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Diastereoisomerization and X-ray Crystal Structure of *meso*-di-(2*H*-Chromene-2-yl) Ether[#]

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It was shown by X-ray crystal structure analysis that di-(2*H*-chromene-2-yl)-ether (**1**) exists in the *meso*-form, *i.e.* as (2*S*, 2'*R*)-**1**. The X-ray structural data indicate, also, that geometries of the two 2*H*-1-benzopyran parts, of which the skeleton of **1** consists, are not identical, that is the molecule is pseudosymmetrical. The *meso*-**1** undergoes thermally induced electrocyclic ring opening and reclosure. Thus, *meso*-**1** equilibrates with enantiomers (2*S*, 2'*S*)-**1** and (2*R*, 2'*R*)-**1**, as confirmed by their ^{1}H-NMR spectra after preparative separation of stereoisomers using liquid chromatography on triacetylcellulose.

INTRODUCTION

2*H*-Chromenes or 2*H*-1-benzopyrans have been the subject of extensive studies largely because of their photochromism, which is based on a reversible photoisomerization involving a rupture of the C(sp^3)-O bond.[1] Some of such systems have found use in the display and storage of information as well as solar energy conversion.[2] Compared to the relatively numerous studies on photochromisms of 2*H*-chromenes,[1,2] relatively few similar studies on thermochromic behaviour of non-spiro 2*H*-chromenes,[3,4] structurally related spiro [chromene-2,2'-indolines][5] and spiro [chromene-2,1'-(2)oxaindans][6] are available. In the cases of spiro-chromenes, the presence of dias-

[#] Chiral 2*H*-Pyrans, Part 5; Part 4: Ref. 18.

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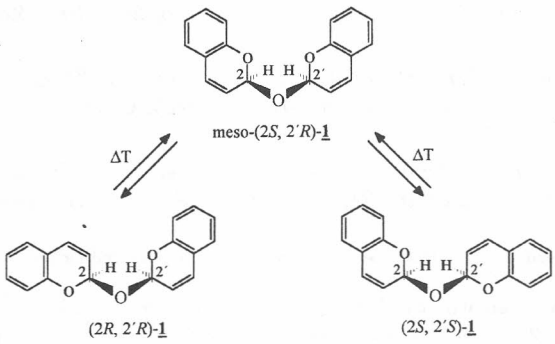
tereotopic groups was necessary for the application of the variable-temperature ^{1}H-NMR spectroscopy. Our interest in chiral chromenes was related, therefore, to separation of enantiomers and determination of the barriers to electrocyclic ring opening *via* thermal racemization of enantiomers.[7–9] While reports on dichromenyl ether exist,[10,11] studies on diasterteoisomerization of chromenes are, to our knowledge, not available. Thus, the aim of this work was to study thermally induced diastereoisomerization of the so called »double chromene« with two chiral centres.

RESULTS AND DISCUSSION

Di-(2*H*-chromen-2-yl) ether (**1**)[10] was prepared by reduction of coumarine by diisobutyl aluminium hydride[12] and subsequent treatment of the reaction product by aqueous acetic acid. This molecule possesses two chiral centres and may exist either as *meso*-(2*R*, 2'*S'*) or racemic (2*R*, 2'*R*) and (2*S'*, 2'*S'*) form (*c.f.* Scheme). The X-ray crystal structure analysis revealed the presence of only *meso*-**1** form (Figures 1 and 2).



