The Stereochemistry of the Decarboxylation of β-Lactones to Form Olefins[1,2]

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The decarboxylation of β-lactones to olefins is shown to be a stereospecific *cis* elimination. *threo*-α-Methyl-β-bromo-β-(*p*-chlorophenyl)propionic acid has been stereoselectively converted to a mixture of *cis*-α-methyl-β-(*p*-chlorophenyl)-β-propiolactone (6) and *cis*-1-(*p*-chlorophenyl)propene (4). In water at pH 6.2, 75% of lactone 6 undergoes decarboxylation to give pure 4; the remainder adds water stereospecifically with inversion to give *threo*-α-methyl-β-hydroxy-β-(*p*-chlorophenyl)propionic acid. Similar results have been obtained with the *trans* isomers.

The recent reviews of the chemistry of β-lactones, by Zaugg[3] and by Etienne and Fischer,[4] point out the general instability of this class of compounds, and a variety of reactions which they may undergo. The thermal decomposition to give carbon dioxide and an alkene has been observed in several instances. The transitory formation of the β-lactone of β-hydroxy-β-phenylpropionic acid was first proposed by Erlenmeyer[5] in 1880 to account for the formation of styrene from alkaline solutions of β-bromo-β-phenylpropionic acid. Senter and Ward[6] similarly proposed the transitory existence of the β-lactone to explain the results of the treatment of the bromo acid with ammonia. The preparation of β-lactones is often accompanied by the formation of olefins, but it is not clear in which instances the olefin is a subsequent decomposition product of the β-lactone and in which instances it is the direct product of the synchronous loss of hydrogen bromide and carbon dioxide.

It is reported by Einhorn[7] that the β-lactone derived from β-bromo-β-(*o*-nitrophenyl)propionic acid decomposes in boiling water to *o*-nitrostyrene and carbon dioxide.

Though the stereochemistry of the decomposition of β-bromo acids to olefins has been admirably elucidated by Cristol and Norris[8] and by Grovenstein and Lee,[9] there is little information bearing on the stereochemistry of the decarboxylation of β-lactones to olefins.

Bartlett and Liang[10] have shown that the major products (63%) from the decomposition in aqueous solution of β-methyl-β-hydroxybutyric acid β-lactone are isobutylene and carbon dioxide; the minor product (37%) is the hydroxy acid.

Thermal decomposition of the β-lactones from 5-hydroxy-6-carboxy B-nor steroids takes place smoothly around 150°.[11-13]

Similar decompositions of the β-lactones derived from 5-hydroxycamphoric acid[14] and 5-hydroxyisofenchocamphoric acid[15] were observed by Toivonen[14] and his co-workers and by Hirsjarvi.[15] These reactions are necessarily *cis* decompositions, but whether this decarboxylation is a general *cis* elimination remains an open question.

As we were interested in the stereochemistry of this decarboxylation in connection with other studies regarding the mechanism of the synchronous decarboxylation and dehydration of β-hydroxy acids,[16,17] we have undertaken an investigation of the stereochemical nature of the decomposition of β-lactones. The system chosen for study was the pair of lactones derived from the two stereoisomers of α-methyl-β-hydroxy-β-(*p*-chlorophenyl)propionic acid. The choice of this particular system was dictated by several considerations: the α-methyl group is necessary to afford the possibility of *cis* and *trans* isomers in the resulting propenylbenzene; the *p*-chlorophenyl moiety was chosen to give a desired balance of reactivity and stability, as well as close relationship to other compounds for which additional kinetic and mechanistic data were available. Additionally this system is uniquely suitable for determination of stereochemistry through use of magnetic resonance spectroscopy.

Results and Discussion

The method of synthesis is outlined in Chart I; α-methyl-*p*-chlorocinnamic acid (1) was prepared by the Reformatsky reaction. Previous workers have assigned the *trans* configuration to the isomer, mp 166–167°.[18,19]

Confirmation for this assignment comes from the nmr spectrum of the ethyl ester. The peak at τ 7.94 is split into a doublet (J = 1.5 cps) by long-range coupling of the methyl group with the *trans*-β hydrogen. For this type of spin–spin interaction Jackman[20] cites values of 0.5–2.0 cps. A similar coupling constant (J = 1.5 cps) is observed in the spectrum of *cis*-1-(*p*-chlorophenyl)propene (4) but is completely absent in the spectrum of the *trans* isomer (5).

Addition of hydrogen bromide in acetic acid to 1 gave largely a single stereoisomer of α-methyl-β-bromo-β-(*p*-chlorophenyl)propionic acid (2), as shown by the sharp melting point of the product after a single crystallization, and by the nmr spectrum of the methyl

(1) Previous paper: D. S. Noyce, S. K. Brauman, and F. B. Kirby, *J. Am. Chem. Soc.*, **87**, 4335 (1965).

