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Promotion of Sandmeyer hydroxylation (homolytic hydroxydediazoniation) and hydrodediazoniation by chelation of the copper catalyst: bidentate ligands† ‡

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Relative to the rate observed for the hexa-aqua ion, $Cu(OH_2)_6^{2+}$, chelation of the copper catalyst by certain bidentate ligands enhances the rate of hydroxydediazoniation reaction (Sandmeyer hydroxylation); the ligands also provide a source of hydrogen in competitive hydrodediazoniation (H-transfer) reactions. By using the cyclisation of 2-benzoylphenyl radical as a radical clock, it has been possible to evaluate absolute rate constants for both processes effected by a variety of complexes involving one or two bidentate ligands (2-aminocarboxylate, 2-hydroxycarboxylate, 1,3-dicarboxylate, 1,2-diamine). The radical exhibits electrophilic character in both processes. The pattern of behaviour observed suggests the rate determining step in hydroxylation is reaction of the aryl radical at the metal centre to form an organocopper adduct which is rapidly converted into products. The relative reactivities of different complexes are explained qualitatively in terms of variations in the ligand field and Jahn–Teller distortion splittings of the copper d orbitals. Hydrodediazoniation is an S_H2 H-abstraction process. Generally, coordination by Cu^{2+} deactivates the first added ligand relative to its reactivity as a free species in the same state of protonation. For the majority of complexes studied, the relative reactivity as H-donors of 1 : 1 and 1 : 2 complexes is statistically determined but an additional electronic effect is discerned for doubly charged ions.

In 1977 Cohen and co-workers[2] showed that homolytic hydroxydediazoniation of arenediazonium ions, catalysed by a Cu(II)/Cu(I) couple, is a useful alternative to thermolysis for the synthesis of phenols. The reaction is thus an apparent late addition to the family of Sandmeyer reactions, recognised a century after its first members.[3] Operationally, Cohen's procedure[2] differs from that of traditional Sandmeyer reactions.[4] In the former, the diazonium ion is added to a solution of Cu^{2+}aq in which is suspended Cu_2O and the [Cu(II)]/[Cu(I)] ratio in solution is thus high whereas, in traditional Sandmeyer reactions, the diazonium salt is added to a solution of Cu(I) halide or cyanide and Cu(II) is generated *in situ* by their reaction and the [Cu(II)]/[Cu(I)] ratio is consequently low. Assuming that hydroxylation and traditional Sandmeyer reactions occur by the same general mechanism, this requirement for different resting states of the catalyst can be explained by disparate rates of reaction (3) of the catalytic cycle in the two circumstances.

$$ArN_2^+ + Cu^{I}X_n \longrightarrow ArN_2^{\bullet} + Cu^{II}X_n \quad (1)$$

$$ArN_2^{\bullet} \longrightarrow Ar^{\bullet} + N_2 \quad (2)$$

$$Ar^{\bullet} + Cu^{II}X_n \longrightarrow ArX + Cu^{I}X_{(n-1)} \quad (3)$$

Previously,[5,6] we have shown hydroxylation and chlorination may be competitive and have determined for the 2-benzoylphenyl radical a hydroxylation rate constant of $(1.47 \pm 0.17) \times 10^6$ dm^3 mol^{-1} s^{-1} for $Cu(OH_2)_6^{2+}$, which compares with chlorination rate constants of 8.8×10^6 dm^3 mol^{-1} s^{-1} for $CuCl(OH_2)_5^+$ and 1.0×10^8 dm^3 mol^{-1} s^{-1}, when statistically adjusted, for both $CuCl_2(OH_2)_4$ and $CuCl_3(OH_2)_3^-$. These figures show hydroxylation by $Cu(OH_2)_6^{2+}$ to occur 100–200 times less rapidly than chlorination by the chlorocuprate(II) complexes which occur in Sandmeyer reaction conditions. Because hydroxylation is comparatively slow, Cohen's reaction requires a high concentration of Cu^{2+} if the aryl radicals are not to be lost to side-reactions and hence the yield of phenol reduced.

The ligand transfer [reaction (3)] may, in principle, occur in several mechanistically distinct ways:

$$Ar^{\bullet} + Cu^{II}X_n \longrightarrow Ar^+ + Cu^{I}X_n \longrightarrow ArX + Cu^{I}X_{(n-1)} \quad (3a)$$

$$Ar^{\bullet} + Cu^{II}X_n \longrightarrow [Ar{-}X{-}CuX_{(n-1)}]^{\ddagger} \longrightarrow ArX + Cu^{I}X_{(n-1)} \quad (3b)$$

$$Ar^{\bullet} + Cu^{II}X_n \longrightarrow Ar{-}Cu^{III}X_n \longrightarrow ArX + Cu^{I}X_{(n-1)} \quad (3c)$$

Reaction (3a) implies the outer sphere transfer of an electron from the aryl radical to copper followed by trapping of a ligand by the aryl cation so produced. This is improbable in view of the unique ability of copper complexes in bringing about the process when more powerful oxidants fail and in view of the high yields of traditional Sandmeyer products when the reactive complex is produced *in situ* in an aqueous medium. If a free aryl cation were to be involved, its solvolysis to phenol under traditional Sandmeyer conditions would be much more important than is the case.

Reaction (3b) can be regarded in two ways. First, if bond formation between Ar and X occurs synchronously with bond breakage between X and Cu, the aryl radical abstracts X from the complex much as it would abstract a chlorine atom from CCl_4 and the reaction is of S_H2 character. Alternatively, reaction (3b) can be regarded as an inner sphere electron transfer in which the relay of the electron between the radical and its oxidant is effected by the ligand which is transferred. This process can be dissected into simpler steps:[7] (i) association

† Sandmeyer reactions. Part 8. For part 7 see ref. 1.
‡ Electronic supplementary information (ESI) available: EPR evidence for the formation of binuclear complexes by 2-hydroxycarboxylates; reprise of the radical clock results for 2-hydroxycarboxylates. See http://www.rsc.org/suppdata/ob/b4/b404699d/

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of the reactants into the precursor complex; (ii) activation of the precursor complex to a configuration which allows transfer of the electron so forming the successor complex and (iii) dissociation of the successor complex. Any one of these elementary steps might, in principle, be that which determines the rate of the transfer. Either variant of reaction (3b) allows rationalisation of the transfer of a specific ligand and is the mechanism usually assumed applicable to traditional Sandmeyer reactions.[8] In our previous work[5] we have argued that the transition states for chloride ligand transfers occupy locations in a continuum between end-members having S_H2 character and inner sphere electron transfer character which are dependent on substitution in the radical and the number of chloride ligands on copper.

In reaction (3c), the radical attacks the *metal* centre to form an adduct containing a C–Cu bond which undergoes reductive (of the metal) elimination to give products. There is a wealth of evidence from mechanistic,[9] flash photolytic[10] and pulse radiolytic studies[11,12] that aliphatic radicals R$^{\bullet}$ combine with Cu(II) complexes to produce transient adducts, R–Cu^{III}X$_n$, which in some cases may be observed spectroscopically. The adducts may decompose to form products other than that from ligand transfer. These include alkenes (if R contains an appropriate β-proton) and solvolysis products. In cases where R may form a relatively stable carbocation, the solvolysis products and some of the ligand transfer products may exhibit characteristic skeletal rearrangement.[9] The rearranged products were inferred to derive from ionisations of the adduct such as:

$$R\text{–}Cu^{III}X_n \longrightarrow R\text{–}CuX_{(n-1)}{}^{+},\ X^{-} \longrightarrow R^{+} + Cu^{I}X_n{}^{-}$$

When more than one product was formed, it was deduced that the rate determining step for the oxidation of R$^{\bullet}$ precedes and is separate from those which determine the product distribution, *i.e.* it is the adduct-forming step.[9] To the best of our knowledge there is no direct evidence, spectroscopic or otherwise, which points to the formation of aryl radical/Cu(II) adducts in the traditional Sandmeyer reaction sequence although there is circumstantial mechanistic evidence that arylcopper species may be involved in the formation of Sandmeyer reaction by-products such as biaryls and azoarenes in conditions where the concentration of Cu(I) is high.[13] However, since Sandmeyer hydroxylation is considerably slower than the transfer of traditional ligands, the possibility arises that, in this case, the aryl radical may attack the metal rather than a water ligand. In both aromatic[5] and aliphatic systems[9] the rate constants for direct ligand transfers [reaction (3b)] in traditional Sandmeyer ligands exceed 10^8 dm^3 mol^{-1} s^{-1} whereas those for addition of neutral aliphatic radicals to aquacopper(II) range from 7.4×10^5 dm^3 mol^{-1} s^{-1} (Me$^{\bullet}$) to 3×10^7 dm^3 mol^{-1} s^{-1} (HOCH$_2$CH$_2^{\bullet}$) to 1.6×10^8 dm^3 mol^{-1} s^{-1} (HOCH$_2^{\bullet}$)[12] an interval which includes our value of 1.47×10^6 dm^3 mol^{-1} s^{-1} for the 2-benzoylphenyl radical.[6]

We have previously found[14] that certain multidentate ligands, such as citrate, can promote hydroxydediazoniation in the sense that lower concentrations of copper suffice to optimise phenol yield in the presence of the ligand than otherwise. The purpose of this paper is to report an investigation into the effects of catalyst ligation on the rates of hydroxylation of aryl radicals by Cu(II) complexes by use of the 2-benzoylphenyl radical clock and, since introduction of organic ligands L into the system introduces sources of hydrogen, to report also the parallel behaviour of the Cu(II) complexes as reductants of the radical clock. Owing to the complexity of ligation by citrate and other multidentate ligands which can give rise to multiple mono- and bi-nuclear complexes, we restrict coverage here to bidentate ligands, L, where for the most part, complexes of the types Cu^{II}L(OH$_2$)$_4$, Cu^{II}L$_2$(OH$_2$)$_2$ and perhaps Cu^{II}L$_3$ are expected. We use the terms 'hydroxylation' and 'hydrogen transfer' without preconceptions as to the mechanisms of the processes; we do assume, however, that the reactivity of a copper complex in hydroxylation depends on it having coordinated water and in hydrogen transfer on it having a coordinated organic ligand.

Results

(i) Distributions of copper(II) complexes

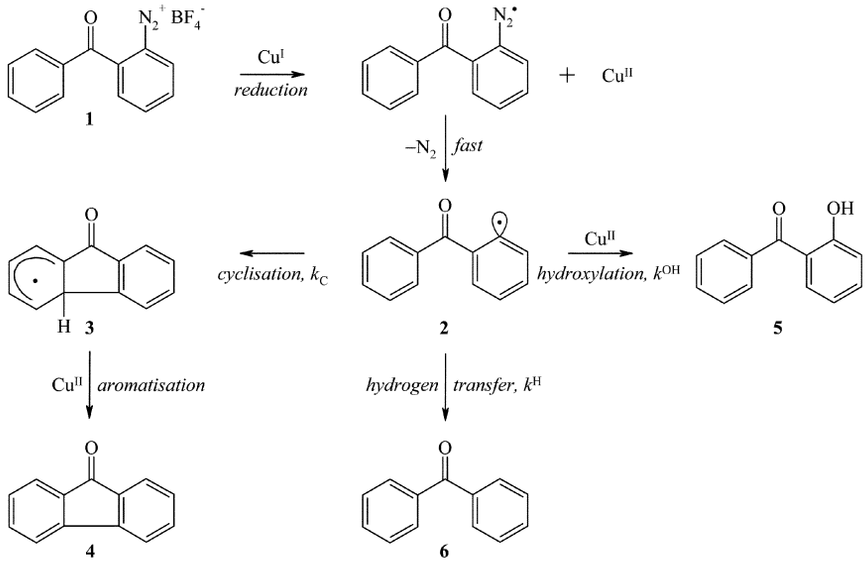
Copper may form complexes of mixed stoichiometry with a particular ligand. The primary requirement for understanding the behaviour of such a system is obviously a knowledge of the distribution of species which, since the chosen ligands and copper–aqua complexes have acid/base properties, is pH-dependent. The required distributions of complexes were calculated as functions of pH using the computer program ES4EC1.[15] Except where otherwise stated, for each ligand we have used protonation constants ($-pK_a$) and stability constants ($\log\beta_n$) for 298 K and unit ionic strength taken from *Critical Stability Constants* compiled by Martell and Smith;[16] for convenience, these are given in ESI.

(ii) The 2-benzoylphenyl radical clock

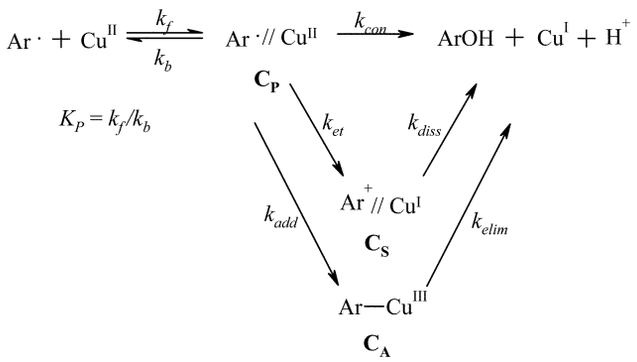
Homolysis of 2-benzoylbenzenediazonium ion, **1**, when dissolved in a solution of mixed Cu(II) complexes at a given pH, may be initiated by the addition of a small amount of ascorbic acid (~0.5 mol% relative to copper). The Cu(I) so produced reduces **1** in the rate determining step for the whole Sandmeyer sequence,[17] giving an aryldiazenyl radical which rapidly loses nitrogen to form the 2-benzoylphenyl radical, **2** (Scheme 1). The latter radical may then undergo three processes which together determine the product distribution. Irreversible cyclisation produces the hydrofluorenyl π-radical, **3**, which is rapidly aromatised by Cu(II) to give 9-fluorenone, **4**, and Cu(I).[18] The cyclisation rate constant, k_C, is the fiducial value relative to which the constants for other reactions of **2** are measured.[6] The second process undergone by **2** is hydroxylation which involves a copper(II) complex and produces 2-hydroxybenzophenone, **5** and Cu(I); the third reaction is reduction to benzophenone, **6**. The organic products **4**–**6** separate from the aqueous medium and do not interfere with reaction in solution.[19]

The mechanistic possibilities described above [reactions (3b) and (3c)] are further addressed in Scheme 2. The aryl radical Ar$^{\bullet}$ (*i.e.* **2**), encounters a copper(II) complex bearing a water ligand and *rapidly and reversibly* forms a precursor complex $\mathbf{C_P}$ which may be activated for reaction in different ways. If, within $\mathbf{C_P}$, Ar$^{\bullet}$ attacks a water ligand with a concerted breakage of the bond between the ligand and the metal, the reaction follows an S_H2 route for which k_{con} is the rate-limiting constant. A routine application of the steady state approximation to $\mathbf{C_P}$ identifies the hydroxylation rate constant k^{OH} as $k_{con}k_f/k_b = k_{con}K_P$ where K_P is the equilibrium constant which defines $\mathbf{C_P}$. If the making and breaking of bonds on activation of $\mathbf{C_P}$ are not synchronous, the complex may attain a vibrational state of which the geometry and energy permit the transfer of an electron between the two participating reactants through the bridging water ligand to give the successor complex $\mathbf{C_S}$. If Ar^{+} were to form it would be expected to react rapidly and irreversibly (k_{diss}) with the bridging water molecule resulting in the rapid conversion of $\mathbf{C_S}$ to products. The electron transfer step would thus be rate-limiting in the formation of products. Application of the steady state approximation now identifies k^{OH} as $k_{et}K_P$.

