

## A CONVENIENT SYNTHESIS OF SUBSTITUTED PYRIDYLGLYCOLS PROMOTED BY AQUEOUS TITANIUM TRICHLORIDE

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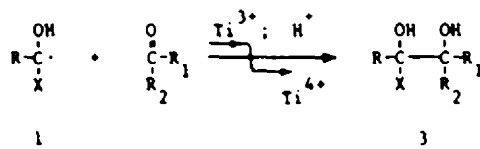
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**Abstract.** 2- and 4-Acetylpyridines, and 2- and 4-pyridinealdehydes when allowed to react with two-equiv. of aqueous titanium trichloride add to the carbonyl carbon atom of simple ketones (acetone, cyclopentanone, cyclohexanone) and aldehydes (acetaldehyde, 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<sup>1,2</sup> that Ti(III) ion promotes the reductive hydrodimerization of pyridineketones and pyridinealdehydes in high yields under quite simple experimental conditions. Next<sup>3,4</sup> 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<sup>1</sup> and the stereochemistry of the reaction (dl/meso ratio<sup>2</sup>) 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<sup>6,7</sup>, has an high concentration in the reaction medium and dimerizes in very good yields.

Though capto-dative substitution seems to mainly favour the whole process of dimerization<sup>6,8</sup>, recent reports<sup>3,4</sup> 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:

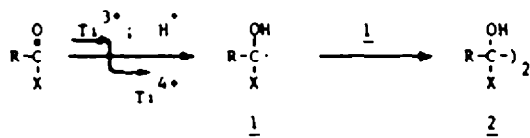


R = Ph; X = CN, COOH, COOR;  
 R<sub>1</sub>-R<sub>2</sub>=CH<sub>3</sub>; R<sub>1</sub> = H, R<sub>2</sub> = CH<sub>3</sub>, Ph.

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<sup>9</sup>, the synthesis of unsymmetrical diols might have a greater synthetic potential, mostly in relation to their pinacol re-



R = H, CH<sub>3</sub>, Ph; (dl, meso)  
 R = 2-, 3-, 4-Py<sup>1,2</sup>, CN<sup>3</sup>, COOH<sup>4</sup>, COOCH<sub>3</sub><sup>4</sup>, CHO<sup>5</sup>.

Scheme 1.



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<sup>12</sup> :

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

is valid in acidic solution where Ti(IV) is present as soluble  $\text{TiO}^{2+}$ ) 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<sup>2</sup> in accord with the increase of the reducing power of Ti(IV)/Ti(III) redox system with increasing the pH (the equation<sup>12</sup> :

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

is valid in basic medium where Ti(IV) is present as insoluble  $\text{TiO}_2$ );

c) simple aliphatic ketones and aldehydes (acetone, cyclopentanone, cyclohexanone, and valeraldehyde) require a stronger reducing agent, such as Ti(0) powder (from  $\text{TiCl}_3/\text{K}$  or  $\text{TiCl}_3/\text{Li}$  systems<sup>13</sup>), to be reduced to the corresponding intermediate radicals<sup>13,14</sup> :  $\text{R}'_2\text{C}^{\cdot}-\text{O}-\text{Ti}(I)$ .

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<sup>6</sup>;

f) supposing the formation of a carbanion is thermodynamically possible, we should obtain, in our reaction conditions ( $\text{pH} \leq 1$ ), the corresponding pyridylcarbinols<sup>15</sup> 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 alkoxy radical 6 (path ii). Rapid reduction of 6 (path iii) and subsequent proton transfer give 4.

