.

iii) *tert*-BuOOH, **13d**, benzene, 8 h, 80°C.

Extended investigations in this area will be reported in due time.

EXPERIMENTAL

Apparatus.

The ^{1}H-nmr spectra were obtained on a JEOL GX 400 spectrometer at 400 MHz using various deuterated solvents depending upon the solubilities of each compound. Chemical shifts are reported in ppm relative to tetramethylsilane. Melting points were determined on a Wagner+Munz melting apparatus and are uncorrected. Column chromatography was run on silica gel 50-200 μm (Fa. Baker) and 32-63 μm (Fa. ICN) for flash chromatography. Infrared spectra were measured as potassium bromide plates using a Perkin Elmer FT-IR 1600 Series IR Spectrometer. Mass spectra were recorded on a Hewlett-Packard 5989A mass spectrometer (EI: electron impact, 70 eV, direct inlet or CI: chemical ionisation with methane as the reagent gas). Gas chromatography was performed with a Perkin Elmer 8320 capillary gas chromatograph (carrier gas: nitrogen, 14.5 psig, equipped with a flame ionisation detector (FID) or a Hewlett-Packard capillary gas chromatograph HP 5890 series II equipped with a Hewlett-Packard HP 5971A mass selective detector and helium as carrier gas (12 psig). Microanalyses were carried out using an Analysator CHN-O-Rapid of Fa. Heraeus.

Materials.

3-Hydroxy-2-methyl-4-pyrone (maltol) was purchased from Fluka (Buchs, Switzerland) and was used as received. The starting material 3-benzyloxy-2-methyl-4(1H)-pyranone **1** was made from maltol by the method of Harris [14]. 1-(3-Methoxy-2-furyl)-1-ethanone (isomaltolmethyl ether) **9** was synthesized by methylation [15] of isomaltol [16]. Solvents were dried in the usual manner and purified by distillation.

General Procedure.

N-Alkyl-3-hydroxy-2-methyl-4-pyridones **5a,b,c** and **e** (procedure A, according to an improved literature method [8]) and *N*-aryl-3-hydroxy-2-methyl-4-pyridones **5f,g** and **h** (procedure B) are reported. Compound **5d** was prepared according to another method.

Procedure A.

A mixture of **1** (4.32 g, 20 mmoles) and the appropriate aliphatic amine (40 mmoles) in 60 ml of ethanol/water (3:1) was heated under reflux. After 4 hours an additional 40 mmoles of amine was added and heating was continued for 6 hours. The solvent and most of the excess amine were removed by evaporation under reduced pressure.

Procedure B.

Ten mmoles (2.16 g) of **1** and 20 mmoles of the appropriate aromatic amine were heated at 120° for 8 hours in a dry flask without any solvent.

Both procedures continue as follows:

The substances were purified by repeated column chromatography or flash chromatography on silica gel (eluent stated) and the fractions containing the product were combined. The

solution was evaporated and dried *in vacuo* to give **2a,b,c,e** and **h** as pure (nmr) red-brown colored oils and **2f** and **g** as solid residues. To a solution of tlc pure **2a,c,e,f** and **h** in 50 ml of ethanol or methanol/ethanol (1:1) respectively for **2b** and **g** was added carefully 50 mg of palladium on activated charcoal (10%). After stirring overnight at ambient temperature under an atmosphere of hydrogen the catalyst was filtered and washed with methanol (10 ml). The filtrate was evaporated under reduced pressure to dryness. Recrystallization (solvent stated) of crude **5a,b,c,e,f,g** and **h** gave analytically pure compounds.

3-Hydroxy-2-methyl-1-propyl-4(1*H*)-pyridone (**5a**).

Compound **2a** was obtained from **1** and propylamine (6.58 ml, 80 mmoles) after elution with ethyl acetate/methanol (4:1 v/v, r_f = 0.4), yield, 3.80 g (74%). Catalytic hydrogenation of 2.57 g (10 mmoles) of **2a** yielded crude **5a** which was recrystallized from ethyl acetate as colorless needles, 1.37 g (82%), mp 163°, lit [1a]; ^{1}H nmr (deuteriochloroform): δ 0.98 (t, J = 7.2 Hz, 3H, $CH_2CH_2CH_3$), 1.77 (sext, J = 7.2 Hz, 2H, $CH_2CH_2CH_3$), 2.39 (s, 3H, Me), 3.83 (t, J = 7.2 Hz, 2H, $CH_2CH_2CH_3$), 4.00 (broad s, 1H, O*H*, deuterium oxide exchangeable), 6.38 (d, J = 7.2 Hz, 1H, 5-*H*), 7.22 (d, J = 7.2 Hz, 1H, 6-*H*); ms: (EI): m/z (relative intensity) 167 (69, $M^{+\cdot}$), 152 (34), 125 (100), 96 (39), 69 (13) and 55 (20).

Anal. Calcd. for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.38. Found: C, 64.76; H, 7.75; N, 8.46.

3-Hydroxy-1-(3-hydroxypropyl)-2-methyl-4(1*H*)-pyridone (**5b**).

Compound **2b** was obtained from **1** and 3-amino-1-propanol (6.12 ml, 80 mmoles) after elution with ethyl acetate/methanol (7:3 v/v, r_f = 0.36), yield, 4.43 g (81%). Catalytic hydrogenation of 2.73 g (10 mmoles) of **2b** yielded crude **5b** which was recrystallized from acetonitrile or ethanol as colorless needles, 1.61 g (88%), mp 117-118°, lit [17]; ^{1}H nmr (methanol-d_4): δ 1.94 (m, J = 5.8 Hz, 2H, N_1-$CH_2CH_2CH_2OH$), 2.45 (s, 3H, Me), 3.59 (m, J = 5.8 Hz, 2H, N_1-$CH_2CH_2CH_2OH$), 4.15 (m, J = 5.8 Hz, 2H, N_1-CH_2-CH_2CH_2OH), 6.40 (d, J = 7.3 Hz, 1H, 5-*H*), 7.59 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 183 (100, $M^{+\cdot}$), 152 (65), 139 (78), 125 (79), 96 (45) and 55 (45).

Anal. Calcd. for $C_9H_{13}NO_3$: C, 59.00; H, 7.15; N, 7.65. Found: C, 58.62; H, 7.57; N, 7.60.

1-(2-Diethylaminoethyl)-3-hydroxy-2-methyl-4(1*H*)-pyridone (**5c**).

Compound **2c** was obtained from **1** and *N,N* diethylethylenediamine (11.24 ml, 80 mmoles) after elution with ethyl acetate/methanol (7:3 v/v, r_f = 0.18), yield, 4.81 g (76.5%). Catalytic hydrogenation of 3.14 g (10 mmoles) of **2c** yielded crude **5c** which was crystallized from ethyl acetate as pale yellow plates, 1.9 g (85%), mp 130°, lit [18]; ^{1}H nmr (methanol-d_4): δ 0.95-0.99 (m, J = 7 Hz, 6H, $N(CH_2CH_3)_2$), 2.45 (s, 3H, Me), 2.52-2.57 (m, J = 7 Hz, 4H, $N(CH_2CH_3)_2$), 2.73 (t, J = 6.6 Hz, 2H, $CH_2N(CH_2CH_3)_2$), 4.08 (t, J = 6.6 Hz, 2H, N_1-CH_2CH_2), 6.38 (d, J = 7.3 Hz, 1H, 5-*H*), 7.58 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 224 (1.3, $M^{+\cdot}$), 149 (1.3), 100 (3), 86 (100) and 58 (11).

Anal. Calcd. for $C_{12}H_{20}N_2O_2$: C, 64.26; H, 8.98; N, 12.49. Found: C, 64.31; H, 9.06; N, 12.36.

