Tetrahedron, 1958, Vol. 2, pp. 304–307. Pergamon Press Ltd., London

STEREOCHEMISTRY OF THE LITHIUM ALUMINUM DEUTERIDE REDUCTION OF THE THIIRANE RING*

G. K. HELMKAMP and N. SCHNAUTZ
University of California, Riverside, California

(*Received* 6 *November* 1957)

Abstract—Inversion of configuration has been demonstrated for the opening of the thiirane ring using lithium aluminum deuteride. This is based on a comparison of the optical activity of butane-2-D obtained from 2,3-dimethylthiirane with that from reductive displacement of other functional groups.

THE ready availability of optically active four-carbon compounds from a bacterial fermentation of carbohydrates[1] has resulted in a convenient series of compounds for the stereochemical evaluation of lithium aluminum deuteride reductions. The action of *Bacillus polymyxa* on glucose yields (RR)-2,3-butanediol† in a high state of optical purity. This, in turn, can be converted to (RR)-2,3-epoxybutane,[2,3] (R)-2-butanol,[4] (R)-2-methanesulfonoxybutane,[5] (S)-2-bromobutane,[6] and (SS)-2,3-dimethylthiirane,[7] all with established configuration.

With the exception of the alcohols mentioned above, the functional groups of these compounds can be replaced by deuterium using lithium aluminum deuteride, leading to butane-2-D from the aliphatic compounds, 2-butanol-3-D from the epoxide, and 2-butanethiol-3-D from the thiirane. Furthermore, the last two can be converted to butane-2-D by appropriate reductions. A measurable optical rotatory power for butane-2-D was predicted by Fickett[8] and subsequently verified experimentally.[9,10] The use of this property has been a convenient tool in comparing the steric route of reductions of the type in question.

The oxygen and sulfur heterocyclic compounds were carried through the reaction sequences shown in Fig. 1, so that introduction of the deuterium atom took place during ring opening.

The results of observations of the optical activity of the various butane-2-D samples are given in Table 1. In our previous studies[5,9] an absolute configuration was assigned to the butane-2-D isomers on the basis of three principal pieces of evidence: (1) *trans*-opening of the epoxide ring, using lithium aluminum hydride, was observed in the

---

* This work, and related work on deuteride reductions,[5,9] was supported by grants from Research Corporation.

† The configuration of optically active compounds is indicated by the (RS) method proposed by R. S. Cahn, C. K. Ingold and V. Prelog *Experientia* **12**, 81 (1956).

[1] D. Rose and S. King *Canad. J. Res.* **23F**, 79 (1945).

[2] H. J. Lucas and C. W. Gould, Jr. *J. Amer. Chem. Soc.* **63**, 2541 (1951).

[3] H. J. Lucas and H. K. Garner *J. Amer. Chem. Soc.* **70**, 990 (1948).

[4] P. J. Leroux and H. J. Lucas *J. Amer. Chem. Soc.* **73**, 41 (1951).

[5] G. K. Helmkamp and B. F. Rickborn *J. Org. Chem.* **22**, 479 (1957).

[6] P. A. Levene and R. E. Marker *J. Biol. Chem.* **91**, 405 (1931).

[7] C. C. Price and P. F. Kirk *J. Amer. Chem. Soc.* **75**, 2396 (1953).

[8] W. Fickett *J. Amer. Chem. Soc.* **74**, 4204 (1952).

[9] G. K. Helmkamp, C. D. Joel and H. Sharman *J. Org. Chem.* **21**, 844 (1956).

[10] A. F. LeC. Holding and W. A. Ross *Soc. Chem. Ind., Lond.* 1276 (1956).

bicyclic epoxides;[11] (2) second-order kinetic data was obtained for the reduction of primary alkyl bromides with the same reagent;[12] and, (3) the sign associated with the optical rotatory power of (R)-butane-2-D, as calculated by Fickett,[8] was positive. This indicates that dextrorotatory butane-2-D must be assigned the (R)-configuration. As indicated in Fig. 1, the successive reaction of (SS)-2,3-dimethylthiirane with lithium aluminum deuteride and Raney nickel led to dextrorotatory, hence (R), butane-2-D.