(2) Supported in part by a grant from the National Science Foundation, G.P. 1572.

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(5) H. Erlenmeyer, *Ber.*, **13**, 303 (1880).

(6) G. Senter and A. M. Ward, *J. Chem. Soc.*, **127**, 1847 (1925).

(7) A. Einhorn, *Ber.*, **16**, 2208 (1883).

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(9) E. Grovenstein, Jr., and D. E. Lee, *ibid.*, **75**, 2639 (1953).

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(15) P. Hirsjarvi, *Chem. Abstr.*, **48**, 651 (1954).

(16) D. S. Noyce and R. A. Heller, *J. Am. Chem. Soc.*, **87**, 4325 (1965); D. S. Noyce, P. A. King, and G. L. Woo, *J. Org. Chem.*, **26**, 624 (1961).

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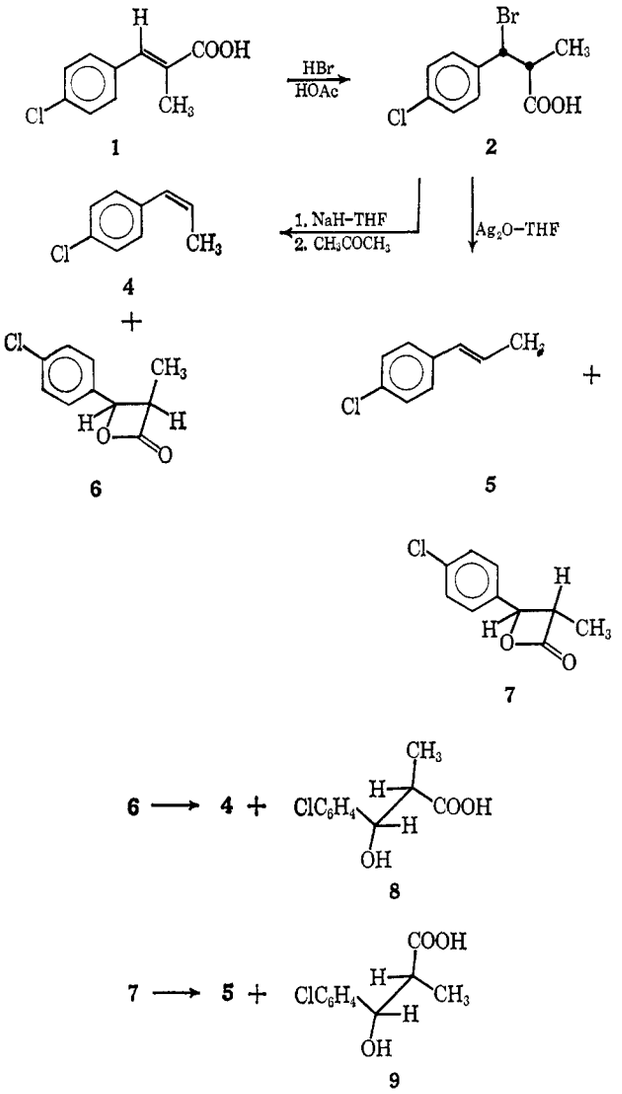
(19) N. L. Wehrmeister, *J. Org. Chem.*, **27**, 4418 (1962).

(20) L. M. Jackman, "Nuclear Magnetic Resonance Spectroscopy," Pergamon Press Ltd., Oxford, 1959, p 85.

CHART I



ester (**3**). Examination of the nmr spectrum of the methyl ester (**3**) allows the assignment of the *threo* configuration to **2**. Most pertinent is the large coupling constant (J = 10.5 cps) between the α and β hydrogens. This value is consistent with the results of Canciell, Basselier, and Jacques[21] on both epimers of α-methyl-β-hydroxy-β-arylpropionic acid derivatives as well as results of Brauman[22] on similar compounds. Further, the recent careful studies of Vaughan and Caple[23] on the stereochemistry of the addition of hydrogen bromide in acetic acid to several α,β-unsaturated acids are likewise in accord with this configurational assignment. They conclude that the initially formed product is isomerized under the reaction conditions to give the thermodynamically more favored configuration, *i.e.*, the net result is often an apparent *cis* addition to the double bond. Finally the observed behavior of the acid **2** upon conversion to β-lactones is in accord with this configurational assignment.

Treatment of bromo acid **2** with sodium hydride in dry tetrahydrofuran, followed by isolation of the sodium salt and reaction in dry acetone stereoselectively produced only *cis*-β-lactone (**6**) and *cis*-1-(*p*-chlorophenyl)propene. The composition of this mixture as determined by nmr analysis (comparison of methyl peak areas) was 12.4% lactone and 87.6% propene.

