Pergamon

Tetrahedron Letters, Vol. 35, No. 20, pp. 3349-3352, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0513-W

Synthesis of New Conduritol Analogues Derived from Bicyclooctatriene: *Bis*-homo-conduritol-D and *Bis*-homo-conduritol-F

Yunus Kara and Metin Balcı*

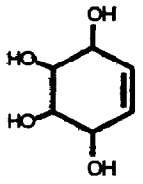
Atatürk University, Department of Chemistry, Faculty of Science, 25240 Erzurum, TURKEY

Susan A. Bourne and William H. Watson[1]

Department of Chemistry, Texas Christian University, Fort Worth, 76129, U.S.A.

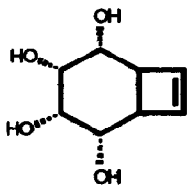
Abstract: The first synthesis of conduritol analogues **2** and **3** is reported. The key compound **7** reacted with $KMnO_4$ and m-chloroperbenzoic acid in a stereospecific manner to give *syn*-addition products **9** and **10**, respectively. Zinc-dust elimination of **10** followed by epoxide opening resulted in the formation of **3b**. The free tetrol **3** was obtained by ammonolysis. The other tetrol isomer **2** was obtained by similar synthetic steps.

Conduritols are tetrahydroxylated cyclohexene derivatives. Two stereoisomers, conduritol-A and conduritol-F of these compounds are known to occur in the nature[2]. All the possible conduritol isomers have been synthesized and their biological importance has been studied. Potential use of some conduritol and conduritol derivatives as inhibitors for glycosidases[3] adds further relevance to this area. Recently, we have reported the synthesis of various conduritol isomers[4]. In this communication we report about the synthesis and characterization of new conduritol analogues derived from bicyclooctatriene such as, *bis*-homo-conduritol-D **2**, and *bis*-homoconduritol-F **3**.



