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Synthesis of the (±)-Carbocyclic Analogues of Ascorbic and Isoascorbic Acid

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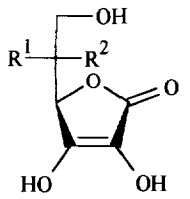
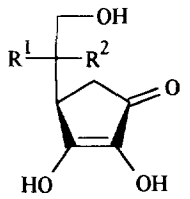
Abstract: The synthesis of compounds **2**, the racemic carbocyclic analogues of ascorbic acid **1a** and isoascorbic acid **1b**, has been accomplished starting from the cyclopentenone **4**. Benzylation followed by diastereoselective addition to *tert*-butyldimethylsilyloxy acetaldehyde gave rise to a mixture of the adducts (±)**6a** and (±)**6b**. Removal of the silyl- and *tert*-butyl protecting groups proceeded cleanly to furnish reductone ethers (±)**8a** and (±)**8b**, which were finally converted by catalytic hydrogenation to (±)**2a** and (±)**2b**, respectively.

Recently we have reported on the synthesis of both racemic sulfur[2] and aza[3] analogues of vitamin C **1a**. In continuation of our efforts to modify this specific lactone moiety, we now wish to report a straightforward access to the hitherto unknown racemic carbocyclic analogues of ascorbic acid **1a** and isoascorbic acid **1b**, which for brevity's sake are referred to as carbaascorbic and carbaisoascorbic acid (±)**2a** and (±)**2b**, respectively (scheme1).

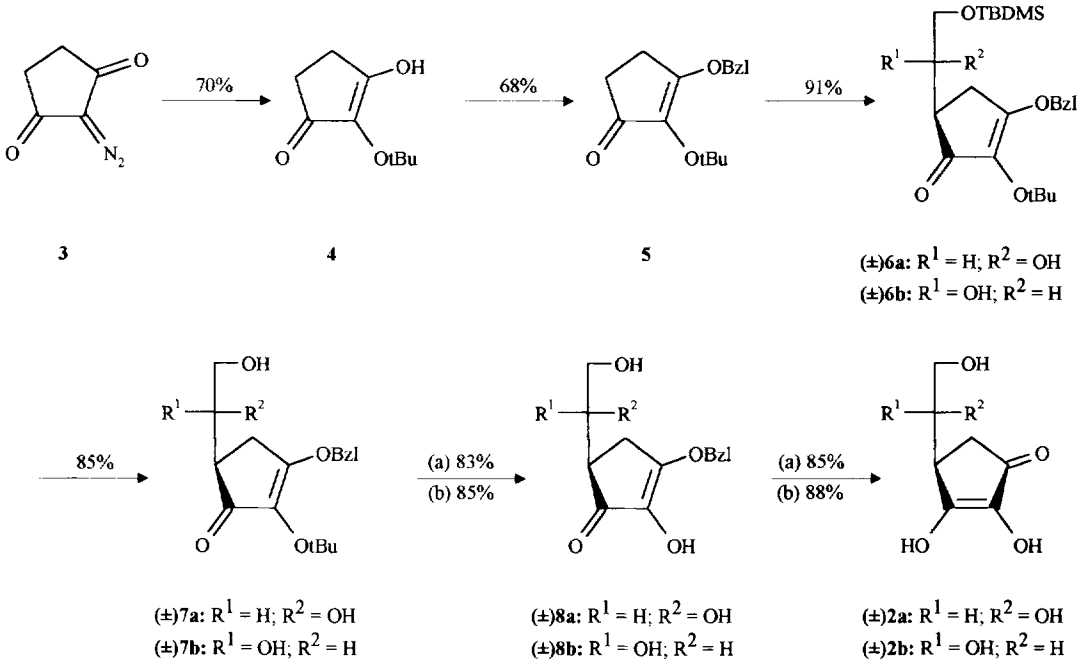




1a: R^1 = H; R^2 = OH (±)**2a:** R^1 = H; R^2 = OH
1b: R^1 = OH; R^2 = H (±)**2b:** R^1 = OH; R^2 = H

Scheme 1

Starting from 2-diazo-1,3-cyclopentanedione **3**[4] and *tert*-butanol, we obtained a good yield of endiol ether **4** by using rhodium acetate assisted O-H insertion. Subsequent alkylation of **4** with benzyl bromide in the presence of Hünig's base led to the crystalline diether **5**, which was employed in an aldol reaction with *tert*-butyldimethylsilyloxy acetaldehyde[5] to give a mixture of the diastereomeric aldols **6**. The product ratio of the isomeric mixture **(±)6a/(±)6b** was determined by HPLC analysis as 34:66 and shifted to 27:73 after we allowed transmetallation[6] with chloro titanium tri-isopropoxide of the lithium salt of **5**, formed initially. If we assume that the aldol addition has taken place adjacent the carbonyl group, then the diastereomer favored by the chelation-controlled reaction should be the isomer represented by formula **6b** (scheme 2). This configuration may be assigned *erythro* in analogy to the denomination of isoascorbic acid **1b**.



