The Syntheses of Some Optically Active ε-Caprolactones

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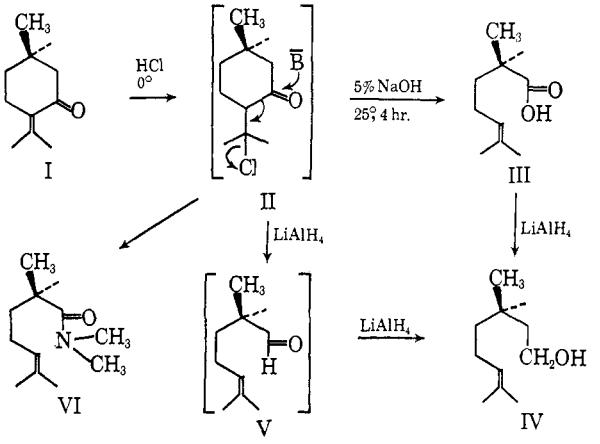
Abstract: The syntheses of (*R*)-(−)-β-methyl-ε-caprolactone, (*R*)-(+)-γ-methyl-ε-caprolactone, (*R*)-(−)-δ-methyl-ε-caprolactone, and (*R*)-(+)-α-bromo-δ-methyl-ε-caprolactone from (*R*)-(+)-pulegone are reported.

The syntheses of optically active, methyl-substituted ε-caprolactones[2] were undertaken for two reasons, firstly because it was of interest to investigate the conformation[3] of the seven-membered ring, and secondly because the lactones were to be employed in the preparation of optically active polyesters which were the subject of another study.[4]

Syntheses

The most suitable approach selected for the preparation of these materials was by the degradation of natural products of known absolute configuration and high optical purity. Initially, natural (*R*)-(+)-citronellal[5-13,16] appeared to be an attractive starting material, but because of its low optical purity,[10,11,16] attention was then directed to the conversion of nearly 100% optically pure (*R*)-(+)-pulegone (I) to (*R*)-(+)-citronellic acid by the procedure of Plesek.[14,15] By passing dry hydrogen chloride gas through (*R*)-(+)-pulegone at low temperature and then without isolating the intermediate pulegone hydrochloride (II) simply adding it to dilute sodium hydroxide at room temperature, good yields of (*R*)-(+)-citronellic acid (III) with the double bond exclusively in the isopropylidene position were obtained. Reduction of the acid III with lithium aluminum hydride afforded (*R*)-(+)-citronellol[17] (IV) in 90% yield. Fragmentation reactions of this type are rather general[18] and have been confined to bases such as hydroxyl ions and Grignard reagents.[19]



It was of interest to us to extend this type of reaction to other bases. Attempts to effect cleavage of pulegone hydrochloride (II) with dimethylamine led only to dehydrohalogenation. Lithium dimethylamide, however, in a mixture of ether–hexane gave a 47% yield of pure (*R*)-(−)-N,N-dimethylcitronellamide (VI). Fragmentation with excess lithium aluminum hydride led to a 16.1% yield of *R*-(+)-citronellol[20] (IV). In this case citronellal (V) was probably formed as an intermediate which was immediately reduced to the alcohol. Because of the low yield and low chemical purity,[20] this latter preparation of (*R*)-(+)-citronellol has little practical value.

Oxidation of (*R*)-(+)-citronellol (IV) by a modified Lemieux–von Rudloff periodate–permanganate[21,22] oxidation led to a quantitative yield of (*R*)-(+)-6-hydroxy-4-methylhexanoic acid (VII).[23]

(1) Taken from the dissertation of H. Kaye submitted to the faculty of the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1965.

(2) Other nomenclature: 6-hydroxyhexanoic acid lactone, 2-oxepinone, and 2-oxohexamethylene oxide.

(3) C. G. Overberger and H. Kaye, *J. Am. Chem. Soc.*, **89**, 5646 (1967)

(4) C. G. Overberger and H. Kaye, to be published.

(5) H. E. Eshinzai, *J. Org. Chem.*, **26**, 3072 (1961).

(6) F. A. Mills and W. Klyne, *Progr. Stereochem.*, 1, 177 (1954).

(7) A. J. Birch, *Chem. Soc. Ann. Rept.*, 47, 191 (1951).

(8) J. L. Simonsen, "The Terpenes," Vol. I, Cambridge University Press, New York, N. Y., 1947.

(9) E. J. Eisenbraun and S. M. McElvain, *J. Am. Chem. Soc.*, 77, 3383 (1955).

(10) Pino[11] found that natural (*R*)-(+)-citronellal is only 77–78% optically pure. As an independent verification of this fact we have compared the specific rotations of both (*R*)-(+)-β-methyladipic acid[12] and (*R*)-(+)-3-methylcyclopentanone[12] prepared from (*R*)-(+)-pulegone[13] and (*R*)-(+)-citronellal[12]. For the (*R*)-(+)-β-methyladipic acid[12] in chloroform the percentage of optical purity was 7.6°/9.5° = 80.0% while for the (*R*)-(+)-3-methylcyclopentanone in methanol the percentage of optical purity was 126.2°/153° = 82.6%. From (*R*)-(+)-citronellal prepared from (*R*)-(+)-pulegone[14,15] and natural (*R*)-(+)-citronellal it could also be shown that natural citronellal is 4.44°/5.51° = 80.5% optically pure, in good agreement with the results of Pino.

(11) F. Clandelli and P. Pino, *Ric. Sci. Rend.*, A4 [5], 694 (1965).

(12) The author is grateful to Mr. Richard Abbott for carrying out these preparations.

(13) C. Djerassi and G. W. Krakower, *J. Am. Chem. Soc.*, **81**, 237 (1959).

(14) J. Plesek, *Chem. Listy*, **50**, 1854 (1956); *Chem. Abstr.*, **51**, 4314 (1957).

(15) R. Lukes, A. Zabacova, and J. Plesek, *Croat. Chem. Acta*, **29**, 201 (1957); *Chem. Abstr.*, **53**, 17898 (1957).

(16) G. W. O. Donnell, and M. D. Sutherland, *Australian J. Chem.*, **19**, 528 (1966).

(17) V. R. Rienacker and G. Ohloff, *Angew. Chem.*, **73**, 240 (1961), have prepared citronellols of high optical purity from (+)- and (−)-pinane.

(18) M. G. Reinecke, *J. Org. Chem.*, **28**, 3574 (1963), and references given therein.

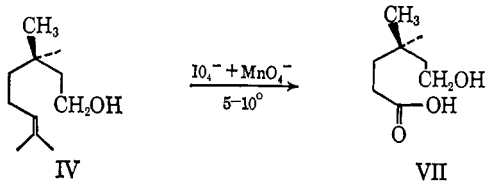
(19) A. Eschenmoser and A. Frey, *Helv. Chim. Acta*, **35**, 1660 (1952).

(20) This product had an infrared spectrum identical with that of authentic (*R*)-(+)-citronellol, but vapor phase chromatography indicated two unidentical impurities in 8.02 and 5.38%, which were probably pulegols.

