

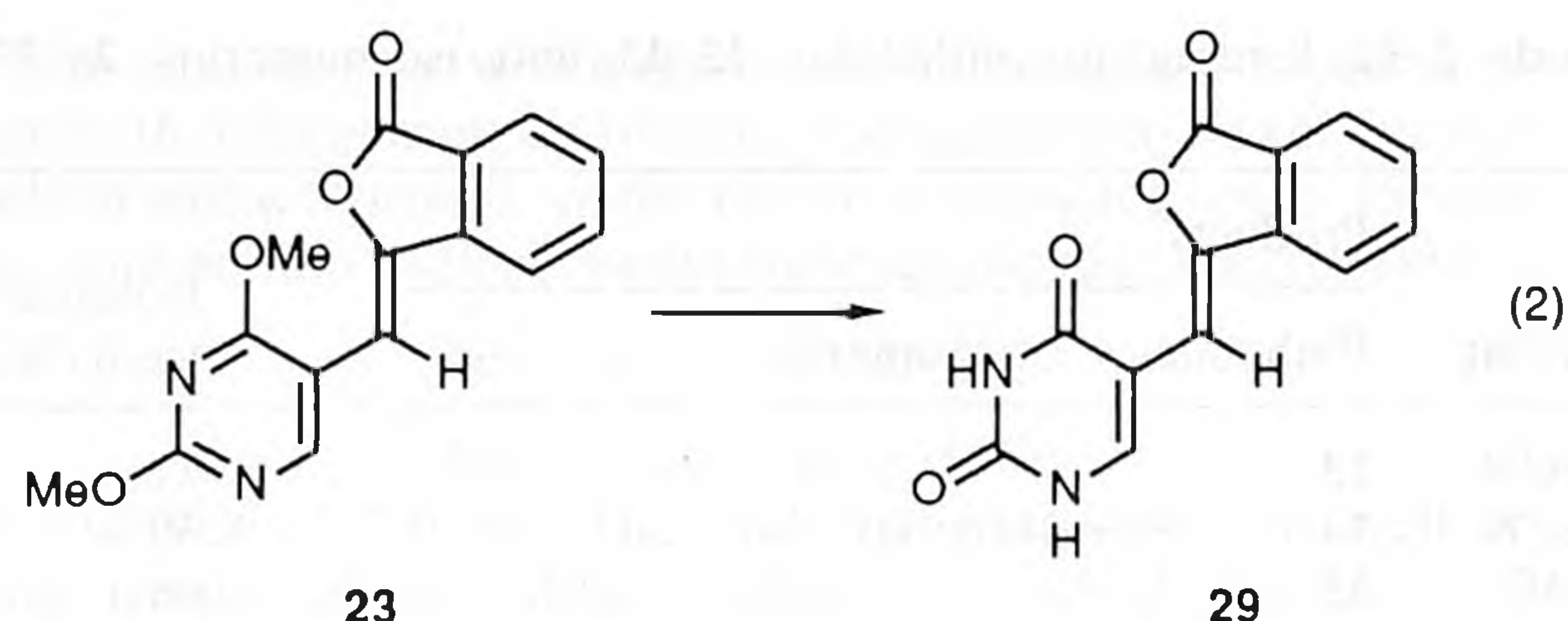
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oids.¹³ Again, compound **23** was demethylated to a novel 5-substituted uracil derivative **29** of potential biological interest [eqn. (2)].⁹ Also, the alkylidene phthalides are precursors to other compounds (indones, indandiones) of biological interest.¹⁴

The mechanism of the reaction can be envisaged to proceed according Scheme 1.^{15,16‡}

Thus, we have described the first successful palladium-catalysed reaction for the synthesis of phthalides from readily available starting materials. The method is easy to carry out under relatively mild conditions, catalytic in palladium reagents, and does not involve any toxic reagents. The process is thus amenable to the synthesis of various phthalide-containing naturally occurring substances and compounds of biological interest.

