General Procedure for Preparation of Alkenes 3. Into a thick-walled (ca. 3 mm) Pyrex ampule (10 × 1 cm o.d.) was placed 2.5 mmol of the solid β-lactone **2**. The constricted ampule was sealed under vacuum [ca. −78 °C (0.1 torr)] and subsequently heated in a metal furnance at 180 °C for 6 h. The ampule was cooled to dry ice temperature and opened, and the olefin product was bulb-to-bulb distilled or sublimed and recrystallized. The results are summarized in Table III.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, the National Institutes of Health, the National Science Foundation, the Deutsche Forschungsgemeinschaft, and the Fonds der Chemischen Industrie for generous financial support.

Registry No. 1a, 70982-82-0; **1b**, 75245-30-6; **1c**, 77984-31-7; **1d**, 77984-32-8; **1e**, 78003-77-7; **2a**, 70982-93-3; **2b**, 75245-54-4; **2c**, 77984-33-9; **2d**, 77984-34-0; **2e**, 77984-35-1; **3a**, 692-48-8; **3b**, 77984-36-2; **3c**, 77984-37-3; **3d**, 77984-38-4; **3e**, 77984-39-5; 3,3-dimethylbutanoic acid, 1070-83-3; tricyclo[3.3.1.1^{3,7}]decane-1-acetic acid, 4942-47-6; 2,2-dimethylpropanol, 630-19-3; tricyclo[3.3.1.1^{3,7}]decane-1-carboxaldehyde, 2094-74-8; tricyclo[3.3.1.1^{3,7}]decylidenemethanone, 54781-13-4.

Triphenylphosphine–Tetrachloromethane Promoted Chlorination and Cyclodehydration of Simple Diols

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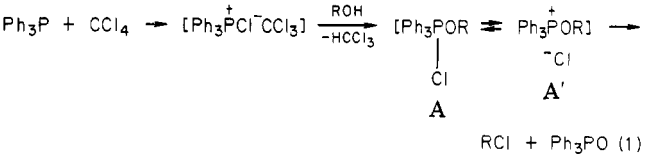
Introduction

The reactions of a variety of alcohols with triphenylphosphine (TPP) and tetrachloromethane (CCl_4) are well documented.[1] As a contribution to the storehouse of useful synthetic methodology, these "three-component"[1] reactions are characterized as (i) mild[2] and (ii) highly stereoselective, occurring with predominant inversion of stereochemistry at the carbinyl carbon.[3] But while new applications of this and analogous chlorination procedures are rapidly accruing, interest has recently focused on the intimate, mechanistic details of the substitution process, with particular emphasis on the modes of decomposition of chloroalkoxytriphenylphosphorane (A)[3c,d,4] and alkoxytriphenylphosphonium chloride (A′)[3c,d,4] to alkyl chlorides as shown in the *simplified*[1] reaction scheme of eq 1.

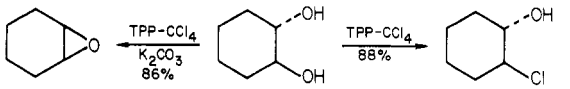


RCl + Ph_3PO (1)

On the basis of previous experience with reactions of diethoxytriphenylphosphorane [$Ph_3P(OEt)_2$] with diols affording cyclic ethers,[7] we became interested in developing other mild, effective, cyclodehydrating media for diols and triols. To our knowledge, general applications of the TPP–CCl_4 reagent to the synthesis of cyclic ethers from diols have not been previously made, and in this report, we describe our findings from the reactions of TPP–CCl_4 with simple diols.

Results and Discussion

When *trans*-1,2-cyclohexanol (**1**) is treated with equimolar TPP in excess CCl_4, a 88% yield of *trans*-2-chlorocyclohexanol (**2**), along with starting diol **1**, can be realized by ^1H and ^{13}C NMR and GLC analyses of the reaction mixture. We obtained no evidence for formation of either *cis*-2-chlorocyclohexanol (**3**) or *trans*-1,2-dichlorocyclohexane which would be expected from a single or sequential chloride ion displacement (respectively) of triphenylphosphine oxide (TPPO) from **1**. Formation of **2** by Cl^- displacement of TPPO from **1** with retention of stereochemistry is unlikely,[3,4] and we, therefore, suspected the intermediacy of cyclohexene oxide (**4**). In fact, reaction of **4** with hydrochloric acid (HCl) generated in solution was easily proven by repeating the reaction in the presence of finely ground potassium carbonate (K_2CO_3) and realizing an 86% yield of **4**.[8] It is doubtful that **4** comes from intramolecular alkoxide displacement of chloride ion from **2** since **2** appears to be relatively stable in the presence of solid K_2CO_3 in CCl_4 solvent. Thus, it seems certain that cyclohexane oxide must arise from TPP–CCl_4-mediated cyclodehydration of diol **1**.



