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Chirality-directed Self-assembly of Supramolecular Propellers of Dialkyltartrate Trimers with Hydronium, Ammonium and Primary Aminium Ions in CI Mass Spectra†

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The specific non-covalent gas phase association of chiral dialkyltartrates M with multiprotic onium ions $A \cdot H^+$, such as hydronium, ammonium and primary aminium ions, was investigated by chemical ionization (CI) mass spectrometry. The method applies enantiomer-labeled racemates of dimethyl-(S)- and [$^2H_6$]dimethyl-(R)-tartrate (s and r) and diisopropyl-(S)- and [$^2H_{14}$]diisopropylyl-(R)-tartrate (S and R). Unusually stable trimer adduct clusters $M_3 \cdot AH^+$ were observed (5%–50% of the substrate ions). The abundances of the four diastereomers rrr · AH^+, rrs · AH^+, rss · AH^+ and sss · AH^+ did not show the statistics 1:3:3:1, but a pattern ranging from 1:1:1:1 to 5:3:3:5. Thus the homochiral clusters rrr · AH^+ and sss · AH^+ are three to five times more favored than the heterochiral ions. For the primary amines 1–10 as base A the chiral effect mainly depends on the CI conditions and hardly on the amine properties (proton affinity, steric crowding, chirality). For ammonia and water as base A the chiral effect was 2.1 and 2.7–3.6 respectively. The effect was not found in $M_3 \cdot AH^+$ with diprotic onium ions from alcohols and secondary amines. It is assumed that the homochiral clusters $M_3 \cdot AH^+$ have an especially stable supramolecular propeller structure as supported by PM3 calculations. The clusters allow CI experiments for molecular and chiral recognition. © 1997 by John Wiley & Sons, Ltd.

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INTRODUCTION

Chemical ionization (CI) mass spectrometry[1] can be applied to stereochemical investigations of organic molecules in the gas phase.[2] Whereas the more conventional studies deal with stereospecific CI fragmentation reactions, the more recent work deals with stereospecific non-covalent interactions under CI conditions, i.e. the formation of specific adducts, host–guest complexes and supramolecular structures. The latter approach has also proved successful in other mass spectrometric methods, such as fast atom bombardment (FAB), matrix-assisted laser desorption ionization (MALDI), electrospray ionization (ESI) and Fourier transform ion cyclotron resonance (FTICR) mass spectrometry, especially for larger biological molecules.[3]

Various examples of specific interactions in gaseous ion aggregates of relatively small organic molecules are known. Recognition of bifunctional oxygen compounds is possible under aminoethanol CI.[4] *Cis/trans* differentiation has been shown for protonated dimers and trimers of cyclic diols[5] and anhydrosugars.[6] Epimeric monosaccharides and α/β-linked disaccharides are distinguishable in FAB-generated metal-co-ordinated heterocomplexes.[7] Chiral discrimination of dialkyltartrates occurs in their protonated dimers[8–10] and trimers[11] and metal heterocomplexes.[12] Chiral recognition of organic ammonium ions in host–guest complexes with crown ethers[13,14] and cyclodextrins[15] has been described. Special stability has been attributed to protonated polyether–water clusters[16] and 'magic number' alcohol–water clusters.[17] Gaseous complementary nucleobase pair ions have been reported.[18] Alkali-ion-labeled (3:3) complexes[19] and chloride-ion-attached (1:3) complexes[20] with a cyanuric acid–melamine lattice and transition-metal-co-ordinated helical and toroidal complexes of heteroaromatic ligands[21] have been detected by ESI mass spectrometry. Specific K^+ adducts of isoguanosine tetramers appeared under FAB conditions.[22] The structures of gaseous ammonium and hydronium adducts with crown ethers and similar complexes have been attributed to specific hydrogen bond systems.[23] Recently, cluster systems with a trigonal symmetry consisting of a protonated hydrazine tetramer[24] and a hydronium-diethylether trimer[25] respectively have been reported.

The supramolecular clusters of the propeller type $M_3 \cdot A \cdot H^+$ were brought to our attention in dialkyltartrate CI measurements for chiral recognition of amines. The approach uses racemic mixtures of

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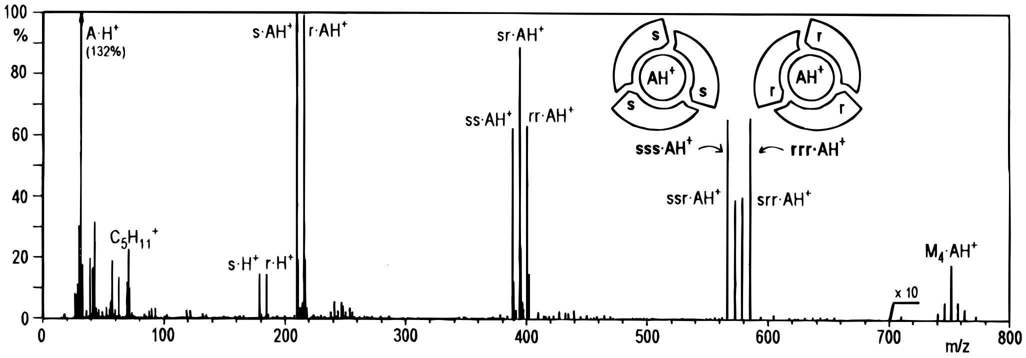