(21) The Lemieux–von Rudloff periodate–permanganate reagent[22] was impractical on a large preparative scale because of the enormous dilutions necessary to keep enough sodium periodate in solution for the reaction to proceed. It was, therefore, necessary to modify this reagent by conducting the reaction under much higher concentrations, utilizing acetone–water as a medium in the absence of a buffer.

(22) R. U. Lemieux and E. von Rudloff, *Can. J. Chem.*, **33**, 1701 (1955).

(23) It is interesting to point out that titration of the crude freshly prepared hydroxy acid VII indicated only 67% carboxyl groups, but after storage for 1 month at −9°, the per cent hydroxy acid increased



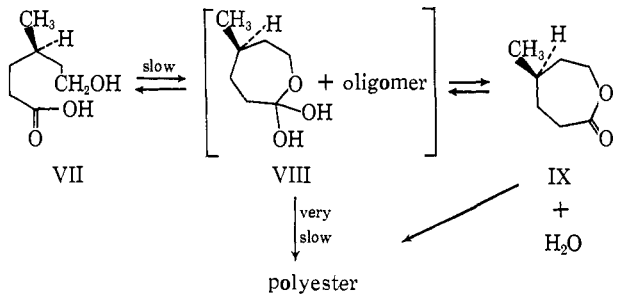
IV VII

The hydroxy acid VII was a very viscous, water-soluble oil which could not be purified by distillation because of polycondensation. Purification was effected by formation of the sodium salt, followed by regeneration of the hydroxy acid and molecular distillation.

Attempts to form the lactone by thermal cyclization,[24] benzenesulfonic acid catalyzed high dilution cyclization in refluxing benzene,[24] and dicyclohexylcarbodiimide cyclization[27,28] were not completely successful.

As an improved method of preparation (*R*)-(+)-γ-methyl-ε-caprolactone (IX) was obtained in 35% yield by a closed system, hydrogen chloride acid catalyzed cyclization carried out in methylene chloride, in the presence of 4A molecular sieves at 25° for 60 hr.

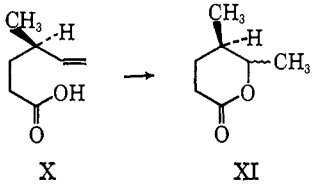
to 91%. The optical rotation of a freshly prepared water solution of the hydroxy acid VII (96% by titration) was found to decrease with time, while the highest percentage of hydroxy acid, 99%, was attained only from a sample which had just been regenerated from the sodium salt. After a few months of storage at −9°, low polyester was detected in the hydroxy acid mixture by its insolubility in water. All of these data are consistent with a reversible equilibrium which slowly goes to polyester as indicated below.



VII VIII IX

Whether the proposed intermediate VIII is stable is uncertain. The fact that the optical rotation decreases with time suggests that it might be, since formation of lactone IX should increase the rotation.

(24) Several attempts were made to thermally cyclize the (*R*)-(+)-6-hydroxy-4-methylhexanoic acid (VII); however, in all cases the desired lactone was contaminated with varying amounts of (*R*)-4-methyl-5-hexanoic acid (X) which was identified by elemental analysis and the infrared bands at 3100, 2620, 1717, 1650, 1420, 1272, 995, and 915 cm^{-1} after a preparative vapor phase separation. Vapor phase chromatography also showed contamination by a few per cent of a nonacidic unidentified material which had a slightly smaller retention time than the lactone IX. This compound might possibly be the six-membered lactone XI which would readily be expected to form from the unsaturated acid. Attempts to cyclize the hydroxy acid with a high-dilution apparatus using benzenesulfonic acid in refluxing benzene[25] led to the same mixture of products. Recently the formation of unsaturated acids from the pyrolysis of steroid lactones has also been reported.[26]



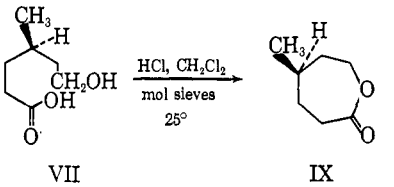
X XI

(25) M. von Stoll and A. Rouve, *Helv. Chim. Acta*, **18**, 1087 (1935).

(26) D. Rosenthal, A. O. Niedermeyer, and J. Fried, *J. Org. Chem.*, 30, 510 (1965).

(27) Reaction of (*R*)-(+)-6-hydroxy-4-methylhexanoic acid (VII) with dicyclohexylcarbodiimide[28] at 4° in ether led to a poor yield of the impure lactone IX with the major portion of the product as polymer.

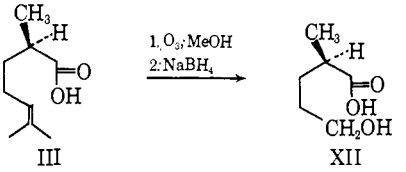
(28) A. Buzas, C. Engell, and P. Freon, *Compt. Rend.*, **255**, 945 (1962).



VII IX

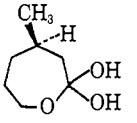
Vapor phase chromatography indicated 93.5% purity with three unidentified impurities in 3%, 3.5%, and one trace amount which could all be readily removed on a preparative vapor phase fractometer. The infrared spectrum of the 100% pure material was identical with that of racemic γ-methyl-ε-caprolactone prepared by the Baeyer–Villiger oxidation of 4-methylcyclohexanone.

Reductive ozonolysis (at −50 to −60°) of (*R*)-(+)-citronellic acid with sodium borohydride[29] led to a 68.6% yield of (*R*)-(+)-6-hydroxy-3-methylhexanoic acid (XII). This material, a water-soluble viscous



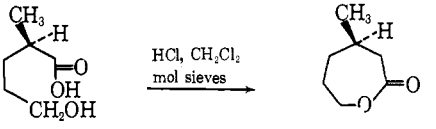
III XII

oil, behaved similarly to (*R*)-(+)-6-hydroxy-4-methylhexanoic acid (VII) described in footnote 23.[30]



XIII

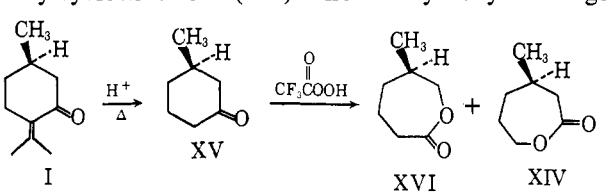
Cyclization of (*R*)-(+)-6-hydroxy-3-methylhexanoic acid was carried out by the closed system hydrogen chloride catalyzed method used for the γ-methyl lactone giving a 59.2% yield of (*R*)-(−)-β-methyl-ε-caprolactone (XI).



XII XIV

Vapor phase chromatography indicated 97.5% purity with 2.5% of one unidentified impurity. The impurity was readily removed by preparative vapor phase chromatography giving 100% pure (*R*)-(−)-β-methyl-ε-caprolactone (XIV).

Conversion of (*R*)-(+)-pulegone (I) to (*R*)-(+)-3-methylcyclohexanone (XV) followed by Baeyer–Villiger



I XV XVI XIV

(29) D. G. M. Diaper and D. L. Mitchell, *Can. J. Chem.*, **38**, 1976 (1960).