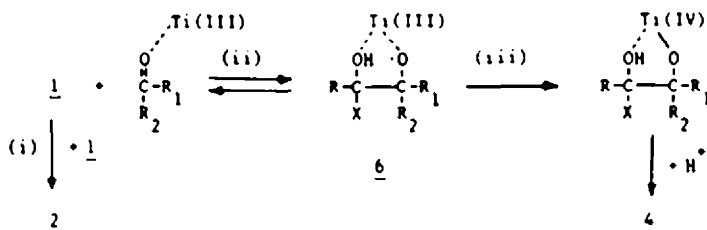
Although alkyl radical additions to carbonyl carbon have been previously proposed<sup>16-18</sup>, path (i) is a well known reversible process<sup>19</sup>. In our reaction conditions, a fundamental role in minimizing the reversibility of path (i) is played by Ti(III) ion<sup>20</sup> which reduces the strong electrophilic alkoxy radical 6 in an especially rapid and competing irreversible process<sup>21</sup> (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 alkoxy 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<sup>22,23</sup> : in fact, dimer 2m

instantaneously 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 60 at 70 eV; <sup>1</sup>H NMR spectra on a Varian A-90 and HA-100 with Me<sub>4</sub>Si 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<sub>3</sub> 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<sub>1</sub>-CO-R<sub>2</sub>, 225 mmol) in glacial acetic acid (10-15 ml), a 15% TiCl<sub>3</sub> 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<sub>2</sub>SO<sub>4</sub> 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<sup>1</sup> and its recovery was achieved only by subsequent continuous extraction by percolation with ethyl acetate. As revealed by <sup>1</sup>H NMR spectra, the crude mixtures obtained after work-up contain almost exclusively the unsymmetrical diols 4a, 4b, 4c, and 4f (which can be further purified by recrystallization) or a mixture of 4d, 4e, and 4e, 4e. 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	$\begin{array}{c} \text{R}-\text{C}-\text{R}_2 \\   \\ \text{O} \end{array}$	Products isolated yield (%) <sup>a)</sup>			Overall yield (%) <sup>a)</sup>
			2	4	5	
<u>a</u>	(4)Py-C(=O)-CH <sub>3</sub>	acetone	25	63	-	88
<u>b</u>	"	cyclopentanone	24	71	-	95
<u>c</u>	"	cyclohexanone	25	62	-	87
<u>d</u>	"	acetaldehyde	25	traces	60	85
<u>e</u>	"	propionaldehyde	24	28	41	93
<u>f</u>	"	benzaldehyde	10	85	-	95
<u>g</u>	(2)Py-C(=O)-CH <sub>3</sub>	acetone	14	80	-	94
<u>h</u>	"	cyclopentanone	17	68	-	85
<u>i</u>	"	cyclohexanone	16	72	-	88
<u>j</u>	"	acetaldehyde	18	42	30	90
<u>k</u>	"	propionaldehyde	40	44	traces	84
<u>l</u>	"	benzaldehyde	16	47	-	63
<u>m</u>	(4)Py-C(=O)-H	acetone	78	20	-	98
<u>n</u>	"	benzaldehyde	77	20	-	97
<u>p</u>	(2)Py-C(=O)-H	acetone	40	35	-	98 <sup>b)</sup>
<u>q</u>	"	benzaldehyde	31	40	-	89 <sup>b)</sup>

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, j); 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<sup>1</sup>. The crude mixture obtained after work-up was contaminated with the dl isomer of 2m which was separated from diol 4m or 4n by preparative thin layer chromatography (eluent: 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 (eluent:

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);  
<sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 1.05 (s, 3H, CH<sub>3</sub>), 1.22 (s, 3H, CH<sub>3</sub>), 1.6 (s, 3H, CH<sub>3</sub>), 3.0-3.5 (broad, 2H, 2OH, D<sub>2</sub>O exch.), 7.45 (m, 2H, Py-H<sub>B</sub>), 8.5 (m, 2H, Py-H<sub>A</sub>); IR (nujol)  $\nu_{\text{max}}$  3300 (OH, s), 3150 (OH, br) cm<sup>-1</sup>; MS m/e 182 (M+1)<sup>24</sup>, 164 (M-H<sub>2</sub>O), 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);  $^1\text{H NMR}$  ( $\text{CDCl}_3 + \text{CD}_3\text{OD}$ )  $\delta$  1.5-2.0 (m, 11H,  $\text{CH}_3$  and  $(\text{CH}_2)_4$ ), 4.5 (broad, 2H, 2OH,  $\text{D}_2\text{O}$  exch.), 7.6 (m, 2H,  $\text{Py-H}_\beta$ ), 8.5 (m, 2H,  $\text{Py-H}_\alpha$ );