Alternatively, treatment of bromo acid **2** with anhydrous silver oxide in dry tetrahydrofuran produced the corresponding *trans* isomers. In this case the product distribution was 17.8% *trans*-β-lactone (**7**) and 77.3% *trans*-1-(*p*-chlorophenyl)propene (**5**). The remaining 4.9% was shown to be **4**, but no *cis*-β-lactone could be detected.

Attempts at separation of this mixture by vapor phase chromatography and by column chromatography were unsuccessful as the lactone did not survive under the conditions used.

For the purpose of this study, pure samples of the β-lactones are not required, although such sample would have been desirable. The β-lactones were therefore used as components of mixtures as the relative proportion and identity of the contaminants were easily established.

The corresponding propenes, **4** and **5**, were also clearly recognizable by their nmr spectra. In *trans*-propene **5**, the methyl protons appear as a simple doublet at τ 8.13 (J = 5 cps), while the 1 and 2 protons appear as a multiplet at 3.7–4.2. The methyl protons of *cis*-propene **4** appear as a doublet (J = 7 cps) centered at τ 8.16. However, each peak of the doublet is split once again (J = 1.5 cps) by long-range coupling with the 1 proton across the double bond. Furthermore, the complex multiplet at τ 3.4–4.4 due to 1 and 2 protons can easily be resolved into two sets of quartets. One set (τ 3.55 and 3.76, J = 1.5 cps) is assigned to the 1 proton while the other set (τ 4.18 and 4.38, J = 7 cps) clearly is due to the 2 proton.

Assignment of configuration to the β-lactones was made on the basis of their nmr spectra. In both compounds the methyl protons appear as a doublet, J = 7.5 cps. The doublet appears at a normal τ 8.51 in the case of *trans*-β-lactone **7**. However the methyl protons of *cis*-β-lactone **6** experience significant shielding by the adjacent aromatic ring; the doublet is consequently shifted upfield and is observed at τ 9.11. Similar examples of such shielding effects in both three- and five-membered ring compounds are well documented. Closs and Moss[24] have used exactly the same shielding phenomenon to assign configurations for various *cis*- and *trans*-1-phenyl-2,3-dimethylcyclopropanes. Resonances for methyl groups *cis* to the aromatic ring were shifted upfield by 0.43 ppm relative to methyl groups *trans* to the aromatic ring. Curtin and Gruen[25] similarly observed that the tertiary protons in *trans*-1,2-diphenylcyclopentane appear at τ 7.11 while tertiary protons of the *cis* isomer (no shielding) appear at τ 6.71.

The reaction of *cis*-β-lactone **6** in buffer solution (pH 6.2) either at 25 or 100° appears to be completely stereospecific. Approximately 75% of this lactone decarboxylates with retention of configuration to give the *cis*-propene **4**. The remaining 25% of *cis*-lactone adds the elements of water to give *threo*-hydroxy acid (**8**). This corresponds to stereospecific "backside" nucleophilic attack by water on the β-carbon atom.

(21) J. Canciell, J. Basselier, and J. Jacques, *Bull. Soc. Chim. France*, 1906 (1963).

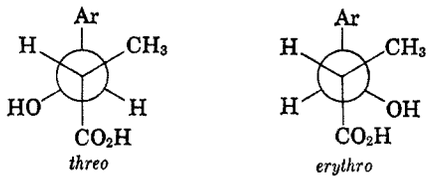
(22) D. S. Noyce and S. L. K. Brauman, unpublished observations; *cf.* S. L. Kruse, Dissertation, University of California at Berkeley, 1965.

(23) W. R. Vaughan and R. Caple, *J. Am. Chem. Soc.*, **86**, 4928 (1964).

(24) G. L. Closs and R. A. Moss, *ibid.*, **86**, 4042 (1964).

(25) D. Y. Curtin and H. Gruen, *Chem. Ind.* (London), 1205 (1958).

None of the diastereoisomeric *erythro*-hydroxy acid (**9**) was formed. The configuration of **8** was established by conversion to the methyl ester (**10**) and examination of the nmr spectrum. In the spectrum of **10** the signal for the β hydrogen (at τ 5.37) was a doublet (J = 8.5 cps) characteristic of the *threo* configuration, as shown by the work of Canciell, Basselier, and Jacques[21] and extended by Brauman.[22]



Similarly, the reaction of *trans*-β-lactone **7** in buffer solution (pH 6.2) either at 25 or 100° appears to be highly stereoselective. Approximately 80% of the *trans*-lactone decarboxylates with retention of configuration to give pure *trans*-propene **5**. The remaining 20% of *trans*-lactone is converted to hydroxy acid. Nmr analysis showed that most of this product consisted of *erythro*-hydroxy acid **9**, but some of the *threo* diastereoisomer is also present. Although the latter result is not so clean-cut as in the *cis* series, the pattern of reaction is clearly the same in both series.