Scheme 2

The crude mixture of the adducts **6** was desilylated by use of aqueous acetic acid to give the glycols **(±)7a** and **(±)7b**, which could conveniently be separated by flash chromatography.

Debutylation of the reductone ethers **(±)7** was best performed by reaction with trifluoromethanesulfonic acid in trifluoroethanol[7] which afforded the partially protected endiols **(±)8a** and **(±)8b** in good yield.

X-ray diffraction analysis of the main product **(±)8b**, shown as an ORTEP drawing in figure 1, confirmed the structure and the assumed *erythro* configuration.

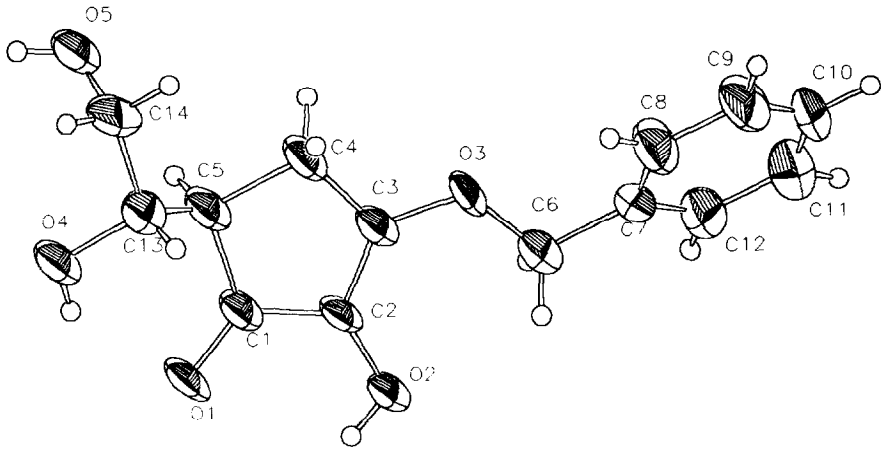


Figure 1: ORTEP drawing of **(±)8b**

Finally, the remaining benzyl groups in ethers **(±)8a** and **(±)8b** were removed by catalytic hydrogenation over Pearlman's catalyst to produce the respective reductones.

As regards the possible tautomerism of these compounds, the crucial question was whether the enolization resembles the preceeding endiol derivatives **8a/b** or whether they are true analogues of ascorbic and isoascorbic acid **1a/b**. This question is answered for the highly crystalline *erythro* isomer **(±)2b** by X-ray diffraction analysis. The plot (figure 2) shows that debenzylation of **(±)8b** is accompanied by a change of enolization to yield **(±)2b** corresponding to isoascorbic acid (erythorbic acid) **1b**.

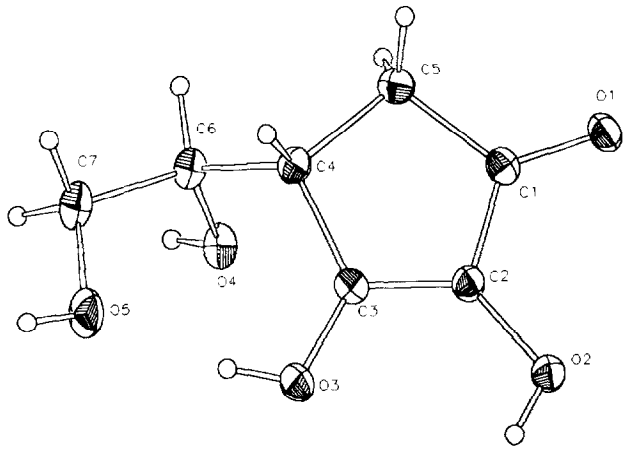


Figure 2: ORTEP plot of **2b**

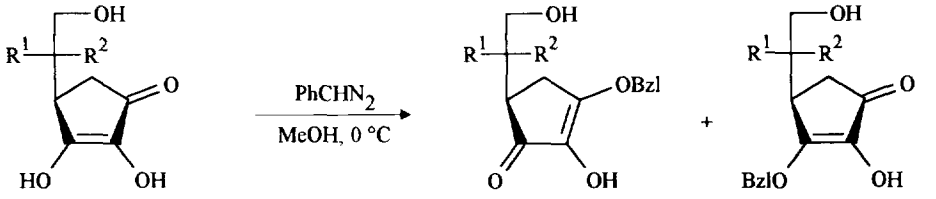
The crystallographic data clearly indicate that the selected sample is enantiopure, presumably due to spontaneous resolution of the racemate. Unfortunately, however, the absolute configuration could not be

assigned. The rings as well as the side chains of **2b** are linked mutually *via* hydrogen bonds and in this way resemble closely the naturally occurring *D*-isoascorbic acid[8]. Furthermore carbaisoascorbic acid **2b** displays a strong intramolecular hydrogen bond between O-3 and O-5 forming a stable seven-membered ring.

