Multinuclear Magnetic Resonance Studies on Aluminium Chelates. Part I. Chelates with Catechol and Disodium 4,5-Dihydroxybenzene-1,3-disulfonate

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The complexation of Al^{3+} with catechol and tiron (disodium 4,5-dihydroxybenzene-1,3-disulfonate) has been studied by NMR spectroscopy. The complexes in solution at different pH values were identified by multinuclear (^{27}Al, ^{13}C and ^{1}H) magnetic resonance spectra, and spectrophotometric and potentiometric data. Aluminium formed 1 : 1, 1 : 2 and 1 : 3 chelates with both catechol and tiron depending on the pH and ligand concentration. Disproportionation of the 1 : 1 chelate with tiron at pH 7 gave a mixture of 1 : 2 and 1 : 3 chelates leaving a major amount of aluminium in an uncomplexed form. Both *meridional* and *facial* isomers of $[AlL_3]^{9-}$ (Na_2H_2L = tiron) have been characterised by ^{13}C and ^{1}H NMR. Hydrolysis of the 1 : 1 $Al-L^{4-}$ chelate leading to the formation of $[Al(OH)_4]^-$ occurs *via* the formation of the tetrahedral chelate $[AlL(OH)_2]^{3-}$ (δ 53) as an intermediate. In the Al–catechol (H_2cat) system three complex species coexist with $[Al(OH)_4]^-$ in a 1 : 2 mixture at pH 12.5. Unlike in the Al–tiron system, a tetrahedral 1 : 2 Al–cat chelate (δ 58.5) is also formed during hydrolysis of the octahedral 1 : 2 Al–cat complex.

Phenols, phenolic acids, complex polymeric phenols, fulvic acid and humic acid are the major organic compounds[1] present in soil. Most of these are known to form stable complexes with aluminium and other polyvalent cations. Humic substances may play a considerable role in soil chemistry in modifying the reactivity of aluminium on oxide surfaces, reducing its toxicity in acid soils and binding aluminium in natural fulvic acids. The observation of significant levels of aluminium in certain human pathological conditions such as Alzheimer's disease and the detrimental effects of elevated levels of this element on aquatic life have stimulated considerable research on its co-ordination chemistry in recent years.[2–4] From a detailed study of binding of aluminium to human serum transferrin in the presence of several chelating agents Harris and Sheldon[5] concluded that certain diphenolic ligands might be good candidates for aluminium uptake. Tiron (disodium 4,5-dihydroxybenzene-1,3-disulfonate) is one such chelating agent which does not bind either Ca or Zn. Sulfonation of catechol (benzene-1,2-diol) results in an increase in its solubility in water and complexing ability coupled with improved oxidative stability near neutral pH. Potentiometric studies on chelates of aluminium with catechol[6,7] and tiron[8] have shown the formation of 1 : 1, 1 : 2 and 1 : 3 complexes; for tiron the formation of dimeric and polymeric complexes has been postulated. Martell *et al.*[9] have recently reviewed results of potentiometric studies on aluminium complexes of hydroxy-aliphatic and -aromatic ligands in aqueous systems highlighting the problems encountered and suggested possible solutions. The Al^{3+} ion, by virtue of its low effective ionic radius (0.54 Å), has a very strong tendency to undergo hydrolysis in aqueous medium. At very low concentration (μmol dm^{-3}) mononuclear hydrolytic species are formed, with dinuclear and polynuclear species forming at higher concentrations (mmol dm^{-3}).[1] Complexation of aluminium with simple ligands is slow and equilibration may take hours to days. Also the complex species formed are dependent on the aluminium concentration and pH, and metastable species may also be formed. Hence the conclusions reported by different authors differ in many cases. Martell and Motekaitis[7] have suggested using ^{13}C and ^{1}H NMR studies for characterising the complex species existing in highly alkaline media.

Aluminium-27 NMR spectroscopy is a valuable tool for speciation of aluminium chelates. Formation of $[Al(OH)_4]^-$ gives rise to a sharp signal at δ ≈80 and tetrahedral complexes may also form in alkaline medium. The formation of the latter has not been taken into account in the earlier potentiometric studies. Though detailed ^{27}Al NMR studies have been reported on chelates with aminopolycarboxylic acids[10] and aliphatic hydroxycarboxylic acids[11] very little work has been reported on chelates with phenolic ligands.[12,13] In this paper the results of our ^{27}Al, ^{13}C and ^{1}H NMR as well as spectrophotometric studies on complexes of aluminium with catechol and tiron are reported. Potentiometric studies reported earlier have been utilised for interpretation of some of the results and additional data were collected wherever required.

Experimental

The $AlCl_3$ solution was prepared by dissolving reagent grade crystalline $AlCl_3{\cdot}6H_2O$ in water and was standardised by ethylenediaminetetraacetic acid (H_4edta) titration. Catechol and tiron were obtained from Eastman Organic Chemicals and BDH Chemicals Ltd. respectively. Catechol was purified by vacuum sublimation, while all other chemicals used were of reagent grade. Stock solutions of various complexes were prepared by mixing the $AlCl_3$ solution and ligand in the required molar ratio. As catechol undergoes oxidation at higher pH, stock solution was prepared in deaerated water and maintained at pH 3. Hydrazine hydrate (0.5%) was added to prevent oxidation and the pH was adjusted by addition of either NH_4OH, NaOH or HCl under argon. For the $AlCl_3$–catechol system, precipitation was observed in the pH range 4–7, and the supernatant solutions were used for recording NMR spectra.

