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Stereospecific Synthesis of Conduramine-F_4 and Conduritol-F (*Leucanthemitol*)

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SUMMARY: Stereospecific synthesis of Conduramine-F_4 and Conduritol-F has been achieved by fully stereospecific cyloaddition of singlet oxygen to cyclohexadiene ketal **1** followed by reductive extrusion of one oxygen atom. The obtained monoepoxide **3** has been smoothly opened to conduritol-F **4** and conduramine-F_4 **6** by water and ammonia, respectively.

Aminocyclitols show interesting inhibitor activity for some glycosidases[1] and serve as important intermediates in the synthesis of aminoinositols[2]. Nakajima et al. have synthesized many aminocyclitols[2b] starting from *cis*- and *trans*-benzene diol isomers. Epoxidation of *cis*- and *trans*-benzene diol isomers gave two epoxy-diol mixture in both cases which have to be separated. Herein we report an efficient and stereospecific route to protected epoxy-benzene diol **3** which is the key intermediate in the synthesis of conduramine-F_4[3] **6** and conduritol-F **4**.

The cyclohexadiene acetonide **1** was obtained by quantitative protection of cyclohexadienediol which is available by microbial oxidation of benzene using *Pseudomonas putida*. Photooxygenation of **1** in CCl_4 (150 Watt, projection lamp) at room temperature using tetraphenylporphyrin as the sensitizer followed by silica gel chromatography afforded **2**[4] in 95% yield. The spectral data have revealed exclusively the formation of *anti*-isomer **2**. Especially a six-line ^{13}C

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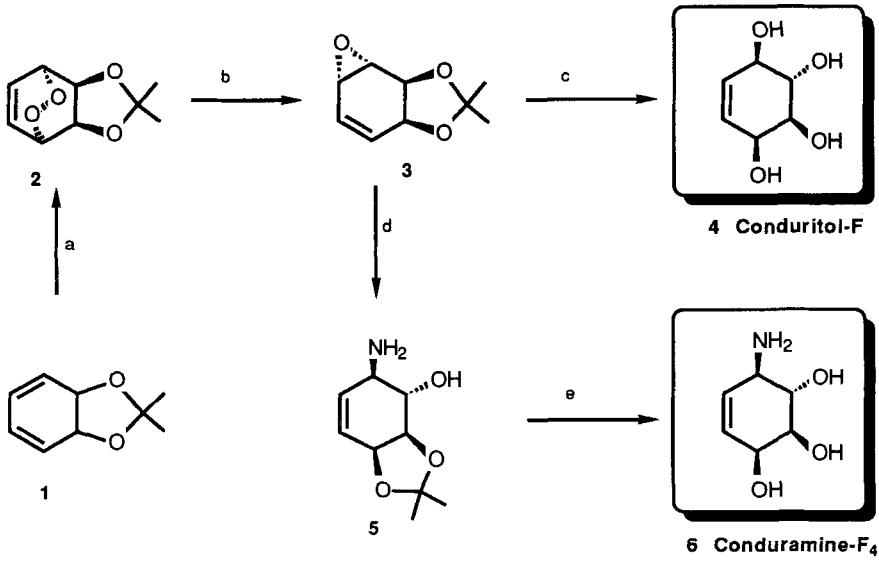

a) O_2, Tetraphenylporphyrin, CCl_4 b) $CHCl_3$, $POEt_3$ c) H_2SO_4, H_2O, $BaCO_3$ d) MeOH, NH_3 e) H_2SO_4, H_2O, $BaCO_3$

NMR indicates the expected symmetry in the molecule. The exact stereochemistry of **2** was determined by chemical transformation of **2** to known conduritol-A[4]. 1,4-Cycloaddition of singlet oxygen to1,3-dienes followed by reductive extrusion of one oxygen atom with trivalent phosphorus compounds provides a convenient entry to the unsaturated epoxides[5]. Triethyl phosphite deoxygenation of endoperoxide **2** gave rise to a single monoepoxide **3** (yield 55%) whose stereochemistry is well defined. The ^{1}H- and ^{13}C-NMR spectra of the epoxide **3** support the expected unsymmetrical structure. Epoxyketal **3** was submitted to acid-catalyzed ring-opening reaction in acidified water. Analysis of the reaction mixture has revealed that only one product was formed in quantitative yield which was identified as conduritol-F[6] (*Leucanthemitol*) **4**. The other expected product, conduritol-C was not formed by this ring-opening reaction because water attacks the epoxide-ring only at the allylic position.

Opening of the epoxide-ring by NH_3 in methanol provided the corresponding, protected aminoconduritol **5**. Hydrolysis of **5** in acidified water gave the conduramine-F_4 **6** in high yield. The fact, isolation of only one isomer,

indicates clearly that ammonia attacks again the epoxide-ring at allylic position. Characteristics of **6** were comparable to those reported by Nakajima et al[2b].

