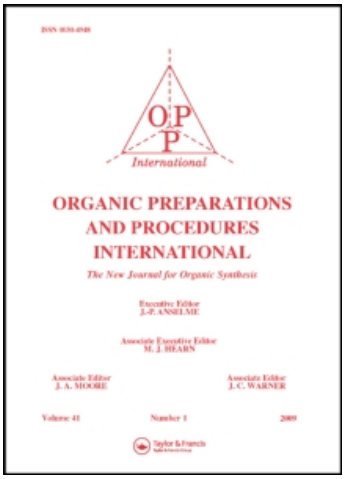


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

ULTRASOUND-PROMOTED SODIUM BOROHYDRIDE REDUCTION OF PENTACYCLO[5.4.0.0^{2,6}.0^{3}.^{10}.0^{5,9}]UNDECANE-8,11-DIONE (PCUD-8,11-DIONE) AND OF 4,4-DIMETHOXY-2,3,5,6-TETRACHLORO-PCUD-8,11-DIONE

Alan P. Marchand[a]; G. Madhusudhan Reddy[a]
[a] Department of Chemistry, University of North, Texas Denton, TX

To cite this Article Marchand, Alan P. and Reddy, G. Madhusudhan(1990) 'ULTRASOUND-PROMOTED SODIUM BOROHYDRIDE REDUCTION OF PENTACYCLO[5.4.0.0^{2,6}.0^{3}.^{10}.0^{5,9}]UNDECANE-8,11-DIONE (PCUD-8,11-DIONE) AND OF 4,4-DIMETHOXY-2,3,5,6-TETRACHLORO-PCUD-8,11-DIONE', Organic Preparations and Procedures International, 22: 4, 528 — 531
To link to this Article: DOI: 10.1080/00304949009356319
URL: http://dx.doi.org/10.1080/00304949009356319

REFERENCES

1. a) M. Goldstein and S. Gerber, Nature, 187, 147, (1960); b) E. Demet and A. Halaris, Biochem. Pharmacol., 28, 3043, (1979).

2. J. Axelrod, I. J. Kopin and J. D. Mann, Biochim. Biophys. Acta., 36, 576, (1959).

3. a) T. H. Maugh, Science, 214, 39, (1981); b) J. R. Cooper, F. E. Bloom and R. H. Ross, "The Biochemical Basis of Neuropharmacology", 5th ed., p. 271, Oxford New York, 1986.

4. M. J. Hubber-Smith, R. Nesse, M. Mazhar and D. S. McCann, J. Chromat., 377, 91, (1986).

5. T. Dennis and B. Scatton, J. Neurosci. Methods, 6, 369, (1982); See reference 1b and G Maardh, B. Sjoequist and E. Aenggard, J. Neurochem., 41, 246, (1983).

6. A. Davis, D. A. Durden and A. A. Boulton, J. Chromat., 374, 227, (1986).

7. S. Murray, T. A. Bailie and D. S. Davies, J. Labelled Cmpd., 18, 1135, (1981); S. P. Markey, K. Powers, D. Dubinsky and I. J. Kopin, ibid., 17, 103, (1980).

8. M. D. Armstrong, A. McMillan and K. N. F. Shaw, Biochim. Biophys. Acta, 25, 422, (1957).

****

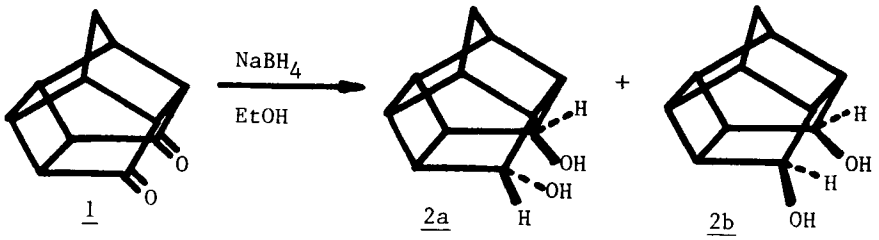
ULTRASOUND-PROMOTED SODIUM BOROHYDRIDE REDUCTION OF PENTACYCLO[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]UNDECANE-8,11-DIONE (PCUD-8,11-DIONE) AND OF 4,4-DIMETHOXY-2,3,5,6-TETRACHLORO-PCUD-8,11-DIONE

Submitted by (08/04/89) Alan P. Marchand* and G. Madhusudhan Reddy

Department of Chemistry
University of North Texas
Denton, TX 76203-5068

In connection with a continuing study of the synthesis and chemistry of substituted pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-diones (PCUD-8,11-diones),[1] a substantial quantity of PCUD-endo, endo-8,11-diol (2a) was needed. Sodium borohydride reduction of PCUD-8,11-dione (1) has been reported to afford a mixture of 2a and PCUD-exo,endo-8,11-diol (2b).[2,3] This method for reducing 1 has several drawbacks, i.e., it requires (i) the use of a large excess of sodium borohydride, (ii) long reaction times (i. e., 24 hrs), and (iii) tedious separation of 2a from the product mixture.[2] Accordingly, this procedure does not lend itself

readily to large scale preparation of 2a.