NMR Spectra.—The ^{27}Al-{^{1}H} NMR spectra were recorded on a Varian XL 300 spectrometer operating at 78.157 MHz (pulse width, 15–27 μs; flip angle, 90°; acquisition time, 1 s; digital resolution, 0.97 Hz per point; 16 000 data points; spectral width, 8000 Hz, 50–2500 transients; line broadening, 2–20 Hz). Samples were taken in 10 mm NMR tubes with a concentric 5 mm tube containing C_6D_6 for locking. All the chemical shifts are relative to external $[Al(H_2O)_6]^{3+}$ (in H_2O containing 20% D_2O) as reference.

The ^1H and ^{13}C-$\{^1H\}$ NMR spectra were recorded in D_2O on a Bruker 200-AC spectrometer operating at 200.13 and 50.33 MHz respectively (pulse width, 6.2 and 4.9 μs; flip angle, 90°; 8000 data points; spectral width, 3000 and 10 000 Hz; line broadening, 2–8 Hz for ^{13}C; 1–100 transients for ^1H and 1000–5000 for ^{13}C). Sodium 4,4-dimethyl-4-silapentane-1-sulfonate was used as internal reference.

Potentiometric Studies.—Potentiometric titrations were carried out in an atmosphere of high purity argon at an ionic strength of 0.1 mol dm^{-3} KCl using an Elico model LI-120 pH meter equipped with a combination electrode. The concentration of aluminium employed was 10^{-3} mol dm^{-3} and the solution temperature was maintained at 27 ± 1 °C; KOH (0.1 mol dm^{-3}) was used as titrant. The pH meter was calibrated using dilute HCl and KOH solutions adjusted to 0.1 mol dm^{-3} ionic strength as standards.

Spectrophotometry.—Spectrophotometric measurements were carried out on a Shimadzu UV-190 double-beam spectrophotometer at room temperature using 1 cm quartz cells, with water as solvent.

Results and Discussion

The nature of the complex species existing at different pH values was deduced from NMR, potentiometric and spectrophotometric data. Before considering the individual systems it is important to demonstrate the methodology used for interpreting the ^{27}Al NMR spectra. The change in chemical shift on stepwise replacement of co-ordinated water in octahedral $[Al(H_2O)_6]^{3+}$ by monodentate ligands such as acetonitrile is nearly linear which has aided the characterisation even of *cis*/*trans* isomers by consideration of both chemical shift and linewidth.[14] This process is complicated in the case of chelating ligands, and no systematic analysis of the data has been reported except for octahedral aluminium chelates with aminopolycarboxylic acids for which a nearly linear relationship was reported between the ^{27}Al chemical shift and denticity of the ligand.[10] The chemical shifts reported in the literature for octahedral chelates containing five- or six-membered chelate rings indicate a greater shielding in the latter. For tris(bidentate) chelates in which chelation is through either oxygen or both nitrogen and oxygen, chelates with five-membered rings show resonances in the range δ 24–36 while for those with six-membered rings resonances are in the range δ 4.5–8.[15–17] The maximum chemical shift values were found for multidentate ligands (δ 41.2 for edta and 41.5 for alumichrome C[18]). Replacement of H_2O by OH^- in octahedral geometry results in deshielding by 1.5–2 ppm,[10] and the formation of a dimer containing a four-membered ring involving hydroxo bridges also results in a ≈1.5 ppm downfield shift.[19]

These results indicate that it is only possible to distinguish between the chelates AlL_n and AlL_{n-1} (OH) for five-membered chelate rings (H_2L = bidentate ligand, charges and water molecules not indicated, $n = 2$ or 3). Identification of dimers is not possible. Another important aspect is the quantification of the total Al in solution. Of the hydroxo complexes formed during the hydrolysis of aluminium salts, only the polynuclear species $[Al_{13}(OH)_{24}O_4(H_2O)_{12}]^{7+}$ gives a sharp NMR signal due to the tetrahedral aluminium.[1] The octahedral Al surrounding the tetrahedral Al only gives rise to a broad base. Hydrolytic species with very low symmetry may not give any signal. (In some cases as much as 47% of the total aluminium is not accounted for.) The linewidth of the ^{27}Al resonance is dependent on the symmetry around Al and the rate of chemical exchange. Even when the complex species in solution remains the same over a certain pH range, variation in linewidth has been observed possibly due to a change in rate of chemical exchange. In view of the above, quantification of the distribution of the total aluminium among the various species is very difficult. The results of studies on Al^{3+} complexation are discussed in detail below.

Complexes of Catechol (H_2cat).—The aluminium–catechol chelate is very susceptible to oxidation and hence utmost care was necessary to prevent oxidation in the alkaline pH range. The ^{27}Al NMR data for the $AlCl_3$–catechol system are summarised in Table 1. All the potentiometric studies reported previously have shown the formation of 1 : 1 (pH 3–6), 1 : 2 (pH 4.5–8.5) and 1 : 3 (pH > 6.5) chelates with deprotonation of the hydroxyl groups when $c_L/c_{Al} > 3$. In addition, Martell and Motekaitis[7] detected minor amounts of [Al(Hcat)(cat)] and $[Al(Hcat)(cat)_2]^{2-}$ while Ohman and Sjoberg[20] identified $[Al_3(OH)_3(cat)_3]$ (pH 4.5–6.5) and $[Al(OH)(cat)_2]^{2-}$ (pH 6.5–9) as minor species. The 1 : 3 chelate is formed quantitatively at pH 9 when $c_{H_2cat}/c_{Al} = 6$. The species present above pH 9 have not been characterised.