The third possible mode of activation of $\mathbf{C_P}$ is by attack of Ar$^{\bullet}$ on the metal centre to give the addition complex $\mathbf{C_A}$ [*cf.* reaction (3c)]. If the addition step is rate-determining ($k_{add} < k_{elim}$), by analogy with the earlier examples k^{OH} is identified as $k_{add}K_P$. However, adducts of aliphatic radicals which do not readily form carbocations may show decomposition rates which



Scheme 1



Scheme 2

are slower than those of their formation, *e.g.* Me$^{\bullet}$ adds to Cu^{2+}aq with a rate constant of 7.4×10^5 dm^3 mol^{-1} s^{-1} whereas the resultant adduct may decompose to Cu^+ and MeOH with a rate constant of 7.2×10^2 s^{-1}.[10] The question therefore arises as to whether an aryl radical might behave similarly hence making k_{elim} rate determining. We suggest not, on the ground that Ph$^{\bullet}$ has a lower ionisation potential than Me$^{\bullet}$. The experimental gas phase ionisation potential of Me$^{\bullet}$ is 9.84 eV[20] agreeing well with the calculated values[21,22] for the $^2A_2'' \longrightarrow {}^1A_1'$ transition of 9.747 and 9.756 eV, respectively, for the adiabatic and vertical ionisations. By contrast, the experimental ionisation potentials for Ph$^{\bullet}$ are 8.32eV (adiabatic) and 8.67 (vertical)[20] which correspond to the $^2A_1 \longrightarrow {}^3B_1$ ionisation of a π-electron and agree well with calculated values[21,22] of 8.419 and 8.576 eV, respectively. These agreements give confidence in the values of 7.614 eV (adiabatic) and 8.419 eV (vertical) calculated for the $^2A_1 \longrightarrow {}^1A_1$ transition, *i.e.* ionisation of the SOMO. [All calculations were performed with the Gaussian 98 program[21] using the B3LYP functional[22] and the 6-32G(d,p) basis set. In all cases the minima were fully characterised by the absence of imaginary vibrational frequencies]. Such values suggest ionisation of the SOMO of Ph$^{\bullet}$ to be comparable with that of propyl radicals [2-Pr$^{\bullet}$: 7.37 eV (adiabatic) and 7.67 eV (vertical); 1-Pr$^{\bullet}$: 8.09 eV (adiabatic) and 8.35 (vertical)].[20] In aqueous solution these energies will be attenuated by solvation of the cations but nevertheless a parallelism of values is expected.[23] It thus seems possible that an adduct Ph–Cu^{III}aq might ionise to Ph$^+$ Cu^{I}aq or exhibit a polarity which facilitates solvolysis or reductive elimination with a *cis*-water ligand to produce PhOH and Cu^{I}aq.[24] Although the 2-benzoyl substituent in **2** will affect the ionisation potential of the SOMO in comparison to that of Ph$^{\bullet}$, we suggest that if such behaviour is possible for a phenyl adduct it could also occur for $\mathbf{C_A}$.

The mechanism expected for reaction of **2** with a wholly organic aliphatic species such as free ligand is H-abstraction *via* an S_H2 transition state to produce **6** and a ligand-derived radical.[25] Copper(II) complexes of organic ligands are expected to react likewise but there is now also the consideration that **2** might conceivably add to the metal centre giving an organometallic intermediate ($\mathbf{C_A}$) which forms **6** upon protonolysis. However, in view of the arguments given above suggesting cationoid character for the aryl moiety in any adduct formed with Cu(II), it seems improbable that protonolysis of the C–Cu^{III} bond in $\mathbf{C_A}$ would occur. Aliphatic radicals add to Cu(I) much more rapidly than to Cu(II) and protonolysis of the C–Cu^{II} bonds in such adducts of Cu(I) occurs to give C–H bonds and Cu(II);[10,26] protonolysis of any adduct of Cu(I) formed in our system would thus interfere with the catalytic cycle. However, Cu(I) concentrations are very low and the catalytic cycle runs efficiently, normally giving product accountabilities in excess of 80%. We conclude therefore that protonolytic routes to **6** are unlikely to be significant and expect that reduction of **2** will occur by S_H2 reaction.

If **6** is formed by S_H2 H-abstraction, the course of reaction is unclear, particularly when the H-donor is a copper(II) complex, but it is probable that any *C*-centred radicals produced will ultimately be oxidised by the excess of Cu(II) with regeneration of Cu(I). Provided copper and ligand are used in large excess over **1** so that negligible amounts of ligand are lost, the lability of ligand exchange on Cu(II)[27] ensures the relative proportions of the Cu(II) complexes remain essentially constant at their equilibrium values throughout the course of a particular decomposition of **1**. The hydroxylation step, irrespective of mechanism [reactions (3b) or (3c)], and cyclisation/aromatisation step both regenerate Cu(I).

Again assuming rapid, reversible formation of $\mathbf{C_P}$, for H-transfer we identify the rate constant, k^H as $k_{abs}K_P$ where k_{abs} is the rate constant for hydrogen abstraction and K_P is the formation constant for the precursor complex ($\mathbf{C_P}$) common to all bimolecular reactions of **2** with a particular copper species. The competitive bimolecular reactions of **2** thus have rate constants of the form kK_P. The value of K_P is likely to vary somewhat between different copper species as a result of their differing diffusive properties; however, since **2** is neutral, coulombic forces should be negligible and we expect values of K_P to approach unity.[28] That being the case, the experimental rate constants obtained using the radical clock are considered to be determined essentially by the various competitive elementary steps.

Table 1 Rate constants[a] for the hydroxylation of 2-benzoylphenyl radical, **2**, by copper(II) complexes of 2-aminocarboxylates and 1,3-dicarboxylates

Entry	Ligand	$10^{-6}k_1^{OH}$/dm^3 mol^{-1} s^{-1}	$10^{-6}k_2^{OH}$/dm^3 mol^{-1} s^{-1}
1	Aminoethanoate (glycinate)[b]	4.71 ± 0.65	7.63 ± 0.93
2	(*S*)-2-Aminopropanoate (L-alaninate)[b]	6.63 ± 1.67	23.0 ± 2.97
3	2-Amino-2-methylpropanoate[b]	3.26 ± 0.73	14.6 ± 1.73
4	Propanedioate (malonate)[b]	4.09 ± 1.49	24.7 ± 2.95
5	Propanedioate (malonate)[c]	5.45 ± 1.01	25.7 ± 2.98
6	2-Methylpropanedioate[c]	7.53 ± 2.14	19.7 ± 2.98
7	2,2-Dimethylpropanedioate[c]	5.61 ± 0.91	14.3 ± 1.78

[a] Uncertainties are the 95% confidence intervals. [b] Distribution of complexes calculated using stability constants for ionic strength I = 1 mol dm^{-3} (ref. 16, see ESI). [c] Distribution of complexes calculated using stability constants for ionic strength I = 0.1 mol dm^{-3} (ref 30, see ESI).

(iii) Rate constants for hydroxylation of 2 by Cu(II) complexes of 2-aminocarboxylates and 1,3-dicarboxylates

If hydroxylation can be effected by any copper(II) complex which retains water in its inner coordination sphere, the rate of formation of **5** in a particular mixture is given by eqn. (4):

$$d[\mathbf{5}]/dt = k_0^{OH}[Cu][\mathbf{2}] + k_1^{OH}[CuL][\mathbf{2}] + k_2^{OH}[CuL_2][\mathbf{2}] \quad (4)$$

where [Cu], [CuL] and [CuL$_2$] are the equilibrium concentrations of non-, mono- and bis-ligated Cu(II) complexes (for convenience water ligands and ionic charges are omitted) and k_0^{OH}, k_1^{OH} and k_2^{OH} are their respective second order rate constants. The oxidation of **3** being fast and irreversible,[6,18] the rate of production of **4** is given by eqn. (5):

$$d[\mathbf{4}]/dt = k_C[\mathbf{2}] \quad (5)$$

where k_C is the first order rate constant for cyclisation of **2**. Hence the ratio, R^{OH}, of the products **4** and **5** equals the ratio of the rates at which they are formed, whence:

$$R^{OH} = (k_0^{OH}/k_C)[Cu] + (k_1^{OH}/k_C)[CuL] + (k_2^{OH}/k_C)[CuL_2] \quad (6)$$

Since the distribution of complexes is a function of pH, R^{OH} also varies with pH. It is thus possible, with prior knowledge of the value of k_C, to evaluate rate constants k_n^{OH} from experimental product ratios, R^{OH}, found as a function of pH, by multiple linear regression of their values upon the equilibrium concentrations of copper(II) species calculated for the appropriate pH. This direct procedure has, however, a practical disadvantage. At low pH values the principal Cu-containing species in solution are [referring to eqn. (6)], Cu (*i.e.* Cu^{2+}aq) and CuL and, as pH is increased, the concentration of the former decreases while that of the latter increases. The pH range where this change occurs is narrow and is sampled few times experimentally. The consequence is that the values of k_0^{OH} and k_1^{OH} found are similar in magnitude and with large errors. However, in calibrating the 2-benzoylphenyl radical clock, we have previously[6] found k_0^{OH}/k_C = (1.84 ± 0.02) and k_C = (8.0 ± 0.9) × 10^5 s^{-1} hence eqn. (6) may be simplified as eqn. (7) which has only two explanatory (*i.e.* independent) variables:

$$\{R^{OH} - 1.84[Cu]\} = (k_1^{OH}/k_C)[CuL] + (k_2^{OH}/k_C)[CuL_2] \quad (7)$$

The rate constants k_1^{OH} and k_2^{OH} can be obtained from the coefficients found from regression of the left hand side of eqn. (7) upon the equilibrium concentrations [CuL] and [CuL$_2$] at the various pH values. The regressions were made without intercept since no other process produces **5** (heterolysis of **1** is insignificant at ambient temperature over the duration of the experiments[29] and results were independent of the presence of air). This procedure has given the rate constants for the 2-aminocarboxylates and 1,3-dicarboxylates in Table 1; the uncertainties on their values are 95% confidence intervals which include the corresponding uncertainty propagated from k_C; the small error in the 1.84 factor was ignored. If an intercept was allowed, either it was not significantly different from zero and the rate constants evaluated were consequently no different from those in Table 1, or, if was different from zero, its absolute value was small in magnitude and the rate constants then varied somewhat from those tabulated with, in general, an increased uncertainty interval for k_1^{OH}. Stability constant data at unit ionic strength for 2-methyl- and 2,2-dimethylpropanedioate complexes of copper(II) are unavailable in Martell and Smith's compendium.[16] Rate constants for propanedioate (malonate) itself were calculated from equilibrium distributions obtained using stability constants reported[16] for both I = 1 mol dm^{-3} and I = 0.1 mol dm^{-3} and they were found to be the same within the 95% confidence interval (see Table 1). The rate constants for the two methylated propanedioates were therefore obtained (at I = 1 mol dm^{-3}) from species distributions calculated using equilibrium constants[30] for I = 0.1 mol dm^{-3} on the assumption that for these ligands, too, the change of ionic strength would not be significant for present purposes.

In the case of aminoethanoate (glycinate) as ligand, equilibrium distributions of complexes as functions of pH were calculated for six or seven analytical copper concentrations and four [Cu]$_t$: [L]$_t$ ratios, (*i.e.* 2 : 1, 1 : 1, 2 : 3 and 1 : 2) giving 27 distributions in total. Fig. 1 shows the plot of experimental values of R^{OH} against values calculated *via* eqn. (6) using the values of k_1^{OH} and k_2^{OH} given for the ligand in Table 1 with k_0^{OH} = 1.47 × 10^6 dm^3 mol^{-1} s^{-1} and k_C = 8.0 × 10^5 s^{-1}.

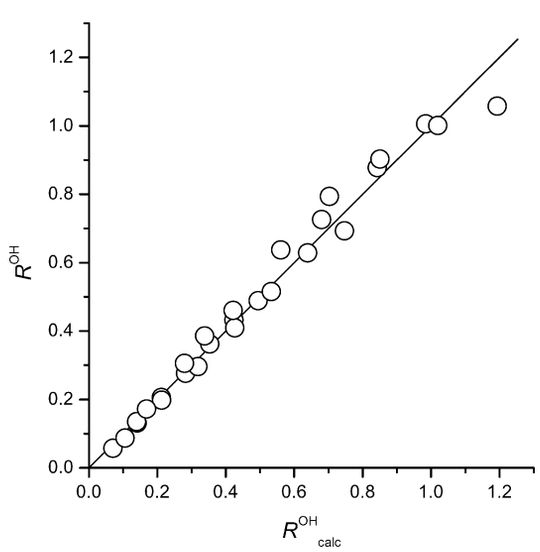


Fig. 1 Plot of R^{OH} *versus* R^{OH}_{calc} for Cu(II) complexes of aminoethanoate; the line has unit gradient.

For the remaining ligands of Table 1, rate constants were evaluated from 12–14 distributions calculated for a single analytical copper concentration (*ca.* 0.05 mol dm^{-3}) with [Cu]$_t$: [L]$_t$ = 1 : 2. It is evident that monoligation produced species which are more reactive than Cu^{2+}aq in the hydroxylation of **2** and the introduction of a second bidentate ligand further

Table 2 Rate constants[a] for H-transfer to 2-benzoylphenyl radical, **2**, from 2-aminocarboxylates and 1,3-dicarboxylates and their complexes with copper(II)

Entry	Ligand	$10^{-6}k_0^H$/dm^3 mol^{-1} s^{-1}	$10^{-6}k_1^H$/dm^3 mol^{-1} s^{-1}	$10^{-6}k_2^H$/dm^3 mol^{-1} s^{-1}
1	Aminoethanoate (glycinate)[b]	*not signif.*	1.04 ± 0.29	2.01 ± 0.34
2	Aminoethanoate (glycinate)[c]	0.75 ± 0.12	0.75 ± 0.12	1.50 ± 0.24
3	(*S*)-2-Aminopropanoate (alaninate)[b]	0.38 ± 0.16	2.22 ± 0.46	5.54 ± 0.66
4	(*S*)-2-Aminopropanoate (alaninate)[d]	0.23 ± 0.12	2.68 ± 0.32	5.36 ± 0.64
5	2-Amino-2-methylpropanoate[b]	0.34 ± 0.15	0.63 ± 0.18	1.03 ± 0.14
6	2-Amino-2-methylpropanoate[e]	0.48 ± 0.06	0.48 ± 0.06	1.03 ± 0.13
7	Propanedioate (malonate)[b,f]	1.77 ± 0.67	1.67 ± 1.16	9.88 ± 1.18
8	Propanedioate (malonate)[f,g]	1.73 ± 0.26	1.73 ± 0.26	9.87 ± 1.16
9	Propanedioate (malonate)[b,h]	1.31 ± 0.77	2.79 ± 1.16	10.1 ± 1.20
10	Propanedioate (malonate)[g,h]	1.90 ± 0.28	1.90 ± 0.28	10.2 ± 1.21
11	2-Methylpropanedioate[b,h]	*not signif.*	23.1 ± 4.60	54.1 ± 7.18
12	2-Methylpropanedioate[e,h]	13.4 ± 0.21	13.4 ± 0.21	54.9 ± 6.67
13	2,2-Dimethylpropanedioate[b,h]	0.23 ± 0.05	0.74 ± 0.12	1.44 ± 0.18
14	2,2-Dimethylpropanedioate[d,h]	0.24 ± 0.04	0.73 ± 0.08	1.45 ± 0.16

[a] Uncertainties are the 95% confidence intervals. [b] Rate constants found independently. [c] Relative reactivity of L_{free}, CuL and CuL_2 assumed to be statistically determined. [d] Relative reactivity of CuL and CuL_2 assumed to be statistically determined. [e] Equal reactivities assumed for HL and CuL. [f] Distribution of complexes calculated using stability constants for ionic strength I = 1 mol dm^{-3} (ref. 16, see ESI). [g] Equal reactivities assumed for uncoordinated ligand and CuL. [h] Distribution of complexes calculated using stability constants for ionic strength I = 0.1 mol dm^{-3} (ref. 30, see ESI).

enhances the hydroxylation rate although the pattern of variation of rate constant with extent of methylation then differs between the two types of ligand.