IR (nujol)  $\nu_{\text{max}}$  3340 (OH, s)  $\text{cm}^{-1}$ ; 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);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.2-1.7 (s and m, 13H,  $\text{CH}_3$  and  $(\text{CH}_2)_5$ ), 2.0-3.0 (broad, 2H, 2OH,  $\text{D}_2\text{O}$  exch.), 7.4 (m, 2H,  $\text{Py-H}_\beta$ ), 8.5 (m, 2H,  $\text{Py-H}_\alpha$ );

IR (nujol)  $\nu_{\text{max}}$  3470 (OH, broad), 3120 (OH, s)  $\text{cm}^{-1}$ ; MS m/e 222 (M+1)<sup>24</sup>, 203 (M-H<sub>2</sub>O), 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):  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.8 (d, J=6.6 Hz, 3H,  $\text{CH}_3$ ), 1.52 (d, J=5.1 Hz, 3H,  $\text{CH}_3$ ), 1.6 (s, 3H,  $\text{CH}_3$ ), 3.95 (q, J=6.6 Hz, HO-CH- $\text{CH}_3$ ), 5.28 (q, J=5.1 Hz, 1H, O-CH-O), 7.3 (m, 2H,  $\text{Py-H}_\beta$ ), 8.6 (m, 2H,  $\text{Py-H}_\alpha$ ).

The other isomer (thick oil):  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.33 (d, J=6.6 Hz, 3H,  $\text{CH}_3$ ), 1.4 (s, 3H,  $\text{CH}_3$ ), 1.48 (d, J=4.8 Hz, 3H,  $\text{CH}_3$ ), 3.92 (q, J=6.6 Hz, 1H, O-CH- $\text{CH}_3$ ), 5.2 (q, J=4.8 Hz, 1H, O-CH-O), 7.3 (m, 2H,  $\text{Py-H}_\beta$ ), 8.6 (m, 2H,  $\text{Py-H}_\alpha$ ); IR (film)  $\nu_{\text{max}}$  1160-1050  $\text{cm}^{-1}$  (characteristic bands of dioxolane ring<sup>25</sup>); MS m/e 193 (M), 178 (M- $\text{CH}_3$ ), 149 (M- $\text{CH}_3\text{CHO}$ , base peak), 134, 122, 107, 79.

2-(4-Pyridyl)-2,3-pentanediol (4e, 28%): thick oil, mixture of two stereoisomers;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.9 and 0.95 (2t, 3H,  $\text{CH}_2\text{-CH}_3$ ), 1.2-1.6 (m, 2H,  $\text{CH}_2\text{-CH}_3$ ), 1.5 and 1.58 (2s, 3H,  $\text{CH}_3$ ), 3.51 and 3.52 (2t, 1H, CH-OH), 4.3 (s, 2H, 2OH,  $\text{D}_2\text{O}$  exch.), 7.4 (m, 2H,  $\text{Py-H}_\beta$ ), 8.4 (m, 2H,  $\text{Py-H}_\alpha$ ); IR (film)  $\nu_{\text{max}}$  3300 (OH, very s)  $\text{cm}^{-1}$ ;

MS m/e 182 (M+H)<sup>24</sup>, 181, 163 (M-H<sub>2</sub>O), 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;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.75-1.95 (m, 10H, two  $\text{CH}_2\text{CH}_3$ ), 1.25, 1.35, 1.40 and 1.60 (4s, 3H,  $\text{CH}_3\text{CO}$ ) 3.5-4.0 (4t, 1H, CH-O), 4.9-5.3 (4t, 1H, O-CH-O) 7.3 (m, 2H,  $\text{Py-H}_\beta$ ); 8.55 (m, 2H,  $\text{Py-H}_\alpha$ ); IR (film)  $\nu_{\text{max}}$  1160-1000  $\text{cm}^{-1}$  (characteristic bands of dioxolane ring<sup>25</sup>); MS m/e 221 (M), 206 (M- $\text{CH}_3$ ), 192 (M-C<sub>2</sub>H<sub>5</sub>), 163 (M-2C<sub>2</sub>H<sub>5</sub>, 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.<sup>10</sup> 149-51 °C unknown stereochemistry;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.4 and 1.6 (2s, 3H,  $\text{CH}_3$ ), 4.4 (s, 2H, 2OH,  $\text{D}_2\text{O}$  exch.), 4.7 (s, 1H, CH), 7.0-7.3 (m, 5H, Ph-H), 7.3-7.5 (m, 2H,  $\text{Py-H}_\beta$ ) 8.4 (m, 2H,  $\text{Py-H}_\alpha$ ); IR (nujol)  $\nu_{\text{max}}$  3400 and 3200 (OH, s)  $\text{cm}^{-1}$ ; MS m/e 211 (M-H<sub>2</sub>O), 123, 122, 121, 106 (base peak), 105, 78, 77.