The maximum ^{27}Al chemical shift observed is at δ ≈ 32. The resonances at δ 31.3 and 31.8 ($w_{\frac{1}{2}}$ 340 and 285 Hz respectively) in the spectra of the 1 : 3 and 1 : 2 mixtures can be unequivocally assigned to the 1 : 3 chelate. The $w_{\frac{1}{2}}$ value is approximately half that for the 1 : 3 chelate of aluminium with 3-hydroxy-2-methylpyridine-4-one[21] (δ 37, $w_{\frac{1}{2}}$ 660 Hz) the crystal structure of which shows rigorous three-fold symmetry. Hence it is reasonable to conclude that the 1 : 3 Al–cat chelate is also highly symmetric. In the pH range 4.5–6.5 less symmetric species are formed. The peak at δ 11 in the spectrum of the 1 : 3 Al–H_2cat mixture at pH 4.5 may be assigned to the 1 : 1 chelate while the signal at δ 26 may be attributed to the 1 : 2 Al–cat chelate. From potentiometric studies, it is inferred that the maximum concentration of the monohydroxo 1 : 2 Al–cat chelate occurs at pH 8. The ^{27}Al NMR spectrum of the 1 : 2 Al–H_2cat mixture at pH 7.9 showed a single very broad unsymmetric peak at δ 32 with a shoulder at δ 22–28, which may be attributed to a mixture of $[Al(cat)_3]^{3-}$, $[Al(cat)_2(H_2O)_2]^-$ and $[Al(cat)_2(OH)(H_2O)]^{2-}$. The hydroxo complex could be dimeric. The ^{27}Al NMR studies at high pH revealed the formation of two additional complex species during the reaction of the Al–cat chelate with NaOH leading to the formation of $[Al(OH)_4]^-$. The maximum chemical shift reported so far for an octahedral aluminium chelate is δ ≈41. Hence the resonances observed in the range δ 50–60 may be attributed to tetrahedral complexes. The data for 1 : 1 and 1 : 2 Al–H_2cat mixtures in the pH range 9.5–12.5 are shown in Fig. 1. The spectrum of the 1 : 1 mixture at pH 9.8 shows a broad resonance at δ 53, which is not observed for 1 : 2 mixtures at pH 9.5, 10.5 and 11.5; however, at pH 12.5, a low intensity peak is observed at δ 51.2. Hence the resonance at δ 53 ppm may be assigned to a tetrahedral dihydroxo 1 : 1 Al–cat chelate.

The spectrum of the 1 : 2 Al–H_2cat mixture at pH 9.5 (somewhat noisy) showed an intense peak at δ 56.2 which is shifted downfield to δ 58.1 at 10.5 [Fig. 1(*b*) and (*c*)], and further to δ 58.5 at pH 11.5 and 12.5 [Fig. 1(*d*) and (*e*)]. No peak was observed in this region for the 1 : 1 mixture at pH 9.8 [Fig. 1(*a*)]. An intense peak at δ 60 was reported for aluminium–glycolic acid[22] and -tartaric acid[23] systems in the pH range 9–11 which has been tentatively assigned to a tetrahedrally co-ordinated 1 : 2 Al–carboxylate chelate. Hence the resonance at 58.5 may be assigned to a tetrahedral 1 : 2 Al–catecholate species. Three complex species coexist with $[Al(OH)_4]^-$ in the 1 : 2 Al–H_2cat mixture at pH 12.5.

The ^{13}C spectrum of catechol at pH 7.5 showed three signals. On raising the pH to 12.5 the C^1 resonance was shifted downfield from δ 146.8 to 160.8 due to progressive dissociation of hydroxyl groups. On complexation with aluminium there is a downfield shift of C^1 and C^2 (5–10 ppm) while the other carbon resonances are shifted upfield; however at pH 12.5 C^1 and C^2 are also shifted upfield (3 ppm). The difference may be

Table 1 Aluminium-27 NMR data on aluminium–catechol complexes[a]

pH	$\delta(^{27}Al)$[b]	$w_{\frac{1}{2}}$/Hz	Assignment
4.5	11.0	v br	$[Al(cat)(H_2O)_4]^+$
5.2	26.0	1720	$[Al(cat)_2(H_2O)_2]^- + [Al_3(cat)_3(OH)_3]$[c]
6.5	26.0	1500	$[Al(cat)_2(H_2O)_2]^- + [Al_3(cat)_3(OH)_3]$[c]
7.5	32.0	715	$[Al(cat)_3]^{3-} + [Al(cat)_2(H_2O)_2]^- + [Al(cat)_2(OH)(H_2O)]^{2-}$
8.5	31.5	410	$[Al(cat)_3]^{3-} + [Al(cat)_2(OH)(H_2O)]^{2-}$
9.5	31.3	340	$[Al(cat)_3]^{3-}$

[a] Total concentration of catechol c_{H_2cat} = 0.3 mol dm^{-3}, c_{Al} = total concentration of aluminium = 0.1 mol dm^{-3}. [b] Relative to external $[Al(H_2O)_6]^{3+}$ in H_2O ($AlCl_3$, 1 mol dm^{-3}) containing 20% D_2O. Positive shifts represent deshielding. [c] Deduced from potentiometry.[20] Water molecules not included since the composition is the average of species with different degrees of polymerisation.