(iii) Rate constants for hydrogen-transfer to 2 from copper(II) complexes of 2-amino-carboxylates and 1,3-dicarboxylates

Reasoning analogous to that leading to eqn. (6) gives eqn. (8) for R^H, the ratio of the radical clock products **6** and **4** (Scheme 1):

$$R^H = [\mathbf{6}]/[\mathbf{4}] = (k_0^H/k_C)[L]_{free} + (k_1^H/k_C)[CuL] + (k_2^H/k_C)[CuL_2] \quad (8)$$

where $[L]_{free}$ is the equilibrium concentration of uncoordinated ligand and the k_n^H are the respective second order rate constants for the transfer of hydrogen to **2** from free ligand and the variously ligated copper species in solution. The free ligands may exist in different states of protonation dependent on the pH but attempts to obtain rate constants for the individual forms were not fruitful. The procedure adopted was either to sum all uncoordinated forms within $[L]_{free}$ or to select the predominant form whichever allowed statistically the better fit of the data. Again, multiple regressions were made without intercept. This prevented the occurrence, in some cases, of the regression program fitting the experimental data with a large intercept and one or more negative regression coefficients. Protonolysis reactions being excluded [see (ii) above)], the only other sources of hydrogen in the system were negligible being the initiator, ascorbic acid, which was used in very small amount relative to the ligands, and the intermediate π-radical **3** which is more likely to be oxidised by the excess of Cu(II) than in a rare radical/radical encounter with **2**.

In Table 2 are presented H-transfer rate constants found for the previously mentioned 2-aminocarboxylates and 1,3-dicarboxylates. For the former, it is noticeable that when regression coefficients, and hence rate constants, are found independently for the three explanatory variables $[L]_{free}$, [CuL] and $[CuL_2]$ (entries 1 and 3), the values of k_2^H are close to twice the value of k_1^H indicating that the relative reactivity of the complexes CuL and CuL_2 may be statistically determined. Also, for 2-amino-2-methylpropanoate (entry 5) the rate constants for free ligand and CuL are equal within the uncertainties (95% confidence intervals). When rate constants for 2-aminopropanoate are evaluated with the prior assumption that relative reactivity is statistically determined for CuL and CuL_2, by use of eqn. (9), the precision is improved (entry 4). On the other hand, for 2-amino-2-methylpropanoate, the best account of the data is obtained by assuming that HL and CuL react at the same rate [eqn. (10)].

$$R^H = (k_0^H/k_C)[L]_{free} + (k_1^H/k_C)\{[CuL] + 2[CuL_2]\} \quad (9)$$

$$R^H = (k_{0,1}^H/k_C)\{[HL] + [CuL]\} + (k_2^H/k_C)[CuL_2] \quad (10)$$

It is noticeable that the first methylation of aminoethanoate enhances the hydrogen transfer rate constants for both CuL and CuL_2 (*cf.* entries 1 and 4) but the second methylation reduces them below those of the aminoethanoate itself (*cf.* entries 1 and 6). This supports the expectation that H-transfer is an S_H2 abstraction of a methylene hydrogen atom from the coordinated ligand by **2**, a process which would give a *C*-centred radical stabilised by the first methylation. The second methylation would, however, substitute the remaining readily abstractable methylene hydrogen resulting in the reduced reaction rate. In the case of aminoethanoate, the free ligand was found to be insignificant when three explanatory variables were used (entry 1). With the prior assumption that the relative reactivities of HL, CuL and CuL_2 are all statistically determined, the use of eqn. (11) allows assignment of a rate constant to the free ligand (entry 2) but this is at the cost of a greater fractional uncertainty on k_2^H; also, since the regression becomes simple, a significant intercept is found. Furthermore, the rate constant ascribed to the free ligand is greater than those found for 2-aminopropanoate (entries 3 and 4) which seems chemically unreasonable in view of the stabilisation afforded by methylation in this case to the *C*-centred radical product. It is concluded therefore that H-abstraction from the free ligand is unimportant for aminoethanoate.

$$R^H = (k_{0,1}^H/k_C)\{[L]_{free} + [CuL] + 2[CuL_2]\} + C \quad (11)$$

The results for propanedioate show that, as for the hydroxylation reaction, within experimental uncertainty the rate constants obtained are independent of the ionic strength for which the equilibrium distributions of complexes were calculated (*cf.* entries 7 and 9). Also in the case of propanedioate, the individually calculated constants (entries 7 and 9) show the free ligand and the mono-ligated complex have rate constants of comparable magnitudes. If the assumption is made that their reactivities are equal, by use of eqn. (10) with $[L]_{free}$ in place of [HL], the uncertainty on $k_{0,1}^H$ is reduced and the value of k_2^H is unaffected (entries 8 and 10). In the case of 2-methylpropanedioate, when all uncomplexed ligand species were summed in $[L]_{free}$, this term was found not to be significant (entry 11). However, examination of the species distributions shows [HL] to have a similar pH-profile to [CuL] but with somewhat lower concentrations. If HL and CuL are assumed to have the same reactivity as H-donors, by use of eqn. (10), the

Table 3 Rate constants[a] for the reactions of 2-benzoylphenyl radical, **2**, with 1,2-diaminoethane and its complexes with copper(II)

	Hydrogen transfer		
Reactive species: Entry	L_{free} $10^{-6}k_0^H$/dm^3 mol^{-1} s^{-1}	CuL $10^{-6}k_1^H$/dm^3 mol^{-1} s^{-1}	CuL_2 $10^{-6}k_2^H$/dm^3 mol^{-1} s^{-1}
1	0.102 ± 0.079	0.686 ± 0.265	3.05 ± 0.36
	Hydroxylation		
		$10^{-6}k_1^{OH}$/dm^3 mol^{-1} s^{-1}	$10^{-6}k_2^{OH}$/dm^3 mol^{-1} s^{-1}
2		3.88 ± 0.60	1.11 ± 0.25

[a] Uncertainties are the 95% confidence intervals.

rate constant found in common ($k_{0,1}^H$) has a lower fractional error than that found for CuL alone and the precision of the rate constant for CuL_2 (k_2^H) is also improved. 2,2-Dimethylpropanedioate behaves like aminoethanoate and 2-aminopropanoate in that the relative reactivities of [CuL] and [CuL_2] are statistically determined (entry 14). The effect of methylation in the 1,3-dicarboxylates is again consistent with S_H2 abstraction (Fig. 2): $R^H(CHMe) > R^H(CH_2) \gg R^H(CMe_2)$.

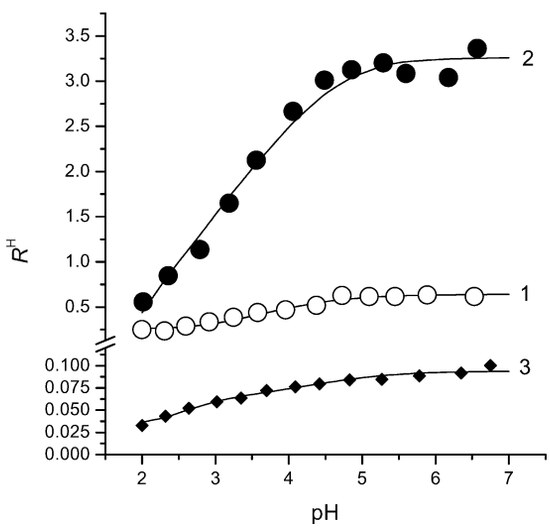


Fig. 2 Variation with pH of R^H for Cu(II) complexes of 1,3-dicarboxylates: 1, propanedioate; 2, 2-methylpropanedioate; 3, 2,2-dimethylpropanedioate. Discrete points are experimental values, lines are predictions given by the rate constants of Table 2, entries 10, 12 and 14, respectively.

(iv) Rate constants for reactions of 2 with Cu(II) complexes of diamines

We have investigated the reactions of copper(II) complexes of two diamines: 1,2-diaminoethane (ethylenediamine) and 1,2-bis(dimethylamino)ethane (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine, TMEN). 1,2-Diaminoethane behaves like the 2-aminocarboxylates and 1,3-dicarboxylates above in forming complexes CuL and CuL_2 but, for steric reasons,[31,32] TMEN forms only a 1 : 1 complex, CuL, which undergoes hydrolysis and olation reactions giving CuL(OH) and $Cu_2L_2(OH)_2$ as the pH is increased. Although the binuclear complex may crystallise without axial water ligands,[33] one crystalline dihydrate has such ligands on either side of the molecular plane, one on each Cu centre.[34] Stability constants have also been proposed[31] for complexes of TMEN having compositions $CuL(OH)_2$, $Cu_2L(OH)$ and $Cu_3L(OH)_4$ but, under the conditions of our experiments, these have negligible concentrations (<1% of the total copper).

1,2-Diaminoethane. Fig. 3 shows the distribution, as a function of pH, of the species present when Cu(II) coordinates 1,2-diaminoethane under conditions where $[Cu^{II}]_t = 0.0555$ mol dm^{-3} and $[L]_t = 0.111$ mol dm^{-3} and also the corresponding variations in the ratios of products obtained from the reactions of **2** with the various species. Cyclisation is always the major reaction of **2**, 9-fluorenone, **4**, being never less than 75% of the combined clock products although both 2-hydroxybenzophenone, **5**, and benzophenone, **6**, each attain almost 15% of the combined product in different parts of the pH range. At pH 3.12 there is very little reduction of **2** but as the pH is increased, R^H increases in a sigmoid fashion, levelling off in parallel with [CuL_2]. Analysis of the variation in R^H *via* eqn. (8) gave the rate constants presented in Table 3, entry 1.

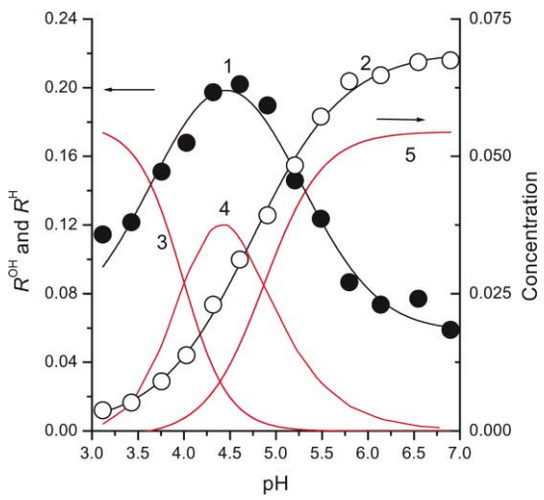


Fig. 3 Variation with pH of R^{OH}, R^H and the species distribution (red) for Cu(II) complexes of 1,2-diaminoethane: 1, R^{OH}; 2, R^H; 3, [Cu]; 4, [CuL]; 5, [CuL_2].

The behaviour of R^{OH} is very different: at pH 3.12 the copper occurs mainly (98%) as Cu^{2+}aq and hence, at this pH, essentially all of the hydroxylation of **2** is due to this species. It is seen that as the pH is increased, the value of R^{OH} increases to a maximum and then declines to values less than that at pH 3.12; the pH at which R^{OH} is maximised corresponds to that at which [CuL] is also greatest. It is thus evident from the R^{OH}/pH profile, that the mono-ligated complex CuL must be more effective than Cu^{2+}aq at hydroxylation of **2** but that the bis-ligated complex CuL_2 must be less so. This reactivity order is confirmed by the rate constants, found *via* eqn. (7), which are given in Table 3, entry 2. Prior assumptions of statistical factors controlling the relative reactivities of CuL and CuL_2, whether in reduction or hydroxylation, do not improve the precision of any of the constants.

