Inorganica Chimica Acta, 28 (1978) L161–L162

Coordination Catalysis: The Comparative Effects of Complex Charge and Ligand Structure on the Activation of Amino Acids Coordinated to Cobalt(III)

P. R. NORMAN* and D. A. PHIPPS†

Department of Chemistry and Biochemistry, Liverpool Polytechnic, Byrom Street, Liverpool, L3 3AF, U.K.

Received April 1, 1978

The base-catalysed reactions such as ^1H–^2H exchange or the Knoevenagel-type condensations with aldehydes, which occur at the α-carbon of the amino acid ligand in complexes of the type $[Co^{III}(en)_2AA]^{2+}$ (where AA is the anion of an amino acid) are thought to proceed via a carbanion intermediate [1, 2]. This labilisation of the C–H bond reflects an activation induced by coordination and the effects of changing the metal, and of ligand conformation for related amino-carboxylate complexes, have been outlined in earlier communications [3, 4]. As a continuation of these investigations into the general phenomenon of ligand activation, we now wish to describe the initial results of our investigatons into the comparative effects of variations in the overall charge on the complex and alterations in ligand structure.

Previous reports by Buckingham *et al.* [2] and by Dabrowiak and Cooke [5] indicated that the reactivity in the base-catalysed condensation of acetaldehyde with glycine bound to cobalt(III) seemed to decrease with decreasing positive charge on the complex. Thus the order of reactivity was found to be $[Co^{III}(en)_2gly]^{2+} > [Co^{III}(gly)_3]^{o} > [Co^{III}(ox)_2gly]^{2-}$ and $[Co^{III}(en)_2gly]^{2+} > [Co^{III}en(gly)_2]^{+}$ though the relative position of $[Co^{III}en(gly)_2]^{+}$ in the series is uncertain since the two experiments were carried out under different conditions, and the results were only qualitative; moreover differences were noted between geometrical isomers of this latter complex. We have therefore extended these observations by studying the base catalysed exchange of ^2H for ^1H at the methylene and methine hydrogens of coordinated amino acids in a variety of complexes.

The effect of complex charge was examined in the complexes $[Co^{III}(en)_2gly]^{2+}$, N-1,2,6-$[Co^{III}(gly)_3]^{o}$ and *trans*-N-$[Co^{III}ox(gly)_2]^{-}$. The rate of exchange was determined by dissolving each complex in mildly alkaline deuterium oxide and following the disappearance of the resonance assigned to the methylenic protons of the glycine. In the case of the oxalate complex the glycine ligands are equivalent, but for N-1,2,6, -$[Co^{III}(gly)_3]$ where two stereochemically distinct types glycinate ligands can be distinguished the data in Table I refers to exchange of the more activated ligand [4]. The rate constants given in the table are corrected for base concentration but uncorrected for decomposition and disproportionation. As expected the rate decreases in the order $[Co^{III}(en)_2gly]^{2+} > [Co^{III}(gly)_3] > [Co^{III}ox(gly)_2]^{-}$.

TABLE I. Rate Constants for the ^1H–^2H Exchange in Amino Acids Coordinated to Cobalt(III) (corrected for pH) at 30 °C.

Complex	$k/min^{-1}\ mol^{-1}\ dm^3$
$[Co^{III}(en)_2gly]^{2+}$	7.0
$[Co^{III}(en)_2L\text{-ala}]^{2+}$	0.7 (3.20²)
$[Co^{III}(en)_2$ D-phegly$]^{2+}$	3.0×10^3
N-1,2,6 $[Co^{III}(gly)_3]^{o}$	0.4
trans-N-$[Co^{III}(ox)(gly)_2]^{-}$	3.0×10^{-2}

The effect of substitution within the amino acid ligand was then investigated by similar experiments with the series of complexes of the types $[Co^{III}(en)_2AA]$ where the amino acids used were D-phenylglycine, glycine and L-alanine. Some difficulties were encountered with the phenylglycine complex which readily disproportionated, a phenomenon encountered whenever the amino acid has a bulky side chain [6], but these were overcome by preparing the complex *in situ* in the n.m.r. tube. The results are also shown in Table I.

The value quoted in Table I for $[Co^{III}(en)_2(L\text{-ala})]^{2+}$ differs from that from the work of Buckingham *et al.* [2], but this can be accounted for by considering the inaccuracies in the measurement of pH (pD) together with the decomposition and disproportionation. Though the two data are not entirely in agreement the data given in Table I is internally consistent and clearly shows the trends in reactivity.

The changes within this latter series are more readily rationalised since complex formation should activate each ligand similarly, resulting in an increase in the absolute reactivity for each, but no change in the relative labilities. As expected all the coordinated amino acids did indeed show a much greater reactivity than the corresponding free ligands, which are effectively inert under the conditions used, with the order within the series $[Co^{III}(en)_2D\text{-phegly}l]^{2+} > [Co^{III}(en)_2gly]^{2+} > [Co^{III}(en)_2L\text{-ala}]^{2+}$. This can be attributed to the comparative efficiencies of the phenyl, hydrogen and methyl groups in stabilising the

*Present address: *Department of Chemistry, University of Stirling, Stirling FK9 4LA, Scotland.*

†Author to whom enquiries should be addressed.

carbanion intermediate. Similar effects have been reported [7] for the racemisation of N-benzoyl-L-amino acid anilides in which a carbanion mechanism is also thought to operate.

The effect of changing the overall charge on the complex is comparable with the effect of altering the substituents on the 2-carbon of the ligand, so that it seems that the metal acts as a polarising centre whose influence is controlled by the rest of the coordination sphere. What remains unanswered is whether this is the dominant effect or whether other factors also contribute. Certainly, recent calculations [8] on model systems have shown that coordination can significantly alter the electron density in σ-bonds remote from the sites of coordination, but clearly if the reaction involves proton abstraction from the 2-carbon by hydroxide ion, a positive charge on the complex will favour this through ion-pairing with the nucleophile, though such interactions are not sufficient in themselves to account for the observed changes. Equally entropy effects related to changes in solvation brought about by the changes in charge between reactant and transition state must be considered, but cannot easily be quantified; nor can conformational effects in the ligand since these cannot even be discussed without accurate structural data which is at present unavailable.

Nevertheless, whatever the detailed explanation, it is clear that the more electron withdrawing capabilities the complex possesses, such a high formal overall positive charge or electron withdrawing groups in the ligand active site, the greater will be the labilisation of the 2–C–H bond and this should be remembered when designing systems for synthetic purposes.

Acknowledgement

We wish to thank the S.R.C. for the award of a research grant in support of this work.

References

1 D. H. Williams and D. H. Busch, *J. Am. Chem. Soc., 87,* 4644 (1965).
2 D. A. Buckingham, L. G. Marzilli and A. M. Sargeson, *J. Am. Chem. Soc., 89,* 5133 (1967).
3 P. R. Norman and A. A. Phipps, *Inorg. Chim. Acta, 17,* L19 (1976).
4 P. R. Norman and D. A. Phipps, *Inorg. Chim. Acta, 24,* L35 (1977).
5 J. C. Dabrowiak and D. W. Cooke, *Inorg. Chem., 14,* 1305 (1975).
6 J. H. Dunlop, R. D. Gillard and R. Ugo, *J. Chem. Soc. A,* 15440 (1966).
7 M. Sato, T. Tatsuno and N. Matsuoko, *Chem. Pharm. Bull., 18(a),* 1791 (1970).
8 D. Demoulin, I, Fischer-Hjalmars, A. Henriksson Enflo, J. A. Pappas, M. Sundbom, *Int. J. Quant. Chem.,* in press.