Figure 1. Methylamine (A)–isopentane CI mass spectrum of racemic S-d_0- and R-d_6-dimethyltartrate (s and r). Insets show schematic structures of propellers sss · AH$^+$ and rrr · AH$^+$ with opposite helicity.

enantiomer-labeled dialkyltartrates.[8,9] Such racemates, in which the (R)-antipode has deuterated alkyl groups, were dimethyl-(2S, 3S)-tartrate and [$^2H_6$]dimethyl-(2R, 3R)-tartrate (compound notation s and r respectively) and diisopropyl-(2S, 3S)-tartrate and [$^2H_{14}$]diisopropyl-(R)-tartrate (S and R respectively). The diastereomeric interactions which can occur between the chiral molecules in the clusters allow the differentiation of bulk aggregates from chirospecific dimers or other supramolecular structures.* In the following sections we report that the clusters $M_3 \cdot A \cdot H^+$ are generally formed by dialkyltartrate (M) trimers with multiprotic onium ions ($A \cdot H^+$), such as hydronium, ammonium and primary aminium ions. The formation of the clusters is essentially controlled by the chirality of the dialkyltartrates and can be utilized for chiral recognition studies.

EXPERIMENTAL

The dialkyltartrate enantiomers and their deuterated analogs were available from earlier work.[9,11] The amines were obtained from Fluka (Buchs, Switzerland). Methylamine gas was from Merck (Darmstadt, Germany).

The mass spectrometer used was a Varian MAT 112 instrument with an EI–CI source. CI reagent gases were isobutane, isopentane, ammonia, methylamine, ethanol and water applied at 0.10–0.15 mbar. A low ion source temperature of 50 °C was applied to obtain sufficient abundances of aggregation products. From a temperature-controlled direct probe the diisopropyltartrate mixtures were evaporated at 80–100 °C and the dimethyltartrate mixtures at 120–140 °C. The amine and alcohol additives were introduced using a gas chromatograph under helium flow with a 20 mm × 0.3 mm i.d. directly coupled capillary column DB-1 (80–200 °C). The GC conditions allowed 20 mass spectral scans per eluted peak. The scan rate was 2.5 or 5 s per scan. The spectra were usually scanned 10–20 times and averaged values were determined for the tabulated spectra and the reported chirality effects. The spectra in Figs 1–5 are single-scan raw data.

Semiempirical molecular orbital calculations using PM3 parameters[26] were performed for trimer adducts within the InsightII MOPAC package of the Biosym/MSI software on an Indigo Iris R3000 workstation.

RESULTS AND DISCUSSION

Dialkyltartrate aggregation under ammonia and amine CI

The results of the complexation studies of the enantiomer-labeled dimethyltartrates (DMT) and diisopropyltartrates (DIPT) with amines and ammonia under CI conditions are given in Figs 1 and 2 and Tables 1 and 2.

Chirality-directed cluster formation

Figure 1 shows a spectrum which was measured with a mixture of isopentane and methylamine (A) as CI reagent gas and a racemic mixture of the labeled S-d_0- and R-d_6-dimethyltartrate (s and r) as substrate. At an ion source temperature of 50 °C the substrate concentration in the ion source was increased to a level where the abundance of the $A \cdot H^+$ reagents ions was decreased to 10% of the total ion yield. The resulting spectrum is dominated by the peak multiplets for adducts of methylammonium with the monomers, dimers, trimers and tetramers of dimethyltartrate.

The trimer adducts $M_3 \cdot AH^+$ are unusually abundant and comparable with the stability of the monomer and dimer aducts.* This is in contrast with the usual monotonic decrease in the cluster abundance with increasing cluster size. In addition, the multiplet of the diastereomeric trimer adducts sss · AH$^+$, ssr · AH$^+$, srr · AH$^+$ and rrr · AH$^+$ shows a substantial deviation from the statistical abundance pattern 1:3:3:1. The observed abundance pattern is about 5:3:3:5. Thus the

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* The dimer adducts of DMT show a chiral discrimination in favor of homochiral ss · AH$^+$ and rr · AH$^+$ versus heterochiral sr · AH$^+$, similar to the behavior of the protonated dimers.[8–11].

homochiral trimer adducts sss · AH^+ and rrr · AH^+ are substantially favored versus the heterochiral trimer adducts ssr · AH^+ and srr · AH^+.

