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Tartaric Acid Chloralides: Isolation and X-ray Analysis of the Third Existing Stereoisomer. Force-Field and AM1 Calculation of all Six Possible Structures

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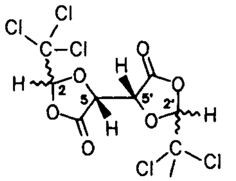
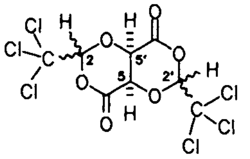
Isolation of a third diastereoisomer (1c) of (*R*,*R*)-tartaric acid chloralide is described. A comparison of structural data derived by X-ray analysis with calculated parameters is given. Structures are generated by the ALCHEMY force-field program as well as by AM1 calculations.

Several years ago[1)] an X-ray structure analysis of tartaric acid "chloralides" **1a** and **1b** has been reported. These are diastereoisomeric condensation products of two equivalents of prochiral chloral hydrate with (*R*,*R*)-tartaric acid. However, so far none of the authors[1)] have considered the possibility that there should be three diastereoisomers in the product mixture, according to the four asymmetric carbon atoms in the molecule.



1a–c



2a–c

1,2	Configuration at position			
	2	5	5'	2'
a	*S*	*R*	*R*	*S*
b	*S*	*R*	*R*	*R*
c	*R*	*R*	*R*	*R*

In the course of our work on the reductive cleavage of tartaric acid chloralide[2)], we found by TLC analysis the third diastereoisomer **1c** which we were able to isolate in one recrystallization step followed by preparative chromatography.

Surprisingly, the new compound has a much higher melting point (205°C) than the chloralides **1a** (175°C) and **1b** (162°C), but a very similar ^{1}H-NMR spectrum to **1a** which is highly symmetrical. The ^{13}C-NMR spectra (Table 1) exhibit again just four different carbons like **1a**, whereas the less symmetrically compound **1b** shows two pairs of four carbons. According to the intensity of the carbon signals the concentration ratio **1a**:**1b**:**1c** in the crude reaction product is 3.8:9.4:1.0.

Table 1. Optical rotation (c = 0.9, acetone) and ^{13}C-NMR data of **1a**–**1c** ($CDCl_3$)

1	$[\alpha]_D^{22}$	C-2	CCl_3	C-5	C-4
a	+28.4	74.27	97.25	105.39	166.00
b	+49.0	73.19[a)] 75.01[a)]	95.23[b)] 97.00[b)]	103.79[c)] 105.16[c)]	165.17[d)] 166.36[e)]
c	+54.0	73.46	95.25	104.22	166.07

Off-resonance multiplicity: [a)] d, 160 Hz; [b)] d, 12 Hz; [c)] d, 190 Hz; [d)] d, 5 Hz; [e)] dd, 3 and 3 Hz.

Considering the significantly higher melting point and the NMR spectra one is not able to distinguish the newly found diastereoisomer **1c** from one of the two possible symmetrical six-membered dioxanone structures **2** which should be at least equally possible. NOE experiments did not give any helpful hint, either. A significant effect of 9 ± 1% was only found for nonsymmetrical **1b** (for 2-H with high-field 5-H, probably that in *cis* position[3)]), but none in this order of magnitude for **1a** and **1c**.

Therefore, an X-ray analysis was performed to assign the new structure **1c** or **2**.