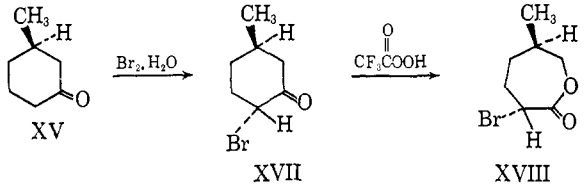
(30) Existence of intermediate XIII or oligomers was indicated by the fact that the optical rotation of a freshly prepared solution of the hydroxy acid XII (84.5% by titration) increased with time, whereas if lactone were forming it would have decreased and become more negative. This result further supports the reversible equilibrium scheme suggested in footnote 23.

oxidation with trifluoroperacetic acid yielded a mixture of (*R*)-(−)-δ-methyl-ε-caprolactone (XVI) and (*R*)-(−)-β-methyl-ε-caprolactone (XIV).

Attempts to separate this mixture by vapor phase chromatography and column chromatography failed. Formation of a mixture of the quinine salts followed by fractional crystallization was not successful due to the high solubility of the salts.

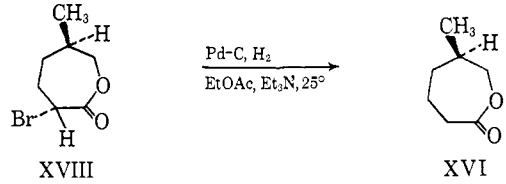
(*R*)-(−)-δ-Methyl-ε-caprolactone (XVI), mp 32.2–32.4°, was finally obtained in the pure state by low-temperature recrystallization at −10 to −20° in 5.9% over-all yield.

As proof of structure for this lactone the following synthesis was carried out.



(*R*)-(+)-3-Methylcyclohexanone (XV) was converted into *trans*-(*R*)-(−)-2-bromo-5-methylcyclohexanone (XVII) with bromine and water in 12.8% yield by the procedure of Djerassi, *et al.*[31] A Baeyer–Villiger[32] reaction on this with trifluoroperacetic acid led to an 86.7% yield of *trans*-(*R*)-(−)-α-bromo-δ-methyl-ε-caprolactone (XVIII). The fact that this reaction went exclusively one way within the limits of detection was shown by the fact that the nuclear magnetic resonance spectrum did not show any α-protons corresponding to the other isomer in the vicinity of δ 2.89, even under maximum resolution; the α-proton on the α-bromo lactone appeared at δ 4.74 ppm. Attempts to remove the α-bromine by treatment with bases such as pyridine or lithium chloride in dimethylformamide led to salt formation and double bond rearranged mixtures.[36] This particular approach was discontinued because of the danger of racemization at the allylic asymmetric center in XX. An attempt was also made to remove the α-bromine by conversion to the enol phosphate *via* the Perkow reaction[37] followed by acidolysis. Reaction of XVIII under a variety of conditions with triethyl phosphite unfortunately always led to a major portion of phosphonate instead.

Success was achieved by hydrogenolysis of the α-bromo lactone XVIII in the presence of triethylamine[38] and palladium on carbon giving a 37.5% yield of (*R*)-(−)-δ-methyl-ε-caprolactone (XVI). The infrared spectrum and optical rotation were identical with that of the material obtained by fractional crystallization and did not show any mixture melting point depression, thus proving the structure of (*R*)-(−)-δ-methyl-ε-caprolactone (XVI).



Experimental Section

1. General. Optical rotations were taken on a Rudolph photoelectric spectropolarimeter, Model 200AS/800/650.

All ultraviolet spectra were taken on a Perkin-Elmer Model 350. A Perkin-Elmer Model 21 was used for infrared work and a Varian HR-60 operating at 60 Mc at 25° using tetramethylsilane set at zero parts per million was used for all nmr measurements. Analysis by vapor phase chromatography was carried out on a Perkin-Elmer Model 154-B, and preparative work was carried out on a Model 154-D. It should be pointed out that all reported retention times are subject to error due to the change of column characteristics with use. All melting points are corrected and all boiling points are uncorrected. Microanalyses were performed by Alfred Bernhardt Mikroanalytisches Laboratorium, Mülheim (Ruhr), Germany.

2. (*R*)-(+)-3-Methylcyclohexanone (XV). The procedure of Eisenbraun and McElvain[9] was used. From 500 g (3.29 moles) of pulegone, $[\alpha]^{25}D$ +44.87° (*l* 2 dm, neat), $n^{25}D$ 1.4808, and 500 ml of concentrated hydrochloric acid was obtained 235.5 g (64%) of the ketone, bp 83–87° (60 mm), $n^{25}D$ 1.4419. Vapor phase chromatography on a column of polyglycol (Ucon LB-550-X) indicated 93.5% purity. On redistillation through a 45-cm column packed with glass helices was obtained (*R*)-(+)-3-methylcyclohexanone, bp 166° (753.2 mm), $n^{25}D$ 1.4440, $[\alpha]^{25}D$ +24.40° (*l* 2 dm, neat), 179.5 g (48.6%) (by the same procedure, bp 166–167°, $n^{25}D$ 1.4440, $[\alpha]^{26}D$ +12.01° (*l* 1 dm, neat), 69%).[9] Vapor phase chromatography on the same column indicates 100% purity.

3. (*R*)-(−)-δ-Methyl-ε-caprolactone (XVI). The procedure of Sager and Duckworth[39] for the synthesis of ε-caprolactone was used. From 265 g (1.26 moles) of trifluoroacetic anhydride, 36.3 g (0.965 mole) of 90% hydrogen peroxide, and 103 g (0.916 mole) of (*R*)-(+)-3-methylcyclohexanone, $[\alpha]^{25}D$ +24.40° (*l* 2 dm, neat), was obtained a mixture of (*R*)-(−)-δ-methyl-ε-caprolactone and (*R*)-(−)-β-methyl-ε-caprolactone, bp 52° (0.1 mm), $n^{25}D$ 1.4580, 75.7 g (64.3%) (by oxidation of the racemic ketone with peracetic acid to a racemic mixture, bp 87° (3 mm), $n^{30}D$ 1.4568, 81%).[40] Vapor phase chromatography on a column of polyethylene glycol succinate at 194° indicated a single peak in 100% purity, retention time 29.5 min. The lactone mixture crystallized when cooled to −10°. After standing for 6 hr at −10°, the crystals were filtered and drained on a jacketed coarse-fritted glass filter under slight nitrogen pressure at −10° for 4 hr. The crude lactone melted at 18°. After dissolving the lactone in 600 ml of pentane, drying over 4A molecular sieves for 2 hr, and cooling to −20°, 16.2 g of lactone melting at 29° was obtained. A further recrystallization after drying over 4A molecular sieves yielded 11.9 g of white needles melting at 32.2–32.4°, and a final recrystallization from dry pentane at −10° yielded 6.9 g (5.9%) of (*R*)-(+)-δ-methyl-ε-caprolactone, mp 32.2–32.4°, $[\alpha]^{25}D$ −36.11° (*c* 0.46, $CHCl_3$), $[\alpha]^{25}_{450}$ −66.96° (*c* 0.46, $CHCl_3$), d^{25} 1.14 g/cm³ from unit cell dimensions, ΔH_f = 6.3 cal/g.[41]

(31) C. Djerassi, L. E. Geller, and E. J. Eisenbraun, *J. Org. Chem.*, **25**, 1 (1960).