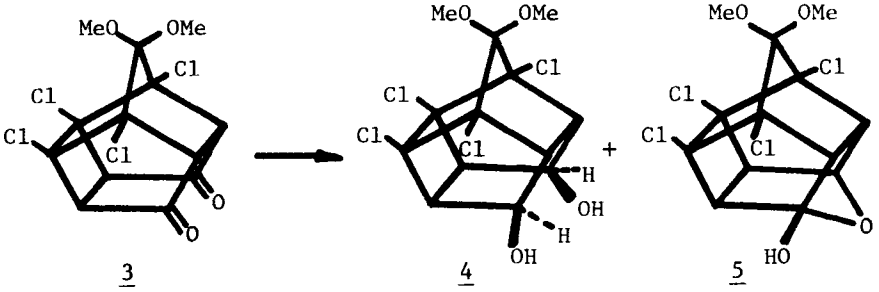


1 2a 2b

Recently we reported that sodium borohydride, when used in conjunction with cerium (III) chloride heptahydrate, promotes stereospecific reduction of the ketone carbonyl moiety in PCUD-8-en-11-one to afford the corresponding endo alcohol 2a.[4] In addition, several recent reports extoll the virtues of sonication to facilitate heterogeneous chemical reactions.[5] In an effort to improve the yield of 2a, we have reexamined the $NaBH_4$-MeOH reduction of 1 by performing the reaction with and without added $CeCl_3$ and, in both instances, with simultaneous ultrasound irradiation.

Without added $CeCl_3$, the sonicated $NaBH_4$-MeOH reduction of 1 at 15° was completed within 15 min. Under these conditions, a mixture of 2a and 2b was obtained (67% and 30% yield, respectively). In contrast to this result, the corresponding reduction of 1, when performed in the presence of $CeCl_3$, afforded isomerically pure 2a in 98% yield.

Several years ago, we reported that 4,4-dimethoxy-2,3,5,6-tetrachloro-PCUD-8,11-dione (3) was reduced by $NaBH_4$ in 95% aqueous ethanol to afford the corresponding exo,endo-8,11-diol, 4 (82% yield), along with a small amount of hemiketal 5.[6] Subsequently, methanolic 3 was found to be inert to $NaBH_4$-$CeCl_3$, even under forcing conditions.[4] In the present study, sonication was observed to promote smooth reduction of the ketone carbonyl groups in 3 by $NaBH_4$-EtOH in the absence of $CeCl_3$. The exclusive product of this reduction is the corresponding exo,endo-8,11-diol 4 which is produced in 90% yield.



3 4 5

Conditions		
$NaBH_4$, 95% EtOH, 0°C → 25 °C → reflux	82%	"small amount"
$NaBH_4$, 95% EtOH, 25 °C, sonicate	90%	0%

EXPERIMENTAL SECTION

Melting points are uncorrected. Sonication was performed by using an American Brand ultrasonic cleaner, model ME 4.6 (input 85 W). WARNING: The toxicological properties of 1-4 are not known. Adequate precautions, consistent with safe laboratory practice, should be taken when performing the operations described below to avoid powder inhallation and also to avoid skin contact with these potentially hazardous compounds.

Reduction of 1 with $NaBH_4$.- A solution of 1 (17.4 g, 100 mmol) in methanol (500 mL) was placed in the ultrasound apparatus and cooled to 15°. Sodium borohydride (7.60 g, 200 mmol) was added portionwise during 10 min to the sonicated reaction mixture. During this time, the temperature of the reaction mixture was never allowed to exceed 15°. Sonication was continued for 15 min after the addition of the reducing agent had been completed. The reaction mixture was concentrated in vacuo, and water (500 mL) was added to the residue. The resulting mixture was extracted with warm ethyl acetate (3 x 400 mL). The combined extracts were washed with water (300 mL), dried (anhydrous sodium sulfate) and filtered, and the filtrate was concentrated in vacuo. The residue, which consisted of a mixture of 2a and 2b, was purified via column chromatography on silica gel (40% ethyl acetate-hexane mixed solvent as eluent). Compounds 2a (11.9 g, 67%) was thereby obtained; recrystallization of this material from ethyl acetate-hexane afforded pure 2a as a colorless microcrystalline solid, mp. 275-276°, lit.[2] mp. 276.0-276.5°; ^{13}C NMR ($CDCl_3$): δ 34.40 (t), 38.24 (d), 39.73 (d), 42.86 (d), 45.39 (d), 71.47 (d).