Because of the virtual, and not true, equilibrium under CI conditions, the observed chiral discriminations generally reflect differences both in the thermodynamic stability and in the kinetics of formation for the cluster species in the particular CI experiment. Therefore measurements under conditions of FTICR spectrometry are in progress to obtain quantitative data for the chiral discriminations in terms of relative cluster stabilities.[27]

As a measure for the chirality effect on the trimer adduct formation, we introduce here the term *chiral discrimination ratio* (CDR). It is defined as the observed ratio of the sums of the homochiral versus heterochiral trimer adduct abundances divided by the corresponding statistical ratio of one-third:

$$\mathrm{CDR} = \frac{3([\mathrm{sss} \cdot \mathrm{AH}^+] + [\mathrm{rrr} \cdot \mathrm{AH}^+])}{[\mathrm{ssr} \cdot \mathrm{AH}^+] + [\mathrm{srr} \cdot \mathrm{AH}^+]}$$

This definition includes that the measurements are performed with equimolar or almost equimolar mixtures of the dialkyltartrates s and r (or S and R). For the above experiment the averaged chirality effect was CDR = 4.9 ± 0.2.

We assume that the homochiral clusters $M_3 \cdot AH^+$ have propeller-shaped supramolecular structures which are schematically depicted as insets in Fig. 1. Their geometry should allow an extremely efficient charge solvation. They can be considered as self-assembled multicomponent analogs of the well-known gas phase complexes between crown ethers and alkyl-substituted or neat ammonium ions.[13,14,23] Also, a related achiral cluster system with a trigonal symmetry consisting of a protonated hydrazine tetramer has been reported recently in ion drift source experiments.[24]

The nature of the supramolecular propellers $M_3 \cdot AH^+$ was explored by three further experiments shown in Fig. 2. (In Figs 2–5 the peak multiplets of the relevant propeller clusters are printed as bold lines for clarity.) The conditions used for these spectra were different from above and more appropriate for screening of numerous systems. The dialkyltartrates were introduced by the direct probe and the amine species A (hexylamine) was introduced by a GC inlet together with the helium carrier gas into the isobutane CI plasma within the ion source.

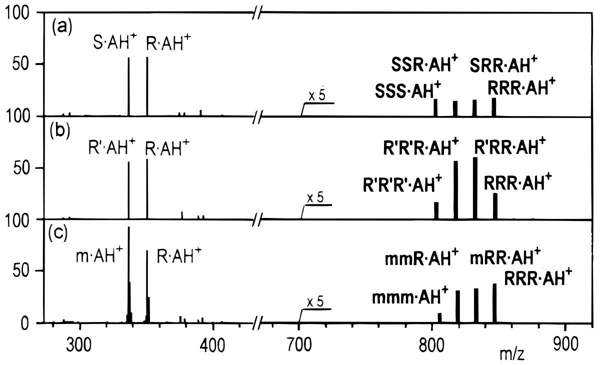

Figure 2. Partial hexylamine (A)–isobutane CI mass spectra of equimolar diisopropyltartrate mixtures. (a) S-d_0- and R-d_{14}-DIPT (S and R); (b) R-d_0- and R-d_{14}-DIPT (R′ and R); (c) meso-d_0- and R-d_{14}-DIPT (m and R).

The chiral discrimination on the trimer adducts is clearly confirmed by the experiments using the homologous racemic diisopropyltartrates S and R and hexylamine as base A [Fig. 2(a)]. Because of the changed conditions, the abundance of the trimer adducts is about one-tenth of that in Fig. 1. The peak multiplet shows a less specific 1:1:1:1 pattern which reflects a chiral discrimination by a factor of three versus the 1:3:3:1 statistics. However, this is still an unusually strong effect in chiral mass spectrometry.

The experiment in Fig. 2(b) was performed with the monochiral mixture of R-d_0- and R-d_{14}-DIPT (R′ and R). The trimer adduct peaks give a straight 1:3:3:1 multiplet (CDR = 1.05 ± 0.07). This practically excludes any isotope effect on the deutero-alkyl groups.

Figure 2(c) shows an experiment with an equimolar diastereomeric mixture of meso-d_0- and R-d_{14}-DIPT (m and R) which have an *erythro* and a *threo* configuration respectively. The chiral propeller RRR · AH^+ is 5.4 times more abundant than the achiral propeller species mmm · AH^+. Apparently, the meso-dialkyltartrate molecules are not suitable for efficient charge solvation in a trimer adduct. The *threo* configuration of the chiral R- and S-dialkyltartrates must be essential for the unusual stability of the homochiral clusters $M_3 \cdot AH^+$ and their supramolecular structure.