3-Hydroxy-2-methyl-1-(2-phenylethyl)-4(1*H*)-pyridone (**5e**).

Compound **2e** was obtained from **1** and phenethylamine (10.05 ml, 80 mmoles) after elution with ethyl acetate/methanol (4:1 v/v, r_f = 0.57), yield, 5.24 g (82%). Catalytic hydrogenation of 3.19 g (10 mmoles) of **2e** yielded crude **5e** which was crystallized from ethyl acetate as colorless needles, 1.95 g (85%), mp 158°; ^{1}H nmr (deuteriochloroform): δ 2.33 (s, 3H, Me), 3.00 (t, J = 7.3 Hz, 2H, N_1-CH_2CH_2), 3.68 (broad s, 1H, O*H*), 4.09 (t, J = 7.3 Hz, 2H, N_1-CH_2CH_2), 6.29 (d, J = 7.3 Hz, 1H, 5-*H*), 6.98 (d, J = 7.3 Hz, 1H, 6-*H*), 7.04-7.06 (m, 2H, Ar'*H*), 7.25-7.32 (m, 3H, Ar'*H*); ms: (EI) m/z (relative intensity) 229 (65, $M^{+\cdot}$), 169 (16), 149 (41), 138 (46), 125 (41), 105 (100) and 57 (43); ir: ν 3022 (OH), 1623 (C=O), 1567 (C=C), 1531, 1505, 1355, 1240, 842, 755, 698 cm^{-1}.

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.38; H, 6.55; N, 6.11. Found: C, 73.34; H, 6.49; N, 6.30.

3-Hydroxy-2-methyl-1-phenyl-4(1*H*)-pyridone (**5f**).

Compound **2f** was obtained from **1** and aniline (1.82 ml, 20 mmoles) after elution with ethyl acetate/methanol (9:1 v/v, r_f = 0.53), yield: 1.92 g (66%). Catalytic hydrogenation of 1.46 g (5 mmoles) of **2f** yielded crude **5f** which was crystallized from ethanol as colorless crystals, 0.82 g (82%), mp 219-220°, lit [9a]; ^{1}H nmr (deuteriochloroform): δ 2.10 (s, 3H, Me), 5.23 (broad s, 1H, O*H*), 6.47 (d, J = 7.3 Hz, 1H, 5-*H*), 7.25-7.32 (m, ~3H, 6-*H*, Ar'*H*, includes chloroform), 7.51-7.56 (m, 3H, Ar'*H*); ms: (EI) m/z (relative intensity) 201 (55, $M^{+\cdot}$), 200 (100), 172 (5), 154 (8), 77 (29), 55 (13) and 51 (25).

Anal. Calcd. for $C_{12}H_{11}NO_2$: C, 71.66; H, 5.47; N, 6.96. Found: C, 71.53; H, 5.62; N, 6.93.

3-Hydroxy-1-(2-hydroxyphenyl)-2-methyl-4(1*H*)-pyridone (**5g**).

Compound **2g** was obtained from **1** and 2-aminophenol 2.18 g (20 mmoles) after elution with ethyl acetate/methanol (9:1 v/v, r_f = 0.57), yield, 1.47 g (48%). Catalytic hydrogenation of 1.54 g (5 mmoles) of **2g** yielded crude **5g** which was crystallized from methanol as white crystals, 0.70 g (64%), mp 301°; ^{1}H nmr (methanol-d_4): δ 2.1 (s, 3H, Me), 6.47 (d, J = 7.3 Hz, 1H, 5-*H*), 6.97-7.03 (m, 2H, Ar'*H*), 7.21 (d, J = 8.0 Hz, 1H, Ar'*H*), 7.37 (t, J = 8.0 Hz, 1H, Ar'*H*), 7.46 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 217 (50, $M^{+\cdot}$), 200 (70), 169 (30), 149 (46), 84 (65) and 66 (100).

Anal. Calcd. for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.42; H, 5.19; N, 6.22.

Ethyl 3-(1,4-Dihydro-3-hydroxy-2-methyl-4-oxo-1-pyridyl)-benzoate (**5h**).

Compound **2h** was obtained from **1** and ethyl 3-aminobenzoate (3.3 g, 20 mmoles) after elution with ethyl acetate/methanol (9:1 v/v, r_f = 0.59), yield, 3.09 (85%). Catalytic hydrogenation of 1.82 g (5 mmoles) of **2h** yielded crude **5h** which was crystallized from methanol/ethyl acetate as white solid, 1.16 g (85%), mp 224°; ^{1}H nmr (methanol-d_4): δ 1.42 (t, J = 7.0 Hz, 3H, Et), 2.13 (s, 3H, Me), 4.42 (q, J = 7.0 Hz, 2H, Et), 6.51 (d, J = 7.3 Hz, 1H, 5-*H*), 7.56 (d, J = 7.3 Hz, 1H, 6-*H*), 7.63 (d, J = 8.0 Hz, 1H, 6'-*H*), 7.72 (t, J = 8.0 Hz, 1H, 5'-*H*), 8.00 (s, 1H, 2'-*H*), 8.22 (d, J = 8.0 Hz, 1H, 4'-*H*); ms: (EI) m/z (relative intensity) 273 (100, $M^{+\cdot}$), 272 (96), 244 (52), 199 (60), 121 (24), 105 (17) and 77 (13).

Anal. Calcd. for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.99; H, 5.59; N, 5.15.

2-(1,4-Dihydro-3-hydroxy-2-methyl-4-oxo-1-pyridyl)acetic Acid (**5d**).

A mixture of 10 g (86.9 mmoles) of sodium glycinate monohydrate and 10 g (46.3 mmoles) of **1** was heated in 60 ml of ethanol/water (1:1) for 8 hours under reflux. After being cooled to room temperature, the *p*H was adjusted to 1-2 with 2 *N* hydrochloric acid at which time a precipitate formed. Precipitation was completed by standing at 8° for 1 hour. Subsequent filtration of the pale yellow solid and recrystallization from methanol/water afforded **2d** (10.7 g, 85%) as colorless needles. A suspension of 100 mg of palladium hydroxide on activated charcoal (20%) in a solution of **2d** (2.73 g, 10 mmoles) in 500 ml of methanol/water (1:1) was stirred overnight at ambient temperature under atmospheric pressure of hydrogen. After removal of the catalyst and washing with water (20 ml), the solution was evaporated under reduced pressure to dryness, and the residue recrystallized from dimethylformamide yielding **5d** (1.37 g, 75%) as colourless needles. mp 260-265° dec, lit [1c]; ^{1}H nmr (deuterium oxide): δ 2.32 (s, 3H, Me), 4.66 (s, 2H, CH_2COOH), 6.53 (d, J = 7.3 Hz, 1H, 5-*H*), 7.59 (d, J = 7.3 Hz, 1H, 6-*H*); ms: [1c]; m/z (relative intensity) 183 (100, $M^{+\cdot}$), 165 (78), 138 (70), 136 (75), 124 (27), 110 (60), 97 (18), 96 (20), 69 (33), 57 (40) and 42 (50).

Anal. Calcd. for $C_8H_9NO_4$: C, 52.46; H, 4.95; N, 7.65. Found: C, 52.18; H, 5.40; N, 7.61.

Formation of *N*-Substituted 3-Benzyloxy-4-methoxy-2-methylpyridinium Tetrafluoroborates **3a, e** and **f**.

To a solution of tlc pure **2a,e** or **f** (5 mmoles) in 30 ml of dry dichloromethane was added 813.5 mg (5.5 mmoles) of trimethyloxonium tetrafluoroborate in one portion. After stirring for 5 hours at room temperature the mixture was filtered and the solvent was removed by rotary evaporation. The resulting oily residue was crystallized at 4-8° from a suitable solvent.

