

Stereochemical Consequences of Methoxyl Participation. The Absolute Configuration of 2-Chloro-5-methoxypentane¹

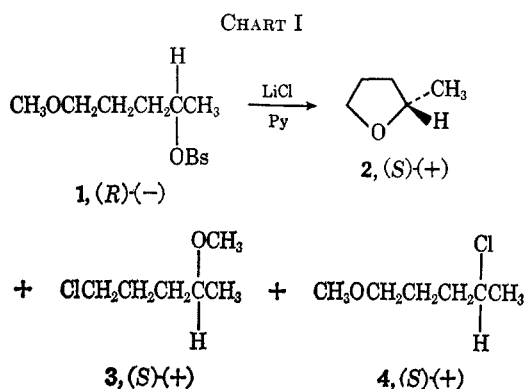
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The absolute configuration of 2-chloro-5-methoxypentane has been determined by the following sequence: (*S*)-(+)-5-hexen-2-ol (absolute configuration known) → (*R*)-(-)-5-chloro-1-hexene (with inversion) → (*R*)-(-)-4-chloro-1-pentanol → (*R*)-(-)-2-chloro-5-methoxypentane. The replacement of hydroxyl by chlorine using triphenylphosphine in refluxing carbon tetrachloride was shown to proceed mainly with inversion. The proof of configuration of 2-chloro-5-methoxypentane shows that lithium chloride in pyridine reacts with 5-methoxy-2-pentyl brosylate partly by direct S_N2 displacement and partly through an intermediate methoxonium ion.

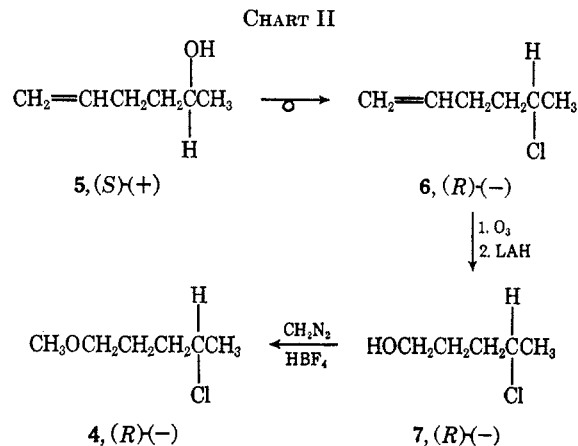
A stereochemical study³ of the action of lithium chloride in pyridine on optically active 5-methoxy-2-pentyl brosylate (**1**) gave the results indicated in Chart I. A few per cent of 2-methyltetrahydrofuran



(**2**) was formed; the major fraction from the reaction consisted of about 60% yield of a mixture of 5-chloro-2-methoxypentane (**3**) and 2-chloro-5-methoxypentane (**4**) in a 1:4 ratio. The absolute configuration of the brosylate **1**, the 2-methyltetrahydrofuran (**2**), and the 5-chloro-2-methoxypentane (**3**) were proved conclusively by relating them to compounds of known configuration. The results showed that the 2-methyltetrahydrofuran was formed from the brosylate **1** with 100% inversion of configuration, and that the 5-chloro-2-methoxypentane (**3**) was 93% inverted with respect to the brosylate **1**. The configuration of the major product, however, the 2-chloro-5-methoxypentane (**4**) was not established definitively, but was assigned on the basis of analogy to other compounds of similar structure and of known absolute configuration.⁴

The present paper presents a conclusive proof of the absolute configuration of **4**, showing that (-)-2-chloro-5-methoxypentane is of *R* configuration; this means that **4** has been formed from the brosylate **1** preponderantly with inversion. The stereochemistry of the process illustrated in Chart I is thus completely defined.

The correlation of **4** with compounds of known absolute configuration is provided by the reactions shown in Chart II. The absolute configurations of 5-hexen-2-ol (**5**) and 5-chloro-1-hexene (**6**) are known as follows. (*S*)-(+)-5-Hexen-2-ol (**5**) is correlated with



(*S*)-(-)- γ -valerolactone.⁵ (*R*)-(-)-5-Chloro-1-hexene (**6**) is correlated with (*S*)-(-)- γ -valerolactone by a sequence involving one inversion;⁶ (*S*)-(-)- γ -valerolactone is correlated with (*S*)-(+)-lactic acid.⁷ Therefore, (+)-5-hexen-2-ol (**5**) has the *S* configuration.

