Tetrahedron Vol 45, No 21, pp 6653 to 6656, 1989
Printed in Great Britain

0040-4020/89 $3 00+ 00
Pergamon Press plc

CYCLOOCTADIENE SYSTEMS DERIVED FROM AUSTROBAILIGNAN-5: REVISED STEREOCHEMICAL ASSIGNMENTS

SUNIL K. CHATTOPADHYAY AND KOPPAKA V. RAO

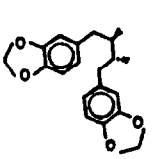
Department of Medicinal Chemistry, College of Pharmacy,
University of Florida, Gainesville, Florida 32610

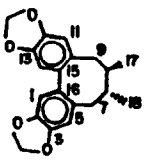
(*Received in USA 26 May* 1989)

Abstract - A number of the stereochemical assignments made in an earlier publication are revised in light of the data based on X-ray crystallographic studies which became available more recently.

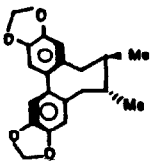
The oxidative conversion of a 1,4-diarylbutane type lignoid to a dibenzocyclooctadiene type, followed by the preparation of the corresponding mono and dioxy derivatives of the latter was the subject of an earlier publication by us[1]. Although the nmr spectral evidence available at the time supported the stereochemical assignments made for these oxy derivatives, these were pointed out to us to be incorrect by Dr.Peter A.Craw, based on the X-ray cystallographic data on a closely related compound[2]. We deeply appreciate Dr. Craw's sharing of this information with us. We also, since, obtained X-ray crystallographic evidence on two key compounds, the details of which will appear shortly[3]. The purpose of the present communication is to provide the corrected stereochemical assignments, as well as clarifications and corrections of other statements which appeared in the earlier paper. Since this paper is limited only to those structures that needed the correction, either interpretative or typographic, a brief narrative description of the compounds in question is given here using the same identification numbers as used in the earlier paper, although they will not be consecutive. The nomenclature of lignans/neolignans used here followed that described by Gottlieb[4] and the numbering system used for the dibenzoocycloctadiene system was that used by Ikeya [5,6] et al.,

Austrobailignan-5[7] 1, more readily isolated from Saururus cernuus as a crystalline solid[1,8] was converted by reaction with dichlorodicyanoquinone (DDQ) in trifluoroacetic acid (TFA) or with Mn^{3+} acetate in TFA to the dibenzocyclooctadiene 10, which has been prepared earlier by Biftu[9] et al., from 1 using vanadium oxyfluoride in TFA. A number of cyclooctadiene type lignoids are naturally occurring and show some biological activity, a notable example being kadsurin 12[10]. All of the naturally occurring compounds of this type are trisubstituted in both the aromatic rings, a situation which restricts the rings to nonplanar conformations. Although 10 is not naturally occurring, its disubstituted aromatic rings represent a system where the above restriction is much less significant. The objective of our earlier study was to prepare some oxy analogues of this type for evaluation of their possible biological activity.

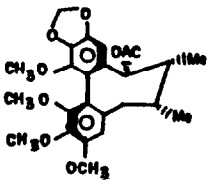




10

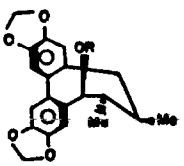


10



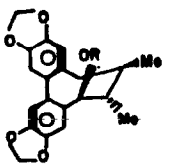
12

Further reaction of 10 with DDQ in acetic acid gave, depending on the amount of reagent and conditions used, a mixture of two mono alcohols 14 and 15 (as their corresponding acetates, 17 and 18) or two dialcohols 22 and 23 (as their corresponding acetates 24 and 25). Oxidation of 14 and 15 gave the same monoketone 16 and that of 22 and 23 gave the same diketone 26.



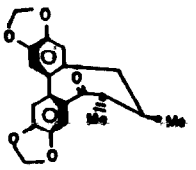
14, R=H

17, R= $-C-CH_3$ (O)

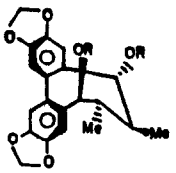


15, R=H

18, R= $-C-CH_3$ (O)

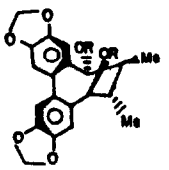


16



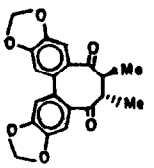
22, R=H

24, R=$COCH_3$



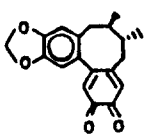
23, R=H

25, R=$COCH_3$

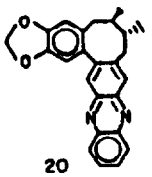


26

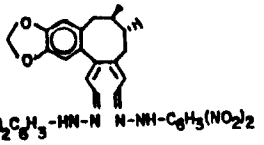
Acid treatment of the monoalcohols 14 or 15 gave the same o-quinone 19, which readily formed 20 when treated with o-phenylenediamine. Reduction of 19 with sodium borohydride gave a product which was not a phenol but appeared to be a dialcohol and on oxidation with periodic acid yielded a dialdehyde, characterized as the bis 2,4-dinitrophenylhydrazone 21.



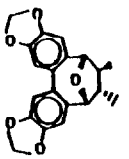
19



20



21



27

The major diol 22 underwent cyclization to the epoxide 27 when treated with triphenylphosphine bromide in acetonitrile. Alternatively, when 22 was treated with BF_3-etherate to effect the same cyclization, the epoxide 27 was formed but part of it was also cleaved to form the monoketone 16. The structures of 18, the acetate of the major mono alcohol, and of 27, the epoxide, were established by x-ray crystallographic evidence[3].