The reaction of *cis*-lactone **6** in buffer solution has been shown to be completely stereospecific. Only *cis*-propene and *threo*-hydroxy acid are produced. Therefore the sequence *threo*-bromo acid **2** → *cis*-β-lactone **6** → *threo*-hydroxy acid **8** leads to over-all retention of configuration with inversion occurring at each step. This result means that the dipolar ion resulting from initial alkyl oxygen cleavage in the β-lactone is indeed best represented by the "intimate ion-pair" envisaged by Bartlett and Liang.[10]

Although the results in the *trans* series are not completely stereospecific, the over-all pattern of reaction is clearly the same as in the *cis* series. The products from **7** are *trans*-propene **5** and *erythro*-hydroxy acid **9** (and minor amounts of the *threo* isomer). The sequence *threo*-bromo acid **2** → *trans*-β-lactone **7** → *erythro*-hydroxy acid **9** leads to net inversion of configuration, a result expected for a single SN2-type displacement.

An attractive possibility for Bartlett's "ion-pair" is an unsymmetrically solvated dipolar ion. In such a species, water molecules may solvate the partially positive β-carbon atom only from the "backside," since the "frontside" is effectively shielded by the negatively charged carboxylate group. If this species collapses with loss of carbon dioxide, the olefin which results must retain the stereochemistry of the lactone. On the other hand, if this species collapses by reaction with water, the resulting β-hydroxy acid must be inverted at the β-carbon atom. Such a picture of the initially formed dipolar ion is completely concordant with the results obtained in the present work.

Experimental Section[26]

α-Methyl-*p*-chlorocinnamic Acid (1).—Ethyl α-methyl-β-hydroxy-β-(*p*-chlorophenyl)propionate was prepared by a Reformatsky reaction from 117 g of redistilled *p*-chlorobenzaldehyde, 163 g of ethyl α-bromopropionate, and 58.9 g of zinc foil in a total of 800 ml of benzene. The crude hydroxy ester in 400 ml of benzene was heated under reflux for 5 hr with 153 g of phosphorus oxychloride to accomplish dehydration and the crude unsaturated ester isolated as an orange-brown oil.

To the crude ester was added 250 ml of ethanol and a solution of 80 g (2 moles) of sodium hydroxide in 300 ml of water, and the mixture was heated under reflux for 8 hr. Most of the ethanol was then removed by distillation and enough water was added to give a clear solution. Several ether washings removed most of the dark color. A honey-colored solid separated upon acidification and was collected by suction filtration. It was washed with cold water and dried overnight in a vacuum desiccator. Pure α-methyl-*p*-chlorocinnamic acid was obtained as broad, heavy, white spears from this solid by two recrystallizations from toluene followed by a third recrystallization from ethanol–water. After drying overnight at 78° (0.3 mm) the acid melted sharply at 167–168° (lit.[18,19] mp 166–167°, 163°) and weighed 101 g (61.6% over-all yield based on *p*-chlorobenzaldehyde): λ_{max}^{EtOH} 272 mμ (ε 21,200) [lit.[27] λ_{max}^{EtOH} 273 mμ (ε 19,400)].

A sample of pure **1** was reconverted to the ethyl ester by refluxing the acid for 24 hr in 30% ethanolic benzene containing a few drops of concentrated sulfuric acid. A Dean–Stark water separator was used to continuously remove water. The mixture was then concentrated to one-half its original volume, cooled, and washed with sodium carbonate solution. After remaining benzene had been distilled off, the crude ester was purified by distillation: bp 93–94° (0.06 mm) [lit.[27] bp 175–180° (20 mm)]; $n^{25}D$ 1.5611; λ_{max}^{EtOH} 273 mμ (ε 21,100). Signals in the nmr spectrum appeared at τ 2.50 (quartet, J = 1.5 cps), 2.73 (singlet), 5.80 (quartet, J = 7 cps), 7.94 (doublet, J = 1.5 cps), and 8.68 (triplet, J = 7 cps). Relative areas of these peaks were 0.8:4.1:2.0:3.0:3.1.

α-Methyl-β-bromo-β-(*p*-chlorophenyl)propionic Acid (2).—Finely pulverized *trans*-α-methyl-*p*-chlorocinnamic acid (11.8 g, 60 mmoles) was placed in a heavy-walled reaction tube (200-ml capacity). Approximately 150 ml of glacial acetic acid was saturated at 0° with hydrogen bromide from a tank and quickly added to the tube. After the contents had been frozen in a Dry Ice–methylene chloride mixture, the tube was sealed in the usual fashion. It was then warmed to room temperature and transferred to an oil bath at 50°. The temperature of the bath was raised rapidly to 100° and maintained at 100–105°. (Higher temperatures result in charring and decomposition of the solution.) After 4 hr at this temperature, the bath was turned off and allowed to cool overnight.