In our work, 5-hexen-2-ol (**5**) was resolved *via* the acid phthalate-brucine route, and was obtained in markedly higher rotation than Levene and Haller reported.^{8a} The alcohol **5** was converted into the chloro compound by four procedures, all of which agreed in their stereochemical result. The brosylate of the (*R*)-(-) alcohol **5** was treated with lithium chloride in ethanol, giving (+) chloride **6**, which must be of *S* configuration.⁸ The (*S*)-(+)-alcohol **5** gave (*R*)-(-) chloride **6** with PCl₅ in ether.^{8a} Finally, the (*R*)-(-) alcohol **5** gave the (+) chloride **6** on reaction with thionyl chloride and pyridine or when refluxed in carbon tetrachloride with triphenylphosphine.⁹ This last result is of some interest, because it appears to be the first case in which the stereochemistry of this convenient procedure has been demonstrated. Thus, this reaction has the same stereochemistry as Wiley's method.¹⁰ There is no reason to suppose that the double bond has participated in any of these transfor-

(5) (a) P. A. Levene and H. L. Haller, *J. Biol. Chem.*, **69**, 169 (1926); (b) *ibid.*, **79**, 485 (1928).

(6) (a) P. A. Levene and H. L. Haller, *ibid.*, **83**, 598 (1925); (b) P. A. Levene and T. Mori, *ibid.*, **78**, 17 (1928).

(7) (a) P. A. Levene and H. L. Haller, *ibid.*, **69**, 165 (1926); (b) *ibid.*, **67**, 329 (1926); (c) *ibid.*, **65**, 49 (1925).

(8) Cf. A. J. H. Houssa, J. Kenyon, and H. Phillips, *J. Chem. Soc.*, 1700 (1929).

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(10) G. A. Wiley, B. M. Rein, and R. L. Hershkovitz, *Tetrahedron Lett.*, 2509 (1964); J. P. Schaefer and D. S. Weinsberg, *J. Org. Chem.*, **30**, 2635 (1965).

(1) Aided by Grant AI-06328 from the National Institutes of Health.

(2) To whom inquiries should be addressed.

(3) E. R. Novak and D. S. Tarbell, *J. Amer. Chem. Soc.*, **89**, 73, 3086 (1967).

(4) Cf. J. A. Mills and W. Klyne, *Progr. Stereochem.*, **1**, 195 (1954).

mations; the infrared and nmr spectra confirm the structure of the chloride.

The chloride 6 was converted into 4-chloro-1-pentanol (7) best by ozonization followed by lithium aluminum hydride reduction; this procedure¹¹ was more expeditious than those in which the ozonide was reduced to γ -chlorovaleraldehyde by dimethyl sulfide¹² or by tetracyanoethylene.¹³ The chloropentanol 7, which is a known compound,¹⁴ was methylated under acidic conditions, to prevent any cyclization to 2-methyltetrahydrofuran,³ using diazomethane and fluoroboric acid in methylene chloride.¹⁵ (*R*)-(-)-4-Chloro-1-pentanol (7) yielded (-) 4, which is thus shown to be (*R*)-(-).

Discussion

It is clear that under the conditions³ specified in Chart I, *i.e.*, with 150 mol % of lithium chloride in pyridine for 12 hr at room temperature, or with brosyl chloride in pyridine with the alcohol corresponding to 1, the 2-chloro-5-methoxypentane (4) is inverted with respect to the brosylate 1. A quantitative statement of the percent inversion in the process shown in Chart I cannot be given because of the difficulty of separating the isomeric chloromethoxy compounds 3 and 4 and because the analysis of the mixture by nmr spectroscopy was not sufficiently accurate.³

The 5-hexen-2-ol in our experiments may not have been obtained completely optically pure; after two crystallizations of the brucine salt of the acid phthalate, the alcohol had $[\alpha]^{25D} +15.7^\circ$ (ether). Two more crystallizations raised the value to $[\alpha]^{25D} +21.8^\circ$,¹⁶ which must be close to optical purity. If one takes the figure of $+21.8^\circ$ for the optically pure alcohol, and calculates the specific rotations of the related compounds, the values obtained are given in Table I. Our actual experiments were carried out with alcohol of $[\alpha]^{25D} +15.7^\circ$ (ether), and the figures in Table I have been corrected for this.

