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A CONVENIENT SYNTHESIS OF SUBSTITUTED PYRIDYLGLYCOLS PROMOTED BY AQUEOUS TITANIUM TRICHLORIDE

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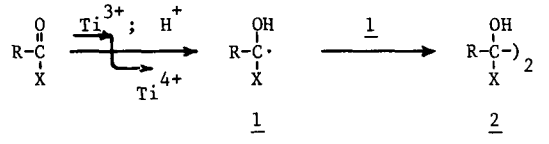
Abstract. 2- and 4-Acetylpyridines, and 2- and 4-pyridinealdehydes when allowed to react with two-equiv. of aqueous titanium trichloride add to the carbonyl carbon atom of simple ketones (acetone, cyclopentanone, cyclohexanone) and aldehydes (acetaldehyde, propionaldehyde, benzaldehyde) affording substituted pyridylglycols in very good yields. The present one-pot method has considerable advantage over the existing procedure. The reaction is discussed in terms of a radical mechanism in which the Ti(III) species plays the fundamental role.

INTRODUCTION

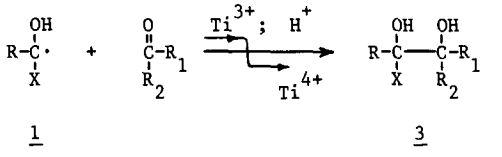
As part of our interest on the reducing properties of titanium trichloride in aqueous acidic or basic solution, we have shown[1,2] that Ti(III) ion promotes the reductive hydrodimerization of pyridineketones and pyridinealdehydes in high yields under quite simple experimental conditions. Next[3,4] we have extended the method to the conversion of other carbonyl compounds, activated towards reduction by an electron withdrawing group (CN, COOH, COOR), to the corresponding symmetrical diols. Both the formation of diols[1] and the stereochemistry of the reaction (dl/meso ratio[2]) have been discussed in terms of a radical mechanism (Scheme 1) in which the intermediate capto-dative radical 1, formed by uptake of one electron from Ti(III) ion, owing to its particular stabilization[6,7], has an high concentration in the reaction medium and dimerizes in very good yields.



R= H, CH_3, Ph; (dl, meso)
R= 2-, 3-, 4-Py[1,2], CN[3], $COOH$[4], $COOCH_3$[4], CHO[5].

Scheme 1.

Though capto-dative substitution seems to mainly favour the whole process of dimerization[6,8], recent reports[3,4] from our laboratory have shown that in the presence of an excess of simple ketones or aldehydes the competitive reaction of Scheme 2 becomes predominant over the dimerization of 1:



R= Ph; X= CN, COOH, COOR;
R_1=R_2=CH_3; R_1= H, R_2= CH_3, Ph.

Scheme 2.

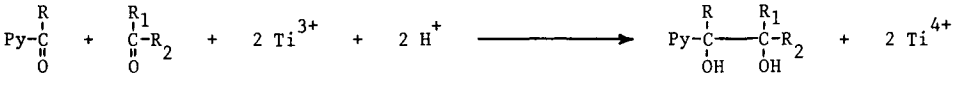
the intermediate radical 1 adds to the carbonyl carbon atom of acetone, acetaldehyde, and benzaldehyde to form the unsymmetrical diols 3 in high yields instead of dimerizing.

Although the synthesis of symmetrical diols represents an excellent alternative to the photochemical, electrochemical and metal reduction methods employed[9], the synthesis of unsymmetrical diols might have a greater synthetic potential, mostly in relation to their pinacol re-

arrangement: in fact, several compounds of this series possess valuable specific adrenal cortical inhibitory activity.

RESULTS

In our effort to develop a generally applicable method for the synthesis of unsymmetrical diols, we, now, report on the convenient preparation of substituted pyridylglycols 4 starting from the corresponding pyridineketones and -aldehydes by one-step procedure. The reaction is depicted in Scheme 3.