The reaction tube was removed from the bath and opened, and the contents were poured over cracked ice. An ivory solid which separated was collected by suction filtration, washed several times with cold water, and taken up in ether. Last traces of acetic acid were removed by washing the ethereal solution several times with water and brine. After drying over sodium sulfate the ether was evaporated to give crude, off-white bromo acid **2**. A single recrystallization from benzene–cyclohexane, followed by drying overnight at 78° (0.3 mm) gave 8.85 g (53%) of pure, white bromo acid, mp 190–192°. Characteristic peaks in the infrared spectrum (Nujol) appeared at 5.85, 6.72, 9.17, 12.05, and 13.79 μ; λ_{max}^{EtOH} 232 mμ (ε 10,500).

Several recrystallizations from benzene–cyclohexane provided an analytical sample, mp 190–191°. It was dried (78°, 0.3 mm) and submitted for analysis; sublimation was found to cause decomposition of the bromo acid.

Anal. Calcd for $C_{10}H_{10}BrClO_2$: C, 43.25; H, 3.63; Br, 28.80; Cl, 12.77. Found: C, 43.08; H, 3.76; Br, 28.58; Cl, 12.64.

Methyl α-methyl-β-bromo-β-(*p*-chlorophenyl)propionate (3) was prepared from **2** (2.78 mg) by treatment with a slight excess of diazomethane in ether. Excess diazomethane was removed in the cold with a rotary evaporator. Evaporation of the ether

(26) All melting points were taken on a Kofler micro hot stage and are uncorrected. Analyses were performed by the Microanalytical Laboratory, University of California at Berkeley. An Aerograph gas chromatograph, Model A-90-P, equipped with either a silicone oil column (20% SF-96, 60–80 firebrick, 15 ft × 3/8 in.) or a Carbowax column (20% Carbowax 20M Chromosorb W, 5 ft × 0.25 in.) was used for vapor phase separations. Helium was used as the carrier gas in all cases. Infrared spectra were measured on a Perkin-Elmer Infracord, Model 137; ultraviolet spectra were obtained on a Cary Model 11 spectrophotometer. All nmr spectra were taken on a Varian Associates A-60 spectrometer using carbon tetrachloride solutions.

(27) A. Psarrea, C. Sandris, and G. Tsatsas, *Bull. Soc. Chim. France*, 2145 (1961).

afforded a viscous, colorless oil which solidified on cooling and rubbing. Recrystallization from ethanol–water gave white crystals of **3**, mp 41–43°. The infrared spectrum (chloroform) exhibited characteristic peaks at 5.75, 6.24, 6.72, 7.30, 8.60, 9.13, and 12.05 μ. Signals in the nmr spectrum appeared at τ 2.72 (singlet), 5.02 (doublet, J = 10.5 cps), 6.27 (singlet), 6.5–7.2 (multiplet), and 9.02 (doublet, J = 7.0 cps). The relative areas of these signals were 4:1:3:1:3.

cis-**1-(*p*-Chlorophenyl)propene (4) and** *trans*-**1-(*p*-Chlorophenyl)propene (5).**—To a vigorously stirred, cooled solution of 2.0 g of sodium bicarbonate in 100 ml of water was added 5.73 g of bromo acid **2**. After 45 min, chloroform (75 ml) was added and stirring was continued for 6 hr. The layers were separated, and the aqueous layer was extracted with an additional portion of chloroform. The dried chloroform layer was evaporated at room temperature, and the residue (3.9 g) was examined. It showed a strong carbonyl absorption at 5.45 μ, which is characteristic of β-lactones.[28] On a Carbowax column at 155° the effluent, however, showed no 5.45-μ band. The two major peaks (retention times 9 and 12 min, respectively) were collected together and analyzed.

Anal. Calcd for C_9H_9Cl: C, 70.81; H, 5.95; Cl, 23.25. Found: C, 70.94; H, 5.93; Cl, 23.52.

Each component was then collected separately from the vpc. Spectral information obtained from these individual samples indicates that the more volatile component (A) is *cis*-1-(*p*-chlorophenyl)propene (**4**) while the less volatile and major component (B) is the corresponding *trans* isomer (**5**).