2-(2-Pyridyl)-3-methyl-2,3-butanediol (4g, 80%): oil;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.1 (s, 3H,  $\text{CH}_3$ ), 1.17 (s, 3H,  $\text{CH}_3$ ), 1.6 (s, 3H,  $\text{CH}_3$ ), 4.3 (broad, 2H, 2OH,  $\text{D}_2\text{O}$  exch.), 7.2 (m, 1H,  $\text{Py-H}_\beta$ ), 7.65 (m, 2H,  $\text{Py-H}_\beta$  and  $\text{Py-H}_\gamma$ ), 8.55 (m, 1H,  $\text{Py-H}_\alpha$ ); IR (film)  $\nu_{\text{max}}$  3400 (OH, s)  $\text{cm}^{-1}$ ; MS m/e 182 (M+H)<sup>24</sup>, 164 (M-H<sub>2</sub>O), 146, 122 (base peak), 79, 59, 43.

1-(2-Pyridyl)-1-(1-cyclopentanol)-ethanol (4h, 68%): m.p. 73-4 °C (from ethyl ether);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.3-2.0 (m, 11H,  $\text{CH}_3$  and  $(\text{CH}_2)_4$ ), 3.5 and 4.8 (broad, 2H, 2OH,  $\text{D}_2\text{O}$  exch.), 7.25 (m, 1H,  $\text{Py-H}_\beta$ ), 7.7 (m, 2H,  $\text{Py-H}_\alpha$  and  $\text{Py-H}_\gamma$ ), 8.55 (m, 1H,  $\text{Py-H}_\alpha$ ); IR (nujol)  $\nu_{\text{max}}$  3360 and 3230 (OH, s)  $\text{cm}^{-1}$ ; 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);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.0-1.7 (m, 13H,  $\text{CH}_3$  and  $(\text{CH}_2)_5$ ), 2.0-3.0 (broad, 2H, 2OH,  $\text{D}_2\text{O}$  exch.), 7.2 (m, 1H,  $\text{Py-H}_\beta$ ), 7.5-7.8 (m, 2H,  $\text{Py-H}_\alpha$  and  $\text{Py-H}_\gamma$ ), 8.5 (m, 1H,  $\text{Py-H}_\alpha$ ); IR (nujol)  $\nu_{\text{max}}$  3320 and