4 1 2

The results with **1** and TPP–CCl_4 may not be too surprising in light of the results from analogous reactions using tris(dimethyamino)phosphine (TDAP). For example, Anselmi et al.[9] have demonstrated that oxytris(dimethylamino)phosphonium α-trifluoroacetate salts form epoxides in 2 N NaOH while Boigegrain and Castro[10] have shown the *meso*-dihydrobenzoin and *o,o′*-dimethoxy *meso*-hydrobenzoin with 2 equiv of TDAP in CCl_4 afford epoxides in 66% and 97% yields, respectively. However, the fact that we observe no *cis*- or *trans*-1,2-dichloro-

(1) For an excellent review, see: Appel, R.; Halstenberg, M. In "Organophosphorus Reagents in Organic Synthesis"; Cadogan, J. I. G., Ed.; Academic Press: New York; 1979, pp 378–424.

(2) (a) Brett, D.; Downie, I. M.; Lee, J. B.; Matough, M. F. S. *Chem. Ind. (London)* **1969**, 1017. (b) Axelrod, E. H.; Milne, G. M.; van Tamelen, E. E. *J. Am. Chem. Soc.* **1970**, *92*, 2139. (c) Stork, G.; Jung, M. E.; Colvin, E.; Noel, Y. *Ibid.* **1974**, *96*, 3684. (d) Georgoulis, C.; Ville, G. *Bull. Soc. Chim. Fr.* **1975**, 607. (e) Goering, H. L.; Trenbeath, S. L. *J. Am. Chem. Soc.* **1976**, *98*, 5016. (f) Kocienski, P. J.; Cernigliaro, G.; Feldstein, G. *J. Org. Chem.* **1977**, *42*, 353. (g) Miller, R. D.; Schneider, M.; Dolce, D. L. *J. Am. Chem. Soc.* **1973**, *95*, 8469. (h) Hunt, L. B.; MacSweeney, D. F.; Ramage, R. *Tetrahedron* **1971**, *27*, 1491.

(3) (a) Friederang, A. W.; Tarbell, D. S. *J. Org. Chem.* **1968**, *33*, 3797. (b) Bestmann, H. J. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 349. (c) Jones, L. A.; Sumner, C. E.; Franzus, B.; Haung, T. T.-S.; Snyder, E. I. *J. Org. Chem.* **1978**, *43*, 2821–2827. (d) Slagle, J. D.; Haung, T. T.-S.; Franzus, B. "Abstracts of Papers", 181st National Meeting of the American Chemical Society, Atlanta, GA., Mar 29–Apr 3, 1981; American Chemical Socity: Washington, DC, 1981; ORGN-124.

(4) Until recently,[3d] there were two views of the TPP–CCl_4-mediated *inversion* of stereochemistry by chloride ion at the carbinyl carbon of alcohols. Jones et al.[3c] and Weiss and Snyder[5] have suggested that the decomposition of the chloroalkoxytriphenylphosphorane intermediate occurs by cleavage of the P–Cl bond first, followed by cleavage of the C–O bond. Alternatively, Aneja and Davies[6] argue that fragmentation of the phosphorane intermediate is consistent with a symmetry allowed [$_\sigma 2_s + {}_\sigma 2_a$] thermal pericyclic process. However, Franzus et al.[3d] have presented recent evidence favoring *clustered* ion pairs in the chlorination reaction.

(5) (a) Weiss, R. G.; Synder, E. I. *J. Org. Chem.* **1970**, *35*, 1627. (b) Weiss, R. G.; Synder, E. I. *Ibid.* **1971**, *36*, 403.

(6) (a) Aneja, R.; Davies, A. P.; Knaggs, J. A. *J. Chem. Soc., Chem. Commun.* **1973**, 110–111. (b) Aneja, R.; Davies, A. P. *J. Chem. Soc., Perkin Trans. 1* **1974**, 141–145.