In solution the enolization of **2b** may take another course. The ^{1}H- and ^{13}C-NMR spectra of **2b**, recorded in deuterated aqueous methanol, each displays only one set of signals with no evidence for a bicyclic hemiketal structure as reported for the aza ascorbic acid[3]. However, the question which of the two endiol tautomers is predominant, must be left open.

Because it forms poor crystals the *threo* isomer (±)**2a** could not be characterized by X-ray diffraction analysis. Nevertheless the observed similarity of its NMR- and IR-spectra as well as computer-aided calculations employing semi-empirical methods[9] strongly suggest that the racemic vitamin C carbon analogue (±)**2a** exists in the same tautomeric form as its diastereomer (±)**2b**.

Benzylation of both reductones (±)**2a** and **b** with excess phenyldiazomethane yielded in each case a mixture of two isomeric monobenzyl ethers, **8a** and **9a** or **8b** and **9b**, respectively in a ratio of 4:6 (scheme 3).



(±)**2a**
(±)**2b**

(±)**8a**
(±)**8b**

(±)**9a**: $R^1 = H$; $R^2 = OH$
(±)**9b**: $R^1 = OH$; $R^2 = H$

Scheme 3

The reductones (±)**2a** and (±)**2b** are nearly as strongly acidic as the ascorbic acids **1**. A comparison of the respective pK_a values[10] is listed in table 1. Both endiols **2** instantaneously decolourize iodine solution as well as Tillmans reagent. According to the redox potentials[11] (table 1) the reductones are stronger reducing agents than ascorbic and isoascorbic acid. It is worth mentioning that using ceric sulfate, the rapid consumption of the theoretical amount of oxidant is pursued by a second, remarkably sluggish reaction, this contrasts with ascorbic acid **1a** and isoascorbic acid **1b**, which can sharply be titrated employing this method.

Table 1: Redox electrode potentials and pK_a-values

	E_p^* [mV]	pK_{a1}	pK_{a2}
1a	433	4.17	11.57
1b	430	4.07	11.56
(±)**2a**	418	4.49	11.92
(±)**2b**	407	4.29	11.90

[*]: E_p refers to the electrode potential of a half-oxidized solution.

In cyclic voltammetry[12] carbaascorbic acid (±)**2a** exhibits a non-reversible type oxidation wave as do L-ascorbic acid **1a** and thioascorbic acid[2], illustrated synoptically by figure 3.

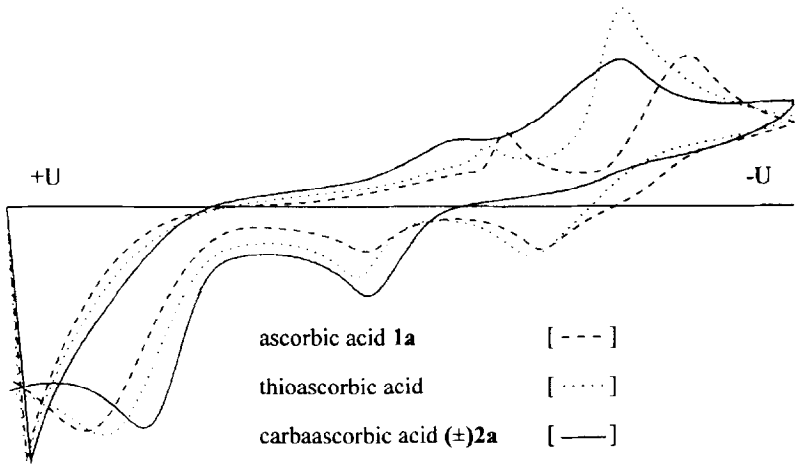


Figure 3: Cyclovoltammograms of **1a**, (±)**2a** and thioascorbic acid

Experimental

Melting points were determined using a Gallenkamp Melting Point Apparatus and are uncorrected. Column chromatography was carried out on silica gel (230 - 400 mesh) from Fa. Merck. ^{1}H-NMR spectra were recorded at 400 MHz using Me_4Si as internal standard, ^{13}C-NMR spectra at 100 MHz on JEOL GSX 400. Mass spectra were obtained with Varian CH7. Infrared spectra were measured as KBr plates using a Perkin-Elmer 710B IR-Spectrometer. UV analysis was performed in methanolic solutions on Uvikon 810 Anakomp 220. HPLC analysis was performed using Merck-Hitachi L-6000A/L-4000A and LiChrospher® 100 DIOL, 10 µm and Hibar® 250-25 LiChrosorb® DIOL, 7 µm (Fa. Merck). Microanalyses were carried out applying an Analysator CHN-O-Rapid of Fa. Heraeus.

