study of reaction mechanism using tritium and deuterium labeled compounds.

[5] (a) Alfred P. Sloan Fellow, 1958–1962; (b) National Science Foundation Postdoctoral Fellow, 1961–1962.

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THE STEREOCHEMISTRY OF CHALCOSE, A DEGRADATION PRODUCT OF CHALCOMYCIN

Sir:

The chemistry and structure of chalcose[1] were reported recently. We now wish to report data indicating that crystalline methyl chalcoside [m.p. 101.5–102°; $[\alpha]^{27}\text{D}$ −21° (chloroform)] and chalcose [m.p. 96–99°; $[\alpha]^{24}\text{D}$ +120° (2 min.) → +97° (10 min.) → +76° (3 hr. and 26 hr.) (water)] may be represented sterically as I and II, respectively.

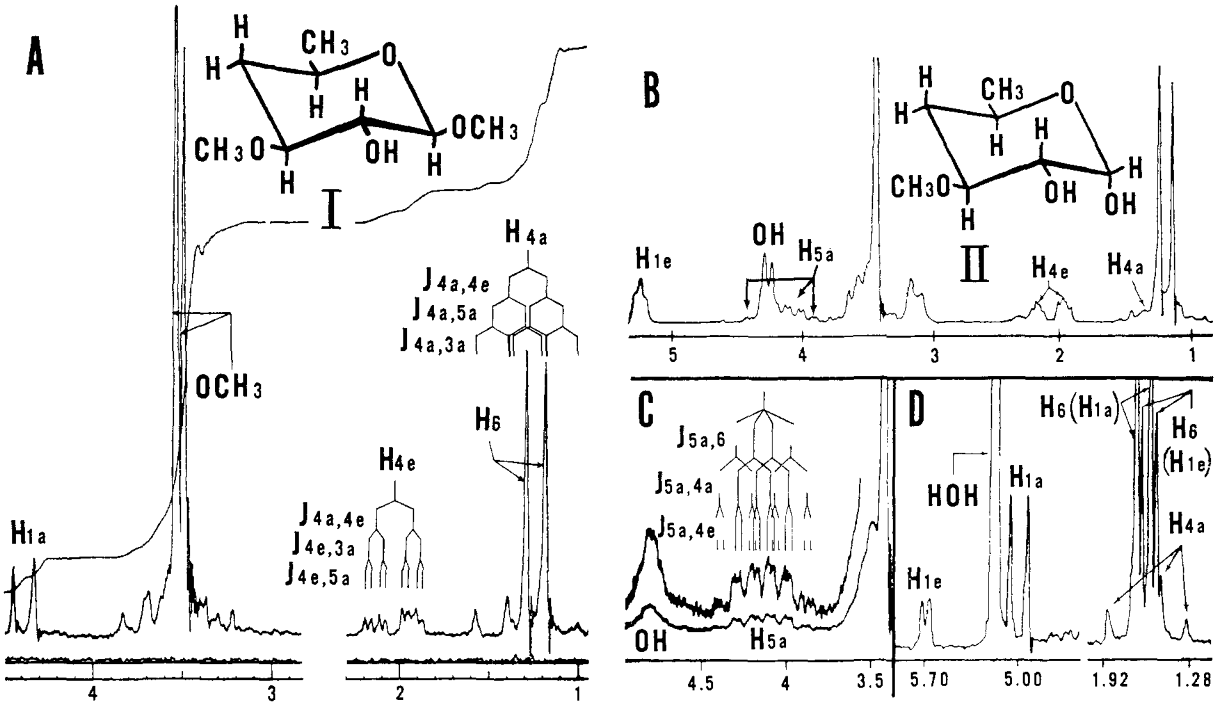

Fig. 1.—N.m.r. spectra at 60 mc. with chemical shifts given in ppm. from tetramethylsilane as zero: (A) methyl chalcoside in pyridine, also showing area integration curve and theoretical splitting patterns derived from assumed constants[4b]; (B) chalcose in deuteriochloroform: (C) the C-5 hydrogen of chalcose in deuteriochloroform (under slightly different conditions from those for Fig. 1B) showing theoretical splitting patterns[4b]; (D) chalcose in deuterium oxide.

