Aminoindanes in Oxygen Transfer Reactions, 2[◇]

Copper Complexes as Functional Models for Dopamine β-Hydroxylase − Stereospecific Oxygen Atom Transfer

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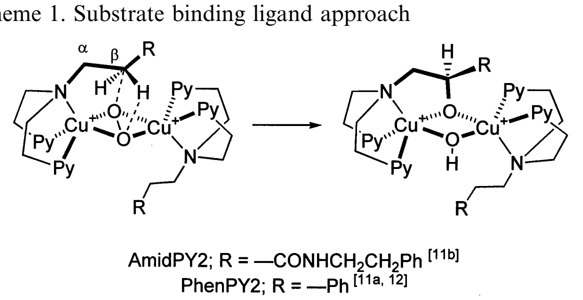
The stereochemistry of oxygen atom transfer mediated by copper–oxygen species has been studied through a substrate binding ligand approach. Copper(II) [(IndPY2)Cu]$(CF_3SO_3)_2$ (**2a**) and copper(I) [(IndPY2)Cu]PF_6 (**5a**) complexes were prepared and exposed to O_2 in media of benzoin/NEt_3/CH_2Cl_2 and CH_2Cl_2, respectively. In both cases, highly regio- and stereoselective oxygen atom transfer to the benzylicC–H bond of the indane ligand occurred. Using deuterium-labelled copper complexes **2b** and **5b**, we found that, in both cases, the oxygen atom transfer occurs with retention of configuration. The high deuterium kinetic isotope effects (7.6 and 11, respectively), determined by ^{13}C-NMR spectroscopy, strongly suggest the intermediacy of two different copper–oxygen reactive species.

Introduction

The mechanism of dioxygen activation by copper-containing monooxygenases such as dopamine β-hydroxylase (DBH)[1], peptidylglycine α-hydroxylating monooxygenase (PHM)[2], and particulate methane monooxygenase (pMMO)[3] is of current interest.[4] Given that these enzymatic processes involve the formation of highly reactive copper/oxygen radical species, which are responsible for hydrogen atom abstraction from the substrate, the Cu/O_2 chemistry has been the subject of recent investigations.[5] From these studies, it has become apparent that copper(I) complexes derived from tridentate ligands {RPY2[5a][6], HB(3,5-iPr$_2$pz)$_3$[5b][7], P(2,4-iPr$_2$im)$_3$[8], and iPr$_3$tacn[9]} lead to side-on $[L_2Cu_2(\mu\text{-}\eta^2{:}\eta^2\text{-}O_2)]^{2+}$ species upon reaction with O_2. In some cases, these side-on peroxo species are capable of inserting an oxygen atom into a C−H bond of the ligand.[10] In earlier papers, we described the substrate binding ligand approach in the chemical modelling of the copper-containing monooxygenase active site.[11] This approach involves the study of copper complexes derived from RPY2-type ligands in which a "substrate" is covalently bound to the tertiary amino group of the ligand such that an intramolecular oxygen atom transfer from copper to the ligand is favoured. Using such complexes, both ourselves[11b] and Itho's group[12] have described hydroxylation at the β-position of the tertiary amino group (Scheme 1). Herein, we describe the study of new RPY2 ligands in which we chose to attach a 2-aminoindane group as the "substrate". This substituent possesses two stereogenic centres in benzylic positions, each bearing two hydrogen atoms, and thus the stereochemistry of aminoindanols obtained after hydroxylation can be regarded as indicating the stereoselectivity of the oxygen atom transfer.

Scheme 1. Substrate binding ligand approach



Results and Discussion

Syntheses

Ligands **1a** and **1b** were obtained by Michael-type addition of 2-aminoindane and *cis*-1-deutero-2-aminoin-

[◇] For Part 1, see ref.[21].

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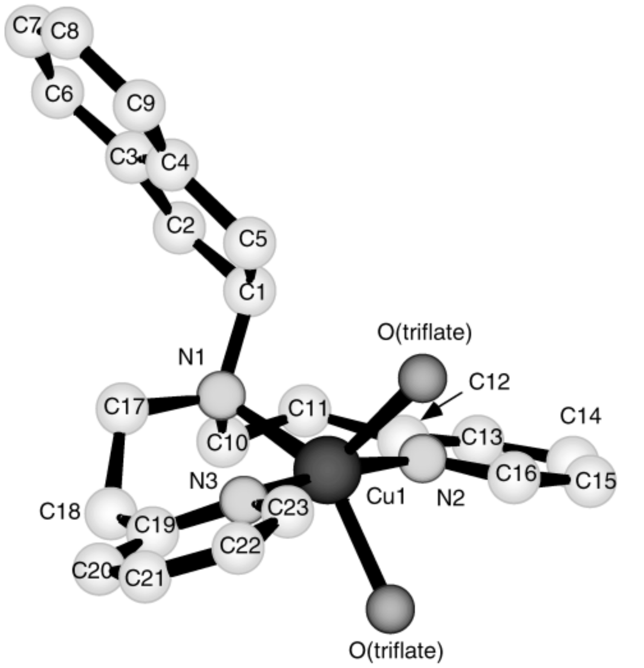
dane[13], respectively, to freshly distilled vinylpyridine in a MeOH/AcOH mixture.[10a] The corresponding copper(II) complexes **2a** and **2b** were quantitatively prepared by reaction of **1a** and **1b**, respectively, with $Cu(CF_3SO_3)_2$ in MeOH. Crystallization of $[(IndPY2)Cu](CF_3SO_3)_2$ (**2a**) from CH_2Cl_2/Et_2O gave blue crystals suitable for X-ray analysis (Table 1, Figure 1).