Differentiation of amine types. The role of the amine type on the formation of the propeller cluster $M_3 \cdot AH^+$ was examined with the racemate of enantiomer-labeled diisopropyltartrates. The details are shown in Table 1. The same GC inlet conditions as described above were used for the amines **2**–**14**. The spectra for methylamine **1** and ammonia **15** were measured using these compounds as neat CI gases.

All the primary amines **1**–**10** studied here show distinct chiral discriminations for the trimer adducts $M_3 \cdot AH^+$. The observed CDR values generally fall within a relatively small range from 2.9 to 3.6. For compounds **2**–**10**, measured under the same conditions, the deviations are close to the spectral error and difficult to correlate to molecular parameters of the amines, such as proton affinity (PA) or steric shape.

In spite of the PA difference for benzylamine **3** (219.7 kcal mol^{-1}) and trifluoroethylamine **4** (203.3 kcal mol^{-1}),[28] the spectral abundances and the CDR values of their propeller clusters are the same. Apparently, the ammonium ion of the weaker base **4** provides also a stable co-ordination center for the cluster. The more bulky α-methyl-benzylamines **6** and **7** give slightly reduced abundances and chiral effects for the clusters $M_3 \cdot AH^+$ compared with benzylamine **3**. Further, the chirality of the amine antipodes **6** and **7** does not distinctly influence the chiral effect on the clusters.

The secondary amines **11**–**13** give generally much smaller peaks for the clusters $M_3 \cdot AH^+$ and the chiral discrimination is practically absent. A minor effect (1.11 ± 0.13) may occur for diethylamine **11**. The tertiary amine **14** does not form the cluster species. Finally, ammonia **15** which is included here along the amine categories behaves similarly to the primary amines. A

Table 1. Partial CI mass spectra of amines (A) as mixtures with S-d_0- and R-d_{14}-diisopropyltartrate (S and R) and chiral discrimination ratios (CDR) of trimer adducts[a]

		Dimers[c]			Dimer adducts			Trimer adducts				
Amine A	PA[b]	$SS \cdot H^+$	$SR \cdot H^+$	$RR \cdot H^+$	$SS \cdot AH^+$	$SR \cdot AH^+$	$RR \cdot AH^+$	$SSS \cdot AH^+$	$SSR \cdot AH^+$	$SRR \cdot AH^+$	$RRR \cdot AH^+$	CDR
1 Methylamine	214.1	0	0	0	35	76	42	15.4	17.0	18.0	19.0	2.9 ± 0.1
2 Hexylamine	220.1	13	16	15	14	28	16	3.5	3.1	3.4	4.3	3.6 ± 0.2
3 Benzylamine	219.7	12	15	14	8	16	9	2.0	2.2	2.3	2.7	3.1 ± 0.3
4 Trifluoroethylamine	203.3	22	25	26	5	11	5	2.9	3.1	3.0	3.5	3.1 ± 0.3
5 Ethanolamine		17	22	21	9	18	10	2.3	3.4	3.6	3.0	2.3 ± 0.1
6 D-α-Me-Benzylamine		9	12	11	3	5	3	0.28	0.39	0.39	0.32	2.3 ± 0.2
7 L-α-Me-Benzylamine		9	11	10	4	9	5	0.53	0.67	0.72	0.62	2.5 ± 0.3
8 Aniline	211.5	12	14	14	6	11	6	1.0	1.1	1.2	1.3	3.0 ± 0.3
9 *tert*-Butylamine	221.3	10	15	12	7	16	8	1.7	2.1	2.2	2.1	2.5 ± 0.2
10 Adamantylamine		14	16	16	6	15	8	3.0	3.2	3.2	3.7	3.3 ± 0.3
11 Diethylamine	225.1	0.1	0.1	0.1	16	32	18	0.5	1.3	1.4	0.5	1.1 ± 0.1
12 Diisopropylamine	228.9	2	3	2	5	11	5	0.03	0.05	0.05	0.02	0.8 ± 0.3
13 L-Prolinol		7	9	8	3	5	3	0.02	0.07	0.08	0.03	1.3 ± 0.4
14 Triethylamine	231.3	6	7	6	1	2	1	0	0	0	0	—
15 Ammonia	205.0	0	0	0	13	26	14	1.2	1.8	1.9	1.4	2.1 ± 0.3

[a] Spectral data as % relative abundance.

[b] Proton affinities (kcal mol^{-1}) of representative amines.[28]

[c] For **2**–**10** and **12**–**14** the excess of $C_4H_9^+$ versus $A \cdot H^+$ reagent ions gives rise to protonated dimers $M_2 \cdot H^+$ and, to a lesser extent, trimers $M_3 \cdot H^+$.

distinct chiral discrimination of 2.1 is observed. In summary, only the ammonium ion and the monosubstituted aminium ions can be accommodated in the supramolecular propellers with homochiral dialkyltartrate trimers. The additional substituents in secondary and teriary aminium ions hinder the assembly of the trimer adducts.