(7) (a) Chang, B. C.; Conrad, W.; Denney, D. B.; Denney, D. Z.; Edelman, R.; Powell, R. L; White, D. W. *J. Am. Chem. Soc.* **1971**, *93*, 4004. (b) Evans, S. A., Jr.; Grote, T. H. "Abstracts of Papers", 176th National Meeting of the Americal Chemical Society Miami, FL, Sept 11–15, 1978; American Chemical Socity: Washington, DC, 1978; ORGN-15.

(8) When the reaction is allowed to proceed in the presence of 2 equiv of pyridine, the course of the reaction remains unchanged.

(9) Anselmi, C.; Berti, G.; Macchia, B.; Macchia, R.; Monti, L. *Tetrahedron Lett.* **1972**, 1209–1212.

(10) Boigegrain, R.; Castro, B. *Tetrahedron* **1976**, *32*, 1283–1288.

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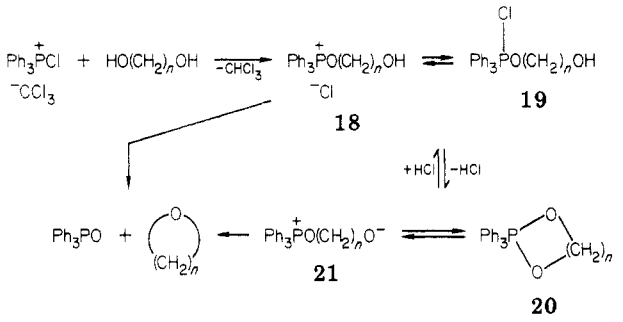
cyclohexanes is significant since it has been shown that cyclohexene oxide reacts with TPP–CCl_4 to give largely *cis*-1,2-dichlorocyclohexane.[11] The apparent survival of **4** under our experimental conditions probably means that most of the "active" phosphorus reagents are consumed in the transformation **1** → **4**.

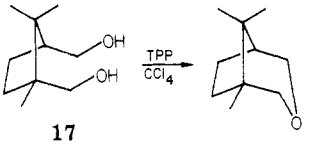
Treatment of 1,3-propanediol (**5**) with TPP–CCl_4 in CH_3CN gives predominantly 3-chloropropanol (75%) and 1,3-dichloropropane (16%) but no oxetane (**6**). The absence of **6** under these conditions is not totally unexpected in view of the consistently low yields obtained from other cyclodehydrating schemes[12] for effecting the transformation **5** → **6**. It is also unlikely that some 3-chloropropanol is a consequence of ring opening of **6** with HCl[13] since repeating the reaction in the presence of potassium carbonate, an HCl scavenger, gave identical results. By contrast, tris(dimethylamino)phosphonium salts of 2,2-disubstituted-1,3-propanediols react with sodium methoxide in methanol and exhibit a high propensity for closure to the 2,2-disubstituted oxetanes.[14] This is, however, consistent with expectations based on the tenets of the "*gem*-dialkyl effect".[15]

We have observed that 1,4-butanediol (**7**), *cis*-2-butene-1,4-diol (**8**), and *cis*-1,2-bis(hydroxymethyl)cyclohexane (**9**) react smoothly with TPP–CCl_4 to afford tetrahydrofuran (**10**), 2,5-dihydrofuran (**11**), and *cis*-8-oxabicyclo-[4.3.0]nonane (**12**) in 78%, 65%, and 84% yields, respectively. Reaction of 1,5-pentanediol (**13**) with TPP–CCl_4 gives 52% 5-chloropentanol (**14**), tetrahydropyran (11%), and 1,5-dichloropentane (25%) while 1,6-hexanediol (**15**) affords 6-chlorohexanol (48%) and 1,6-dichlorohexane (39%).

