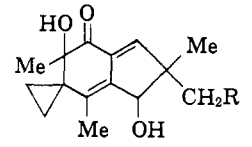
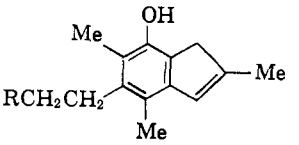
τ[4] 8.92 and 7.33 (triplet and quartet, ethyl); 7.79, 7.72 (aromatic methyls); 7.89 (broad singlet, olefinic methyl); 3.48 (quartet, olefinic proton); 6.83 (singlet, cyclic methylene); and 5.7 (very broad peak, hydroxyl); and a residue $C_{15}H_{20}O_2$ (IIb), m.p. 147–149°. This has very similar properties to IIa, but it contains a methoxyl group (singlet at τ 6.63) which results from solvent interaction during hydrogenation. With ethanol as solvent, the corresponding ethoxyl compound $C_{16}H_{22}O_2$ (IIc), m.p. 121–123°, is obtained.

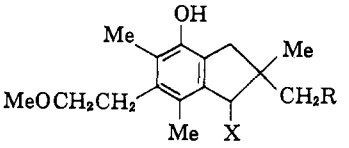
These idenes are smoothly hydrogenated to the corresponding indanes. They react readily with tetrachloro-1,2-benzoquinone to give adducts (1,4-dioxenes).[5] Ozonization of IIb (with phenolic hydroxyl methylated)



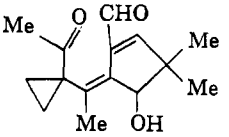
Ia, R = OH
b, R = H



IIa, R = H
b, R = OMe
c, R = OEt



IIIa, R = H, X = OH
b, R = X = H
c, R = X = OH



IV

gives a stable ozonide, $C_{16}H_{22}O_5$, m.p. 95–96°.[6]

Illudin M has λ_{max}^{EtOH} 228, 318 mμ (ϵ 13,900, 3,600); ν_{max} 1695, 1661, 1595 cm.$^{-1}$). It forms a monoacetate, m.p. 75–76°, which still shows hydroxyl absorption in the infrared. Hydrogenation (methanol, *ca.* 1.5-mole uptake) gives the phenol $C_{16}H_{24}O_3$ (IIIa), m.p. 163–165°; τ 8.98, 8.76 (*gem*-dimethyl); 7.77, 7.65 (aromatic methyls); 6.62 (methoxyl); 5.40 (proton α to hydroxyl); 8.5, 5.40 (hydroxyls); 7.5–6.4 (cyclic methylene and $-CH_2CH_2OMe$).

Hydrogenolysis of IIIa yields the compound IIIb, m.p. 123–125°; τ 8.82 (*gem*-dimethyl); 7.86, 7.78 (aromatic methyls); 7.37, 7.30 (two singlets, two cyclic methylenes); 7.25–6.34 ($-CH_2\cdot CH_2-O$ Me); 6.62 (methoxyl) and 5.60 (hydroxyl).

By analogy with IIIa, a primary hydrogenation product of illudin S may be represented by IIIc. Illudin S itself possesses a hydroxymethyl group as evidenced by a singlet at τ 6.53 (2 protons) which on acetylation moves to 5.94 (AB spectrum J_{AB} = 11 c.p.s., δ_{AB} = 0.16 p.p.m.).

The 1,3-glycol system of IIIc would cleave under acidic conditions ("reverse Prins reaction")[7] to give IIb and formaldehyde (which also has been isolated).

The illudins exhibit a multiplet in the region τ 9.7–8.95 (cyclopropyl protons). The cyclopropane ring opens on hydrogenation to give the fragment $-CH_2-CH_2OMe$ in III.[8] The ready formation of these phenols indicates a hydrindane-type skeleton for the illudins. Since the aromatic ring in the phenols is fully substituted, the olefinic proton (singlet at τ 3.5) in their precursors is placed on the double bond exocyclic to the six-membered ring and its position defines that of the carbonyl group.