Figure 1. Perspective view of copper(II) complex **2a** displaying the numbering scheme and selected bond distances and angles[a]

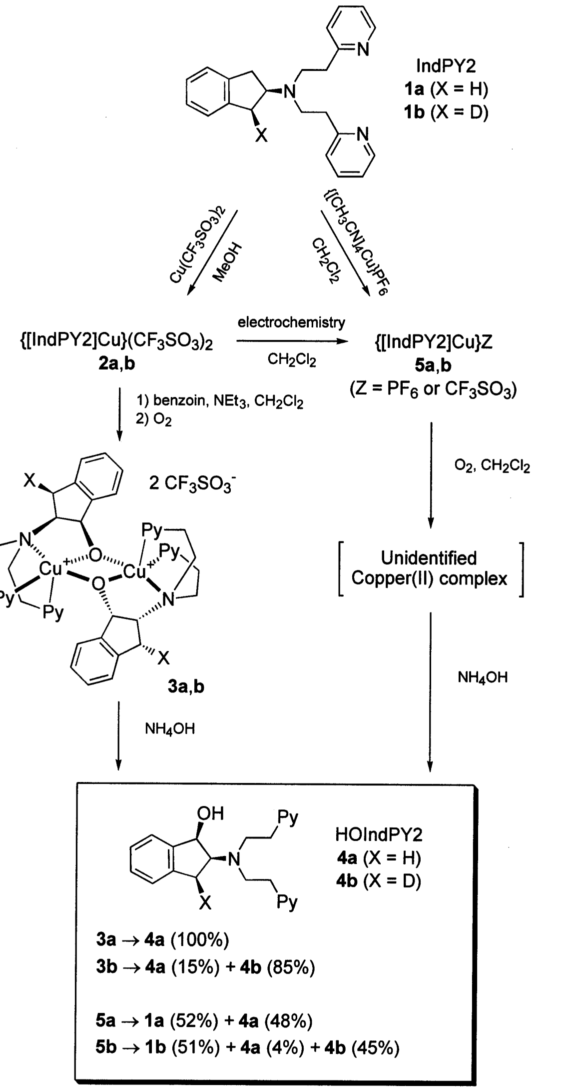


[a] Bond lengths in Å: Cu1−O2 2.108(7), Cu1−O4 2.210(7), Cu1−N1 2.019(7), Cu1−N2 2.042(6), Cu1−N3 1.977(8). Bond angles in°: O2−Cu1−O4 97.5(3), O2−Cu1−N1 148.4(3), O2−Cu1−N2 86.3(3), O2−Cu1−N3 85.0(3), O4−Cu1−N1 114.0(3), O4−Cu1−N2 88.7(3), O4−Cu1−N3 91.5(3), N1−Cu1−N2 92.1(3), N1−Cu1−N3 95.9(3), N2−Cu1−N3 171.2(3). Numbers in parentheses denote the estimated standard deviation in the least significant digits.

Reactions with Dioxygen

When the copper(II) complex **2a** was treated with 2 equiv. of benzoin/NEt_3 in CH_2Cl_2 at 25°C under Ar[14], reduction to a copper(I) complex occurred in less than one hour. This was clearly demonstrated by the complete disappearance of the *d-d* absorption at 671 nm in the electronic spectrum, which is characteristic for copper(II) complexes, and the silent EPR spectrum of the reaction mixture obtained after 40 min. Upon exposure to O_2 atmosphere, a new copper(II) complex **3a** was obtained in quantitative yield. Demetallation with 35% aqueous ammonia and analysis of the organic products indicated that complete conversion to the *cis*-2-amino-1-indanol derivative (**4a**) had occurred (Scheme 2). The stereochemistry of **4a** was assigned by comparison of its spectral data with those of an authentic sample prepared by Michael-type addition of *cis*-2-amino-1-indanol[15] to vinylpyridine, and was confirmed by X-ray analysis of the green crystals of complex **3a** obtained after recrystallization from CH_2Cl_2/MeOH (Table 1, Figure 2).

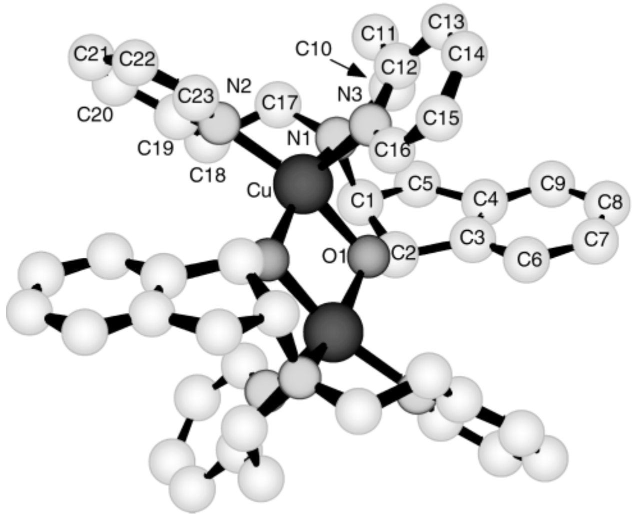
Scheme 2. Reactions with O_2 involving copper complexes **2a** and **5a**



Since the first step in this reaction sequence is reduction to a copper(I) complex, we examined the reaction of the copper(I) complex [(IndPY2)Cu]Z (**5a**; Z = PF_6 or CF_3SO_3) with O_2 in CH_2Cl_2. Complex **5a** was either prepared in situ by reaction of ligand **1a** with $[(CH_3CN)_4Cu]PF_6$ in CH_2Cl_2, or by electrolysis of the copper(II) complex **2a**. The voltammetric behaviour of **2a** is depicted in Figure 3, which shows a single quasi-reversible process characteristic of the Cu^{II}/Cu^{I} transition. Upon electrolysis of **2a** under a constant potential of 0 V vs. SCE, the solution turned from blue to pale-yellow after an equivalent charge of 1 electron had been passed. As expected for a reversible electron transfer, the cyclic voltammetry (CV) curve relating to the Cu^{II}/Cu^{I} couple had not changed.