1,2-Bis(dimethylamino)ethane. There are two papers dealing with the protonation of TMEN and its complexation by Cu^{2+} and in which there is a good measure of agreement between the values of the stability constants given.[31,35] The values are given in ESI Table 1. There is reasonable agreement between all the constants except one, *i.e.* $\log\beta_{1,1,-1}$, the stability constant of the

Table 4 Rate constants[a] for the reactions of 2-benzoylphenyl radical, **2**, with copper(II) complexes of 1,2-bis(dimethylamino)ethane

Hydrogen transfer

Reactive species:		HL	CuL	CuL(OH)	$Cu_2L_2(OH)_2$	Statistical summary[b]				
		$10^{-6}k_0^H$/	$10^{-6}k_{1a}^H$/	$10^{-6}k_{1b}^H$/	$10^{-6}k_{2,2b}^H$/					
Entry	Footnote	$dm^3\ mol^{-1}\ s^{-1}$	$dm^3\ mol^{-1}\ s^{-1}$	$dm^3\ mol^{-1}\ s^{-1}$	$dm^3\ mol^{-1}\ s^{-1}$	R^2	n	s	F	F_{sig}
1	[c]	8.50 ± 2.42	6.09 ± 0.90	*not signif.*	23.6 ± 5.78	0.995	20	0.032	1761.4	2.299×10^{-20}
2	[d]	8.25 ± 2.47	6.11 ± 0.91	11.6 ± 2.86	23.2 ± 5.72	0.995	20	0.032	1757.3	2.342×10^{-20}
3	[d,e]	6.51 ± 0.79	6.51 ± 0.79	13.5 ± 1.68	27.0 ± 3.36	0.994	20	0.033	3219.4	1.186×10^{-22}

Hydroxylation

Reactive species:		CuL	CuL(OH)	$Cu_2L_2(OH)_2$	Statistical summary[b]				
		$10^{-6}k_{1a}^{OH}$/	$10^{-6}k_{1b}^{OH}$/	$10^{-6}k_{2,2b}^{OH}$/					
Entry	Footnote	$dm^3\ mol^{-1}\ s^{-1}$	$dm^3\ mol^{-1}\ s^{-1}$	$dm^3\ mol^{-1}\ s^{-1}$	R^2	n	s	F	F_{sig}
4	[c]	1.17 ± 0.16	(−46.4 ± 19.0)	6.73 ± 1.53	0.972	20	0.006	299.0	2.950×10^{-14}
5	[f]	1.02 ± 0.15	—	3.29 ± 0.49	0.923	20	0.009	216.6	8.043×10^{-13}
6	[g]	1.02 ± 0.15	1.02 ± 0.15	3.22 ± 0.49	0.921	20	0.009	210.1	1.031×10^{-12}
7	[d]	1.02 ± 0.15	1.59 ± 0.27	3.18 ± 0.54	0.920	20	0.009	206.6	1.183×10^{-12}

[a] Uncertainties are the 95% confidence intervals. [b] R, correlation coefficient; n, number of data points; s, standard error of the estimate; $F = R^2(n-m)/(1-R^2)(m-1)$, $(m-1)$ is the number of explanatory variables; F_{sig} is the significance of F. [c] Rate constants calculated independently for each complex. [d] Relative reactivity of CuL(OH) and $Cu_2L_2(OH)_2$ assumed to be 1 : 2. [e] HL and CuL assumed to be equally reactive. [f] CuL(OH) assumed unreactive. [g] CuL and CuL(OH) assumed to be equally reactive.

hydrolysis product CuL(OH). The consequence of this difference is that the distributions of CuL(OH) and its dimer differ markedly between the two sets of authors. According to Sóvágó and Gergely,[35] for solution concentrations $[Cu]_t$ = 0.0555 mol dm^{-3} and $[L]_t$ = 0.111 mol dm^{-3}, [CuL(OH)] exceeds $[Cu_2L_2(OH)_2]$ over the whole range of pH that we have examined (pH 3.77–8.15) whereas according to Paoletti and co-workers[31] [CuL(OH)] is always small, never exceeding 3.2% of $[Cu]_t$, and hence $Cu_2L_2(OH)_2$ is the predominant species at the higher pH values. For solution concentrations $[Cu]_t$ = 0.0555 mol dm^{-3} and $[L]_t$ = 0.111 mol dm^{-3} above pH 8, the constants of Sóvágó and Gergely predict that the copper in binuclear form will comprise 60% of the total whereas the constants of Paoletti *et al.* predict in excess of 90%. Since Cu(II) has a d^9 electron configuration, the formation of binuclear species in which the unpaired d electrons can interact antiferromagnetically will result in a reduced EPR signal intensity. For the concentrations specified above, we observed a 95% loss of EPR signal intensity at pH 8.4 relative to a $Cu(NO_3)_2$ standard indicating the constants of Paoletti and co-workers[31] to be preferable.

Using the method described above for other complexes, we have correlated values of the radical clock product ratios R^H and R^{OH}, measured as functions of pH with the equilibrium concentrations of the various complexes at the particular pH values. It is immediately apparent from the product ratios that the complexes of TMEN are *much* better H-donors than hydroxylating agents: R^H reaches *ca.* 1.4 in the higher pH range showing that H-transfer becomes the principal reaction of **2** whereas R^{OH} does not exceed 0.15. On correlating R^H with TMEN species distributions found using the stability constants of Paoletti and co-workers,[31] it is found that the total concentration of uncoordinated ligand, $[L]_{free}$, is statistically insignificant. Unlike the case of 1,2-diaminoethane where the diprotonated ligand is the only uncoordinated species in significant concentration, with TMEN, the monoprotonated form HL reaches concentrations comparable with those of CuL. Chemically, it is expected that an unprotonated dimethylamino group should activate H-abstraction from the adjacent methylene group and, indeed if [HL] is used in place of $[L]_{free}$, the term is significant [eqn. (12)].

$$R^H = (k_0^H/k_C)[HL] + (k_{1a}^H/k_C)[CuL] + (k_{1b}^H/k_C)[CuL(OH)] + (k_{2,2b}^H/k_C)[Cu_2L_2(OH)_2] \quad (12)$$

As previously, we also examined the correlations in the light of prior assumptions regarding the relative reactivity of complexes dependent on the numbers of ligands of a particular type contained. The results are presented in Table 4 along with a statistical summary of each correlation to aid comparison.

Entries 1–3 relate to hydrogen transfer reactions of TMEN and its Cu(II) complexes. When rate constants are found independently, CuL(OH) is found to be not significant (entry 1) but the other rate constants are unaffected if the relative reactivity of CuL(OH) and its dimer is assumed to be statistically determined (entry 2); if, in addition, it is assumed that HL and CuL are also equally reactive, the precision of all the rate constants is improved (entry 3).

When **1** is homolysed in the presence of the copper complexes of TMEN, the yields of hydroxybenzophenone, **5**, are very low and experimental error results in scatter. Nevertheless, they do bear a relationship to the distributions of complexes. Fig. 4 shows the variation with pH of the concentrations of TMEN-containing complexes together with that of $\{R^{OH} - 1.84[Cu]\}$. It is clear that hydroxylation increases across the pH

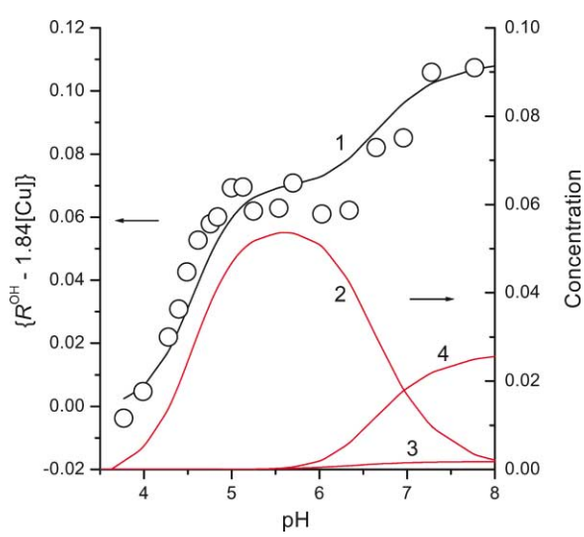


Fig. 4 Variation with pH of $\{R^{OH} - 1.84[Cu]\}$ and the species distribution (red) for Cu(II) complexes of 1,2-bis(dimethylamino)-ethane: 1, $\{R^{OH} - 1.84[Cu]\}$; 2, [CuL]; 3, [CuL(OH)]; 4, $[Cu_2L_2(OH)_2]$. The continuous line in 1 is the prediction given by the rate constants of Table 4, entry 5.

range as the species distributions vary. Entries 4–7 of Table 4 relate to the hydroxylation properties of the TMEN complexes. When rate constants are found for each complex independently *via* eqn. (13) (entry 4), a statistically significant but physically meaningless negative value results for CuL(OH). This is likely to be due to the scatter in the experimental data and the fact that [CuL(OH)] is small, amounting to <3% of total copper.

$$\{R^{OH} - 1.84[Cu]\} = (k_{1a}{}^{OH}/k_C)[CuL] + (k_{1b}{}^{OH}/k_C)[CuL(OH)] + (k_{2,2b}{}^{OH}/k_C)[Cu_2L_2(OH)_2] \quad (13)$$

Entries 5–7 tabulate the results of various assumptions about the relative reactivities of the TMEN complexes; it is seen that the statistical quality of their accounts of the experimental observations deteriorates progressively. The best assumption is that CuL(OH) is unreactive (entry 5) though the statistical summaries in Table 4 show there is very little difference in regarding CuL(OH) as having no reactivity (entry 5), or the same reactivity as CuL (entry 6) or half that of its binuclear dimer (entry 7); the rate constants for CuL and $Cu_2L_2(OH)_2$ are essentially unchanged by these different assumptions. The species distributions obtained by use of the stability constants of Paoletti and co-workers[31] thus allow an adequate account of the weak hydroxylating properties of the copper complexes of TMEN. Since negligible hydroxylation is brought about by CuL(OH), that which does occur at higher pH must be due to the binuclear complex $Cu_2L_2(OH)_2$. Although any effect of deprotonation of CuL on hydroxylation is undetectable, it enhances its H-donating capacity two-fold (*i.e.* $k_{1b}{}^{H}/k_{1a}{}^{H} = \sim 2$). Dimerisation of CuL(OH) restores hydroxylating capacity to about three times that of CuL (*i.e.* 1.5-fold per copper centre) but the reactivity per TMEN ligand in H-transfer is unaffected.

(v) Rate constants for the reactions of 2 with copper(II) complexes of 2-hydroxycarboxylates

Hydroxyethanoate and 2-hydroxy-2-methylpropanoate. Fig. 5 illustrates the variation with pH of the product-ratios obtained when **1** was homolysed in the presence of the copper(II) complexes formed by hydroxyethanoate (glycolate), ([Cu] = 0.0555 mol dm^{-3} and [L] = 0.111 mol dm^{-3}). Both plots, but especially that of R^H, show positive curvature towards higher pH values. Such curvature necessitates the presence in solution of a species the concentration of which is rising in the higher pH range and which is particularly reactive in H-donation.

Martell and Smith's compendium[16] quotes stability constants only for CuL and CuL_2 (see ESI) as does the more recent electronic version[36] and these prescribe equilibrium concentrations which are almost constant above pH 4.5. It follows that no mixtures of these complexes can account for the increasing trends observed for R^H and R^{OH} above pH 4.5. A comparable situation holds for the R^{OH} values obtained for 2-hydroxy-2-methylpropanoate (values of R^H are very low for this ligand across the whole pH range owing to the substitution of the readily abstractable methylene hydrogens by methyl groups).

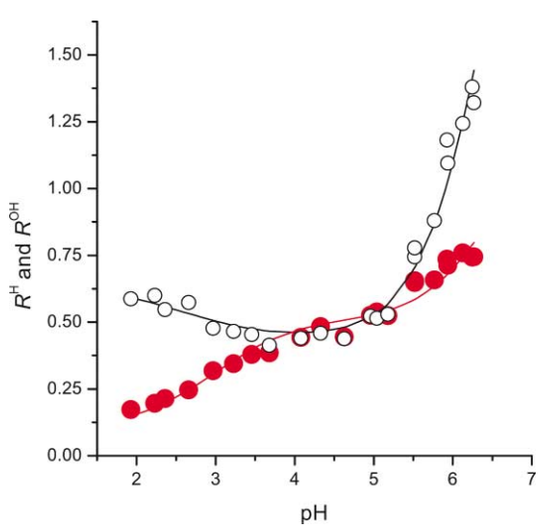


Fig. 5 Variation with pH of R^H (black) and R^{OH} (red) for Cu(II) complexes of hydroxyethanoate. Lines are predictions given by the rate constants of Table 5, entries 1 and 6, respectively.

Piispanen and Lajunen[37] have measured stability constants at an ionic strength of 0.5 mol dm^{-3} for complexes formed by copper(II) with various 2-hydroxycarboxylate ligands. Their values for the CuL and CuL_2 complexes of both hydroxyethanoate and 2-hydroxy-2-methylpropanoate are very close to those quoted by Martell and Smith[16] for unit ionic strength. However, Piispanen and Lajunen also report values for the deprotonated complex $CuLH_{-1}$. When included in the species distributions, this complex has a significant rising concentration in the pH range 4.5–6.0 for both ligands. Table 5 presents the best rate constants found for complexes of both 2-hydroxycarboxylates, evaluated as for earlier ligands; the continuous curves of Fig. 5 were calculated using the rate constants for hydroxyethanoate.

The easy abstraction of an α-hydrogen atom from hydroxyethanoate (and its parent acid) makes it an effective H-donor and the free ligand contributes importantly to reaction with **2** (entry 1). Coordination by the metal ion reduces its H-donating capacity which accounts for the minimum occurring in the pH profile of R^H for this ligand (Fig. 5). This deactivation can be understood in terms of coordination reducing the availability of lone-pair electrons on the hydroxyl oxygen atom for stabilising the *C*-centred radical formed by H-abstraction. Conversely, if the proton lost from CuL in forming $CuLH_{-1}$ is the ligand's hydroxyl proton rather than one from a coordinated water molecule, the lone-pair availability on the hydroxyl oxygen is enhanced and the heightened reactivity of $CuLH_{-1}$ can be understood.

The rate constants for the hydroxylation of **2** by like complexes of both ligands are quite similar (entries 6 and 7) but show rather large uncertainties. This could be because, for both ligands, the rates of change of [CuL] and [CuL_2] as functions of pH are rather low and both have comparable values over much of the pH range; furthermore, [$CuLH_{-1}$] in the case of 2-hydroxy-2-methylpropanoate is considerably smaller than in the case of hydroxyethanoate. [Another reason may be the involvement of binuclear species (see ESI).] Nevertheless, it is evident that the presence of one bidentate ligand enhances the hydroxylation rate relative to that of the Cu^{2+}aq by 2–3-fold (recall $k_0{}^{OH} = 1.47 \times 10^6$ dm^3 mol^{-1} s^{-1}) and that deprotonation of CuL further activates its rate of hydroxylation as does the coordination of a second bidentate ligand.

2-Hydroxypropanoate. For 2-hydroxypropanoate (lactate) as ligand, the pH profiles of R^H and R^{OH} both show a positive curvature in the upper pH range like the 2-hydroxycarboxylates above and, as in their cases, the stability constants quoted by Martell and Smith[16] for the simple unhydrolysed mononuclear complexes [of the (*R*)-enantiomer] do not provide species distributions which are adequate for modelling the experimental data. Piispanen and Lajunen[37] have claimed that 2-hydroxypropanoate (stereochemistry unspecified) does not form a complex of stoichiometry CuL_2 in solution (though a crystal structure of such a complex of the racemic ligand has been reported[38]) but that, below pH 4, only CuL occurs and above pH 4 a binuclear species, $Cu_2L_3H_{-1}$, forms additionally; appropriate stability constants were given (see ESI). Unfortunately, the distributions calculated using these constants are also inadequate for modelling the pH profiles of R^H and R^{OH} in the upper pH range as the concentrations of $Cu_2L_3H_{-1}$ prove to be essentially stationary.