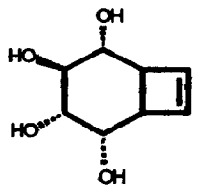
1

Conduritol



2

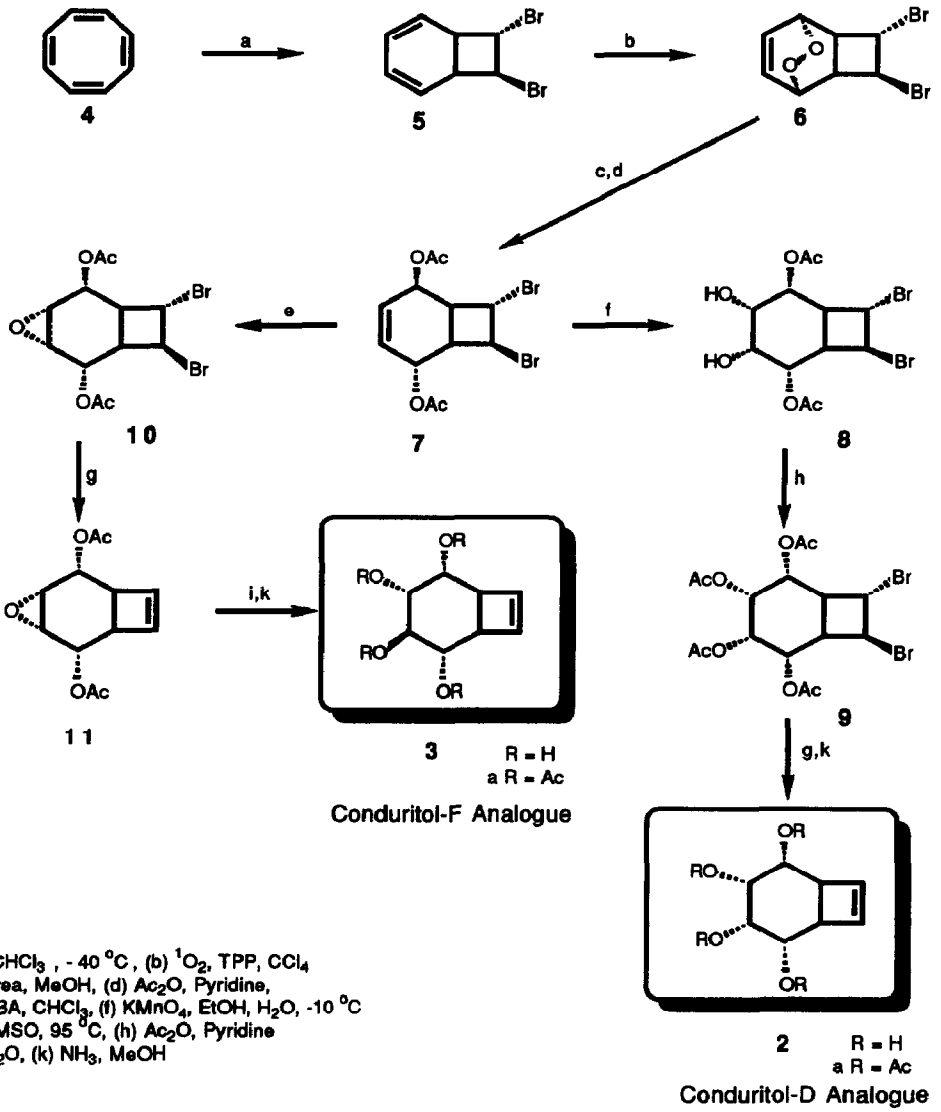
Bis-homo-conduritol-D



3

Bis-homo-conduritol-F

Our starting material was dibromobicyclooctadiene which has been synthesized by bromination of cyclooctatetraene[5]. Photooxygenation of *trans*-7,8-dibromobicyclo[4.2.0]octa-2,4-diene in methylene chloride using tetraphenylporphyrine as sensitizer gave the endoperoxide[6] in 80% yield. The reduction of



endoperoxide with thiourea in methanol followed by acetylation in pyridine gave the diacetate 7[6a] in 75 % yield which was the key compound for the synthesis of our target molecules **2**, and **3**. Hydroxylation of diacetate **7** with $KMnO_4$ at -10 °C in ethanol led exclusively to **8** which was characterized as its tetraacetate **9** (overall yield 68 %). The NMR spectral data confirmed the hydroxylation of the double bond but it was not possible to assess from these data whether the stereochemical course of the hydroxylation was *syn* or *anti*. In order to make a clear-cut differentiation between these two possible structures we carried out an X-ray crystal analysis[7] of this compound (Figure 1). All *cis*-stereochemistry of four acetate groups was determined unequivocally. The stereochemical outcome of this latter reaction was explained by inspection of Dreiding models. This shows the *syn*-face of the cyclohexene double bond is considerably more accessible than the *anti*-face which is blocked by the *endo*-bromine atom.

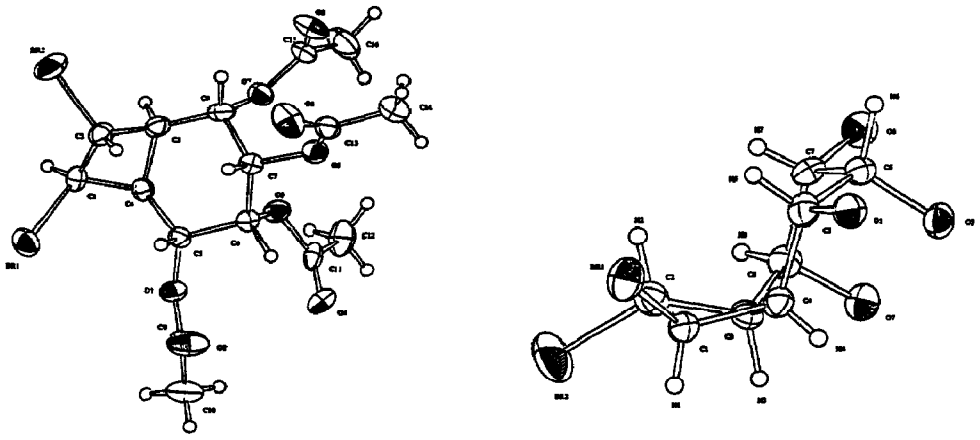


Figure 1. X-ray crystal structure for 9. a) Complete Structure, b) Rings with attached atoms