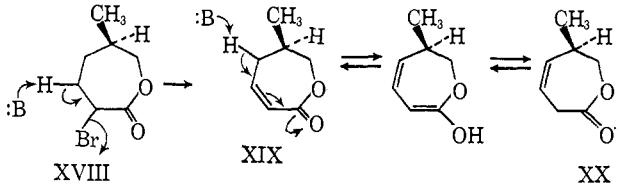
(32) Reactions of this type are known in steroid chemistry;[33] the preferential migration might be rationalized on the basis of the withdrawal of electron density by the inductive effect of the bromine atom, thereby allowing the more electron-rich bond to migrate. For a more detailed discussion of the Baeyer–Villiger reaction, see Hassall[34] and Smith.[35]

(33) P. Wieland and K. Miescher, *Helv. Chim. Acta*, **32**, 1768 (1949).

(34) C. H. Hassall, *Org. Reactions*, **9**, 73 (1957).

(35) P. A. S. Smith in "Molecular Rearrangements," Vol. I, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, p 457.

(36) A suggested mechanism for the formation of the double bond rearranged products is shown below.



The reaction mixtures were analyzed by vpc and structure XIX was assigned on the basis of a 1715-cm⁻¹ infrared band and nmr peaks at 5.48 and 6.36 ppm, while XX was assigned from a 1735-cm⁻¹ infrared band and nmr peaks at 3.23 and 5.74 ppm.

(37) F. W. Lichtenthaler, *Chem. Rev.*, **61**, 607 (1961).

(38) M. G. Reinecke, *J. Org. Chem.*, **29**, 299 (1964).

(39) F. Sager and A. Duckworth, *J. Am. Chem. Soc.*, 77, 188 (1955).

(40) P. S. Starcher and B. Phillips, *ibid.*, **80**, 4079 (1958).

(41) The heat of fusion was determined by Mr. Zory Glaser, Polytechnic Institute of Brooklyn, with a Perkin-Elmer differential scanning calorimeter, Model DSC-1.

Anal. Calcd for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.46; H, 9.21.

Recrystallizations carried out by slowly reducing the temperature of more highly diluted solutions to −10° have led to formation of 4- and 5-in. needles.

The infrared spectrum indicated a strong carbonyl peak at 1740 cm^{-1} and a strong carbon–ether oxygen stretching band at 1170 cm^{-1} indicative of a lactone. Ultraviolet analysis detected a weak peak at 221 ± 1 mμ (ε 60.0), and a strong peak below 179 mμ (ϵ_{174} 3.02 × 10^3), in heptane. The nuclear magnetic resonance spectrum in carbon tetrachloride showed a methyl doublet at δ 0.95 ppm, a methyl multiplet at δ 1.75 ppm, and α-proton triplet at δ 2.43 ppm, and an ε-proton doublet at δ 3.82 ppm, consistent with the structure of the (*R*)-(−)-δ-methyl-ε-caprolactone. The unit cell was found[42] to be monoclinic, $P2_1$, $Z = 2$, $a = 6.00$ A, $b = 5.41$ A, $c = 11.25$ A, $\beta = 98° 10'$.

4. *trans*-(*R*)-(−)-2-Bromo-5-methylcyclohexanone (XVII). The procedure of Djerassi, Geller, and Eisenbraun[31] was used. From (*R*)-(+)-3-methylcyclohexanone, $[\alpha]^{25}D$ +24.40° (*l* 2 dm, neat), $n^{25}D$ 1.4440, 108 g (0.962 mole), 328 ml of water, and 154 g (1.93 moles) of bromine was obtained 30.22 g of crude bromo ketone. Recrystallization from *n*-pentane yielded 23.53 g (12.8%) of *trans*-(*R*)-(−)-2-bromo-5-methylcyclohexanone, mp 82–82.2°, $[\alpha]^{25}D$ −63.78° (*c* 0.947, toluene) (by the same procedure mp 83.5–84°, $[\alpha]^{25}D$ −64.4° (*c* 1.06, toluene), 21%).[31]

Nuclear magnetic resonance in carbon tetrachloride showed the methyl doublet at δ 1.02 ppm, the ring methylene proton multiplet at δ 2.09 ppm, the six-position doublet at δ 2.89 ppm, and the two-position quartet at δ 4.35 ppm, consistent with the structure for *trans*-(*R*)-(−)-2-bromo-5-methylcyclohexanone.

5. *trans*-(*R*)-(−)-α-Bromo-δ-methyl-ε-caprolactone (XVIII). To 130 ml of chloroform at 0° was added 7.2 g of 90% hydrogen peroxide. The suspension was stirred rapidly at 0° while 53.0 g (0.252 mole) of trifluoroacetic anhydride was added dropwise so that the temperature remained between 0 and 5°. After the addition the stirring was continued for 0.5 hr at 0° and 23.5 g (0.180 mole) of (*R*)-(−)-*trans*-2-bromo-5-methylcyclohexanone, $[\alpha]^{25}D$ −63.78° (*c* 0.947, toluene), was slowly added in 25 ml of chloroform so that the temperature remained between 0 and 5°. The reaction mixture was stirred for 3 hr at 0° after which time 100 ml of chloroform and 36.7 g of potassium carbonate in 50 ml of water was added slowly. The yellow color of the reaction was then discharged and 50 ml more of water was added. The organic phase was extracted with 25 ml of water, and the combined water washings were extracted with 50 ml of chloroform. After combining the chloroform washings, drying over anhydrous magnesium sulfate for 12 hr, and removing the chloroform on a rotating evaporator, 22.10 g (86.7%) of crude (*R*)-(−)-*trans*-α-bromo-δ-methyl-ε-caprolactone was left as a colorless viscous oil. A portion of this, 0.85 g, was purified by distillation through a microdistillation apparatus, bp 81–81.5 (0.09 mm), $n^{25}D$ 1.5056, $[\alpha]^{25}D$ −15.40° (*c* 0.646, $CHCl_3$).

Anal. Calcd for $C_7H_{11}O_2Br$: C, 40.40; H, 5.81; Br, 38.41. Found: C, 40.23; H, 5.76; Br, 38.22.

The infrared spectrum showed two carbonyl peaks at 1745 and 1725 cm^{-1}, respectively. The intensity of the 1745-cm^{-1} peak was slightly larger than the 1725-cm^{-1} peak. Two carbon–ether oxygen stretching peaks at 1153 cm^{-1} (weaker) and 1138 cm^{-1} (stronger) along with two more carbon–ether stretching peaks at 1040 cm^{-1} (weaker) and 1052 cm^{-1} (stronger) were present. The ultraviolet spectrum in trifluoroethanol showed one broad peak at 239 mμ (ϵ_{231} 66.5).

