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CONFORMATIONAL DISPARITY OF (R,R)-TARTARIC ACID ESTERS AND AMIDES

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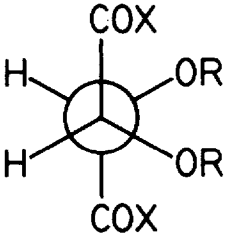
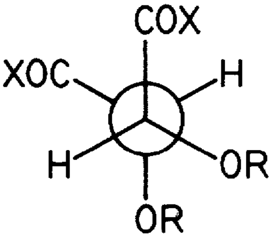
Abstract: Exciton chirality method is used to determine anti and gauche conformations, respectively, of ester and dialkylamide derivatives of (R,R)-tartaric acid. Gauche conformation of (R,R)-N,N,N'-tetramethyltartamide and its O,O-dibenzoyl derivative is found in the solid state by X-ray analysis.

(R,R)-Tartaric acid and its derivatives play an important role in organic and pharmaceutical chemistry. The chirality of the acid and the presence of polar groups in the molecule have led to the successful use of tartaric acid and O,O-dibenzoyl tartaric acid in resolution of racemates[1]. Dialkyl tartares have been recently used as chiral ligands for titanium - catalyzed asymmetric epoxidation of allylic alcohols[2] and sulfides[3]. In addition, tartaric acid diamides have been applied to resolutions of racemates by crystallization[4] and by high pressure liquid chromatography[5].

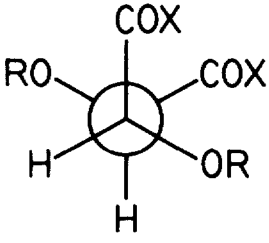
It is generally accepted that for (R,R)-tartaric acid molecules there is strong preference for anti (T) conformation of the carbon chain. This is indicated by ^{13}C NMR data for the acid[6] and its esters[7] as well as by Raman[8] and vibrational[9] CD measurements. In addition, a planar carbon chain is found in (R,R)-tartaric acid[10] and in monoammonium[11], monopotassium[12], disodium[13] and calcium[14] salts of (R,R)-tartaric acid by X-ray analysis. Recent *ab initio* calculations (6-31G/STO-3G level) on intramolecularly OH---O=C hydrogen-bonded conformers of (R,R)-tartaric acid show that conformer T is lower in energy compared to the G^+ and G^- conformers by 5.4 and 8.5 kcal/mol, respectively[9].



T



G^-



G^+

We have recently used circular dichroism measurements to study configurations and conformations of acyclic polyol benzoates[15], using the benzoate exciton chirality method[16]. When applied to (R,R)-tartaric acid derivatives, negative exciton Cotton effect of the O,O-dibenzoate is expected for conformer T (negative RO-C-C-OR torsional angle) and a positive one - for conformer G$^-$ (positive RO-C-C-OR torsional angle). Conformer G$^+$ is expected to give no exciton Cotton effect, as the two benzoate groups are coplanar.

As shown in Figure 1, the O,O-dianisoate derivative of (R,R)-diethyl tartrate (**1**) shows a negative exciton Cotton effect (A = -35.4), characteristic of conformer T, while the O,O-dianisoate derivative of (R,R)-N,N,N',N'-tetramethyltartramide (**2**) gives a positive exciton Cotton effect (A = +59.0), due to the dominance of conformer G$^-$. That these Cotton effects originate from coupling of the anisoate charge-transfer transition moments is made clear by comparison with the Cotton effects of O-anisoate derivatives of (R)-malic acid **3** and **4**, which are weak and monosignate.