3-Benzyloxy-4-methoxy-2-methyl-1-propyl-pyridinium Tetrafluoroborate (**3a**).

This compound was obtained from **2a** (1.29 g, 5 mmoles) by the above procedure. Crystallisation from ether/ethyl acetate yielded 0.99 g (55%) of **3a** as colourless needles. Recrystallisation from ethyl acetate gave an analytical sample, mp 103°; ^{1}H nmr (deuteriochloroform): δ 0.98 (t, J = 7.3 Hz, 3H, $CH_2CH_2CH_3$), 1.83 (sext, J = 7.3 Hz, 2H, $CH_2CH_2CH_3$), 2.47 (s, 3H, Me), 4.18 (s, 3H, OCH_3), 4.33 (t, J = 7.3 Hz, 2H, $CH_2CH_2CH_3$), 5.12 (s, 2H, $OCH_2C_6H_5$), 7.37 (s, 5H, $OCH_2C_6H_5$), 7.51 (d, J = 7.3 Hz, 1H, 5-*H*), 8.53 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 272 (11, $M^{+\cdot}$, corresponding to the cation), 257 (32), 180 (65), 151 (47), 138 (47), 109 (41), 91 (100) and 65 (49).

Anal. Calcd. for $C_{17}H_{22}NO_2BF_4$: C, 56.85; H, 6.17; N, 3.90. Found: C, 56.61; H, 6.14; N, 3.87.

3-Benzyloxy-4-methoxy-2-methyl-1-(2-phenyl-ethyl)pyridinium Tetrafluoroborate (**3e**).

This compound was obtained from **2e** (1.60 g, 5 mmoles) by the above procedure. Crystallisation from ethyl acetate yielded 1.26 g (60%) of **3e** as colourless needles. Recrystallisation from ethyl acetate gave an analytical sample, mp 98°; ^{1}H nmr (deuteriochloroform): δ 2.22 (s, 3H, Me), 3.05 (t, J = 7.3 Hz, 2H, N_1-CH_2CH_2), 4.05 (s, 3H, OCH_3), 4.52 (t, J = 7.3 Hz, 2H, N_1-CH_2-CH_2), 4.98 (s, 2H, $OCH_2C_6H_5$), 6.94-6.96 (m, 2H, Ar'*H*), 7.16-7.32 (m, ~9H, Ar'*H*, $OCH_2C_6H_5$, 5-*H*, includes chloroform), 8.32 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 334 (2, $M^{+\cdot}$, corresponding to the cation), 319 (12), 242 (22), 213 (16), 185 (8), 105 (87), 104 (31), 91 (100), 79 (28) and 65 (42).

Anal. Calcd. for $C_{22}H_{24}NO_2BF_4$: C, 62.73; H, 5.74; N, 3.33. Found: C, 62.62; H, 5.78; N, 3.42.

3-Benzyloxy-4-methoxy-2-methyl-1-phenylpyridinium Tetrafluoroborate (**3f**).

This compound was obtained from **2f** (1.46 g, 5 mmoles) by the above procedure. Crystallization (**No heating** because of decomposition!) from methanol/ethyl acetate yielded 1.37 g (70%) of **3f** as colourless needles. Recrystallization from methanol/ethyl acetate gave an analytical sample, mp 190°; ^{1}H nmr (methanol-d_4): δ 2.21 (s, 3H, Me), 4.05 (s, 3H, OCH_3), 5.24 (s, 2H, $OCH_2C_6H_5$), 7.40-7.43 (m, 7H, Ar'*H*, $OCH_2C_6H_5$), 7.62-7.67 (m, 4H, Ar'*H*, 5-*H*), 8.36 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 306 (5, $M^{+\cdot}$, corresponding to the cation), 305 (17), 291 (15), 215 (33), 214 (100), 186 (28), 91 (47) and 77 (51).

Anal. Calcd. for $C_{20}H_{20}NO_2BF_4$: C, 61.10; H, 5.13; N, 3.56. Found: C, 61.31; H, 5.21; N, 3.63.

General Methods for the Formation of **4**.

Method A.

Reaction of *N*-Substituted 3-Benzyloxy-4-methoxy-2-methylpyridinium Tetrafluoroborates **3a, e** and **f** with Amines.

To a solution of **3a,e** or **f** respectively (1 mmole) in 20 ml of dry dichloromethane was added 3 mmoles of the appropriate amine *via* a syringe and the mixture was stirred at room temperature for 3 hours. After additional 3 hours of heating under reflux the solvent and most of the excess amine was removed by rotary evaporation. The oily residue was crystallized from a suitable solvent in the refrigerator.

Method B.

Preparation of **4a** and **d** from 3-Benzyloxy-2-methyl-4(1*H*)-pyranone **1**.

Trimethyloxonium tetrafluoroborate (813.5 mg, 5.5 mmoles) was suspended in a solution of **1** (1.08 g, 5 mmoles) in 30 ml of anhydrous dichloromethane. After stirring for 5 hours at room temperature the mixture was cooled to 0° and the appropriate amine (20 mmoles) was added with stirring *via* a syringe dropwise over a period of 10 minutes. The solution was warmed to ambient temperature and was allowed to stir for 16 hours. Evaporation of the solvent and the excessive amine afforded an oily product which crystallized from ethyl acetate at 0°.

3-Benzyloxy-2-methyl-1-propyl-4-propylaminopyridinium Tetrafluoroborate (**4a**).

This compound was prepared from propylamine (1.65 ml, 20 mmoles) and **1** using method B. The resulting product was recrystallized from ethyl acetate to yield 1.52 g (79%) of **4a** as colorless prisms, mp 138°; ^{1}H nmr (deuteriochloroform): δ 0.90 (t, J = 7.3 Hz, 3H, C_4-$NHCH_2CH_2CH_3$), 0.98 (t, J = 7.3 Hz, 3H, N_1-$CH_2CH_2CH_3$), 1.53 (sext, J = 7.3 Hz, 2H, C_4-$NHCH_2CH_2$-CH_3), 1.79 (sext, J = 7.3 Hz, 2H, N_1-$CH_2CH_2CH_3$), 2.42 (s, 3H, Me), 3.18 (q, J = 7.3 Hz, 2H, C_4-$NHCH_2CH_2CH_3$), 4.12 (t, J = 7.3 Hz, 2H, N_1-$CH_2CH_2CH_3$), 4.95 (s, 2H, $OCH_2C_6H_5$), 5.93 (broad t, 1H, N*H*, deuterium oxide exchangeable), 6.75 (d, J =

7.3 Hz, 1H, 5-*H*), 7.38-7.41 (m, 5H, $OCH_2C_6H_5$), 8.03 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 298 (3, $M^{+\cdot}$, corresponding to the free base), 255 (4), 207 (28), 169 (38), 150 (29), 119 (25) and 91 (100).

Anal. Calcd. for $C_{19}H_{27}N_2OBF_4$: C, 59.08; H, 7.05; N, 7.25. Found: C, 58.82; H, 6.82; N, 7.28.