Sodium borohydride reduction of Ib gives a triol $C_{15}H_{22}O_3$, m.p. 142–144°, λ_{max}^{EtOH} 256 mμ (ϵ 22,400) (conjugated diene),[9] which is oxidized by sodium periodate to the aldehyde IV, m.p. 102–103°. This has τ 0.3 (aldehyde); 9.2, 8.65 (two quintets, two pairs of equivalent cyclopropyl protons); 8.98, 8.80, 7.92, 7.80 (four methyls); 7.58 (hydroxyl); 5.70 (proton α to hydroxyl); 3.22 (olefinic proton).

The α-ketol in I can also be demonstrated by cleavage with sodium periodate.

The methyl groups in Ia give singlets at τ 8.82 (tertiary methyl), 8.65 (methyl α to hydroxyl) and 8.32 (olefinic methyl) and in Ib at 8.92, 8.81 (*gem*-dimethyl), 8.67 (methyl α to hydroxyl) and 8.33 (olefinic methyl). There is clearly only one position for attachment of the cyclopropane ring. The orientation of substituents in the aromatic ring of II and III follows from the structure of I.

(4) N.m.r. spectra were determined by Dr. D. P. Hollis of Varian Associates, California, whom we thank for helpful discussion regarding their interpretation.

(5) L. M. Jackman, in "Advances in Organic Chemistry; Methods and Results," Vol. 2, Interscience Publishers, Inc., New York, N. Y., 1960, p. 335.

(6) P. S. Bailey, *Chem. Rev.*, **58**, 928 (1958).

(7) T. E. Maggio and J. English, Jr., *J. Am. Chem. Soc.*, **83**, 968 (1961).

(8) *Cf.* spiro[2,5]octa-1,4-diene-3-one; R. Baird and S. Winstein, *ibid.*, **79**, 4238 (1957).

(9) The cyclopropane ring is expected to contribute a bathochromic shift. See L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, pp. 318–320.

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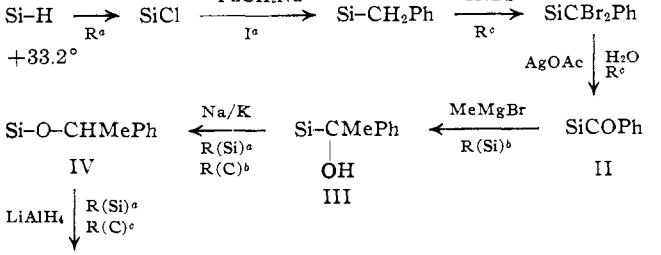
RECEIVED JANUARY 15, 1963

STEREOCHEMISTRY OF α-SILYLCARBINOL REARRANGEMENTS. II. THE ABSOLUTE CONFIGURATION OF ASYMMETRIC SILANES

Sir:

Recently we reported the stereochemistry at the asymmetric silicon atom involved in the synthesis and rearrangement to its isomeric silyl ether of methyl-α-naphthylphenylsilyldiphenylcarbinol.[1] We now wish to report a related Walden cycle which permits the assignment of the stereochemistry at both asymmetric centers (silicon and carbon) in methyl-α-naphthylphenylsilylmethylphenylcarbinol (III) and as well permits the assignment of the absolute configuration of (+)-methyl-α-naphthylphenylsilane (I) and all of its derivatives which are formed by reactions of known stereochemistry.

The Walden cycle, summarized below, results in overall inversion with respect to the silicon atom and logically follows the same stereochemical course at silicon as was reported earlier,[1] *viz.*, inversion of configuration during coupling of the chlorosilane with organometallic and retention during rearrangement from the carbinol to the ether. Treatment of the intermediate optically active benzoylsilane (II) with methyl Grignard reagent introduces an asymmetric carbon atom. This reaction and the subsequent steps proceed with considerable se-



Attached to Si in each case are methyl, α-naphthyl, and phenyl. R = retention; I = inversion. [a] Previous assignment.[1,10] [b] Assignment this work. [c] Reaction does not involve asymmetric center.