Comparisons of the ether–chlorohydrin–dichloride product distributions reveal a parallelism with the established trend for efficiency of chain closure involving 3- → 7-membered rings.[16] In fact, the formation of cyclic ethers decreases in order of the following ring size: $3 \approx 5 > 6 > 4 \approx 7$. This trend is essentially analogous to the one reported by Martin et al.[12] where the cyclodehydration of a variety of diols with a diaryldialkoxysulfurane has been described. This trend is a consequence of the collective energy differences arising from ring strain and the entropy of ring formation during intramolecular displacement reactions.[17] Therefore, the relatively high yields of ether **10**, bicyclic ether **12**, and dihydrofuran **11** are predicted on the basis of the facility with which intramolecular cyclization occurs. In fact, this may also explain the exclusive formation of trimethyl-3-oxabicyclo[3.2.1]octane (**16**) from 1,2,2-trimethyl-1,3-bis(hydroxymethyl)cyclopentane (**17**) with TPP–CCl_4.[18] Although ether **16** possesses a six- and seven-membered ring, diol **17** actually *simulates* a 1,4-diol due to the configurational constraints of the *cis*-1,3-bis-(hydroxymethyl) groups.

Scheme I





17 16 (80–90%)

In previous reports[9,10] detailing the cyclodehydration of diols with TDAP–CCl_4, either 2 equiv of TDAP was required or 1 equiv of base was necessary to effect closure of the (hydroxyalkoxy)tris(dimethylamino)phosphonium chlorides. The experimental results described here as well as those used in conversion of **17** → **16** are characterized by *equimolar* diol and TPP concentrations. While these differences have mechanistic importance requiring further elaboration in a future publication, we offer only a brief comment here.

It seems reasonable that the initial formation of the (hydroxyalkoxy)triphenylphosphonium chloride (**18**) occurs by interception of (trichloromethyl)triphenylphosphonium chloride by the diol (Scheme I). Loss of HCl from **18** or (hydroxyalkoxy)chlorotriphenylphosphorane (**19**) would ultimately give dioxytriphenylphosphorane (**20**) and/or betaine **21** which could eventually undergo intramolecular displacement of TPPO to the cyclic ether. If intramolecular displacement if slow (e.g., **20** or **21** → ether), **18** and /or **19** can undergo chloride ion displacement of TPPO to chlorohydrin. Alternatively, Ph_3PCl_2, which is formed during TPP–CCl_4 reactions,[1] can readily chlorinate hydroxyl groups. However, loss of HCl from **18** may not be a prerequisite for ultimate closure to the ether; **18** may undergo an uncatalyzed intramolecular cyclization. For example, Heine et al.[19] have shown that a 1.5 M aqueous solution of 4-chlorobutanol gives tetrahydrofuran (73%) on standing at 40 °C. It is also apparent that for those diols where ring closure is energetically unfavorable, chlorohydrin competes for (trichloromethyl)triphenylphosphonium chloride and/or Ph_3PCl_2 (and perhaps, HCl) to give dichlorides.

As a preparative scheme for cyclic ethers, the TPP–CCl_4 reagent appears to be best suited for 1,4-diols and perhaps 1,2-diols in the presence of K_2CO_3.

Experimental Section

Melting points were obtained with a Mel-Temp melting point apparatus with an open capillary tube and they are uncorrected.

(11) (a) Actually, a trace (5%) of *trans*-1,2-dichlorocyclohexane and 80% *cis*-1,2-dichlorocyclohexane is obtained from the reaction of **4** and TPP in refluxing CCl_4 (1–2 h). See: Isaacs, N. S.; Kirkpatrick, D. *Tetrahedron Lett.* **1972**, 3869–3870. (b) It has also been shown that dichlorotriphenylphosphorane (Ph_3PCl_2) in CH_3CN reacts with **4** to give an equimolar mixture of the diastereoisomeric 1,2-dichlorocyclohexanes as well as some cyclohexene. See: Thakore, A. N.; Pope, P.; Oehlschlager, A. C. *Tetrahedron* **1971**, *27*, 2617–2626.

(12) Martin, J. C.; Franz, J. A.; Arhart, R. J. *J. Am. Chem. Soc.* **1974**, *96*, 4604–4611.

(13) Virtanen has determined the rates of acid-catalyzed ring opening of oxetane and oxirane and concludes that the rates are of the same order or magnitude. See: Virtanen, P. O. I. *Suom. Kemi.* **1967**, *B40*, 185–189, 193–198.

(14) Castro, B.; Selve, C. *Tetrahedron Lett.* **1973**, 4459–4460. For the preparation of the alkoxytris(dimethylamino)phosphonium salts, see: Boigegrain, R.; Castro, B.; Selve, C. *Tetrahedron Lett.* **1975**, 2529–2530; Castro, B.; Selve, C. *Ibid.* **1973**, 4455–4458.