3-Benzyloxy-4-(2-diethylaminoethylamino)-2-methyl-1-propylpyridinium Tetrafluoroborate (**4b**)

This compound was prepared from *N,N*-diethylethylenediamine (422 µl, 3 mmoles) and **3a** (359 mg, 1 mmole) using method A. The resulting product was crystallized from ether/ethyl acetate to yield 408 mg (92%) of **4b** as colorless needles, mp 95°; ^{1}H nmr (deuteriochloroform): δ 0.93-1.01 (m, 9H, C_4-$NHCH_2CH_2N(CH_2CH_3)_2$, N_1-$CH_2CH_2CH_3$), 1.80 (sext, J = 7.3 Hz, 2H, N_1-$CH_2CH_2CH_3$), 2.44 (s, 3H, Me), 2.49-2.56 (m, J = 7 Hz, 4H, C_4-$NHCH_2CH_2N(CH_2CH_3)_2$), 2.69 (t, J = 7 Hz, 2H, C_4-$NHCH_2CH_2N(CH_2CH_3)_2$), 3.30 (m, 2H, C_4-$NHCH_2CH_2N(CH_2CH_3)_2$), 4.15 (t, J = 7.3 Hz, 2H, N_1-$CH_2CH_2CH_3$), 4.88 (s, 2H, $OCH_2C_6H_5$), 6.77 (broad t, 1H, N*H*), 6.88 (d, J = 7.3 Hz, 1H, 5-*H*), 7.40 (s, 5H, $OCH_2C_6H_5$), 8.12 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 355 (3, $M^{+\cdot}$, corresponding to the free base), 269 (56), 169 (26), 91 (56), 68 (86), 57 (100) and 55 (95).

Anal. Calcd. for $C_{22}H_{34}N_3OBF_4$: C, 59.60; H, 7.73; N, 9.48. Found: C, 59.36; H, 7.76; N, 9.38.

3-Benzyloxy-2-methyl-1-phenyl-4-propylaminopyridinium Tetrafluoroborate (**4c**).

This compound was prepared from propylamine (247 µl, 3 mmoles) and **3f** (393 mg, 1 mmole) using method A. The resulting product was crystallized from ethyl acetate to yield 399 mg (95%) of **4c** as colorless crystals, mp 133-134°; ^{1}H nmr (deuteriochloroform): δ 0.90 (t, J = 7.3 Hz, 3H, C_4-$NHCH_2CH_2CH_3$), 1.55 (sext, J = 7.3 Hz, 2H, C_4-$NHCH_2CH_2CH_3$), 2.09 (s, 3H, Me), 3.27 (q, J = 7.3 Hz, 2H, C_4-$NHCH_2CH_2$-CH_3), 5.05 (s, 2H, $OCH_2C_6H_5$), 6.29 (broad t, 1H, N*H*), 6.90 (d, J = 7.3 Hz, 1H, 5-*H*), 7.37-7.55 (m, 10H, Ar'*H*, $OCH_2C_6H_5$), 7.81 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 332 (16, $M^{+\cdot}$, corresponding to the free base), 289 (23), 241 (100), 213 (30), 184 (78), 91 (75), 77 (44) and 65(47).

Anal. Calcd. for $C_{22}H_{25}N_2OBF_4$: C, 62.88; H, 6.00; N, 6.66. Found: C, 62.74; H, 6.24; N, 6.51.

4-Anilino-3-benzyloxy-2-methyl-1-phenylpyridinium Tetrafluoroborate (**4d**).

This compound was prepared from aniline (1.82 ml, 20 mmoles) and **1** using method B. The resulting product was recrystallized from ethyl acetate to yield 1.50 g (66%) of **4d** as pale yellow crystals, mp 138°; ^{1}H nmr (deuteriochloroform): δ 2.28 (s, 3H, Me), 5.22 (s, 2H, $OCH_2C_6H_5$), 7.00 (d, J = 7.3 Hz, 1H, 5-*H*), 7.14-7.57 (m, ~16H, C_4-N*H*Ar*H*, $OCH_2C_6H_5$, Ar'*H*, includes chloroform), 7.74 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 366 (41, $M^{+\cdot}$, corresponding to the free base), 275 (65), 259 (100), 130 (13), 91 (25) and 77(51).

Anal. Calcd. for $C_{25}H_{23}N_2OBF_4$: C, 66.10; H, 5.10; N, 6.17. Found: C, 66.16; H, 5.02; N, 6.18.

3-Benzyloxy-2-methyl-1-(2-phenylethyl)-4-propylaminopyridinium Tetrafluoroborate (**4e**).

This compound was prepared from propylamine (247 µl, 3 mmoles) and **3e** (421 mg, 1 mmole) using method A. The resulting product was crystallized from ethyl acetate to yield 415 mg (93%) of **4e** as colorless needles, mp 110°; ^{1}H nmr (deuteriochloroform): δ 0.87 (t, J = 7.3 Hz, 3H, C_4-$NHCH_2CH_2CH_3$), 1.47 (sext, J = 7.3 Hz, 2H, C_4-$NHCH_2CH_2CH_3$), 2.22 (s, 3H, Me), 3.05-3.14 (m, 4H, C_4-$NHCH_2CH_2CH_3$, N_1-$CH_2CH_2Ar'H$), 4.37 (t, J = 7.3 Hz, N_1-$CH_2CH_2Ar'H$), 4.84 (s, 2H, $OCH_2C_6H_5$), 5.86 (broad t, 1H, N*H*), 6.62 (d, J = 7.3 Hz, 1H, 5-*H*), 7.07-7.09 (m, 2H, N_1-$CH_2CH_2Ar'H$), 7.22-7.39 (m, ~8H, $OCH_2C_6H_5$, N_1-$CH_2CH_2Ar'H$, includes chloroform), 7.87 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 360 (16, $M^{+\cdot}$, corresponding to the free base), 317 (16), 270 (24), 269 (58), 212 (18), 165 (15), 121 (24), 105 (100), 91 (49), 79 (23) and 65 (26).

Anal. Calcd. for $C_{24}H_{29}N_2OBF_4$: C, 64.33; H, 6.47; N, 6.25. Found: C, 64.09; H, 6.74; N, 6.21.

3-Benzyloxy-4-(3-hydroxypropylamino)-2-methyl-1-(2-phenylethyl)pyridinium Tetrafluoroborate (**4f**).

This compound was prepared from 3-amino-1-propanol (230 µl, 3 mmoles) and **3e** (421 mg, 1 mmole) using method A. The resulting product was crystallized from methanol/ethyl acetate to yield 327 mg (71%) of **4f** as colorless plates, mp 57°; ^{1}H nmr (deuteriochloroform): δ 1.76 (quint, J = 5.8 Hz, 2H, C_4-$NHCH_2CH_2CH_2OH$), 2.11 (s, 3H, Me), 3.02 (t, J = 7.3 Hz, 2H, N_1-$CH_2CH_2Ar'H$), 3.37 (q, J = 5.8 Hz, 2H, C_4-$NHCH_2CH_2CH_2OH$), 3.69 (t, J = 5.8 Hz, 2H, C_4-$NHCH_2CH_2CH_2OH$), 4.30 (t, J = 7.3 Hz, 2H, N_1-$CH_2CH_2Ar'H$), 4.79 (s, 2H, $OCH_2C_6H_5$), 6.69 (d, J = 7.3 Hz, 1H, 5-*H*), 6.79 (broad t, 1H, N*H*), 7.03-7.05 (m, 2H, N_1-$CH_2CH_2Ar'H$), 7.22-7.29 (m, ~3H, N_1-$CH_2CH_2Ar'H$, includes chloroform), 7.35 (s, 5H, $OCH_2C_6H_5$), 7.76 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 376 (1, $M^{+\cdot}$, corresponding to the free base), 284 (30), 256 (46), 165 (33), 105 (49), 91 (100) and 65 (62).

Anal. Calcd. for $C_{24}H_{29}N_2O_2BF_4$: C, 62.08; H, 6.29; N, 6.03. Found: C, 62.07; H, 6.14; N, 6.19.

4-(2-Acetamidoethylamino)-3-benzyloxy-2-methyl-1-(2-phenylethyl)pyridinium Tetrafluoroborate (**4g**).