Solvents were purified according to standard laboratory techniques.

(4R*)-(±)-4-[(1S*)-1,2-Dihydroxyethyl]-2,3-dihydroxy-2-cyclopenten-1-one (*rac*-carbaascorbic acid, (±)2a):

A methanolic suspension of 1.32 g (5 mmol) **(±)8a** and 100 mg $Pd(OH)_2/C$ was hydrogenated under atmospheric pressure with H_2 for 3 h. After filtering through a small pad of reversed phase silica gel (Silica gel 100, C_{18}-RP, Fa. Fluka) the solution was concentrated to dryness *in vacuo* without external warming. The remaining residue was triturated with diethyl ether/butanol to furnish colourless crystals of the endiol **(±)2a**, m.p. 165 °C (butanol/methanol, dec.). Yield 0.74 g (85%). - IR: ν = 3600 - 2000 cm^{-1} br., 3489, 3293, 3098, 2922, 2623, 1713, 1552 br., 1465. - UV: λ_{max}(lg ε) = 267 nm (3.895).- ^{1}H-NMR (CD_3OD/D_2O, 1:1)[13]: δ = 4.12 (m, 1 H, H_{C-6}), 3.59 (m, 2 H, H_{C-7}), 2.77 (m, 1 H, H_{C-4}), 2.47 (m, 2 H, H_{C-5}). - CH-COSY (CD_3OD/D_2O, 1:1): δ = 189.7; 183.9; 133.1; 70.6 (C-6); 65.0 (C-7); 42.9 (C-4); 28.0 (C-5). - Anal. ($C_7H_{10}O_5$) Calcd C,48.28; H,5.79; found C,48.21; H,5.87%. - MS: 174 (M^+, CI).

(4R*)-(±)-4-[(1R*)-1,2-Dihydroxyethyl]-2,3-dihydroxy-2-cyclopenten-1-one (*rac*-carbaisoascorbic acid, (±)2b):

A suspension of 1.32 g (5 mmol) **(±)8b** and 100 mg $Pd(OH)_2/C$ in 50 ml freshly distilled methanol was hydrogenated with H_2 under atmospheric pressure for 3 h, then filtered through a small pad of reversed phase silica gel (Silica gel 100, C_{18}-RP, Fa. Fluka) and evaporated to dryness *in vacuo* without the aid of heating. The residue was recrystallized from aqueous methanol employing ultrasound to give rise to colourless crystals of **(±)2b**, m.p. 163 °C (methanol/water, dec.). Yield 0.77 g (88%). - IR: ν = 3600 - 2000 cm^{-1} br., 3267, 2936, 2663, 1712, 1576, 1472. - UV: λ_{max}(lg ε) = 268 nm (3.832). - ^{1}H-NMR (CD_3OD/D_2O, 1:1): δ = 3.86 (m, 1 H, H_{C-6}), 3.64 (m, 2 H, H_{C-7}), 2.85 (m, 1 H, H_{C-4}), 2.58 (m, 1 H, H_{C-5}), 2.30 (m, 1 H, H'_{C-5}). - ^{1}H-NMR (D_2O): δ = 3.77 (m, 1 H), 3.52 (m, 2 H), 2.74 (m, 1 H), 2.47 (dd, 1H, J_1 = 6.6 Hz; J_2 = 18.0 Hz), 2.17 (d, 1 H, J = 18.0 Hz).- CH-COSY (CD_3OD/D_2O, 1:1): δ = 188.4; 186.8; 134.8; 75.0 (C-6); 66.2 (C-7); 44.2 (C-4); 33.3 (C-5). - Anal. ($C_7H_{10}O_5$) Calcd C,48.28; H,5.79; found C,48.08; H,5.99%. - MS: 174 (M^+, CI).

X-Ray Data Collection and Structure Solution: A crystal with dimensions 0.17 x 0.40 x 0.47 mm was transferred into a glass capillary and measured at room temperature. $C_7H_{10}O_5$, M = 174.15, orthorhombic, space group $Pna2_1$, with a = 13.608(3) Å, b = 5.6121(9) Å, c = 9.517(3) Å, V = 726.8(3) $Å^3$, Z = 4, d_c = 1.591 g/cm^3, absorption coefficient = 0.137 mm^{-1}, F(000) = 368, Diffractometer ENRAF-NONIUS CAD4, Mo-K_α, oriented graphite monochromator: 2Θ-range: 4° - 46°, scan width = 0.50 + 0.35tanΘ °, max time per scan 60 s. index range h k ±l, no. of reflections collected: 1271, no. of unique reflections: 1270 (Ri = 0.0823), no. of observed reflections (I>2σI) 1226. Lorentz and polarisation corrections applied. Programs used: SHELXS for solution by direct methods, SHELXL-93 for full matrix least squares refinement on F^2, riding hydrogens with fixed U. Weighting by $w = 1/ [\sigma^2F_o^2 + (0.0482\ P)^2 + 0.1264\ P]$ with $P = (F_o^2 + 2F_c^2)/3$, no. of variables 114 and 1 restraint, extinction coefficient 0.066(6). R1 = 0.0274 wR2 = 0.0722 for 1226 data, R1 = 0.0284 and wR2 = 0.0729 for all data, goodness of fit = 1.048, largest difference peak : 0.153 $eÅ^{-3}$.