Further gradient elution of the chromatography column with 80-100% ethyl acetate-hexane afforded 2b (5.40 g, 30%), which was recrystallized from acetone to afford a colorless microcrystalline solid, mp. 273°, lit.[2] mp. 274°; ^{13}C NMR (CD_3OD): δ 35.66 (t), 39.76 (d), 40.61 (d), 41.97 (d), 43.47 (d), 44.77 (d), 45.94 (d), 47.76 (d), 50.17 (d), 73.45 (d), 74.03 (d).

Reduction of 1 with $NaBH_4$-$CeCl_3$.- To a solution of 1 (17.4 g, 100 mmol) in methanol (500 mL) was added cerium (III) chloride heptahydrate (74.5 g, 200 mmol). The reaction mixture was placed in the ultrasound apparatus and cooled externally to 15°. Sodium borohydride (7.60 g, 200 mmol) was added portionwise during 10 min to the sonicated reaction mixture. During this time, the temperature of the reaction mixture was never allowed to exceed 15°. Sonication was continued for 15 min after the addition of the reducing agent had been completed. The reaction mixture was concentrated in vacuo, and water (1000 mL) was added to the residue. The resulting mixture was extracted with ethyl acetate (3 x 300 mL). The combined extracts were washed with water (300 mL), dried (anhydrous sodium sulfate), filtered and the filtrate was concentrated in vacuo. Diol 2a (17.4 g, 98%) was thereby obtained; recrystallization of this material from ethyl acetate-hexane afforded pure 2a as a colorless microcrystalline solid, mp. 275-276°, lit.[2] mp. 276-276.5°.

Reduction of 3 with $NaBH_4$.- A solution of 3 (200 mg, 0.537 mmol) in ethanol (15 mL)

was placed in the ultrasound apparatus at room temperature. Sodium borohydride (50 mg, 0.13 mmol) was added, and the reaction mixture was sonicated for 3 hrs. The reaction mixture was concentrated in vacuo, and water (20 mL) was added to the residue. The resulting mixture was extracted with ethyl acetate (3 x 30 mL). The combined extracts were washed with water (30 mL), dried (anhydrous sodium sulfate) and filtered, and the filtrate was concentrated in vacuo. Diol 4 (182 mg, 90%) was thereby obtained; recrystallization of this material from ethyl acetate-hexane mixed solvent afforded pure 4 as a colorless microcrystalline solid, mp. 255-256°, lit.[9] mp. 256-257°); ^{13}C NMR (acetone-d_6): δ 48.74 (d), 51.02 (d), 51.46 (d), 52.50 (q), 53.49 (q), 54.05 (d), 69.21 (d), 70.36 (d), 75.60 (s), 76.78 (s), 78.22 (s), 78.86 (s), 104.07 (s).

Acknowledgement.- We thank the Robert A. Welch Foundation (Grant B-963), the Air Force Office of Scientific Research (Grant AFOSR-88-0132), and the University of North Texas Faculty Research Committee for financial support of this study.

REFERENCES

1. See A. P. Marchand in "Advances in Theoretically Interesting Molecules", Vol. 1, pp. 357-399, R. P. Thummel, Ed., JAI Press, Greenwich, CT, 1989 and references cited therein.

2. R. C. Cookson, E. Crundwell, R. R. Hill and J. Hudec, J. Chem. Soc., 3062 (1964).

3. G. J. Kent, S. A. Godleski, E. Osawa and P. von R. Schleyer, J. Org. Chem., 42, 3852 (1977).

4. A. P. Marchand, W. D. LaRoe, G. V. M. Sharma, S. C. Suri and D. S. Reddy, ibid., 51, 1622 (1986).

5. a) B. H. Han and P. Boudjouk, Tetrahedron Lett., 23, 1643 (1982); b) B. H. Han and P. Boudjouk, Organometallics, 2, 771 (1983); c) P. Boudjouk, R. Sooriyakumaran and B. H. Han, J. Org. Chem., 51, 2818 (1986); d) J. Lindley and T. J. Mason, Chem. Soc. Rev., 16, 275 (1987); e) R. F. Abdulla, Aldrichimica Acta, 21, 31 (1988); f) C. Einhorn, J. Einhorn, and J.-L. Luche, Synthesis, 787 (1989); g) A. V. Eremeev, R. Nurdinov and F. D. Polyak, J. Org. Chem. USSR, 22, 2049 (1986).

6. A. P. Marchand and T.-C Chou, Tetrahedron, 31, 2655 (1975).

****