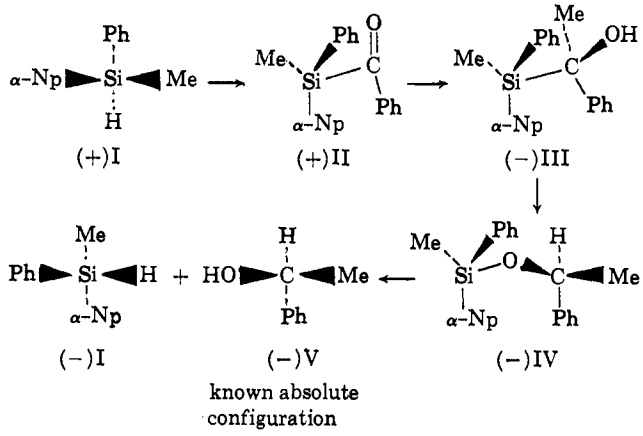
(1) A. G. Warner and C. M. Warner, *Tetrahedron Letters*, **18**, 815 (1962).

lectivity at the carbon atom since the 1-phenylethanol ultimately produced is a 72:28 mixture of (−) and (+)-enantiomers, based on its observed rotation.

Cram's rule of asymmetric induction[2] should apply in the addition of methyl Grignard reagent to benzoylmethyl-α-naphthylphenylsilane (II) and thus the configuration of the asymmetric carbon atom in the predominant diastereomer formed is defined relative to the configuration of the silicon atom.[3]

Provided that the subsequent reactions of rearrangement or reduction do not alter the configuration at carbon, the isolation of (−)-1-phenylethanol of known absolute configuration[4] can be used to establish the absolute configuration of the predominant carbinol. Reduction of the silyl ether will not affect the configuration since the cleavage occurs at the Si–O bond.[5] The rearrangement of the silylcarbinol by sodium–potassium alloy in diethyl ether is believed to involve an intermediate carbanion or species of considerable carbanionic character.[6] Cram has found that related carbanions under similar conditions retain their configuration,[7] and this, together with the great rapidity with which the rearrangement occurs, leads us to believe that the configuration at the asymmetric carbon atom is retained during rearrangement. Indeed, if the two diastereomeric carbinols were formed in the ratio 72:28, the rearrangement is completely stereospecific and at the very worst had essentially only one carbinol been produced, the rearrangement was significantly stereoselective.

Knowing the absolute configuration of (−)-1-phenylethanol (V) and assuming that the configuration at carbon, established by Grignard addition according to Cram's rule, is retained during the rearrangement of the silylcarbinol to the silyl ether, then the absolute configuration of the key compounds in the Walden cycle are



It is of interest to note that the absolute configuration of (+)-methyl-α-naphthylphenylsilane derived above is in accord with that predicted by Brewster's rules of atomic asymmetry,[8] accepting that α-naphthyl is more polarizable than phenyl. If α-naphthyl is assigned a polarizability value of 4, and Brewster's values are used for other groups, then the directions of rotation of all optically active silanes in the methyl, α-naphthyl, phenyl series for which polarizability data are available are correctly predicted on the basis of the stereochemical transformations of retention or inversion reported by Sommer and Frye.[5,9,10] Thus the chlorosilane known to be formed from (+)-silane (α-Np > Ph > Me > H, clockwise) by retention of configuration[9,10] would be predicted to be levorotatory (Cl > α-Np > Ph > Me, anticlockwise) by Brewster's rules, as is found experimentally. Further work is in progress.

The following are typical experimental data: Treatment of (+)-methyl-α-naphthylphenylsilane, $[\alpha]^{25}D$ +33.2° (cyclohexane, *c*, 5.3), with chlorine gave chlorosilane $[\alpha]^{25}D$ −6.22° (cyclohexane, *c* 9.1). Treatment with benzylsodium in ether–toluene gave 54% benzylsilane, m.p. 69–70° after several recrystallizations from methanol–ethanol, $[\alpha]^{25}D$ −6.68° (cyclohexane, *c* 6.0).

Bromination with two moles of N-bromosuccinimide[11] gave a 94.7% yield of dibromobenzyl compound, m.p. 114–114.5°, $[\alpha]^{25}D$ 12.90° ($CHCl_3$, *c* 6.5) which on hydrolysis with silver acetate in benzene–acetone–water[11] gave, after recrystallization from ethanol, 94% of yellow benzoylsilane, m.p. 68–70°, $[\alpha]^{25}D$ 6.72° (C_6H_6, *c* 9.45).