Complete details of the structure investigation are available on request from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, England on quoting the names of the authors and the journal citation.

2-*tert*-Butoxy-3-hydroxy-2-cyclopenten-1-one (4):

A mixture of 2.50 g (20 mmol) diazoketone **3** and 50 mg rhodium acetate in 15 ml freshly distilled *tert*-BuOH was kept in a closed reaction vessel at 110 °C for 8 h. After cooling the mixture the volatiles were removed *in vacuo* and the remaining residue recrystallized from diisopropyl ether/ethyl acetate to give pure **4** as colourless crystals, m.p. 173 °C (diisopropyl ether/ethyl acetate, dec.). Yield 2.40 g (70%). - IR: ν = 3300 - 2200 cm^{-1} br., 2976, 2934, 2597, 1684, 1572, 1439. - UV: λ_{max}(lg ε) = 254 nm (3.960). - ^{1}H-NMR ([D6]-DMSO): δ = 11.36 (s, 1 H, OH), 2.33 (m, 4 H), 1.19 (s, 9 H). - Anal. ($C_9H_{14}O_3$) Calcd C,63.51; H,8.29; found C,63.34; H,8.31%. - MS: 170 (M^+, CI).

3-Benzyloxy-2-*tert*-butoxy-2-cyclopenten-1-one (5):

A mixture of 1.70 g (10 mmol) *tert*-butyl ether **4** , 1.80 g benzyl bromide (10.5 mmol) and 1.35 g (10.5 mmol) ethyl diisopropylamine in 50 ml dichloromethane was left to stand 12 h at r.t. and thereafter adsorbed onto silica gel *in vacuo*. Column chromatography using 66% ethyl acetate/hexane furnished pure **5** as colourless shimmering plates, m.p. 99 °C (hexane/diisopropyl ether). Yield 1.77 g (68%). - IR: ν = 3060 cm^{-1}, 2970, 2940, 2882, 1685, 1611, 1462. - UV: λ_{max}(lg ε) = 257 nm (4.307). - ^{1}H-NMR ($CDCl_3$): δ = 7.37 (m, 5 H), 5.28 (s, 2 H), 2.62 (m, 2 H), 2.37 (m, 2 H), 1.39 (s, 9 H). - Anal. ($C_{16}H_{20}O_3$) Calcd C,73.82; H,7.74; found C,73.45; H,8.11%. - MS 260 (M^+, CI).

(5R*)-(±)-5-[(1R*)-2-(*tert*-Butyldimethylsilyloxy)-1-hydroxyethyl]-3-benzyloxy-2-*tert*-butoxy-2-cyclopenten-1-one ((±)6a):

To an ice-cooled solution of 0.26 ml (2 mmol) diisopropyl amine in 5 ml dry THF was added under N_2 0.65 ml (1 mmol) of a 1.6 M solution of *n*-butyllithium in hexane. After 15 min the mixture was cooled to -78 °C and a solution of 0.26 g (1 mmol) **5** in 2 ml THF added dropwise. After stirring for 45 min at this temp. 0.18 g (1 mmol) *tert*-butyldimethylsilyloxy acetaldehyde in 0.5 ml THF was added all at once. Five minutes later the mixture was quenched by addition of sat. aq. citric acid solution and extracted thrice with ethyl acetate. After drying the combined organic phases with Na_2SO_4 the volatiles were removed *in vacuo* and the residue was finally chromatographed using 33% ethyl acetate/hexane as eluant to give 395 mg (91%) of an inseparable mixture of the two diastereomers **(±)6a** and **(±)6b**. An analytical sample of each diastereomer was obtained by using semi-preparative HPLC (DIOL 7 µm, eluent: 17% ethyl acetate/hexane, 9 ml/min, ret. time **(±)6a**: 16 min, **(±)6b**: 10 min). The ratio of **(±)6a/(±)6b** was calculated to 34:66.