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‡ Compound **28** was converted mainly to the phthalide either with (Ph₃P)₂PdCl₂ (cat.), CuI (cat.), Et₃N in benzene at room temp. for 20 h, or, (Ph₃P)₂PdCl₂ (cat.), NaHCO₃ in DMF at 60 °C for 12 h, or, (Ph₃P)₂PdCl₂ (cat.), Et₃N in benzene at room temp. for 20 h¹⁸ proving compound **28** to be an intermediate towards the phthalide synthesis.

Redox Behaviour of Novel Copper(II) Crown Ether-Pyrazole Complexes

Constantinus F. Martens,^a Albert P. H. J. Schenning,^a Robertus J. M. Klein Gebbink,^a Martinus C. Feiters,^a Johannes G. M. van der Linden,^b Jürgen Heck^b and Roeland J. M. Nolte^{*a}

^a Departments of Organic and ^bInorganic Chemistry, NSR Center, University of Nijmegen, Toernooiveld, 6525 ED Nijmegen, The Netherlands

A novel dinuclear copper(II) diazacrown ether complex reduces in solution to the copper(I) state; the related mononuclear copper(II) monoazacrown ether complex undergoes reduction, when K⁺-ions are added.

One of the most challenging themes in bioinorganic chemistry is the mimicking of the dinuclear copper sites in copper proteins such as haemocyanin and dopamine-β-hydroxylase.¹ The former protein is responsible for dioxygen transport in arthropods and molluscs,² the latter enzyme is vital for the biosynthesis of noradrenaline.³ The binding of dioxygen to

haemocyanin occurs through the cooperative action of both copper ions present in the active centres⁴ and can be influenced by pH,⁵ anions⁶ and cations.⁷ Model systems mimicking this behaviour could provide insight into the mechanistic action of these biomolecules.

In the literature only a few examples are known of dinuclear

copper(II) complexes that reduce to the copper(I) state.⁸ We present here a novel dinuclear copper(II) crown ether-dimethylpyrazole complex **1**, which in methanol solution is reduced to the copper(I) state, even in the presence of air. The related complex **2** undergoes a much slower reduction under these conditions. This process, however, can be enhanced and controlled by the addition of alkali metal ions.

The ligands from which **1** and **2** are derived were synthesized by treating α -bromo- α' -{bis[2-(3,5-dimethyl-1-pyrazolyl)ethyl]amino}-*m*-xylene† with the corresponding diaza- and aza-crown ethers in dimethylformamide (DMF). The yield after column chromatography (silica 60H, eluent CHCl_3 -MeOH-triethylamine, 97.5:2:0.5, v/v/v) for both ligands was approximately 55%. The ligands were mixed with 2 equiv. (for **1**) and 1 equiv. (for **2**) of $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ in methanol to give the di- and mono-nuclear complexes **1** and **2** in 77 and 80% yield, respectively.‡ During the synthesis of **2** a dark-green colour developed, typical for this type of copper(II) complex. The homogeneous solution of **1**, however, decolorized rapidly, indicating the formation of a copper(I) complex. Proof that **1** indeed had reduced to the copper(I) state came from electrochemical experiments on samples of **1** and **2**, obtained from these reactions. A solution of **2** in acetonitrile [0.1 mol dm^{-3} (Bu^n)₄PF₆, Pt-electrode] showed a reversible wave with $E_{1/2} = 0.29 \text{ V}$ (vs. Fc⁺/Fc, $\Delta E_p = 0.12 \text{ V}$, $i_b/i_f = 1$). The equilibrium potential ($E_{\text{c}q}$) of the solution was 0.50 V, proving that **2** indeed is a Cu^{II} complex. Complex **1** also showed a reversible wave at approximately the same potential ($E_{1/2} = 0.31 \text{ V}$, $\Delta E_p = 0.18 \text{ V}$, $i_b/i_f = 1$) as found for **2**. The equilibrium potential of this solution was 0.15 V, clearly indicating that **1** was present in the form of a reduced complex. In view of the broad forward oxidation peak and the presence of two copper atoms, it is clear that **1** can be oxidized in two consecutive one-electron steps following an EE-reaction path. The half-wave potentials of these steps were calculated by the method of Richardson and Taube and amounted to $E_{1/2}(\mathbf{1}) = 0.29 \text{ V}$ and $E_{1/2}(\mathbf{2}) = 0.32 \text{ V}$.⁹