Component A, *cis*-**Propene (4).**—Characteristic peaks in the infrared appear at 6.24, 6.72, 7.33, 9.18, 9.87, and 11.85 μ; ultraviolet λ_{max}^{EtOH} 247 mμ (ϵ 16,800). Signals in the nmr spectrum appear at τ 2.82 (doublet, J = 1.5 cps), 3.5–4.5 (multiplet), and 8.16 (doublet, J = 7 cps; each peak of the doublet is split once more, J = 1.5 cps). The relative areas of these three groups of peaks are 4.2:1.9:3.0. It is possible to resolve the τ 3.4–4.5 multiplet into four quartets. Two of these quartets have J = 1.5 cps and are centered at τ 3.55 and 3.76. The remaining two quartets are centered at τ 4.18 and 4.38 (J = 7 cps).

Component B, *trans*-**Propene (5).**—Characteristic peaks in the infrared spectrum appear at 6.24, 6.72, 7.30, 9.18, 9.88, 10.36, and 11.85 μ; ultraviolet λ_{max}^{EtOH} 255 mμ (ϵ 21,800). Signals in the nmr spectrum appear at τ 2.83 (singlet), 3.7–4.2 (multiplet), and 8.13 (doublet, J = 5 cps) with relative areas of 4.3:1.9:3.0.

α-Methyl-β-(*p*-chlorophenyl)-β-propiolactone. A. Sodium Hydride Method. *cis*-**β-(*p*-Chlorophenyl)-α-methyl-β-propiolactone (6).**—A 100-ml, round-bottomed flask containing a magnetic stirring bar was flushed out with dry nitrogen. Enough sodium hydride (50% dispersion in mineral oil) was weighed out into the flask to give 5 mmoles of active hydride. The sodium hydride was quickly covered with 20 ml of anhydrous tetrahydrofuran (dried over potassium hydroxide and freshly distilled from lithium aluminum hydride), and the flask was closed with a fitting which bore a rubber serum cap and a calcium chloride drying tube.

Bromo acid **2** (1.806 g, 6.5 mmoles) was weighed out in a separate flask and dissolved in 40 ml of dry tetrahydrofuran. The resulting clear, colorless solution was injected with a syringe into the stirred suspension of sodium hydride. Another 20 ml of dry tetrahydrofuran was added to keep the heavy white suspension which formed mobile enough to stir. After the suspension had been stirred vigorously at room temperature for 2 hr, the white bromo acid sodium salt was collected with suction on a finely fritted glass funnel. Excess bromo acid was recovered from the filtrate.

The white sodium salt was transferred to a new 100-ml, round-bottomed flask. After 60 ml of anhydrous acetone (dried over potassium carbonate and distilled from phosphorus pentoxide) had been added, the flask was closed with a drying tube and the contents were stirred at room temperature for 2–3 hr. During this time the suspension became thinner in consistency and paler in color. The suspension was filtered with suction through a finely fritted funnel to remove most of the white solid (NaBr). A small amount of sodium bromide is dissolved by acetone and was removed by evaporating acetone from the filtrate, replacing it with dry pentane, and refiltering. Evaporation of the pentane afforded 765 mg of a clear, colorless oil.

This oil exhibited the strong, characteristic carbonyl absorption of β-lactones at 5.45 μ. In all other respects the spectrum was similar to that of *cis*-propene **4** and lacked completely the intense band at 10.35 μ which is due to *trans*-propene **5**. The nmr spectrum showed all the peaks of **4**; in addition a doublet (J = 7.5 cps) appeared at τ 9.11. This doublet can be assigned to the α-methyl group of *cis*-β-lactone. (The other peaks of **6** are mixed with those of **4** at τ 2.82, and 3.5–4.5.) It is shifted upfield relative to the α-methyl of the *trans*-lactone (*vide infra*) due to the shielding effect of the adjacent aromatic ring. Comparison of the integrated area of the α-methyl signal of **4** to that of the *cis*-β-lactone signal indicates that the mixture is composed of 87.6% **4** and 12.4% *cis*-lactone (**6**).

A vapor phase chromatogram of this oil using the Carbowax column revealed a single, sharp peak with a retention time of 9 min (**4**). A trace of *trans*-propene **5** was noted, but amounted to no more than 0.2% of the total by integration.

B. Silver Oxide Method. *trans*-**β-(*p*-Chlorophenyl)-α-methyl-β-propiolactone (7).**—The silver oxide procedure described here is patterned after the work of Westfahl and Gresham[29] and Kandiash[30] who used it in special cases to successfully synthesize β-lactones.

A magnetic stirring bar, 200 mg of silica gel, 20 ml of anhydrous tetrahydrofuran, and 580 mg (2.5 mmoles) of anhydrous silver oxide (prepared as described by Westfahl and Gresham[29]) were placed in a 100-ml, round-bottom flask. A solution of bromo acid **2** (1.388 g, 5 mmoles) in 20 ml of anhydrous tetrahydrofuran was added, and after the flask had been closed with a calcium chloride drying tube, the mixture was stirred overnight at room temperature. Solids were removed by filtration; evaporation of the clear filtrate and removal of last traces of solvent under reduced pressure provided 900 mg of a clear, colorless oil which possessed a distinctive licorice-like odor.