Nuclear magnetic resonance did not show the presence of any protons at δ 2.89 ppm excluding the existence of (*R*)-ε-bromo-β-methyl-ε-caprolactone as a reaction product. The spectrum indicated a methyl doublet at δ 1.03 ppm, a methylene multiplet at δ 2.16 ppm, an ε-proton multiplet at δ 4.18 ppm, and the α-proton quartet at δ 4.74 ppm consistent with the structure for *trans*-(*R*)-(−)-α-bromo-δ-methyl-ε-caprolactone.

6. (*R*)-(−)-δ-Methyl-ε-caprolactone by Hydrogenolysis of *trans*-(*R*)-(−)-α-Bromo-δ-methyl-ε-caprolactone. *trans*-(*R*)-(−)-α-Bromo-δ-methyl-ε-caprolactone (crude product from part 5), 11.06 g (0.0534 mole), was hydrogenolyzed in a Parr bottle with 100 ml of triethylamine, 100 ml of ethyl acetate, and 10 g of 10% palladium on carbon for 24 hr at 45 psi of hydrogen. At the end of this time the mixture was filtered, and the solvent was removed on a rotating evaporator. On distillation through a 6-in. Vigreux column 3.06 g (43.8%) of (*R*)-(−)-δ-methyl-ε-caprolactone, bp 57° (0.2 mm), was obtained. On momentary contact of the bottom of the receiver with Dry Ice, crystallization of the material was initiated. This material was dissolved in 100 ml of pentane, dried over molecular sieves, filtered through a coarse sintered-glass funnel, and slowly cooled until, at −2°, larger white needles began to precipitate. The bath temperature was reduced to −10° and kept at this temperature for 0.5 hr at which time the crystals were filtered in a jacketed sintered-glass funnel at −10° under a nitrogen atmosphere yielding 1.67 g (24.5%) of (*R*)-(−)-δ-methyl-ε-caprolactone, mp 32.7–33.4°, $[\alpha]^{25}D$ −35.58° (*c* 0.312, $CHCl_3$).

Anal. Calcd for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.55; H, 9.48.

The infrared spectrum of this compound was identical with that of the material prepared by the Baeyer–Villiger reaction in part 3. A mixture melting point with the material from part 3 showed no depression.

Vapor phase chromatography on a column of polyethylene glycol succinate at 202° indicated 100% purity, retention time 16 min.

7. (*R*)-(+)-Citronellic Acid (III). The procedure of Plesek[14,15] was used. Pulegone, $[\alpha]^{25}D$ +44.87° (*l* 2 dm, neat), $n^{25}D$ 1.4808, 505.7 g (3.32 moles), was cooled to 0°, and 178 g of dry hydrogen chloride was bubbled in at a rate such that the temperature remained between 0 and 8° with slow stirring. The reaction mixture was allowed to stand for 12 hr in an ice bath at which time it was slowly added to 10,500 g of 5% sodium hydroxide at 16°. After vigorous stirring for 12 hr at this temperature, the reaction mixture was extracted with two 1000-ml portions of ether which were then separated from the aqueous phase. Upon acidification of the clear yellow basic solution with 800 ml of concentrated hydrochloric acid an immediate light yellow oil formed on the surface and was then taken up by extraction with three 500-ml portions of ether. The ether was removed on a rotating evaporator after drying over anhydrous sodium sulfate for 12 hr, and the remaining light yellow oil was then distilled through a 25-cm glass helix packed column yielding 290.5 g (51.5%) of (*R*)-(+)-citronellic acid, bp 80.5–81° (0.07 mm), $[\alpha]^{25}D$ +8.48° (neat), $n^{25}D$ 1.4520, d^{25}_4 0.9226. Vapor phase chromatography on a silicone oil column at 200° indicated 97.8% purity, retention time 6 min, and 2.2% of an unidentified impurity, retention time 3 min.

In an alternate procedure the pulegone hydrochloride was added to the sodium hydroxide at 36° and the reaction mixture was vigorously stirred for 4 hr, bp 82–82.5° (0.1 mm), $[\alpha]^{25}D$ +8.72° (neat), $[\alpha]^{25}D$ +10.2° (*c* 2.48, $CHCl_3$), $n^{25}D$ 1.4510, d^{25}_4 0.9226 (51.5%) (by adding the pulegone hydrochloride at room temperature with vigorous stirring for 4 hr, bp 112–113° (0.6 mm), $[\alpha]^{25}D$ +8.40° (neat), $n^{20}D$ 1.4540, d^{20}_4 0.9256, 59.5%).[14,15] The infrared spectrum indicated a strong carbonyl peak at 1710 cm^{-1}, a weak CH stretching band at 2660 cm^{-1}, and an OH deformation peak at 940 cm^{-1} along with bands at 1300 and 1228 cm^{-1} indicative of a carboxyl group. A peak at 1410 cm^{-1} may be the CH_2 deformation associated with the α-hydrogens. The carbon–carbon double bond stretching vibration was too weak to detect; however a shoulder at 3030 cm^{-1} for the CH stretching vibration and a band at 825 cm^{-1} for the CH out-of-plane deformation indicated the presence of the double bond.

The nuclear magnetic resonance spectrum indicated a methyl doublet at δ 0.96 ppm, a methylene multiplet at δ 1.31 ppm, an isopropylidene doublet at δ 1.62 ppm, a α-proton–allylic proton multiplet at δ 2.05 ppm, an olefinic proton triplet at δ 5.02 ppm, and a carboxyl proton singlet at δ 11.56 ppm.

8. (*R*)-(−)-N,N-Dimethylcitronellamide. Pulegone ($[\alpha]^{25}D$ +44.87° (*l* 2 dm, neat), $n^{25}D$ 1.4808, 407.1 g (2.68 moles)) was cooled to 0°, and 205 g of dry hydrogen chloride was bubbled in at rate such that the temperature remained between 0 and 8° with slow stirring. The pulegone hydrochloride mixture was allowed to stand for 12 hr in an ice bath at which time the excess hydrogen chloride was removed by vigorously bubbling in dry nitrogen gas while under reduced pressure for 4 hr.