Colourless needles, m.p. 122 °C (hexane/diisopropyl ether). - IR: ν = 3436 cm^{-1}, 2954, 2923, 2851, 1684, 1616, 1460. - UV: λ_{max}(lg ε) = 259 nm (4.246). - ^{1}H-NMR ($CDCl_3$): δ = 7.33 - 7.41 (m, 5 H), 5.30 (dd, 2 H, J = 12.0 Hz), 4.04 (m, 1 H), 3.75 (dd, 1 H, J_1 = 4.7 Hz; J_2 = 10.3 Hz), 3.65 (dd, 1 H, J_1 = 7.3 Hz, J_2 = 10.3 Hz), 2.82 (dd, 1 H, J_1 = 2.1 Hz, J_2 = 17.1 Hz), 2.61 (dd, 1 H, J_1 = 7.3 Hz, J_2 = 17.1 Hz), 2.53 (d, 1 H, OH, J = 4.2 Hz), 2.51 (m, 1 H), 1.33 (s, 9 H), 0.89 (s, 9 H), 0.08 (s, 3 H), 0.07 (s, 3 H). - Anal. ($C_{24}H_{38}O_5Si$) Calcd C,66.32; H,8.81; found C,66.32; H,8.69%. - MS: 434 (M^+, CI).

(5R*)-(±)-5-[(1S*)-2-(*tert*-Butyldimethylsilyloxy)-1-hydroxyethyl]-3-benzyloxy-2-*tert*-butoxy-2-cyclopenten-1-one ((±)6b):

Colourless needles, m.p. 108 °C (hexane/diisopropyl ether). - IR: ν = 3434 cm^{-1}, 2974, 2955, 2931, 2884, 2851, 1686, 1618, 1472, 1458. - UV: λ_{max}(lg ε) = 260 nm (4.232). - ^{1}H-NMR ($CDCl_3$): δ = 7.34 - 7.41 (m, 5

H), 5.28 (s, 2 H), 4.12 (d, 1 H, OH, J = 1.3 Hz), 3.75 (m, 1 H), 3.66 (m, 2 H), 2.73 (m, 1 H), 2.59 (m, 2 H), 1.32 (s, 9 H), 0.88 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H). - Anal. ($C_{24}H_{38}O_5Si$) Calcd C,66.32; H,8.81; found C,66.30; H,8.69%. - MS: 434 (M^+, CI).

***tert*-Butyldimethylsilyloxy acetaldehyde**[5]:

To a solution of 10.0 ml (115 mmol) oxalyl chloride in 300 ml dry dichloromethane, precooled to -60 °C, was added dropwise a mixture of 20.0 ml (282 mmol) DMSO in 50 ml dichloromethane. After stirring 5 min at this temp. 17.6 g (100 mmol) 2-*tert*-butyldimethylsilyloxy ethanol[14], dissolved in 50 ml dichloromethane, was added dropwise. Another 15 min later 85.0 ml (480 mmol) ethyl diisopropylamine was slowly added with stirring. After 5 min the cooling bath was removed and the mixture allowed to reach r.t. The organic phase was thoroughly washed with water, dried with Na_2SO_4, filtered and evaporated to dryness. The resulting residue was purified chromatographically (hexane/diethyl ether, 5:1) and finally distilled under reduced pressure, b.p. 66 °C/15 Torr (Lit[5]: 65 °C/17 Torr). Yield 10.4 g (60%).

(5R*)-(±)-5-[(1R*)-1,2-Dihydroxyethyl]-3-benzyloxy-2-*tert*-butoxy-2-cyclopenten-1-one ((±)7a):

The diastereomeric mixture **(±)6a,b** (435 mg, 1 mmol) was dissolved in acetic acid, THF and water (3:1:1, 10 ml) and left to stand at r.t. for 16 h. The volatiles were removed *in vacuo* and the remaining residue chromatographed on silica gel using ethyl acetate to furnish in the order of elution **(±)7a** and then **(±)7b**.
Colourless crystals, m.p. 115 °C (diisopropyl ether/ethyl acetate). Yield 92 mg (29%). - IR: ν = 3328 cm^{-1} br., 2980, 2949, 2885, 1686, 1610, 1466. - UV: λ_{max}(lg ε) = 259 nm (4.301). - ^{1}H-NMR (CD_3CN): δ = 7.38 - 7.44 (m, 5 H), 5.28 (s, 2 H), 3.96 (m, 1 H), 3.49 (m, after add. of D_2O: d, J = 5.9 Hz, 2 H), 3.06 (d, 1 H, OH, J = 4.4 Hz), 3.01 (t, 1 H, OH, J = 6.0 Hz), 2.77 (dd, 1 H, J_1 = 2.9 Hz, J_2 = 17.6 Hz), 2.69 (dd, 1 H, J_1 = 6.6 Hz, J_2 = 17.6 Hz), 2.48 (m, 1 H), 1.24 (s, 9 H). - Anal. ($C_{18}H_{24}O_5$) Calcd C,67.48; H 7.55; found C,67.40; H,7.63%. - MS 320 (M^+, CI).