When copper(I) complex **5a** (Z = PF_6 or CF_3SO_3) was placed under an O_2 atmosphere, the pale-yellow solution rapidly turned green. A new copper(II) complex was quantitatively obtained. Demetallation with 35% aqueous am-

Figure 2. Perspective view of copper(II) complex **3a** displaying the numbering scheme and selected bond distances and angles[a]



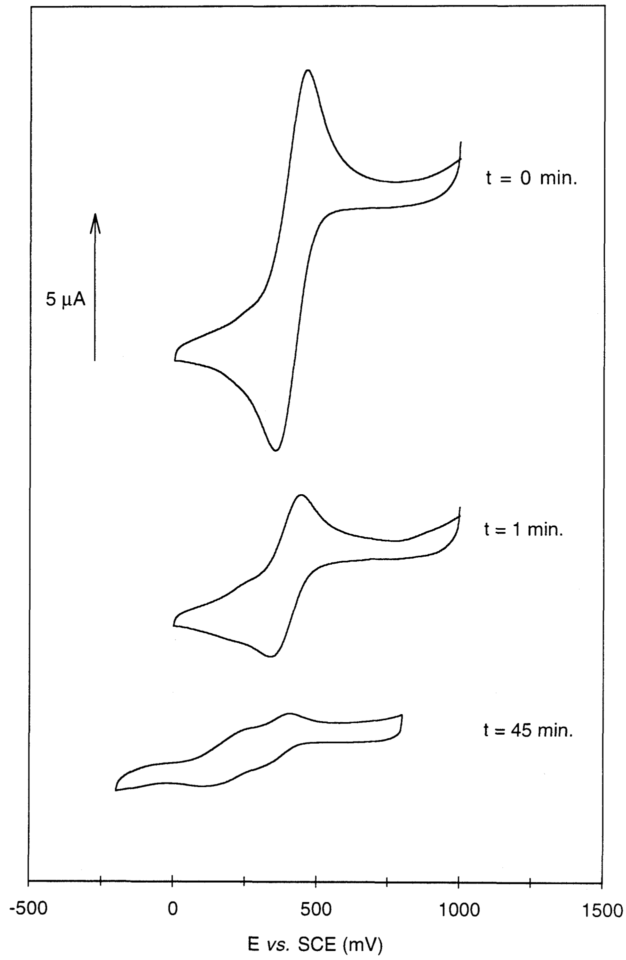
[a] Bond lengths in Å: Cu−O1 1.927(5), Cu−N1 2.057(7), Cu−N2 2.208(7), Cu−N3 1.984(7). Bond angles in°: O1−Cu−N1 85.7(2), O1−Cu−N2 96.5(2), O1−Cu−N3 165.0(3), N1−Cu−N2 99.0(2), N1−Cu−N3 94.5(3), N2−Cu−N3 98.3(3). Numbers in parentheses denote the estimated standard deviation in the least significant digits.

monia and analysis of the organic products revealed that 52% of unchanged ligand **1a** had been recovered, besides 48% of the *cis*-2-amino-1-indanol derivative **4a**. The reaction of **5a** (Z = CF_3SO_3) with O_2 was followed by CV. As can be seen in Figure 3, consumption of **5a** by O_2 progressively gives rise to a double-wave electrochemical signal. This result, as well as the smaller value of the peak currents, is consistent with either: (i) the formation of a dimeric complex with two non-equivalent copper(II) ions such as **A** (Scheme 5), or (ii) the formation of a mixture of symmetrical dimeric complexes such as **3a** and $[(IndPY2)_2Cu_2(\mu\text{-}OH)_2]^{2+}$ **B**. This second hypothesis is supported by the fact that two types of crystals (green and blue) are obtained after crystallization of the copper(II) complex from CH_2Cl_2/MeOH. Unfortunately, these crystals were not suitable for carrying out an X-ray structure analysis.

Stereoselectivity of Oxygen Atom Insertion

The aforementioned hydroxylations are highly stereoselective, and we propose, as is generally accepted, a process involving oxygen atom insertion into the benzylic C−H bond. The question then arises as to whether this insertion occurs with retention or inversion of configuration. Indeed, the hydroxylation can be envisaged as being either the result of a concerted mechanism in which oxygen atom insertion occurs at a *cis* C−H bond, or the result of a two-step process in which C−H bond scission and formation of the C−O bond occur at the same face (*cis* with respect to the amino group). In both cases, the product would be formed with retention of configuration at the benzylic carbon atom (Scheme 3). Another possibility is that the hydroxylation takes place via a two-step process involving *trans* C−H bond scission and *cis* formation of the C−O bond. If this

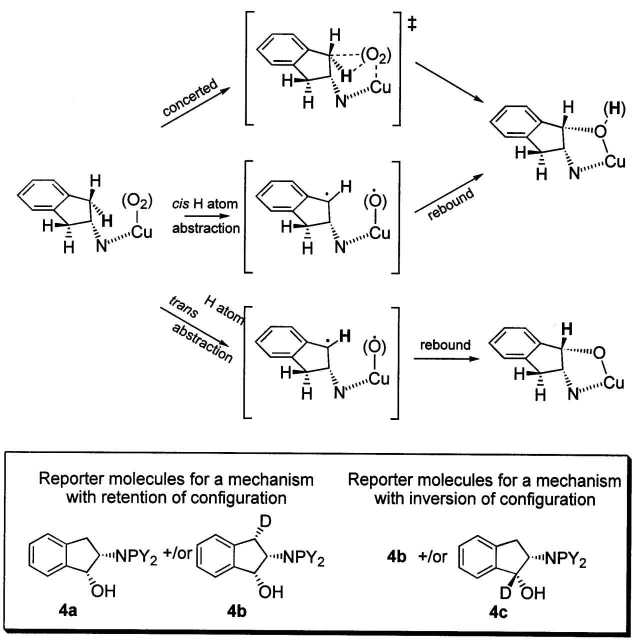
Figure 3. Cyclic voltammograms of **2a** after electrolysis at 0 V vs. SCE and reaction with O_2 in CH_2Cl_2, $n$$Bu_4NCF_3SO_3$ 0.1 M at 50 mV s^{-1}: (*solid line*) **2a** or **5a**; (*dotted line*) **5a** after 1 min. O_2 bubbling and (*bold line*) **5a** after 45 min. O_2 bubbling (steady-state CV)