An infrared spectrum (chloroform) of this oil exhibited the strong, characteristic carbonyl absorption of β-lactones at 5.45 μ. The intense bands characteristic of **5** were also present. The nmr spectrum was similar to that of pure **5** except that in addition a new singlet appeared at τ 2.68 and a new doublet (J = 7.5 cps) appeared at 8.51. No peaks were observed in the τ 9.1 region (*cis*-lactone). The doublet at τ 8.51 is assigned to the α-methyl group of *trans*-lactone **7**. The new peak at τ 2.68 is no doubt due to the four aromatic protons of *trans*-lactone. Comparison of the integrated areas of the methyl signal of **5** to that of the *trans*-lactone α-methyl signal indicated the mixture was composed of 82.2% propene **5** and 17.8% *trans*-lactone **7**.

A vapor phase chromatogram of this oil using the Carbowax column revealed a sharp, major peak corresponding in retention time to **5** (12 min). Several minor peaks were also noted. The largest of these correspond in retention time to *cis*-propene **4**. The ratio of **5** to **4** is 94:6.

Combination of the information obtained by nmr and vpc analyses reveals that the oily product of this reaction consists of 17.8% *trans*-β-lactone, 77.3% *trans*-propene **5**, and 4.9% *cis*-propene **4**.

Decarboxylation of *cis*-**β-Lactone 6.**—The mixture of 12.4% *cis*-lactone and 87.6% *cis*-propene (**4**) as prepared above was decarboxylated by addition to boiling buffer solution at pH 6.2. A 500-ml, three-necked, round-bottomed flask was flushed with nitrogen, 150 ml of citrate buffer of pH 6.2 was introduced, and the solution was heated to boiling. After distillation had begun, the lactone–propene mixture (225 mg in 7 ml of methanol) was injected slowly beneath the surface of the boiling liquid at such a rate that the distillation rate was not altered. The pot solution became very cloudy, but cleared as the organic material steam distilled. Additional water was added as necessary in order to maintain a fairly constant level in the flask. After approximately 75 ml of distillate had been collected, the distillation was halted. The pot solution was immediately poured over cracked ice.

Volatile organic material was isolated by extracting the steam distillate with two 20-ml portions of clean pentane. The extracts were combined, dried (sodium sulfate), filtered, and saved for vpc analysis.

The cold buffer solution was extracted first with two 100-ml portions of clean pentane to remove any hydrocarbons. Evaporation of the dried pentane extracts left no residue (less than 1 mg).

(28) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, p 188.

(29) J. C. Westfahl and T. L. Gresham, *J. Org. Chem.*, **21**, 1145 (1956).

(30) A. Kandiash, *J. Chem. Soc.*, 1215 (1932).

The buffer solution was next acidified with hydrochloric acid to pH 1 and extracted two times with 80-ml portions of clean ether. The combined ether extracts were dried, filtered, and saved.

A second sample of **6** (226 mg) was decarboxylated in a similar fashion, except that it was introduced into the aqueous buffer solution at room temperature. After 1 hr the mixture was steam distilled.

A third sample (721 mg) was introduced into 330 ml of buffer solution at room temperature. After 3 hr steam distillation was carried out.

Vpc Analysis of Steam Distillates.—The dried pentane extracts were examined directly on a Carbowax column. All three samples gave the same chromatogram. A single, sharp peak corresponding in retention time to *cis*-propene was observed. A trace peak corresponding in retention time to *trans*-propene was also observed, but it was no larger than in the freshly prepared *cis*-propene *cis*-lactone mixture; *i.e.*, it amounted to no more than 0.2% of the total.

Examination of the Ether Extracts.—The ether extracts from the first sample yielded 13.8 mg of clear, viscous oil which was a mixture of citric acid and α-methyl-β-hydroxy-β-(*p*-chlorophenyl)propionic acid. The ether extracts of the third sample yielded a total of 47 mg of a clear, viscous oil. This oil was dissolved in 10 ml of ether and treated with ethereal diazomethane until the yellow color persisted. Evaporation of the ether from the methylated residual oil afforded a new, highly viscous oil, readily soluble in carbon tetrachloride. The nmr spectrum of this oil showed peaks at τ 2.77 (singlet, ArH), 5.37 (doublet, J = 8.5 cps, β-H), 6.38 (singlet, OMe), *ca.* 7.10 (multiplet, α-H), and 9.04 (doublet, J = 7 cps, α-Me). Both the position of the methyl ester peak, and the coupling constant for the β hydrogen support the assignment of the *threo* configuration to this material. In addition the spectrum showed the four sharp peaks characteristic of methyl citrate at τ 6.23, 6.36, 6.72, and 7.27. By integration of the relative areas of the peaks assigned to **10** and to methyl citrate, the composition of the mixture was determined to be 56% **10** and 44% methyl citrate. Thus of the lactone originally present, 25% was converted to the hydroxy acid **8**. This value is obviously subject to some uncertainty.