Treatment of benzoylmethyl-α-naphthylphenylsilane in ether at −60° with one mole of methylmagnesium bromide (inverse addition) over 75 min. gave on work-up 86% of a sirupy carbinol mixture, $[\alpha]^{25}D$ −16.0° (C_6H_6, *c* 9.43). Without attempting to separate the diastereomers, the carbinol mixture was treated in ether over 1.7 hours with 2 drops of Na–K alloy. Work-up gave a clear gummy silyl ether in 89% yield, $[\alpha]^{25}D$ −23.7° (cyclohexane, *c* 8.2), which was reduced with lithium aluminum hydride in butyl ether to give by crystallization 98% of crude methyl-α-naphthylphenylsilane, $[\alpha]D$ −25.4°, twice recrystallized from pentane to give 68% of material, m.p. 63–64°, $[\alpha]^{25}D$ −33.5° (cyclohexane, *c* 10.3), and by distillation 38% of 1-phenylethanol, b.p. 47–49° (0.08 mm.), $[\alpha]^{25}D$ −23.2° ($CHCl_3$, *c* 12.79) (reported[12] $[\alpha]^{20}D$ 54.13° ($CHCl_3$, *c* 5.4)), together with additional alcohol which co-distilled with the dibutyl ether, isolated in 10% yield as crude acid phthalate, $[\alpha]^{20}D$ 8.3°. Analyses and infrared spectra were in agreement with the expected structures.

Acknowledgment.—Part of this research was supported by the National Research Council of Canada. Grateful acknowledgment is also made to Dow–Corning Silicones of Canada for a gift of chemicals and for a Fellowship held by W. W. L. during the period 1961–1962.

(2) D. J. Cram and F. A. Abd Elhafez, *J. Am. Chem. Soc.*, **74**, 5828 (1952).

(3) The selectivity of the Grignard addition is markedly temperature sensitive. With addition at room temperature the diastereomeric mixture of carbinols had $[\alpha]D$ +3.03, whereas addition at −60° gave $[\alpha]D$ −16.0° with the specific rotations of the derived 1-phenylethanol being −7.26° and −23.1°, respectively. The actual proportions of diastereomers is not as yet established.

(4) P. A. Levene and S. A. Harris, *J. Biol. Chem.*, **113**, 55 (1936); P. A. Levene and P. G. Stevens, *ibid.*, **89**, 471 (1930).

(5) L. H. Sommers and C. L. Frye, *J. Am. Chem. Soc.*, **82**, 4118 (1960).

(6) A. G. Brook, *ibid.*, **80**, 1886 (1958).

(7) D. J. Cram, A. Langemann and F. Hauck, *ibid.*, **81**, 5750 (1959).

(8) J. H. Brewster, *ibid.*, **81**, 5475 (1959).

(9) L. H. Sommer and C. L. Frye, *ibid.*, **81**, 1013 (1959); **82**, 3796 (1960); **83**, 2210 (1961).

(10) C. L. Frye, Ph.D. Thesis, Pennsylvania State University, 1960.

(11) A. G. Brook, *J. Am. Chem. Soc.*, **79**, 4373 (1957).

(12) R. H. Pickard and J. Kenyon, *J. Chem. Soc.*, **105**, 1115 (1914).

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STUDIES ON POLYPEPTIDES. XXVI. PARTIAL SYNTHESIS OF AN ENZYME POSSESSING HIGH RNASE ACTIVITY[1-3]

Sir:

We wish to describe experiments which appear to represent the first partial laboratory synthesis of an

(1) The authors wish to express their appreciation to the U. S. Public Health Service, the National Science Foundation and the American Cancer Society for generous support of this investigation.

(2) The peptides and peptide derivatives mentioned are of the L-configuration. In the interest of space conservation the customary L-designation for individual amino acid residues is omitted.

(3) See *J. Am. Chem. Soc.*, **84**, 4481 (1962), for paper XXV in this series.