3200 (OH, s)  $\text{cm}^{-1}$ ; 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%):  $^1\text{H NMR}$  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):  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.92 (d, 3H,  $\text{CH}_3$ ), 1.53 (s, 3H,  $\text{CH}_3$ ), 3.87 (q, 1H, CH), 4.0-5.0 (broad, 2H, 2OH,  $\text{D}_2\text{O}$  exch.), 7.0-8.0 (m, 3H, Py-H<sub>Y</sub> and Py-H<sub>B</sub>), 8.5 (m, 1H, Py-H<sub>Y</sub>). The other isomer (oil):  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.1 (d, 3H,  $\text{CH}_3$ ), 1.46 (s, 3H,  $\text{CH}_3$ ), 3.9 (q, 1H, CH), 4.0 and 5.0 (broad, 2H, 2OH,  $\text{D}_2\text{O}$  exch.), 7.0-8.0 (m, 3H, Py-H<sub>Y</sub> and Py-H<sub>B</sub>), 8.5 (m, 1H, Py-H<sub>Y</sub>); IR (film)  $\nu_{\text{max}}$  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):  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.45 (d,  $J=6.3$  Hz, 3H, O-CH- $\text{CH}_3$ ), 1.45 (s, 3H,  $\text{CH}_3$ ), 1.46 (d,  $J=4.8$  Hz, 3H, O-C( $\text{CH}_3$ )-O), 4.2 (q,  $J=6.3$  Hz, 1H, O-CH- $\text{CH}_3$ ), 5.15 (q,  $J=4.8$  Hz, 1H, O-CH-O), 7.15 (m, 1H, Py-H<sub>B</sub>), 7.65 (m, 2H, Py-H<sub>B</sub> and Py-H<sub>Y</sub>), 8.6 (m, 1H, Py-H<sub>O</sub>). The other isomer (oil):  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.81 (d,  $J=6.6$  Hz, 3H, O-CH- $\text{CH}_3$ ), 1.55 (d,  $J=5.1$  Hz, 3H, O-C( $\text{CH}_3$ )-O), 1.73 (s, 3H,  $\text{CH}_3$ ), 4.5 (q,  $J=6.6$  Hz, 1H, O-CH- $\text{CH}_3$ ), 5.3 (q,  $J=5.1$  Hz, 1H, O-CH-O), 7.15 (m, 1H, Py-H<sub>B</sub>), 7.65 (m, 2H, Py-H<sub>Y</sub> and Py-H<sub>B</sub>), 8.6 (m, 1H, Py-H<sub>O</sub>); IR (film)  $\nu_{\text{max}}$  1160-1050  $\text{cm}^{-1}$  (characteristic bands of dioxolane ring<sup>25</sup>); MS  $m/e$  193 (M), 178 (M- $\text{CH}_3$ ), 149 (M- $\text{CH}_2\text{CHO}$ , 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;

$^1\text{H NMR}$  ( $\text{CDCl}_3$ ),  $\delta$  0.85-1.45 (m, 5H,  $\text{C}_2\text{H}_5$ ), 1.5 and 1.6 (2s, 3H, HO-C- $\text{CH}_3$ ), 3.4-3.7 (2t, 1H, CH- $\text{C}_2\text{H}_5$ ), 3.0-5.0 (broad, 2H, 2OH,  $\text{D}_2\text{O}$  exch.), 7.3 (m, 2H, Py-H<sub>B</sub>), 7.7 (m, 1H, Py-H<sub>Y</sub>), 8.55 (dd, 1H, Py-H<sub>O</sub>); IR (film)  $\nu_{\text{max}}$  3380 (OH, s)  $\text{cm}^{-1}$ ; MS  $m/e$  181 (M), 163 (M- $\text{H}_2\text{O}$ ), 122, 121, 79, 78 (base peak), 58.

1-Phenyl-2-(2-pyridyl)-1,2-propanediol (4l, 47%): threo and erythro mixture (1:1); m.p. 85-9 °C, lit.<sup>10</sup> 119-21 °C, HCl salt of unknown stereochemistry;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.40 and 1.52 (2s, 3H,  $\text{CH}_3$ ), 4.3 (s, 2H, 2OH,  $\text{D}_2\text{O}$  exch.), 4.8 and 4.82 (2s, 1H, CH), 7.2 (m, 7H, 5Ph-H and 2Py-H<sub>B</sub>), 7.6 (m, 1H, Py-H<sub>Y</sub>), 8.5 (m, 1H, Py-H<sub>O</sub>); IR (nujol)  $\nu_{\text{max}}$  3410 and 3310 (OH, s)  $\text{cm}^{-1}$ ; MS  $m/e$  229 (M), 211 (M- $\text{H}_2\text{O}$ ), 194 (M- $\text{H}_2\text{O}$ -OH), 123, 122, 106 (base peak), 105, 77.

