

## Pyridinediols as HCl Receptors; Formation of an Unusual Pyridine·HCl Complex in Conjunction with the Preparation of Lewis Acidic Titanium(IV) Centres

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Reaction of pyridinediols **1** with TiCl<sub>4</sub> affords in one case an unusual dehydration–HCl complexation; in conjunction with these results, reaction of **1** with HCl indicates a strong affinity of these diols for (Lewis) acids.

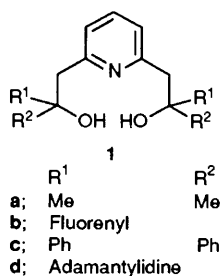
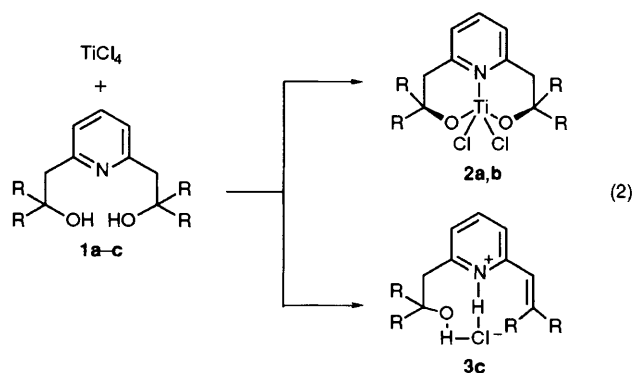
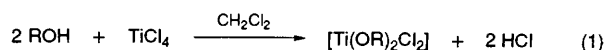
Pyridinediols **1**<sup>1a–e</sup> are special cases of metal receptors. The combination, in one ligand, of two hydroxy groups and the pyridine ring nitrogen atom makes these systems suitable, either as free ligands or as dialkoxy ligands for the complexation of a variety of metals including Mo, Fe, Co and Zn. The Mo<sup>1d–g</sup> and Zn<sup>2a,b</sup> complexes have been used as models for biomimetic studies of enzymes such as zinc alcohol dehydrogenases, carboxypeptidases<sup>2c</sup> and oxygen transferases.

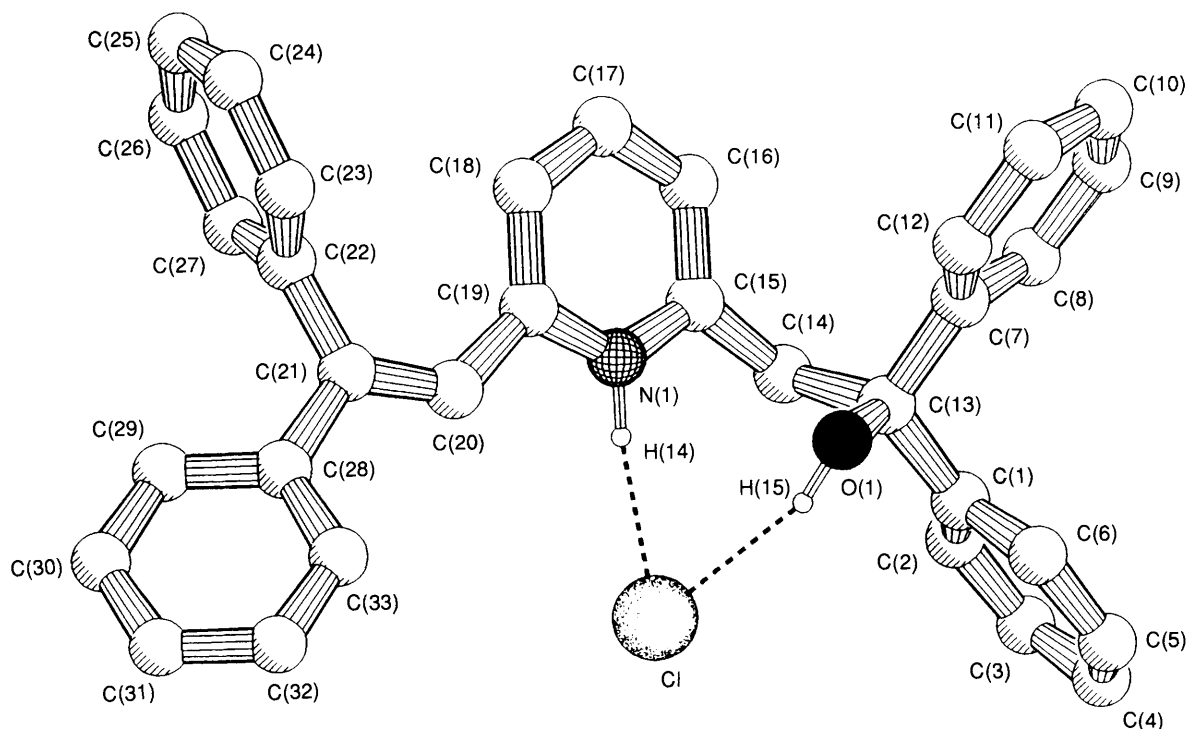
Alkoxo ligands stabilise metals in a rather broad variety of oxidation states.<sup>3</sup> Therefore, within the field of catalytic organic synthesis, alkoxides have been used to support a number of metal mediated stereoselective asymmetric reactions of which the Lewis acid based ene reactions<sup>4h,i</sup> and catalysed Diels–Alder reactions<sup>4a–g</sup> are important examples.