(15) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. "Conformational Analysis"; Interscience: New York, 1965; Chapter 4, pp 189–192.

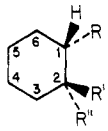
(16) (a) Capon, B. *Q. Rev., Chem. Soc.* **1964**, *18*, 45. (b) Page, M. I. *Chem. Soc. Rev.* **1973**, *2*, 295–324. (c) DeTar, D. F.; Brooks, W., Jr. *J. Org. Chem.* **1978**, *43*, 2245–2248. (d) An interesting discussion has been presented regarding the ease of formation of three- and five-membered rings. See: Stirling, C. J. M. *J. Chem. Educ.* **1973**, *50*, 844–845.

(17) Ruzicka, L. *Chem. Ind. (London)* **1935**, *54*, 2.

(18) Erickson, G. W.; Fry, J. L. *J. Org. Chem.* **1980**, *45*, 970–972.

(19) Heine, H. W.; Miller, A. D.; Barton, W. H.; Greiner, R. W. *J. Am. Chem. Soc.* **1953**, *75*, 4778–4779.

Table I. Carbon-13 NMR Spectral Data of 1,2-Disubstituted Cyclohexanes[a]



compd	R	R′	R″	C1	C2	C3	C4	C5	C6	other carbons
2	OH	Cl	H	75.30	67.37	33.27	24.07*	25.65*	35.25	
3	OH	H	Cl	70.58	66.06	30.81	26.37*	25.69*	32.00	
1	OH	OH	H	75.83	75.83	33.15	24.38	24.38	33.15	
9	CH_2OH	H	CH_2OH	40.26	40.26	27.36	24.20	24.20	27.36	CH_2OH, 64.12
12	CH_2O	H	CH_2O	38.21	38.21	25.37	23.00	23.00	25.37	CH_2O, 71.86

[a] Experimental details of the ^{13}C data collection process are given in the Experimental Section. Carbons whose chemical shifts cannot be assigned with a high level of certainty and may be interchangeable are labeled with an asterisk.

Proton magnetic resonance (^1H NMR) spectra were recorded on Varian Model XL-100-12 and Perkin-Elmer Model R24B NMR spectrometers. The ^{13}C NMR FT spectra were recorded on the Varian Model XL-100-12 NMR spectrometer controlled by a 620/f computer. All FT spectra were obtained at ambient temperature (ca. 30 °C) and Fourier transformations were based on 8K data points with noise decoupling. All ^1H and ^{13}C chemical shifts of samples as 5–15 (w/w%) deuteriochloroform ($CDCl_3$) or tetrachloromethane (CCl_4) solutions are presented in parts per million (δ) downfield from internal tetramethylsilane (Me_4Si).

Gas chromatographic analyses were obtained on a Hewlett-Packard Model 5754B research gas chromatograph, using a stainless-steel column [0.125 in. (i.d.) × 6 ft packed with 20% Carbowax 20M on Chromosorb W-HP-AW-DMCS, 100–120 mesh].

Triphenylphosphine, 1,3-propanediol, 1,4-butanediol, 1,5-pentanediol, 1,6-hexanediol, *cis*-2-butene-1,4-diol, oxetane, oxepane, and tetrahydropyran are commercially available from Aldrich Chemical Company and were used without further purification. Tetrachloromethane was dried and distilled over phosphorus pentoxide[20] while acetonitrile was used without additional purification. Cyclohexene oxide was obtained from Research Organic/Inorganic Chemical Corporation.

General Procedure for Reaction of Ph_3P–CCl_4 with Diols. The diol (16.5 mmol) was added to a solution of triphenylphosphine (4.93 g, 16.5 mmol) in anhydrous tetrachloromethane (30 mL) and acetonitrile (10 mL).[21] The solution was refluxed for 24 h and cooled to ambient temperature, and its composition was determined by ^1H and ^{13}C NMR analyses as well as GLC comparisons with retention times of authentic materials. The ^{13}C NMR spectra of the cyclohexyl derivatives are summarized in Table I.