were the case, we should observe inversion of configuration. In order to decide in favour of one of these mechanisms, we studied the reaction of deuterium-labelled copper complexes **2b** and **5b**. If the stereochemical course were to proceed with inversion of configuration, we would expect the formation of a mixture of deuterated compounds **4b** and **4c**. However, if the configuration was retained, we would expect the formation of a mixture of non-deuterated **4a** and its deuterated analogue **4b**.

Under standard conditions (benzoin, NEt_3, CH_2Cl_2, 25°C), the copper(II) complex {(*cis*-[D]-IndPY2)Cu}$(CF_3SO_3)_2$ **2b** (D content of 99 ± 0.1% determined by FAB-MS) was quantitatively transformed into complex **3b** (D content of 87.57 ± 0.16%). Demetallation with 35% aqueous ammonia gave the deuterated hydroxy ligand **4b** as the main product of the reaction. This is clearly evident from the ^{1}H-NMR spectrum, which shows a doublet of doublets at δ = 3.41 ($^3J_{2\text{-H},3\text{-H}cis}$ = 7 Hz and $^3J_{2\text{-H},1\text{-H}cis}$ = 5 Hz) instead of the doublet of doublet of doublets ($^3J_{2\text{-H},3\text{-H}trans}$ = 9 Hz, $^3J_{2\text{-H},3\text{-H}cis}$ = 7 Hz and $^3J_{2\text{-H},1\text{-H}cis}$ = 5 Hz} observed for the non-deuterated hydroxy ligand **4a**. The ^{13}C-NMR spectrum reveals the

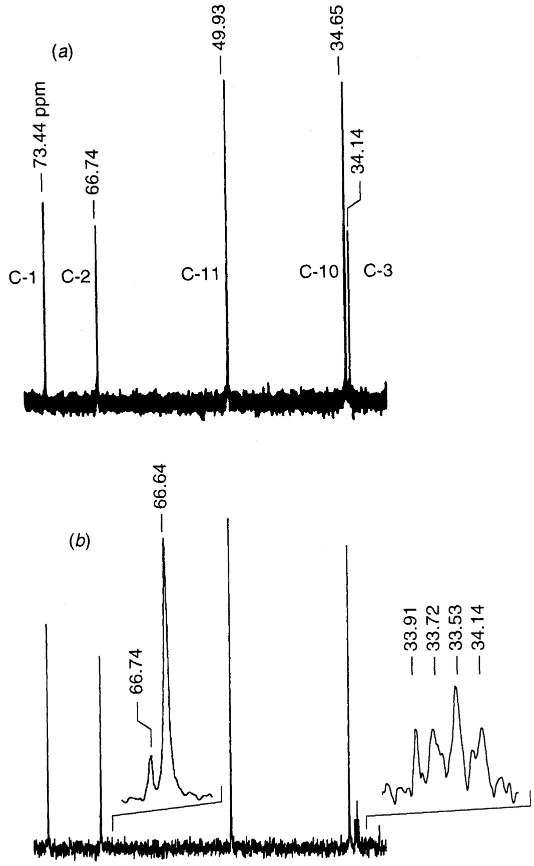
Scheme 3



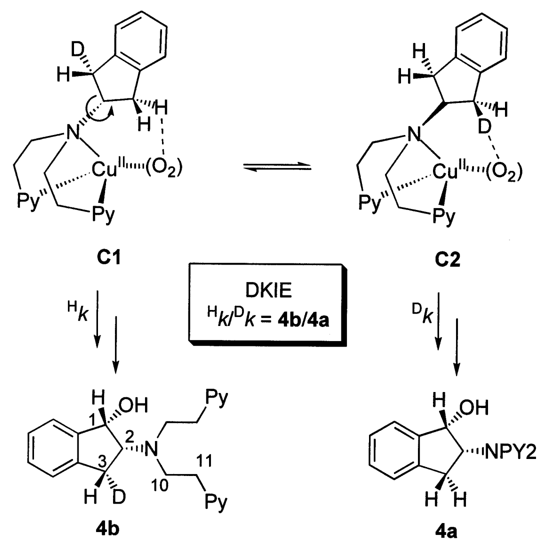
presence of a small amount of **4a** (singlet at δ = 34.14, C-3; Figure 4a) in addition to **4b** (triplet at δ = 33.72, $^{1}J_{13\,\mathrm{C,D}}$ = 21 Hz, C-3; Figure 4b), but no signals corresponding to a hypothetical deuterated hydroxy ligand **4c**, which might have arisen from a mechanism involving inversion of configuration, were observed. Moreover, the ^{13}C-NMR spectrum shows a singlet at δ = 66.64 attributable to C-2 of compound **4b**, in addition to the corresponding signal of **4a** (δ = 66.74). Integration of these signals after a DEPTCH sequence led to a **4b**/**4a** ratio of 7.6 ± 0.5. This ratio was confirmed by mass spectrometry analysis (FAB-MS) of complex **3b**, for which an 87.57 ± 0.16% deuterium content was found [**4b**/**4a** = 87.57/(100 − 87.57) = 7.04 ± 0.02]. Using the same methodology under standard conditions (O_2, CH_2Cl_2, 25°C), the deutero-copper(I) complex **5b** was quantitatively transformed into a copper(II) complex, which, after demetallation with 35% aqueous ammonia, also gave a mixture of **4b** and **4a** (**4b**/**4a** = 11.0 ± 0.7).