An important advantage of ligand system **1** is its facile preparation<sup>1,2</sup> and the possibility of introducing chiral building blocks<sup>2c</sup> by simply choosing a suitable ketone.

Following our interest in the coordination chemistry of **1** with Lewis acidic metals,<sup>5</sup> we tried to prepare the corresponding Ti<sup>IV</sup> complexes according to a procedure reported by Flamini *et al.*<sup>6a</sup>

This method involves the reaction of TiCl<sub>4</sub> with 2 equiv. of alcohol [eqn. (1)] and results in the almost quantitative formation of [Ti(OR)<sub>2</sub>Cl<sub>2</sub>] with concomitant evolution of HCl. If necessary, an additional amount of base (*e.g.* NEt<sub>3</sub>) may be added to neutralise the HCl. In our case, the reaction of TiCl<sub>4</sub> with **1a,b** provided cleanly the corresponding [Ti(L)Cl<sub>2</sub>] **2a,b** in yields ranging from 43–56% [eqn. (2)] as





**Fig. 1** Perspective drawing of **3c**. Selected bond distances (Å) and angles (°). H(14)–N(1) 0.92(1), H(14)···Cl 2.15(4), O(1)–H(15) 0.86(5); N(1)–H(14)···Cl 173(4), O(1)–H(15)···Cl 160(4).

was demonstrated by spectroscopic and analytical methods.<sup>5a†</sup>

However, the tetraphenyl derivative **1c** did not, upon reaction with  $\text{TiCl}_4$ , give the expected  $\text{Ti}^{\text{IV}}$  alkoxide. Instead, a crystalline solid **3c**<sup>8</sup> was isolated in modest yield (32%), analysis of which established the absence of titanium. Unlike the relatively simple and symmetrical  $^1\text{H}$  NMR spectra of the  $\text{Ti}^{\text{IV}}$  complexes **2a,b** that of **3c** indicated the absence of symmetry.

An X-ray diffraction analysis<sup>‡</sup> of the crystals revealed the

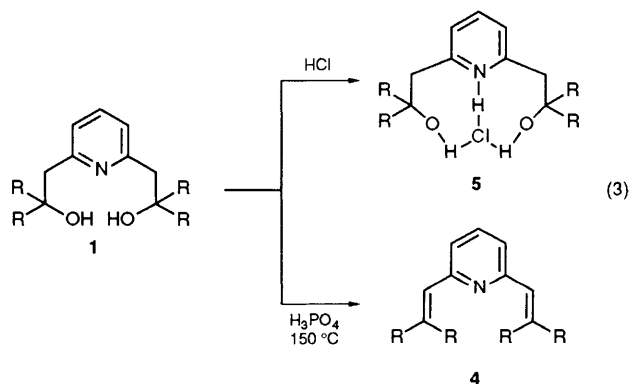
<sup>†</sup> *Experimental procedure* for the preparation of **3c**. A solution of 13 g (27.6 mmol) of **1c** in 250 ml  $\text{CH}_2\text{Cl}_2$  was treated with 1.2 equiv. of  $\text{TiCl}_4$ . The mixture was stirred for 1 h. A solid formed which was collected and recrystallized from  $\text{MeOH}-\text{CH}_2\text{Cl}_2$  to yield 4.3 g (8.8 mmol) of **3c** as white crystals, m.p. 188–193 °C;  $^1\text{H}$  NMR ( $\text{CD}_3\text{OD}$ ) 4.27 (s, 2H), 5.67 (br, OH), 6.33 (d, 1H), 7.23–7.45 (m, 22H), 7.92 (s, NH);  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{OD}$ ) 44.65 (t), 77.42 (s), 126.04 (d), 129.36 (d), 138.26 (s), 145.37 (s), 145.40 (s). Satisfactory C, H and Cl analyses were obtained.