For want of satisfactory stability constants for 2-hydroxypropanoate complexes and in view of the success in modelling

Table 5 Rate constants[a] for reactions of 2-benzoylphenyl radical, **2**, with mononuclear copper(II) complexes of 2-hydroxycarboxylates

Entry	Reactive species:	L_{free} $10^{-6}k_0^H$/ dm³ mol⁻¹ s⁻¹	CuL $10^{-6}k_{1a}^H$/ dm³ mol⁻¹ s⁻¹	$CuLH_{-1}$ $10^{-6}k_{1b}^H$/ dm³ mol⁻¹ s⁻¹	CuL_2 $10^{-6}k_2^H$/ dm³ mol⁻¹ s⁻¹
Hydrogen transfer					
1	Hydroxyethanoate[b]	4.59 ± 0.89	2.51 ± 0.72	43.3 ± 5.87	5.02 ± 1.44
2	2-Hydroxy-2-methylpropanoate[c]	0.070 ± 0.045	0.070 ± 0.045	1.49 ± 1.10	0.611 ± 0.177
3	(±)-2-Hydroxypropanoate[b]	11.0 ± 1.36	4.10 ± 0.62	63.9 ± 8.52	8.20 ± 1.24
4	(*S*)-2-Hydroxypropanoate[b]	7.89 ± 1.89	3.45 ± 0.77	61.8 ± 8.03	6.90 ± 1.09
5	2-Hydroxypropanoate *means*	9.44 ± 1.16	3.77 ± 0.49	62.8 ± 5.85	7.55 ± 0.70
Hydroxylation					
			$10^{-6}k_{1a}^{OH}$/ dm³ mol⁻¹ s⁻¹	$10^{-6}k_{1b}^{OH}$/ dm³ mol⁻¹ s⁻¹	$10^{-6}k_2^{OH}$/ dm³ mol⁻¹ s⁻¹
6	Hydroxyethanoate[d]		3.29 ± 1.37	18.6 ± 3.19	12.8 ± 2.56
7	2-Hydroxy-2-methylpropanoate[d]		3.96 ± 1.11	26.2 ± 7.89	11.9 ± 1.96
8	(±)-2-Hydroxypropanoate[d]		3.78 ± 0.51	26.5 ± 3.21	9.16 ± 1.16
9	(*S*)-2-Hydroxypropanoate[d]		4.88 ± 1.57	27.6 ± 4.82	10.9 ± 2.58
10	2-Hydroxypropanoate *means*		4.33 ± 0.82	27.0 ± 2.89	10.0 ± 1.41

[a] Uncertainties are the 95% confidence intervals. [b] Relative reactivity of CuL and CuL_2 assumed to be 1 : 2. [c] Free ligand and CuL assumed to be equally reactive. [d] Rate constants calculated independently for each complex.

the experimental results for the other 2-hydroxycarboxylates in terms of CuL, CuL_2 and $CuLH_{-1}$, we interpolated $\log\beta_{p,q,r}$ values for each of these species where L is 2-hydroxypropanoate, which are the means of Piispanen and Lajunen's corresponding values for hydroxyethanoate and 2-hydroxy-2-methylpropanoate. (Such averaging is equivalent to assuming that the incremental changes in $\Delta G^{\ominus}_{p,q,r}$ on two successive *C*-methylations of hydroxyethanoate are equal, which does not seem chemically unreasonable.) The interpolated values for CuL and CuL_2, 2.53 and 4.04, respectively, agree with experimental values 2.52 ± 0.01[37] and 4.08 ± 0.1[16] which gives confidence in the value (−3.92) interpolated for $CuLH_{-1}$. The interpolated stability constants allowed a satisfactory modelling of the pH profiles of R^H and R^{OH} for both racemic and (*S*)-2-hydroxypropanoate. The derived rate constants are given in Table 5, entries 3–5 and 8–10.

It is expected that any particular complex which contains a single 2-hydroxypropanoate ligand should have the same reactivity irrespective of whether it is formed from the racemic or an optically resolved precursor and inspection of the data of Table 5 shows this to be the case. However, for CuL_2 there are different diastereoisomeric possibilities: $Cu(^SL)_2$ from the (*S*)-precursor, but this along with $Cu(^RL)_2$ and $Cu(^SL)(^RL)$ from the racemic precursor. The racemic complex crystallises in the latter form.[38] In principle, the hetero-enantiomeric form might show reactivity different from the homo-enantiomeric forms should it predominate sufficiently in solution but it is clear from Table 5 that in neither H-transfer (entries 3–5) nor hydroxylation (entries 8–10) is there any discernible difference in the reactivity of CuL_2 according to its provenance.

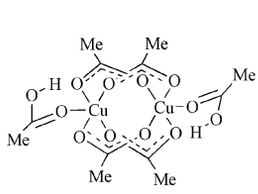
It is evident that the methylation of hydroxyethanoate to 2-hydroxypropanoate increases the reactivity of all species as H-donors. This is analogous to the situation found for the 2-aminocarboxylates and propanedioates (*cf.* Table 2). Interestingly, the hydroxylation rate constants for the three 2-hydroxycarboxylates are all very similar. Change in the extent of methylation has little effect on them except perhaps for $CuLH_{-1}$ between hydroxyethanoate (Table 5, entry 6) and the 2-hydroxypropanoates (entries 8 and 9).

(vi) EPR evidence of the formation binuclear complexes by 2-hydroxycarboxylates

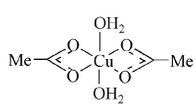
In view of the suggestion by Piispanen and Lajunen[37] of the formation of a binuclear complex by copper(II) and 2-hydroxypropanoate, we undertook experiments in which the EPR signal intensities of solutions containing $Cu(NO_3)_2$ and 2-hydroxycarboxylate ligands, in the same concentrations as used in the radical clock experiments, were monitored as functions of pH. Any formation of binuclear species in which the unpaired d^9 electrons of the individual copper(II) centres are able to interact is expected to result in a loss of initial paramagnetic signal intensity. The results which indicate a degree of binuclear complex formation by all the hydroxycarboxylates are given as ESI.

(vii) Rate constants for the reactions of 2 with copper(II) complexes of ethanoate

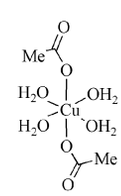
Ethanoate ion has the potential to be a bidentate ligand. Both copper(I)[39] and copper(II)[40] form binuclear 'paddlewheel' complexes in which the copper centres are bridged by ethanoate ions, *e.g.* **7**. The behaviour of **7** in solution is not simple.[41] In ethanoic acid, on initial addition of water, the displacement of the axial ethanoic acid ligands by water is energetically favourable but **7** dissociates to mononuclear forms as the percentage of water in the solvent is further increased. Structures **8** and **9** have been proposed to be present in dilute solutions containing Cu^{2+} and ethanoate ions.[42] Evidence from EPR spectra (*g*-value and hyperfine splitting) indicates that ethanoate remains coordinated to the copper in dilute aqueous solution.[43]



7



8



9

Stability constants for complexes of copper(II) with ethanoate are given by Martell and Smith[16] for CuL_n, n = 1–4 (see ESI). According to these constants, solutions of $Cu(NO_3)_2$ (0.05 mol dm⁻³) and KO_2CMe (0.10 mol dm⁻³), contain the complexes CuL, CuL_2 and CuL_3 in significant concentrations (≥1 × 10⁻³ mol dm⁻³) in some part of the pH range between 2.1 and 5; above pH 5.1, the solutions become turbid and may deposit a pale blue precipitate [presumably $Cu(OH)_2$]. When **1** is homolysed in solutions containing 0.05 mol dm⁻³ copper(II)

Table 6 Rate constants[a] for reactions of 2-benzoylphenyl radical, **2**, with ethanoate complexes of copper(II)

Hydrogen transfer					
Reactive species:		L_{free}	CuL	CuL_2	CuL_3
Entry	Footnote	$10^{-6}k_0^{H}$/dm^3 mol^{-1} s^{-1}	$10^{-6}k_1^{H}$/dm^3 mol^{-1} s^{-1}	$10^{-6}k_2^{H}$/dm^3 mol^{-1} s^{-1}	$10^{-6}k_3^{H}$/dm^3 mol^{-1} s^{-1}
1	[b,c]	0.264 ± 0.039	0.939 ± 0.152	*not signif.*	*not signif.*
2	[d,e]	0.287 ± 0.038	0.701 ± 0.091	1.40 ± 0.18	2.10 ± 0.27
Hydroxylation					
Entry	Footnote		$10^{-6}k_1^{OH}$/dm^3 mol^{-1} s^{-1}	$10^{-6}k_2^{OH}$/dm^3 mol^{-1} s^{-1}	$10^{-6}k_3^{OH}$/dm^3 mol^{-1} s^{-1}
3	[c]		4.14 ± 0.71	6.22 ± 1.67	*not signif.*
4	[f]		4.10 ± 0.50	5.12 ± 0.63	6.83 ± 0.84

[a] Uncertainties are the 95% confidence intervals. [b] L_{free} taken as ($HL + L^-$). [c] Rate constants calculated independently for each species. [d] L_{free} taken as HL only. [e] Relative reactivities of Cu complexes assumed to be statistically determined. [f] Relative reactivities found *via* eqn. (14).

ethanoate in the pH range 2.1–5.0, it is apparent that cyclisation of the radical clock is the predominant reaction: both R^{H} and R^{OH} are less than unity though both increase sigmoidally over the range. Hydrogen transfer is very much the minor reaction ($0.04 < R^{H} < 0.055$) consistent with the expectation that H-abstraction from the methyl group of ethanoate to produce a primary radical would be relatively difficult. When R^{H} is correlated with equilibrium concentrations of free ligand and the three copper complexes independently, it is found that $[CuL_2]$ and $[CuL_3]$ are not statistically significant (Table 6, entry 1). A better account of the experimental data is given if it is assumed that only the predominant protonated free ligand is reactive and that the relative reactivities of the three copper complexes are statistically determined (entry 2). A coordinated ethanoate ion thus reacts as an H-donor almost 2.5-fold faster than free ethanoic acid.

Hydroxylation of **2** by the mixed copper ethanoate complexes rises to about 20% of the total product over the pH range 2.1–5.0 and for a 0.05 molar analytical concentration of copper ethanoate. Examination of the dependence of $\{R^{OH} - 1.84[Cu]\}$ upon the equilibrium concentrations of the various complexes showed $[CuL_3]$ not to be statistically significant when the concentrations of all three complexes were taken as explanatory variables. The rate constants obtained for CuL and CuL_2, given in Table 6, entry 3, show that ethanoate ligands promote hydroxylation but they imply nothing for the structures of the complexes.

However, with the prior assumptions that the copper is six-coordinate in all three complexes, that the ethanoate ligands are *monodentate* in each and that the activation per residual ligated water molecule is constant for each ethanoate ligand added, the experimental data may be expressed by eqn. (14), where the intercept C is introduced to enable simple linear regression.

$$\{R^{OH} - 1.84[Cu]\} = (k_{act}^{OH}/k_C)\{[CuL]/5 + [CuL_2]/4 + [CuL_3]/3\} + C \quad (14)$$

When the experimental data are fitted by eqn. (14), C is found to be not significantly different from zero and the gradient allows evaluation of k_{act}^{OH} as $(20.5 \pm 2.51) \times 10^6$ dm^3 mol^{-1} s^{-1}. The derived rate constants for the individual complexes are given in Table 6, entry 4; those for CuL and CuL_2 show improved precision relative to their counterparts in entry 3 and a value is now assigned to CuL_3. Fig. 6 shows the variation of R^{OH} as a function of the analytical concentration of copper ethanoate. The discrete points are experimental[44] values of R^{OH} obtained using copper ethanoate solutions up to four times more concentrated than those used in finding the rate constants and acidified to prevent turbidity; the continuous line gives values of R^{OH} predicted by application of the rate constants of Table 6, entry 4 to the distributions of copper-containing species at pH 4.3.

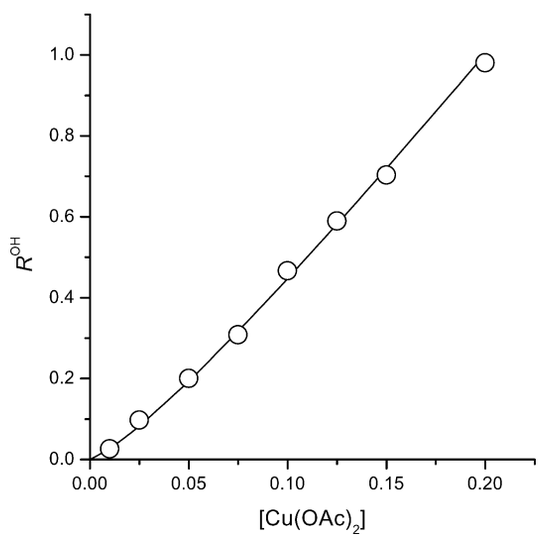


Fig. 6 Variation of R^{OH} with the concentration of copper(II) ethanoate; discrete points are experimental values, the line is the prediction given by the rate constants of Table 6, entry 4.

Discussion

(i) Hydrogen transfer

Free ligands. There are no literature precedents for rate constants for hydrogen abstraction from any of the various ligands by **2** or by phenyl radical, Ph$^{\bullet}$, which is expected to react at rates comparable to **2**.[6] However, estimates for Ph$^{\bullet}$ can be inferred from other known constants as follows. The radicals Ph$^{\bullet}$, HO$^{\bullet}$ and Me$^{\bullet}$ react with methanol with respective rate constants[45–47] of 1.2×10^6, 9.7×10^8, and 2.2×10^2 dm^3 mol^{-1} s^{-1} indicating relative rate constants of $k(Ph^{\bullet})/k(OH^{\bullet}) = 1.2_4 \times 10^{-3}$ and $k(Ph^{\bullet})/k(Me^{\bullet}) = 5.4_5 \times 10^3$. These can be used as interpolation factors to estimate rate constants for reactions of the ligands with Ph$^{\bullet}$ (and **2**) from the known constants for their reactions with HO$^{\bullet}$ and Me$^{\bullet}$. The values obtained for the parent members of each ligand family are collected in Table 7 (comment has already been made on the effects of *C*-methylation on rates within each family).