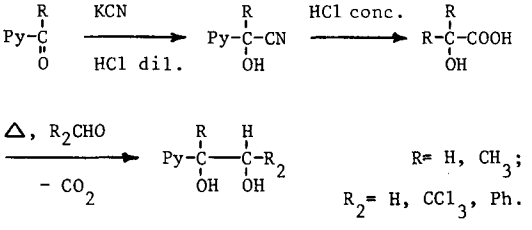


Py= 2- or 4-pyridine ring; R= H, CH_3;
R_1= R_2= CH_3; R_1, R_2= $-(CH_2)_4-$, $-(CH_2)_5$;
R_1= H and R_2= CH_3, C_2H_5, Ph.

Scheme 3.

When acetaldehyde or propionaldehyde are used, unsymmetrical diols 4 are accompained by dioxolanes 5 which result from subsequent condensation of 4 with the starting aldehydes. Symmetrical diols 2 are always formed in variable amount according to Scheme 1. Isolated yields of 2, 4, and 5 are reported in Table 1. The overall stoichiometry for the reaction in Scheme 3 is 2:1 with respect to the Ti(III) ion/carbonylpyridines ratio, and a molar ratio of 1:2:15 (substrate/Ti(III) ion/R_1R_2CO) has been used in all reactions. A great excess of ketones and/or aldehydes has been utilized in order to minimize the formation of 2 in favour of 4[3]. Rapid instead of dropwise addition of the reducing solution has been adopted, for an excess of Ti(III) ion in the reaction medium improves the yield of 4 and reduces the formation of 2. The ^{1}H NMR spectra of crude dioxolanes 5 reveal that two out of four (dl pairs) possible stereoisomers are present in higher yield. The ^{1}H NMR spectra of crude diols 4 obtained with aldehydes suggest that these compounds are formed as a mixture of threo and erythro isomers. In some cases (see experimental section) the isomers' separation was achieved by column and preparative thin layer chromatography, but any attempt to analyse their stereochemistry by spectroscopic methods has been hitherto unsuccessful.

As far as the synthesis of pyridylglycols 4 is concerned, only two patents[10,11] are reported in the literature which recall their pharmaceutical interest as intermediates. It is worth to underline that several steps are needed for their preparation as shown in Scheme 4:



Scheme 4.

Furthermore, this method, considerably less advantageous over our one-step procedure, does have limitation, for its applicability is re-

stricted to aldehydes (R_2CHO) only.

DISCUSSION

The mechanism involved in the reaction of Scheme 3 deserves some more comments. It is known that, at low pH, the Ti(III) species is a very mild reducing agent (the equation[12] :

$$E = 0.100 - 0.1182\ pH + 0.0591\ lg \left[TiO^{2+} / Ti^{3+}\right]$$

is valid in acidic solution where Ti(IV) is present as soluble TiO^{2+}) and we experimentally observed that:

a) only carbonyl compounds substituted with electron-withdrawing groups (X), capable of effecting the necessary activation of the carbon-oxygen bond, are reduced to the corresponding intermediate radicals 1 by Ti(III) ion in acidic medium;

b) simple aromatic ketones and aldehydes (benzophenone, acetophenone, and benzaldehyde), while are not affected by Ti(III) ion in acidic medium, undergo rapid one-electron reduction to symmetrical diols in basic solution[2] in accord with the increase of the reducing power of Ti(IV)/Ti(III) redox system with increasing the pH (the equation[12]:

$$E = 0.029 - 0.236\ pH - 0.0591\ lg \left[Ti^{3+}\right]$$

is valid in basic medium where Ti(IV) is present as insoluble TiO_2);

c) simple aliphatic ketones and aldehydes (acetone, cyclopentanone, cyclohexanone, and valeraldehyde) require a stronger reducing agent, such as Ti(0) powder (from $TiCl_3$/K or $TiCl_3$/Li systems[13]), to be reduced to the corresponding intermediate radicals[13,14]: $R'R''\dot{C}$-O-Ti(I).

Therefore, on the basis of the above evidence given, a mixed radicals coupling is not the process which would lead to unsymmetrical diols 4. The alternate hypothesis that Ti(III) ion further reduces the intermediate radical 1 to the corresponding anion, and this latter would effect a nucleophilic addition to the carbonyl carbon atom of simple ketones or aldehydes, is in contrast with the following considerations:

d) the already mentioned low reducing power of Ti(III) ion in acidic medium;

e) the redox potential of radical 1 which, though unknown, must be high (in negative value) for the presence of adjacent donor and acceptor groups greatly stabilizes the radical while, on the contrary, destabilizes the corresponding anion[6];

f) supposing the formation of a carbanion is thermodynamically possible, we should obtain, in our reaction conditions ($pH \leqslant 1$), the corresponding pyridylcarbinols[15] instead of the symmetrical and unsymmetrical diols 2 and 4.