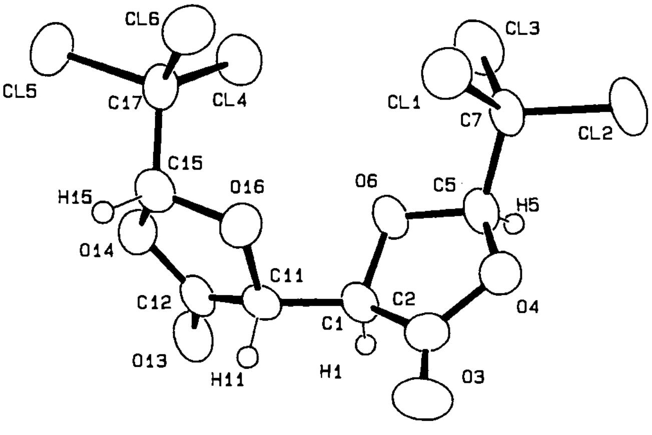


Figure 1. ORTEP drawing of **1c**, thermal ellipsoids in 50% probability scale

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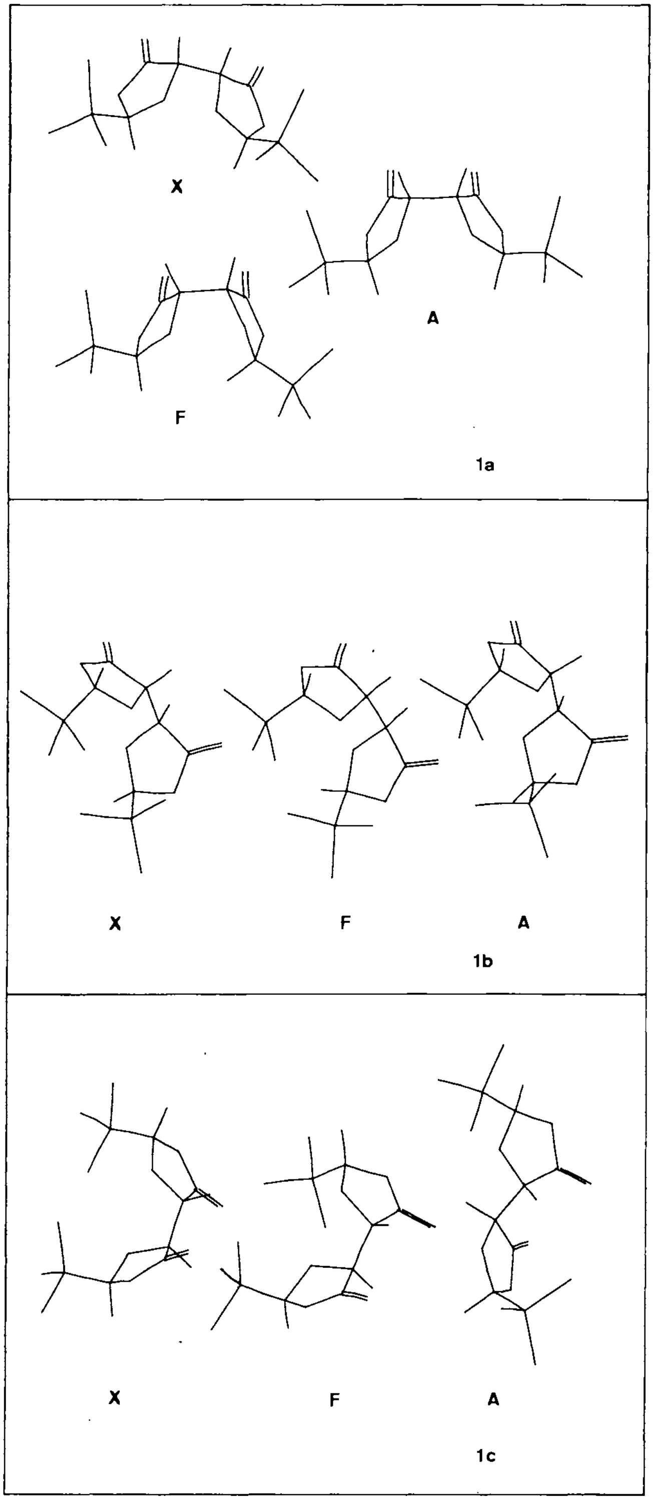

Figure 2. Comparison of X-ray structures (X) with the structures generated by force-field (F) and AM1 calculations (A) for **1a**–**1c**; oxygens and chlorines are not enhanced especially (original ALCHEMY plot has coloured atoms)

Figure 1 shows that the new compound is in fact the hitherto unknown third diastereoisomeric five-membered chloralide **1c**. It is the sterically most hindered *cis-cis* isomer. Interestingly, in the crystal a rather crowded conformation is adopted which one would not expect. The two trichloromethyl groups are quite close with distances of 3.7 and 3.8 Å between Cl4 and Cl1 or Cl3, respectively.

Table 2. Puckering amplitudes q and C2–C5–C5′–O1′ torsional angles τ for compounds **1a**–**1c**

	1a			**1b**			**1c**		
	ring 1	ring 2	τ	ring 1	ring 2	τ	ring 1	ring 2	τ
X-ray	0.04	0.10	−30	0.04	0.16	−24	0.13	0.22	−11
FF	0.26	0.19	−27	0.24	0.25	−21	0.18	0.26	17
AM1	0.07	0.08	−13	0.06	0.08	−19	0.06	0.06	130

The two five-membered rings of **1c** deviate slightly from planarity (Table 2). Puckering amplitudes are comparable to the one five-membered ring of **1b** with (R) configuration at the trichloromethyl-bound carbon. For *trans-trans* isomer **1a** both rings were found to be planar[1]. The relative position of the two rings with respect to the adjoining bond as measured by the torsional angle C2–C5–C5′–O1′ is surprisingly very similar for all three diastereoisomers. The torsional angles O1–C5–C5′–O1′ for **1a** and **1b** (−63°) and for **1c** (−44°) are also similar. This might be due to a preferred *anti* position of the two carbonyl groups.