Scheme

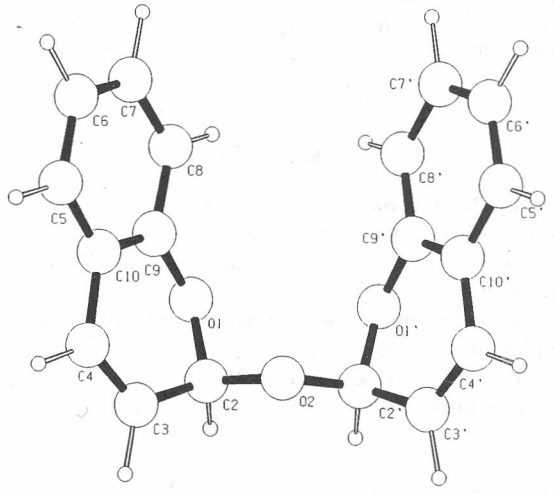


Figure 1. Perspective view and atom numbering of di-(2*H*-chromene-2-yl)-ether (**1**).

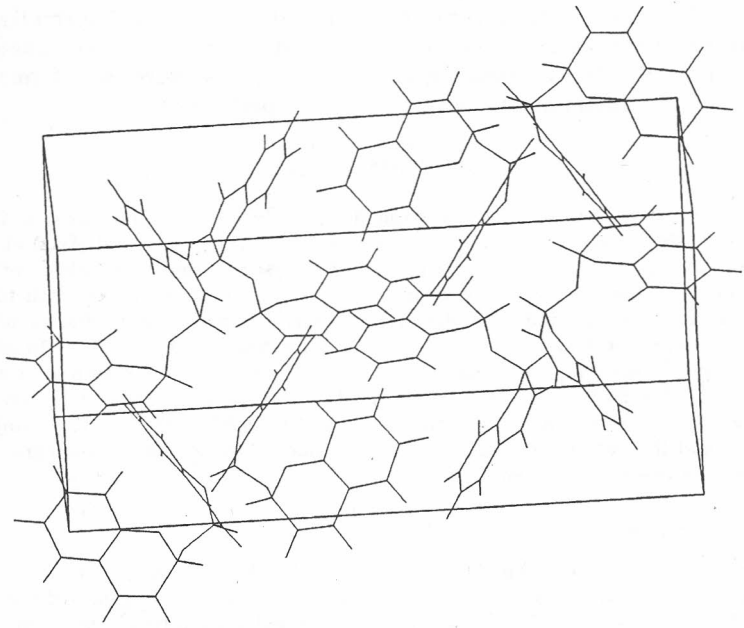


Figure 2. Packing diagram in the unit cell of **1**.

Analysis of the structural data shows that the skeleton of **1** consists of two 2*H*-1-benzopyran parts connected by the bridging ether bond C(2)-O(2)-C(2') (Figure 1). The angle of these bonds is 114.7°. This value is in good agreement with the corresponding values of glycosidic link in structurally related loganin[13] and gentiopicin.[14] The dihedral angle between the planes of 2*H*-1-benzopyran moieties is 104.6°. The values of bond lengths and angles (Table II) are very similar in both 2*H*-1-benzopyran rings, that is their geometry is almost identical, but not the same. Thus, internal stereochemical relation between both 2*H*-1-benzopyran parts of the molecule is only apparently symmetrical, and the molecule is, therefore, pseudosymmetrical. As fas as we are aware, the literature contains no reference to this specific point.

In order to induce thermal conversion of **1** into its diastereomers (2*R*, 2'*R*)-**1** and (2*S*, 2'*S*)-**1** (Scheme), this compound was heated in a thermostated ^{1}H-NMR tube and the reaction was followed by ^{1}H-NMR spectroscopy. Analysis showed that, besides signals of the starting *meso*-compound and those which were to be expected for diastereomers, additional signals in the ^{1}H-NMR spectrum of the reaction product were present. Therefore, that mixture was separated by low pressure liquid chromatograhy on triacetylcellulose (TAC). This chromatography allowed separation of the *meso*-**1** from its diastereomers consisting of the racemic mixture of (2*R*, 2'*R*) and (2*S'*, 2'*S'*)-**1**, as clearly indicated by an analytical chromatogram showing the presence of two enantiomeric peaks. However, preparative separation of enantiomers was not accomplished. ^{1}H-NMR spectrum of the reaction product after equilibration proved the presence of a mixture consisting of the *meso*-**1** and its diastereomers: (2*R*, 2'*R*)- and (2*S'*, 2'*S'*)-**1** (Figure 3) in the ratio of 1:1.5:0.5, as established from the peak areas

of the analytical chromatogram. From this it follows that the thermally induced ring opening and reclosure of the C(sp^3)-O bonds in **1** occurred to form diastereomers (2*R*, 2'*R*)- and (2*S'*, 2'*S'*)-**1**. However, because of various byproducts formed in this thermal reaction, kinetic measurements were not performed.