The most likely sequence of reactions to rationalize the formation of pyridylglycols 4 is produced in Scheme 5: the intermediate radical 1 either dimerizes to 2 (path i) or adds to the carbonyl carbon atom to form the alkoxyl radical 6 (path ii). Rapid reduction of 6 (path iii) and subsequent proton transfer give 4.

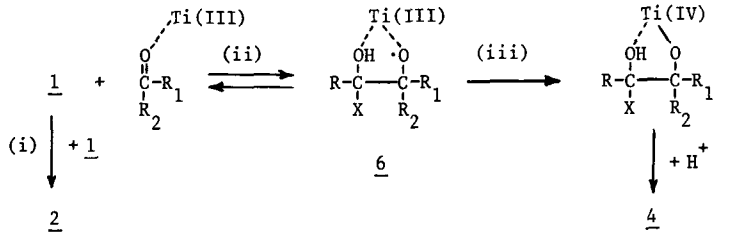
Although alkyl radical additions to carbonyl carbon have been previously proposed[16-18], path (ii) is a well known reversible process[19]. In our reaction conditions, a fundamental role in minimizing the reversibility of path (ii) is played by Ti(III) ion[20] which reduces the strong electrophilic alkoxyl radical 6 in an especially rapid and competing irreversible process[21] (path iii).

Supporting evidence is that dropwise addition of the reducing solution increases the yields of 2, while rapid mixing of the reagents gives the best yields of 4, i.e. an high concentration of Ti(III) ion favours the alkoxyl radical reduction, practically eliminates the reversibility of path ii, and reduces the formation of 2.

The high yields of symmetrical diol obtained with 4-pyridinealdehyde turns in favour of a reversible dimerization of 1 to 2 (path i) even at room temperature[22,23] : in fact, dimer 2m

istantaneously precipitates from the reaction mixture as insoluble hydrochloride and would not serve anymore as a reservoir for the reactive monomer 1.

ether (3x50 ml) of the crude mixture. The residual aqueous layers, added with 20 ml of 30% dibasic ammonium citrate solution to prevent foaming, were made alkaline with a 30% NaOH



Scheme 5.

EXPERIMENTAL

General data. The physical data were obtained as follows: melting points in a Koffler apparatus (uncorrected); IR spectra on a Perkin-Elmer E 177; mass spectra on a Hitachi-Perkin-Elmer RMU 6D at 70 eV; ^{1}H NMR spectra on a Varian A-90 and HA-100 with Me_4Si as an internal standard. Column and preparative thin layer chromatography were carried out by using Merck silica gel 60 (0.06-0.24 mm) and Merck Kieselgel G F-254 (2mm) plates respectively. All chemicals employed were reagent grade, and the $TiCl_3$ solution (15% v/v in acidic water) was standardized against Ce(IV) 0.1 N solution. All new compounds gave satisfactory elementary (C,H,N) analyses. All compounds were isolated and their structural assignments are completely consistent with the spectral and analytical data given below.

General procedure. To a well stirred solution of the substrate (Py-CO-R, 15 mmol) and the ketones or aldehydes (R_1-CO-R_2, 225 mmol) in glacial acetic acid (10-15 ml), a 15% $TiCl_3$ solution (30 mmol) was added all at once. The reaction mixture was allowed to react for 3 h at room temperature under nitrogen.

General work-up procedure. In all reactions (except with acetone) the unreacted ketone or aldehyde was separated by extraction with ethyl

solution and then extracted with ethyl acetate (3x150 ml). The combined organic extracts were washed with distilled water, dried over Na_2SO_4 and concentrated in vacuo.

Because of the different solubility of the reaction products, the respective procedures for their isolation are given.