Influence of CI reaction conditions. The lowest accessible temperature (50 °C) gave the best abundances and accuracy in the spectra and was used throughout this study. Under the instrumental conditions used for the amines **2**–**14** listed in Table 1, the GC inlet limited the possible amine concentration in the ion source. Nevertheless, the composition of the CI reaction mixture could be controlled over a wide range by experiments in which the amine species was directly used as CI reagent gas. Accordingly, the influence of the CI plasma composition on the trimer species $M_3 \cdot AH^+$ was studied with methylamine as base A and racemic S-d_0- and R-d_6-dimethyltartrate (DMT) and S-d_0- and R-d_{14}-diisopropyltartrate (DIPT) respectively as ligands M. The spectral data are summarized in Table 2.

Under methylamine CI without any buffer gas the spectra of racemic DMT and DIPT both show very similar abundances and chiral discriminations for $M_3 \cdot AH^+$ as observed for the other primary amines **2**–**10** of Table 1. However, the amount of trimer adducts could be enhanced efficiently by the addition of a buffer gas into the CI reaction system. Admixing isopentane in the methylamine CI experiment with DMT removes the higher amine clusters $A_2 \cdot H^+$, $A_3 \cdot H^+$ and $A_4 \cdot H^+$ from the reagent ion system. This reduces the abundance of the two-amine-containing clusters $M \cdot A_2H^+$ from 30% to 2% and increases the abundance of the trimer adducts $M_3 \cdot AH^+$ from 10% to 33% (Table 2). A similar increase in the yield of $M_3 \cdot AH^+$ was found in the study of DIPT under ethanol addition. In both cases the abundance changes were accompanied by a substantial increase in the chiral discrimination. The CDR values of 2.8 and 2.9 increased by a factor of almost two to 4.9 and 4.5 respectively.

Incidentally, the same spectral improvement for the cluster $M_3 \cdot AH^+$ under methylamine CI was obtained in experiments designed for chiral recognition of tartrate-related enantiomers. D-Threitol and 1,4-dibenzyl D-threitol were introduced into the ion source as a three-component mixture with racemic DMT. The evaporated threitol compounds were not detectable in the spectra because of their lower proton affinity compared with the DMT ester. Apparently, the threitol species can thermally stabilize the clusters $M_3 \cdot AH^+$ by collisions very efficiently. Their abundances are 47% and 41% respectively and the CDR values are again increased to about 4.9 (Table 2).

Dialkyltartrate aggregation under water and alcohol CI

The observation of the propellers $M_3 \cdot AH^+$ also for the weak base trifluoroethylamine and the earlier reports on alcohol–water clusters $(ROH)_9 \cdot H_3O^+$ and crown ether H_3O^+ complexes[17,23] prompted us to extend our investigations to CI with alcohol and water. The water CI mass spectrum of the racemic dimethyltartrates at high sample concentrations (inlet probe temperature 140 °C, ion source temperature 50 °C) is shown in Fig. 3. It contains two series of cluster ions. The normal protonated species $M_n \cdot H^+$ ($n = 1$–4) are dominating for the smaller cluster sizes. The more interesting hydronium ion adducts $M_n \cdot H_3O^+$ ($n = 1$–4) are observed in high abundances for larger cluster sizes.

Table 2. Partial methylamines (A) CI mass spectra of racemic dialkyltartrates (M) and CDR values of $M_3 \cdot AH^+$ clusters[a]

M	Buffer	$M \cdot AH^+$	$M \cdot A_2H^+$	$M_2 \cdot AH^+$	$M_3 \cdot AH^+$	CDR
DMT	—	31	30	29	10	2.8 ± 0.1
DMT[b]	Isopentane	31	2	34	33	4.9 ± 0.3
DMT	D-Threitol	9	17	26	47	4.9 ± 0.2
DMT	1,4-Bz$_2$-D-Threitol	13	20	26	41	4.8 ± 0.1
DIPT[c]	—	36	24	27	13	2.9 ± 0.1
DIPT	Ethanol	35	6	29	30	4.5 ± 0.2

[a] Spectral abundances for peak multiplets, as normalized to 100%.
[b] See single scan in Fig. 1.
[c] See entry **1** of Table 1.

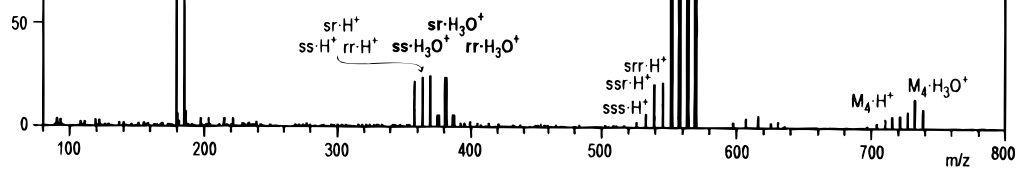

Figure 3. Water CI mass spectrum of S-d_0- and R-d_6-dimethyltartrate (s and r). Note isobaric ions rrr · H^+ and sss · H_3O^+ as indicated.