TABLE I

CALCULATED ROTATIONS^a FOR OPTICALLY PURE SUBSTANCES

Compd	$[\alpha]^{25D}^b$	$[\alpha]^{25D}^c$
(<i>S</i>)-5-Hexen-2-ol (5)	+21.8°	+24.2°
(<i>S</i>)-2-Brosyloxy-5-hexene	+13.4°	+14.9°
(<i>R</i>)-5-Chloro-1-hexene (6)	-61.8°	-68.5°
(<i>R</i>)-4-Chloropentanol-1-ol (7)	-49.2°	-54.6°
(<i>R</i>)-2-Chloro-5-methoxypentane (4)	-44.5°	-49.4°

^a In ether. ^b Based on $[\alpha]^{25D} +21.8^\circ$ for 5-hexen-2-ol (observed value, this paper). ^c Based on $[\alpha]^{25D} -27.7^\circ$ for γ -valerolactone.

An alternative calculation gives somewhat higher results, indicating that the specific rotation of optically pure 5-hexen-2-ol is close to $+25^\circ$ (Table I). This is based on the following observations. (*S*)- γ -Valero-

(11) J. A. Sousa and A. L. Bluhm, *J. Org. Chem.*, **25**, 108 (1960).

(12) J. J. Pappas, W. P. Keaveney, E. Gancher, and M. Berger, *Tetrahedron Lett.*, 4273 (1966).

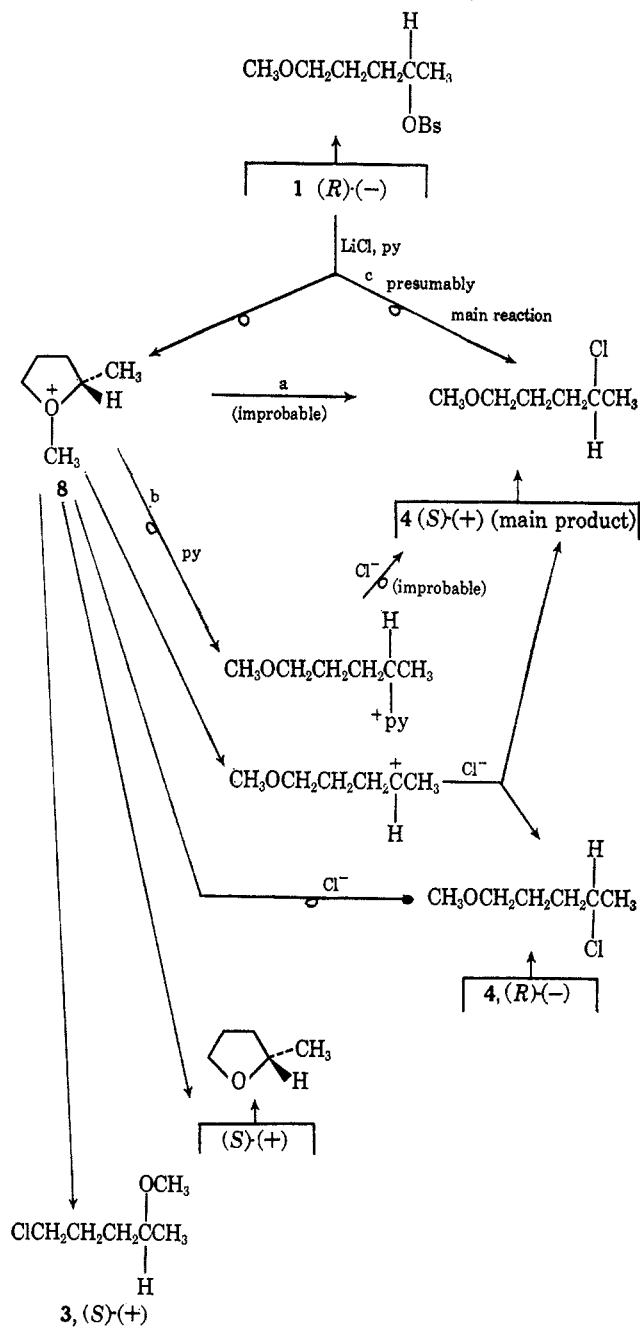
(13) R. Criegee and P. Guenther, *Chem. Ber.*, **96**, 1564 (1963).