To 5.08 l. of 1.65 *N* butyllithium (8.4 moles) in *n*-hexane and 400 ml of ether was added 458 g (10.2 moles) of anhydrous dimethylamine in 2 l. of ether dropwise with stirring under a nitrogen atmosphere at 25° with cooling in an ice bath. After the addition of 600 ml of ether, the white suspension of lithium dimethylamide was stirred for 1 hr at 25°. The pulegone hydrochloride was then added dropwise with stirring under nitrogen with the temperature maintained at 25–30° with an ice bath. Stirring was continued for 2.5 hr at 20° after the addition and at the end of this time 2.5 l. of water was added first slowly and, after the remaining lithium

(42) All X-ray analyses were carried out by Mr. Rubin Rudman of the Polytechnic Institute of Brooklyn and are reported in the ASTM X-Ray Powder Data File.

dimethylamide was destroyed, more rapidly. The white suspension eventually dissolved in the water phase after vigorous stirring. The aqueous phase was separated and washed with 300 ml of ether which was then combined with the bulk of the organic phase and this in turn was reduced in volume to 2 l. by distillation of the ether and hexane. After drying the solution over anhydrous sodium sulfate for 12 hr, the solvent was removed on a rotating evaporator and the remaining oil distilled through a 25-cm stainless steel packed column. The first low-boiling fraction of pulegone, bp 42° (0.1 mm), was discarded. As soon as pure (*R*)-(−)-N,N-dimethylcitronellamide began coming over, the packed column was replaced with a 20-cm Vigreux column and the distillation continued giving 248 g (47%) of (*R*)-(−)-N,N-dimethylcitronellamide, bp 70.5° (0.1 mm), $[\alpha]^{25}D$ −4.91° (neat), $n^{25}D$ 1.4690, d^{25}_4 0.8958.

Vapor phase chromatography on a column of silicone oil at 198° showed 100% purity, retention time −13.5 min.

Anal. Calcd for $C_{12}H_{23}ON$: C, 73.04; H, 11.75; N, 7.095; [M]D, 61.96°. Found: C, 73.27; H, 11.69; N, 7.21; [M]D, 61.60°.

The infrared spectrum indicated a strong peak at 1650 cm^{-1} and a weak peak at 8.25 cm^{-1} consistent with an unsaturated tertiary amide structure. Peaks were also observed at 1492, 1450, 1390, 1270, 1143, 1108, 1068, and 980 cm^{-1}.

The nuclear magnetic resonance spectrum showed the methyl doublet at δ 0.90 ppm, the methylene proton multiplet at δ 1.31 ppm, the isopropylidene doublet at δ 1.62 ppm, the allylic proton triplet at δ 1.92 ppm, the carbonyl proton peak at δ 2.13 ppm, the N,N-dimethyl doublet at δ 2.92 ppm, and the olefinic proton triplet at δ 5.10 ppm consistent with the structure for (*R*)-(−)-N,N-dimethylcitronellamide.

9a. (*R*)-(+)-Citronellol (IV). Pulegone ($[\alpha]^{25}D$ +44.87° (*l* 2 dm, neat), $n^{25}D$ 1.4808, 78 g (0.511 mole)) was converted to pulegone hydrochloride with 50 g of dry hydrogen chloride by the method described above. The excess hydrogen chloride was then removed by vigorously bubbling in dry nitrogen gas while under reduced pressure for 4 hr. This was then added slowly under nitrogen with stirring to 26.5 g (0.7 mole) of lithium aluminum hydride in 2.5 l. of ether with the temperature maintained at 20–25° with an ice bath. After the addition the reaction was stirred at room temperature for 9 hr, at which time 100 ml of water was cautiously added followed by 500 ml of 6 *N* hydrochloric acid. Once the solids dissolved, the ether phase was washed with two 100-ml portions of saturated sodium bicarbonate and two 100-ml portions of water and dried over anhydrous sodium sulfate overnight. Upon removal of the ether on a rotating evaporator and distillation through a 25-cm column packed with glass helices, 13.2 g (16.1%) of (*R*)-(+)-citronellol, bp 65° (0.3 mm), $[\alpha]^{25}D$ +2.10° (neat), $n^{25}D$ 1.4554, was obtained (by the $LiAlH_4$ reduction of (*R*)-(+)-citronellic acid, bp 110° (11 mm), $[\alpha]^{20}D$ +5.37° (neat), $n^{20}D$ 1.4558, d^{20}_4 0.8558, 94%).[15]

Vapor phase chromatography on a column of polyglycol (Ucon LB-550-X) at 200° indicated 86.6% purity, retention time 10.5 min, with 8.02% of one unidentified component, retention time 9.5 min, and 5.38% of a mixture of other unidentified components, retention time 8.5 min. The infrared spectrum was identical with that of authentic citronellol.

9b. (*R*)-(+)-Citronellol (IV). The procedure of Lukes, Zabacova, and Plesek was used.[15] To 3 l. of ether containing 33 g (0.883 mole) of lithium aluminum hydride was added 105 g (0.616 mole) of (*R*)-(+)-citronellic acid, $[\alpha]^{25}D$ +8.72° (neat), in 500 ml of ether at a rate sufficient to maintain reflux under nitrogen. The reaction mixture was stirred at room temperature for 24 hr at which time 50 ml of water was cautiously added, followed by 400 ml of 6 *N* hydrochloric acid; stirring was continued for 1 hr followed by separation of the ether layer and washing with 100 ml of saturated sodium bicarbonate and two 100-ml portions of water. After drying the ether solution over anhydrous sodium sulfate for 12 hr, the ether was removed by distillation leaving a colorless oil which was then distilled through a 25-cm column packed with glass helices yielding 86.8 g (90%) of (*R*)-(+)-citronellol, bp 68° (0.8 mm), $[\alpha]^{25}D$ +5.51° (neat), $n^{25}D$ 1.4530 (by the same procedure, bp 110° (100 mm), $[\alpha]^{20}D$ +5.37° (neat), $n^{20}D$ 1.4558, d^{20}_4 0.8558, 94%).[15] Vapor phase chromatography on a column of polyglycol (Ucon LB-550-X) at 177° indicated 96.5% purity, retention time 20 min, with 3.5% of an unidentified component, retention time 17.2 min, which could not be removed by distillation through a spinning-band column at a reflux ratio of 500:1.

The infrared spectrum showed a strong sharp peak at 3340 cm^{-1} for the hydroxyl stretching frequency and a strong carbon–oxygen stretching vibration or hydroxyl deformation bond at 1153 cm^{-1} indicative of an alcohol. A very weak carbon–carbon double bond stretching vibration was observed at 1675 cm^{-1} and the CH out-of-plane deformation at 825 cm^{-1} indicated the presence of the double bond.

Nuclear magnetic resonance showed the methyl doublet at δ 0.89 ppm, the methylene multiplet at δ 1.37 ppm, the isopropylidene doublet at δ 1.59 ppm, the allylic proton triplet at δ 1.97 ppm, the α-hydroxyl proton triplet at δ 3.51 ppm, and the olefinic proton triplet at δ 4.50 ppm, consistent with the structure of citronellol.

10. (*R*)-(+)-6-Hydroxy-4-methylhexanoic Acid (VII). (*R*)-(+)-Citronellol ($[\alpha]^{25}D$ +5.51° (neat), $n^{25}D$ 1.4530, 76.9 g (0.492 mole)) was slowly added to a solution of sodium periodate, 420 g (1.76 moles), dissolved in 1430 ml of acetone and 1800 ml of water with stirring. The stirred solution was cooled in an ice bath to 5° and then potassium permanganate, 13 g (0.083 mole) in 500 ml of water, was added simultaneously with 500 ml of acetone at 5–10° over a 4-hr period under nitrogen. Stirring was continued for 12 hr at 5–10° at which time the blue-violet reaction media was decanted from the red-brown residue, the acetone removed under reduced pressure, and the remaining aqueous phase extracted with five 600-ml portions of ether. After reducing the aqueous phase to dryness on a rotating evaporator, the remaining solids were combined with the above red-brown residue and washed with 1200 ml of ether followed by extraction in a soxhlet extractor with an additional 600 ml of ether for 24 hr. The ether washings were combined and dried over anhydrous sodium sulfate for 48 hr and the ether removed on a rotating evaporator leaving 73.8 g (102%) of crude (*R*)-(+)-6-hydroxy-4-methylhexanoic acid as a faintly yellow, viscous oil, $n^{25}D$ 1.4424, hydroxy acid by titration 67%.