The ^{13}C nmr frequencies of the various dibenzocyclooctadienes described here are listed in Table 1 using the corrected numbering system. Finally, the structure 28 assigned in the earlier paper to the product of an acid-catalyzed transformation of 23 is withdrawn until a satisfactory alternative, consistent with the evidence is found.

TABLE 1: ^{13}C NMR DATA FOR THE DIBENZOCYCLOOCTADIENE DERIVATIVES

Carbon Number	10	14	15	22	23
1	109.0 (x2,C-14)	109.0	107.1	108.3 (x2,C-14)	106.4 (x2,C-14)
2	145.4 (x2,C-13)	145.2	145.5	145.3 (x2,C-13)	145.3 (x2,C-13)
3	147.0 (x2,C-12)	145.9	147.0	146.0 (x2,C-12)	146.8 (x2,C-12)
4	108.4 (x2,C-11)	111.1	109.0	107.5 (x2,C-11)	105.8 (x2,C-11)
5	133.3 (x2,C-10)	135.6	141.0	135.8 (x2,C-10)	141.1 (x2,C-10)
6	42.0 (x2,C-9)	66.5	70.8	66.3 (x2,C-9)	70.7 (x2,C-9)
7	40.7 (x2,C-8)	43.7	47.0	43.5 (x2,C-8)	47.2 (x2,C-8)
8		31.4	39.4		
9		34.6	42.0		
10		133.0	135.4		
11		107.7	106.4		
12		145.9	147.0		
13		145.2	145.5		
14		108.5	107.1		
15	135.5 (x2,C-16)	131.5	132.3	130.6 (x2,C-16)	130.3 (x2,C-16)
16		131.2	131.1		
17	23.5 (x2,C-18)	19.5	24.0	15.7 (x2,C-18)	19.3 (x2,C-18)
18		15.8	18.0		
OCH_2O	100.8 (x2)	100.8 (x2)	101.0 (x2)	100.8 (x2)	100.8 (x2)

Experimental

The instrumentation used and the details of the experimental methods are essentially the same as described earlier[1]. Only necessary alterations or corrections of the data are presented here, each item being referred to the appropriate section of the earlier paper.

Conversion of 1 to 10 with Mn^{3+} acetate: The procedure was analogous to that described for DDQ except that 1 (5g) was treated with Mn^{3+} acetate (7g; 1:2 molar ratio). The product, 10 was crystallized from benzene to form rosettes, yield, 3.8g; m.p. 219-220°.

Conversion of 10 to 14 and 15: ... ^{1}H nmr of 15: ... δ 2.02, a distorted t, J=14.4 and 15.3 Hz.

Preparation of the Acetates 17 and 18: The acetate 18 crystallized from MeOH as small cubes. ^{1}H nmr of 18 : ... δ 6.66, 6.67, 2s, 4ArH .... $[\alpha]_D$ of 17, -105°; ^{1}H nmr of 17 : ... δ 6.70, S, 2ArH ....

Oxidation of 15 to 16: ... 1655cm^{-1}...; ^{1}H nmr of 16: ... δ0.92, 1.0, 2d, J=6Hz; 2.80, dd and 2.95, dd J=4.5 Hz.

Reduction of 16 to 14 and 15: A methanolic solution of 16 (0.05g) was treated with $NaBH_4$(0.04g) at 20°. Dilution with water, extraction with ether and concentration of the extract gave a solid consisting of 14 and 15 in a ratio of 9:1. Crystallization of the mixture gave 14, yield, 0.02g.

Conversion of 14 to 19: ... ^{1}H nmr of 19: ... δ 7.0, 2s, 2H; ...

Preparation of 20 from 19: ... ^{1}H nmr of 20: ... δ 0.90, 1.33, 2d, J=6Hz; 2 CH-CH_3 ....

Oxidation of 22 to 26: To a solution of 22 (0.1g) ...

Preparation of 27: ... C_3H_6O = acetone. ... ^{1}H nmr of 27: .... δ 1.85, 2.20, 2m, 2 CH-CH_3 ...

Conversion of 22 to 16 and 27: Compounds 16 and 27 were identified on the basis of their physical (m.p., tlc)and spectral (uv, ir, ^{1}H nmr and ms) characteristics.

References

1. S.K. Chattopadhyay and K.V. Rao, Tetrahedron 43, 669 (1987).
2. J.S. Buckleton, R.C. Cambie, G.R. Clark, P.A. Craw, C.E.F. Rickard, T.S. Rutledge and P.D. Woodgate, Austr. J. Chem., 41, 305 (1988).
3. Z.Y. Zhang, G.J. Palenik, S.K. Chattopadhyay and K.V. Rao, Acta Crys., Sec. C (in press).
4. O.R. Gottlieb, Progr. in the Chem. Org. nat. Prod. 35, 11 (1979).
5. Y. Ikeya, H. Taguchi, I. Yosioka and H. Kobayashi, Chem. Pharm. Bull. 27, 2695 (1979).
6. Y. Ikeya, H. Taguchi, H. Sasaki, K. Nakajima and I. Yosioka, Chem. Pharm. Bull. 28, 2414, 1547 (1980).
7. S.T. Murphy, E. Ritchie and W.C. Taylor, Austral. J. Chem., 28, 81 (1975).
8. K.V. Rao and F.M. Alvarez, J. Nat. Prod. 48, 592 (1985).
9. T. Biftu, B.G. Hazra and R. Stevenson, J.C.S. Perkin I, 2276 (1979).
10. Y.P. Chen, R. Liu, H.Y. Hsu, S. Yamamura, Y. Shizuri and Y. Hirata, Tetrahedron Lett. 4257 (1973).