This compound was prepared from *N*-acetylethylenediamine (306 mg, 3 mmoles) and **3e** (421 mg, 1 mmole) using method A. The resulting product was crystallized from methanol/ ethyl acetate to yield 450 mg (92%) of **4g** as colorless crystals, mp 143°; ^{1}H nmr (methanol-d_4): δ 1.93 (s, 3H, $NHCOCH_3$), 2.21 (s, 3H, Me), 3.07 (t, J = 7.3 Hz, 2H, N_1-$CH_2CH_2Ar'H$), 3.35-3.43 (m, 4H, C_4-$NHCH_2CH_2NHCOCH_3$), 4.40 (t, J = 7.3 Hz, 2H, N_1-$CH_2CH_2Ar'H$), 4.91 (s, 2H, $OCH_2C_6H_5$), 6.85 (d, J = 7.3 Hz, 1H, 5-*H*), 7.10-7.12 (m, 2H, N_1-$CH_2CH_2Ar'H$), 7.24-7.44 (m, 8H, N_1-$CH_2CH_2Ar'H$, $OCH_2C_6H_5$), 7.80 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 403 (4, $M^{+\cdot}$, corresponding to the free base), 312 (20), 270 (14), 213 (9), 105 (69), 91 (100) and 65 (55).

Anal. Calcd. for $C_{25}H_{30}N_3O_2BF_4$: C, 61.11; H, 6.15; N, 8.55. Found: C, 61.06; H, 6.12; N, 8.61.

Hydrogenation and Deprotonation of **4a,b,c,e,f** and **g**. General Procedure for the Preparation of **7a,b,c,e,f** and **g**.

To a solution of 1 mmole of **4a,b,c,e,f** and **g** in 60 ml of methanol/ethanol (1:1) was carefully added 50 mg of palladium on activated charcoal (10%), and the suspension was stirred at room temperature overnight under an atmosphere of hydrogen. At the end of this period, the catalyst was filtered, washed with methanol (10 ml), and the filtrate was evaporated under reduced

pressure to give **8a,b,c,e,f** and **g** as unpurified products. The residue was dissolved in 20 ml of 2 *N* aqueous sodium hydroxide and 10 ml of methanol, and the mixture was allowed to stir at ambient temperature for 16 hours. Most of the methanol was removed by evaporation, and the aqueous layer was extracted with dichloromethane for 6 hours. The organic layer was evaporated to dryness.

Compounds **7c,f** and **g** were obtained as solids which were suspended in a suitable solvent under heating. After cooling the solids were collected by suction filtration and dried *in vacuo* to afford analytically pure **7c,f** and **g**.

Compounds **7a,b** and **e** were obtained as oils. Compounds **7a** and **e** were used for the synthesis of **13c** or **13e** respectively without further purification; **7b** was purified by distillation.

Compound **7d** was prepared according to another method.

1,4-Dihydro-2-methyl-1-propyl-4-propylimino-3-pyridinol (**7a**).

Method A.

From **4a** (386 mg, 1 mmole), according to the general procedure to give pyridonimine **7a** as an oily product, yield, 191 mg (92%).

Method B.

A solution of 100 mg (0.55 mmole) of **6a** and propylamine (1.00 ml, 12.1 mmoles) was heated in a bomb tube for 7 hours at 120°. After evaporation of the excess propylamine the brown oil was separated by thin-layer chromatography using 20 x 20 cm glass plates coated with a 0.5 mm thickness of silica gel 60 F_{254} (Fa. Merck) with ethyl acetate/methanol (6:4 v/v) as eluent. The compound **7a** was eluted from the band with an R_f value of 0.38 with hot dichloromethane. The solvent was removed under reduced pressure, and the residue was dried *in vacuo* to afford **7a** as an oily product, 80.1 mg (70%); ^{1}H nmr (deuteriochloroform): δ 0.87-0.95 (m, 6H, N_1-$CH_2CH_2CH_3$, C_4=$NCH_2CH_2CH_3$), 1.62 (sext, J = 7.3 Hz, 2H, C_4=$NCH_2CH_2CH_3$), 1.72 (sext, J = 7.3 Hz, 2H, N_1-$CH_2CH_2CH_3$), 2.45 (s, 3H, Me), 3.13 (t, J = 7.3 Hz, 2H, C_4=$NCH_2CH_2CH_3$), 3.85 (t, J = 7.3 Hz, 2H, N_1-$CH_2CH_2CH_3$), 6.10 (d, J = 6.6 Hz, 1H, 5-*H*), 6.40 (broad s, 1H, O*H*, deuterium oxide exchangeable), 6.87 (d, J = 6.6 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 208 (26, $M^{+\cdot}$), 179 (33), 165 (16), 151 (22), 137 (43), 124 (29), 111 (19), 97 (31), 83 (36), 71 (57) and 57 (100).

4-(2-Diethylaminoethylimino)-1,4-dihydro-2-methyl-1-propyl-3-pyridinol (**7b**).

From **4b** (443 mg, 1 mmole), according to the general procedure, pyridonimine **7b** was obtained as a waxy yellow product, yield, 257 mg (97%). Distillation afforded an analytically pure sample, bp 250°/0.4 torr; ^{1}H nmr (deuteriochloroform): δ 0.97 (t, J = 7.3 Hz, 3H, N_1-$CH_2CH_2CH_3$), 1.08 (t, J = 7.3 Hz, 6H, C_4=$NCH_2CH_2N(CH_2CH_3)_2$), 1.80 (sext, J = 7.3 Hz, 2H, N_1-$CH_2CH_2CH_3$), 2.52 (s, 3H, Me), 2.64 (q, J = 7.3 Hz, 4H, C_4=N-$CH_2CH_2N(CH_2CH_3)_2$), 2.78 (t, J = 7.3 Hz, 2H, C_4=N-$CH_2CH_2N(CH_2CH_3)_2$), 3.38 (t, J = 7.3 Hz, 2H, C_4=$NCH_2CH_2N(CH_2CH_3)_2$), 3.96 (t, J = 7.3 Hz, 2H, N_1-$CH_2CH_2CH_3$), 6.36 (d, J = 6.6 Hz, 1H, 5-*H*), 6.87 (broad s, 1H, O*H*), 7.11 (d, J = 6.6 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 265 (4, $M^{+\cdot}$), 179 (100), 166 (29), 137 (33), 124 (10), 86 (46) and 58 (15).

Anal. Calcd. for $C_{15}H_{27}N_3O$: C, 67.88; H, 10.25; N, 15.83. Found: C, 67.90; H, 10.19; N, 15.45.

1,4-Dihydro-2-methyl-1-phenyl-4-propylimino-3-pyridinol (**7c**).

From **4c** (420 mg, 1 mmole), according to the general procedure, pyridonimine **7c** was obtained as a beige solid, yield, 215 mg (89%). Workup as described afforded an analytically pure sample, mp 228; ^{1}H nmr (methanol-d_4): δ 1.03 (t, J = 7.3 Hz, 3H, C_4=$NCH_2CH_2CH_3$), 1.73 (sext, J = 7.3 Hz, 2H, C_4=$NCH_2CH_2CH_3$), 2.20 (s, 3H, Me), 3.40 (t, J = 7.3 Hz, 2H, C_4=$NCH_2CH_2CH_3$), 6.84 (d, J = 6.6 Hz, 1H, 5-*H*), 7.44 (m, 2H, N_1-Ar'*H*), 7.62 (m, 3H, N_1-Ar'*H*), 7.81 (d, J = 6.6 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 242 (65, $M^{+\cdot}$), 227 (52), 213 (100), 199 (56), 179 (58), 167 (24), 149 (48), 86 (37), 77 (66) and 51 (46).

Anal. Calcd. for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56. Found: C, 74.18; H, 8.10; N, 11.47.