In summary, a short and fully stereocontrolled synthesis of an important aminoconduritol **6** and conduritol-F **4** was accomplished. The key step, synthesis of monoepoxide **3** was achieved in good yield and free of the other isomers. Further application of this synthetic methodology to other systems are currently under progress.

EXPERIMENTAL

***anti*-3,5,7,8-Tetraoxa-4,4-dimethyl-tricyclo[5.2.2.$0^{2,6}$]undec-10-ene 2.** To a stirred solution of ketal **1**[7] (1.0 g, 6.57 mmol) in 50 mL of carbon tetrachloride was added 20 mg of tetraphenyl porpyrine. The resulting mixture was irradiated with a projection lamp (150 Watt) while oxygen is being passed through solution and the mixture was stirred for 4 hours. The solvent was removed by evaporation at room temperature. The residue (1.21 g, quantitative yield) was recrystallized from methylene chloride/n-hexane, m.p. 108 °C.

^{1}H-NMR (200 MHz, $CDCl_3$, TMS) δ 6.55 (dd, XX'-part of AA'BB'XX'-system, olefinic protons, 2H), 4.71(m, BB'-part of of AA'BB'XX'-system, bridgehead protons, 2H), 4.50 (m, AA'-part of AA'BB'XX'-system, alkoxy protons, 2H), 1.30 (s, methyl protons, 6H).

^{13}C-NMR (50 MHz, $CDCl_3$, TMS) δ 130.52, 110.31, 71.47, 71.68, 25.69, 25.39.

IR (KBr, cm^{-1})3000, 1375, 1200, 900.

(1α,2β,4β,7α)-3,8,10-trioxa-9,9-dimethyl-tricyclo-[5,3,0,$0^{2,4}$]doc-5-ene 3. The endoperoxide **2** (450 mg, 2.44 mmol) was dissolved in 50 mL of chloroform. A solution of triethylphosphite ($POEt_3$, 410 mg, 2.44 mmol) in 5 mL of chloroform was added dropwise in 1 h to a stirred solution of the endoperoxide cooled to 0 °C. After stirring at room temperature for 1h, the solvent was evaporated. The residue was purified by column chromatography on neutral alumina (25 g Al_2O_3, Activity III, ethyl acetate/n-hexane 1:20) yielding 225 mg (yield 55%) of a colourless oil which was identified as **3**.

^{1}H-NMR (200 MHz, $CDCl_3$, TMS) δ 6.10 (ddd, A-part of AB system, J_{56}= 10.2 Hz, J_{67}= 1.8 Hz, J_{46}= 1.5 Hz, H_6), 5.8 (br. d, B-part of AB system, J_{56}= 10.2 Hz, H_5), 4.74 (br. d, A-part of AB system, J_{17}= 7.0 Hz, H_1), 4.42 (dt, B-part of AB system, J_{17}= 7.0 Hz, J_{57}= J_{67}= 1.8Hz, H_7), 3.51 (dd, A-Part of AB system, J_{24}= 3.7 Hz, J_{12}= 1.9 Hz, H_2), 3.30 (br. t, H_4), 1.37 (s, 2 CH_3).
^{13}C-NMR (50 MHz, $CDCl_3$, TMS) δ 132.51, 123.96, 110.97, 71.33, 71.20, 49.66, 46.93, 28.25, 26.41.
IR (KBr, neat, cm^{-1}) 2985, 1650, 1445, 1380, 1290, 1220, 1170, 1050, 950, 860, 685, 650.

(1α,2α,3β,4α)-1,2,3,4-Tetrahydroxy-cyclohex-5-ene 6 Conduritol-F. The epoxy-ketal **3** (0.4 g, 2.4 mmol) was dissolved in 10 mL of 1 N H_2SO_4 and the resulting solution was stirred at room temperature for 1 h. The acid was neutralized with $BaCO_3$. After stirring for additional 10 min. the precipitate was filtered. Evaporation of the solvent under reduced pressure gave conduritol-F nearly in quantitative yield (m.p. 106-108 °C, 103-104 °C[6b], 106-107 °C[6d])recrystallized from MeOH/n-hexane).
^{13}C-NMR (50 MHz, D_2O, TMS) δ 135.34, 129.67, 75.36, 75.32, 73.71, 69.56. For other spectral data see ref 6d.