Figure 2 shows a comparison of the X-ray structures for **1a**–**1c** with the structures generated by force-field[4] as well as by semiempirical molecular orbital (AM1)[5] calculations. Both methods provide a satisfactory description of the energetic (Table 3) as well as structural aspects (Table 2 and Figure 3) of the investigated compounds. The minimum energy conformation for **1c** as calculated by AM1 differs considerably from both the force-field and experimental results. However, the potential energy curve for rotation around C5–C5′ (Figure 3) is very flat over a wide range of about 130°. At the X-ray value of $\tau = -11°$ the AM1-calculated energy is only less than 1 kcal/mol higher.

Table 3. Sterical energies (force field) and heats of formation (AM1) for compounds **1a**–**1c** and **2a**[a]–**2c** [kcal mol^{-1}]

	1a	**1b**	**1c**	**2a**	**2b**	**2c**
FF	7.0	5.6	8.3	3.1	2.1	0.9
AM1	−251.0	−249.4	−248.7	−234.8	−240.8	−242.3

[a] Lettering of **2** corresponds to the stereochemistry of **1**.

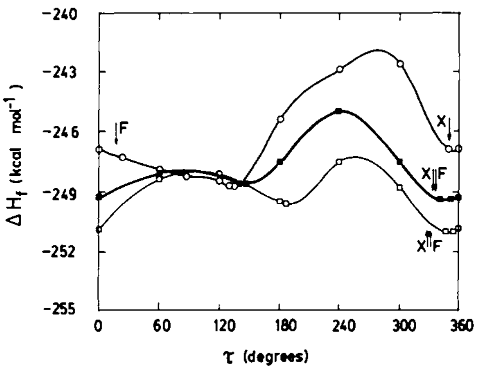

Figure 3. Calculated (AM1) potential energy curves for rotation around the C5–C5′ bond (□: **1a**, ■: **1b**, ○: **1c**); experimental (X) as well as force-field (F) torsional angles τ are marked by arrows

Experimental

NMR: Varian XL 200 (TMS as internal standard). – Optical rotation: Perkin-Elmer polarimeter 441, 10-cm cell. – Preparative chromatography: FMI pump RPD, 2 bar, silica gel (GRACE) 35–70 µm.

Separation of Chloralides **1a–c**

(2R,2′R,5R,5′R)-2,2′-Bis(trichloromethyl)-5,5′-bis(1,3-dioxolane-4,4′-dione) (**1c**): Identification of the diastereoisomers was achieved by TLC (toluene; Kieselgel 60, Merck): $R_f = 0.53$ for **1a**, 0.33 for **1b**, and 0.21 for **1c**. The identity of **1a** and **1b** was checked by comparison of the ^{1}H-NMR data and mp's (ref.[1] 176 and 162°C, respectively). Fractional recrystallization of 20.4 g (50 mmol) of the crude condensation product [from (*R,R*)-tartaric acid and chloral hydrate[2]] from 70 ml of CCl_4 gave after 1 h at 20°C 6.0 g (29%) of pure **1b**. After 3 h, additional 4.5 g of precipitate was collected which gave after 2 more recrystallizations 3.2 g (16%) of more pure **1b**. The combined filtrates were evaporated, and a solution of the residue in 50 ml of toluene was separated on 500 g of silica gel with toluene at 2 bar. Complete separation of **1a** was achieved (yield 4.9 g, 24%), as well as of **1c** (0.4 g, 2%). A second fraction of 2 g containing a 7:3 mixture of **1b** and **1c** yielded after another chromatographic run 1.3 g (6%) of pure **1b** and 0.4 g (2%) of **1c**. The latter was recrystallized from CCl_4 to give the analytically pure sample, m.p. 204–205°C, which was also used for X-ray analysis.