1-(2-Pyridyl)-2-methyl-1,2-propanediol (4p, 35%): oil;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.1 (s, 3H,  $\text{CH}_3$ ), 1.2 (s, 3H,  $\text{CH}_3$ ), 4.5 (s, 1H, CH), 4.6 (s, 2H, 2OH,  $\text{D}_2\text{O}$  exch.), 7.2 (m, 1H, Py-H<sub>B</sub>), 7.3-7.8 (m, 2H, Py-H<sub>B</sub> and Py-H<sub>Y</sub>), 8.5 (m, 1H, Py-H<sub>O</sub>); IR (film)  $\nu_{\text{max}}$  3340 (OH, s)  $\text{cm}^{-1}$ ; MS  $m/e$  167 (M), 149 (M- $\text{H}_2\text{O}$ ), 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.<sup>26</sup> threo isomer 151-2 °C, erythro isomer 133-7 °C;  $^1\text{H NMR}$  ( $\text{CD}_3\text{OD}$ )  $\delta$  4.0 (s, 2H, 2OH,  $\text{D}_2\text{O}$  exch.), 4.78-5.10 (two AB systems, 2H, H<sub>1</sub>-C(OH)-C(OH)-H<sub>2</sub>); one AB system  $\delta_{\text{H}_1}$  4.82,  $\delta_{\text{H}_2}$  4.91,  $J_{\text{H}_1\text{H}_2} = 6$  Hz; the other AB system  $\delta_{\text{H}_1}$  4.98,  $\delta_{\text{H}_2}$  5.02,  $J_{\text{H}_1\text{H}_2} = 5.4$  Hz, 7.2 (m, 7H, 5Ph-H and 2Py-H<sub>B</sub>), 7.5 (m, 1H, Py-H<sub>Y</sub>), 8.5 (m, 1H, Py-H<sub>O</sub>); IR (nujol)  $\nu_{\text{max}}$  3500-3000 (OH, s)  $\text{cm}^{-1}$ ; MS  $m/e$  197 (M- $\text{H}_2\text{O}$ ), 109 (base peak), 108, 107, 106, 105, 79, 78, 77.

1-(4-Pyridyl)-2-methyl-1,2-propanediol (4m, 20%):  $^1\text{H NMR}$  ( $\text{CDCl}_3 + \text{CD}_3\text{CO}$ )  $\delta$  1.1 and 1.2 (2s, 6H, 2 $\text{CH}_3$ ), 4.0 (s, 2H, 2OH,  $\text{D}_2\text{O}$  exch.), 4.5 (s, 1H, CH), 7.4 (m, 2H, Py-H<sub>B</sub>), 8.5 (m, 2H, Py-H<sub>O</sub>); IR (nujol)  $\nu_{\text{max}}$  3350 (OH, s)  $\text{cm}^{-1}$ ; MS  $m/e$  167 (M), 149 (M- $\text{H}_2\text{O}$ ), 109, 108 (base peak), 79, 78, 59, 58.

1-Phenyl-2-(4-pyridyl)-1,2-ethanediol (4n, 202):  
 threo and erythro mixture; m.p. 173-5 °C, Lit.<sup>27</sup>  
 threo isomer 177-8 °C, erythro isomer 175-6 °C;  
<sup>1</sup>H NMR (CD<sub>3</sub>OD + CF<sub>3</sub>COOD) δ 4.85-5.20 (two AB  
 systems practically overlapped, 2H, H<sub>1</sub>-C(OH)-  
 C(OH)-H<sub>2</sub>, δ<sub>H1</sub> 4.9, δ<sub>H2</sub> 5.15, J<sub>H1H2</sub> ≈ 6 Hz), 7.3  
 (s, 5H, Ph-H), 7.9 (m, 2H, Py-H), 8.7 (m, 2H,  
 Py-H<sub>α</sub>); IR (nujol) ν<sub>max</sub> 3400 (OH, br) cm<sup>-1</sup>;  
 MS m/e 197 (M-H<sub>2</sub>O), 109 (base peak), 108, 107,  
 106, 105, 79, 78, 77.

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- 21- The rapid reduction of **6** by Ti(III) ion is a plausible finding. For the reaction
 
$$\text{Ti}^{3+} + \text{-OH} \xrightarrow{K_{\text{red}}} \text{Ti}^{4+} + \text{OH}^-$$
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