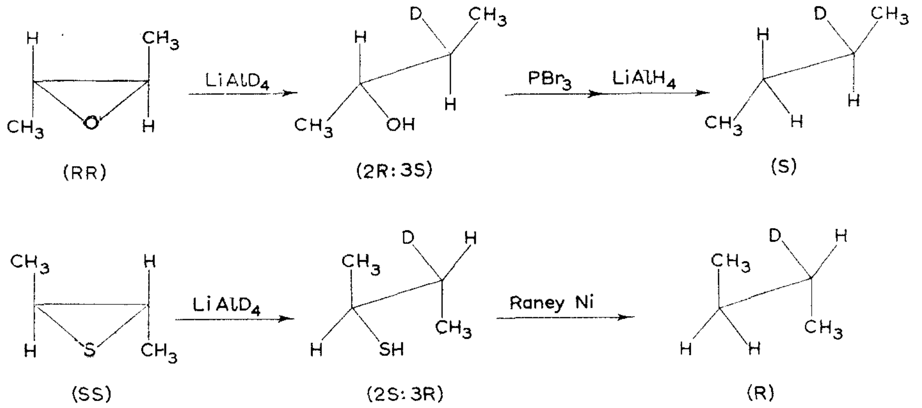

FIG. 1. Stereospecific introduction of deuterium by ring opening.

Consequently, ring opening was accompanied by inversion of configuration, and the (2S:3R) configuration must be assigned to the 2-butanethiol-3-D intermediate. Our interpretation is consistent with the observation of Bordwell *et al.*[13] that the ring of methylthiirane is opened at the 1-position with lithium aluminum hydride.

TABLE 1. OPTICAL ROTATION OF BUTANE-2-D OBTAINED BY VARIOUS LITHIUM ALUMINUM DEUTERIDE REDUCTIONS

Parent compound	Butane-2-D, $[\alpha]_D^{25}$
(RR)-2,3-Epoxybutane	−0·56°[9]
(SS)-2,3-Dimethylthiirane	+0·36°
(R)-2-Methanesulfonoxybutane	−0·47°[5]
(S)-2-Bromobutane	+0·50°[5]

As in the case of the deuterobutanol, which was converted into (SR)- and (SS)-isomers of butane-2,3-D_2 (Fig. 2),[5] an attempt was made to convert (2S:3R)-2-butanethiol-3-D into butane-2,3-D_2. This proved unsuccessful, for deuteride reduction of the methanesulfonate ester of the thiol yielded mainly the original thiol, as reported for similar esters.[14] Also, it has been established that Raney nickel desulfurization is non-stereospecific for simple systems with no participating adjacent groups.[15]

---

[11] L. W. Trevoy and W. G. Brown *J. Amer. Chem. Soc.* **71**, 1675 (1949).

[12] D. J. Malter, J. H. Wotiz and C. A. Hollingsworth *J. Amer. Chem. Soc.* **78**, 1311 (1956).

[13] F. G. Bordwell, H. M. Andersen and B. M. Pitt *J. Amer. Chem. Soc.* **76**, 1082 (1954).

[14] J. Strating and H. J. Backer *Rec. Trav. Chim. Pays-Bas* **69**, 638 (1950).

[15] W. A. Bonner *J. Amer. Chem. Soc.* **74**, 1034 (1952).

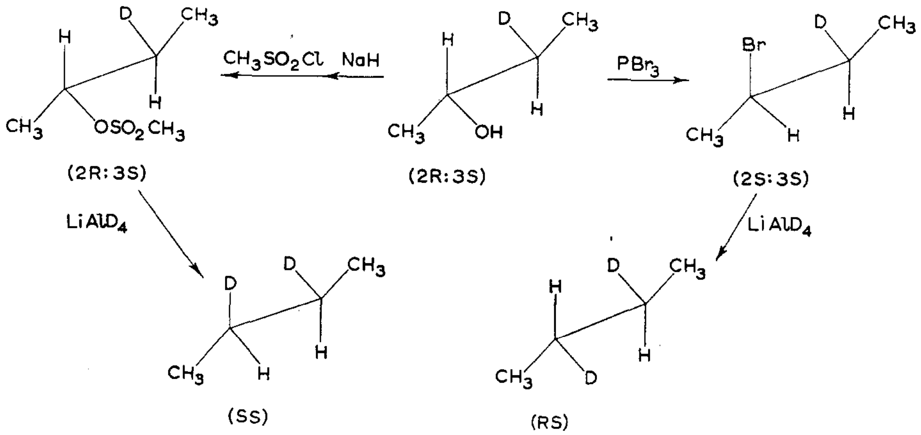

FIG. 2. Stereoisomers of butane-2,3-D_2.

