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CHIRALITY EFFECTS IN THE CHEMICAL IONIZATION MASS SPECTRA OF DIALKYL TARTRATES

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Abstract. - The earlier discovered chirality effect in the chemical ionization mass spectra of dialkyl tartrates (Fales and Wright, 1977) has been studied further under structural and analytical aspects. Thus, enantiomers of the dialkyl tartrate type apparently interlock by H bonds to rigid diastereomeric protonated dimers MMH^+ with definite chirospecificity. Within the homologous series, the enantiomeric configuration of an "unknown" chiral substrate M exposed to an enantiomer-labeled racemic reagent D plus L is indicated by the more abundant homochiral species of the competitive mixed dimers MDH^+ and MLH^+.

The detection of molecular chirality with a mass spectrometer was reported first in 1977 by Fales and Wright[1]. Their studies showed that the chirality of dialkyl tartrates strongly influences the stability of the diastereomeric bimolecular attachment ions DDH^+, DLH^+ and LLH^+ which can be observed in the isobutane chemical ionization (CI) mass spectrum of the enantiospecifically deuterium-labeled racemate D plus L. The homochiral dimers are more stable than the heterochiral dimers by a factor of 2.2 and 1.3 for the diisopropyl and dimethyl tartrates, respectively. Gas-phase chiral interactions have also been studied in the areas of neutral collisions[2a] and chiral carrier-gas additives.[2b]

Whereas general stereochemical effects in mass spectrometry[3] have always been important topics, the molecular chirality[4] became of potential interest only after the introduction of the CI technique. However, the various interesting observations on complementary binding in CI mass spectra[1,5] are not yet well understood. Recent thermodynamic measurements on stabilities and hydrogen bonding in gaseous complexes of H_3O^+ and $CH_3OH_2^+$ ions[6] and RNH_3^+ ions[7] with polyethers and crown ethers give insight into related multiple coordination complex structures. Parallels with condensed-phase molecular recognition models[4,8] should also be expected; studies in the tartaric acid field include configurational assignment[9] and chromatographic separation[10] of enantiomers.

In this paper we outline our approach to exploring the structural correlations and the analytical aspects of the CI mass spectral chirality effect[1] and report some initial results. We applied a new technique with chiral competition for mixed-dimer formation in the CI spectra of three-component samples. This internal standard or enantiomer labeling method improves the experimental reproducibility, so that a basis for quantitative matching of substrates and for energy-increment studies is given. In our measurements (Table 1), 10-mg samples equimolar of the chiral substrate M and the enantiospecifically labeled racemic reagent components diisopropyl-d_0 D-tartrate (d_0D or D) and diisopropyl-d_{14} L-tartrate (d_{14}L or L), were introduced by a direct probe into the CI ion source of the mass spectrometer (VG Micromass ZAB 2F) at an isobutane pressure of 0.3 Torr and a source temperature of ~120 °C. The probe temperature was adjusted to give a sample pressure at which the dimer intensity ranged from 1 to 5 percent of the total sample ionization. These conditions also applied to the two-component spectra (Table 2). The investigated compounds[11] belonged to the earlier dialkyl tartrate homologs[1] and related groups. Fragment ions were absent or negligible ($<2\%$ $(MH - C_3H_6)^+$ versus 100% MH^+ in diisopropyl ester spectra).

The data evaluation of the chiral-additive CI spectra based on dimer-peak intensities is done by means of the equations (1) and (2). The chirality effect or the chirospecific ratio of the virtual equilibrium constants K_{DD}/K_{DL} ($= K_{LL}/K_{DL}$) is defined here arbitrarily as the stability of the homochiral versus the heterochiral dimers (eq. 1). Thus the observed ratio of the DDH^+ or LLH^+ versus the DLH^+ dimers is weighted with the statistical square relation $([DH^+] + [LH^+])^2$ showing the 1:2:1 pattern. If a third chiral component M (substrate) is added to the above racemate D plus L (reagent), a new chirality effect term K_{MD}/K_{ML} (eq. 2) must be introduced for the "mixed" or external dimers MDH^+ and MLH^+ as defined by their intensity ratio versus the reagent composition $[DH^+]/[LH^+] = ([DDH^+]/[LLH^+])^{1/2}$. The substrate/reagent chirality effect K_{MD}/K_{ML} (for homochiral MDH^+ dimers) or its reciprocal value K_{ML}/K_{DL} (homochiral MLH^+) can be compared with the internal reagent chirality effect K_{DD}/K_{DL}. Within series of homologous compounds, matching chirality effect values should allow the correlation of the absolute configuration of enantiomers on a phenomenological basis.

$$\text{internal reagent chirality effect} \quad K_{DD}/K_{DL} = 2\sqrt{[DDH^+][LLH^+]}\ /\ [DLH^+] \tag{1}$$

$$\text{substrate/reagent chirality effect} \quad K_{MD}/K_{ML} = ([MDH^+]/[MLH^+])/\sqrt{[DDH^+]/[LLH^+]} \tag{2}$$

The results of the chiral assignment experiments applying CI are shown in Fig. 1 and Table 1. The dimethyl and diethyl tartrate enantiomers as the first test substrates give the expected chirality effects of about 1.5 ± 0.1 and therefore clearly demonstrate the feasibility and accuracy of the approach. However, initial data from D-tartaric acid dipyrrolidide indicate the predicted direction, but a smaller size of K_{MD}/K_{ML}. The respective mixed dimers are even suppressed to a 3 % level, apparently reflecting the different basicities of the monomers. The observations on functional group change are in line with similar solution-phase[4,8] chiral recognition problems.