Our study of the copper/aminoethanoate system was carried out in the pH range 4.5–6.25. Under these conditions the predominant form of the free ligand was always $H_3N^+CH_2CO_2^-$ (*i. e.* HL) which exceeded $H_2NCH_2CO_2^-$ (L) by factors never

Table 7 Comparisons between interpolated rate constants for H-abstraction by phenyl radical from free ligands, per CH_2 group, and those found for 2-benzoylphenyl radical, **2**

Entry	Free ligand species	H-abstraction by HO$^{\bullet}$		H-abstraction by Ph$^{\bullet}$, *interpolation 1*[a]	H-abstraction by Me$^{\bullet}$		H-abstraction by Ph$^{\bullet}$, *interpolation 2*[b]	H-abstraction by **2**[c], per CH_2 group
		dm^3 mol^{-1} s^{-1}	Ref.[d]	dm^3 mol^{-1} s^{-1}	dm^3 mol^{-1} s^{-1}	Ref.	dm^3 mol^{-1} s^{-1}	dm^3 mol^{-1} s^{-1}
1	$H_3N^+CH_2CO_2^-$	1.7×10^7	48	2.1×10^4	~4	49	2.2×10^4	*none*
2	$H_3N^+CH_2CO_2H$	1.0×10^7	48	1.2×10^4				
3	$H_2NCH_2CO_2^-$	5.3×10^9	50	6.6×10^6	~1.2×10^2	49	6.5×10^5	
4	$MeCO_2H$	1.1×10^7[e]	51	1.4×10^4	1.3×10^2[e]	52	7.1×10^5	$(1.91 \pm 0.25) \times 10^5$[f]
5	$MeCO_2^-$	4.9×10^7[e]	51	6.1×10^4				
6	$HO_2CCH_2CO_2H$	1.6×10^7	53	2.0×10^4				$(1.73 \pm 0.26) \times 10^6$
7	$^-O_2CCH_2CO_2^-$	2.4×10^8	54	3.0×10^5				{
8	$HOCH_2CO_2H$	5.4×10^7	55	6.7×10^5	3.6×10^3	52	2.0×10^7	$(4.93 \pm 0.71) \times 10^6$
9	$HOCH_2CO_2^-$	1.2×10^9	55	1.5×10^6				{
10	$H_3N^+CH_2CH_2NH_3^+$							$(5.10 \pm 3.95) \times 10^4$[g]
11	$H_2NCH_2CH_2NH_2$	2.7×10^9[h]	50	3.3×10^6				
12	$Me_2NCH_2CH_2NHMe_2^+$							$(6.51 \pm 0.79) \times 10^6$

[a] Interpolation factor $1.2_4 \times 10^{-3}$. [b] Interpolation factor $5.4_5 \times 10^3$. [c] Uncertainties are 95% confidence intervals, a brace indicates that different protonated forms of the ligand have significant concentrations within the pH range examined and the observed rate is therefore the weighted sum of rate constants for reactions of **2** with the different forms. [d] Rate constants are cited from the on-line compilation of the Radiation Chemistry Data Center of Notre Dame Radiation Laboratory (http://allen.rad.nd.edu); owing to adoption of consistent rates for reference reactions, values may differ somewhat from those of the original reference. [e] Cited value with a statistical correction of 2/3 applied. [f] Value from Table 6, entry 2 with a statistical correction of 2/3 applied. [g] Value from Table 3, entry 1 with a statistical correction of 1/2 applied. [h] Cited value with a statistical correction of 1/2 applied.

less than 1.6×10^3 and $H_3N^+CH_2CO_2H$ (H_2L) by factors never less than 1.2×10^2. Both interpolations (Table 7, entry 1) suggest a rate constant of about 2×10^4 dm^3 mol^{-1} s^{-1} for the reaction of Ph$^{\bullet}$ with $H_3N^+CH_2CO_2^-$. In the various experimental runs, the highest concentration of $H_3N^+CH_2CO_2^-$ encountered was 1.2×10^{-2} mol dm^{-3} implying a maximum expected contribution to the value of R^H from the free ligand of $k_0^H[HL]/k_C = (2 \times 10^4) \times (1.2 \times 10^{-2})/(8 \times 10^5) = 3 \times 10^{-4}$ which is within the experimental error. The failure to find a rate constant for H-transfer from aminoethanoate to **2** is thus consistent with the magnitude of the interpolated rate constant.

Excepting entry 1 (and 3), it is noticeable that interpolation 1 based on reaction rates of HO$^{\bullet}$ underestimates rate constants found for **2** whereas interpolation 2 based on reaction rates of Me$^{\bullet}$ overestimates them. We suggest this stems from the different reactivities and hence selectivities of the two radicals used for interpolation. The very reactive HO$^{\bullet}$ is expected to discriminate less kinetically between substrates than the much less reactive Me$^{\bullet}$ and the interpolated rate constants for Ph$^{\bullet}$ with reactivity/selectivity expected to lie between those of HO$^{\bullet}$ and Me$^{\bullet}$ reflect this difference.

Rate constants for H-abstraction by HO$^{\bullet}$ are available for the differently protonated forms of the ligands and from these, the corresponding interpolated rate constants for abstraction by Ph$^{\bullet}$ are given in Table 7. When more than one form are present in significant concentrations in the experimental pH range, the actual abstraction rate by **2** must be the weighted sum of rates of the different forms. In cases when this occurs, a brace is used in Table 7 to indicate the observed rate constant relates to more than one free ligand species. For example, for hydroxyethanoate both the anion and the acid were present so the first interpolated constant for Ph$^{\bullet}$ lies in the range $(0.7–1.5) \times 10^6$ dm^3 mol^{-1} s^{-1} (entries 8 and 9); the observed rate constant for **2**, $(4.93 \pm 0.71) \times 10^6$ dm^3 mol^{-1} s^{-1}, is indicated by the adjacent brace to result from reaction of **2** with both $HOCH_2CO_2H$ and $HOCH_2CO_2^-$. In the case of propanedioate, rate constants for reactions of HO$^{\bullet}$ with $CH_2(CO_2H)_2$ and $CH_2(CO_2^-)_2$ are available (entries 6 and 7). In the pH range of our experiments, the monoanion $HO_2CCH_2CO_2^-$ occurs in significant concentrations but, as it is likely that this reacts at a rate intermediate between those of the acid and dianion, the range of interpolation 1 is unchanged at $(0.2–3.0) \times 10^5$ dm^3 mol^{-1} s^{-1}.

Although the rate constant found for the reaction of **2** with 1,2-diaminoethane is similar in magnitude to that interpolated for aminoethanoate (*cf.* entries 10 and 1), in the case of the diamine an H-abstraction rate constant for the free ligand was measurable because the equilibrium concentrations of the reacting form are larger and it has the advantage of two equivalent methylene groups. The apparent great difference in reactivity found between 1,2-diaminoethane and 1,2-bis-(dimethylamino)ethane (*cf.* entries 10 and 12) occurs because the concentration of the monocationic form is much more important for the latter. Although the distributions of the low-reactivity dicationic forms are comparable for the two diamines, the presence of the tertiary amine function in the monocation of 1,2-bis(dimethylamino)ethane activates abstraction from the adjacent CH_2 group. Entry 11 also shows that the presence of free amine groups leads to a large rate constant. The fact that protonation of 1,2-diaminoethane greatly reduces its capacity as an H-donor to aryl radicals confirms ambiphilic aryl radicals manifest electrophilic character in this reaction as expected.[25]

Overall, the data of Table 7 show that the order of substituent effects on reactivity of the CH_2 groups of the free ligands with **2** is consistent with expectation from the reactions of HO$^{\bullet}$, *i.e.* $H_3N^+ < H < CO_2H < CO_2^- < OH < NMe_2$. Although some of the rate constants found do not relate to single species and although they have been extracted from experimental data by curve-fitting of product-ratio/pH profiles rather than by substrate-specific measurement, they do clearly

Table 8 H-abstraction rate constants[a] per available methylene hydrogen atom from complexes of Cu(II) with bidentate ligands together with the standard enthalpies of complexation

Ligand:	1,2-Diaminoethane	2-Aminocarboxylates	2-Hydroxycarboxylates	1,3-Dicarboxylates
C-Unmethylated				
$\Delta H_1^{\ominus}$/kJ mol^{-1} [b]	−55.2	−25	−1	+5.8
$k_1^{H}{}_{corr}$/dm^3 mol^{-1} s^{-1}	(1.71 ± 0.66) × 10^5 [c]	(5.20 ± 1.45) × 10^5 [d]	(1.25 ± 0.36) × 10^6 [e]	(9.50 ± 1.40) × 10^5 [f]
$\Delta H_2^{\ominus}$/kJ mol^{-1} [b]	−107	−54.3	−2	+5.0
$k_2^{H}{}_{corr}$/dm^3 mol^{-1} s^{-1}	(3.81 ± 0.45) × 10^5 [g]	(5.02 ± 1.70) × 10^5 [h]	(1.25 ± 0.36) × 10^6 [i]	(2.55 ± 0.30) × 10^6 [j]
C-Monomethylated				
$\Delta H_1^{\ominus}$/kJ mol^{-1} [b]		−22	+0.8	+9.2
$k_1^{H}{}_{corr}$/dm^3 mol^{-1} s^{-1}		(2.68 ± 0.32) × 10^6 [k]	(3.77 ± 0.49) × 10^6 [l]	(1.34 ± 0.02) × 10^7 [m]
$\Delta H_2^{\ominus}$/kJ mol^{-1} [b]		−49.3	+4.0	+10.0
$k_2^{H}{}_{corr}$/dm^3 mol^{-1} s^{-1}		(2.68 ± 0.32) × 10^6 [n]	(3.77 ± 0.49) × 10^6 [o]	(2.75 ± 0.33) × 10^7 [p]

[a] Uncertainties are 95% confidence intervals. [b] Values from ref. 36. [c] From Table 3, entry 1, $k_1^{H}/4$. [d] From Table 2, entry 1, $k_1^{H}/2$. [e] From Table 5, entry 1, $k_{1a}^{H}/2$. [f] From Table 2, entry 10, $k_1^{H}/2$. [g] From Table 3, entry 1, $k_2^{H}/8$. [h] From Table 2, entry 1, $k_2^{H}/4$. [i] From Table 5, entry 1, $k_2^{H}/4$. [j] From Table 2, entry 10, $k_2^{H}/4$. [k] From Table 2, entry 4, k_1^{H}. [l] From Table 5, entry 5, k_{1a}^{H}. [m] From Table 2, entry 12, k_1^{H}. [n] From Table 2, entry 4, $k_2^{H}/2$. [o] From Table 5, entry 5, $k_2^{H}/2$. [p] From Table 2, entry 12, $k_2^{H}/2$.

have chemical significance which gives confidence in the findings for the copper(II) complexes.

Copper(II) complexes—ligand deactivation. In order to assess the effect of coordination on the reactivity of a ligand as a hydrogen donor, it must be borne in mind that a *coordinated* ligand is not usually in the same state of protonation as the predominant form(s) of the *free* ligand. The only cases where a significant concentration of the predominant form of the free ligand is the same as the coordinated ligand are the 2-hydroxycarboxylates in the upper pH ranges examined. For example, for hydroxyethanoate above pH 4, $HOCH_2CO_2^-$ is the predominant form of the free ligand and this is also the form which binds to the metal. Entry 1 of Table 5 shows that $k_{1a}^{H} < k_0^{H}$, *i.e.* coordination reduces the reactivity of the ligand as a hydrogen donor (*cf.* the minimum in Fig. 5) and the statistical advantage of CuL_2 over CuL is required to compensate the loss in reactivity per mole.

For the structurally analogous aminoethanoate, the coordinated ligand is $H_2NCH_2CO_2^-$ but the free ligand is predominantly $H_3N^+CH_2CO_2^-$. Since experimental rate constants are unavailable for H-abstractions by **2,** or by Ph$^{\bullet}$, from $H_2NCH_2CO_2^-$, we make use of the interpolated value given in Table 7, interpolation 1 (remembering that it is probably an *under*estimate). Entry 3 of Table 7 therefore indicates an expectation of at least 6.6 × 10^6 dm^3 mol^{-1} s^{-1} for the rate constant for H-abstraction by Ph$^{\bullet}$, and hence by **2**, from $H_2NCH_2CO_2^-$. The value observed for the coordinated ligand is k_1^{H} = (1.04 ± 0.29) × 10^6 dm^3 mol^{-1} s^{-1} (Table 2, entry 1). Again, coordination evidently reduces the ligand's reactivity as a hydrogen donor. A similar situation arises for 1,2-diaminoethane where the interpolated rate constant, per CH_2 group, for reaction of Ph$^{\bullet}$ (hence **2**) is at least 3.3 × 10^6 dm^3 mol^{-1} s^{-1} (Table 7, entry 11) whereas the observed values, *per CH_2 group*, for k_1^{H} and k_2^{H} are, respectively, (3.43 ± 1.32) × 10^5 and (7.62 ± 0.9) × 10^5 dm^3 mol^{-1} s^{-1} (data from Table 3, entry 1, with the appropriate statistical corrections applied). Here, although the intrinsic reactivity per CH_2 group is higher in CuL_2 than in CuL, the approximately ten-fold reduction in the reactivity of L brought about by ligation in CuL is not fully compensated by the increase.

Propanedioate coordinates copper(II) as $^-O_2CCH_2CO_2^-$ but, in our conditions, the free ligand occurs predominantly as $HO_2CCH_2CO_2H$ at pH 2–2.5 and as $HO_2CCH_2CO_2^-$ at pH 2.5–5; the dianion is the predominant form of free ligand only in the pH range 5.5–6.5 but then its concentration is low, attaining a maximum of *ca.* 6% of total ligand in this range. Entries 8 and 10 of Table 2 indicate H-abstractions by **2** from free ligand and from CuL to occur at the same rate but, since the protonated forms in which the free ligand exists are expected to be poorer H-donors than the dianion, it is again apparent that coordination of the first ligand to copper(II) causes a decrease in its H-donating capacity.

The interpolated reactivity of Ph$^{\bullet}$ with ethanoate anion relative to that with ethanoic acid is 6.1/1.4 = 4.3$_6$ (Table 7 entries 4 and 5, interpolation 1); the observed reactivity of **2** with coordinated ethanoate anion relative to free ethanoic acid is k_1^{H}/k_0^{H} = 0.701/0.287 = 2.44 (Table 6, entry 2). Since the interpolated figure is likely to be an underestimate, it is evident that ethanoate is no exception to the general finding that coordination by Cu^{2+} diminishes the H-donating reactivity of a ligand relative to that of the free ligand in the same state of protonation as that in which it is complexed.

Copper complexes—relative reactivities. In Table 8 are presented the H-abstraction rate constants, $k_1^{H}{}_{corr}$ and $k_2^{H}{}_{corr}$, corrected for the numbers of available methylene hydrogens contained in complexes CuL and CuL_2, together with standard enthalpies of complexation of the complexes.[36] On traversing the Table from left to right, the complexes range from the most exothermic to the endothermic. Also, the rate constants show an apparent increasing trend from left to right. However, comparing their uncertainties, it is evident that the rate constants for 2-amino-carboxylates and 2-hydroxycarboxylates may not be significantly different from each other [the mean values for the two families of ligand are: *C*-unmethylated, $k_1^{H}{}_{corr} = k_2^{H}{}_{corr}$ = (7.0 ± 1.0) × 10^5 dm^3 mol^{-1} s^{-1}; *C*-monomethylated, $k_1^{H}{}_{corr} = k_2^{H}{}_{corr}$ = (3.1 ± 0.2) × 10^6 dm^3 mol^{-1} s^{-1}]. The values of $k_1^{H}{}_{corr}$ and $k_2^{H}{}_{corr}$ are equal because the uncorrected relative reactivity of CuL and CuL_2 for these families of ligand depends only on the numbers of available methylene hydrogens (the prior assumption that this was the case resulted in improved precision of the evaluated rate constants). By contrast, the fact that $k_1^{H}{}_{corr} \neq k_2^{H}{}_{corr}$ for the complexes of 1,2-diaminoethane and the two 1,3-dicarboxylates indicates that, for these H-donors, other factors are responsible for the relative reactivity of CuL and CuL_2.

1,2-Diaminoethane is distinguished from the other ligands in that the stability constants for CuL and CuL_2 are both are very large (see ESI) and mainly enthalpically determined (see Table 8); furthermore, both complexes are dicationic. On the assumption of transfer of electron density to copper, positive charge will be transferred from the metal to the donor N-atoms and thence inductively to the methylene H atoms; this will inhibit attack by **2**, the somewhat electrophilic aryl radical (*cf.* the similar but larger effect of protonation of the free ligand). The value of $k_2^{H}{}_{corr}/k_1^{H}{}_{corr}$ in the complexes of 1,2-diaminoethane is 2.2 showing that CuL is more deactivated than CuL_2. Assuming six-coordination in both complexes, the donor atoms are 2 × N and 4 × O in the case of aquated CuL but 4 × N and 2 × O in

the case of aquated CuL_2. Since O is more electronegative than N, it seems reasonable to conclude that the polarisation of N should be greater in the case of CuL with the consequence that this complex has the more deactivated ligand.