(1α,2β,3α,6α)-2-hydroxy-3-amino-7,9-dioxa-8,8-dimethyl-bicyclo[4.3.0]non-4-ene 5. Epoxyketal **3** (0.1 g, 0.55 mmol) was dissolved in 25 mL of absolute methanol. While dry NH_3 is being passed through solution, the mixture was stirred for 24 hours at room temperature. The solvent was evaporated and the residue recrystallized from ethanol: 0.104 g (95%), colourless crystals m.p. 142-143 °C.
^{1}H-NMR (200 MHz, $CDCl_3$, TMS) δ 5.75-5.89 (AB-system, J_{45}= 10.0 Hz, H_4 and H_5), 4.62 (dd, J_{56}= 2.4 Hz, J_{16}= 5.8 Hz, H_6), 4.06 (t, J_{12}= J_{23}= 7.4 Hz, H_2), 3.3 (m, H_1 and H_3), 2.17 (br. s, OH and NH_2) 1.51 (s, CH_3), 1.39 (s, CH_3).
^{13}C-NMR (50 MHz, $CDCl_3$, TMS) δ 130.20, 129.87, 114.26, 80.15, 75.59, 73.36, 55.17, 30.20, 28.00.
IR (KBr, cm^{-1}) 3360, 2980, 1620, 1510, 1380, 1240, 1160, 1060, 900, 870, 820.

(1α,2α,3β,4α)-1,2,3-trihydroxy-4-amino-cyclohex-5-ene 5

Conduramine F_4. The ketal **5** (50 mg (0.24 mmol) was dissolved in 10 mL of 1.0 N H_2SO_4 and the resulting solution was stirred at room temperature for 3 hours. The acid was neutralized with $BaCO_3$. After stirring for additional 10 min. the precipitate was filtered and the solvent was evaporated under reduced pressure. The aminoconduritol **5** was obtained nearly in quantitative yield (40 mg). The residue was recrystallized from methanol/ethanol, m.p: 189 °C (188-189 °C[2b]).

^{1}H-NMR (200 MHz, D_2O, TMS) δ 5.85 (ddd, A-part of AB-system, J_{56}= 10.1 Hz, J_{16}= 5.0 Hz, J_{46}= 2.1 Hz, H_6), 5.70 (dd, B-part of AB-system, J_{56}= 10.1, J_{45} =1.4 Hz, H_5), 4.23 (dd, J_{16}= 5.0 Hz, J_{12}= 3.8 Hz, H_1), 3.6 (dd, A-part of AB-system, J_{12}= 3.8 Hz, J_{23}= 10.4 Hz, H_3), 3.52 (dd, B-part of AB-system, J_{23}= 10.4 Hz, J_{34}= 8.5 Hz, H_3), 3.31 (br. d, J_{34}= 8.5Hz, H_4).

^{13}C-NMR (50 MHz, D_2O, TMS) δ 134.63, 129.73, 75.46, 74.32, 69.50, 57.09.

IR (KBr, cm^{-1}) 3360, 2980, 1620, 1510, 1380, 1240, 1160, 1060, 900, 870, 820.

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REFERENCES

1) a) T. Postermak, *The Cyclitols*, Hermann, Paris, **1965**.
b) S. Umezawa, *Adv. Carbohydr. Chem. Biochem.* **1974**, 30, 111.
c) K.L. Rinehart, Jr., T. Suami (Eds.) *Aminocyclitol Antibiotics*, ACS Symposium Series 125, Washington, **1980.**
d) M. Balcı, Y. Sütbeyaz, H. Seçen, *Tetrahedron*, **1990**, 46, 3715.b

2) a) M. Nakajima, N. Kurihara, *Chem.Ber.* **1961**, 94, 515.
b) M. Nakajima, A. Hasegawa, N. Kurihara, *Chem.Ber.* **1962**, 95, 2709.

c) Nakajima, N. Kurihara, A. Hasegawa, T. Kurokawa, *Ann. Chem.* **1965,** 689, 243.

d) Nakajima, N. Kurihara, A. Hasegawa, *Ann. Chem.* **1965,** 689, 235.

3) For conduramine synthesis see:

a) T. Hudlicky, H. F. Olivo, *Tetrahedron Lett.* **1990**, 43, 6077.

b) H. Paulsen, W. Röben, F. R. Heiker, *Chem.Ber.* **1981**, 114, 3242.

c) S. Ogawa, T. Toyokuni, T. Suami, *Chem. Lett.* **1981**, 947.

d) S. Ogawa, T. Toyokuni, T. Suami, *Chem.Lett.* **1980**, 713.

4) Y. Sütbeyaz, H. Seçen, M. Balcı, *J. Chem. Soc. Chem. Commun.* **1988,** 1330.

5) M. Balcı, *Chem.Rev.* **1981**, 81, 91.

6) a) V. Plouvier, *C. r. hebdomad. Sc' Acad. Sci.* Paris, **1962**, 225, 360.

b) M. Nakajima, I. Tomida, S. Takei, *Chem.Ber.* **1959**, 92, 163.

c) H. Seçen, Y. Sütbeyaz, M. Balcı, *Tetrahedron Lett.* **1990**, 31, 1323.

d) C. L. Drian, J. P. Vionnet, P. Vogel, *Helv. Chim. Acta,* **1990**, 73, 161.

7) N. C. Yang, M. J. Chen, P. Chen, *J. Am. Chem. Soc.* **1984**, 106, 7310.

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