EXPERIMENTAL RESULTS

(*RR*)-*2,3-epoxybutane*. The active epoxide was prepared by the procedure of Lucas *et al.*[2,3] from (RR)-2,3-butanediol.* The epoxide had $[\alpha]_D^{25}$ +57·2°, indicating an optical purity of 97 per cent based on the best previous value, +59·05°.[3]

(*SS*)-*2,3-dimethylthiirane*. This was prepared from the epoxide according to the thiourea method of Bordwell and Andersen.[16] Yield, 73 per cent; b.p. 88–89° (735 mm); n_D^{25} 1·4587; d_4^{25} 0·8863; MR_D, Calcd. 27·13, Found 27·08; $[\alpha]_D^{25}$ −129·0° (In reference 7 n_D^{25} 1·4390; $[\alpha]_D^{25}$ − 94·33°).

(2*S*:3*R*)-*2-butanethiol*-3-D. Reduction of the active thiirane was carried out in refluxing ethyl ether using a 1:1 molar ratio of lithium aluminum deuteride.[17] In preliminary studies, more efficient use of the reducing agent was sought by the use of lithium aluminum hydride and lithium hydride mixtures, but the advantages were doubtful. In all instances, with reaction times of up to 12 hr, the product was contaminated with starting material, and isolation required removal of the latter by

TABLE 2. PHYSICAL CONSTANTS OF BUTANETHIOLS

	(2S:3R)-2-Butanethiol-3-D	(SR)-2-Butanethiol	Literature
B.p	82–82·5° (735 mm)	83° (735 mm)	84–85°[19]
n_D^t	1·4303 (25°)	1·4302 (25°)	—
d_4^t	0·8277 (25°)	0·8185 (25°)	0·8299 (17°)[19]
d_4^{25}, calcd.[18]	0·8277	—	—
MR_D, Calcd., Found	28·37, 28·48	28·37, 28·47	—
$[\alpha]_D^t$,	+32·0° (25°)	—	+15·7° (20°)[20]

---

* The authors are indebted to Dr. R. W. Watson of the National Research Council of Canada for the culture of *Bacillus polymyxa* used in the biosynthesis of the diol.

[16] F. G. Bordwell and H. M. Andersen *J. Amer. Chem. Soc.* **75**, 4959 (1953).

[17] M. Mousseron, R. Jacquier, M. Mousseron Canet and R. Zagdoun *Bull. Soc. Chim. Fr.* 1042 (1952).

[18] A. McLean and R. Adams *J. Amer. Chem. Soc.* **58**, 804 (1935).

[19] S. Reymann *Ber. Dtsch. Chem. Ges.* **7**, 1287 (1874).

[20] P. A. Levene and L. A. Mideska *J. Biol. Chem.* **63**, 85 (1925).

extraction with pentane from an aqueous solution of potassium hydroxide. The yield of purified product was about 35 per cent.

(*R*)-*butane*-2-D. The reduction of the thiol was carried out with Raney nickel in refluxing ethanol.[21] From 3·4 g (0·037 mole) of the thiol was obtained 1·7 g butane-2-D in 7 hr: yield, 77 per cent; d_4^{25} 0·5856; α_D^{25} +0·21°; $[\alpha]_D^{25}$ +0·36° (Lit.: d_4^{25}, Calcd.,[18] 0·5836; $[\alpha]_D^{25}$ 0·56°.[5] Chromatographic analysis of the sample indicated the presence of 3·3 per cent *trans*-2-butene and 5·3 per cent *cis*-2-butene. This was sufficient alkene to account for the high density of the sample.

SUMMARY

The reductive opening of the thiirane ring with lithium aluminum deuteride has been demonstrated to proceed with inversion of configuration. This is consistent with the steric course of similar reductions of 2-bromobutane, 2-methanesulfonoxybutane, and 2,3-epoxybutane.

[21] R. Mozingo, D. E. Wolf, S. A. Harris and K. Folkers *J. Amer. Chem. Soc.* **65**, 1013 (1943).