(5R*)-(±)-5-[(1S*)-1,2-Dihydroxyethyl]-3-benzyloxy-2-*tert*-butoxy-2-cyclopenten-1-one ((±)7b):

Colourless crystals, m.p. 112 °C (diisopropyl ether/ethyl acetate). Yield 180 mg (56%). - IR: ν = 3448 cm^{-1} br., 3034, 2971, 2931, 2883, 1684, 1611, 1458. - UV: λ_{max}(lg ε) = 260 nm (4.297). - ^{1}H-NMR (CD_3CN): δ = 7.37 - 7.43 (m, 5 H), 5.27 (s, 2 H), 3.98 (d, 1 H, OH, J = 2.9 Hz), 3.72 (m, 1 H), 3.56 (m, after add. of D_2O: J = 5.1 Hz, 2 H), 3.08 (t, 1 H, OH, J = 6.0 Hz), 2.87 (dd, 1 H, J_1 = 7.0 Hz, J_2 = 18.0 Hz), 2.57 (m, 2 H), 1.23 (s, 9 H). - Anal. ($C_{18}H_{24}O_5$) Calcd C,67.48; H,7.55; found C,67.56; H,7.45%. - MS: 320 (M^+, CI).

(5R*)-(±)-5-[(1R*)-1,2-Dihydroxyethyl]-3-benzyloxy-2-hydroxy-2-cyclopenten-1-one ((±)8a):

To a solution of **(±)7a** (3.20 g, 10 mmol) in 25 ml CF_3CH_2OH were added five drops of trifluoromethanesulfonic acid. After standing 8 h at r.t. the volatiles were removed *in vacuo* and the remaining residue rinsed with a small amount of ethyl acetate. Colourless crystals, m.p. 124 °C (ethyl acetate). Yield 2.20 g (83%). - IR: ν = 3500 - 3000 cm^{-1} br., 3332, 2936, 1700, 1623, 1499, 1457. - UV: λ_{max}(lg ε) = 272 nm (4.182). - ^{1}H-NMR (CD_3OD): δ = 7.30 - 7.43 (m, 5 H), 5.44 (s, 2 H), 3.81 (m, 1 H), 3.63 (d, 2 H, J = 5.1 Hz), 2.67 (m, 2 H), 2.49 (m, 1 H). - CH-COSY (CD_3OD): δ = 201.8 (C-1), 166.8 (C-3), 138.0, 134.6, 128.6 - 129.7 (C_{arom}), 73.7 (C-13), 73.2 (C-6), 64.7 (C-14), 45.4 (C-5), 27.9 (C-4). - Anal. ($C_{14}H_{16}O_5$) Calcd C,63.63; H,6.10; found C,63.46; H,6.26%. - MS: 264 (M^+, CI).

(5R*)-(±)-5-[(1S*)-1,2-Dihydroxyethyl]-3-benzyloxy-2-hydroxy-2-cyclopenten-1-one ((±)8b):

This compound was prepared in the same manner as its diastereomer **(±)8a** using 3.20 g (10 mmol) **(±)7b**. Colourless crystals, m.p. 150 °C (ethyl acetate). Yield 2.24 g (85%). - IR: ν = 3361 cm^{-1} br., 2942, 2882, 1695, 1613, 1500, 1470, 1458. - UV: λ_{max}(lg ε) = 270 nm (4.267). - ^{1}H-NMR (CD_3OD): δ = 7.30 - 7.47 (m, 5 H), 5.46 (s, 2 H), 4.07 (m, 1 H), 3.53 (m, 2 H), 2.50 - 2.70 (m, 3 H). - Anal. ($C_{14}H_{16}O_5$) Calcd C,63.63; H,6.10; found C,63.72; H,5.83. - MS: 264 (M^+, CI).

X-Ray Data Collection and Structure Solution: A crystal with dimensions 0.20 x 0.53 x 0.57 mm was transferred into a glass capillary and measured at room temperature. $C_{14}H_{16}O_5$, M = 264.27, triclinic space group P-1 (no.2), with a = 7.710(9) Å, b = 8.162(5) Å, c = 10.946(5) Å, α = 104.34(4)°, β = 94.64(6)°, γ = 95.29(9)°, V = 660.6(9) $Å^3$, Z = 2, d_c = 1.329 g/cm^3, absorption coefficient = 0.101 mm^{-1}, F(000) = 280, Diffractometer ENRAF-NONIUS CAD4, Mo-K_α, oriented graphite monochromator: 2Θ-range: 4° - 46°, scan width = 1.00 + 0.35tanΘ °, max time per scan 60 s. index range h k ± l, no. of reflections collected: 1939, no. of unique reflections: 1825 (Ri = 0.0130), no. of observed reflections (I>2σI) 1369. Lorentz and polarisation corrections applied. Programs used: SHELXS for solution by direct methods, SHELXL-93 for full matrix least squares refinement on F^2, riding hydrogens with fixed U. Weighting by $w = 1/ [\sigma^2F_o^2 + (0.1879\ P)^2 + 0.3805\ P]$ with $P = (F_o^2 + 2F_c^2)/3$, no. of variables 175, R1 = 0.0954 wR2 = 0.2645 for 1369 data, R1 = 0.1127 and wR2 = 0.2802 for all data, goodness of fit = 0.864, largest difference peak : 0.706 $eÅ^{-3}$.
Complete details of the structure investigation are available on request from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, England on quoting the names of the authors and the journal citation.