(14) (a) S. Murahashi and N. Hagihara, *Mem. Inst. Sci. Ind. Research, Osaka Univ.*, **6**, 102 (1948); *Chem. Abstr.*, **45**, 10197g (1951); (b) N. I. Shuikin, I. F. Bel'skii, and I. E. Grushko, *Zh. Obshch. Khim.*, **29**, 2591 (1959); *Chem. Abstr.*, **54**, 10988a (1960); (c) S. G. Kuznetsov and D. V. Ioffe, *Zh. Obshch. Khim.*, **31**, 2289 (1961); *Chem. Abstr.*, **56**, 3439hi (1962).

(15) M. C. Caserio, J. D. Roberts, M. Neeman, and W. S. Johnson, *J. Amer. Chem. Soc.*, **80**, 2584 (1958); *Tetrahedron*, **6**, 36 (1959); M. Neeman and W. S. Johnson, *Org. Syn.*, **41**, 9 (1961).

(16) The reported value¹⁶ is $+18.2^\circ$.

CHART III



lactone, $[\alpha]^{25D} -27.75^\circ$ (probably without solvent), was converted into γ -hydroxyvaleric acid, $[\alpha]^{22D} +14^\circ$ (water)^{5a}. 5-Hexen-2-ol, $[\alpha]^{22D} +18.2^\circ$ (ether), was converted into γ -hydroxyvaleric acid, $[\alpha]^{24D} +10.5^\circ$ (water).^{5b} Assuming that the γ -valerolactone is 100% optically pure,¹⁷ and applying the appropriate ratios, the figures in the second column of Table I are obtained. γ -Valerolactone, obtained by a series of degradations from guaioil,¹⁸ was reported to have $[\alpha]^{23D} -35.1^\circ$ (no solvent given); use of this figure leads to values higher by about 25% than those in column 2 of Table I. The values in Table I, of course, assume that the transformations involved are stereochemically homogeneous.

(17) Cf. J. I. Braumann and A. J. Pandell, *J. Amer. Chem. Soc.*, **89**, 5424 (1967).

(18) K. Takeda and H. Minato, *Tetrahedron Lett.*, No. 22, 33 (1960).

Under solvolytic conditions, the brosylate **1** reacts with anchimeric acceleration.¹⁹ As shown above, in the reaction with lithium chloride in pyridine, however, the main product (80% of the mixture of the isomeric chloromethoxypentanes, which has been obtained in about 58% yield), 2-chloro-5-methoxypentane (**4**), is formed by an odd number of inversions. As shown in Chart III, this result could be explained by three mechanisms: (a) frontside attack of chloride ion on the methoxonium ion **8** (with retention, *i.e.*, one inversion between **1** and **4**), (b) backside attack of pyridine on this intermediate **8**, followed by S_N2 displacement of pyridine by chloride (*i.e.*, three inversions between **1** and **4**), or (c) direct S_N2 reaction of the brosylate **1** with chloride ion. As discussed in an earlier paper,³ the most probable mechanism is the direct displacement of the brosyloxy group by chloride ion. However, to account for the product ratio, in this case the rate of the methoxy participation must be slower than the rate of the attack by chloride ion.

A semiquantitative comparison of the reactivity under this S_N2-like condition (LiCl, pyridine)²⁰ shows that 5-methoxy-2-pentyl brosylate (**1**) reacts at least 1.5 times faster than 2-pentyl brosylate, *i.e.*, at best two-thirds of the starting material **1** can react by direct S_N2 displacement; therefore, some of the 2-chloro-5-methoxypentane (**4**) must be formed by the anchimeric assisted way, presumably by backside ring opening of the methoxonium ion with a second inversion, *i.e.*, leading partially to racemization of the product **4**.

Experimental Section²¹

Allylacetone²² was prepared from ethyl allylacetate,²³ and was reduced to 5-hexen-2-ol (**5**) with lithium aluminum hydride^{22a} in 85% yield: bp 138–141°; n_D^{25} 1.4271.²⁴ The product was homogeneous when examined by vpc and tlc. The infrared spectrum had bands at 3320 (OH), 3080 (C=C), 1820 (overtone), 1645 (vinyl), 1110 (secondary alcohol), 990 and 910 (vinyl); nmr signals (CDCl₃) were at δ 1.18 (d, 3), *ca.* 1.6 (m, 2), *ca.* 2.1 (m, 2), *ca.* 3.65 (s, 1, OH), *ca.* 3.75 (m, 1), 5.1 (t, 2), *ca.* 5.8 (m, 1).