EXPERIMENTAL

M.p.s were determined on a Kofler Mikroheitztisch (Reichert, Wien) and are not corrected. The ^{1}H-NMR spectra were recorded on a Bruker ARX-400 (Pft mode, 400 MHz) at 24 ± 2 °C with the measuring accuracy of ± 0.002 ppm. Low pressure liquid chromatography, column 300 x 25 mm, at a flow rate of 210 cm^3 min^{-1}, Δp = 2.5 – 3.0 bar on TAC with the particle diameter of 0.02 – 0.03 mm and ethanol:water, 96:4 (*v*/*v*), or methanol as eluents at 22–25 °C, was used for preparative separation of stereoisomers. Injected quantities were 5–10 mg in 1 cm^3 of solvent. High pressure liquid chromatography (HPLC), column 250 x 10 mm at a flow rate of 1 cm^3 min^{-1}, Δp = 90 bar on TAC with the particle diameter of 0.007–0.015 mm and ethanol:water, 96:4 (*v*/*v*), or methanol as eluents at 23 °C, was used for analytical separation. Sample injection and the detector system, along with other details of the chromatographic equipment, have been described previously.[15]

Meso-*di-(2*H*-chromene-2-yl)-ether (**1**)*[10]

A solution of coumarine (2.0 g, 0.014 mol) in 60 ml of dry toluene was reduced at approximately –40 °C by dropwise addition of 17 ml of 1.2 M diisobutylaluminium hydride (0.20 mol) in hexane for about 30 min. Oxygen was excluded by bubbling nitrogen through a solution. The mixture was stirred under cooling to maintain the temperature of –40 to –30 °C for 3 hrs after which time the solution was poured into a mixture containing 53 ml of acetic acid, 50 ml of water and 50 g of ice. The aqueous phase was extracted with 250 ml of chloroform, the organic layer washed with water and aqueous sodium carbonate, and dried over magnesium sulfate. The oily residue, obtained after removing the solvent under reduced pressure, crystallized from ethanol after standing overnight in the refrigerator. Yield 47%, m.p. 158–160 °C. This product was recrystallized from acetone by slow evaporation of the solvent at room temperature to give colourless crystals of m.p. 159–160 °C (Ref. 10, m.p. 163 °C). ^{1}H-NMR ($CDCl_3$): δ 5.86 (dd, ^3J = 3.9 Hz, $^3J_{AB}$ = 9.7 Hz, 2H, 3,3'-H), 6.10 (d, ^3J = 3.9 Hz, 2H, 2,2'-H), 6.70 (d, $^3J_{AB}$ = 9.7 Hz, 2H, 4,4'-H), 6.9-7.3 (m, 8H, Ar-H) (*cf.* Scheme), HPLC: TAC/MeOH, k'^{**} = 4.11; TAC/EtOH, k'^{**} = 18.2.