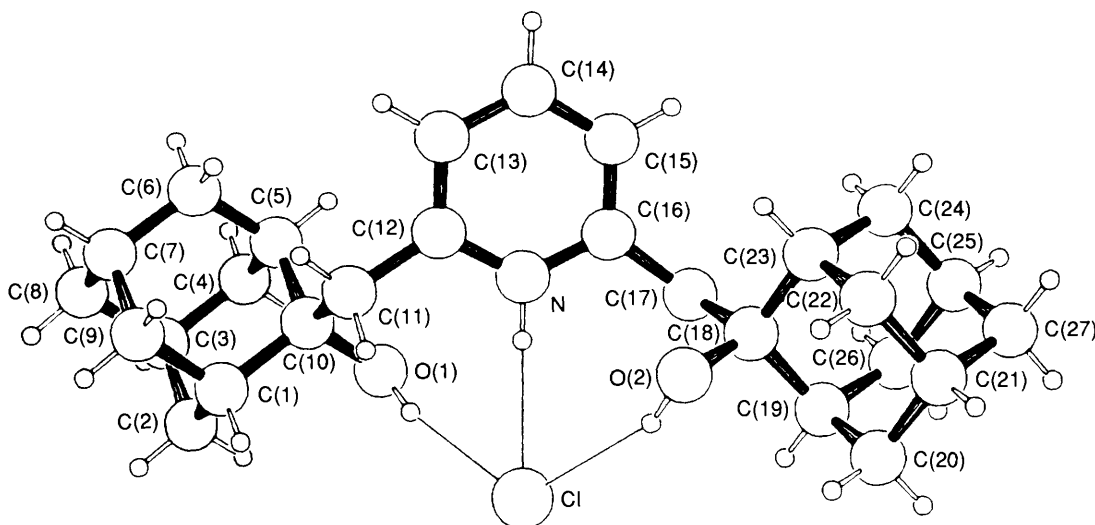
<sup>‡</sup> *Crystal data* for **3c**:  $\text{C}_{33}\text{H}_{28}\text{NOCl}_2$ , plate-shaped crystal (0.1 × 0.5 × 0.6 mm), triclinic, space group  $P1$  (no. 2) with  $a = 5.721(2)$ ,  $b = 9.107(2)$ ,  $c = 25.170(5)$  Å,  $\alpha = 88.52(2)$ ,  $\beta = 86.14(2)$ ,  $\gamma = 79.45(2)^\circ$ ,  $V = 1286.1(6)$  Å<sup>3</sup>,  $Z = 2$ ,  $D_c = 1.265$  g cm<sup>-3</sup>,  $F(000) = 516$ ,  $\mu(\text{Mo}-\text{K}\alpha) = 1.7$  cm<sup>-1</sup>, 9984 reflections measured, 5903 independent ( $0.81 < I < 27.5^\circ$ ,  $R_{\text{int}} = 0.042$ ,  $\omega$ - $2\theta$  scan,  $T = 298$  K, Mo-K $\alpha$  radiation Zr-filtered,  $\lambda = 0.71073$  Å) on an Enraf-Nonius CAD 4 diffractometer. Data were corrected for Lorentz polarization; no significant linear decay of the reference reflections (<1%) during 31.5 h of X-ray exposure time was observed; no absorption correction was applied. The structure was solved by automated Patterson methods (SHELXS86). Refinement on  $F$  was carried out by full-matrix least-squares techniques (SHELXL76); final  $R = 0.061$ ,  $R_w = 0.049$ ,  $w^{-1} = 1/[\sigma^2(F) + 0.000094F^2]$ ,  $S = 0.85$  for 332 parameters and 2681 reflections with  $I > 2.5\sigma(I)$ . Hydrogen atoms were included in the refinement on calculated (C–H = 0.98 Å) positions riding on their carrier atoms. All non-hydrogen atoms were refined with anisotropic thermal parameters; the H-atoms were refined with an overall isotropic thermal parameter of 0.064(2) Å<sup>2</sup>. Weights were introduced in the final refinement cycles. A final Fourier map showed no residual density outside  $-0.30$  and  $0.29$  e Å<sup>-3</sup>.

detailed structure of **3c**. Instead of the expected  $\text{Ti}^{\text{IV}}$  complex, the HCl salt of singly dehydrated **1c** has been formed. The molecule, as depicted in Fig. 1, is constituted by a planar pyridine backbone with the alkenyl fragment lying in the same plane [ $\angle(\text{pyridine}, \text{alkenyl}) 16.3(2)^\circ$ ]. The two phenyl substituents of this fragment are severely twisted with respect to this plane [angles 79.9(2) and 31.1(2)° for the rings containing C(22) and C(28), respectively] in order to minimize steric interaction.