A portion of the crude product, 10.37 g, was refluxed with 206 ml of 0.5 *N* potassium hydroxide in methanol under nitrogen for 8 hr, at which time it was cooled and 33 ml of 1.66 *N* hydrochloric acid was added to neutralize the solution. After removing water on a rotating evaporator the remaining light yellow oil was triturated under 200 ml of ether. The ether was then discarded and the semisolid oil placed under high vacuum to remove traces of ether. Water (100 ml) was added, and the resulting solution after washing with Darco G60 adsorbing charcoal became colorless. To this was added 5.51 ml of 12 *N* hydrochloric acid and the acidic solution extracted with four 100-ml portions of ether which was then dried over anhydrous sodium sulfate for 4 hr and on a rotating evaporator, leaving 5.36 g of colorless hydroxy acid. Molecular distillation of 2.1 g at 70° (3×10^{-4} mm) led to pure (*R*)-(+)-6-hydroxy-6-methylhexanoic acid, $[\alpha]^{25}D$ +6.37° (*c* 1.64, H_2O), $n^{25}D$ 1.4589, hydroxy acid by titration 96%; after standing in a water solution at 25° for 6.5 hr, $[\alpha]^{25}D$ +5.64° (*c* 1.64, H_2O); after 2 weeks, $[\alpha]^{25}D$ +5.41° (*c* 1.64, H_2O).

Anal. Calcd for $C_7H_{14}O_3$: C, 57.51; H, 9.65. Found: C, 57.23; H, 9.82.

The infrared spectrum showed peaks at 3333 (s), 2640 (m), 1710 (s), 1050 (m), and 1282 cm^{-1}, indicative of a hydroxy acid.

11. (*R*)-(+)-6-Hydroxy-3-methylhexanoic Acid (XII). Ozone from a Welsbach T-23 ozonizer was passed through a solution of citronellic acid, $[\alpha]^{25}D$ +8.48° (neat), $n^{25}D$ 1.4520, 50 g (0.294 mole), in 150 ml of methanol at −55° with stirring until no more ozone was taken up by the solution as evidenced by the rapid formation of the brown triiodide ion in a trap containing an acidic solution of 2% potassium iodide connected to the reaction vessel exit gas outlet. After flushing the solution with oxygen and then nitrogen and allowing the solution to reach room temperature, it was added dropwise to a solution of 22.2 g (0.588 mole) of sodium borohydride and 18 g of sodium hydroxide dissolved in 150 ml of methanol and 50 ml of water with stirring and cooling such that the temperature remained at 10°. During the addition a mild evolution of a gas occurred, and the solution became cloudy. After the addition the mixture was stirred at 25° for 12 hr at which time the solution was refluxed for 10 min, and then the water and methanol were removed on a rotating evaporator leaving a solid white residue. This was dissolved in 100 ml of water and cooled to 0° at which time 100 ml of concentrated hydrochloric acid was added slowly with immediate formation of a white precipitate. After extraction of the mixture with 900 ml of chloroform, 200 ml of water and 100 ml of concentrated hydrochloric acid were added to the remainder of the aqueous phase, and this in turn was extracted twice more with 900-ml portions of chloroform. Upon combining the chloroform washings, drying over anhydrous sodium sulfate for 12 hr, and removing the chloroform on a rotating evaporator, 29.52 g (68.6%) of (*R*)-(+)-6-hydroxy-3-methylhexanoic acid remained as a colorless viscous oil, $n^{25}D$ 1.4570, hydroxy acid by titration 89.4%. A 2-g sample was purified by molecular distillation giving

pure (*R*)-(+)-6-hydroxy-3-methylhexanoic acid, $[\alpha]^{24}D$ +6.11° (*c* 1.76,H_2O), $n^{25}D$ 1.4558, hydroxy acid by titration 84.5%; after 3 weeks at 25° in a water solution $[\alpha]^{25}D$ +7.47° (*c* 1.76, H_2O).

Anal. Calcd for $C_7H_{14}O_3$: C, 57.51; H, 9.65. Found: C, 57.99; H, 9.47.

The infrared spectrum showed peaks at 3333 (s), 2640 (m), 1710 (s), 1050 (m), and 1285 cm^{-1} indicative of an hydroxy acid.

12. (*R*)-(+)-3-Methyl-6-oxohexanoic Acid. (*R*)-(+)-Citronellic acid ($n^{25}D$ 1.4536, 11.70 g (0.069 mole)) in 40 ml of acetic acid and 5 ml of water was ozonized at 0–7° by passing a stream of ozone from a Welsbach Model T23 through the solution until the potassium iodide trap at the end of the chain rapidly turned brown. The ozinate was then added dropwise to 10 g of powdered zinc in 100 ml of water with very rapid stirring while the temperature rose to 51° during the first 10 min. Stirring was continued for 1.5 hr at which time the clear solution was decanted away from the zinc and extracted with six 50-ml portions of ether which were then dried over anhydrous sodium sulfate for 12 hr. Removal of the ether and acetic acid on a rotating evaporator left 8 g of a light green oil which was distilled through a 6-in. Vigreux column giving 3.56 g (36%) of (*R*)-(+)-3-methyl-6-oxohexanoic acid, $[\alpha]^{25}D$ +20.82° (*c* 2.93, $CHCl_3$), $n^{25}D$ 1.4490, d^{25}_4 1.0698.

Anal. Calcd for $C_7H_{12}O_3$: C, 58.31; H, 8.39; [M]D, 36.08; neut equiv, 144.17. Found: C, 58.06; H, 8.30; [M]D, 36.14°; neut equiv, 145.21.

The infrared spectrum indicated the characteristic carboxylic acid peak at 1710 cm^{-1} (s) and the characteristic aldehyde peaks at 2720 cm^{-1} (w) and 1725 cm^{-1} (s). A medium peak at 1410 cm^{-1} was also observed.

13. *dl*-γ-Methyl-δ-caprolactone. The procedure of Sager and Duckworth[43] for the synthesis of ε-caprolactone was used. From 453 g (2.16 moles) of trifluoroacetic anhydride, 61.89 g (1.63 moles) of 90% hydrogen peroxide, and 172.5 g (1.54 moles) of 4-methylcyclohexanone, $n^{26}D$ 1.4435, was obtained 156.1 g (79.2%) of *dl*-γ-methyl-ε-caprolactone, bp 83–84° (2 mm), $n^{25}D$ 1.4566, d_4^{25} 1.0327 (by oxidation with peracetic acid, bp 103° (5 mm), $n^{30}D$ 1.4550, 83.7%).[43] Vapor phase chromatography on a column of polyethylene glycol succinate at 196° indicated 100% purity, retention time 15 min.