Runs a - f. Dimer 2a, 2,3-di(4-pyridyl)-2,3-butanediol has a very low solubility in most of the common organic solvents[1] and its recovery was achieved only by subsequent continuous extraction by percolation with ethyl acetate. As revealed by ^{1}H NMR spectra, the crude mixtures obtained after work-up contain almost exclusively the unsymmetrical diols 4a, 4b, 4c, and 4f (wich can be further purified by recrystallization) or a mixture of 4d, 5d, and 4e, 5e. Preparative column chromatography on silica gel, using the gradient elution method (hexane/ethyl acetate from 8:1 to 1:1) afforded the separation of dioxolanes 5d or 5e from diols 4d or 4e. The elution order was: dioxolane, diol.

Runs g - l. Dimer 2g, 2,3-di(2-pyridyl)-2,3-butanediol is soluble in ethyl acetate, but its quantitative recovery was achieved by continuous extraction. Dimer 2g was separated from the crude reaction mixtures obtained after work-up by column chromatography on silica gel (eluant: hexane/

Table 1. Yields of isolated products.

Run	Substrate	$R-\overset{\overset{O}{\|}}{C}-R_2$	Products isolated yield (%)[a]			Overall yield (%)[a]
			2	4	5	
a	(4)Py-$\overset{\overset{O}{\|}}{C}$-$CH_3$	acetone	25	63	-	88
b	"	cyclopentanone	24	71	-	95
c	"	cyclohexanone	25	62	-	87
d	"	acetaldehyde	25	traces	60	85
e	"	propionaldehyde	24	28	41	93
f	"	benzaldeyhde	10	85	-	95
g	(2)Py-$\overset{\overset{O}{\|}}{C}$-$CH_3$	acetone	14	80	-	94
h	"	cyclopentanone	17	68	-	85
i	"	cyclohexanone	16	72	-	88
j	"	acetaldehyde	18	42	30	90
k	"	propionaldehyde	40	44	traces	84
l	"	benzaldehyde	16	47	-	63
m	(4)Py-$\overset{\overset{O}{\|}}{C}$-H	acetone	78	20	-	98
n	"	benzaldehyde	77	20	-	97
p	(2)Py-$\overset{\overset{O}{\|}}{C}$-H	acetone	40	35	-	98[b]
q	"	benzaldehyde	31	40	-	89[b]

a) products isolated and overall yields are based on the starting substrate; b) 23% and 18% of methyl-2-pyridylcarbinol were respectively recovered in runs p and q; in all other runs the corresponding carbinols were always less than 5%.

ethyl acetate from 9:1 to 1:1). The elution order was: dimer 2g, diol 4 (runs g, h, i, l); dioxolane 5j, dimer 2g, diol 4j (run j); and dioxolane 5k, dimer 2g, diol 4k (run k).

Runs m and n. Dimer 2m, 1,2-di(4-pyridyl)-1,2-ethanediol (meso isomer) precipitated instantaneously from the reaction mixture as insoluble dihydrochloride[1]. The crude mixture obtained after work-up was contamined with the dl isomer of 2m which was separated from diol 4m or 4n by preparative thin layer chromatography (eluant: hexane/ethyl acetate/methanol 4.5:4.5:1).

Runs p and q. Dimer 2p, 1,2-di(2-pyridyl)-1,2-ethanediol was separated from diol 4p or 4q by column chromatography on silica gel (eluant: hexane/ethyl acetate/methanol 4.5:4.5:1). The elution order was: 4p or 4q, methyl-2-pyridylcarbinol (see note b) in Table 1.), and 2p.

Spectroscopic data. For spectroscopic assignments of 2a, 2g, 2m, and 2p see Ref. 1. The structures of products 4 and 5 were deduced as follows:

2-(4-Pyridyl)-3-methyl-2,3-butanediol (4a, 63%): m.p. 148-51 °C (from chloroform/methanol 9:1); ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 3H, CH_3), 1.22 (s,3H, CH_3), 1.6 (s, 3H, CH_3), 3.0-3.5 (broad, 2H, 2 OH, D_2O exch.), 7.45 (m, 2H, Py-H_β), 8.5 (m, 2H, Py-H_α); IR (nujol) ν_{max} 3300 (OH, s), 3150 (OH, br) cm^{-1}; MS m/e 182 $(M+1)^{24}$, 164 $(M-H_2O)$, 148, 123, 122 (base peak), 106, 80, 79, 59.