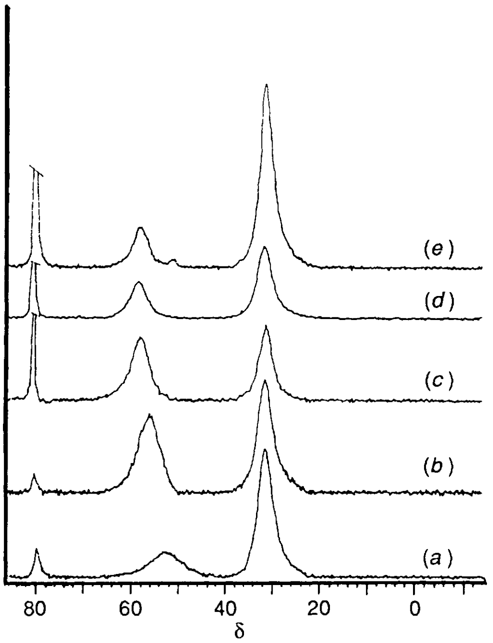

Fig. 1 ^{27}Al NMR spectra of mixtures of (*a*) $AlCl_3$–catechol (1:1), c_{Al} = 0.1 mol dm^{-3}, pH 9.8, and $AlCl_3$–catechol (1:2), c_{Al} = 0.1 mol dm^{-3}, at pH 9.5 (*b*), 10.5 (*c*), 11.5 (*d*) and 12.5 (*e*)

attributed to the fact that while complete deprotonation of the OH groups occurs in the ligand, the O groups are co-ordinated to Al with a high extent of covalency in the complex.

The spectrum of 1:2 Al–H_2cat mixture at pH 7.5 showed only three resonances. However, line broadening indicates the presence of more than one complex (potentiometry showed three species while ^{27}Al NMR spectra suggested at least two). At pH 9.5, the spectrum suggests the existence of two complexes. Only one complex is found in the 1:3 Al–H_2cat mixture at pH 9.5 which exhibits resonances at δ 157.2 and 118.7 assigned to C^1 and C^4, respectively. Accordingly, the resonances at δ 157.2 and 118.6 in the 1:2 Al–H_2cat mixture at pH 9.5 can be attributed to the 1:3 Al-chelate. For the second species, the C^1 resonance was observed upfield and C^4 downfield with respect to those of the 1:3 chelate (Table 3). This suggests that this complex is a tetrahedral chelate, confirming the structure inferred earlier from ^{27}Al NMR data. The other spectra do not show the presence of either free catechol or more than one complex species, though these are known to exist in some cases.

At pH 9.5, the ^1H NMR spectrum of free catechol showed two *ortho*-coupled doublets at δ 6.64 (J = 5.5, H^6 and H^3) and 6.74 (J = 5.5 Hz, H^5 and H^4), which were shifted upfield to δ 6.20 and 6.10 respectively at pH 12.5. On complexation both these peaks shifted upfield and appeared as one signal. A 1:3 $AlCl_3$–catechol mixture at pH 9.5 gave only one broad multiplet at δ 6.6.

Table 2 Aluminium-27 NMR data on aluminium–tiron complexes[a]

c_L/c_{Al}	pH	$\delta(^{27}Al)$[b]	$w_{\frac{1}{2}}$/Hz	Assignment
1	7.0	27.5	795	$[AlL_2(H_2O)_2]^{5-}$
1	7.0	36.1	705	$[AlL_3]^{9-}$
1	10.5	36.4	470	$[AlL_3]^{9-}$
1	10.5	80.2	23	$[Al(OH)_4]^-$
2	7.2	27.5	555	$[AlL_2(H_2O)_2]^{5-}$
2	7.2	36.3	795	$[AlL_3]^{9-}$
2	9.0	35.5	475	$[AlL_3]^{9-}$
2	9.0	80.0	75	$[Al(OH)_4]^-$
2	10.5	36.1	450	$[AlL_3]^{9-}$
2	10.5	80.3	20	$[Al(OH)_4]^-$
2	13.5	36.1	575	$[AlL_3]^{9-}$
2	13.5	53.0	—	$[AlL(OH)_2]^{3-}$
2	13.5	80.3	30	$[Al(OH)_4]^-$
3	3.0	0.10	50	$[Al(H_2O)_6]^{3+}$
3	3.0	15.7	v br	$[AlL(H_2O)_4]^-$
3	6.1	36.2	1120	$[AlL_3]^{9-}$
3	7.0	35.1	675	$[AlL_3]^{9-}$
3	10.0	35.6	711	$[AlL_3]^{9-}$
3	12.6	36.5	505	$[AlL_3]^{9-}$
3	13.5	36.0	525	$[AlL_3]^{9-}$

[a] c_{Al} = 0.1 mol dm^{-3}. [b] Relative to external $[Al(H_2O)_6]^{3+}$ in H_2O ($AlCl_3$, 1 mol dm^{-3}) containing 20% D_2O. Positive shifts represent deshielding.

Complexes of Tiron (Na_2H_2L).—Tiron forms soluble chelates over the entire pH range and no precipitation was observed even when the $AlCl_3$–tiron mole ratio was 1:1. Aluminium-27 NMR data for the Al–tiron system are summarised in Table 2.

In some cases the ^{27}Al spectra are very broad and show a lot of noise. This is more pronounced in the presence of either excess of Al or of ligand. The broad resonances of the 1:3 Al–L^{4-} ^{13}C spectra obtained at pH 7 were resolved on raising the pH to 9.0.

At pH 7, the ^1H NMR spectrum of free tiron in D_2O shows two *meta*-coupled doublets (J = 1.8 Hz) at δ 7.66 and 7.42 assigned to H^2 and H^6 respectively. In the ^{13}C NMR spectrum all six carbon resonances are well resolved with the substituted carbons having weak signals. Of these, C^4 and C^5 are the furthest downfield with resonances for $C^1 > C^3 > C^2 > C^6$. The ^{13}C and ^1H chemical shifts of tiron are dependent on the pH [Fig. 2(*a*) and (*b*)]. Both the ^{13}C C^4 and C^5 resonances undergo downfield shifts of up to 20 ppm with increase in pH, while C^1 and C^2 are shifted upfield by *ca.* 5 ppm. In the ^1H NMR spectra H^2 and H^6 are shifted upfield by *ca.* 0.4–0.7 ppm upon increase in pH. These shifts can be explained by the deprotonation of hydroxyl groups at higher pH resulting in reduction in electron density at the carbons bearing the hydroxyl groups (C^4 and C^5) and an increase in the electron density at C^2 and C^6.