In both reactions, ratios of non-deuterated **4a** to the deuterated compound **4b** are very large (7.6 and 11). These findings can be explained if we assume that the copper/oxygen species responsible for the observed hydroxylations exist as two conformers, **C1** and **C2**, which are in equilibrium (Scheme 4). It is clear that conformer **C2**, which exposes a deuterium atom to the copper−oxygen core, must react with a lower rate than conformer **C1**, which exposes a hydrogen atom. Since conformers **C1** and **C2** are in rapid equilibrium, the deuterium kinetic isotope effect (DKIE) expressed by the k_H/k_D ratio is directly related to the **4b**/**4a** ratio.[16] The large DKIEs (7.6 vs. 11) indicate that the hydroxylations occur with retention of configuration in a process in which the benzylic C−H bond is broken in the rate-determining step.[17]

Figure 4. Aliphatic region of ^{13}C-NMR spectra of aminoindanols **4a**, **b**: (*a*) reaction of **2a** with benzoin/NEt_3/O_2 or **5a** with O_2 in CH_2Cl_2; (*b*) reaction of **2b** with benzoin/NEt_3/O_2 or **5b** with O_2 in CH_2Cl_2



Scheme 4.

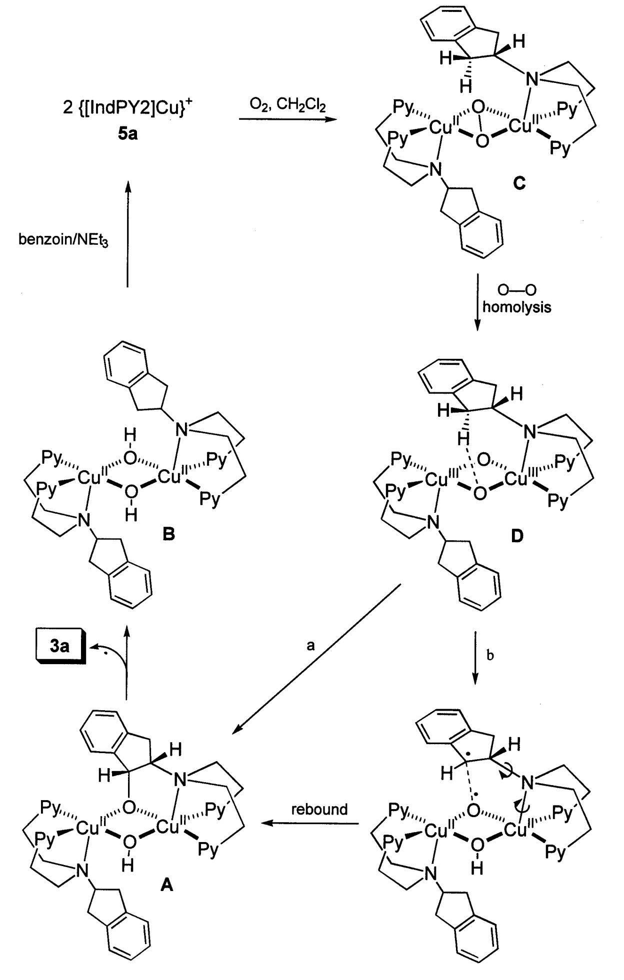


Dioxygen Adducts and Mechanistic Hypothesis

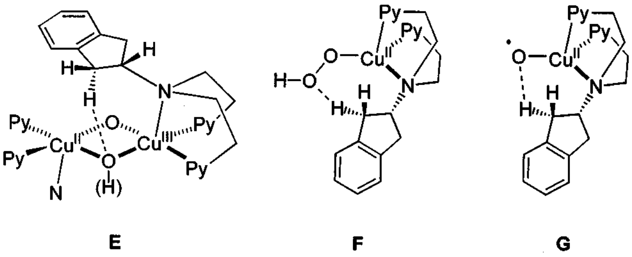
Finally, we turn to the question of the dioxygen adduct that may be involved in these hydroxylations. At present, for the reaction of the copper(I) complex **5a** with O_2 in CH_2Cl_2, it is difficult to obtain structural information concerning copper/oxygen species, because, even at $-80\,°C$, such species are too reactive to be amenable to structural analysis, e.g. by UV/vis or X-ray spectroscopy. However, since copper(I) complexes derived from tridentate ligands are known to lead to $[L_2Cu_2(\mu\text{-}\eta^2{:}\eta^2\text{-}O_2)]^{2+}$ species by reaction with O_2[5a][6], we can reasonably expect the formation of this type of intermediate (**C**) upon reaction of **5a** with O_2 (Scheme 5). Kitajima has observed that the $\{[HB(3,5\text{-}Me_2pz)_3]_2Cu_2(\mu\text{-}\eta^2{:}\eta^2\text{-}O_2)\}$ complex is capable of oxidising cyclohexene to 2-cyclohexen-1-ol and 2-cyclohexen-1-one.[18] To account for this finding, a mechanism was proposed involving: (i) formation of the radical $\{[HB(3,5\text{-}Me_2pz)_3]Cu{-}O^{\bullet}\}$ by homolysis of the peroxo bond; (ii) abstraction of a hydrogen atom from cyclohexene, and (iii) subsequent reaction of these intermediates with O_2 to generate the observed products. Given that we did not observe any formation of an indanone derivative, and that the oxygen atom transfer proceeds with high DKIEs and high *cis* stereoselectivity, we can rule out the possibility that the hydroxylated ligand is formed by a mechanism akin to that postulated for Kitajima's cyclohexene oxidation. More recently, Tolman has reported that $[Cu^{II}_2(\mu\text{-}\eta^2{:}\eta^2\text{-}O_2)]^{2+}$ species exist in equilibrium with a bis(μ-oxo)dicopper species with a formal $[Cu^{III}_2(\mu\text{-}O)_2]^{2+}$ oxidation state, and it was demonstrated that these species behave like electrophilic radicals.[19] Considering these findings and the fact that oxidation of **5a** by O_2 results in stereospecific *cis*-hydroxylation in yields not exceeding 50%, Scheme 5 illustrates possible pathways whereby hydroxylation can occur via the $\{[IndPY2]_2Cu^{III}_2(\mu\text{-}O)_2\}^{2+}$ species (**D**): (i) by a concerted mechanism (pathway *a*), or (ii) by abstraction of a *cis* benzylic hydrogen atom forming a benzylic radical and a copper/oxygen radical species, which recombine at the same face to give the observed copper(II) complex in an overall mechanism with retention of configuration (pathway *b*).