1-(4-Pyridyl)-1-(1-cyclopentanol)-ethanol (4b, 71%): m.p. 135-6 °C (from chloroform/methanol 9:1); ^{1}H NMR ($CDCl_3$ + CD_3OD) δ 1.5-2.0 (m, 11 H, CH_3 and $(CH_2)_4$), 4.5 (broad, 2H, 2OH, D_2O exch.), 7.6 (m, 2H, Py-H_β), 8.5 (m, 2H, Py-H_α); IR (nujol) ν_{max} 3340 (OH, s) cm^{-1}; MS m/e 207 (M), 190 (M-OH), 123 (base peak), 122, 85, 79.

1-(4-Pyridyl)-1-(1-cyclohexanol)-ethanol (4c, 62%): m.p. 134 °C (from chloroform/ethyl ether 1:1); ^{1}H NMR ($CDCl_3$) δ 1.2-1.7 (s and m, 13 H, CH_3 and $(CH_2)_5$), 2.0-3.0 (broad, 2H, 2 OH, D_2O exch.), 7.4 (m, 2H, Py-H_β), 8.5 (m, 2H, Py-H_α); IR (nujol) ν_{max} 3470 (OH, broad), 3120 (OH, s) cm^{-1}; MS m/e 222 (M+1)^{24}, 203 (M-H_2O), 123 (base peak), 122, 79.

2,4,5-Trimethyl-5-(4-pyridyl)-1,3-dioxolane (5d, 60%): thick oil; the NMR spectrum of the crude product shows a mixture of four diastereomers, two forms were predominant and their separation was achieved by preparative column chromatography using the gradient elution method (hexane/ethyl acetate from 9:1 to 1:1).

One isomer (oil): ^{1}H NMR ($CDCl_3$) δ 0.8 (d, J= 6.6 Hz, 3H, CH_3), 1.52 (d, J= 5.1 Hz, 3H, CH_3), 1.6 (s, 3H, CH_3), 3.95 (q, J= 6.6 Hz, HO-CH-CH_3), 5.28 (q, J= 5.1 Hz, 1 H, O-CH-O), 7.3 (m, 2H, Py-H_β), 8.6 (m, 2H, Py-H_α).

The other isomer (thick oil): ^{1}H NMR ($CDCl_3$) δ 1.33 (d, J= 6.6 Hz, 3H, CH_3), 1.4 (s, 3H, CH_3), 1.48 (d, J= 4.8 Hz, 3H, CH_3), 3.92 (q, J= 6.6 Hz, 1 H, O-CH-CH_3), 5.2 (q, J= 4.8 Hz, 1 H, O-CH-O), 7.3 (m, 2H, Py-H_β), 8.6 (m, 2H, Py-H_α); IR (film) ν_{max} 1160-1050 cm^{-1} (characteristic bands of dioxolane ring[25]); MS m/e 193 (M), 178 (M-CH_3), 149 (M-CH_3CHO, base peak), 134, 122, 107, 79.

2-(4-Pyridyl)-2,3-pentanediol (4e, 28%): thick oil, mixture of two stereoisomers; ^{1}H NMR ($CDCl_3$) δ 0.9 and 0.95 (2t, 3H, CH_2-CH_3), 1.2-1.6 (m, 2H, CH_2-CH_3), 1.5 and 1.58 (2s, 3H, CH_3), 3.51 and 3.52 (2t, 1 H, CH-OH), 4.3 (s, 2H, 2 OH, D_2O exch.), 7.4 (m, 2H, Py-H_β), 8.4 (m, 2H, Py-H_α); IR (film) ν_{max} 3300 (OH, very s) cm^{-1}; MS m/e 182 (M+H)^{24}, 181, 163 (M-H_2O), 123 (base peak), 122, 80, 79, 78, 59.