$C_8H_4Cl_6O_6$ (408.8)	Calcd.	C 23.50	H 0.99	Cl 52.03
	Found	C 23.25	H 1.03	Cl 51.40

Calculated from the ^{13}C-NMR data, the diastereoisomeric mixture contained 27% of **1a**, 66% of **1b**, and 7% of **1c**. Hence, the recovery of **1a** was 4.9 g (89%), of **1b** 10.5 g (78%), and of **1c** 0.8 g (57%). – ^{1}H-NMR ($CDCl_3$): **1c**: $\delta = 4.98$ and 5.87 ppm (dd each, $J = 1.1, 0.3$ Hz); NOE: 0.5 ± 0.2%. The spectrum is almost identical with that of **1a**[1] which gives signals at $\delta = 5.1$ and 6.0 (d each, $J = 1.0$ Hz); with **1a** no NOE could be detected. **1b** is different and has been described in ref.[1]. An NOE of 9 ± 1% could be found for the high-field 5-H which should be in *cis* position to 2-H[3].

X-ray Analysis of **1c**[6]: Crystals were obtained by vaporization of a concentrated CCl_4 solution [crystal size 0.3 × 0.3 × 0.3 mm; $F(000) = 404$; space group $P2_1$; $a = 9.184(8)$, $b = 5.814(4)$, $c = 13.689(11)$ Å; $\beta = 106.86(6)°$; $V = 699.4$ Å^3; $Z = 2$]. Cell parameters were determined by least-squares refinement of the angular positions of 10 reflections in the range $20° \leqslant 2\Theta \leqslant 35°$.

Data were collected on a modified STOE four-circle diffractometer with Mo-K_α radiation ($\lambda = 0.71069$ Å, graphite monochromator). 2485 unique reflections [2288 with $F > 4\sigma(F)$] were measured with ω-scan technique ($\Delta\omega = 1.0°$) to a limit of $2\Theta = 50°$. Three standard reflections were periodically monitored (every 100 reflections). Their intensities fluctuated by less than 5.5%. Intensity data were corrected for Lorentz and polarisation effects, but not for extinction or absorption ($\mu = 12.5$ cm^{-1}).

The structure was solved by locating the chlorine atoms from a patterson map. A subsequent tangent expansion and two cycles of structure optimization[7] yielded the positions of all nonhydrogen and two hydrogen atoms.

Table 4. Fractional atomic coordinates (× 10^4) and equivalent temperature parameters (× 10^4) [Å^2] for **1c**

	x/a	y/b	z/c	U_{eq}
C1	1499 (4)	-56 (7)	1225 (3)	357 (20)
H1	590 (41)	-653 (63)	708 (28)	389 (105)
C2	1129 (4)	2335 (8)	1516 (3)	411 (24)
O3	1031 (4)	4048 (6)	1047 (2)	589 (21)
O4	860 (3)	2168 (5)	2427 (2)	445 (17)
C5	1037 (4)	-159 (8)	2755 (3)	366 (21)
H5	112 (49)	-830 (79)	2704 (33)	555 (128)
O6	1766 (3)	-1323 (5)	2141 (2)	386 (15)
C7	1969 (4)	-299 (7)	3876 (3)	358 (20)
CL1	3744 (1)	1006 fix	4070 (1)	509 (6)
CL2	951 (1)	1121 (3)	4607 (1)	542 (6)
CL3	2182 (2)	-3203 (3)	4218 (1)	614 (8)
C11	2839 (4)	-107 (8)	788 (3)	371 (21)
H11	2689 (36)	970 (66)	293 (27)	292 (93)
C12	3052 (4)	-2278 (8)	265 (3)	411 (24)
O13	2185 (3)	-3351 (6)	-381 (2)	536 (18)
O14	4542 (3)	-2872 (6)	629 (2)	480 (17)
C15	5321 (4)	-1258 (8)	1365 (3)	397 (22)
H15	5996 (40)	-308 (65)	1035 (28)	397 (102)
O16	4231 (3)	241 (5)	1558 (2)	405 (15)
C17	6188 (4)	-2465 (7)	2339 (3)	392 (22)
CL4	5015 (1)	-4198 (3)	2830 (1)	558 (7)
CL5	7610 (1)	-4192 (3)	2056 (1)	586 (6)
CL6	7073 (1)	-344 (3)	3224 (1)	524 (6)

Refinement[8] of positional and anisotropic thermal parameters (hydrogens isotropic) by full-matrix least squares led to a residual $R = 0.0364$, $R_w = 0.0343$ ($1/\sigma^2$ weights, 196 parameters, 2288 observables). Atomic coordinates and equivalent temperature parameters are shown in Table 4.

CAS Registry Numbers

1a: 119717-54-3 / **1b**: 119717-55-4 / **1c**: 119717-56-5 / **2a**: 119639-09-7 / **2b**: 119717-57-6 / **2c**: 119717-58-7 / $Cl_3CCH(OH)_2$: 302-17-0 / $\text{-}\!\!\!\!+\,CH(OH)CO_2H]_2$: 87-69-4

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