X-Ray Crystal Structure Study

Single crystals of **1**, suitable for X-ray structure analysis, were prepared by growth under slow evaporation at room temperature of a dilute solution of benzene. A colourless crystal, dimensions 0.35 x 0.39 x 0.64 mm, was mounted on a Philips PW 1100 diffractometer upgraded by Stoe; data were collected in the ω=2θ scan mode (2-θ-30°), graphite-monochromated Mo K_α radiation; lattice parameters from a least-squares refinement of 19 reflections (24.2–2θ –35.8°); monitored reflections (0,1,–10; 6,0,4 and 2,5,2) showed only statistical variations in intensities; 4121 independent reflections were measured (h = 0.15; k = 0.16; l = 0.32), 1103 ≥ 2σ(I); Lorentz-polarization corrections were applied; structure was solved by direct methods, block-cascade least squares refinment, H atoms were located in the difference map but were allowed to ride at fixed distances from the attached atoms,

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** Capacity factors that correspond to the stabilities of diastereoisomeric sorbates[15,19]

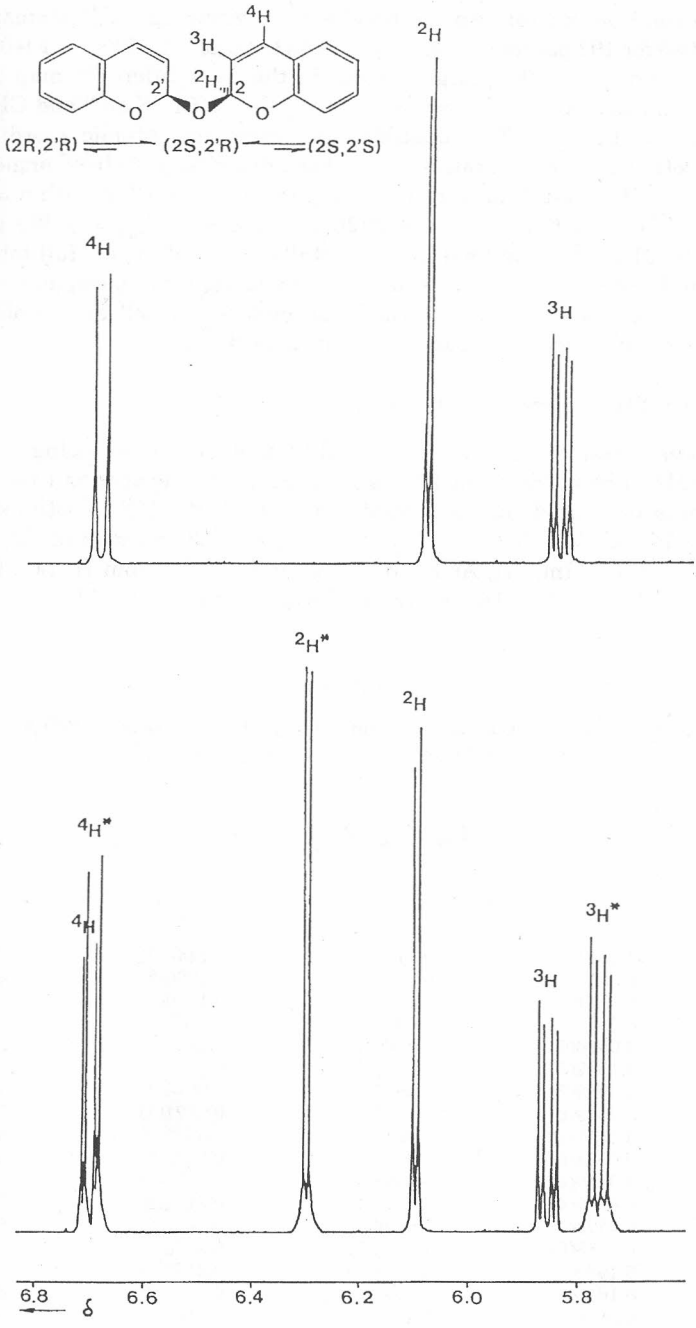

Figure 3. ^{1}H-NMR in $CDCl_3$ of the ^{2}H, ^{3}H and ^{4}H protons of *meso*-(**1**) (top) and the mixture of *meso*-, (2*R*, 2'*R*)- and (2*S*, 2'*R*)-**1** (bottom) after equilibration. Signals of racemate are denoted by asterices.