***trans*-1,2-Cyclohexanediol (1).** Cyclohexene (82 g, 1 mol) was added slowly to a mixture of 30% hydrogen peroxide (140 mL) and 88% formic acid (600 mL). The resulting mixture was stirred at 40 °C for 1.5 h and then overnight at ambient temperature. Formic acid and water were removed under reduced pressure (rotary evaporator) to give a residue which was treated with a cold solution of sodium hydroxide (80 g, 2 mol) in water (150 mL). This solution was extracted with ethyl acetate (7 × 250 mL). The organic portions were combined and concentrated (rotary evaporator) to an approximate volume of 300 mL. The mixture was cooled (ice bath) and *trans*-1,2-cyclohexanediol (70 g, 60%) was obtained by suction filtration, mp 99–101 °C (lit.[22] mp 101.5–103.0 °C).

***trans*-2-Chlorocyclohexanol (2).** Cyclohexene (123 g, 1.5 mol) was treated with a slight excess of a 3.5% aqueous solution of hypochlorous acid. The resulting mixture was saturated with sodium chloride and distilled. The distillate was saturated with sodium chloride and extracted with diethyl ether (3 × 250 mL). The combined ethereal solutions were dried (anhydrous sodium sulfate) and concentrated to dryness (rotary evaporator) to afford an oily residue. Distillation of this residue under reduced pressure (2 torr) gave *trans*-2-chlorocyclohexanol (57 g, 29%), bp 86–90 °C (2 torr) [lit.[23] bp 88–89 °C (2 torr)].

***cis*-2-Chlorocyclohexanol (3).** A mixture of *cis*- and *trans*-2-chlorocyclohexanols[24] (110 g, 0.82 mol) was stirred with 0.5 N sodium hydroxide (1.36 L) at 10–15 °C for 1 h. The resulting mixture was extracted with diethyl ether (4 × 200 mL) and the ethereal solution was concentrated to dryness (rotary evaporator) to afford an oil. Distillation of the oil through a 16-in. Vigreux column gave *cis*-2-chlorocyclohexanol (33.5 g, 30%): bp 76–83 °C (13 torr) [lit.[25] bp 76–82 °C (13 torr)]; ^1H NMR ($CDCl_3$) δ 1.06–2.20 (m, 8 H, CH_2), 2.82 (br, 1 H, OH), 3.85 (m, 1 H, CH–O), 4.30 (m, 1 H, CHCl).

***cis*-1,2-Bis(hydroxymethyl)cyclohexane (9).** A solution of diethyl *cis*-hexahydrophthalate[26] (228 g, 1 mol) in diethyl ether (750 mL) was added dropwise to a suspension of lithium aluminum hydride (50 g, 1.32 mol) in 1 L of anhydrous diethyl ether. After being stirred for 1 h at ambient temperature, the suspension was treated with water (50 mL), 15% sodium hydroxide (50 mL), and more water (150 mL). The solid residue was separated by filtration and the ethereal solution was washed with water (3 × 250 mL) and dried (anhydrous magnesium sulfate). Removal of the solvent (rotary evaporator) gave an oil which was distilled under reduced pressure to afford diol **9** (97 g, 68%): bp 132–137 °C (3 torr) [lit.[27] bp 134–136 °C (3 torr)]; mp 37–43 °C (lit.[27] mp 43.0–43.5 °C).

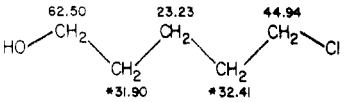
2,5-Dihydrofuran (11). *cis*-2-Butene-1,4-diol (50 g, 0.57 mol) was refluxed with a catalytic quantity of iodine (750 mg). The dihydrofuran azeotrope (16 g) with boiling range 60–80 °C (760 torr) [lit.[28] bp 64–65 °C (760 torr)]; was collected by distillation through a 12-in. Vigreux column: ^{13}C NMR ($CDCl_3$) δ 75.39 (CH_2), 126.30 (CH=CH); ^1H NMR ($CDCl_3$) δ 4.66 (d, 4 H, $J < 1$ Hz, CH_2), 5.90 (s, 2 H, CH=CH).

***cis*-8-Oxabicyclo[4.3.0]nonane (12).** *cis*-1,2-Bis(hydroxymethyl)cyclohexane (20 g, 0.14 mol) was dissolved in dry acetone (300 mL) containing 2 mL of concentrated sulfuric acid. The mixture was stirred over anhydrous sodium sulfate at ambient temperature for 48 h. Solid sodium bicarbonate was added to neutralize the H_2SO_4 and the resulting mixture was filtered. Acetone solvent was removed (rotary evaporator) to afford an oil. Distillation under reduced pressure gave bicyclic ether **12** (4.2 g, 24%): bp 50–55 °C (10 torr) [lit.[30] bp 54–55 °C (10 torr)]; ^1H NMR ($CDCl_3$) δ 1.02–1.83 (m, 8 H, CH_2), 2.00–2.40 (m, 2 H, CH), 3.48–4.02 (m, 4 H, CH_2–O).