2,4-Diethyl-5-methyl-5-(4-pyridyl)-1,3-dioxolane (5e, 41%): thick oil, mixture of four stereoisomers; ^{1}H NMR ($CDCl_3$) δ 0.75-1.95 (m, 10 H, two CH_2CH_3), 1.25, 1.35, 1.40 and 1.60 (4s, 3H, CH_3CO), 3.5-4.0 (4t, 1 H, CH-O), 4.9-5.3 (4t, 1 H, O-CH-O), 7.3 (m, 2H, Py-H_β); 8.55 (m, 2H, Py-H_α); IR (film) ν_{max} 1160-1000 cm^{-1} (characteristic bands of dioxolane ring[25]); MS m/e 221(M), 206 (M-CH_3), 192 (M-C_2H_5), 163 (M-2 C_2H_5, base peak), 148, 134, 122. 121, 78, 58.

1-Phenyl-2-(4pyridyl)-1,2-propanediol (4f, 85%): threo and erythro mixture (1:1); m.p. 150-2 °C (from chloroform), Lit.[10] 149-51 °C unknown stereochemistry; ^{1}H NMR ($CDCl_3$) δ 1.4 and 1.6 (2s, 3H, CH_3), 4.4 (s, 2H, 2 OH, D_2O exch.), 4.7 (s, 1 H, CH), 7.0-7.3 (m, 5H, Ph-H), 7.3-7.5 (m, 2H, Py-H_β), 8.4 (m, 2H, Py-H_α); IR (nujol) ν_{max} 3400 and 3200 (OH, s) cm^{-1}; MS m/e 211(M-H_2O), 123, 122, 121, 106 (base peak), 105, 78, 77.

2-(2-Pyridyl)-3-methyl-2,3-butanediol (4g, 80%): oil; ^{1}H NMR ($CDCl_3$) δ 1.1 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.6 (s, 3H, CH_3), 4.3 (broad, 2H, 2 OH, D_2O exch.), 7.2 (m, 1 H, Py-H_β), 7.65 (m, 2H, Py-H_β and Py-H_γ), 8.55 (m, 1H, Py-H_α); IR (film) ν_{max} 3400 (OH, s) cm^{-1}; MS m/e 182 (M+H)^{24}, 164 (M-H_2O), 146, 122 (base peak), 79, 59, 43.

1-(2-Pyridyl)-1-(1-cyclopentanol)-ethanol (4h, 68%): m.p. 73-4 °C (from ethyl ether); ^{1}H NMR ($CDCl_3$) δ 1.3-2.0 (m, 11 H, CH_3 and $(CH_2)_4$), 3.5 and 4.8 (broad, 2H, 2 OH, D_2O exch.), 7.25 (m, 1 H, Py-H_β), 7.7 (m, 2H, Py-H_β and Py-H_γ), 8.55 (m, 1 H, Py-H_α); IR (nujol) ν_{max} 3360 and 3230 (OH, s) cm^{-1}; MS m/e 207 (M), 190 (M-OH), 123 (base peak), 122, 104, 80, 79, 78.

1-(2-Pyridyl)-1-(1-cyclohexanol)-ethanol (4i, 72%): m.p. 76-8 °C (from petrol ether/ethyl ether 9:1); ^{1}H NMR ($CDCl_3$) δ 1.0-1.7 (m, 13 H, CH_3 and $(CH_2)_5$), 2.0-3.0 (broad, 2H, 2 OH, D_2O exch.), 7.2 (m, 1 H, Py-H_β), 7.5-7.8 (m, 2H, Py-H_β and Py-H_γ), 8.5 (m, 1 H, Py-H_α); IR (nujol) ν_{max} 3320 and

3200 (OH, s) cm^{-1}; MS m/e 221 (M), 204 (M-OH), 123 (base peak), 122, 104, 99, 80, 79, 78.

