The Determination of the Stereochemistry of Erythro-1,2-Diphenyl-1,2-Ethanediol

An Undergraduate Organic Experiment

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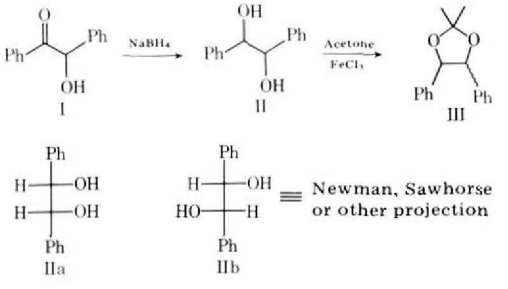
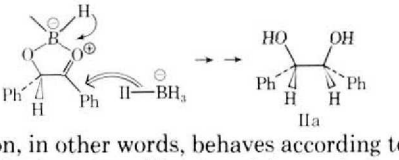
The determination by chemical means of the configurations at centers of chirality in the threo- and erythro-isomers of most α-glycols and related compounds is no easy chore. Attention has been focussed in recent years upon the use of NMR spectroscopy in making the appropriate configurational assignments in cyclic derivatives of the compounds. One report utilizes the detection of an intramolecular nuclear Overhauser effect (NOE) or W-type long-range coupling in the ^{1}H NMR spectra of the acetonide, oxazolidine, or thiazolidine derivatives to make the assignments (*1*). An earlier study demonstrated the feasibility of the use of ^{1}H NMR spectroscopy in characterizing numerous symmetrical and unsymmetrical erythro- and threo-glycols by examination of the corresponding acetonides (*2*).

For several years we have conducted a first-year organic experiment which illustrates the power of ^{1}H NMR spectroscopy in a configuration determination of the type cited. The structure involves the reduction of benzoin (I) with sodium borohydride[1] ($NaBH_4$) followed by conversion of the resulting diol (II) to the acetonide [a 2,2-dimethyl-4,5-diphenyl-1,3-dioxolane (III)].



The sequence provides a fine opportunity to correlate a number of points with topics covered in organic lectures. Experience is gained in the use of $NaBH_4$, a reagent employed routinely as a reducing agent in the latest organic laboratory manuals (*3*) and discussed in detail in all organic textbooks. The projection formulas and the various conformations of the erythro (*R,S*)-1,2-diphenyl-1,2-ethanediol (IIa) and its threo (SS,RR) isomer (IIb) serve to emphasize the stereochemical aspects of acyclic systems. The formation of the acetonide provides a good backdrop for a general discussion of ketals and acetals. Their importance in carbohydrate chemistry may be noted. The ^{1}H NMR analysis of the two possible acetonides leads to (or reviews) inspection of the presence and importance of symmetry elements and diastereotopic hydrogens. Finally, the stereoselectivity of the $NaBH_4$ reduction may be rationalized on the basis of Cram's rule.

Reduction of benzil by $NaBH_4$ (*4*) or benzoin (I) by lithium aluminum hydride (*5*) produces the erythro (meso) diol IIa contaminated by the threo (dl) isomer (IIb). When conducted as described in the Experimental section, benzoin (I) is reduced by $NaBH_4$ to the erythro diol (IIa) with good stereoselectivity [mp 133–136° C for unrecrystallized product: mp 137° C for pure erythro, mp 119° C for pure threo.] The stereochemistry of the reaction may be explained on the basis of the preferential attack by hydride ion upon the least hindered face of the carbonyl group in the complex

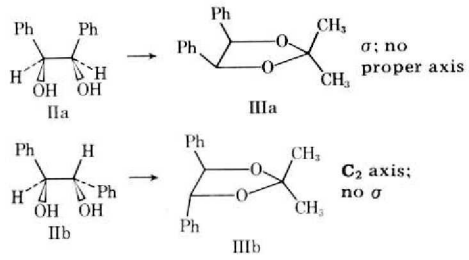


The reduction, in other words, behaves according to "Cram's Rule" (*6*). A single recrystallization of the crude product from acetone-petroleum ether gives the erythro diol IIa of excellent purity.

A recent report described the efficient preparation of acetonides of various carbohydrates by treatment with acetone in the presence of anhydrous ferric chloride (*7*). Following this procedure, the erythro diol (IIa) is converted with ease to the acetonide by heating under reflux for 20 min. Longer periods of reflux give rise to contamination of the crude acetonide (IIIa) with what is apparently diacetone alcohol, produced by an aldol condensation of the acetone. Traces of the aldol product do not interfere with the crystallization of the product when the reaction is conducted for the specified time. Catalysis by $FeCl_3$ greatly reduces the reaction times of 8–24 hr needed when anhydrous copper sulfate is used (*2*).