isotropicthermal parameters were refined for two groupings of H atoms; R = 0.086 and ωR = 0.088 for 192 parameters and 1103 reflections, $w = 2.1536/[\sigma^2(F)+0.00389(F)^2]$ I; S = 2.450; $(\Delta/\sigma)_{max}$ = 0.002; largest peaks in the final difference map : +0.38 and –0.50 e Å^{-3}. All calculations were performed with the SHELXS 86[16] and CRYSRULER package[17] on a IBM PC/AT compatible microcomputer. Atomic coordinates with equivalent isotropic thermal parameters and bond distances with bond angles are given in Tables I and II. Crystal data for $C_{18}H_{14}O_3$: space group *Pbca* with a = 11.572(3), b = 10.771(2), c = 22.669(3) Å, V = 2826(1) Å^3, Z = 8, d_{calc} = 1.309 g cm^{-3} and μ(Mo K_α) = 0.827 cm^{-1}. Additional X-ray crystallographic data, *i.e.* full tables of bond distances and bond angles, tables of anisotropic thermal parameters, hydrogen atomic coordinates with isotropic termal parameters, as well as the observed and calculated structure factors (9 pages) are given as deposit.

*(+) and (–)-Di-(2*H*-Chromene-2-yl)-ether(**1**)*

These were obtained after d_8-toluene solution of the *meso*-**1** being thermostated in the ^{1}H-NMR tube at 95 °C for 24 hrs, by preparative separation from the *meso*-**1** using low pressure liquid chromatography on TAC[15]. ^{1}H-NMR of both (+)- and (–)-**1** ($CDCl_3$): δ 5.76 (dd, ^3J = 3.9 Hz, $^3J_{AB}$ = 9.7 Hz, 2H, 3,3'-H), 6.69 (d, $^3J_{AB}$ = 9.7 Hz, 2H, 4,4'-H) 6.95–7.29 (m, 8H, Ar-H), impurity at δ 7.5–7.7 ppm HPLC: TAC/MeOH, $k_1'^{**}(-)_{365}$=2.7, $k_2'^{**}(+)$=4,1; TAC/EtOH, $k_1'^{**}(+)_{365}$=8.3; $k_2'^{**}(-)$ = 11.7.

TABLE I

Atomic coordinates and equivalent isotropic thermal parameters (x 10^4) with e.s.d.'s in parentheses in the structure of $C_{18}H_{14}O_3$

$$U_{eq} = \frac{1}{3}\sum_i \sum_j U_{ij} a_i^* a_j^* a_i a_j$$

Atom	x	y	z	U_{eq}
O1	–0.1484(4)	0.9191(5)	0.1440(2)	650(19)
C2	–0.0548(7)	0.8515(7)	0.1696(3)	637(29)
C3	–0.0164(7)	0.7463(7)	0.1319(4)	712(28)
C4	–0.0323(6)	0.7477(6)	0.0747(4)	658(32)
C5	–0.0980(6)	0.8706(7)	–0.0131(3)	569(26)
C6	–0.1562(7)	0.9725(7)	–0.0359(4)	658(30)
C7	–0.2080(7)	1.0547(7)	0.0018(4)	709(32)
C8	–0.2049(6)	1.0398(6)	0.0621(4)	580(26)
C9	–0.1451(5)	0.9357(6)	0.0843(3)	475(24)
C10	–0.0938(6)	0.8517(6)	0.0469(3)	494(25)
O2	–0.0440(4)	0.9291(4)	0.1778(2)	479(14)
O1'	–0.0372(4)	1.1119(4)	0.2171(2)	537(16)
C2'	0.0379(6)	1.0094(7)	0.2281(3)	536(26)
C3'	0.1588(6)	1.0509(7)	0.2399(3)	557(26)
C4'	0.1990(6)	1.1529(7)	0.2161(3)	543(26)
C5'	0.1618(7)	1.3349(7)	0.1488(3)	605(28)
C6'	0.0846(7)	1.4076(7)	0.1188(4)	649(28)
C7'	–0.0327(7)	1.3813(7)	0.1199(3)	608(28)
C8'	–0.0737(6)	1.2807(6)	0.1531(3)	572(24)
C9'	0.0061(5)	1.2066(6)	0.1821(3)	412(19)
C10'	0.1240(5)	1.2319(6)	0.1817(3)	451(21)

