Configuration of the major stereoisomer of Zn/AcOH reduction product of 4-oxo-4*H*-chromene-3-carbaldehyde

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Under modified Clemmensen reduction condition 4-oxo-4*H*-chromene-3-carbaldehyde gave two 1,2-diol products of which the configuration of the major diol was determined by X-ray crystallography

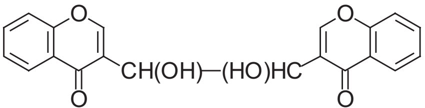
Keywords: 4-oxo-4*H*-chromene-3-carbaldehyde, configuration, diastereomers, modified Clemmensen reduction, H-bonding, X-ray crystal structure

Chiral 1,2-dihydroxy compounds are important building block in synthetic organic chemistry. Chirality of the hydroxy group can also be used for controlling/generating stereochemistry at other sites. Recently, metal mediated organic reactions in aqueous media have drawn considerable attention of synthetic organic chemists.[1-8] Aromatic aldehydes are known to undergo bimolecular reductive coupling yielding pinacols under a variety of reducing condition.[9-13]

In connection with our study of the reaction of different oxygen heterocycles having unsaturated carbonyl moiety, in modified Clemmensen reduction condition, we have considered 4-oxo-4*H*-chromene-3-carbaldehyde as easily available starting material. Concurrent to this work, Bandyopadhyay *et al.*[14] reported the formation of only one 1,2-diol compound from 4-oxo-4*H*-chromene-3-carbaldehyde in modified Clemmensen reduction condition and they did not mention the configuration of their reported compound. Formation of only one 1,2-diol compound from 4-oxo-4*H*-chromene-3-carbaldehyde encouraged us to reinvestigate the reaction under similar reaction conditions. Reduction of 4-oxo-4*H*-chromene-3-carbaldehyde under almost the same condition afforded two isomeric 1,2-diol products, which was indicated from analytical and spectral studies. It may be mentioned here that the melting point of the major product (*meso* isomer) *i.e.*, *meso*-1,2-dihydroxyethylenebis(chromen-4-one) (Fig. 1) obtained by us was the same as that of the stereoisomer of **1** reported by Bandyopadhyay *et al.*[14] So, it is interesting that there was no indication for the formation of minor 1,2-diol product in the report of Bandyopadhyay *et al.*[14] although it was formed during our reaction.

In our present study, we tried to determine the configuration of the *meso* isomer (major product) obtained by Zn/AcOH reduction of 4-oxo-4*H*-chromene-3-carbaldehyde. With the aim of achieving the configuration of the *meso* isomer, the type of H-bondings and gaining a deeper insight into the structural aspect responsible for the observed physical and spectral properties, X-ray crystallographic analysis of the *meso* isomer (**2**) was carried out. X-ray structural analysis supports the observed physical properties and ^{1}H NMR spectral data of the hydroxyl protons of both diastereomers and it also shows that the hydroxyl groups bearing chiral carbons of the major diol are in a tetrahedral environment (Fig. 2).

The ordinary pinacols such as ArCHOH–CHOHAr (Ar = Ph, *o*-Cl–C_6H_4 *etc.*) can have only one type of H-bonding but diastereoisomers of **1** can have two types of H-bonding as shown below (Fig. 3). The hydroxyl hydrogen of ArCHOH–CHOHAr absorb around δ 3.0 while that of both *rac* and *meso* form of **1** are found to absorb around δ 5.5. This observation strongly supports that the hydrogen bonding of the type-A is present in the diastereoisomers and this was also confirmed by X-ray analysis of the *meso* isomer. This view is also supported by the closeness of chemical shift of hydroxyl hydrogen of the diastereoisomers with that of (α-hydroxybenzyl)flavones (**3**) (Fig. 4) recently reported by Dhara *et al.*[15]



(**1**)

Fig. 1 Major product of Zn/AcOH reduction of 4-oxo-4*H*-chromene-3-carbaldehyde (**1**).