For the reaction $\text{Cu}^{\text{I},\text{I}} + \text{Cu}^{\text{II}} \rightleftharpoons 2\text{Cu}^{\text{I},\text{II}}$ we can calculate from the $\Delta E_{1/2}$ (30 mV) a comproportionation constant $K_c = 4$.§ This value suggests that there is hardly any interaction between the two copper centres in the electrochemical reduction of **1**. This is not unexpected in view of the large metal-metal distance [$\sim 18 \text{ \AA}$ from Corey-Pauling-Koltun (CPK) models] in the complex. The chemical reduction reaction follows a pathway different from the electrochemical oxidation/reduction of **1**. We assume that in the former case a cooperative action between the two copper(II)-centres is necessary to achieve the observed reduction of complex **1**. This is based on our observation that formaldehyde is produced during the reaction (fuchsine test): a two electron

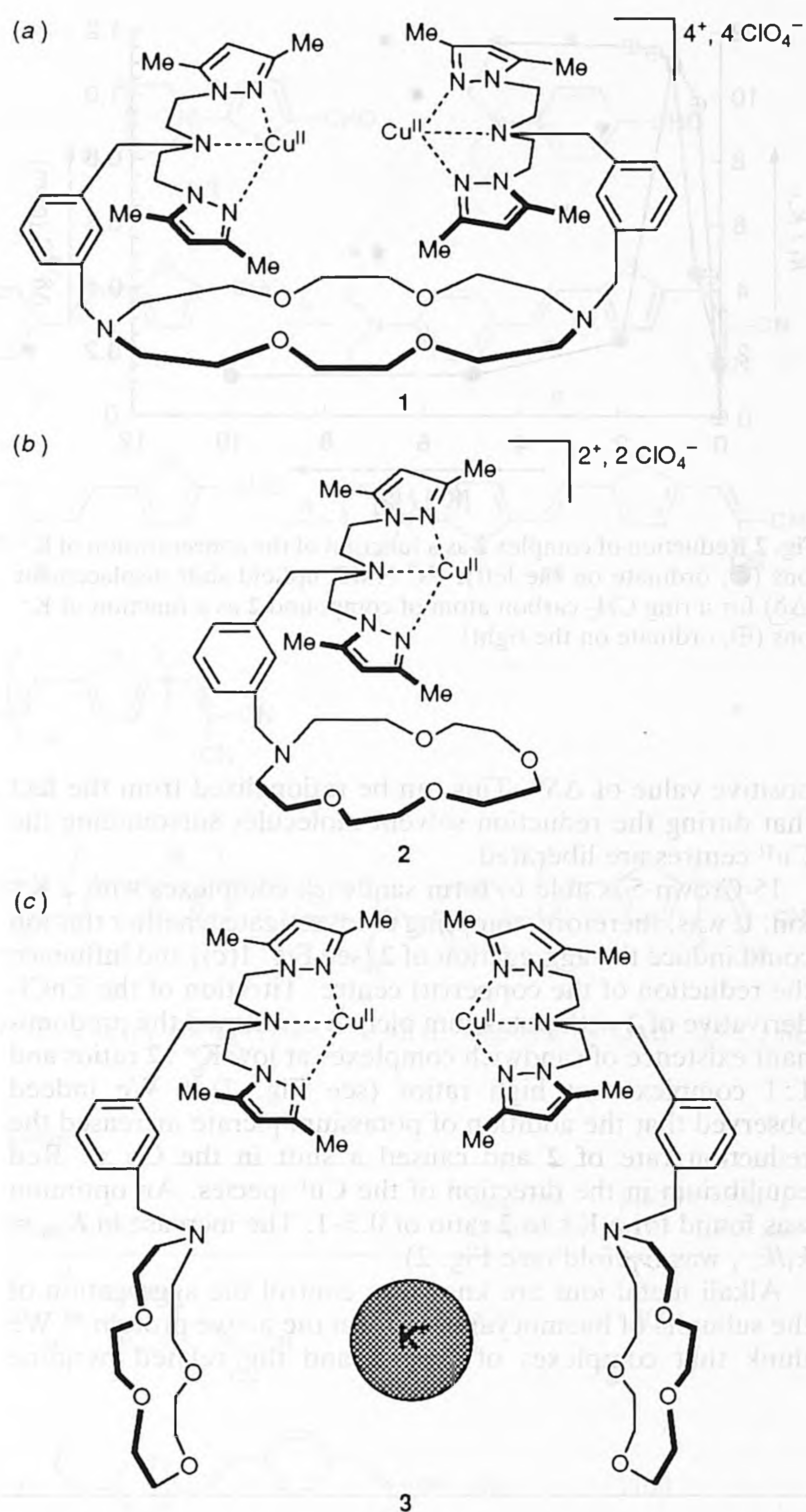


Fig. 1

oxidation of methanol requires two copper(II) ions as electron acceptors. This reaction probably takes place in a μ -alkoxo (or μ -hydroxo) bridged complex, as described by Nelson and Drew.^{8a} Subsequent electron transfer and liberation of the aldehyde will yield the dinuclear copper(I) complex.

The progress of the reduction of **1** (2.5 mmol dm^{-3} , acetonitrile-methanol 1:1, v/v) was followed by UV-VIS spectroscopy, measuring the decrease of the d-d absorption band at 700 nm as a function of time and temperature. Rate constants and equilibrium constants were obtained by standard procedures assuming the equilibrium $\text{Ox} \xrightleftharpoons[k_{-1}]{k_1} \text{Red}$.¶