Δ^5 -2-Hexenyl Hydrogen Phthalate.—5-Hexen-2-ol (**5**) (55.0 g), phthalic acid anhydride (81.4 g), and 90 ml of anhydrous pyridine were stirred at room temperature for 4 days. The resulting clear solution was poured into ice, and this mixture was acidified by addition of ice-cold concentrated hydrochloric acid. The ester was extracted with chloroform, the combined chloroform solutions were washed with three portions of ice-cold 2 N HCl and three portions of ice-cold sodium chloride solution and dried, and the solvent was evaporated. The resulting oil was dissolved in a slight excess of ice-cold 2 N Na₂CO₃ solution, extracted three times with ether, acidified with 2 N HCl, and extracted with chloroform. The combined organic layers were washed with ice-cold sodium chloride solution, dried, and con-

centrated. Petroleum ether (bp 30–60°) was added, and on standing overnight in the refrigerator the hydrogen phthalate crystallized. The yield after recrystallization from ether-petroleum ether was 95.0 g (70%), mp 52–56° (lit.^{22b} 58°).

Resolution of Δ^5 -2-Hexenyl Hydrogen Phthalate.^{5b}—The crystalline hydrogen phthalate (106 g) and brucine (200 g) were refluxed on a steam bath in 1000 ml of acetone until a clear solution resulted (*ca.* 20 min). Upon cooling, the crystalline brucine salt of the hydrogen phthalate separated. It was filtered, pressed and washed with acetone. After two recrystallizations from acetone, the brucine salt (109.5 g) was dissolved in 150 ml of hot ethanol and a slight excess of 2 N HCl was added. The mixture was diluted with water to about 600 ml and extracted four times with ether. The combined ether extracts were washed with 2 N HCl and water, dried, filtered, and evaporated. After seeding the mixture with racemic material and allowing it to stand at 0° for 24 hr, the substance was partially crystalline. A sample of the crystals had a specific rotation of $[\alpha]_D^{25} +54.5^\circ$ (ether) [lit.^{5b} $[\alpha]_D^{25} +43.75^\circ$ (ether)].

The (+)-hydrogen phthalate was hydrolyzed with 150 ml of 2 N sodium hydroxide, and the 5-hexen-2-ol was isolated by steam distillation. The two layers of the distillate were separated, and the aqueous layer was extracted three times with chloroform. The combined organic solutions were dried and fractionated; the yield was 10.4 g (49% based on the racemic hydrogen phthalate, 34% based on the racemic alcohol): bp 138–140°; $[\alpha]_D^{25} +15.7^\circ$ (ether) [lit.^{5b} $[\alpha]_D^{25} +18.2^\circ$ (ether)]. A sample of the brucine salt was recrystallized twice more; the alcohol obtained from it had then a specific rotation of $[\alpha]_D^{25} +21.8^\circ$ (ether). The nmr and infrared spectra of optically active and of racemic alcohol were identical. The mother liquor of the first crystallization was concentrated to about 300 ml. On cooling, crystals of brucine salt precipitated, which yielded 8.2 g (27% based on the racemic alcohol) of (–)-5-hexen-2-ol: bp 138–140°; $[\alpha]_D^{25} -13.7^\circ$ (ether) [lit.^{5b} $[\alpha]_D^{25} -14.1^\circ$ (ether)].

The resolution was also attempted with (S)-valine and *p*-toluenesulfonic acid²⁵ but was unsuccessful.

2-Brosyloxy-5-hexene.—Brosyl chloride (7.8 g) in 20 ml of anhydrous pyridine was added during 30 min to a solution of (R)-(–)-5-hexen-2-ol (2.0 g), $[\alpha]_D^{25} -13.7^\circ$ (ether), in 30 ml of anhydrous pyridine, with cooling in an ice-salt bath. After stirring at –10 to 0° for 12 hr, the mixture was poured into ice-water and acidified with ice-cold 6 N HCl. The oily brosylate was extracted with ether; the combined ether solutions were washed three times with ice-cold 6 N HCl and three times with ice-water, and dried, and the solvent was evaporated under vacuum at 0°. The resulting oil contained some starting material (nmr), therefore it was purified by column chromatography on neutral alumina, activity I. Elution with 300 ml of petroleum ether (30–60°) and evaporation of the solvent at 0° gave an oil, which crystallized on standing in the refrigerator, mp 36–37° (petroleum ether): yield 1.8 g (28%); $[\alpha]_D^{25} -8.43^\circ$ (ether). Infrared bands were at 3110, 1660 (vinyl), 1590 (aromatic), 1380 and 1200 (R–SO₂–OR'), 1000 and 910 cm^{–1} (vinyl); nmr signals (CDCl₃) were at δ 1.19 (d, 3, *J* = 6.5 Hz, methyl), *ca.* 4.9 (m, 3, vinyl and R–SO₂–O–CH), *ca.* 5.6 (m, 1, vinyl), and 7.80 (s, 4, aromatic).