1,4-Dihydro-2-methyl-1-phenyl-4-phenylimino-3-pyridinol (**7d**).

To a solution of 908.5 mg (2 mmoles) **4d** in 30 ml of dry ethanol was added sodium ethanolate (272 mg, 4 mmoles, 10% in ethanol). After stirring for 2 hours at room temperature, most of the ethanol was removed under reduced pressure and 30 ml of water was added. The mixture was extracted with dichloromethane (2 x 25 ml), 50 mg of palladium on activated charcoal (10%) was added and the suspension was stirred at ambient temperature overnight under an atmosphere of hydrogen. After filtration of the catalyst and washing with methanol (10 ml), the solvent was removed by rotary evaporation to give crude **7d**, 514 mg (93%). Recrystallization from methanol/ethyl acetate afforded yellow crystals, mp 180°; ^{1}H nmr (methanol-d_4): δ 2.23 (s, 3H, Me) 7.09 (d, J = 7.3 Hz, 1H, 5-*H*), 7.19-7.63 (m, 11H, 6-*H*, C_4=NAr*H*, N_1-Ar'*H*); ms: (EI) m/z (relative intensity) 276 (48, $M^{+\cdot}$), 275 (83), 169 (25), 105 (27), 78 (68) and 58 (100).

Anal. Calcd. for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84; N, 10.14. Found: C, 78.37; H, 5.71; N, 10.21.

1,4-Dihydro-2-methyl-1-(2-phenylethyl)-4-propylimino-3-pyridinol (**7e**).

From **4e** (448 mg, 1 mmole), according to the general procedure, pyridonimine **7e** was obtained as an oily product, yield, 251 mg (93%); ^{1}H nmr (deuteriochloroform): δ 0.92 (t, J = 7.3 Hz, 3H, C_4=$NCH_2CH_2CH_3$), 1.61 (sext, J = 7.3 Hz, 2H, C_4=$NCH_2CH_2CH_3$), 2.48 (s, 3H, Me), 2.96 (t, J = 7.3 Hz, 2H, N_1-CH_2CH_2Ar'H), 3.11 (t, J = 7.3 Hz, 2H, C_4=$NCH_2CH_2CH_3$), 4.14 (t, J = 7.3 Hz, 2H, N_1-CH_2CH_2Ar'H), 6.04 (d, J = 6.6 Hz, 1H, 5-*H*), 6.75 (d, J = 6.6 Hz, 1H, 6-*H*), 7.00 (d, J = 8.0 Hz, 2H, N_1-CH_2CH_2Ar'*H*), 7.17-7.23 (m, ~3H, N_1-CH_2CH_2Ar'*H*, includes chloroform); ms: (EI) m/z (relative intensity) 270 (27, $M^{+\cdot}$), 241 (20), 137 (26), 124 (39), 105 (100) and 79 (21).

1,4-Dihydro-4-(3-hydroxypropylimino)-2-methyl-1-(2-phenylethyl)-3-pyridinol (**7f**).

From **4f** (464 mg, 1 mmole), according to the general procedure, pyridonimine **7f** was obtained as a beige solid, yield, 249 mg (87%). Workup as described afforded an analytically pure sample, mp 175°; ^{1}H nmr (methanol-d_4): δ 1.85 (quint, J = 6.6 Hz, 2H, C_4=$NCH_2CH_2CH_2OH$), 2.46 (s, 3H, Me), 3.07 (t, J = 7.3 Hz, 2H, N_1-CH_2CH_2Ar'H), 3.38 (t, J = 6.6 Hz, 2H, C_4=$NCH_2CH_2CH_2OH$), 3.66 (t, J = 6.6 Hz, 2H, C_4=NCH_2-CH_2CH_2OH), 4.33 (t, J = 7.3 Hz, 2H, N_1-CH_2CH_2Ar'H), 6.35 (d, J = 6.6 Hz, 1H, 5-*H*), 7.10 (d, J = 7.3 Hz, 2H, N_1-

$CH_2CH_2Ar'H$), 7.17 (d, J = 6.6 Hz, 1H, 6-*H*), 7.24-7.26 (m, 3H, N_1-$CH_2CH_2Ar'H$); ms: (EI) m/z (relative intensity) 286 (8, $M^{+\cdot}$), 255 (19), 241 (12), 124 (29), 105 (100) and 79 (28).

Anal. Calcd. for $C_{17}H_{22}N_2O_2$: C, 71.30; H, 7.74; N, 9.78. Found: C, 71.29; H, 7.78; N, 9.75.

N-2-[1,4-Dihydro-3-hydroxy-2-methyl-1-(2-phenylethyl)-4-pyridylidenamino]ethyl acetamide (**7g**).

From **4g** (491 mg, 1 mmole), according to the general procedure, pyridonimine **7g** was obtained as a beige solid, yield, 285 mg (91%). Workup as described afforded an analytically pure sample, mp 210°; ^1H nmr (methanol-d_4): δ 1.92 (s, 3H, NH-COC*H*$_3$), 2.46 (s, 3H, Me), 3.09 (t, J = 7.3 Hz, 2H, N_1-CH_2-C*H*$_2$Ar'H), 3.37-3.41 (m, 4H, C_4=N-C*H*$_2$C*H*$_2$NHCOCH$_3$), 4.35 (t, J = 7.3 Hz, 2H, N_1-C*H*$_2$CH$_2$Ar'H), 6.42 (d, J = 6.6 Hz, 1H, 5-*H*), 7.10 (d, J = 7.3 Hz, 2H, N_1-$CH_2CH_2Ar'H$), 7.17-7.26 (m, 4H, 6-*H*, N_1-$CH_2CH_2Ar'H$); ms: (EI) m/z (relative intensity) 313 (5, $M^{+\cdot}$), 241 (27), 149 (15), 105 (100), 104 (40), 79 (22), 78 (22) and 77 (38).

Anal. Calcd. for $C_{18}H_{23}N_3O_2$: C, 69.00; H, 7.40; N, 13.40. Found: C, 68.98; H, 7.50; N, 13.32.

4-Methoxy-2-methyl-1-propylpyridinium-3-olate (**6a**).

Method A.

A mixture of 501 mg (3 mmoles) of **5a** and 444 mg (3 mmoles) of trimethyloxonium tetrafluoroborate in 30 ml of dry dichloromethane was stirred at room temperature for 5 hours. After this period 10 ml of water and 2,2,6,6-tetramethylpiperidine (557 µl, 3.3 mmoles) was added and stirring was continued for 30 minutes. The aqueous layer was separated and the organic layer was extracted with water (3 x 10 ml). The aqueous layers were combined, washed with 5 ml of dichloromethane and evaporated *in vacuo* to give **6a** as colorless crystals, 299 mg (55%). An analytical sample was recrystallized from water.

Method B.

A solution of 4.20 g (30 mmoles) of isomaltol methyl ether **9** and 2.40 g of propylamine (40 mmoles) in 20 ml of water/ethanol (1:1 v/v) was heated under reflux for 6 hours. Most of the solvent and the excessive amine was removed by rotary evaporation and the mixture was diluted with water. After extraction with dichloromethane the organic layer containing **10** was separated and the remaining aqueous layer was evaporated under reduced pressure to dryness affording **6a** as colorless crystals, 2.20 g (40%). An analytical sample was prepared by recrystallization from water, mp 157°; ^1H nmr (methanol-d_4) δ 0.99 (t, J = 7.3 Hz, 3H, N_1-$CH_2CH_2CH_3$), 1.86 (sext, J = 7.3 Hz, 2H, N_1-$CH_2CH_2CH_3$), 2.53 (s, 3H, Me), 3.95 (s, 3H, OC*H*$_3$), 4.25 (t, J = 7.3 Hz, 2H, N_1-C*H*$_2$CH$_2$CH$_3$), 7.00 (d, J = 7.3 Hz, 1H, 5-*H*), 7.65 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (EI) m/z (relative intensity) 181 (100, $M^{+\cdot}$), 166 (11), 152 (31), 138 (62), 110 (50), 109 (36), 93 (22), 67 (29) and 53 (32).