The protonated dimers $M_2 \cdot H^+$ show the well-known chiral discrimination.[8–11] The diastereomeric ions ss · H^+, sr · H^+ and rr · H^+ (statistics 1 : 2 : 1) are about equally abundant and thus the homochiral species are favored by a factor of almost two in this experiment. There are some new special cluster features in Fig. 3 which will not be discussed here. They include the unusual abundances of the $M \cdot (H_2O)_2 \cdot H^+$ hydrates and of the heterochiral sr · H_3O^+ dimer adducts.*

The clusters of interest here are the trimer adducts sss · H_3O^+, ssr · H_3O^+, srr · H_3O^+ and rrr · H_3O^+. They give the most abundant peaks in the spectrum and show a distinct chiral specificity of 2.7 ± 0.1 in favor of the homochiral diastereomers. This effect is comparable with the CDR values for the clusters $M_3 \cdot AH^+$ of the primary amines and ammonia.

For the homologous diisopropyltartrates the observed chiral discrimination of the hydronium clusters $M_3 \cdot H_3O^+$ was 3.6 ± 0.2 [Fig. 4(a)]. This value is somewhat higher than that in the above water CI experiment with DMT. On the other hand, the protonated trimers $(DIPT)_3 \cdot H^+$ are relatively more abundant than the ions $(DMT)_3 \cdot H^+$. This could be explained by the slightly higher proton affinity of DIPT compared with DMT, which supports proton transfer from the hydronium ion.

In the outcome, the formation and stabilization of the clusters $M_3 \cdot H_3O^+$ with a hydronium ion center can be very efficient in spite of the low proton affinity of water (166.5 kcal mol^{-1})[28] compared with the PA of the ester ligands. This agrees with the earlier observations of the alcohol and crown ether solvated hydronium ion clusters[17,23] and a recent ICR study on hydronium ions specifically co-ordinated by three diethylether molecules.[25] In all these systems the PA of the water oxygen atom is substantially increased by the solvation of the water hydrogen atoms and thus the proton transfer to the ligands becomes a less favorable reaction. This PA shift is related to the proton affinity increase of molecule pairs.[28]

Ethanol and glycerol were used as alcohol bases A in the studies of the clusters $M_3 \cdot AH^+$ in combination with the racemic dialkyltartrates. The ethanol adduct complex $M_3 \cdot EtOH_2{}^+$ showed only very low abundances comparable with the protonated trimers $M_3 \cdot H^+$ and a chiral discrimination (CDR = 1.10 ± 0.22) was hardly detectable [Fig. 4(b)]. Thus the assumed diprotic ethoxonium ion is unable to co-ordinate three tartrate ligands efficiently to give a supramolecular propeller structure, similar to the observation with protonated secondary amines discussed before.

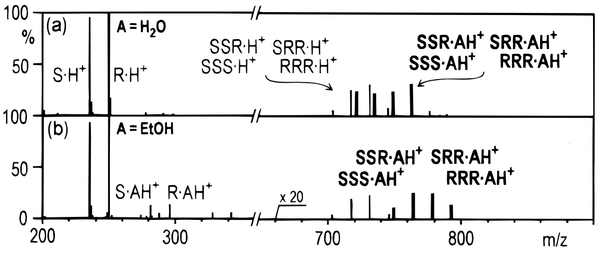

Figure 4. Partial CI mass spectra of S-d_0- and R-d_{14}-diisopropyltartrate (S and R). (a) water CI; (b) ethanol CI.

In the experiment with glycerol as base A the isotopomeric trimer adducts $M_3 \cdot AH^+$ showed very strong relative abundances of 11%, 39%, 43% and 16%. However, the pattern is definitely not chirospecific (CDR = 0.99 ± 0.06) and thus a completely different cluster structure must be assumed.

Chiral recognition in mixed trimer adduct clusters

The special association in the propeller structure $M_3 \cdot AH^+$ represents a self-assembled analog of a crown ether host species M_3 which binds a guest species AH^+. This cluster system can be used for a new type of molecular and chiral recognition studies in the gas phase. Two different binding sites for analyte molecules A or M are available which are in the central part of the periphery of the propeller respectively. As already noted before, molecular recognition of A allows the differentiation of primary amines and ammonia from secondary and tertiary amines and the differentiation of water from alcohols, among the corresponding onium ions.