Comparable reasoning explains the behaviour of the complexes of propanedioate and 2-methylpropanedioate. In these cases, as the ligands are dianionic, the CuL species are neutral complexes in which the reactivities as H-donors are indistinguishable experimentally from those of the free, mixed, mono- and di-protonated forms (see above); addition of a second ligand produces dianionic complexes, CuL_2, which are endothermic species indicating the enthalpy gain from the binding of the ligand does not compensate that lost by displacement of water; the negative charge is largely retained by the donor O-atoms of the ligands as the most electronegative sites in the complex. Local D_{4h} symmetry requires the net negative charge to be equally distributed over the ligands' four donor O-atoms. The methylene hydrogens in the CuL_2 complexes are thus flanked by accumulations of negative charge which inductively enhances their reactivity towards electrophilic aryl radicals. The CuL_2 complexes are thus better donors than the CuL complexes; the values of $k_2^{H}{}_{corr}/k_1^{H}{}_{corr}$ are 2.7 and 2.0, respectively, for propanedioate and 2-methylpropanedioate.

In the cases of the 2-aminocarboxylates and the 2-hydroxycarboxylates the CuL complexes are monocationic. Part of this charge, transferred to the ligand, accounts for the reduced reactivity of the coordinated ligands by comparison with free ligands in the same states of protonation. Coordination of a second ligand produces neutral complexes but the reduction in net charge does not result in noticeably increased reactivity ($k_2^{H}{}_{corr} = k_1^{H}{}_{corr}$). Since, in the cases discussed above, the postulated ligand polarisation effects produced by double net charges resulted in rate enhancements of 2–3-fold, it seems reasonable that those produced by single charges might be insufficient to be detectable in our experiments. Loss of positive charge by deprotonation of CuL complexes does, however, noticeably increase reactivity: the loss of the ligands' hydroxyl protons in the cases of hydroxyacids (Table 5, entries 1 and 5) and hydrolysis (deprotonation of coordinated water) in the case of 1,2-bis(dimethylamino)ethane (Table 4, entry 3) give species more reactive as H-donors than the initial CuL complexes.

For those ligands where the methylene group is fully methylated, the reactivities in H-donation of the corresponding Cu(II) complexes are much reduced on account of the loss of mesomeric stabilisation of the incipient radical by adjacent groups. Nevertheless, complexes of the ligands $XCMe_2CO_2^-$ show a decrease in the magnitudes of both k_1^H and k_2^H on change of X in the order $CO_2^- > NH_2 > OH$ (*cf.* Table 2 entries 6 and 14; Table 5 entry 2) which parallels the increase in electronegativity in the donor atoms in X and is as expected for H-abstraction by an electrophilic radical. Of these ligands, $HOCMe_2CO_2^-$ is the only one where the relative reactivity of CuL and CuL_2 is apparently not statistically determined. Possibly, this intrinsically unreactive system allows discrimination of the difference that was not discernable for 2-hydroxy- and 2-amino-acids in abstractions of methylene hydrogens; certainly, the effect of deprotonation is significant (*cf.* Table 5 entry 2). However, this is the poorest H-donor of all those we have examined, the yields of **6** do not exceed 3% of the radical clock products and the experimental values of R^H are consequently small and somewhat scattered. The apparently greater relative reactivity of CuL_2 could equally be an artefact of the scatter.

(ii) Hydroxylation reactions

Evidence against S_H2 mechanism

The tabulated rate constants show that all CuL complexes investigated, with the exception of that of TMEN, hydroxylate **2** faster than does Cu^{2+}aq (*i.e.* $k_1^{OH} > k_0^{OH}$) and that, with the exception of the complexes of 1,2-diaminoethane, CuL_2 complexes hydroxylate **2** faster than the corresponding 1 : 1 complex (*i.e.* $k_2^{OH} > k_1^{OH}$). Fig. 7 shows a plot of $\log k_n^{OH}$ *versus* $\log\beta_n$ for the bidentate ligands investigated. For the 2-amino-, 2-hydroxy- and 1,3-di-carboxylate ligands, lines are drawn from the intercept which correspond to $\log k_0^{OH}$ through the points having coordinates: [mean $\log\beta_1$, mean $\log k_1^{OH}$] and [mean $\log\beta_2$, mean $\log k_2^{OH}$]. It is apparent that approximate linear free energy relationships hold.

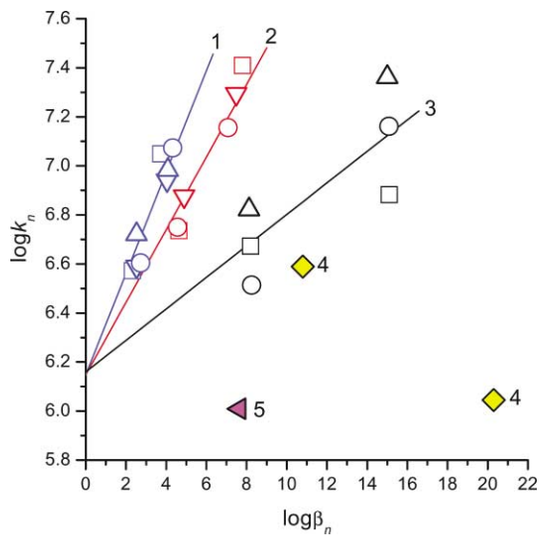


Fig. 7 Plots of $\log k_n$ *versus* $\log\beta_n$ for bidentate ligands: 1 (blue), 2-hydroxycarboxylates; 2 (red), 1,3-dicarboxylates; 3 (black), 2-aminocarboxylates; 4, 1,2-diaminoethane; 5, 1,2-bis(dimethylamino)-ethane. In plots 1–3: □, parent ligand; Δ, (*S*)-monomethylated ligand; ∇, achiral or (±)-monomethylated ligand; ○, dimethylated ligand.

In the overall hydroxylation process, a Cu(II) complex is reduced to Cu(I) so our first consideration was whether these relationships support the supposition that the k_n^{OH} values might relate to this reduction step [*i.e. via* the S_H2 variant of reaction (3b)]. The $\log\beta_n$ values measure the extent to which association of the Cu^{2+} ion with a ligand is preferred over that with water; also, it is well established that, for six-coordinate Cu^{2+}, where the coordination sphere is tetragonally distorted from octahedral by the operation of the normal Jahn–Teller effect, there is an inverse correlation of the mean length of equatorial bonds with the lengths, and hence strengths, of axial bonds.[56] We therefore considered the possibility that the more stable complexes might be the better water ligand transfer agents because they hold axially ligated water less tightly than the less stable complexes.

Here the implicit assumption is that the transition states for water ligand transfer resemble the reactants. However, for all the ligands investigated, the donor atoms are hard and hence are expected to stabilise Cu^{2+} better than Cu^+. Data are scarce for the latter but, for the complexes $Cu^{II}L_2$ and $Cu^{I}L_2$ where L is aminoethanoate, $\log\beta^{II}{}_2 = 15.1$ and $\log\beta^{I}{}_2$ is 10.1,[36] confirming this expectation. With respect to these complexes therefore, the transfer of a water ligand to **2** would be endergonic by 28.5 kJ mol^{-1} and a similar situation is expected for the other complexes. According to Hammond's postulate, the transition state for an endergonic reaction step should resemble the reaction products, not the reactants. The circumstantial evidence afforded by the correlations of Fig. 7 is therefore against k_n^{OH} values relating to S_H2 transfer of water ligands but rather in favour of relating to an elementary step not involving the reduction of Cu(II).

Notwithstanding similarities of rate constant between complexes of analogous stoichiometry, differences are discernible between complexes of different charge-type:

Dication: 3 examples,
k_n^{OH} range = (1.02–3.88) × 10^6 dm^3 mol^{-1} s^{-1}
Monocation: 6 examples,
k_n^{OH} range = (3.26–6.63) × 10^6 dm^3 mol^{-1} s^{-1}
Neutral: 9 examples,
k_n^{OH} range = (5.45–23.0) × 10^6 dm^3 mol^{-1} s^{-1}
Dianion: 3 examples,
k_n^{OH} range = (14.3–23.7) × 10^6 dm^3 mol^{-1} s^{-1}

It is clear that cationic complexes react less rapidly than anionic complexes and that neutral complexes span the difference between them. This suggests the attack of **2** upon the copper complexes has a degree of *electrophilic* character and the fact that deprotonation of the cationic CuL complexes of 2-hydroxy-carboxylates gives hydroxylating species of enhanced reactivity (*cf.* Table 5) further supports the suggestion. This finding stands in marked contrast to the case of Sandmeyer chlorination where it was found[5] that the attack of aryl radicals upon chlorocuprate(II) complexes has nucleophilic character, being assisted by electron donating substituents in the aryl ring and by a high reduction potential for the chlorocuprate couple involved. It is believed that, in chlorination, the radical attacks the ligand[5,9] but the correlations of Fig. 7 were taken as circumstantial evidence that in hydroxylation it does not. The stability constants for bis-aminoethanoate complexes of Cu^+ and Cu^{2+} quoted above imply, *via* the Nernst equation, a standard reduction potential of −0.135 V, for the couple $Cu^{II}L_2/Cu^{I}L_2$ (L, aminoethanoate). If hydroxylation were to relate to the standard reduction potential of the catalytic copper couple, as does chlorination, the reaction involving the aminoethanoate-ligated couple would proceed less rapidly than that involving Cu^{2+}aq ($E^{\ominus}$ = +0.159 V)[57] which is not the case. It thus appears that although Sandmeyer hydroxylation and chlorination may be competitive, they are mechanistically different in their product determining steps.

Evidence supporting adduct formation. We therefore suggest that aryl radicals add to Cu(II) species in the same way as alkyl radicals and that k_n^{OH} values relate to this addition step.[9–12] Significant in this regard is the observation by Freiberg and Meyerstein[12] that the rates of addition of alkyl radicals to Cu^{2+}aq are increased by inductively electron withdrawing substituents in the radical (see the examples given above in the introduction). The additions of both alkyl and aryl radicals to copper(II) species thus have electrophilic character which is consistent with the formation of formally Cu(III) adducts from Cu(II) reactants. The combination of organic radicals in aqueous solution usually occurs with little activation barrier and hence close to the diffusion controlled rate (k_{comb} = 10^9–10^{10} dm^3 mol^{-1} s^{-1}).[58] By contrast, the rate constants of the reactions of **2** with the complexes we have found (k_n^{OH} = 1 × 10^6–2.5 × 10^7 dm^3 mol^{-1} s^{-1}) imply free energies of activation of 31–38 kJ mol^{-1} despite both **2** and any Cu(II) complex being odd-electron species. Such barriers must originate in structural and orbital changes in the complex which are necessary for reaction to occur.

The operation of the normal Jahn–Teller effect in notionally octahedral Cu^{2+}aq results in a tetragonal distortion which lowers the symmetry from O_h to D_{4h} and separates the degenerately occupied $2e_g$ molecular orbitals (largely metal $d_{x^2-y^2}$ and d_{z^2}) to give a singly occupied b_{1g} orbital (SOMO) (metal $d_{x^2-y^2}$) of raised energy and a doubly occupied a_{1g} orbital (metal d_{z^2}) of lowered energy.[56] The SOMO thus lies in the equatorial plane of the metal and provides very little σ-overlap with a radical SOMO approaching along the *z*-axis upon which the most loosely bound water ligands lie. On the other hand, the a_{1g} orbital *is* directed along the *z*-axis and could provide σ-overlap with a radical approaching in that direction. Such interaction of the radical SOMO with a *filled* orbital of the complex of somewhat lower energy would confer electrophilic character consistent with observation. However, in order for all orbitals to become doubly occupied, passage to the transition state would also require an orbital and geometric reorganisation which could contribute to the activation barrier. This argument assumes **2** attacks six-coordinate Cu^{2+}aq (*I*-mechanism)[27] but similar conclusions also follow the assumption that **2** attacks five-coordinate Cu^{2+}aq (*D*-mechanism).[27] Since water ligands exchange on Cu^{2+}aq at a rate which is much higher than the addition reactions of interest [k_{ex} = (4.4 ± 0.1) × 10^9 s^{-1}],[59] it is conceivable that $[Cu(OH_2)_5]^{2+}$ might be a reactive pre-equilibrium species.[60] Assuming for this a square pyramidal geometry of C_{4v} symmetry, the SOMO is b_1 (largely metal $d_{x^2-y^2}$) with the doubly occupied a_1 orbital (largely metal d_{z^2}) at lower energy and directly analogous arguments apply as for the six-coordinate case.

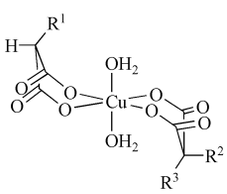
Although variations in number, structure, and donor atoms of the organic ligands will cause differences in strict molecular symmetries, provided the sequence of d orbital energies of the derived complexes may be regarded as those of an effective D_{4h} (or C_{4v}) symmetry ($d_{x^2-y^2}$ > d_{z^2} > d_{xy} > d_{xz}, d_{yz}) so that the SOMO of the complex remains in the *xy* plane, analogous argument can apply here also. This proviso seems reasonable given that all the ligands are σ-donors, none is a π-acceptor and all but the diamines are π-donors though any π-effects are expected to be small given the contracted nature of the d-orbitals on copper. Satisfactory assignments of d–d transitions in the electronic spectra of crystalline copper(II) complexes have been made on this proviso.[55,61] The differences in reactivity between different complexes would then relate to the differences in the energies of their molecular orbitals which are of largely d_{z^2} character and which are subject to variation under tetragonal distortion. Different ligands may also differ in their capacity sterically to hinder access of **2** to the metal centre. We suggest it is to the combination of such electronic and steric factors that the observed range of activation barriers owes its origin.

Support for the suggestion comes from an analysis of the effect of *C*-methylation on the ligands used. For the 2-amino-carboxylates and the 1,3-dicarboxylates, the first methylation enhances the reactivity of the CuL complexes (k_1^{OH}) by up to *ca.* 40% depending on the family (Table 1, entries 1 and 2, 5 and 6). As the methyl group is inductively electron donating this increase is consistent with attack by **2** having electrophilic character. The second methylation of the ligands, however, decreases these enhanced values suggesting that methylation can cause steric hindrance as well as electronic rate enhancement. The methyl group of a monomethylated bidentate ligand is located to one side of the equatorial plane of the copper ion in CuL and is thus able to exert its electronic effect without hindering an axial approach of the radical to the other side. However, the second methylation results in methyl groups on both sides and, in general, hindrance to both sides annuls the combined electronic effect [*i.e.* $k_1^{OH}(CHMe)$ > $k_1^{OH}(CH_2)$ ≈ $k_1^{OH}(CMe_2)$].