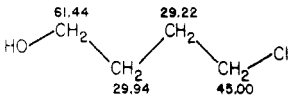
5-Chloro-1-pentanol (14). 5-Chloro-1-pentylacetate[31] (60 g, 0.36 mol) was shaken with 200 mL of ethanol and 255 mL of 2 N sodium hydroxide until the mixture became homogeneous. The solution was stirred at ambient temperature for 48 h. Ethanol

(20) Gordon, A. J.; Ford, R. A. "The Chemist's Companion"; John Wiley & Sons: New York, 1972; p 432.
(21) A number of the diols exhibited limited solubility in CCl_4; however, addition of CH_3CN gave a homogeneous solution.
(22) Roebuck, A.; Adkins, H. "Organic Syntheses"; Wiley: New York, 1955; Collect. Vol. 3, 217.
(23) Coleman, G. H.; Johnstone, H. F. "Organic Syntheses"; Wiley: New York, 1941; Collect. Vol. 1, p 158.
(24) Prepared by the sodium borohydride reduction of 2-chlorocyclohexanone.
(25) Stevens, H. C.; Grummitt, O. *J. Am. Chem. Soc.* **1952**, *74*, 4876.
(26) Cope, A. C; Herrick, E. C. "Organic Syntheses"; Wiley: New York, 1963, Collect. Vol. 4, p 304.
(27) Bailey, J. W.; Golden, H. R. *J. Chem. Soc.* **1953**, 4780.
(28) Brace, N. O. *J. Am. Chem. Soc.* **1955**, *77*, 4157.
(29) Haggis, G. A.; Owen, L. N. *J. Chem. Soc.* **1953**, 389.
(30) Kops, J.; Spanggard, H. *Makro. Chem.* **1974**, *175*, 3077.
(31) Synerholm, M. E. *J. Am. Chem. Soc.* **1947**, *69*, 2581.

solvent was removed (rotary evaporator) and the aqueous solution was extracted with benzene (4 × 150 mL). The benzene solution was concentrated (rotary evaporator) to afford an oil which was distilled under reduced pressure to give chlorohydrin 14 (36.5 g, 57%), bp 56–57 °C (0.7 torr) [lit.[32] bp 57 °C (0.7 torr)]. The ^{13}C NMR chemical shift assignments in $CDCl_3$ are shown below. (Carbons with the asterisk may be interchangeable.)

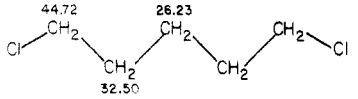


4-Chloro-1-butanol. Tetrahydrofuran (114 g, 1.58 mol) was heated to its boiling point and a slow stream of hydrochloric acid gas was bubbled into the liquid. After 8 h, the internal temperature of the reaction mixture had reached 100 °C and the reaction mixture was allowed to cool. Excess THF was removed (rotary evaporator) and the residue was distilled under reduced pressure to give the chlorohydrin (88 g, 45%): bp 65–76 °C (7 torr) [lit.[33] bp 65–75 °C (7 torr)]; ^1H NMR ($CDCl_3$) δ 1.48–2.02 (m, 4 H, CH_2), 3.20–3.82 (m, 4 H, CH_2Cl and CH_2OH), and 3.90 (s, 1 H, OH). The ^{13}C NMR chemical shift assignments in $CDCl_3$ are shown below.



1,3-Dichloropropane. A mixture of 1,3-propanediol (67 g, 0.88 mol, 63 mL) and concentrated hydrochloric acid (685 mL) was heated at 80 °C for 48 h. The resulting mixture was extracted with toluene (4 × 250 mL) and the resulting organic solution was dried (anhydrous potassium carbonate). Removal of the toluene solvent (rotary evaporator) gave an oily residue which was distilled under reduced pressure to afford 1,3-dichloropropane (9.6 g, 10%): bp 120–121 °C (760 torr) [lit.[34] bp 120.3–120.5 °C (760 torr)]; ^{13}C NMR ($CDCl_3$) δ 35.07 (CH_2), 41.43 (CH_2Cl).