On the other hand, the potential of chiral recognition for ligands M is demonstrated with 'unknown' enantiomers of dialkyltartrate homologs in Fig. 5. The racemate of S-d_0- and R-d_6-dimethyltartrate (s and r) is applied for the chiral reagent ion system. The corresponding clusters sss · AH^+, ssr · AH^+, srr · AH^+ and rrr · AH^+ provide an internal CDR reference value in the spectrum. The homologous diethyltartrate enantiomers (with the same labels R and S here which are used for DIPT above) have been applied as chiral analytes M.

As indicated by the broken lines in the spectra, the assay systems give two groups of mixed trimer adduct clusters which contain one or two molecules of M. These peak groups show opposite abundance shifts for the two antipodes in the spectra [Figs 6(a) and 6(b)] which are characteristic of the chirality of the analyte M. The absolute configuration of M is indicated by the more abundant homochiral propeller clusters among the competitive species of the ssM · AH^+/rrM · AH^+ and sMM · AH^+/rMM · AH^+ cluster pairs. The corre-

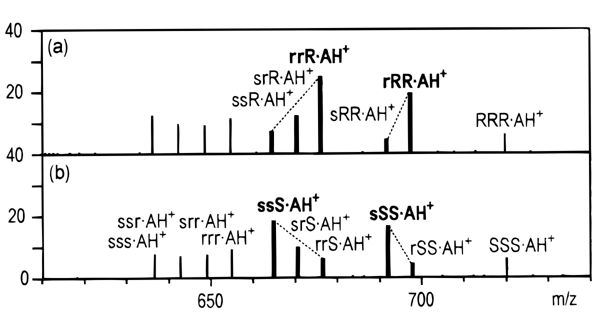

Figure 5. Partial hexylamine (A)-isobutane CI mass spectra with S-d_0- and R-d_6-DMT (s and r) as chiral reagents and with chiral analytes M. (a) M ≡ R-diethyltartrate. (b) M ≡ S-diethyltartrate.

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* The dimer adducts $M_2 \cdot H_3O^+$ show an unusual chiral discrimination in the opposite direction in favor of the heterochiral ions sr · H_3O^+, similar to the inverse chiral effect for the $M_3 \cdot H^+$ trimers.[11] Also, the observation for $M_2 \cdot H_3O^+$ was found under ICR conditions.[29]

sponding *chirospecific abundance ratios* or CAR values for R and S (and the reciprocals for S) were as follows:

M	$\frac{[\text{rrM} \cdot \text{AH}^+]}{[\text{ssM} \cdot \text{AH}^+]}$	$\frac{[\text{rMM} \cdot \text{AH}^+]}{[\text{sMM} \cdot \text{AH}^+]}$
R	3.9 ± 0.4	4.4 ± 0.5
S	0.28 ± 0.02 (3.6 ± 0.3)	0.24 ± 0.01 (4.2 ± 0.2)

The CAR values of 3.6–4.4 for the homochiral clusters are in the range expected from the CDR of the racemic DMT. Water CI measurement with the same three-enantiomer mixtures gave similar CAR values.[30] As an example of a non-tartrate enantiomer, S-diisopropylmalate M was investigated with the DMT/hexylamine system. The CDR value of DMT was 3.5 ± 0.5 and the ratios for the chiral recognition of M were $[\text{ssM} \cdot \text{AH}^+]/[\text{rrM} \cdot \text{AH}^+] = 1.3 \pm 0.1$ and $[\text{sMM} \cdot \text{AH}^+]/[\text{rMM} \cdot \text{AH}^+] = 1.4 \pm 0.1$. Apparently, the S configuration of M is correctly assigned, but with much lower specificity than for the actual dialkyltartrate enantiomers. This indicates the complexity of the chiral recognition approach.

The principle of the chiral recognition process for the ligand M is illustrated in Fig. 6. The components of the system can self-assemble to form host molecule aggregates $M_2 \cdot AH^+$ which do not belong to the crown ether type. They rather have chiral clefts which are receptors for chiral guest molecules.

From the different chirocompetitive association reactions in the CI system, two typical cases are shown. (a) The self-assembled enantiomeric host species $\text{rr} \cdot \text{AH}^+$ and $\text{ss} \cdot \text{AH}^+$ compete to bind the analyte R. (b) the analyte R forms the homochiral host $\text{RR} \cdot \text{AH}^+$ which selects one of the reagent gas monomers r or s. Both reactions contribute to the mixed homochiral propellers $\text{rrR} \cdot \text{AH}^+$ and $\text{rRR} \cdot \text{AH}^+$ which then give the diagnostic peaks in the spectra.

Molecular modeling studies

A full conformational analysis of the cluster system $M_3 \cdot AH^+$ is very complicated. We have applied semi-empirical molecular orbital calculations by the PM3 method[26] to shed some light on this problem. Arbitrarily, the homochiral and heterochiral propeller structures of the methylammonium dimethyltartrate trimer clusters $(\text{DMT})_3 \cdot \text{CH}_3\text{NH}_3{}^+$ are represented here by the related pair of local minima in Fig. 7.