The effect of methylation on the reactivity of the CuL_2 complexes is somewhat more complicated. In the formation of CuL_2 with (*S*)-2-aminopropanoate, the product appropriate to the ambient temperature conditions of our experiments is the complex which is *trans* in respect of the donor atoms in the equatorial plane.[62] This, on account of the ligand being homo-enantiomeric, has both methyl groups on one side of the plane; the methyl groups therefore exert no steric effect on the other side but enhance reactivity there by their combined electronic effect. As a consequence, the value of k_2^{OH} for (*S*)-2-aminopropanoate as ligand shows a large (200%) increase over the corresponding value for aminoethanoate (*cf.* Table 1 entries 1 and 2). Introduction of a second methyl group into the ligand gives 2-amino-2-methylpropanoate for which k_2^{OH} is lower than for the monomethylated ligand (*cf.* Table 1, entries 2 and 3), reflecting steric hindrance now on both sides of the equatorial

plane, but still higher than k_2^{OH} for aminoethanoate showing that the combined electronic effect in bis-ligation exceeds the combined steric effect for 2-aminocarboxylate ligands.

The complex CuL_2 (L, propanedioate) has the centrosymmetric structure **10a** in which the metallocycles each have a boat conformation.[63] In principle, 2-methylpropanedioate can form two diastereoisomeric CuL_2 complexes and it is likely that the solution contains the mixed isomers **10b** and **10c** (assuming retention of the parent structure upon methylation). It seems reasonable to suppose that the preferred position for methyl groups is on the pseudo-axial bonds in order to minimise their steric interaction with flanking carbonyl groups; this, however, will hinder an axial approach to the metal of an attacking radical. In the CuL_2 complex of 2,2-dimethylpropanoate, such hindrance will be maximised. The fact that the values of k_2^{OH} decrease stepwise with the extent of methylation in the case of the three 1,3-dicarboxylates (Table 1, entries 5–7) implies the hindering effect of methylation outweighs electronic activation in this ligand family. It is reasonable that this should be the case as the complexes are dianions with, as indicated in (i) above, the negative charge accumulated on the ligands' donor oxygen atoms. There will thus be no inductive electron-demand upon the methyl groups with a resultant lack of electronic discrimination between the different degrees of methylation.



10a $R^1 = R^2 = R^3 = H$
b $R^1 = R^2 = Me$, $R^3 = H$
c $R^1 = R^3 = Me$, $R^2 = H$

For the 2-hydroxycarboxylates, the variations in k_n^{OH} values with methylation are small and, given their uncertainties, may not be real (*cf*. Table 5, entries 6–10). The CuL_2 complexes of hydroxyethanoate and 2-hydroxy-2-methylpropanoate have equal reactivities (entries 6 and 7) indicating that, for this family of ligands, any electronic promotion of the addition of **2** by dimethylation is negated by the concomitant steric hindrance. The crystalline form of the CuL_2 complex of *rac*-2-hydroxypropanoate ligand is a *trans* complex, in respect of the donor atoms, which contains both enantiomers of the ligand.[38] Consequently, this complex has a methyl group on each side of the equatorial plane. If it is predominant in solution (it has the statistical advantage), the counterbalance of the steric and electronic effects of methylation explains why k_2^{OH} for this complex is little different from the values of the complexes of the un- and di-methylated ligands. By analogy with the homo-enantiomeric complex of 2-aminopropanoate, a significantly enhanced value of k_2^{OH} might be expected for the homo-enantiomeric complex of 2-hydroxypropanoate, but this is not observed. [The lack of difference in reactivity between CuL_2 complexes derived from racemic and resolved 2-hydroxypropanoate was noted earlier; see Results (v).] However, the stability constants of the complexes of the amino- and hydroxy-carboxylates are very different, those used for 2-hydroxypropanate [$\log K_1 = 2.53$ and $\log\beta_2 = 4.04$, respectively; see Results (v)] being much smaller than those of 2-aminopropanoate ($\log K_1 = 8.09$ and $\log\beta_2 = 14.9$, respectively, see ESI).[16] The values for the complexes of 2-hydroxypropanoate indicate that $\log K_2 = 1.51$. This relatively small value implies the association of CuL with L to be fairly readily reversible and the equilibrium mixture might plausibly contain both *cis* and *trans* isomers. The presence of the *cis* isomer, which has methyl groups on each side of the equatorial plane, would allow some counterbalancing of the electronic and steric effects of methylation to operate in the homo-enantiomeric CuL_2 complex. It should also be recalled that, for want of better, the same interpolated constants were used for the complexes of both stereoisomers of 2-hydroxypropanoate and this might influence their apparent pattern of behaviour.

Relative to Cu^{2+}aq ($k_0^{OH} = 1.47 \times 10^6$ dm^3 mol^{-1} s^{-1}), in the hydroxylation of **2** the CuL complex of 1,2-diaminoethane reacts faster whereas that of 1,2-bis(dimethylamino)ethane (TMEN) reacts slower (*cf*. Table 3, entry 2 and Table 4 entry 5). The steric effect of the *N*-methyl groups has been invoked[31,32] to explain the failure of the CuL complex of TMEN to add a second ligand and, we suggest, this is also the likely cause of the low rate at which this complex is attacked by **2**.

Rationale of the relative magnitudes of k_n^{OH}. In general, in the absence of major π-effects, the octahedral ligand field splitting (Δ_0) increases with the strength of σ-bonding.[64] The enthalpies quoted in Table 8 lead to the expectation that such splittings for the ligands we have used should increase in the order 1,3-dicarboxylate < water ≈ 2-hydroxycarboxylate < 2-aminocarboxylate < 1,2-diaminoethane. The energies ($0.6\Delta_0$)[64] of the degenerately occupied e_g orbitals of notional octahedral copper complexes would therefore also increase in this order. However, actual complexes undergo tetragonal (Jahn–Teller) distortion, the magnitude of which relates to the extent of the splitting of the e_g orbitals which removes the degeneracy.[56] The ordering of the energies of the a_{1g} molecular orbitals of largely d_{z^2} character to which we have related the reactivities of different complexes will therefore depend (in the absence of steric effects) on the extent to which their distortion-related stabilisation compensates for the octahedral ligand field splitting. Since tetragonal distortion weakens axial bonds to copper and strengthens equatorial bonds,[56] a larger compensation might be expected for those ligands which form the stronger equatorial bonds, *i.e.* those which cause a large ligand field splitting. The narrow range of the values of $10^{-6}k_1^{OH}$/dm^3 mol^{-1} s^{-1} found for the unmethylated CuL indicates a good measure of compensation and their ordering, in comparison with that expected for the ligand field splitting, shows the large effect for 1,2-diaminoethane: 1,3-dicarboxylate (5.45) > 2-aminocarboxylate (4.71) > 1,2-diaminoethane (3.88) > 2-hydroxycarboxylate (3.74) > water ($10^{-6}k_0^{OH}$/dm^3 mol^{-1} s^{-1} = 1.47). 1,2-Diaminoethane is the only ligand studied where $k_2^{OH} < k_0^{OH} < k_1^{OH}$, behaviour which must be of electronic origin as there are no hindering substituents and the displacements of the methylene groups from the equatorial plane are small;[65] thus here further significant stabilisation of the a_{1g} orbital must accompany the second ligation. That the splitting between the b_{1g} SOMO (largely metal $d_{x^2-y^2}$) and the doubly occupied a_{1g} MO (largely metal d_{z^2}) is large for CuL_2 (L, 1,2-diaminoethane) is shown by the large energy of the electronic transition between the two orbitals [18.0×10^3 cm^{-1};[56] *cf*. (7–10) × 10^3 cm^{-1} for Cu^{2+}aq[66]] and there is also crystallographic[67] and other solution-phase X-ray diffraction[68] and EXAFS evidence[69] of the large tetragonal distortion in CuL_2. In contrast to the diamine, all the carboxylate-containing ligands are anionic. Addition of a second ligand in these cases raises the energy of the filled a_{1g} orbital, narrowing the energy gap to the SOMO of the attacking radical and hence increasing reactivity: $k_2^{OH} > k_1^{OH}$

Adduct decomposition. We initially assumed a water ligand to be necessary for hydroxylation to occur in order to allow for the possibility of S_H2-type ligand transfer. As we have found the latter does not happen, the assumption needs reconsideration. All of the adducts formed between **2** and the copper(II) complexes ultimately form **5** but, since the structures of the transient adducts are unknown, it is not clear how this occurs. It may not be appropriate to infer reductive elimination, *i.e.* an intramolecular reaction in which a ligated water molecule provides the OH function of **5** and intermolecular solvolysis is

probably the safer assumption. In the case of aliphatic radical-adducts, it has been suggested that nucleophilic participation by the solvent at the C-atom bonded to Cu assists the displacement of the bonding pair of electrons towards the metal in the decomposition of the covalent Cu(III) adduct to Cu(I) and a hydroxylated organic molecule.[70] The probable role of axially ligated water in hydroxylation is merely to be readily displaced by the incoming radical.

Conclusions

When 2-benzoylphenyl radical (a radical clock) is produced in solutions containing Cu^{2+} with various bidentate ligands, multiple linear regression may be used to relate pH-dependent ratios of radical-derived products to the equilibrium concentrations of the copper complexes present at a particular pH. Knowing the rate of cyclisation of the radical, rate constants for its reaction with individual complexes may be evaluated from the regression coefficients. If prior assumptions regarding the relative reactivities of solute species lead to rate constants of improved precision in comparison to those obtained with no such assumption, it is inferred that the assumptions reflect chemical fact. The inference is justified by the relative magnitudes of such rate constants being amenable to interpretation in terms of mechanism.

It is concluded that aryl radicals react with Cu(II) complexes of bidentate organic ligands in two competitive reactions, the one leading to the oxidation (hydroxylation) of the radical, the other to its reduction (H-transfer). In both cases the radical attack has electrophilic character. This is shown for the hydroxylation reaction by the effect on reaction rate of the ionic charge and the effect of non-sterically hindering methylation of the ligand. It is shown for the H-transfer reaction by the fact that coordination by Cu^{2+} reduces the reactivity of the ligand relative to that it has as a free species in the same state of protonation.

The mechanism of hydroxylation is suggested to involve reaction of the aryl radical at the copper centre of a complex to produce a transient organometallic intermediate which is formally a Cu(III) species; on this account, the C–Cu bond is expected to be essentially covalent. Addition to the metal centre is supported by the observation of steric hindrance by some patterns of methylation of the ligand and by the fact that comparable adducts of aliphatic radicals are known which have been characterised spectroscopically.

Assuming tetragonally distorted octahedral complexes of an effective symmetry which orders the energies of the molecular orbitals of largely d character as $d_{x^2-y^2} > d_{z^2} > d_{xy} > d_{xz}, d_{yz}$, the SOMO of the complex is in the equatorial plane of the metal ion and hence is hindered by the ligands themselves from significant σ-overlap with the SOMO of the aryl radical. This inaccessibility of the SOMO of the complex results in its effective frontier orbital being the doubly occupied d_{z^2}-weighted MO which can achieve significant σ-overlap with the radical SOMO in the *z*-axis of the complex. Interaction of the radical SOMO with a filled MO of lower energy accounts for the electrophilic character of the radical's attack and the rise in the energy of the d_{z^2}-weighted MO towards that of the radical SOMO on addition of a second ligand accounts for the enhanced reactivity observed for CuL_2 complexes relative to CuL complexes when L is anionic. Conversely, when L is 1,2-diaminoethane, there is no change in ionic charge on ligation and the second ligation stabilises the effective frontier orbital and reduces reactivity. The activation barrier to the addition of two odd-electron species is suggested to stem from the inaccessible nature of the SOMO of the complex and the need for substantial orbital reorganisation in order to arrive at a spin-paired product.

The mechanism of H-transfer is the S_H2 abstraction of ligand methylene hydrogen atoms. This process is enhanced by monomethylation of geminal methylene positions which converts the incipient radical from secondary into tertiary and is greatly inhibited by methylation of both sites which results in derived radicals being primary and without mesomeric stabilisation from adjacent functional groups. For 2-amino-carboxylates and 2-hydroxycarboxylates, the relative reactivity as H-donors of the complexes CuL and CuL_2 is statistically determined; however, for these complexes of 1,3-dicarboxylates and diamines where, respectively, one or both carries a double charge, there is an additional electronic factor which we suggest results from ligand polarisation effects.

Experimental

(i) Materials

An aqueous master solution of $Cu(NO_3)_2$ (*ca.* 1 mol dm^{-3}) was made up gravimetrically and standardised by atomic absorption spectrometry on an accurately diluted sample; the analytical concentration of the master solution was 1.111 mol dm^{-3}. Aliquots (50 cm^3) were diluted 10-fold to give the working copper solutions (0.111 mol dm^{-3}). Commercial concentrated aqueous solutions of hydroxyethanoic acid (glycolic acid) and (±)-2-hydroxypropanoic acid [(±)-lactic acid] were standardised by NaOH titration and diluted to give working solutions (0.555 mol dm^{-3}). Solutions of the same concentration were made up gravimetrically for the remaining ligands

(ii) Radical clock experiments

Procedure varied slightly between experimentalists but the following is typical. To a solution of $Cu(NO_3)_2$ (25 cm^3, 0.111 mol dm^{-3}) contained in a 150 cm^3 beaker was added a solution of a chosen ligand (10 cm^3, 0.555 mol dm^{-3}), a concentrated solution of KOH or HNO_3, dropwise, as necessary to adjust the pH to a convenient value and a weighed amount of KNO_3 [see (iii) below] to adjust the final ionic strength (usually to 1 mol dm^{-3}); water was added to give a volume of 49 cm^3 and the pH checked and recorded to the nearest 0.01 units. To the magnetically stirred solution was added 2-benzoylbenzene-diazonium tetrafluoroborate,[6] **1** (30–35 mg), accurately weighed. When the diazonium salt had dissolved, a solution of ascorbic acid (1 cm^3, 1.5×10^{-2} mol dm^{-3}) was added to initiate the decomposition of **1**. At initiation, the concentrations of copper and ligand were 0.0555 and 0.111 mol dm^{-3}, respectively; the concentration of **1** was $(2.0–2.4) \times 10^{-3}$ mol dm^{-3} and the concentration of initiator was 3×10^{-4} mol dm^{-3}. The reaction mixture was stirred at ambient temperature for 15–20 minutes and then extracted with 25 cm^3 ethyl ethanoate.

(iii) Analysis

The reaction extracts were analysed by GLC using a Varian 3350 chromatograph equipped with an Alltech Econocap FFAP capillary column (30 m) and served by a Varian Star Workstation. The instrumental ratios of radical clock products were corrected to molar ratios by means of correction factors obtained by prior calibration using authentic materials. When reaction accountabilities were required a known amount of dibenzofuran, as internal standard, was included in the extraction solvent.

The distribution of species in each mixture was calculated for a particular pH using the program ES4EC1.[15] An initial set of calculations was run for a wide range of pH values at intervals of 0.5 units. From this set the range of pH was identified in which species concentrations changed most and which was hence useful for experiments (solubility permitting). The intrinsic ionic strengths of the mixture at intervals of 0.5 pH unit were also calculated and the amounts of KNO_3 required to bring the total ionic strength to its chosen value during runs at

any particular experimental pH were found by interpolation between these intervals.

The concentrations of relevant species and the corresponding product ratios were manipulated and analysed using *Essential Regression*,[71] an add-in for the Microsoft Excel spreadsheet.

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