Anal. Calcd. for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73. Found: C, 66.42; H, 8.43; N, 7.76.

2-Methyl-4-methylthio-1-(2-phenylethyl)pyridinium-3-olate (**12a**).

Thiopyridone **11a** was prepared according to a modified literature method [10]. A solution of 229 mg (1 mmole) of **5e** and 212 mg (0.525 mmole) of 2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide in 10 ml of anhydrous 1,2-dichloroethane was heated at 80° for 8 hours. After evaporation of the solvent, the residue was dissolved in 15 ml of methanol and the mixture was allowed to stand at room temperature for several hours at which time **11a** crystallized (118 mg, 48%). Pure **11a** (100 mg, 0.41 mmole) was dissolved in 10 ml of dry dichloromethane and trimethyloxonium tetrafluoroborate (71 mg, 0.48 mmole) was added under stirring in one portion. Stirring was continued for 5 hours, and the resulting white precipitate was collected by suction filtration, dissolved in 10 ml of ethanol, and 68 µl (0.4 mmole) of 2,2,6,6-tetramethylpiperidine was added *via* a syringe. After stirring for one hour at ambient temperature the solvent was removed by evaporation and the crude product was separated by column chromatography (ethyl acetate/methanol, (1:1) v/v, r_f = 0.54). Fractions containing the product were evaporated to dryness yielding 94 mg (91%) of **12a** as oily product. An analytical sample was prepared by crystallization from methanol/ethyl acetate to give white needles, mp 169°; ^1H nmr (deuteriochloroform): δ 2.27 (s, 3H, SC*H*$_3$), 2.50 (s, 3H, Me), 3.02 (t, J = 7.3 Hz, 2H, N_1-CH_2-C*H*$_2$Ar'H), 4.26 (t, J =7.3 Hz, 2H, N_1-C*H*$_2$CH$_2$Ar'H), 6.63-6.67 (m, 2H, 5-*H*, 6-*H*), 6.99 (d, J = 7.3 Hz, 2H, N_1-$CH_2CH_2Ar'H$), 7.17-7.24 (m, 3H, N_1-$CH_2CH_2Ar'H$); ms: (CI) m/z (relative intensity) 260 (100, M + H), 214 (8), 105 (12) and 79 (42).

Anal. Calcd. for $C_{15}H_{17}NOS$: C, 69.46; H, 6.60; N, 5.40. Found: C, 69.28; H, 6.97; N, 5.50.

3-Benzyloxy-2-methyl-4-methylthio-1-(2-phenylethyl)pyridinium Tetrafluoroborate (**12b**).

Thiopyridone **11b** was prepared according to a modified literature method [11]. To a stirring suspension of tlc pure **2e** (638 mg, 2 mmoles) and 489 mg (1.1 mmoles) of phosphorus pentasulfide in 20 ml of dry acetonitrile was added triethylamine (1.12 ml, 8 mmoles) in three portions while cooling the mixture in ice-water. The resulting solution was left stirred at room temperature for 24 hours. After this period, the solvent was removed under reduced pressure and the substance was purified by column chromatography on silica gel with ethyl acetate/methanol ((9:1) v/v, r_f = 0.73) as eluent. The fractions containing the product were combined. Evaporation of the solvent afforded crude **11b** which crystallized from methanol at room temperature, 369 mg (55%). Pure **11b** (335 mg, 1 mmole) was dissolved in 20 ml of dry dichloromethane and trimethyloxonium tetrafluoroborate (148 mg, 1 mmole) was added under stirring in one portion. The brown solution turned colorless within 30 minutes, and stirring was continued for an additional 2 hours. After evaporation of the solvent the solid material was recrystallized from methanol/ethyl acetate to give 367 mg (84%) of **12b**, mp 149°; ^1H nmr (deuteriochloroform/methanol-d_4): δ 2.34 (s, 3H, Me), 2.64 (s, 3H, SC*H*$_3$), 3.18 (t, J = 6.6 Hz, 2H, N_1-CH_2C*H*$_2$Ar'H), 4.66 (t, J = 6.6 Hz, 2H, N_1-C*H*$_2$CH$_2$Ar'H), 4.97 (s, 2H, OC*H*$_2$C$_6$H$_5$), 7.04-7.07 (m, 2H, N_1-$CH_2CH_2Ar'H$), 7.29-7.43 (m, ~8H, N_1-$CH_2CH_2Ar'H$, OC*H*$_2$C$_6$*H*$_5$, includes chloroform), 7.54 (d, J = 7.3 Hz, 1H, 5-*H*), 8.21 (d, J = 7.3 Hz, 1H, 6-*H*); ms: (CI) m/z (relative intensity) 350 (4, $M^{+\cdot}$, corresponding to the cation), 260 (19), 105 (44), 93 (100), 92 (75) and 91 (77).

Anal. Calcd. for $C_{22}H_{24}NOSBF_4$: C, 60.45; H, 5.49; N, 3.20. Found: C, 60.15; H, 5.54; N, 3.43.

General Methods for the Preparation of the Complex Compounds **13a-f** and **14a,b**.

Method A.

A solution of 2 (3) mmoles of **5** or **7** and the appropriate metal salt or metal acetylacetonate (1 mmole) respectively in 20 ml of a suitable solvent is heated under reflux for 2 hours. The reaction mixture was evaporated under reduced pressure to dryness and the residue was recrystallized (solvent stated).

Method B.

One mmole of **4a** or **e** was treated as described in the general procedure to give crude **8** which was dissolved in 20 ml of methanol. Bis(2,4-pentandionato)dioxomolybdenum(VI) (163.08 mg, 0.5 mmole) and triethylamine (0.5 ml) were added, and the mixture was heated for 2 hours under reflux. After removal of the solvent under reduced pressure the oily residue was crystallized from methanol/ethyl acetate.

Bis(1,4-dihydro-2-methyl-4-oxo-1-propyl-3-pyridinolato)-copper(II) (**13a**).

This compound was synthesized from **5a** (334 mg, 2 mmoles) and copper(II) chloride dihydrate (170.45 mg, 1 mmole) in methanol/water (1:1) as solvent using method A. The product was recrystallized from methanol yielding 301 mg of **13a** (76%) as green crystals, mp >300° dec; ir: ν 3100-3000, 2950, 1600, 1550, 1500, 1350, 1290 cm^{-1}.

Anal. Calcd. for $C_{18}H_{24}N_2O_4Cu$: C, 54.60; H, 6.11; N, 7.08. Found: C, 54.69; H, 6.26; N, 6.83.

Bis(1,4-dihydro-2-methyl-4-oxo-1-propyl-3-pyridinolato)oxo-vanadium(IV) (**13b**).

This compound was synthesized from **5a** (334 mg, 2 mmoles) and bis(2,4-pentandionato)oxovanadium(IV) (265.16 mg, 1 mmole) in methanol/water (1:1) as solvent using method A. The product was recrystallized from methanol/ethyl acetate yielding 283 mg of **13b** (71%) as dark blue crystals, mp >300° dec; ir: ν 3050, 3000-2900, 1610, 1550, 1500, 1350, 1270, 1050, 952 cm^{-1}.

Anal. Calcd. for $C_{18}H_{24}N_2O_5V$: C, 54.14; H, 6.06; N, 7.01. Found: C, 54.07; H, 6.44; N, 6.70.