2-(2-Pyridyl)-2,3-butanediol (4j, 42%): ^1H NMR spectrum of the crude product reveals a mixture of the threo and erythro forms. Separation of the two stereoisomers was achieved by preparative column chromatography, using the gradient elution method (hexane/ethyl acetate from 9:1 to 1:1) followed by preparative thin layer chromatography (eluant: hexane/ethyl acetate 7:3). One isomer (oil): ^1H NMR ($CDCl_3$) δ 0.92 (d, 3H, $\underline{CH_3}$-CH), 1.53 (s, 3H, CH_3), 3.87 (q, 1H, CH), 4.0-5.0 (broad, 2H, 2 OH, D_2O exch.), 7.0-8.0 (m, 3H, Py-H_γ and Py-H_β), 8.5 (m, 1H, Py-H_α). The other isomer (oil): ^1H NMR ($CDCl_3$) δ 1.1 (d, 3H, $\underline{CH_3}$-CH), 1.46 (s, 3H, CH_3), 3.9 (q, 1H, CH), 4.0 and 5.0 (broad, 2H, 2 OH, D_2O exch.), 7.0-8.0 (m, 3H, Py-H_γ and Py-H_β), 8.5 (m, 1H, Py-H_α); IR (film) ν_{max} 3400 (OH, s), 2500 (intramolecular H-bond with nitrogen).

2,4,5-Trimethyl-5-(2-pyridyl)-1,3-dioxolane (5j, 30%): two diastereoisomers are predominant and their isolation was achieved by column chromatography on silica gel (hexane/ethyl acetate 9:1). One isomer (oil): ^1H NMR ($CDCl_3$) δ 1.45 (d, J= 6.3 Hz, 3H, O-CH-$\underline{CH_3}$), 1.45 (s, 3H, CH_3), 1.46 (d, J= 4.8 Hz, 3H, O-C(CH_3)-O), 4.2 (q, J= 6.3 Hz, 1H, O-$\underline{CH}$-CH_3), 5.15 (q, J= 4.8 Hz, 1H, O-CH-O), 7.15 (m, 1H, Py-H_β), 7.65 (m, 2H, Py-H_β and Py-H_γ), 8.6 (m, 1H, Py-H_α). The other isomer (oil): ^1H NMR ($CDCl_3$) δ 0.81 (d, J= 6.6 Hz, 3H, O-CH-$\underline{CH_3}$), 1.55 (d, J= 5.1 Hz, 3H, O-C(CH_3)-O), 1.73 (s, 3H, CH_3), 4.5 (q, J= 6.6 Hz, 1H, O-$\underline{CH}$-CH_3), 5.3 (q, J= 5.1 Hz, 1H, O-CH-O), 7.15 (m, 1H, Py-H_β), 7.65 (m, 2H, Py-H_γ and Py-H_β), 8.6 (m, 1H, Py-H_α); IR (film) ν_{max} 1160-1050 cm^{-1} (characteristic bands of dioxolane ring[25]); MS m/e 193 (M), 178 (M-CH_3), 149 (M-CH_3CHO, base peak), 134, 123, 122, 107, 79, 78.

2-(2-Pyridyl)-2,3-pentanediol (4k, 44%): thick oil; mixture of the threo and erythro forms; ^1H NMR ($CDCl_3$), δ 0.85-1.45 (m, 5H, C_2H_5), 1.5 and 1.6 (2s, 3H, HO-C-$\underline{CH_3}$), 3.4-3.7 (2t, 1H, $\underline{CH}$-C_2H_5), 3.0-5.0 (broad, 2H, 2 OH, D_2O exch.), 7.3 (m, 2H, Py-H_β), 7.7 (m, 1H, Py-H_γ), 8.55 (dd, 1H, Py-H_α); IR (film) ν_{max} 3380 (OH, s) cm^{-1}; MS m/e 181 (M), 163 (M-H_2O), 122, 121, 79, 78 (base peak), 58.

1-Phenyl-2-(2-pyridyl)-1,2-propanediol (41, 47%): threo and erythro mixture (1:1); m.p. 85-9 °C, Lit.[10] 119-21°C, HCl salt of unknown stereochemistry; ^1H NMR ($CDCl_3$) δ 1.40 and 1.52 (2s, 3H, CH_3), 4.3 (s, 2H, 2 OH, D_2O exch.), 4.8 and 4.82 (2s, 1H, CH), 7.2 (m, 7H, 5Ph-H and 2Py-H_β), 7.6 (m, 1H, Py-H_γ), 8.5 (m, 1H, Py-H_α); IR (nujol) ν_{max} 3410 and 3310 (OH, s) cm^{-1}; MS m/e 229 (M), 211 (M-H_2O), 194 (M-H_2O-OH), 123, 122, 106 (base peak), 105, 77.