Anal. Calcd for $C_7H_{12}O_2$: C, 65.59; H, 9.44; [M]D, 33.99°; saponification equiv, 128.2. Found: C, 65.27; H, 9.31; [M]D, 33.78°; saponification equiv, 127.6.

The infrared spectrum showed the presence of a carbonyl peak at 1740 cm^{-1} and a carbon–ether oxygen stretching vibration as a doublet centered at 1168 cm^{-1} indicative of a lactone.

Nuclear magnetic resonance indicated a methyl doublet at δ 0.95 ppm, a methylene multiplet at δ 1.75 ppm, the α-proton triplet at δ 2.49 ppm, and the ε-proton triplet at δ 4.05 ppm consistent with the structure for *dl*-γ-methyl-ε-caprolactone.

14. (*R*)-(+)-γ-Methyl-ε-caprolactone (IX). (*R*)-(+)-6-Hydroxy-4-methylhexanoic acid ($n^{25}D$ 1.4424, hydroxy acid by titration 64.5%, 14.35 g (0.0982 mole)) was dissolved in 7 l. of methylene chloride and 300 g of molecular sieves, type 4A, was then added. After standing for 2 hr, 139 g (3.86 moles) of anhydrous hydrogen chloride gas was bubbled through the mixture with stirring over a period of 35 min. The system was then sealed and stirring was continued for 60 hr at room temperature with a closed system stirring assembly. At the end of this time a rapid stream of nitrogen was bubbled through the opened system with stirring for 36 hr to remove the hydrogen chloride gas and then the mixture was filtered yielding a light straw colored solution which was reduced in volume to 1 l. by distillation of the methylene chloride. Extraction with 50 ml of an aqueous solution containing 20 g of potassium carbonate immediately discharged the yellow color to a very faint yellow, and after drying the organic phase over anhydrous magnesium sulfate for 12 hr the methylene chloride was removed on a rotating evaporator leaving a yellow nonviscous liquid which was distilled through a 25-cm column packed with glass helices in the presence of four drops of toluene diisocyanate as drying agent and 2 ml of dibutyl phthalate as chaser yielding 4.41 g (35.1%) of crude (*R*)-(+)-γ-methyl-ε-caprolactone, bp 51° (0.1 mm), which vapor phase chromatography on a column of polyethylene glycol succinate at 196° indicated to be 93.5% (*R*)-(+)-γ-methyl-ε-caprolactone, retention time 18 min, and three unidentified components in 3%, 3.5%, and one in trace amount with retention times of 6.5, 8, and 13 min, respectively. The crude lactone was then passed through a preparative polyethylene glycol succinate column in 0.5-ml portions at 195° and the pure product collected in a tube equipped with a rubber serum cap and calcium chloride drying tube at −78°. This material was then distilled through a microdistillation unit giving 2.14 g (17%) of pure (*R*)-(+)-γ-methyl-ε-caprolactone, bp 51–52° (0.1 mm), $[\alpha]^{25}D$ +51.77° (*c* 3.46, $CHCl_3$), $[\alpha]^{25}D$ +96.69° (*c* 3.46, $CHCl_3$), $[\alpha]^{25}_{350}$ +187.82° (*c* 3.46, $CHCl_3$), $n^{25}D$ 1.4570, d^{25}_4 1.0301. Vapor phase chromatography on a column of polyethylene glycol succinate at 190° indicated 100% purity, retention time 23 min.

Anal. Calcd for $C_7H_{12}O_2$: C, 65.59; H, 9.44; [M]D, 33.99°. Found: C, 65.63; H, 9.27; [M]D, 33.89.

The infrared spectrum was identical with that of *dl*-γ-methyl-ε-caprolactone. Ultraviolet analysis in heptane showed weak absorption at λ_{max} 220 ± 1 mμ (ε 61.0), and very strong absorption below 179 mμ (ε 3020).

15. (*R*)-(−)-β-Methyl-ε-caprolactone (XIV). The same procedure as used for (*R*)-(+)-γ-methyl-ε-caprolactone was used. From (*R*)-(+)-6-hydroxy-3-methylhexanoic acid ($n^{25}D$ 1.4570, hydroxy acid by titration 89.5%, 16.0 g (0.109 mole)) in 8 l. of methylene chloride, 300 g of 4A molecular sieves, and 40 g (1.11 moles) of anhydrous hydrogen chloride was obtained 8.3 g (59.2%) of crude (*R*)-(−)-β-methyl-ε-caprolactone, bp 58–59° (0.5 mm), which vapor phase chromatography on a column of polyethylene glycol succinate at 199° indicated to be 97.5% (*R*)-(−)-β-methyl-ε-caprolactone, retention time 17 min, and 2.5% of an unidentified impurity with a retention time of 6 min. Six grams of this material was purified by being passed through a preparative vapor phase polyethylene glycol succinate column at 200° in 0.5-ml portions and the pure product collected in a tube equipped with a rubber serum cap and a calcium chloride drying tube at −78° followed by distillation through a microdistillation unit, giving 5 g of pure (*R*)-(−)-β-methyl-ε-caprolactone, bp 55° (0.2 mm), $[\alpha]^{25}D$ −32.18° (*c* 1.24, $CHCl_3$), $[\alpha]^{25}_{450}$ −59.84° (*c* 1.24, $CHCl_3$), $[\alpha]^{25}_{350}$ −113.51° (*c* 1.24, $CHCl_3$), $n^{25}D$ 1.4583, d^{25}_4 1.0334. Vapor phase chromatography on a column of polyethylene glycol succinate at 190° indicated 100% purity, retention time 20.8 min.

Anal. Calcd for $C_7H_{12}O_2$: C, 65.59; H, 9.44; [M]D, 33.99°. Found: C, 65.56; H, 9.28; [M]D, 33.90°.

The infrared spectrum indicated strong carbonyl absorption at 1740 cm^{-1} and ether oxygen absorption at 1168 cm^{-1} indicative of a lactone.

The ultraviolet spectrum in heptane showed a peak, λ_{max} 222 ± 1 mμ (ε 62.8), and a very strong peak below 179 mμ (ε 3020). In trifluoroethanol two peaks were observed, λ_{max} 209 ± 1 mμ (ε 107.5) and λ_{max} 181.5 ± 1 mμ (ε 3717), corresponding to the n–π_3* and π–π_3* transitions, respectively.

Nuclear magnetic resonance indicated the methyl doublet at δ 0.94 ppm, the methylene multiplet at δ 1.72 ppm, the α-proton doublet at δ 2.57 ppm, and the ε-proton triplet at δ 4.12 ppm, consistent with the structure for (*R*)-(−)-β-methyl-ε-caprolactone.

(43) P. S. Starcher and B. Phillips, German Patent 1,086,686 (Aug 11, 1962); *Chem. Abstr.*, **56**, 46240 (1962).