Concerning the reaction of **2a** with benzoin/NEt_3, we have shown that under Ar the first step is the reduction to the cuprous state. Upon exposure to O_2, the next step could then be the formation of the peroxo complex **C** and/or its subsequent species **D**. As already described, this reaction sequence could lead to the observed compounds. As an explanation for the quantitative yield of oxidised complex **3a**, we can assume that a 1:1 mixture of complexes **3a** and **B** is obtained, and that only **B** is reduced to the copper(I) complex **2a** by excess benzoin/NEt_3 and is thus able to participate in the hydroxylation reaction once more (Scheme 6). We can effectively demonstrate that complex **3a** does not react with benzoin/NEt_3, even after several hours, but the higher DKIE observed for the reaction of **2a**/O_2 compared to that of **5a**/benzoin/NEt_3/O_2 (11 vs. 7.6) suggests the intermediacy of another reactive species, for which several structures can be proposed. As previously assumed for the active species in pMMO[3], a μ-oxo mixed-valence Cu^{II}/Cu^{III} species **E** derived from a one-electron reduction of species **C** or **D** could be responsible for the present ligand hydroxylation. However, as it is known that the reaction of copper salts with O_2 in the presence of a reducing agent leads to hydroperoxo species[20], another possibility could be the formation of the hydroperoxo species **F** or its subsequent (one-electron reduction) copper radical species **G**. Structural studies of the copper/oxygen species involved in these hydroxylations aimed at elucidating details of the reaction mechanism are currently in progress.

Scheme 5. Proposed mechanism for the ligand hydroxylation



Scheme 6. Possible copper/oxygen intermediates in the reaction of copper(II) complex **2a** with O_2/benzoin/NEt_3



Conclusion

Once again, we have shown that a conformationally-restricted substrate approach can provide valuable information about the mechanism of oxygen atom transfer from copper to a ligand. On the basis of deuterium-labelling experiments, we have demonstrated that oxygen atom insertion into a C−H bond of the ligand occurs at a benzylic position with retention of configuration. This is an important approach, which is of interest because of the possibility of performing parallel enzymatic studies. For example, we have recently found that the DBH-catalysed hydroxylation of 2-aminoindane produces exclusively *trans*-(1*S*,2*S*)-2-amino-1-indanol with 93% *ee*. Studies with stereospecifically deuterium-labelled 2-aminoindanes have further shown that the formation of (1*S*)-aminoindanol is the result of stereospecific *pro*-(*S*) hydrogen abstraction followed by oxygen binding, with overall retention of configuration.[21] Nevertheless, for modelling reactivity of the order of that of DBH, we have to admit that our approach needs to be improved and that we have to find a copper complex with catalytic properties towards an exogenous 2-aminoindane (oxygen atom transfer that does not involve the ligand). To achieve this goal, the problem of 2-aminoindane association in the copper coordination sphere still has to be solved.

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Experimental Section

General: Solvents were freshly distilled under Ar (MeOH/Mg, Et_2O/Na-benzophenone ketyl, CH_3CN/CaH_2, and CH_2Cl_2/P_2O_5). Deoxygenation of solvents and solutions was carried out by 3 vacuum/purge cycles. Preparation and handling of air-sensitive compounds was carried out by using standard Schlenk techniques. Commercial starting materials were used without further purification, except for 2-vinylpyridine, which was distilled prior to use; *cis*-1-deutero-2-aminoindane was obtained by $LiAlD_4$ reduction of *trans*-2-azido-1-bromoindane.[13] − $^1H\{^{13}C\}$-NMR spectra were recorded at 25°C on a Bruker AC-400 spectrometer. Chemical shifts are reported in ppm as δ values downfield from an internal standard of TMS. − IR spectra were recorded on a Nicolet MX 5 spectrometer. − Elemental analyses were obtained with a CHN Technicon microanalyser. − FAB-MS were obtained by the LSIMS ionization technique in thioglycerol (TG) or nitrobenzyl alcohol (NB) lattices.