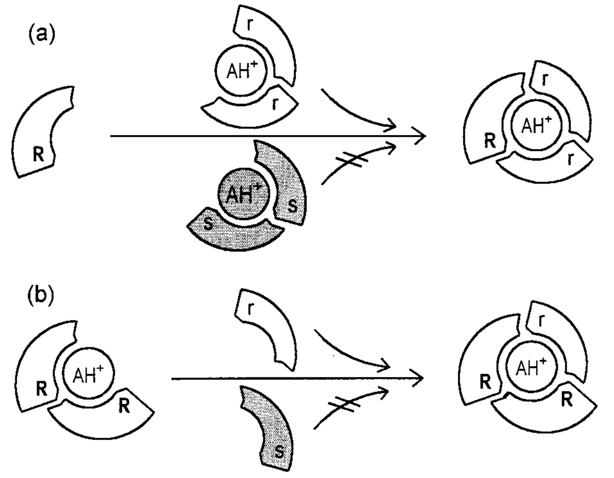

Figure 6. Chiral recognition by self-assembly and host–guest chemistry. (a) guest R selected by $\text{rr} \cdot \text{AH}^+$ or $\text{ss} \cdot \text{AH}^+$; (b) host $\text{RR} \cdot \text{AH}^+$ selects r or s.

The strong hydrogen bonds in the structures are indicated by broken lines. One of the additional N—H---O contacts with the inner OH groups (not marked specifically) is lost in the heterochiral cluster $\text{ssr} \cdot \text{AH}^+$, because in the R antipode this OH group (labeled by an asterisk) points outwards. In principle, the resulting enthalpy difference could explain the preference of the homochiral cluster $\text{sss} \cdot \text{AH}^+$ and thus the observed chiral discrimination. Higher levels of *ab initio* theory are required for more adequate descriptions of hydrogen-bonded structures.[31]

CONCLUSIONS

The specific aggregation yielding ionic four-component clusters $M_3 \cdot AH^+$ in the gas phase could be observed under chemical ionization conditions in the mass

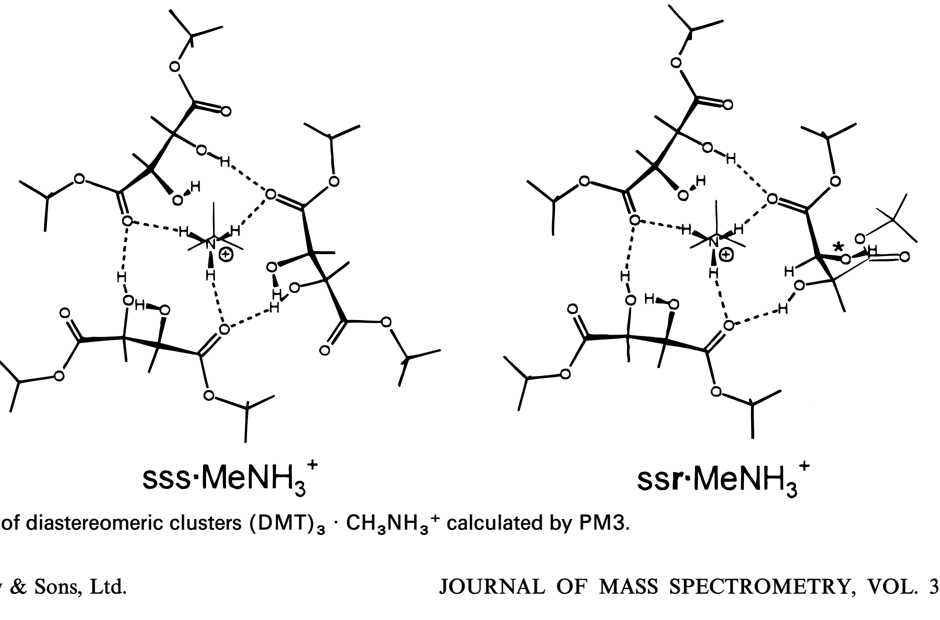

Figure 7. Structures of diastereomeric clusters $(\text{DMT})_3 \cdot \text{CH}_3\text{NH}_3{}^+$ calculated by PM3.

spectrometer. The self-assembly process is directed by the chirality of the dialkyltartrate ligands M. The cluster core is formed by a multiprotic onium ion which can be an ammonium, hydronium or primary aminium ion. The specificity of the supramolecular structure can be used for molecular and chiral recognition studies. In principle, the core and the ligand sites can be exposed to competitive binding of suitable substrates. This technique would be an independent method to correlate the absolute configuration of chiral molecules.

The formation and behavior of the clusters $M_3 \cdot AH^+$ are now being investigated further by application of FTICR[27] and ESI[32] mass spectrometry.

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