Figure 1A shows the n.m.r. spectrum of methyl chalcoside in pyridine. The doublet C-1 anomeric hydrogen signal at $\delta = 4.40$ has a large spin coupling ($J \sim 7$ cps.) which indicates that the C-1 and C-2 hydrogens are axial,[2] as in I. The equatorial C-4 hydrogen signals around $\delta = 2.05$ shows a typical large spin coupling to the axial C-4 hydrogen ($J_{4a,4e} \sim 12.5$ cps.).[2,3] The axial C-4 hydrogen signals around $\delta = 1.00$ to 1.58,[3] partly hidden by the doublet C-methyl signal, have a total width of 34.5 cps. This width is practically equal to the sum of three coupling constants ($J_{4a,5}$, $J_{4a,3}$, $J_{4a,4e}$) with which the axial C-4 hydrogen is coupled to the equatorial C-4 hydrogen and to the two neighboring hydrogens on C-3 and C-5.[4] Thus the sum of $J_{4a,5}$ and $J_{4a,3}$ may be calculated to be approximately 22 cps. To account for this large value, as well as for the splitting pattern observed, the C-3 and C-5 hydrogens are assigned axial configurations as in I.[5]

Similar consideration of the n.m.r. spectrum of crystalline chalcose in deuteriochloroform (Fig. 1B and 1C) and in deuterium oxide (Fig. 1D) indicates the presence of axial hydrogens on C-3 and C-5. The C-2 hydrogen, being *trans* to the C-3 hydrogen, therefore must be axial. The C-1 ano-

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[1] P. W. K. Woo, H. W. Dion and Q. R. Bartz, *J. Am. Chem. Soc.*, **83**, 3352 (1961).

[2] From n.m.r. studies of acetylated pyranose, cyclohexane and related ring systems, R. U. Lemieux, R. K. Kullnig, H. J. Bernstein and W. G. Schneider [*ibid.*, **80**, 6098 (1958)] reported these data pertinent to the present discussion: (a) in β-D-xylopyranose tetraacetate, $J_{5a,5e} = 12$ cps., $\delta_{5e} > \delta_{5a}$ (*cf.* ref. 3); (b) for a number of acetylated pyranoses, $\delta_{1e} = 5.66$–6.11 ppm., $\delta_{1a} = 5.37$–5.75 ppm. (*cf.* ref. 3); (c) for hydrogens on adjacent carbons, $J_{a,a} = 5$–8 cps., $J_{a,e}$ or $J_{e,e} = 2$–3.5 cps. (*cf.* ref. 5).

[3] J. N. Shoolery and M. T. Rogers [*ibid.*, **80**, 5121 (1958)] give other examples showing that the equatorial proton absorbs at a larger δ value than its axial counterpart.

[4] (a) This statement was based on calculations first treating three hydrogens, H_{4a}, H_{4e}, $H_{5a\ (\text{or}\ 3a)}$, as an ABX system [J. A. Pople, W. G. Schneider and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., New York, N. Y., 1959, p. 132], then splitting each of the resulting lines by the fourth hydrogen $H_{3a\ (\text{or}\ 5a)}$. (b) The following constants (in cps.) were used to derive the theoretical patterns shown in Fig. 1A: $J_{4a,3a} = 11.0$, $J_{4a,5a} = 11.0$, $J_{4e,5a} = 2.1$ (or 5.0), $J_{4e,3a} = 5.0$ (or 2.1), $J_{4a,4e} = 12.5$, $\delta_{4e} - \delta_{4a} = 43.0$; and in Fig. 1C: $J_{4a,5a} = 11.4$, $J_{4e,5a} = 2.3$, $J_{5a,6} = 6.5$.