Table 1. Intramolecular Distances Involving the Nonhydrogen Atoms

atom	atom	distance	atom	atom	distance
Br (1)	C (1)	1.94 (1)	C (1)	C (2)	1.53 (1)
Br (2)	C (2)	1.93 (9)	C (1)	C (4)	1.54 (1)
O (1)	C (5)	1.45 (1)	C (2)	C (3)	1.54 (1)
O (1)	C (9)	1.35 (1)	C (3)	C (4)	1.57 (1)
O (7)	C (15)	1.34 (1)	C (3)	C (8)	1.49 (1)
O (7)	C (8)	1.43 (1)	C (4)	C (5)	1.53 (1)
O (3)	C (6)	1.45 (1)	C (5)	C (6)	1.51 (1)
O (3)	C (11)	1.36 (1)	C (15)	C (16)	1.50 (1)
O (2)	C (9)	1.17 (1)	C (9)	C (10)	1.51 (1)
O (8)	C (15)	1.19 (1)	C (6)	C (7)	1.52 (1)
O (5)	C (7)	1.42 (1)	C (7)	C (8)	1.54 (1)
O (5)	C (13)	1.36 (1)	C (13)	C (14)	1.49 (1)
O (6)	C (13)	1.20 (1)	C (11)	C (12)	1.49 (1)
O (4)	C (11)	1.21 (1)			

Table 2. Intramolecular Bond Angles Involving the Nonhydrogen Atoms

atom	atom	atom	angle	atom	atom	atom	angle
C (5)	O (1)	C (9)	115.6 (8)	O (7)	C (15)	C (16)	109 (1)
C (15)	O (7)	C (8)	117.1 (8)	O (8)	C (15)	C (16)	124 (1)
C (6)	O (3)	C (11)	117.8 (7)	O (1)	C (9)	O (2)	125 (1)
C (7)	O (5)	C (13)	116.5 (7)	O (1)	C (9)	C (10)	110 (1)
Br(1)	C (1)	C (2)	116.6 (7)	O (2)	C (9)	C (10)	125 (1)
Br(1)	C (1)	C (4)	121.0 (7)	O (3)	C (6)	C (5)	108.4(7)
C (2)	C (1)	C (4)	89.2 (8)	O (3)	C (6)	C (7)	109.9(7)
Br(2)	C (2)	C (1)	118.4 (7)	C (5)	C (6)	C (7)	108.8(8)
Br(2)	C (2)	C (3)	118.6 (6)	O (5)	C (7)	C (6)	108.2(7)
C (1)	C (2)	C (3)	86.9 (7)	O (5)	C (7)	C (8)	109.7(8)
C (2)	C (3)	C (4)	87.4 (7)	C (6)	C (7)	C (8)	113.0(8)
C (2)	C (3)	C (8)	119.5 (9)	O (7)	C (8)	C (3)	107.6(8)
C (4)	C (3)	C (8)	120.0 (8)	O (7)	C (8)	C (7)	109.7(8)
C (1)	C (4)	C (3)	85.4 (7)	C (3)	C (8)	C (7)	112.1(8)
C (1)	C (4)	C (5)	115.0 (8)	O (5)	C (13)	O (6)	122 (1)
C (3)	C (4)	C (5)	112.6 (7)	O (5)	C (13)	C (14)	111 (1)
O (1)	C (5)	C (4)	106.0 (7)	O (6)	C (13)	C (14)	126 (1)
O (1)	C (5)	C (6)	111.1 (7)	O (3)	C (11)	O (4)	122.7(9)
C (4)	C (5)	C (6)	112.2 (8)	O (3)	C (11)	C (12)	110.5(9)
O (7)	C (15)	O (8)	126.0 (1)	O (4)	C (11)	C (12)	126.7(9)