The following parameters were obtained: forward reaction $\Delta G^\ddagger_{333 \text{ K}} = 88 \text{ kJ mol}^{-1}$, $\Delta H^\ddagger = 48 \text{ kJ mol}^{-1}$, $\Delta S^\ddagger = -120 \text{ J mol}^{-1} \text{ K}^{-1}$ and $E_a = 50.6 \text{ kJ mol}^{-1}$; $\Delta G^\circ = -4 \text{ kJ mol}^{-1}$, $\Delta H^\circ = 17 \text{ kJ mol}^{-1}$ and $\Delta S^\circ = 63 \text{ J mol}^{-1} \text{ K}^{-1}$. The negative entropy of activation points towards a highly ordered transition state, thus supporting our proposed mechanism. The overall reaction is entropy driven as can be seen from the

† This compound was synthesized from 1 equiv. of bis[2-(3,5-dimethyl-1-pyrazolyl)ethyl]amine and 3.5 equiv. of *m*- α,α' -dibromoxylene in tetrahydrofuran-benzene (1:1, v/v). Yield 51% after column chromatography (silica 60H, eluent 3% methanol in chloroform). $R_f = 0.22$. ¹H NMR (CDCl_3) δ 2.1 (s, 6H, CH_3), 2.2 (s, 6H, CH_3), 2.9 (t, 4H, NCH_2CH_2), 3.6 (s, 2H, ArCH_2N), 3.9 (t, 4H, NCH_2CH_2), 4.5 (s, 2H, ArCH_2Br), 6.8 (s, 2H, Pyrazole H), 7.1-7.4 (m, 4H, ArH); Mass spectrometry (m/z) 364 (20%, M - Br).

‡ Selected spectral data for complex **1**: UV-VIS (MeCN-MeOH, 1:1, v/v) $\lambda_{\text{d-d}}$ /nm (ϵ) 695 (140); $\Lambda = 253 \mu\text{S cm}^{-1}$ (1 mmol dm^{-3} in MeCN); FAB-MS: m/z (*m*-nitrobenzylalcohol) 1414 ($\text{M}^+ - \text{ClO}_4^-$), 1314 ($\text{M}^+ - 2 \text{ ClO}_4^-$); IR (CsI, v/cm^{-1}) 1552 (pyrazole), 1097, 624 (ClO_4^-); satisfactory elemental analyses was obtained. For complex **2**: UV-VIS (MeCN-MeOH, 1:1, v/v) $\lambda_{\text{d-d}}$ /nm (ϵ) 691 (80); $\Lambda = 210 \mu\text{S cm}^{-1}$ (1 mmol dm^{-3} in MeCN); FAB-MS: m/z (*m*-nitrobenzylalcohol) 645 ($\text{M}^+ - 2 \text{ ClO}_4^-$); IR (CsI, v/cm^{-1}) 1553 (pyrazole), 1097, 624 (ClO_4^-). No reproducible elemental analysis could be obtained for oil **2**.