[5] J. N. Shoolery ["NMR and EPR Spectroscopy" by Varian staff, Pergamon Press, New York, N. Y., 1960, p. 114] tabulates spin coupling constants for cyclohexane systems: $J_{a,a} = 6$–14 cps., $J_{a,e}$ or $J_{e,e} = 0$–6 cps.

meric hydrogen in deuteriochloroform appears as a triplet at $\delta = 5.26$, being spin coupled to the axial C-2 hydrogen and to the C-1 hydroxyl hydrogen. The small spin coupling observed (2 to 3 cps.) indicates that the C-1 hydrogen in crystalline chalcose is equatorial,[2] as in II.

N.m.r. spectroscopy clearly demonstrates the configurational change at C-1 which accompanies the mutarotation of chalcose. In deuterium oxide (Fig. 1D), the equatorial C-1 hydrogen appears as a doublet at $\delta = 5.70$, $J_{a,e} = 2.7$ cps. The doublet signal at $\delta = 5.00$, being at higher field, is typical of an axial anomeric hydrogen[2,3]; the large spin coupling observed (7 cps.) indicates that in the newly formed anomer of chalcose the C-1 and C-2 hydrogens are axial.[2]

Oxidation of chalcose with nitric acid yielded a crystalline diacid, m.p. 179–182°, $[\alpha]^{24}\text{D}$ +47° (*c* 1.4%, water), [*Anal.* Calcd. for $C_5H_8O_6$: C, 36.59; H, 4.91; neut. eq., 81 (two titratable groups). Found: C, 36.54; H, 4.99; neut. eq., 81; pK'a (water), 2.7, 4.2], which was identical with a synthetic sample of O-methyl-L-tartaric acid (specific rotation, R_f values, mixed melting point, infrared spectrum and X-ray diffraction pattern); the latter was synthesized by partial methylation of dimethyl L-tartrate[6] and saponification. The isolation of O-methyl-L-tartaric acid, which had originated from C-1 to C-4 of chalcose, confirmed the *trans*-relationship between the C-2 and C-3 hydrogens and established the absolute configuration of these two carbons as indicated in II, rather than in the mirror image of II.

According to Hudson's rules of isorotation,[7] the absolute configuration at C-1 of crystalline chalcose, as indicated in II, would result in a mutarotation the magnitude of which decreases with time. This behavior is exactly that observed.

Thus the C-1, C-2 and C-3 configurations of methyl chalcoside (I) and of chalcose (II) have been established by mutually consistent chemical, n.m.r. and rotational data; and the C-5 configuration has been deduced from n.m.r. data.

[6] From L-tartaric acid, $[\alpha]^{25}\text{D}$ +14.6° (*c* 10.1%, water).

[7] C. S. Hudson, "Advances in Carbohydrate Chemistry," **3**, 15 (1948).

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THE EFFECT OF SUBSTRATE STERIC PROPERTIES ON THE STEREOCHEMICAL COURSE OF DIIMIDE REDUCTIONS[1]

Sir:

The action of diimide (H_2N_2) on organic substances has been the subject of recent investigations in this[2] and other[3] laboratories. Although it has been demonstrated that during reduction of olefins and acetylenes *cis* transfer of hydrogen is favored over *trans*,[3a] no examples are available which illuminate the role substrate steric features play in determining the relative configuration at an asymmetric center produced in the process.[4] Since it seemed that such information about this unusually selective, and therefore potentially useful, reagent[5] would be of general interest, we carried out a series of reductions on appropriate, representative olefins. Summarized below are results which indicate that in cases where bulk effects in the olefin are pronounced, reduction is markedly subject to steric approach control.[6] On the other hand, in examples where steric influences are moderate, much less stereochemical discrimination is observed; however, the product stability factor still does not entirely govern the stereochemical course of reaction in these cases.