1-(2-Pyridyl)-2-methyl-1,2-propanediol (4p, 35%): oil; ^1H NMR ($CDCl_3$) δ 1.1 (s, 3H, CH_3), 1.2 (s, 3H, CH_3), 4.5 (s, 1H, CH), 4.6 (s, 2H, 2 OH, D_2O exch.), 7.2 (m, 1H, Py-H_β), 7.3-7.8 (m, 2H, Py-H_β and Py-H_γ), 8.5 (m, 1H, Py-H_α); IR (film) ν_{max} 3340 (OH, s) cm^{-1}; MS m/e 167 (M), 149 (M-H_2O), 109 (base peak), 108, 79, 78, 59, 58.

1-Phenyl-2-(2-pyridyl)-1,2-ethanediol (4q, 40%): threo and erythro mixture; m.p. 146-8 °C, Lit.[26] threo isomer 151-2 °C, erythro isomer 133-7 °C; ^1H NMR (CD_3OD) δ 4.0 (s, 2H, 2 OH, D_2O exch.), 4.78-5.10 (two AB systems, 2H, $\underline{H_1}$-C(OH)-C(OH)-$\underline{H_2}$; one AB system δ_{H_1} 4.82, δ_{H_2} 4.91, $J_{H_1H_2}$ = 6 Hz; the other AB system δ_{H_1} 4.98, δ_{H_2} 5.02, $J_{H_1H_2}$ = 5.4 Hz), 7.2 (m, 7H, 5Ph-H and 2Py-H_β), 7.5 (m, 1H, Py-H_γ), 8.5 (m, 1H, Py-H_α); IR (nujol) ν_{max} 3500-3000 (OH, s) cm^{-1}; MS m/e 197 (M-H_2O), 109 (base peak), 108, 107, 106, 105, 79, 78, 77.

1-(4-Pyridyl)-2-methyl-1,2-propanediol (4m, 20%): ^1H NMR ($CDCl_3$+CD_3CD) δ 1.1 and 1.2 (2s, 6H, $2CH_3$), 4.0 (s, 2H, 2 OH, D_2O exch.), 4.5 (s, 1H, CH), 7.4 (m, 2H, Py-H_β), 8.5 (m, 2H, Py-H_α); IR (nujol) ν_{max} 3350 (OH, s) cm^{-1}; MS m/e 167 (M), 149 (M-H_2O), 109, 108 (base peak), 79, 78, 59, 58.

1-Phenyl-2-(4-pyridyl)-1,2-ethanediol (4n, 20%): threo and erythro mixture; m.p. 173-5 °C, Lit.[27] threo isomer 177-8 °C, erythro isomer 175-6 °C; ^{1}H NMR (CD_3OD + CF_3COOD) δ 4.85-5.20 (two AB systems practically overlapped, 2H, $\underline{H}_1$-C(OH)-C(OH)-$\underline{H}_2$, δ_{H_1} 4.9, δ_{H_2} 5.15, $J_{H_1H_2} \cong$ 6 Hz), 7.3 (s, 5H, Ph-H), 7.9 (m, 2H, Py-H_β), 8.7 (m, 2H, Py-H_α); IR (nujol) ν_{max} 3400 (OH, br) cm^{-1}; MS m/e 197 ($M-H_2O$), 109 (base peak), 108, 107, 106, 105, 79, 78, 77.

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$$Ti^{3+} + \cdot OH \xrightarrow{K_{red}} Ti^{4+} + OH^-$$

a value for K_{red}= $3x10^9$ 1 $mol^{-1}s^{-1}$ has been reported: A. Samuni; D. Meisel and G. Czapsky, J.C.S. Dalton Trans., 1273 (1972); for the reduction of the less electrophilic carbonyl conjugated radical $\cdot CH_2CHO$ by Ti(III) ion, a value of K_{red}= $6x10^5$ 1 mol^{-1} s^{-1} at pH= 0.7 and $K_{red} > 10^7$ 1 $mol^{-1}s^{-1}$ at pH= 9 were estimated: B.C. Gilbert, R.O.C. Norman and R.C. Sealy, J.C.S. Perkin II, 2174 (1973).

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