TABLE II

Bond distances (Å) and bond angles (°) in the structure of $C_{18}H_{14}O_3$

O1 – C2	1.428(9)	O2 – C2'	1.433(8)
O1 – C9	1.366(8)	O1' – C2'	1.427(9)
C2 – C3	1.487(11)	O1' – C9'	1.386(8)
C2 – O2	1.428(9)	C2' – C3'	1.493(10)
C3 – C4	1.310(13)	C3' – C4'	1.309(10)
C4 – C10	1.469(10)	C4' – C10'	1.444(10)
C5 – C6	1.388(11)	C5' – C6'	1.369(11)
C5 – C10	1.376(10)	C5' – C10'	1.407(10)
C6 – C7	1.369(12)	C6' – C7'	1.387(11)
C7 – C8	1.377(13)	C7' – C8'	1.402(10)
C8 – C9	1.410(9)	C8' – C9'	1.386(9)
C9 – C10	1.375(9)	C9' – C10'	1.391(8)
C2 – O1 – C9	116.6(5)	C2' – O1' – C9'	116.7(5)
O1 – C2 – O2	111.2(6)	O2 – C2' – O1'	111.0(5)
O1 – C2 – C3	112.4(6)	O1' – C2' – C3'	111.7(6)
C3 – C2 – O2	106.4(6)	O2 – C2' – C3'	106.1(6)
C2 – C3 – C4	121.2(7)	C2' – C3' – C4'	120.7(7)
C3 – C4 – C10	120.1(7)	C3' – C4' – C10'	120.2(6)
C6 – C5 – C10	120.2(7)	C6' – C5' – C10'	120.8(7)
C5 – C6 – C7	119.5(8)	C5' – C6' – C7'	120.9(7)
C6 – C7 – C8	122.2(7)	C6' – C7' – C8'	119.9(7)
C7 – C8 – C9	117.4(7)	C7' – C8' – C9'	118.3(6)
O1 – C9 – C8	116.4(6)	O1' – C9' – C8'	117.0(6)
C8 – C9 – C10	121.0(7)	C8' – C9' – C10'	122.5(6)
O1 – C9 – C10	122.5(6)	O1' – C9' – C10'	120.2(6)
C5 – C10 – C9	119.8(6)	C5' – C10' – C9'	117.6(6)
C4 – C10 – C9	116.5(6)	C4' – C10' – C9'	118.1(6)
C4 – C10 – C5	123.6(7)	C4' – C10' – C5'	124.4(6)
C2 – O2 – C2'	114.7(5)		

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SAŽETAK

Dijastereoizomerizacija i rendgenska kristalna struktura *meso*-di(2*H*-kromen-2-il)etera

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Rentgenskom strukturnom analizom pokazano je da di-(2*H*-kromen-2-il)eter (**1**) postoji u *mezo*-obliku, tj. (2*S*, 2'*R*)-**1**. Rentgenski strukturni podaci također pokazuju da geometrije dvaju 2*H*-1-benzopiranskih dijelova od kojih se sastoji skelet molekule **1** nisu identične, tj. molekula je pseudosimetrična. Spoj *mezo*-**1** podliježe termički induciranom elektrocikličkom otvaranju i zatvaranju piranskih prstenova. Tako *mezo*-**1** dolazi u ravnotežu s enantiomerima (2*S*, 2'*S*)-**1** i (2*R*, 2'*R*)-**1**, što je potvrđeno spektrima ^{1}H-NMR i preparativnim razdvajenjem stereoizomera s pomoću tekućinske kromatografije na triacetilcelulozi.