Olefin cases selected for study were ones wherein approach of diimide from the less hindered side would afford the less stable of two possible reduc-

TABLE I

STEREOCHEMICAL RESULTS OF DIIMIDE REDUCTIONS

Olefin reduced	Diimide reduction Product (% *cis*:trans)	Catalytic reduction (Pt) product (% *cis*:trans)
1 α-Pinene	99:1[a]	93:7[d]
2 β-Pinene	96:4[a]	84:16[d]
3 2,3-Dimethylcyclohexene	24:76[b]	71:29[e]
4 2-Methylmethylenecyclohexane	61:39[b]	68:32[e]
5 4-*t*-Butylmethylenecyclohexane	49:51[c]	83:17[f]
6 Camphene	92(*endo*):8(*exo*)[a]	75(*endo*):25(*exo*)[d]
7 2-Norbornene-2,3-dicarboxylic acid	*endo-cis* (by isolation of single product in 40% yield)	(*endo-cis*)

[a] In this case, the stereochemical assignment to reduction products was confirmed by hydroboration of starting olefins (H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **81**, 247 (1959); thermal equilibration of the resulting alkyl borane; and then reductive hydrolysis to saturated hydrocarbon. The major product was considered to be also the more stable, *i.e.*, *trans*-pinane and *exo*-isocamphane (see J. C. Braun and G. S. Fisher, *Tetrahedron Letters*, No. 21, 9 (1960)). [b] Comparison with data supplied by the American Petroleum Institute. [c] Tentative assignment of configuration, which is based on application of the von Auwers–Skita rule (N. L. Allinger, *Experientia*, **10**, 328 (1954)) utilizing refractive index data (K. T. Serijan, P. H. Wise and L. C. Gibbons, *J. Am. Chem. Soc.*, **71**, 2265 (1949)), is not crucial here, in that nearly equimolar amounts of isomers were formed. [d] Determined in this laboratory (v.p.c.). [e] S. Siegel and G. V. Smith, *J. Am. Chem. Soc.*, **82**, 6082 (1960). [f] S. Siegel, as quoted by J.-F. Sauvage, R. H. Baker and A. S. Hussey, *ibid.*, **82**, 6090 (1960).

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[1] From the Ph.D. thesis (U. of W.) of R. J. Timmons.

[2] (a) E. E. van Tamelen, R. S. Dewey and R. J. Timmons, *J. Am. Chem. Soc.*, **83**, 3725 (1961); (b) R. S. Dewey and E. E. van Tamelen, *ibid.*, **83**, 3729 (1961); E. E. van Tamelen, R. S. Dewey, M. F. Lease and W. H. Pirkle, *ibid.*, **83**, 4302 (1961).

[3] (a) E. J. Corey, D. J. Pasto and W. L. Mock, *ibid.*, **83**, 2957 (1961); (b) E. J. Corey, W. L. Mock and D. J. Pasto, *Tetrahedron Letters*, No. 11, 347 (1961); S. Hünig, H-R. Müller and W. Thier, *ibid.*, 353 (1961). See also F. Aylward and M. Sawistowska, *Chem. and Ind.*, 404 (1961), and previous papers by Aylward and co-workers.

[4] (a) The stereochemistry of the tetrahydrogibberellic acid produced by hydrazine–air reduction of gibberellic acid (B. E. Cross, *J. Chem. Soc.*, 3022 (1960)) has not been determined. (b) Cholesterol is converted by diimide to cholestanol (20%)[3b] which, however, is the expected product on the basis of either steric approach or product development control.

[5] For example, as noted in other laboratories, dideuteriodiimide (D_2N_2) reduces an isolated double bond with introduction of only the expected two deuterium atoms; whereas catalytic reduction with deuterium gas involves additional deuterium insertion through metal-catalyzed exchange.

[6] W. G. Dauben, G. F. Fonken and D. S. Noyce, *J. Am. Chem. Soc.*, **78**, 2579 (1956).