Anal. Calcd for C₁₂H₁₈O₃SBr: C, 45.15; H, 4.74; Br, 25.03; S, 10.04. Found: C, 45.22; H, 4.82; Br, 25.21; S, 10.12.

5-Chloro-1-hexene. A. **PCl₅ Method.**^{6a}—(S)-(–)-5-Hexen-2-ol (8.4 g), $[\alpha]_D^{25} +15.7^\circ$ (ether), in 20 ml of anhydrous ether was slowly added to a stirred, ice-cooled suspension of phosphorus pentachloride (19.4 g) in 40 ml of anhydrous ether. The mixture was stirred at room temperature for 1.5 hr; the resulting clear solution was hydrolyzed by the slow addition of ice. The ether layer was separated, and the aqueous layer was extracted with three portions of ether. The combined ether solutions were washed five times with sodium chloride solution, dried, and distilled, yielding 4.6 g (46%): bp 119–122° (lit. 30%,^{26a} bp 120–124°,^{26a} 121–125°,^{26b} 119–122°^{6a}); $[\alpha]_D^{25} -44.5^\circ$ (ether) [lit.^{6a} $[\alpha]_D^{25} -43.3^\circ$ (ether)]; ir, 3100 (vinyl), 1830 (overtone), 1650 (vinyl), 990 and 915 (vinyl), 670 cm^{–1} (C–Cl); nmr (CDCl₃), 1.50 (d, 3, *J* = 6.0 Hz, methyl), *ca.* 1.8 and 2.2 (m, 4), 4.00 (sextet, 1, *J* = 6.4 Hz, CH₃(Cl)CH–R), *ca.* 5.0 (m, 2, vinyl), *ca.* 5.6 (m, 1, vinyl).

(25) B. Halpern and J. W. Westley, *Aust. J. Chem.*, **19**, 1533 (1966).

(26) (a) Ch. Courtot and J. Pierron, *C. R. Acad. Sci., Paris*, **190**, 1059 (1930); (b) F. Cortese, *J. Amer. Chem. Soc.*, **52**, 1519 (1930).

(19) E. L. Allred and S. Winstein, *J. Amer. Chem. Soc.*, **89**, 3991 (1967).

(20) E. R. Novak, Ph.D. Thesis, University of Rochester, Rochester, N. Y., 1966.

(21) Nmr spectra were recorded on a Varian Associates A-60 instrument with tetramethylsilane as an internal standard. Chemical shifts are given in δ (ppm) values; relative signal intensities are in parentheses. Ir spectra of thin films were recorded on a Beckman IR 10 spectrophotometer; absorptions are given in wave numbers (cm^{–1}). Optical rotations of compounds in ether solutions in a 1-dm tube were determined using a Schmidt and Haensch polarimeter. Gas-liquid partition chromatographic studies (vpc) were carried out on a F & M 720 instrument with a silicone rubber liquid phase. All boiling points and melting points are uncorrected. Elemental analyses were done by Galbraith Laboratories, Inc., Knoxville, Tenn.

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(23) M. S. Schechter, N. Green, and F. B. La Forge, *J. Amer. Chem. Soc.*, **71**, 3167 (1949).

(24) In agreement with values reported in ref 22b and by K. Kato, *Nippon Kagaku Zasshi*, **83**, 752 (1962); *Chem. Abstr.*, **59**, 5018d (1963).