Bis(1,4-dihydro-2-methyl-1-propyl-4-propylimino-3-pyridino-lato)dioxomolybdenum(VI) (**13c**).

Using method B compound **13c** was synthesized from **4a** (386 mg, 1 mmole) to yield 54 mg (20%) as orange crystals, mp *ca.* 244° dec; ir: ν 2961, 2872, 1613, 1548, 1493, 1378, 1348, 1284, 1254, 1140, 928, 897, 676 cm^{-1}.

Anal. Calcd. for $C_{24}H_{38}N_4O_4Mo$: C, 53.13; H, 7.06; N, 10.33. Found: C, 52.93; H, 7.20; N, 10.38.

Bis(1,4-dihydro-2-methyl-4-oxo-1-(2-phenylethyl)-3-pyridin-olato)dioxomolybdenum (VI) (**13d**).

This compound was synthesized from **5e** (458 mg, 2 mmoles) and bis(2,4-pentandionato)dioxomolybdenum(VI) (326.16 mg, 1 mmole) in methanol/water (4:1) as the solvent using method A. The product was recrystallized from methanol yielding 419.5 mg of **13d** (72%) as yellow powder, mp >300° dec; ir: ν 1613, 1551, 1493, 1267, 1053, 919, 892, 822, 697, 641 cm^{-1}.

Anal. Calcd. for $C_{28}H_{28}N_2O_6Mo$: C, 57.54; H, 4.83; N, 4.79. Found: C, 57.58; H, 4.99; N, 4.55.

Bis(1,4-dihydro-2-methyl-1-(2-phenylethyl)-4-propylimino-3-pyridinolato)dioxomolybdenum(VI) (**13e**).

Using method B compound **13e** was synthesized from **4e** (448 mg, 1 mmole) to yield 132.6 mg (40%) as orange crystals, mp ca. 240° dec; ir: ν 2958, 2865, 1613, 1548, 1493, 1349, 1281, 1249, 924, 901, 669 cm^{-1}.

Anal. Calcd. for $C_{34}H_{42}N_4O_4Mo$: C, 61.28; H, 6.30; N, 8.40. Found: C, 61.16; H, 6.56; N, 8.25.

Bis(1,4-dihydro-2-methyl-1-phenyl-4-phenylimino-3-pyridin-olato)copper(II) (**13f**).

This compound was synthesized from **7d** (552 mg, 2 mmoles) and bis(2,4-pentandionato)copper(II) (262 mg, 1 mmole) in dry dichloromethane as solvent using method A. The product was recrystallized from dichloromethane/ethyl acetate yielding 264 mg of **13f** (43%) as brown crystals, mp ca. 275° dec; ir: ν 1580, 1537, 1466, 1307, 696, 609 cm^{-1}.

Anal. Calcd. for $C_{36}H_{30}N_4O_2Cu$: C, 70.40; H, 4.92; N, 9.12. Found: C, 70.29; H, 4.87; N, 9.25.

Tris(1,4-dihydro-2-methyl-4-oxo-1-(2-phenylethyl)-3-pyridin-olato)iron(III) (**14a**).

This compound was synthesized from **5e** (687 mg, 3 mmoles) and iron(III) chloride (162 mg, 1 mmole) in methanol/water (4:1) as solvent using method A . The product was recrystallized from dichloromethane/ethyl acetate yielding 629 mg of **14a** (85%) as dark red crystals, mp ca. 285° dec; ir: ν 1733, 1594, 1538, 1503, 1355, 1281, 1244, 1055, 809, 748, 701, 625 cm^{-1}.

Anal. Calcd. for $C_{42}H_{42}N_3O_6Fe$: C, 68.10; H, 5.71; N, 5.67. Found: C, 67.95; H, 5.99; N, 5.54.

Tris(1,4-dihydro-2-methyl-4-oxo-1-propyl-3-pyridinolato)man-ganese(III) (**14b**).

This compound was synthesized from **5a** (501 mg, 3 mmoles) and manganese(III) acetate dihydrate (268 mg, 1 mmole) in methanol/water (1:1) as the solvent using method A . The product was recrystallized from dichloromethane/ethyl acetate yielding 288 mg of **14b** (52%) as brown crystals, mp >300° dec; ir: ν 3050, 3000-2900, 1600, 1550, 1495, 1340, 1270 cm^{-1}.

Anal. Calcd. for $C_{27}H_{36}N_3O_6Mn$: C, 58.59; H, 6.56; N, 7.59. Found: C, 58.38; H, 6.92; N, 7.42.

Preliminary Experiments: Oxidation of Olefins using **13** or **14** as Catalysts:

Gas Chromatographic Analysis of the Oxidation Products.

An aliquot of the reaction mixture (0.2 µl) was injected through a split injector onto a 25m x 0.25 mm ID fused capillary column (OV 1701, Fa. Permabond). The flow rate was 0.5 ml/minute and detection was by FID or mass selective detector respectively. The injector and detector temperature was at 280° and the oven temperature was programed as follows: 40° for 4 minutes, 40-80° at 4°/minute, 80-260° at 20°/minute and hold at 260° for 15 minutes. No internal or external standards were used and yields were based on the amount of consumed alkene.

Epoxidation of 1-Methyl-1-cyclohexene.

Method A.

In a modified procedure according to a literature method [12] for olefin-epoxidation with *tert*-butylhydroperoxide 1.18 ml (10 mmoles) of 1-methyl-1-cyclohexene in 20 ml of dry benzene was charged into a 50 ml round-bottomed flask. After adding the catalyst **13c** (27 mg, 0.05 mmoles) the flask was closed by a septum and the atmosphere was replaced with a nitrogen stream. To this magnetically stirred suspension 1.75 ml of *tert*-butylhydro-

peroxide (80% in di-*tert*-butylhydroperoxide, *ca.* 14 mmoles) was injected dropwise during 5 minutes *via* a syringe through the septum. Stirring was continued in an oil-bath at 80° for 22 hours under nitrogen. The reaction products were analyzed by gas chromatography. 1,2-Epoxy-1-methylcyclohexane as main product, small amounts of 1-methyl-1,2-cyclohexandiol, and traces of unconsumed olefin were detected.

Method B.

Epoxidation of Olefins by Oxygen, According to a Modified Literature Method [13].

A solution of 1 ml (11 mmoles) of isobutyraldehyde, 10 µl of acetic acid, 37 mg (0.05 mmole) of **14a** and 300 mg (3.12 mmoles) of 1-methyl-1-cyclohexene in 1,2-dichloroethane (10 ml) was gassed with oxygen for 10 minutes. The septum fitted flask was allowed to stir at 60° in an oil bath for 22 hours. The reaction products were analyzed by gas chromatography. 1,2-Epoxy-1-methylcyclohexane was formed quantitatively (no unconsumed olefin could be detected).

Epoxidation of Cyclooctene.

In a modified procedure according to a literature method [12] for olefin-epoxidation with *tert*-butylhydroperoxide 0.2 ml (1.54 mmoles) of cyclooctene in 5 ml of dry benzene was charged into a 50 ml round-bottomed flask. After adding the catalyst **13d** (45 mg, 0.077 mmole) the flask was closed with a septum and the atmosphere was replaced with a nitrogen stream. To this suspension 1.0 ml of *tert*-butylhydroperoxide (80% in di-*tert*-butylhydroperoxide, ca. 8 mmoles) was injected dropwise during 5 minutes under magnetic stirring *via* a syringe through the septum. Stirring was continued in an oil-bath at 80° for 8 hours under nitrogen. The reaction products were analyzed by gas chromatography. 1,2-Epoxycyclooctene as main product and traces of unconsumed olefin were detected.

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