The lab sequence described is presented as a problem in the determination of which stereoisomer of 1,2-diphenyl-1,2-ethanediol (IIa or IIb) is produced by the $NaBH_4$ reduction of benzoin (I); the answer lies in the analysis of the ^{1}H NMR spectrum of the acetonide. The erythro diol (IIa) produces a meso acetonide (IIIa) which the methyl groups are diastero-

topic while the acetonide (IIIb) of the threo diol (IIb) contains enantiotopic methyl groups:



Inspection of the 1.5–2.0 δ region of the spectrum of the acetonide gives the answer immediately: the magnetically dissimilar methyl groups in IIIa appear as separate singlets at 1.51 and 1.76 δ ($CDCl_3$ solution). The acetonide IIIb, which may be prepared by a different route, gives just one singlet (1.60 δ) for the enantiotopic methyl groups (2). The stereochemistry thus may be assigned in this system without examination of any of the other hydrogens in the structure.

The sequence described above is presented, of course, to students in a manner that does not unmask the identity of the diol until examination of the ^1H NMR spectrum of the acetonide is completed.

Further details may be obtained from the author.

Experimental Procedure

Reduction of Benzoin (I) *by* $NaBH_4$

To a magnetically stirred suspension of 2.00 g (9.42 mmol) of I in 20 ml of absolute ethanol in a 125-ml Erlenmeyer flask is added 0.400 g (10.6 mmol) of $NaBH_4$ through a wide-bore plastic funnel. The borohydride is rinsed into the reaction flask with 5 ml of absolute ethanol and stirring is continued at room temperature for 15 min. The flask then is placed into a 400-ml beaker which is positioned on the magnetic stirrer; crushed ice is added to the beaker. The stirred solution is diluted with 30 ml of water and 1 ml of 6 *M* hydrochloric acid is added *dropwise* (**caution:** foaming!) to the solution. An additional 10 ml of water is added and stirring is continued for a further 15 min.

The white precipitate is collected and rinsed with 100 ml of water. The air-dried 1,2-diphenyl-1,2-ethanediol (IIa) (mp ~133–136°, 1.5 g) is of sufficient purity for conversion to the acetonide. Recrystallization from acetone-petroleum ether gives pure IIa: mp 136–137°; ^1H NMR (60 MHz, ~10% acetone-d_6 solution containing one drop of CF_3CO_2H) δ 4.42 (s, OH, removed by D_2O exchange), 4.83 (s, —CH), 7.38 ("s", C_6H_5). [Lit. mp 137° (*4*); ^1H NMR (220 MHz, $CDCl_3$ solution) δ 4.83 (—CH) (*8*).

Preparation of meso-2,2-Dimethyl-4,5-diphenyl-1,3-dioxolane (IIIa)

A solution of 1.00 g (4.67 mmol) of IIa and 0.30 g (1.9 mmol) of anhydrous $FeCl_3$ in 30 ml of anhydrous acetone is heated under reflux for 20 min (*7*). The cooled mixture is diluted with 10 ml of a 10% aqueous K_2CO_3 solution and 50 ml of water and extracted with two 20-ml portions of methylene chloride. The combined organic extracts are washed with 25 ml of water, dried over anhydrous Na_2SO_4, and evaporated.

The oily acetonide (IIIa) is crystallized by dissolving in 15 ml of boiling petroleum ether (30–60°), filtering to remove unreacted diol (mp 135–137°), concentrating to a volume of 3–4 ml, and cooling in an ice water bath. Crystallization is induced by scratching, whereupon IIIa separates as chunky white crystals. The product is collected and washed with a little cold petroleum ether to give 500–800 mg (42–67%, depending upon the technique of the experimentalist) with mp 57–59°; NMR (60 MHz, ~10% $CDCl_3$ solution) δ 1.51 (s, CH_3), 1.76 (s, CH_3), 5.33 (S, —CH), 6.87 ("s", C_6H_5). [Lit. mp 62° (*9*); ^1H NMR (60 MHz, CCl_4 solution) δ 1.53 (s, CH_3), 1.74 (s, CH_3), 5.37 (s, —CH) (*2*).]

The acetonide IIIa decomposes upon standing at room temperature to give benzaldehyde and benzoic acid (*9*).

[1] **Note Added in Proof:**
The recent report by W. J. leNoble (*Chem. & Eng. News*, 2 (May 9, 1983)) of an explosion which occurred when a student opened a screw-capped bottle of sodium borohydride should be noted by users of this reducing agent. We have experienced no problem with its use as described in the experimental procedure. We have, however, repackaged the sodium borohydride in plastic bottles.

Literature Cited

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