B. Triphenylphosphine-Carbon Tetrachloride Method.⁹—(*R*)-(-)-5-Hexen-2-ol (2.0 g), $[\alpha]_D^{25} -13.7^\circ$ (ether), triphenylphosphine (8.0 g), and carbon tetrachloride (16.0 g) were refluxed for 2.5 hr. After cooling to room temperature, the mixture was diluted with pentane to precipitate most of the phosphorus compounds, filtered, and distilled to give 0.95 g (40%) of 5-chloro-1-hexene, identified by the nmr spectrum: bp 118–121°; $[\alpha]_D^{25} +29.4^\circ$ (ether). The PCl_5 reaction with 5-hexen-2-ol of the same optical purity would give a chloride with a specific rotation of $[\alpha]_D^{25} +38.9^\circ$ (ether).

C. SOCl_2 Method.—Thionyl chloride (1.7 g) was added dropwise to a solution of (-)-5-hexen-2-ol (1.27 g), $[\alpha]_D^{25} -13.7^\circ$ (ether), in anhydrous pyridine (1.2 g) and 3 ml of anhydrous ether. The mixture was refluxed for 5.5 hr. Ice and water were added, and the ether layer was separated, washed, and dried. It had a positive rotation; according to the nmr spectrum it contained 5-chloro-1-hexene, some elimination product, and pyridine. (The latter are not optically active, and therefore do not contribute to the rotation.)

Reaction of (*R*)-(-)-2-Brosyloxy-5-hexene with Lithium Chloride.⁸—(*R*)-(-)-2-Brosyloxy-5-hexene (1.2 g), $[\alpha]_D^{25} -8.43^\circ$ (ether), lithium chloride (0.8 g), and 30 ml of ethanol (95%) were refluxed on a steam bath for 24 hr. After diluting with 10 ml of water, the solution was extracted with three portions of petroleum ether. The combined extracts were dried and concentrated to about 2 ml; this solution was composed largely of 5-chloro-1-hexene (nmr); assuming 100% yield for the conversion of the brosylate into the chloride, it had a specific rotation of $[\alpha]_D^{25} +42.7^\circ$.

4-Chloropentan-1-ol. A. Ozonolysis in Ether and Reduction with Lithium Aluminum Hydride.—(*R*)-(-)-5-Chloro-1-hexene (4.1 g), $[\alpha]_D^{25} -43.3^\circ$ (ether), in 50 ml of anhydrous ether was ozonized at -70° until the blue color of excess ozone appeared. The solution was flushed with dry nitrogen and then added dropwise to a stirred mixture of lithium aluminum hydride (2.8 g) in 100 ml of anhydrous ether. After stirring at room temperature for 45 min, the excess of lithium aluminum hydride was destroyed by dropwise addition of a saturated aqueous solution of sodium tartrate. The precipitate was filtered over celite; the clear filtrate was dried over Molecular Sieves 4A, concentrated, and distilled, giving 2.286 g (54%) of (-)-4-chloropentan-1-ol: bp 70–75° (4.25 mm) [lit. bp 78–80° (10 mm),^{14a} 76–77° (9 mm),^{14b} 77–79° (10 mm);^{14c} $n_D^{20} 1.4454$ (lit. $n_D^{20} 1.4503$,^{14b} $n_D^{20} 1.4490$ ^{14c}); $[\alpha]_D^{25} -35.5^\circ$ (ether); ir, 3340 (OH), 1050 (primary alcohol), 660 cm^{-1} (C-Cl); nmr (CDCl_3), 1.50 (d, 3, $J = 6.5$ Hz, methyl), ca. 1.75 (m, 4), ca. 3.6 (m, 2, $-\text{CH}_2-\text{OH}$), ca. 4.0 (m, 1), 4.82 (s, 1, OH).

Using different solvents (chloroform, methanol, ethanol) and reducing with sodium borohydride gave less satisfactory results.

B. Via γ -Chloroaldehyde.—5-Chloro-1-hexene (2.0 g of racemic material) in 50 ml of anhydrous methanol was ozonized at -70° . The solution of the ozonide was reduced by adding 2 ml of dimethyl sulfide at -15° and working up according to the procedure of Pappas, *et al.*¹² Distillation of the product gave 0.585 g (29%) of γ -chloroaldehyde: bp 65–75° (11 mm) [lit.²⁷ bp 70–71° (16 mm)]; purity ca. 90% (vpc); ir, 3450 (overtone), 2820 and 2720 ($-\text{CHO}$), 1725 (C=O), 660 (C-Cl); nmr (CDCl_3), 1.52 (d, 3, $J = 6.5$ Hz, methyl), ca. 2.0 (m, 2), ca. 2.6 (m, 2), ca. 4.0 (m, 1), 9.65 (t, 1, $J = 1$ Hz, CHO).