The formation of Al complexes is indicated by upfield shifts of H^2 and H^6 (0.2–0.4 ppm), and in the ^{13}C NMR spectrum, significant shifts are observed upon complexation: C^4 and C^5 are shifted downfield, with higher values (7–12 ppm) at lower pH, and C^6 and C^2 exhibit an upfield shift. The ^{13}C resonances of the aluminium–tiron complexes showed less dependence on pH compared to those in free tiron. It is notable that the ^{13}C NMR spectra of the complexes were better resolved at higher pH, whilst the isomers could be characterised at pH 5.5 and 7.0 by the ^1H NMR spectra.

Potentiometric studies[8] have indicated stepwise formation of 1:1, 1:2 and 1:3 Al–L^{4-} chelates depending on the pH. The maximum ^{27}Al chemical shift observed for octahedral Al–L^{4-} chelates is δ 36 and a resonance at this frequency is observed in the spectra of 1 : 1, 1 : 2 and 1 : 3 Al–tiron mixtures in the pH range 7–10 which is assigned to the 1 : 3 Al–L^{4-} chelate.

The formation of a polynuclear 1 : 1 chelate was postulated by Dubey and Mehrotra.[6] Since no precipitation was observed in the 1 : 1 Al–tiron mixture over the entire pH range, a detailed study of this system was carried out. The ^{27}Al NMR spectrum of the 1 : 1 Al–tiron mixture at pH 3 displayed two peaks at δ 0.1 and 15.2. The former is due to $[Al(H_2O)_6]^{3+}$ while the latter is assigned to an octahedral 1 : 1 Al–L^{4-} chelate $[AlL(H_2O)_4]^-$ formed by loss of the protons from both the phenolic hydroxyl groups. The large linewidth at half height ($w_{\frac{1}{2}}$ 990 Hz) indicates that the chelate has a highly distorted symmetry. On raising the pH to 5.1, the resonance at δ 15.2 broadened considerably while the signal due to $[Al(H_2O)_6]^{3+}$ disappeared. At pH 7.0, a noisy spectrum was obtained which contained two resonances at δ 27.5 and 36 indicating the presence of at least two complex species [Fig 3(*b*)].

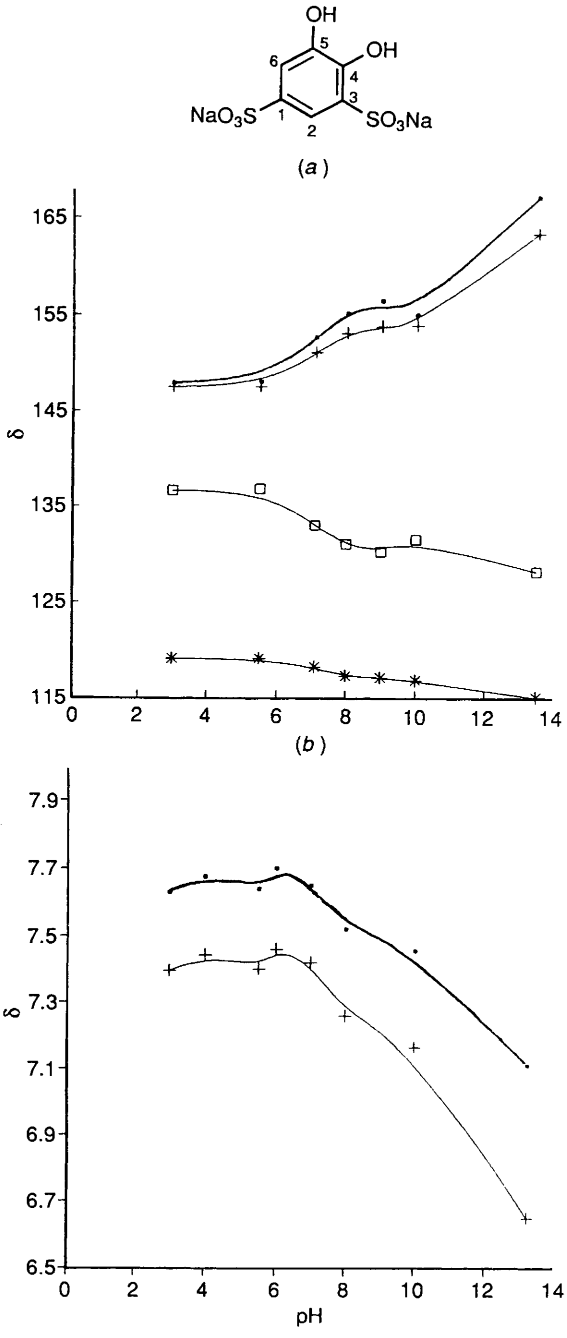

Fig. 2 (*a*) Carbon-13 (●, C^5; +, C^4; *, C^2; □, C^1) and (*b*) ^{1}H (●, H^4; +, H^6) and chemical shifts of tiron in D_2O, at 30 °C as a function of pH

The pH titration curve for the 1 : 1 mixture (c_{Al} = 0.01 mol dm^{-3}) showed the consumption of 3.5 mol KOH per mol Al at pH 7, suggesting the existence of an equimolar mixture of mono- and di-hydroxo 1 : 1 Al–L^{4-} chelates or a polymeric hydroxo 1 : 1 chelate. However, the δ values are much higher than those expected for mono- or di-meric 1 : 1 hydroxo chelates (the formation of dimers through hydroxo bridges resulting in four-membered rings does not cause a chemical shift change). No chemical shift values have been reported so far for polynuclear hydroxo chelates.