§ $K_c = \exp[n_1 n_2 F(\Delta E_{1/2})/RT] = \exp[\Delta E_{1/2}/25.69]$ at 298 K with $n_1 = n_2 = 1$.⁹

¶ The rate constants k_1 and k_{-1} follow from the equilibrium constant $K = k_1/k_{-1}$ and from $k = k_1 + k_{-1}$.¹³ The latter k is obtained by fitting absorbance (A) - time (t) data points to the equation $A_t = [A_0/(K + 1)] \times [1 + (K \times \exp(-k \times t))]$.

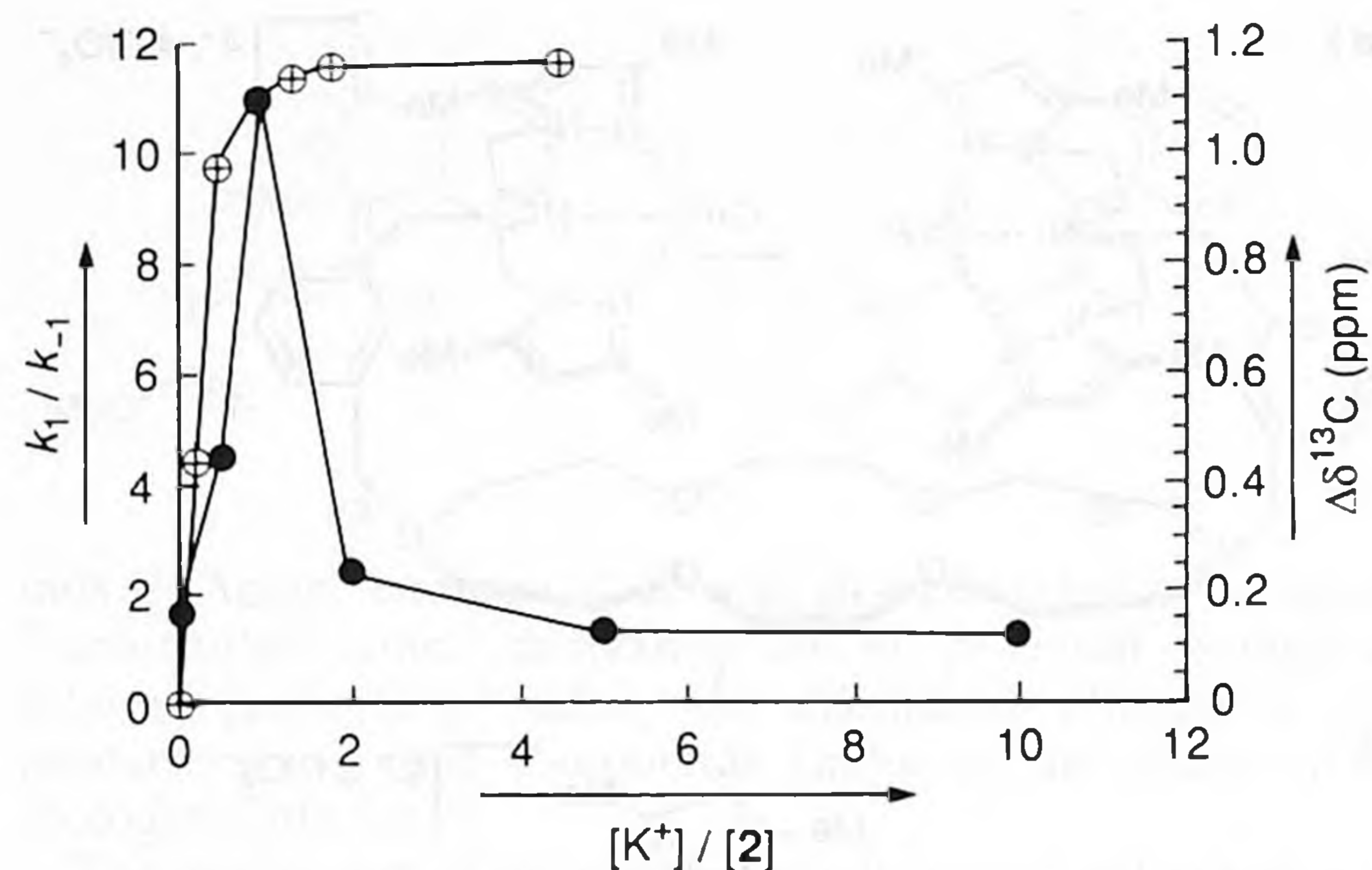


Fig. 2 Reduction of complex **2** as a function of the concentration of K⁺ ions (●, ordinate on the left); ¹³C NMR upfield shift displacement (Δδ) for a ring CH₂ carbon atom of compound **2** as a function of K⁺ ions (⊕, ordinate on the right)

positive value of ΔS[‡]. This can be rationalized from the fact that during the reduction solvent molecules surrounding the Cu^{II} centres are liberated.

15-Crown-5 is able to form sandwich complexes with a K⁺ ion. It was, therefore, tempting to investigate whether this ion could induce the aggregation of **2** [see Fig. 1(c)] and influence the reduction of the copper(II) centre. Titration of the ZnCl₂ derivative of **2** with potassium picrate confirmed the predominant existence of sandwich complexes at low K⁺ : **2** ratios and 1:1 complexes at high ratios (see Fig. 2).¹⁰ We indeed observed that the addition of potassium picrate increased the reduction rate of **2** and caused a shift in the Ox ⇌ Red equilibrium in the direction of the Cu^I species. An optimum was found for a K⁺ to **2** ratio of 0.5–1. The increase in K_{eq} = k₁/k₋₁ was fivefold (see Fig. 2).

Alkali metal ions are known to control the aggregation of the subunits of haemocyanin to form the active protein.¹¹ We think that complexes of type **2** and the related pyridine

complexes may be used to mimic this process. Work along this line is in progress.¹²

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Functionalized Thiophenes: Second-order Nonlinear Optical Materials