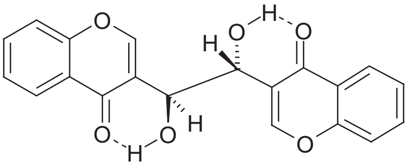
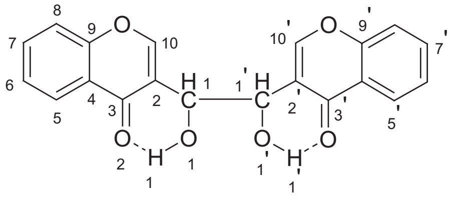
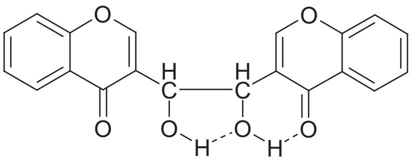


Fig. 2 Configuration major diastereomer (**2**) of 1 (*meso*-configuration).



Type-**A**



Type-**B**

Fig. 3 Types of hydrogen bondings in diastereomer of **1**.

A view of the solid state conformation of compound **2** is given in Fig. 5 and selected bond lengths and angles are given in Table 1. The angle between the groups attached with the chiral carbon *viz.*, C(2)–C(1)–C(1)#1 = 110.21(18)°, O(1)–C(1)–C(2) = 112.05(16)°, O(1)–C(1)–H(1A) = 107.9° and

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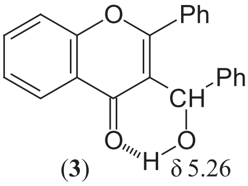

(**3**)

Fig. 4 Chemical shift of hydroxyl hydrogen of the diastereomers with that of (α-hydroxybenzyl)flavones (**3**).

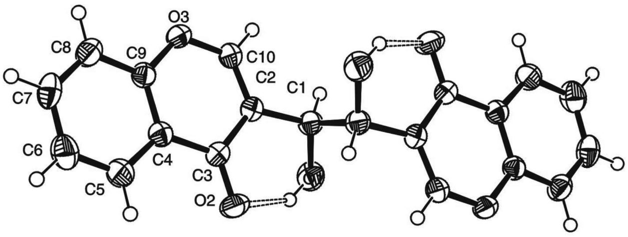

Fig. 5 Molecular structure (thermal ellipsoids are shown at 50% probability level) and atom numbering scheme of compound **2**.

C(2)–C(1)–C(1)#1 = 110.61(19)° are very close to the ideal bond angles between the groups of a regular tetrahedron. Slight deviations in the bond angles may be due to the attachment of the bulkier size of aryl moiety with the chiral carbons and H-bonding between the carbonyl oxygen and H-atom of the adjacent hydroxyl group. The bond distances and angles involved in hydrogen bonded system are: O(1)–H(1) = 0.93(3) Å, O(2)–H(1) = 1.92(3) Å, O(1)–O(2) =2.743 (3) Å, O(1)–H(1)-O(2) = 147(3)°.

Experimental

A mixture of zinc-dust (5 g, 0.077 mole), $HgCl_2$ (250 mg, 0.92 mmol), H_2O (10 ml), conc.HCl (0.2 ml) was stirred for 10 min and then the liquid was decanted. Lumps of solid were broken up and to them were added AcOH (10 ml), 95% ethanol (3 ml) and 4-oxo-4*H*-chromene-3-carbaldehyde (4 mmol) with stirring. The mixture was refluxed and stirred for 1 hr. The liquid was decanted into a separatory funnel and the residue stirred with 20 ml of water for 5 min. The water was also added to the separatory funnel and the residue was stirred with 20 ml of CH_2Cl_2 for 5 min. The residue was washed two more times with 20 ml of CH_2Cl_2 and the CH_2Cl_2 was used to extract the aqueous phase each time. The combined solution was washed with 1N NaOH (until the wash was basic) and with saturated NaCl solution (50 ml) and dried over anhydrous Na_2SO_4. The concentrate of the extract (showed two TLC spots) was separated by column chromatography over silica gel. Single crystal of the major 1,2-diol product was grown by slow evaporation of a chloroform–petroleum ether mixture of the product. The minor 1,2-diol did not give single quality crystals for X- ray structural analysis. Analytical and spectral data for major and minor 1,2-diol are given below:

*Major 1,2-diol (*meso *product)*

$C_{20}H_{14}O_6$, m.p. 245–246°C (lit.[14] m.p. 244–245°C) IR: ν_{max}(KBr): 3390 (O–H), 1630 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.04 (2H, d, J = 9.0 Hz, 2>CHOH), 5.07 (2H, d, J = 9.0 Hz, exchangeable with D_2O, 2 >CHOH), 7.40–7.47 (4H, m, 6,8,6',8'), 7.69 (2H, dt, J = 8,4 and 1,2 Hz, H-7,7'), 8.05 (2H. s, H-10, 10') and 8.20 (2H, dd, J = 7.8 and 1.2 Hz, H-5, 5').

Table 1 Selected bond lengths (Å) and angles (°) for compound 2

O(1)–C(1)	1.425(2)	O(2)–C(3)	1.238(2)
C(1)–C(2)	1.510(3)	C(2)–C(10)	1.338(2)
C(1)–C(1')	1.542(4)	O(1)–H(1)	0.93(3)
O(2)–H(1)	1.92(3)		
O(1)–C(1)–C(2)	112.05(16)	C(10)–C(2)–C(1)	120.34(17)
O(1)–C(1)–C(1')	110.21(18)	C(2)–C(1)–C(1')	110.61(19)
C(3)–C(2)–C(1)	120.07(15)	O(1)–H(1)–O(2)	147(3)

Minor 1,2-diol:

$C_{20}H_{14}O_6$, m.p. 106 – 107°C IR: ν_{max}(KBr): 3360 (O–H), 1630 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.18 (2H, d, J = 7.5 Hz, 2>CHOH), 5.86 (2H, d, J = 7.5 Hz, exchangeable with D_2O, 2 >CHOH), 7.41–7.72 (4H, m, 6,8,6',8'), 7.69 (2H, ddd, J = 7.5, 6.9 and 1.5 Hz, H-7,7'), 8.14 (2H. s, H-10, 10') and 8.20 (2H, dd, J = 7.8 and 1.5 Hz, H-5, 5').

X-ray structure determination

Single crystals of **2** (size 0.50 × 0.35 × 0.10 mm) were grown from chloroform–petroleum ether. Diffraction measurements were made at 293 ± 2°C on an Enraf-Nonius CAD-4 MACH 3 diffractometer using graphite-monochromated Mo–*K*α radiation (λ = 0.71073 Å): orientation matrices and unit cell parameters from the setting angles of 25 centred medium-angle reflections; collection of the diffraction intensities by ω scans. The structure was solved by direct methods and subsequently refined by full-matrix least-squares procedures on F^2 with allowance for anisotropic thermal motion of all non-hydrogen atoms employing the WinGX package[16] with the relevant programs (SIR-97,[17] SHELXL-97,[18] ORTEP-3[19]) implemented therein. ∠ $C_{20}H_{14}O_6$ (350.31); triclinic, P-1, a = 6.7802(10), b = 7.2562(9), c = 9.1336(9) Å, α = 109.98(8), β = 92.467(11), γ = 111.775(9)°, V = 384.69(8) Å^3, Z = 1, d_{calc} = 1.512 g cm^{-3}, μ(Mo–Kα) = 0.113 mm^{-1}; 2.42° ≤ Θ ≤ 25.16°, 2771 reflections collected ($-8 \le h \le +8$, $-8 \le k \le +8$, $-10 \le l \le +10$), 1386 unique (R_{int} = 0.0238); wR = 0.1089 for all data and 122 parameters, R = 0.0387 for 980 structure factors F_o > 4 σ(F_o). Except for the O-bonded hydrogen atom H1, which was free to refine, hydrogen atoms were included in geometrically idealised positions employing appropriate riding models. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition numbers CCDC 629783. Copies of the data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or on application to CCDC, 12 Union Road, Cambridge, UK.

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