1,5-Dichloropentane. A mixture of 1,5-pentanediol (92 g, 0.89 mol, 93 mL) and concentrated hydrochloric acid (685 mL) was heated at 80 °C for 48 h. The resulting mixture was extracted with toluene (4 × 250 mL) and the resulting organic solution was dried (anhydrous potassium carbonate). Removal of the toluene solvent (rotary evaporator) gave an oily substance which was distilled under reduced pressure to give 1,5-dichloropentane (83.2 g, 59%), bp 66–69 °C (11 torr) [lit.[34] bp 64–66 °C (10 torr)]. The ^{13}C NMR chemical shift assignments in $CDCl_3$ are shown below.



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Registry No. 1, 1460-57-7; 2, 6628-80-4; 3, 17002-09-4; 4, 286-20-4; 5, 504-63-2; 7, 110-63-4; 8, 6117-80-2; 9, 15753-50-1; 10, 109-99-9; 11, 1708-29-8; 12, 13149-01-4; 13, 111-29-5; 14, 5259-98-3; 15, 629-11-8; 16, 51097-04-2; 17, 49852-39-3; TPP, 603-35-0; CCl_4, 56-23-5; cyclohexene, 110-83-8; diethyl *cis*-hexahydrophthalate, 17351-07-4; 5-chloro-1-pentylacetate, 20395-28-2; 4-chloro-1-butanol, 928-51-8; 1,3-dichloropropane, 142-28-9; 1,5-dichloropentane, 628-76-2; 6-chlorohexanol, 2009-83-8; 1,6-dichlorohexane, 2163-00-0.

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New Clerodane Diterpenoid from *Teucrium polium* subsp. *aureum*. X-ray Structure Determination

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Continuing our studies on diterpenic compounds from the *Teucrium* species (family Labiatae),[2,3] we have now investigated *T. polium* subsp. *aureum* (Schreber) Arcangeli collected in Western Sicily (Italy) and in Southern Spain. In the case of the Sicilian sample only previously known diterpenoids (gnaphalidin[4] and teucrin P_1[5,6]) were isolated, whereas from the Spanish sample we have extracted 19-acetylgnaphalin[4] and a new product, auropolin, whose structure was established as follows.

Auropolin (1) was isolated as a syrup, and its ^1H NMR spectrum showed signals for a secondary methyl group at δ 1.19 (d, J = 7 Hz), a β-substituted furan ring (two α-furan protons at δ 7.47 and 7.44 and one β-furan proton at δ 6.45), and two acetates (δ 2.10 and 2.06), one of which was placed on a methylene group attached to a fully substituted carbon atom (a two-proton singlet at δ 4.99) and the other one on a secondary carbon atom probably placed between the furan ring and a methylene group (geminal proton as a doublet of doublets at δ 5.90, J_1 = 7.5, J_2 = 5 Hz). In addition, the ^1H NMR spectrum of auropolin (1) showed a one-proton singlet at δ 5.30, which was assigned to an hemiacetalic function placed on a carbon atom without vicinal protons. The closure of this hemiacetal group was revealed by a one-proton singlet at δ 4.13 ($W_{1/2}$ = 1 Hz) which may be attached to a secondary carbon atom placed between fully substituted carbon atoms or, alternatively, by the fact that its dihedral angle with a vicinal proton gave a J value of ~0 Hz. Finally, two one-proton signals at δ 3.05 (dd, J_{gem} = 5.5 Hz, J(long range) = 1.5 Hz) and 2.33 (d, J_{gem} = 5.5 Hz) were assigned to an α,α-disubstituted oxirane ring.[2]

In accord with all the above assignments, Ac_2O–pyridine treatment of auropolin (1) gave a crystalline derivative (2, $C_{26}H_{32}O_{10}$), the ^1H NMR spectrum of which showed the hemiacetalic proton paramagnetically shifted (δ 6.15). CrO_3–pyridine treatment of the natural substance (1) gave a compound (3, $C_{24}H_{28}O_9$) which possessed a γ-lactone group (ν_{CO} 1785 cm^{-1}) instead of the hemiacetalic function found in 1, since the ^1H NMR spectrum of this derivative (3) lacked the signal assigned to the hemiacetalic proton, and the signal attributed to the closure of the hemiacetal

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