To a solution of 0.386 g of this product in a mixture of 10 ml of dioxan and 5 ml of water was added 4.5 g of sodium borohydride. After stirring at room temperature for 1 hr, dilute HCl was added, and the alcohol was extracted with five portions of ether. The combined extracts were dried and distilled, giving 0.309 g (79%) of 4-chloropentan-1-ol, bp 76–81° (10 mm), identical with the product of the above reaction according to infrared and vpc data.

Attempts to get a better yield of γ -chloroaldehyde using the tetracyanoethylene method¹³ were unsuccessful.

(*R*)-(-)-2-Chloro-5-methoxypentane.—A solution of diazomethane (prepared from 25 g of *N*-methyl-*N*-nitroso-*N'*-nitroguanidine) in 200 ml of methylene chloride was dropwise added at about -30° to a stirred solution of (*R*)-(-)-4-chloropentan-1-ol (1.8 g), $[\alpha]_D^{25} -35.5^\circ$ (ether), and ca. 160 mg of HBF_4 (ca. 60%) in 10 ml of ether and 10 ml of methylene chloride. After stirring at 0° for 1 hr the solution was colorless. The small amount of amorphous polymethylene was filtered off, and the solution was extracted with three portions of saturated aqueous potassium hydrogen carbonate solution and three portions of sodium chloride solution, dried, and distilled yielding 0.58 g (30%) of (*R*)-(-)-2-chloro-5-methoxypentane: bp 52–55° (12 mm); $[\alpha]_D^{25} -32.1^\circ$ (ether); ir, 2710 (OCH_3), 1110 (ether), 660 cm^{-1} (C-Cl); nmr (CH_2Cl_2), 1.40 (d, 3, $J = 6.5$ Hz, methyl), ca. 1.65 (m, 4), 3.23 (s, 3, methoxy), ca. 3.3 (m, 2, $-\text{CH}_2-\text{OCH}_3$), ca. 4.0 (m, 1).

Anal. Calcd for $\text{C}_6\text{H}_{13}\text{OCl}$: C, 52.75; H, 9.59; Cl, 25.96. Found: C, 52.53; H, 9.57; Cl, 26.24.

Registry No.—4, 17397-23-8; 5, 17397-24-9; 6, 17397-25-0; 7, 17397-26-1; (*S*)-2-brosyloxy-5-hexene, 17397-27-2; Δ^5 -2-hexenyl hydrogen phthalate, 17408-12-7; (+)- Δ^5 -2-hexene hydrogen phthalate, 17397-28-3; (-)-5-hexen-2-ol, 17397-29-4; γ -chloroaldehyde, 17408-13-8.

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The Acetylation of Phenylcyclopropane¹

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Reaction of phenylcyclopropane with acetyl chloride-aluminum chloride at $0-5^\circ$ affords not only *p*-cyclopropylacetophene (**6**, 78%) but also 1-(4'-acetylphenyl)-2-chloropropane (**3**, 17%). The alkene 1-(4'-acetylphenyl)propene (**7**) is shown not to be an intermediate in the acylation, although **7** can be prepared in good yield from **6** and 80% aqueous sulfuric acid. The minor product **3** may be formed during the acylation from an intermediate such as **5** *via* a hydride shift.

It was recently shown that the products obtained from acetylation of cyclopropane with acetyl chloride and aluminum chloride cannot be accounted for by a conventional carbonium ion mechanism, but are easily rationalized *via* protonated cyclopropanes.³ On

the other hand, acetylation of 1,1-dimethylcyclopropane proceeds by initial isomerization to 2-methyl-2-butene, followed by conventional electrophilic acetylation of the alkene. Methylcyclopropane occupies an intermediate position and the acetylation products can be rationalized either by protonated cyclopropanes or by a combination of two more conventional schemes, a clear choice not yet being possible.

In this paper consideration is given to the acetylation of phenylcyclopropane, which can in principle undergo electrophilic attack at either the phenyl or the cy-

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(3) For a preliminary communication, see H. Hart and R.H. Schlosberg, *J. Amer. Chem. Soc.*, **88**, 5030 (1966); for a full account with additional information, see *ibid.*, **90**, 5189 (1968).