From the ^{27}Al and ^{13}C spectra of 1 : 1, 1 : 2 and 1 : 3 Al–tiron mixtures at pH 7.0 it has been possible to characterise the two complex species present in the 1 : 1 mixture at pH 7.0. The intensities of the ^{27}Al resonances of this mixture at δ 27.5 and 36 are in the approximate ratio 3 : 2, while for the 1 : 2 mixture this ratio is nearly reversed [Fig. 3(*b*) and (*c*)]. In the 1 : 3 mixture a single resonance is observed at δ 35.1; hence the resonance at δ 27.5 can be assigned to the 1 : 2 Al–L^{4-} chelate, which was confirmed by the ^{13}C NMR spectral data (Fig. 4): the most intense resonances in the ^{13}C NMR spectra are in the range δ 110–120 and due to C^2 and C^6. For the 1 : 3 Al–tiron mixture (only the 1 : 3 Al–L^{4-} chelate is present) the resonance at δ 115.5 is more intense than that at δ 112.6. Both of these resonances are present in the same intensity ratio in the spectrum of the 1 : 1 mixture at pH 7.0 confirming the existence of the 1 : 3 Al–L^{4-} chelate. The other two peaks at δ 115.9 and 113.1 which are more intense than that of those due to the 1 : 3 chelate may be assigned to the 1 : 2 Al–L^{4-} chelate. The ^{1}H NMR spectra of 1 : 1, 1 : 2 and 1 : 3 Al–tiron mixtures at pH 7.0 and the 1 : 2 mixture at pH 5.5 showed separate peaks corresponding to different isomers of 1 : 3 Al–L^{4-} complexes. The H^6 protons in particular were well resolved and appeared as three doublets in the ratio 1 : 2 : 1 at δ 6.89, 6.94 and 7.02 for different isomeric 1 : 3 complexes (Table 3). The resonances due to the 1 : 2 Al–L^{4-} chelate appeared downfield at δ 7.06 and 7.46 for H^6 and H^2 respectively. There were no peaks corresponding to 1 : 3 chelates in the 1 : 1 mixture at pH 7.0 (c_{Al} = 0.01 mol dm^{-3}) and the 1 : 2 chelate proton resonances experienced a small upfield shift (0.06 ppm) with respect to those at c_{Al} 0.1 mol dm^{-3}.

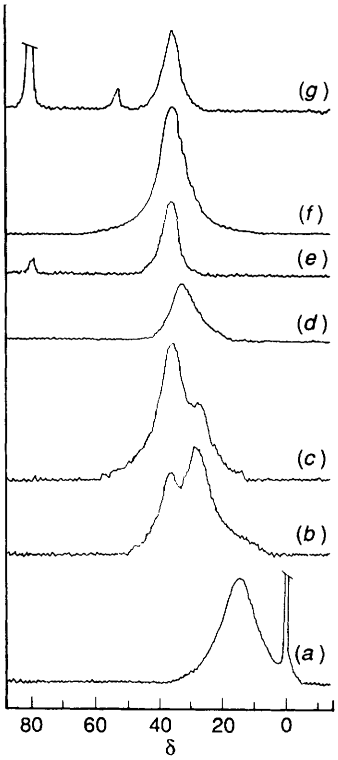

Fig. 3 ^{27}Al NMR spectra of 1 : 1 (*b*, *e* and *g*), 1 : 2 (*a* and *c*) and 1 : 3, (*d* and *f*) Al–tiron mixtures at pH 3(*a*), 7(*b*–*d*), 9(*e*), 10(*f*) and 12.5(*g*)

Table 3 Summary of the ^{27}Al, ^{13}C and ^{1}H NMR data for Al^{III}–catechol (H_2cat) and –tiron(Na_2H_2L) complexes

			δ(^{13}C)*						δ(^{1}H)*	
Complex	pH	δ(^{27}Al)	C^1 (C^5)	C^2 (C^4)	C^3	C^4 (C^2)	C^5 (C^1)	C^6	H^4 (H^2)	H^6
$[Al(cat)_3]^{3-}$	9.5	31.3	157.2	157.2	115.0	118.7	118.7	115.0	6.59	6.59
$[Al(cat)_2]^-$	9.5	58.5	155.7	155.7	114.9	119.8	119.8	114.9	6.61	6.61
$[AlL_2(H_2O)_2]^{5-}$	7.0	27.5	159.0	157.4	126.5	115.9	130.8	113.1	7.46	7.06
$[AlL_3]^{9-}$	7.0	35.1	159.6	158.1	126.2	115.5	130.3	112.6		
fac									7.39	6.93
mer-a									7.37	6.89
mer-b									7.40	6.94
mer-c									7.41	7.02
$[AlL_3]^{9-}$	8.2	36.0								
fac			159.8	158.2	126.2	115.5	130.3	112.6	7.47	7.02
mer-a			159.6	158.2	125.6	115.5	130.0	111.3	7.45	6.96
mer-b			159.7	158.3	126.2	115.6	130.3	112.6	7.47	7.03
mer-c			159.8	158.4	126.6	115.8	130.7	113.1	7.48	7.09

* Labelling in parentheses refers to tiron complexes.