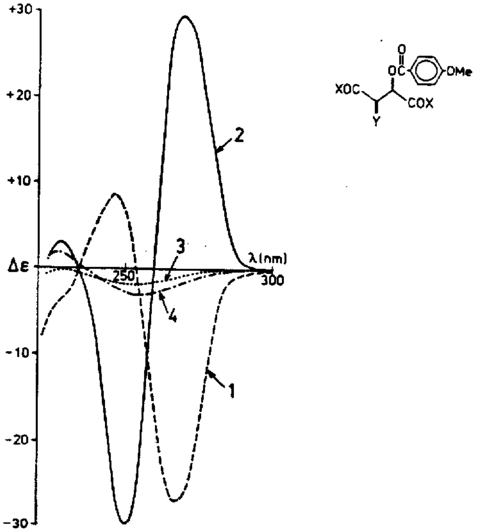


Figure 1. CD spectra (in dioxane) of O-anisoyl derivatives of (R,R)-tartaric (**1**,**2**) and (R)-malic (**3**,**4**) ester and amide:

	X	Y
1	OEt	OC(O)C_6H_4OMe
2	NMe_2	OC(O)C_6H_4OMe
3	OEt	H
4	NMe_2	H

Table 1. CD and UV data for derivatives of (R,R)-tartaric acid XOCCH(OR)CH(OR)COY (solvent dioxane)

Compound no.	X	Y	CD Δε (nm)	UV ε (nm)
	R = p-ClC_6H_4CO			
5	OEt	OEt	-28.0 (250) +4.0 (232)	34,800 (242.5)
6	NMe_2	NMe_2	+26.9 (252) -19.0 (236)	36,000 (242.5)
			+22.8 (252) -18.8 (235)[a]	37,200 (242)[a]
	R = C_6H_5CO			
7	OH	OH	-22.8 (236)[a]	26,300 (231)[a]
8	OEt	OEt	-20.8 (237)	26,200 (231)
9	OH	NEt_2	-13.3 (235)	27,800 (231)
10	OEt	NEt_2	-9.3 (234)	27,200 (230)
11	OEt	DCU[b]	-20.3 (237)	27,900 (231)
12	NEt_2	DCU[b]	+8.2 (242) -14.7 (227)	31,200 (230)
13	NMe_2	NMe_2	+11.1 (240) -10.7 (226)	29,000 (230)

[a] in methanol

[b] DCU = *cyclo*-C_6H_{11}NC(O)NH*cyclo*-C_6H_{11}

Additional CD data on (R,R)-tartaric acid derivatives are in Table 1. Diesters (**5**, **8**), diacid (**7**), and monoamides (**9** - **11**)[17] show preference for the T conformation, while N,N,N',N'-tetraalkyl diamides (**6**, **13**) and acylated N,N'-dicyclohexylurea derivative (**12**)[18] are predominantly in the G^- conformation. Substituting methanol for dioxane does not have any significant effect on the conformational preference of **6**.

In order to compare CD conformational results in solution with the conformation of tartramides in the crystalline state we have performed X-ray analyses of (R,R)-N,N,N',N'-tetramethyltartramide **14** and its O,O-dibenzoyl derivative **13**[19].