Alex K-Y. Jen,* V. Pushkara Rao,* K. Y. Wong and Kevin J. Drost

EniChem America Inc., Research and Development Center, 2000 Cornwall Road, Monmouth Junction, New Jersey 08852, USA

It is shown experimentally that the complete replacement of benzene rings with thiophene rings in a donor–acceptor substituted stilbene significantly enhances its second-order nonlinear optical hyperpolarizability (β); results obtained with a series of thiophene-substituted donor–acceptor compounds with different conjugation lengths reveal a power law dependence of βμ on the molecular conjugation length.

Organic materials with second-order nonlinear optical (NLO) properties have been the subject of intense investigations owing to their exceptionally large nonlinearity and ultrafast response times.¹ These materials have potential applications in areas such as telecommunications, optical information processing and data storage.² Major research efforts have focused on developing NLO chromophores possessing large molecular nonlinearity and good thermal stability as well as improved solubility and processability.

It is well-known that the second-order molecular nonlinear optical hyperpolarizability (β) increases with increasing donor and acceptor strengths and with increasing length of conjuga-

tion.³ Many donor–acceptor conjugated organic molecules reported in the literature fall into the following categories: substituted benzenes, biphenyls, stilbenes, azobenzenes and Schiff bases.^{4–7} In all these classes, benzene ring(s) with or without the π-bridges have been employed as the conjugating moieties to connect donor and acceptor functional groups. However, optical studies on compounds containing more than two benzenoid rings have been limited. This could be attributed, in part, to the difficulty in the synthesis of extended conjugated compounds possessing more than two benzenoid rings as they are practically insoluble in most common organic solvents.