# Unprecedented Carbon–Nitrogen Bond Formation in Aqua(ethylenediaminetripropionato)chromium(III) with Hydroxycarboxylic Acids

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Carbon–nitrogen bond formation is found to occur through the dehydration between the secondary amine in the aqua(ethylenediaminetripropionato) type chromium(III) complexes and the hydroxy group of hydroxycarboxylic acids simply by allowing the aqueous mixture to stand for several days at room temperature.

This paper reports the anomalous reactivity of a secondary amine exhibiting an unprecedented carbon–nitrogen bond formation in the aqua(ethylenediaminetripropionato)chromium(III) {[Cr(edtrp)($H_2O$)]} type complexes. We have recently reported[1] for two of three novel diastereoisomers (I and II) of ethylenediaminetetrapropionatochromium(III) {[Cr(edtp)]$^-$} and its (*S*)-propane-1,2-diamine and (1*S*,2*S*)-*trans*-cyclohexane-1,2-diamine analogues that a facile C–N bond cleavage at the 3-propionate chelate ring occurs in aqueous solution at 60 °C. In each reaction solution for the I and II isomers, small amounts of the three diastereoisomers of the edtp type complexes were found to exist along with a large amount of the edtrp type complexes.[1] Moreover, from the acid hydrolysed solution which was condensed after monitoring the complete decomposition to the edtrp type complexes by HPLC chromatography, the three diastereoisomers of the edtp type complexes were also detected to form after several months. In order to confirm this peculiar reaction—a reversible C–N bond cleavage—in more detail, we have attempted deliberately to reproduce the edtp type isomers simply by mixing the diaminetripropionato type complexes and 3-hydroxypropionic acid in the following manner.

The starting diaminetripropionato complexes[1] (0.01 g, 2–3 × $10^{-5}$ mol) and 3-hydroxypropionic acid (50% aqueous solution, 1 $cm^3$) were allowed to stand at room temperature (28 ± 1 °C) for a week. The QAE-Sephadex A-25 column chromatography ($Cl^-$ form) of the reaction solution gave three bands by eluting with 0.04 mol $dm^{-3}$ NaCl solution after removing the unconverted edtrp type complexes with water. Each band was identified to be the corresponding edtp type diastereoisomers by absorption and/or circular dichroism (CD) spectra.[1] The total formation yields of the edtp type complexes were estimated to be about 35%.

Such a reproduction of the edtp diastereoisomers from the edtrp complex shows that the C–N bond recombination after the C–N bond cleavage occurs through the dehydration between the secondary amine in the *trans-eq* geometrical isomer[2] of the diaminetripropionato complexes and the hydroxy group of 3-hydroxypropionic acid at room temperature. Similar C–N bond formation in the edtrp type complexes was also observed with the other hydroxycarboxylic acids.

To examine the coordination site where the 3-hydroxypropionate was incorporated into the complex, deuteriated 3-hydroxypropionic acid ($HOCH_2CD_2CO_2H$) was employed for the reproduction of the edtp complexes from the edtrp complex. The I and II isomers obtained from the starting materials above give one and two $^2H$ NMR signal(s), respectively, as shown in Fig. 1(*a*) and 1(*b*). The signal of the I isomer corresponds to the shoulder around δ 23 of the I isomers of fully deuteriated [Cr([$^2H_4$]edtp)]$^-$ [Fig. 1(*c*)].[1] The signals of the II isomer are found to coincide with those at δ 20 and 25 of the II isomers of [Cr([$^2H_4$]edtp)]$^-$ as shown in Fig.

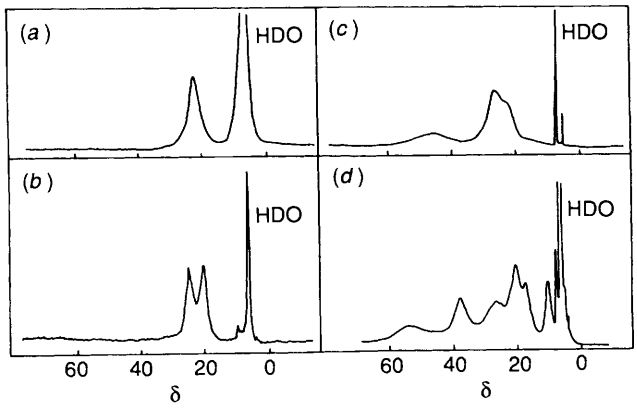
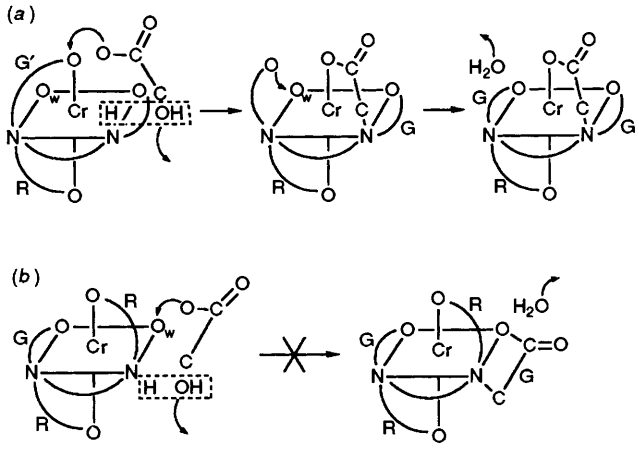



**Fig. 1** The $^2H$ NMR spectra for the diastereoisomers of $[Cr(edtp)]^-$ reproduced from the edtrp complex with deuteriated 3-hydroxypropionic acid [(*a*) I; (*b*) II], and for the fully deuteriated one [(*c*) I; (*d*) II]




**Scheme 1**

1(*d*).[1] For both the isomers, there is no signal around δ 50 assignable to the G-ring[3]. This fact indicates that the deuteriated 3-propionate was incorporated at the R-ring stereoselectively as shown in Scheme 1(*a*), and that no scrambling of the 3-propionate rings occur among the G-ring and R-ring sites. During this incorporation process, the conformational conversions in the six-membered propionato chelates at the R-rings bring about the formation of the three diastereoisomers.

It is found for the analogous ethylenediaminetriacetato complex {[Cr(edtra)($H_2O$)]} that no C–N bond formation occurs with hydroxycarboxylic acids, although an incorporation process through the C–N bond formation in this complex with *cis-eq* configuration[2b] should be much simpler than that in the edtrp type complexes [Scheme 1(*b*)]. In the *trans-eq* edtrp type complexes, the high reactivity even through such a complicated process may arise from the lower acidity of the coordinated water molecule and/or the untypical asymmetric envelope conformation[2] for the diamine chelate as compared with those[2b] of the *cis-eq* edtra complex.

The analogous C–N bond formation in non-aqueous solvents without or with catalysts has been reported for organic compounds.[4,5] In the present case, however, it is to be noted that the C–N bond formation occurs in aqueous solvent in spite of the dehydration reaction and not through the Schiff base condensation as in the generally accepted catalytic reaction pathways.[5] To our knowledge, this is the first example of the C–N bond formation or alkylation in metal complexes which proceeds even under rather mild conditions in acidic aqueous solutions where the C–N bond rupture reaction was found to be promoted with increasing acid concentrations.

Further elucidation of the astonishing C–N bond formation together with the facile C–N bond cleavage in this system could provide a clue to understanding not only the role of metal ions for the enzymatic reversible deamination with ammonialyases,[6] but also the fundamental principles governing the anomalous reactivity for the ligating secondary amine along with the stereochemistry in the complex.

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