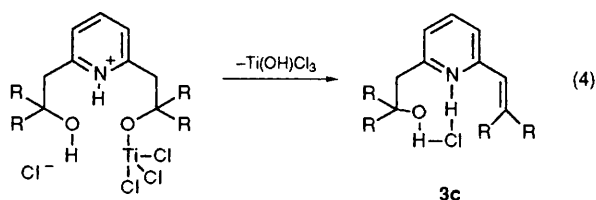
The hydroxyethyl moiety points out of the pyridine plane and is bonded to the  $\text{Cl}^-$  ion via a hydrogen bridge [H(15)···Cl 2.22(5) Å, O(1)–H(15)···Cl 160(4)°]. The  $\text{Cl}^-$  ion is furthermore hydrogen bonded to H(14) of the protonated pyridine nitrogen atom [N(1)–H(14)···Cl 173(4)°].

$\text{TiCl}_4$  rather than HCl alone appears to be involved in the mechanism for the formation of **3c**. Reaction of **1a–d** with dry HCl leads to the formation of the corresponding HCl salts **5** without observable  $\text{H}_2\text{O}$  elimination. The  $^1\text{H}$  NMR spectra are rather simple indicating a symmetrical bonding of HCl in these pyridinium salts. The molecular structure of the HCl derivative **5d** has been determined by X-ray crystallography





**Fig. 2** Perspective drawing of **5d**. Selected bond distances (Å) and angles (°). H(1)–N(1) 0.97(1), H(01)···Cl 2.2137(9), H(02)···Cl 2.286(1), H(N1)···Cl 2.149(1), O(1)–H(01) 0.97(5); O(1)···Cl···O(2) 113.27(7), O(1)···Cl···N(1) 56.10(7), O(2)···Cl···N(1) 57.27(7), H(01)···Cl···H(02) 121.58(5), H(01)···Cl···H(N1) 56.17(5), H(N1)···Cl···H(02) 65.42(3).



and is illustrated in Fig. 2. The molecule attains a pseudo  $C_2$ -symmetry in the solid state, placing the bulky adamantyl groups in a *trans* fashion. The deformation from idealized  $C_2$ -symmetry may be due to crystal packing effects. In analogy with the structure of **3c**, the chloride ion is strongly bonded to the pyridinium ion *via* hydrogen bridges [H(01)···Cl 2.2137(9), H(02)···Cl 2.286(1), H(N1)···Cl 2.149(1) Å].

In order to achieve complete dehydration to the corresponding dienes **4** [eqn. (3)], neat  $H_3PO_4$  has to be used at elevated temperatures.<sup>2b</sup> Initial formation of a **1c**–TiCl<sub>3</sub>–HCl species may occur owing to the competing reaction of the HCl formed with the **1c**–TiCl<sub>3</sub> complex. Elimination of the Ti(OH)Cl<sub>3</sub> fragment would result in the generation of **3c** [eqn. (4)].

§ *Crystal data* for **5d**: C<sub>27</sub>H<sub>38</sub>NO<sub>2</sub>Cl, plate-shaped crystal (0.2 × 0.5 × 0.15 mm), orthorhombic, space group *Pca*2<sub>1</sub> (no. 29) with  $a = 30.177(1)$ ,  $b = 7.061(2)$ ,  $c = 11.250(1)$  Å,  $V = 2397.1(8)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.225$  g cm<sup>-3</sup>,  $F(000) = 952$ ,  $\mu(\text{Mo-K}\alpha) = 1.79$  cm<sup>-1</sup>, 4345 reflections measured, 2547 independent ( $1 < \theta < 32^\circ$ ,  $\omega$ –2 $\theta$  scan,  $T = 298$  K, Mo-K $\alpha$ -radiation Zr-filtered,  $\lambda = 0.71073$  Å) on an Enraf-Nonius CAD 4 diffractometer. Data were corrected for Lorentz polarization; no significant linear decay of the reference reflections (<1%) was observed during data collection; no absorption correction was applied. The structure was solved by direct methods. Refinement on  $F$  was carried out by full-matrix least-squares techniques with final  $R = 0.055$ ,  $R_w = 0.061$ ,  $w^{-1} = 1/[\sigma^2(F)]$ ,  $S = 1.73$  for 349 parameters and 2547 reflections with  $I > 2.5\sigma(I)$ . Hydrogen atoms were included in the refinement on calculated (C–H = 0.97 Å) positions riding on their carrier atoms. All non-H atoms were refined with anisotropic thermal parameters: the H-atoms were refined with an overall isotropic thermal parameter of  $B = 4.0$  Å<sup>2</sup>. Weights were introduced in the final refinement cycles. A final Fourier map showed no residual density outside  $-0.32$  and  $0.57$  e Å<sup>-3</sup>. Atomic coordinates, bond lengths and angles, and thermal parameters for compounds **3c** and **5d** have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

However, it remains to be established why this partial elimination occurs with **1c** but not with **1a**, **b–d**.

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