Ligands **1a** *and* **1b**: To absolute MeOH (8 ml) were added 2-vinylpyridine (3.785 g, 36 mmol), 2-aminoindane (798 mg, 6 mmol) and acetic acid (900 mg, 15 mmol). After refluxing for 5 days, the MeOH was evaporated and 15% NaOH (10 ml) was added. The product was extracted with CH_2Cl_2 (3 × 20 ml) and the combined organic layers were dried over Na_2SO_4. Evaporation of the CH_2Cl_2 under reduced pressure (18 mmHg) left the crude product. Flash chromatography (SiO_2, CH_2Cl_2/MeOH, 90:10) afforded ligand **1a** (**1b**). − **1a**: Yield: 800 mg (2.3 mmol, 40%). − ^1H NMR ($CDCl_3$): δ = 8.51 (ddd, *J* = 5, 2 and 1 Hz, 2 CH-pyr), 7.55 (td, *J* = 8 and 2 Hz, 2 CH-pyr), 7.15−7.07 (m, 8 CH-aryl), 3.74 (qt, *J* = 9 Hz, 2 2-H), 3.07−2.95 (m, 10 H), 2.83 (dd, *J* = 15 and 9 Hz, 2 1-H_{cis}). − ^{13}C NMR ($CDCl_3$): δ = 160.65 (2 C-pyr), 149.25 (2 CH-pyr), 141.75 (2 C-ind), 136.15 (2 CH-pyr), 126.26 (2 CH-ind), 124.42 (2 CH-pyr), 123.36 (2 CH-pyr), 121.07 (2 CH-pyr), 63.25 (C-2), 51.50 (2 C-10), 36.93 (2 C-11), 36.11 (2 C-1). − IR (neat): $\tilde{\nu}$ = 1595 cm^{-1} (C=N), $\tilde{\nu}$ = 1570, 1480, 1440 cm^{-1} (C=C). − **1b**: Yield: 930 mg (2.7 mmol, 45%). − ^1H NMR ($CDCl_3$): δ = 8.50 (ddd, *J* = 5, 2 and 1 Hz, 2 H), 7.53 (td, *J* = 8 and 2 Hz, 2 H), 7.15−7.05 (m, 8 H), 3.74 (q, *J* = 9 Hz, 1 H), 3.07−2.96 (m, 10 H), 2.85 (dd, *J* = 15 and 9 Hz, 1 H). − ^{13}C NMR ($CDCl_3$): δ = 160.70 (2 C-pyr), 149.30 (2 CH-pyr), 141.84 (2 CH-pyr), 141.75 (2 C-ind), 136.19 (2 CH-pyr), 126.32 (CH-ind), 126.35 (CH-ind), 124.49 (CH-ind), 124.46 (CH-ind), 123.41 (2 CH-pyr), 121.11 (2 CH-pyr), 63.21 (C-2), 51.55 (2 C-10), 36.96 (2 C-11), 36.62 (t, $^1J_{13\,C,D}$ = 21 Hz, C-1), 36.17 (C-3).

Complexes **2a** *and* **2b**: To a solution of $Cu(CF_3SO_3)_2$ (362 mg, 1 mmol) in MeOH (15 ml), a solution of **1a** (**1b**) (344 mg, 1 mmol) in MeOH (15 ml) was added dropwise and the mixture was stirred for 30 min. The MeOH was then evaporated in vacuo and Et_2O (50 ml) was added. The resulting precipitate was filtered off, washed with further Et_2O, and dried in vacuo to give complex **2a** (**2b**) as a blue solid. − **2a**: Yield: 634 mg (0.9 mmol, 90%). Recrystallization from CH_2Cl_2/Et_2O gave blue crystals suitable for X-ray analysis. − $C_{25}H_{25}CuF_6N_3O_6S_2$ (705.15): calcd. C 42.58, H 3.57, N 5.96; found C 42.98, H 3.52, N 6.05. − MS (FAB); *m*/*z* (%): 344 (100) [IndPY2 + H]$^+$, 345 (27) [*p* + 1], 343 (2.6) [*p* − 1]. − **2b**: Yield: 635 mg (0.9 mmol, 90%). − MS (FAB); *m*/*z* (%): 345 (100) [*d*-IndPY2 + H]$^+$, 346 (26.54) [*p* + 1], 344 (3.44) [*p* − 1]; deuterium content 99 ± 0.1%.

Complexes **3a** *and* **3b**: To a solution of **2a** (**2b**) (70 mg, 0.1 mmol) in degassed CH_2Cl_2 (6 ml) were added benzoin (42 mg, 0.2 mmol) and NEt_3 (20 mg, 0.2 mmol). This mixture was stirred under Ar for 2 h and then exposed to an O_2 atmosphere for 24 h. The CH_2Cl_2 was subsequently evaporated in vacuo and Et_2O (20 ml) was added. The precipitate thus obtained was filtered off, washed with Et_2O, and dried in vacuo to give complex **3a** (**3b**). − **3a**: Yield: 49 mg (86 µmol, 86%). Recrystallization from CH_2Cl_2/MeOH gave green crystals suitable for X-ray analysis. − $C_{24}H_{24}CuF_3N_3O_4S$ (571.08): calcd. C 50.48, H 4.24, N 7.36; found C 50.55, H 4.27, N 7.56. − MS (FAB); *m*/*z* (%): 360 (100) [IndOHPY2 + H]$^+$, 361 (27.7) [*p* + 1], 359 (1.7) [*p* − 1]. − **3b**: Yield: 48 mg (85 µmol, 85%). − MS (FAB); *m*/*z* (%): 361 (100) [*d*-IndOHPY2 + H]$^+$, 362 (29.7) [*p* + 1], 360 (14.0) [*p* − 1]; deuterium content 87.57 ± 0.16%.