Decarboxylation of *trans*-β-Lactone 7.—Two samples of the mixture of 17.8% *trans*-lactone (**7**), 77.3% *trans*-propene, and 4.9% *cis*-propene were decarboxylated under similar conditions to those used for the *cis*-lactone. Sample A (383 mg) was decarboxylated by addition (in 10 ml of methanol) to boiling buffer solution. Sample B (367 mg) was decarboxylated by adding to buffer solution at room temperature. After stirring for 1.5 hr at room temperature, the mixture was heated, and volatile organic material was allowed to steam distil as before.

Isolation procedures were as described above. The ether extracts of the two experiments were combined.

The pentane extracts of the steam distillates were examined by vpc. The distillate from sample A showed 93% *trans*-propene and 7% *cis*-propane. The distillate from fraction B showed 94% *trans*-propene and 6% *cis*-propene. These values are in good agreement with the composition of the propene fraction before the decarboxylation (94% *trans*-propene and 6% *cis*-propene).

Examination of the Ether Extracts.—The combined ether extracts were concentrated to yield a clear, viscous oil (46 mg). This oil was converted to methyl esters with diazomethane. Examination of the nmr spectrum showed 67% methyl hydroxy ester and 33% methyl citrate. The peaks in the nmr at τ 8.93 (doublet, J = 7 cps) and at 5.01 (doublet, J = 4 cps) were assigned to the *erythro* isomer of methyl α-methyl-β-hydroxy-β-(*p*-(chlorophenyl)propionate (**11**) in analogy to the results of Canciell, Basselier, and Jacques[21] and Brauman.[22] In addition to the peaks for the *erythro* isomer, the doublet for the methyl ester of the *threo* isomer, centered at τ 9.02 (J = 7 cps) was observed. The estimated composition was 40% *erythro* isomer and 27% *threo* isomer. Further, from the weight of lactone taken (133 mg) it may therefore be calculated that 20% of the *trans* lactone was converted to the epimeric α-methyl-β-hydroxy-β-(*p*-chlorophenyl)propionic acids.

Solvent Effects in Nuclear Magnetic Resonance. VI. Conformations of Substituted Cyclohexanones[1]

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Cyclohexanones and tetrahydropyranones, methyl substituted in the β (and γ) position, relative to the carbonyl, give rise to benzene-induced chemical shifts of the order of 22 (equatorial methyl) and 12 cps (axial methyl), differing much less than the previously determined values at the α position, 16 (axial methyl) and −5 cps (equatorial CH_3), carbon tetrachloride being the reference solvent. Nevertheless, the present results are consistent with strong deformations, into a flattened chair or twisted chair conformation, for both molecules **8** and **14**, as well as for **13**. Mixing curves of ketones with benzene are presented and emphasize the need of a careful control of concentration in such conformational studies.

In addition to the accepted use of intramolecular chemical shifts (*e.g.*, *via* the Zürcher rules[3] in the steroid field) another extremely useful technique of nmr spectroscopy has been developed recently:[1,4-8] the chemical shift for some group in a solute can be induced to vary by a change in solvent, and these variations in turn can be related to the structure of the solute. For instance the comparison between the spectrum of a polycyclic ketone as a solute either in a reference solvent ($CDCl_3$ or CCl_4) or in an aromatic solvent (C_6H_6,[4,5] C_6H_5N,[6] or C_4H_4O[7]) affords incremental shifts[8] characteristic of the spatial relationship of the corresponding protons with respect to the carbonyl grouping. When the molecule contains several such C=O groups, the shifts are quite additive.[5]

It is the purpose of the present article to present such measurements on the monocyclic cyclohexanone itself, methyl-substituted in the α, β, and γ positions, therefore enlarging the scope of the previous observations. The Δ variations are believed to be generated by conformational changes since the results are self-coherent within series of compounds. However, it should be pointed out that these Δ variations also depend upon the ease of formation of the postu-

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(4) Reference 3b, Chapter 7.

(5) N. S. Bhacca and D. H. Williams, *Tetrahedron Letters*, 3127 (1964); D. H. Williams and N. S. Bhacca, *Tetrahedron*, **21**, 1641 (1965).

(6) D. H. Williams, *Tetrahedron Letters*, 2305 (1965).

(7) D. H. Williams, private communication.

(8) The notation, $\Delta^{CCl_4}_{C_6H_6}$, etc., will be used, as previously defined.[1]