The debrominated product **2a** has been obtained by heating of **9** with zinc dust, added with a small amount of iodine at 90 °C in dimethylsulfoxide for 4 h. The ^{1}H and ^{13}C NMR spectra of the tetraacetate support the symmetrical structure in which a plane of symmetry bisects the molecule. Alkoxy protons H_3, H_4, H_5, and H_6 (coupled with cyclobutene protons) give rise to an AA'BB'XX' system at δ = 5.3, 5.2 and 3.25 ppm where the double bond protons (H_7 and H_8) resonate at δ = 6.29 as a singlet. An 8 line ^{13}C NMR spectrum is also in full agreement with the proposed structure. Deacetylation of **2a** was carried out with ammonia in methanol to give the free tetrol **2** in nearly quantitative yield (mp. 113-114 °C) which has been characterized properly.

For the synthesis of *bis*-homo-conduritol-F **3** we reacted **7** with m-chloroperbenzoic acid and obtained again only one isomer. The *syn*-stereochemistry of this dibromoepoxy diacetate **10** was confirmed by differential ^{1}H NMR-NOE measurements. The dibromoepoxy diacetate **10** reacted smoothly with Zn-DMSO and gave the epoxy diacetate **11** in 84% yield. *Trans*-ring opening of the epoxide **11** in acidified acetic anhydride proceeded regioselectively to afford in 90% yield the *bis*-homoconduritol-F tetraacetate **3**. All analytical methods indicate the presence of only one isomer and the observed asymmetry in the molecule is in agreement with the proposed structure. Finally, deacetylation of **3a** as described above gave the free tetrol (mp. 119-120 °C) in high yield.

In summary, a short stereocontrolled approach to these new class compounds, *bis*-homo-conduritol-D and -F has been accomplished starting from cyclooctatetraene. Further work starting from the diacetate **7** concerning the synthesis of *bis*-homo-aminoconduritol and *bis*-homo-inositol derivatives are currently under progress.

Acknowledgement: The authors are indebted to the Department of Chemistry and Atatürk University (Grant No 1992/17) for financial support of this work and State Planning Organization (DPT) for purchasing a 200 MHz NMR.

REFERENCES

1) Author to whom inquires concerning the X-ray structure should be directed.

2) For recent reviews see:
   a) Balcı, M.; Sütbeyaz, Y.; Seçen, H. *Tetrahedron*, **1990**, *46*, 3715.
   b) Carless, H. A. J. *Tetrahedron, Asymmetry*, **1992**, *3*, 795.

3) Legler, G., *Adv. Carbohydr. Chem. Biochem.* **1990**, *48*, 319.

4) a) Sütbeyaz, Y.; Seçen, H.; Balcı, M. *J. Chem. Soc. Chem. Commun.* **1988**, 1330.
   b) Seçen, H.; Sütbeyaz, Y.; Balcı, M. *Tetrahedron Lett.* **1990**, *31*, 1323.
   c) Seçen, H.; Maraş, A.; Sütbeyaz, Y.; Balcı, M. *Synthetic Commun.* **1992**,
   d) Seçen, H.; Salamcı, E.; Sütbeyaz, Y.; Balcı, M. *Syn Lett.* **1993**, 609.

5) Georgian, V.; Georgian, L.; Robertson, A. V. *Tetrahedron.* **1963**, *19*, 1219.

6) a) Oda, M.; Kayama, Y.; Kitahara, Y. *Tetrahedron Lett.* **1974**, 2019.
   b) Gözel, Y.; Kara, Y.; Balcı, M. *Doğa - Turk. J. Chem.***1991**, *15*, 274.

7) The absolute configuration of the molecule in the crystal was determined. Crystal data of **9**: $C_{16}H_{20}Br_2O_8$, MW: 500.14, orthorombic, Lattice parameters: a=11.090 (2) A, b=22.523 (3)Å, c=8.180 (2)Å, V=2043 (1)Å^3, Space Group: $P2_12_12_1$ (#19), Z=4, D_{calc}=1.626 g/cm^3, R= 0.038 for 1280 reflections and 268 parameters, $\mu_{(CuK\alpha)}$= 54.15 cm^{-1}.

(*Received in UK* 14 *December* 1993; *revised* 7 *March* 1994; *accepted* 10 *March* 1994)