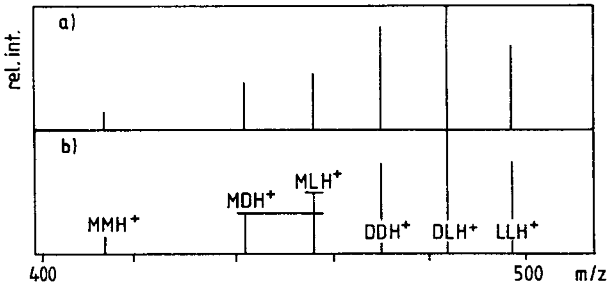


Fig. 1. Dimer region of the isobutane chiral-additive CI spectrum of diethyl L-tartrate (M). Spectrum a) as measured and b) as normalized for equal concentrations of the enantiomer-labeled additives diisopropyl-d_0 D-tartrate (D) and diisopropyl-d_{14} L-tartrate (L).

Table 1. Chiral assignment of homologous tartrate-type enantiomers in isobutane CI spectra with chiral reagent additives $d_0D + d_{14}L$ (see text)

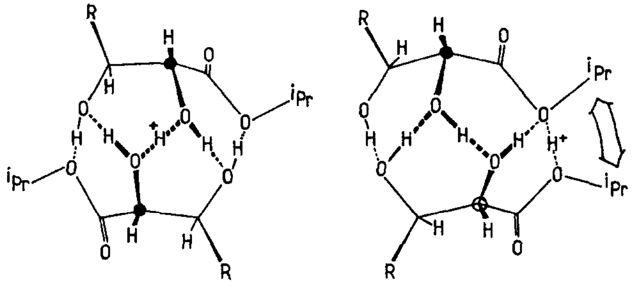
Substrate M	Chirality effects (homochiral stabilization)[a] Reagent (internal) K_{DD}/K_{DL}	for MDH^+ K_{MD}/K_{ML}	for MLH^+ K_{ML}/K_{MD}	rel. effect external/internal
diMe D-tartrate	1.57 ± 0.16	1.54 ± 0.17	(0.65)[b]	0.99 ± 0.12
diMe L-tartrate	1.51 ± 0.06	(0.74)	1.35 ± 0.14	0.88 ± 0.11
diEt D-tartrate	1.47 ± 0.04	1.55 ± 0.10	(0.65)	1.05 ± 0.08
diEt L-tartrate	1.49 ± 0.05	(0.68)	1.46 ± 0.10	0.98 ± 0.08
D-dipyrrolidide	1.43 ± 0.05	1.23 ± 0.14	(0.81)	0.86 ± 0.10

[a] Exper. errors for means of ≥5 scans. Reproducibility (~120 °C): K_{DD}/K_{DL} = 1.43-1.57
[b] ( ) = values <1 indicate heterochiral destabilization of the mixed dimer.

A causal explanation of the observed chirality effect was attempted on the basis of additional experiments (Table 2) and Dreiding stereomodel considerations. The variation of K_{DD}/K_{DL} from 1.5 to 2.2 here and earlier[1] typically reflects changes of the ion source conditions, whereas the absence of an isotope effect[1] due to the enantiomer labeling is clearly confirmed by the $d_0L/d_{14}L$ spectrum. As the meso-tartrate (meso) with the 2R,3S-configuration still gives $K_{DD}/K_{DL} \approx 1.2$ similar to a racemic mixture, the configuration of only one of the chiral centers might be essential for the stability of the diastereomeric adduct ions as depicted for LLH^+ and DLH^+ in Scheme 1.

Table 2. CI spectral chirality effect experiments with two-component mixtures of deuterium-labeled diisopropyl tartrates

Tartrate mixture	CI reagent ion	Type of dimeric ions	Chirality effect (n ≥5) K_{DD}/K_{DL}
$d_0D + d_{14}L$	$t\text{-}C_4H_9^+$	MMH^+	1.71 ± 0.04
$d_0L + d_{14}L$	$t\text{-}C_4H_9^+$	MMH^+	1.01 ± 0.05
meso + $d_{14}L$	$t\text{-}C_4H_9^+$	MMH^+	1.18 ± 0.03
$d_0D + d_{14}L$	NH_4^+	$MMNH_4^+$	0.96 ± 0.05
$d_0D + d_{14}L$	OH^-	$(MM\text{-}H)^-$	0.99 ± 0.06



homochiral dimer LLH$^+$ heterochiral dimer DLH$^+$

Scheme 1.
Chirospecific conformations of diastereomeric protonated dimers MMH$^+$ of diisopropyl tartrates (R = COO^{i}Pr)

● = ***R*** configuration
○ = ***S*** configuration

The above conformations are minimum-energy structures which allow optimal proton solvation with the total possible number of five strain-free linear H bonds. These zip-type chelate complexes with alternating participation of three vicinal sp^3-oxygens from each of the monomers also imply a basket geometry with subtantial rigidity. Therefore a chiral discrimination by a weak dialkyl gauche interaction at one outer H bond in the heterochiral DLH$^+$ adduct may become operative. This agrees with the small stability difference of $-\Delta\Delta G \approx 1.2$ kJ/mol calculated from the chirality effect of $K_{DD}/K_{DL} \approx 1.6$. These values here are higher than those for the chiral behavior of gaseous neutral dimers[2], but similar to solution phase data of ionic or strongly H-bound diastereomeric adducts.[4,8] Further support for the rigid LLH$^+$ and DLH$^+$ models is given by the expected cancellation of the chiral effect under changed CI conditions (Table 2). The deprotonated (MM-H)$^-$ dimers lack two H bonds for complete interlocking, whereas the ammonium adducts MMHN$_4^+$ are more stable as fully solvated NH$_4^+$ complexes because of the higher nitrogen basicity. According to Dreiding models various other structures of MMH$^+$ with five H bonds show additional steric strain.

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