The formation of 1:2 and 1:3 Al–L^{4-} chelates in the mole ratio 3:2 can only occur by disproportionation of the 1:1 chelate leaving 60% of the total aluminium in an uncomplexed form; the question is what form does the aluminium exist in. The ^{27}Al NMR spectrum of the 1:1 mixture at pH 7 is not indicative of uncomplexed aluminium, suggesting that any uncomplexed aluminium species are of very low symmetry. In any case, there are more than 2.5 OH groups per Al^{3+} ion.[1] Addition of a 10% excess of $AlCl_3$ to the 1:1 mixture and readjustment of the pH to 7.0 did not alter the ^{27}Al spectrum appreciably except broadening occurred. On dilution of the 1:1 mixture from 0.1 to 0.01 mol dm^{-3} Al and adjustment to pH 7.0, the spectrum showed only a very broad baseline in the region δ 45–75, with no resonances attributable to complex species. However, the ^{13}C spectrum, though noisy, clearly indicated the presence of a 1:2 Al–L^{4-} chelate (but no 1:3 chelate) [Fig. 4(*a*)]. Spectrophotometric studies at pH 7 using Job's method of continuous variation also showed the existence of a 1:2 Al–L^{4-} complex ($c_{Al} = 2.5 \times 10^{-3}$ mol dm^{-3}).

The ^{27}Al NMR spectrum of the 1:2 $AlCl_3$–tiron mixture at pH 3.0 showed two peaks at δ 0.5 and 15 due to $[Al(H_2O)_6]^{3+}$ and the 1:1 Al–L^{4-} chelate respectively. At pH 5.5, a very broad peak was observed with a plateau in the range δ 28–36. By comparing the ^{13}C spectrum of the 1:2 mixture at pH 5.5 with spectra of the 1:2 and 1:3 Al–L^{4-} chelates (especially the most intense signals due to C^2 and C^6) it could be concluded that the 1:2 mixture contained a mixture of both these chelates, the major component being the 1:3 complex. All of the resonances were broad which could suggest the existence of isomers of both 1:2 and 1:3 chelates.

On raising the pH of the 1:1 Al–tiron mixture to 9, formation of $[Al(OH)_4]^-$ commenced, all the tiron being incorporated in the 1:3 Al–L^{4-} chelate. At pH 12.5, the ^{27}Al NMR spectrum showed three resonances at δ 36.2, 53 and 80.3 [Fig. 3(*g*)], the last of these being due to the highly symmetric tetrahedral $[Al(OH)_4]^-$. The signal at δ 53 was present in the spectrum of the 1:2 mixture at pH 13.5 but not in that of the 1:3 mixture at this pH. This resonance may be assigned to the reasonably symmetric tetrahedral chelate, $[AlL(OH)_2]^{3-}$. Formation of a tetrahedral dihydroxo 1:1 Al–glycolate complex (δ 55.5) was reported previously by Venema *et al.*[22]

Facial and meridional isomers. Since tiron is an unsymmetrical bidentate ligand, the two oxygens are non-equivalent which can give rise to *meridional* and *facial* isomerism in the $[AlL_3]^{9-}$ chelate. In the *facial* isomer the ligands are magnetically equivalent, but in the *meridional* isomer they are symmetrically distinct. The *meridional* and *facial* isomers are expected to exist in a 3:1 ratio purely on the basis of statistical considerations.[24] The ^{27}Al NMR spectra showed the existence of only one 1:3 Al–L^{4-} chelate species. However, both ^{1}H and ^{13}C NMR spectra of 1:3 and 1:6 $AlCl_3$–tiron mixtures in the pH range 8–13.5 indicated the presence of isomers, and as mentioned above, ^{1}H NMR at pH 5.5 and 7.0 also show resolved peaks due to these isomers.

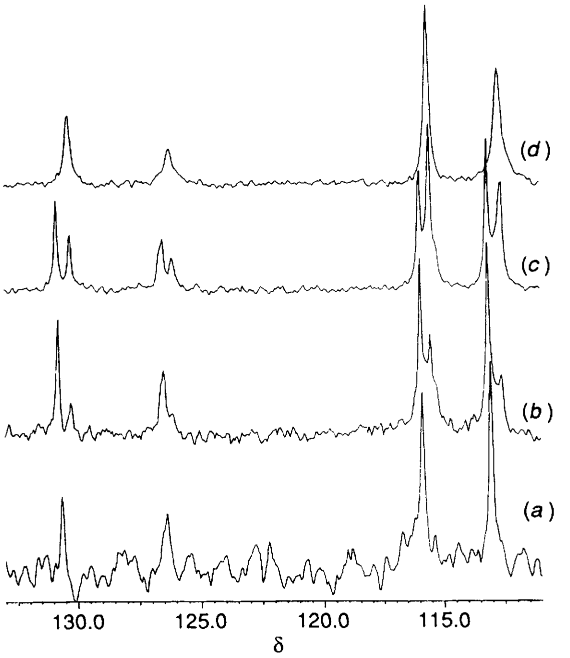

Fig. 4 ^{13}C NMR spectra of 1:1 (*a* and *b*), 1:2 (*c*) and 1:3 (*d*) Al–tiron mixtures at pH 7; c_{Al} = 0.01 (*a*) and 0.1 mol dm^{-3} (*b*–*d*)

Fig. 5(*a*) shows the ^{1}H NMR spectrum of $AlCl_3$–tiron (1:3) in D_2O at pH 8.2, with no peaks corresponding to free tiron. The H^6 resonance consists of two *meta*-coupled peaks of equal intensity on either side of two overlapped *meta*-coupled doublets in the range δ 6.95–7.1. The central peak is an overlapping signal assignable to protons of the *facial* isomer and one of the three non-equivalent ligands in the *meridional* isomer. The outer two resonances are due to those of the other two ligands in the *meridional* isomer. The peak intensities clearly indicate a 3:1 *meridional*-to-*facial* isomer ratio.