(4S*)-(±)-4-[(1R*)-1,2-Dihydroxyethyl]-3-benzyloxy-2-hydroxy-2-cyclopenten-1-one ((±)9a):

To an ice-cooled solution of 175 mg (1 mmol) **(±)2a** in 10 ml methanol/diethyl ether (2:1) was added dropwise freshly distilled phenyldiazomethane in hexane until the faintly red colour persisted. After stirring for 30 min at 0 °C the mixture was quenched by slow addition of 0.5 ml acetic acid. Following removal of the volatiles *in vacuo* the residue was carefully chromatographed using ethyl acetate as eluent. The obtained fractions were checked for purity by HPLC analysis (DIOL, ethyl acetate 1ml/min, ret. time 7.0 min). Colourless crystals m.p. 200 °C (ethyl acetate). Yield 100 mg **(±)9a** (38%) besides a smaller amount of **(±)8a** (72 mg, 27%). - IR: ν = 3500 - 2500 cm^{-1} br., 3445, 3281, 2943, 1696, 1597, 1498, 1455. - UV: λ_{max}(lg ε) = 269 nm (4.176). - ^{1}H-NMR (CD_3OD): δ = 7.32 - 7.45 (m, 5 H), 5.66 (d, 1 H, J = 12.0 Hz), 5.55 (d, 1 H, J = 12.0 Hz), 4.05 (m, 1 H), 3.52 (dd, 1 H, J_1 = 6.4 Hz; J_2 = 11.1 Hz), 3.44 (dd, 1 H, J_1 = 6.4 Hz; J_2 = 11.1 Hz), 2.91 (m, 1 H), 2.37 (d, 1 H, J = 18.0 Hz), 2.22 (dd, 1 H, J_1 = 6.4 Hz; J_2 = 18.0 Hz). - Anal. ($C_{14}H_{16}O_5$) Calcd C,63.63; H,6.10; found C,63.54; H,6.19%. - MS: 264 M^+, CI).

(4S*)-(±)-4-[(1S*)-1,2-Dihydroxyethyl]-3-benzyloxy-2-hydroxy-2-cyclopenten-1-one ((±)9b):

This compound was prepared in an analogous manner to **(±)9a** starting with 175 mg (1 mmol) **(±)2b** in 10 ml methanol/diethyl ether (2:1) and a solution of freshly distilled phenyldiazomethane in hexane. The eluted fractions were monitored by HPLC analysis (DIOL, ethyl acetate 1ml/min, ret. time 7.0 min). Colourless crystals m.p. 120 °C (ethyl acetate). Yield 106 mg **(±)9b** (40%) besides a smaller amount of **(±)8b** (77 mg, 29%). - IR: ν = 3500 - 2500 cm^{-1} br., 3433, 3093, 2927, 2896, 1701, 1603, 1500, 1456. - UV: λ_{max}(lg ε) = 269 nm (4.146).

- ^{1}H-NMR (CD_3OD): δ = 7.32 -7.45 (m, 5 H), 5.62 (d, 1 H, J = 12.0 Hz), 5.55 (d, 1 H, J = 12.0 Hz), 3.83 (m, 1 H), 3.57 (m, 2 H), 3.00 (m, 1 H), 2.43 (dd, 1 H, J_1 = 6.5 Hz, J_2 = 18.0 Hz), 2.30 (dd, 1 H, J_1 = 1.7 Hz, J_2 = 18.0 Hz). - Anal. ($C_{14}H_{16}O_5$) Calcd C,63.63; H,6.10; found C,63,49; H,6.25%. - MS: 264 (M^+, CI).

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REFERENCES AND NOTES

Dedicated to Prof. Rolf Huisgen on the occasion of his 75th birthday

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11. Experimental conditions: 0.1*N* - $Ce(SO_4)_2$, *2N* - H_2SO_4, N_2, 20 °C, combined redox-electrode Pt *vs.* Ag/AgCl (Fa. Ingold).
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