In situ Preparation and Oxidation of Complexes **5a** *and* **5b**: To a solution of $[CH_3CN]_4CuPF_6$ (37.3 mg, 0.1 mmol) in degassed CH_2Cl_2 (50 ml), a solution of **1a** (**1b**) (34.4 mg, 0.1 mmol) in CH_2Cl_2 (50 ml) was added dropwise. The mixture was stirred under Ar for 1 h, and then exposed to an O_2 atmosphere for 24 h. The CH_2Cl_2 was subsequently evaporated in vacuo, Et_2O (50 ml) was added, and the precipitate thus obtained was filtered off, washed with Et_2O, and dried in vacuo to give a mixture of copper(II) complexes. This mixture was redissolved in CH_2Cl_2 (20 ml), washed with 35% NH_4OH (5 ml) and brine (3 × 5 ml), and dried over Na_2SO_4. Evaporation of the CH_2Cl_2 under reduced pressure (18 mmHg) gave the crude product. Flash chromatography (SiO_2, CH_2Cl_2/MeOH, 90:10) afforded ligands **1a** (**1b**) and **4a** (**4b**). − **4a**: Yield: 17.3 mg (48 µmol, 48%). − ^1H NMR ($CDCl_3$): δ = 8.51 (ddd, *J* = 4, 2 and 1 Hz, 2 H-pyr), 7.54 (td, *J* = 8 and 2 Hz, 2 H-pyr), 7.43 (d, *J* = 6 Hz, 1 H-ind), 7.49−7.17 (m, 3 H-ind), 7.11−7.06 (m, 4 H-pyr), 4.97 (d, *J* = 5 Hz, 1-H), 3.41 (ddd, *J* = 9, 7 and 5 Hz, 2-H), 3.24−3.09 (m, 4 H), 3.07−2.95 (m, 6 H). − ^{13}C NMR ($CDCl_3$): δ = 160.05 (2 C-pyr), 149.34 (2 CH-pyr), 143.28 (C-ind), 141.77 (C-ind), 136.50 (2 CH-pyr), 128.70 (CH-ind), 126.95 (CH-ind), 125.52 (CH-ind), 124.81 (CH-ind), 123.57 (2 CH-pyr), 121.39 (2 CH-pyr), 73.44 (C-1), 66.74 (C-2), 49.93 (2 C-10), 34.65 (2 C-11), 34.14 (C-3). − **4b**: Yield: 17.4 mg (48 µmol, 48%). − ^1H NMR ($CDCl_3$): δ = 8.50 (d, *J* = 5 Hz, 2 H-pyr), 7.54 (td, *J* = 8 and 2 Hz, 2 H-pyr), 7.44 (d, *J* = 7 Hz, H-ind), 7.24−7.17 (m, 3 H-ind), 7.11−7.06 (m, 4 H-pyr), 4.96 (d, *J* = 5 Hz, 1-H), 3.41 (dd, *J* = 7 and 5 Hz, 2-H), 3.23−3.10 (m, 4 H), 3.05−2.94 (m, 5.28 H). − ^{13}C NMR ($CDCl_3$): δ = 160.05 (2 C-pyr), 149.26 (2 CH-pyr), 143.30 (C-ind), 141.65 (C-ind), 136.34 (2 CH-pyr), 128.56 (CH-ind), 126.84 (CH-ind), 125.40 (CH-ind), 124.72 (CH-ind),

Table 1. Crystallographic data for copper(II) complexes **2a** and **3a**

Complexes	**2a**	**3a**
Crystal data		
formula	$C_{50}H_{50}Cu_2F_{12}N_6O_{12}S_4$	$C_{24}H_{24}CuF_3N_3O_4S$
M_r	1410.30	571.08
crystal system	triclinic	orthorhombic
space group	$P\bar{1}$	*Pbca*
a [Å]	9.858(1)	13.787(3)
b [Å]	13.023(2)	15.083(3)
c [Å]	27.465(3)	22.935(4)
α [°]	98.85(23)	90.00
β [°]	94.72(29)	90.00
γ [°]	92.19(34)	90.00
V [Å^3]	3467.4	4769(3)
D_{calc} [g cm^{-3}]	1.35	1.59
Z	2	8
F(000) [e]	1432	2344
μ (Mo-K_α) [cm^{-1}]	8.13	10.60
Data collection		
T [K]	294	294
scan mode	ω−2θ	ω−2θ
scan width [°]	0.9 + 0.35 tanθ	0.8 + 0.35 tanθ
$2\theta_{max}$ [°]	48	48
measured refl.	10760	4193
unique refl.	6359	4051
refl. used for refinement	5660	1977
absorption correction	no	no
extinction correction	no	isotropric[25]
extinction coefficient	−	4.19×10^{-8}
Structure refinement		
refined parameters	775	326
H atoms	included, not refined	
R	0.075	0.06
R_w	0.104	0.073
w	$4\,F_0{}^2/[\sigma^2(F_0{}^2) + 0.0025\,F_0{}^4]$	$4\,F_0{}^2/[\sigma^2(F_0{}^2) + 0.0016\,F_0{}^4]$
(shift/e.s.d.)$_{max}$	0.11	0.62
goodness of fit	2.807	2.22
$\Delta\rho_{fin}$(max./min.) [e Å^{-3}]	0.61/0.54	0.606/0.452

123.42 (2 CH-pyr), 121.25 (2 CH-pyr), 73.38 (C-1), 66.64 (C-2), 49.96 (2 C-10), 34.75 (2 C-11), 33.72 (t, $^1J_{13\,C,D}$ = 21 Hz, C-3).

X-ray Structure Analysis: Crystals of complexes **2a** and **3a** of suitable quality and size were mounted in glass capillaries and examined on an Enraf-Nonius CAD4 diffractometer [Mo-K_α radiation, λ(Mo-K_α) = 0.71073 Å]. During data collection, three standard reflections were measured periodically as a general check of crystal and instrument stability. The data reduction was performed with Begin in SDP-Plus.[22] The structures were solved by the Patterson method for **2a** and by direct methods with MULTAN80[23] for **3a**, and were refined with LSFM-Plus. The scattering factors were taken from the International Tables for X-ray Crystallography.[24]

Crystallographic data for the structure(s) reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-101037. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: int. code +44(0)1223/ 336-033, e-mail: deposit@chemcrys.cam.ac. uk].

Electrochemical Measurements: Cyclic voltammetric (CV) experiments were carried out using an EG&G 263A potentiostat with EG&G M270 software. CV curves were obtained at a scan rate of 50 mVs^{-1}. A three-electrode system consisting of a saturated calomel reference electrode, a platinum wire auxiliary electrode, and a gold microelectrode (surface area: 7.8×10^{-3} cm^2) was used throughout. Both the reference and auxiliary electrodes were connected to the solution through porous bridges. Coulometric measurements were made using an EG&G 379 coulometer. Electrolyses were performed using a gold grid (geometric surface: 7 cm^2) under a constant potential.

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