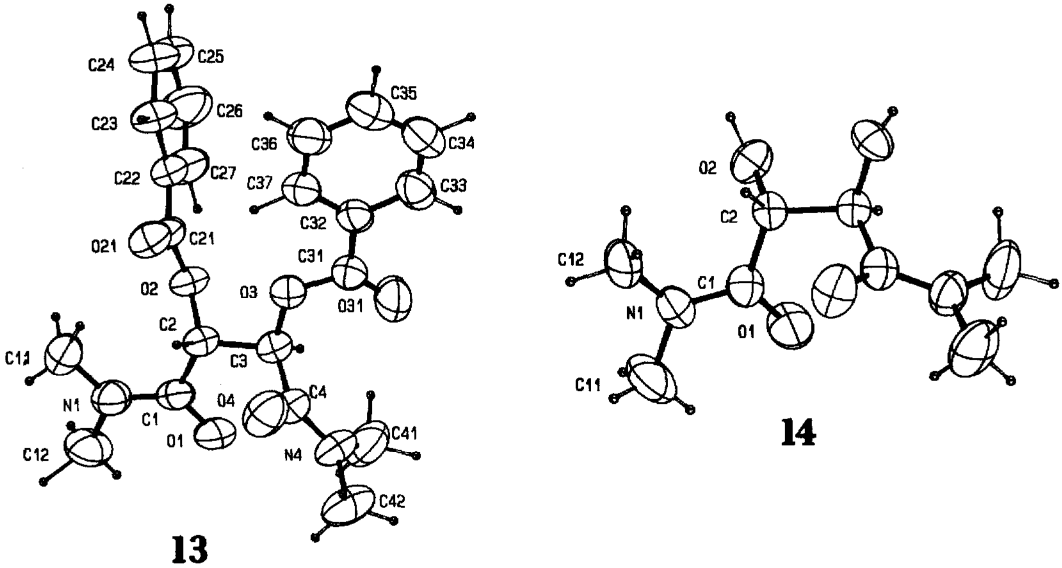


Figure 2. Perspective view of the molecules 13 and 14. The molecule 14 has a two-fold rotation axis coinciding with the crystallographic diad. Selected torsion angles: 13: O(1)-C(1)-C(2)-O(2) = 115.7(2)°, O(3)-C(3)-C(4)-O(4) = 57.6(3)°, C(1)-C(2)-C(3)-C(4) = -67.2(3)°, O(2)-C(2)-C(3)-O(3) = 60.4(2)°; 14: O(1)-C(1)-C(2)-O(2) = 90.5(3)°, C(1)-C(2)-C(2')-C(1') = -52.4(2)°, O(2)-C(2)-C(2')-O(2') = 71.6(2)° (primes denote symmetry related atoms).

As can be seen from Figure 2 both **13** and **14** adopt in the solid state a staggered conformation about the central C-C bond in which both hydroxy (or benzoyloxy) and amide groups are in a gauche arrangement. Thus conformer G^- is favoured in N,N,N',N'-tetraalkyl tartramides both in solution and in the solid state. One particular feature of this conformer is the presence of two gauche bond systems, RO-C-C-OR and XOC-C-C-COX, with the possibility of contributing an attractive gauche effect and thus stabilizing the conformation. This effect is well documented for molecules having vicinal small electronegative groups[20].

Our present findings should help rationalize different effects of tartrates and tartramides as ligands in the Sharpless epoxidation[21] as well as in analyzing enantioselective complex formation of tartramides by means of intermolecular hydrogen bond formation in solution and in the crystal[4,22].

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17. The $^3J_{2H,3H}$ coupling constants for 9 - 11 are 5.6, 4.9, and 4.1 Hz, respectively.
18. Compounds 11 and 12 were obtained, respectively, by the addition of N,N'-dicyclohexylcarbodiimide to O,O-dibenzoyl-(R,R)-tartaric acid monoethyl ester or monoamide 9 in dichloromethane. All compounds are fully characterized by NMR, IR, and elemental analyses.
19. **Crystal data.** **13:** Crystals were obtained from AcOEt - Et$_2$O, $C_{22}H_{24}O_6N_2$, M=410.43, monoclinic, space group P2$_1$, a=9.578(1), b=13.692(1), c=8.508(1) Å, β=102.783(9)°, V=1088.1(2) Å^3, D$_c$=1.26 gcm^{-3}, Z=2, λ=1.54178 Å, μ(CuKα) =0.78 mm^{-1}, F(000)=436. R=0.036, wR=0.050 for 2795 observed reflections (I≥σ(I)) and 285 parameters. **14:** Crystals were obtained from MeOH - AcOEt, $C_8H_{16}O_4N_2$, M=204.23, trigonal, space group P3$_2$2, a=b=9.4366(8), c=10.6896(8) Å, V=824.4(1) Å^3, D$_c$=1.23 gcm^{-3}, Z=3, λ=1.54178 Å, μ(CuKα)= 0.84 mm^{-1}, F(000)=330. R=0.035, wR=0.050 for 736 observed reflections (I≥2σ(I)) and 80 parameters. Intensities were collected on a Syntex P2$_1$ diffractometer, at room temperature. The data were corrected for Lorenz and polarization effects, absorption was ignored. Structures were solved by direct methods and refined using F magnitudes by full-matrix least squares; [$w^{-1}=\sigma^2(F) + 0.0001F^2$]. Details of the X-ray analysis will be reported elswhere.
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