The resonances of the corresponding H^2 protons are not as informative but there is clearly an overlap of identical numbers of *meta*-coupled doublets. The ^{1}H NMR spectra at pH 9.1 and 13 are similar.

The presence of isomeric 1:3 Al–L^{4-} complexes was further corroborated by the ^{13}C NMR spectra over the range pH

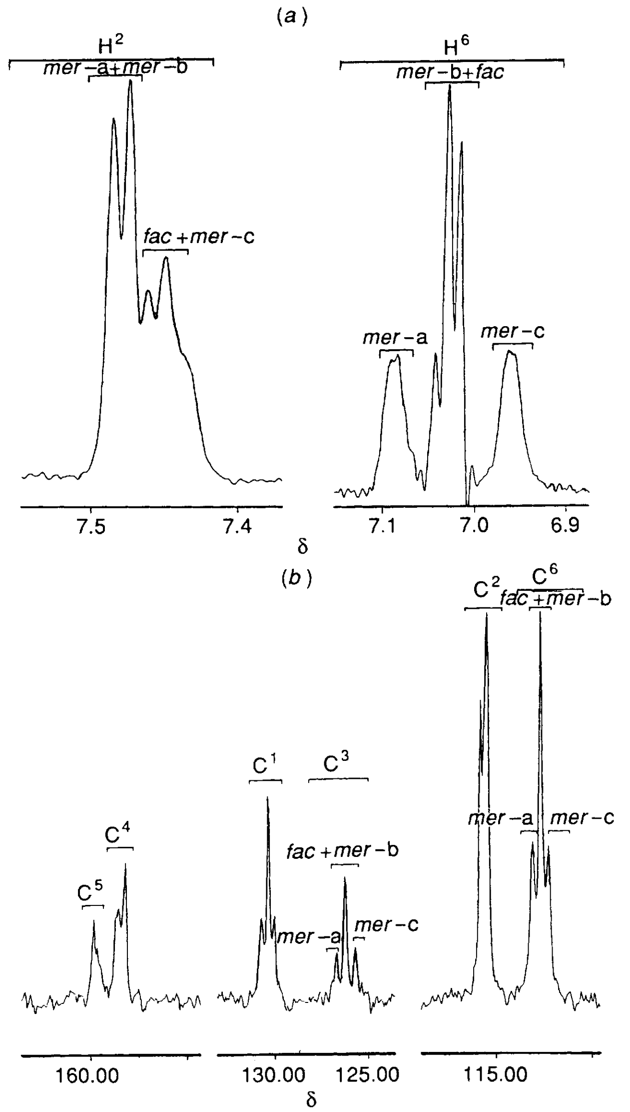

Fig. 5 Proton (*a*) and ^{13}C (*b*) NMR spectra of $AlCl_3$–tiron (1 : 3) at pH 8.2, c_{Al} = 0.1 mol dm^{-3}

8–13.5. At pH 8.2 [Fig. 5(*b*)] six sets of signals are observed (one set for each tiron carbon), with resonances for C^6, C^3 and C^1 appearing as triplets. The intensities of the middle peaks of the triplets are twice those of the side peaks, suggesting that the former are due to the carbons of the *facial* isomers (all three ligands equivalent) and one of the three non-equivalent ligands of the *meridional* isomer, with the latter assigned to the other two ligands of the *meridional* isomer. At pH 13.5, the remaining sets of signals were also resolved. The *meridional*-to-*facial* ratio was again 3 : 1. At higher magnetic field (125 MHz) the C^4 and C^5 resonances could each be resolved into four lines.

The ^{13}C and ^1H spectra of a 1 : 6 Al–tiron mixture at pH 8–10 showed similar behaviour to those of the 1 : 3 mixture, although as a result of its higher relative concentration free tiron was detected in both ^{13}C and ^1H NMR spectra. The presence of *facial* and *meridional* isomers in ^1H NMR spectra was also reported for Si^{IV}–tiron complexes.[24]

A notable feature of the Al–tiron system is the lack of formation of octahedral hydroxo complexes. This may be attributed to the high stability of the chelates with the formation of higher chelates by disproportionation being more favoured than formation of hydroxo chelates. The chelate $[AlL_3]^{9-}$ is remarkably stable at alkaline pH and even at pH 13.5 it is not hydrolysed to $[Al(OH)_4]^-$.

The linear change in chemical shift upon successive co-ordination observed earlier for aliphatic ligands such as lactic acid and aminopolycarboxylic acids does not appear to apply to aromatic ligands. With tiron, the increase in δ(^{27}Al) on conversion from the 1 : 2 to the 1 : 3 Al–L^{4-} chelate is ≈8 ppm, while the expected increase is 14–15 ppm. Hence it may be concluded that steric factors play an important role in lowering the change in chemical shift in this conversion.

It is notable that both the ^{27}Al chemical shift and linewidth of the 1 : 3 Al–L^{4-} chelate are greater than those of the corresponding catechol chelate. The higher δ value is possibly due to the greater stability of $[AlL_3]^{9-}$ while the increased line-width may be attributed to the presence of the negatively charged sulfonate groups in tiron which can give rise to greater distortion in the symmetry around the aluminium nucleus.

In view of the remarkable stability of the aluminium–tiron complexes at pH 7.4 (the physiological pH), tiron is a promising candidate for aluminium uptake, also the presence of the sulfonate groups has been found to reduce the toxicity of catechol: *in vivo* tests with mice have shown that tetrameric 5-sulphodihydroxybenzoyl compounds are acutely non-toxic.[25] Hence the toxicity of tiron is expected to be low.

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