

do not fall very well along the expected line; adsorption of the *m*-nitrophenol may occur, causing the intercept, M/M_0 , to be greater than unity. 2,4-Dinitrophenol was found to be essentially an ideal solute over the small range studied. The chelation in this compound undoubtedly accounts for its difference in behavior compared to *p*-nitrophenol.

Calculation of Equilibrium Constants.—The mean polymerization number, \bar{n} , was found to be a linear function of the concentration, m , for all of the solutes examined. Thus, $\bar{n} = M_0/M = 1 + \alpha m$, where α is a constant. Now Lassette⁷ found that a unique set of equilibrium constants K_L for the formation of polymers would account for this behavior, where L was the order of the individual polymer.

$$K_L = \frac{(\alpha L)^{L-1}}{L!}$$

The equilibrium constant for the dimer ($L = 2$) turns out to be $K_2 = \alpha$. This quantity has been calculated from the author's own data and also

TABLE IX

EQUILIBRIUM CONSTANTS FOR FORMATION OF DIMERS FOR VARIOUS PHENOLS

Solute	$K_2 = \alpha$	Workers
<i>o</i> -Cresol	1.1	This investigation
	0.28	Bury and Jenkins ¹⁰
<i>p</i> -Cresol	1.1	This investigation
	0.42	Bury and Jenkins ¹⁰
<i>m</i> -Nitrophenol	2.3	This investigation
<i>p</i> -Nitrophenol	5.2	This investigation

from that of earlier workers, using the method of least squares. The values for the cresols are in poor agreement, due to the small deviations that must be measured in dilute solutions. The equilibrium constants for the nitrophenols are found to be high, especially for the para compound.

Summary

An apparatus for measuring the freezing points of dilute solutions (0.002 to 0.1 molal) has been described. The freezing points of solutions of triphenylmethane in benzene have been determined, and the cryoscopic constant of benzene was found to be 5.088 - 0.0548 ΔT .

The freezing points of solutions of phenol in benzene have been determined. The results were interpreted as due to the formation of solid solutions of phenol in benzene. The partition coefficient of the solute between solid and liquid benzene was calculated to be 0.41.

Cryoscopic data were obtained for solutions of nitrobenzene in benzene. The ideal law was obeyed to $\approx 2\%$ below 0.1 molal. There was no evidence that nitrobenzene formed solid solutions with benzene.

The freezing points of solutions of *o*-cresol, *p*-cresol, *m*-nitrophenol, *p*-nitrophenol and 2,4-dinitrophenol in benzene have been measured. Equilibrium constants for the formation of dimers have been calculated. Except for 2,4-dinitrophenol, which is chelated, the deviations from ideality increase in the order mentioned.

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RECEIVED AUGUST 7, 1944

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

Isomeric Lactone Pairs Related to Cyclohexanone-2-acetic Acid¹

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Because of their relation to the aglucones of the important cardiac glycosides, unusual interest has attended a study of $\Delta^{\alpha,\beta}$ - and $\Delta^{\beta,\gamma}$ -unsaturated γ -lactones, particularly from the standpoint of a comparison of their properties and reactions.³

Most of the early knowledge concerning the chemistry of isomeric unsaturated lactones was due to the classical work of Thiele,⁴ who reported an extensive series of investigations involving a number of unsaturated lactone pairs prepared by the removal of water from γ -ketonic acids.

To our knowledge, however, no isomeric pair of

unsaturated lactones of the $\Delta^{\alpha,\beta}$ - and $\Delta^{\beta,\gamma}$ -type in which the lactone ring is fused to a second ring has heretofore been reported. The present paper describes such a pair, namely, the unsaturated lactones, IV and V, related to cyclohexanone-2-acetic acid, III, as well as the corresponding pair of stereoisomeric saturated lactones, I and VII. The method used for the synthesis of the lactones is illustrated by the chart.

The lactone, I, prepared according to Coffey⁵ possessed physical constants in agreement with those reported.⁵ Our lactone, however, in direct contrast to that of Coffey, was hydrolyzed to give a quantitative yield of an unusually stable hydroxy-acid, cyclohexanol-2-acetic acid, II. Upon direct oxidation of II with chromic anhydride in acetic acid, cyclohexanone-2-acetic acid, III, was obtained in good yield.

Treatment of III with boiling acetic anhydride

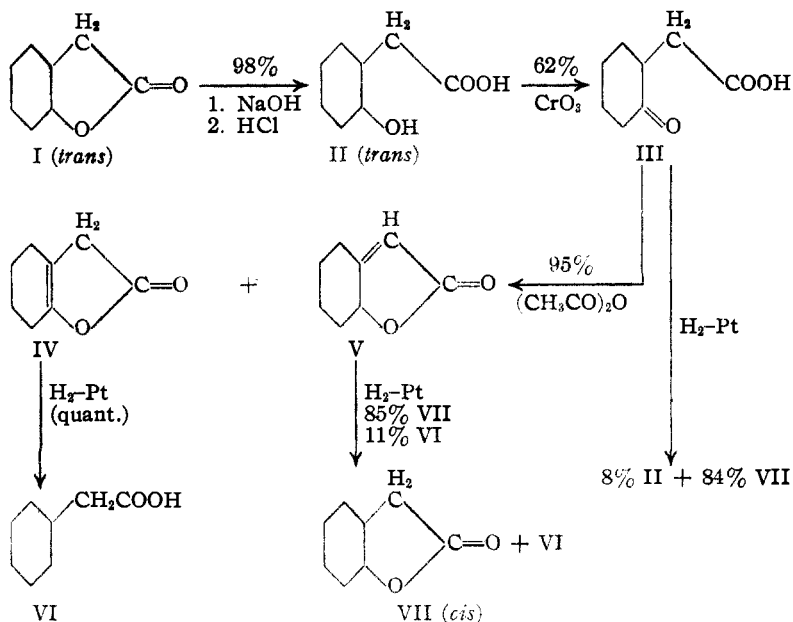
(1) The material in this paper is largely contained in the Ph.D. thesis of C. A. V. W., The Ohio State University, August, 1941.

(2) Now Assistant Professor of Chemistry at the University of Kansas, where several additional experiments were performed.

(3) See for example: (a) Jacobs and Collins, *J. Biol. Chem.*, **61**, 387 (1924); (b) Jacobs, Hoffmann and Gustus, *ibid.*, **70**, 1 (1926); (c) Jacobs and Scott, *ibid.*, **87**, 601 (1930); (d) **93**, 139 (1931); (e) Paist, Blout, Uhle and Elderfield, *J. Org. Chem.*, **6**, 273 (1941).

(4) Thiele, *Ann.*, **319**, 144 (1901), and subsequent articles.

(5) Coffey, *Rec. trav. chim.*, **63**, 387 (1923).



afforded a pair of isomeric unsaturated lactones which were separated by fractional distillation *in vacuo*.

The higher boiling isomer, which proved the major product, was assigned the $\Delta^{\alpha,\beta}$ structure, V, on the basis of the following facts: the lactone (1) did not add bromine and had an iodine number of zero^{3b,6}; (2) gave no benzal derivative⁴; (3) failed to reduce ammoniacal silver nitrate^{3b}; (4) gave a negative Legal test^{3b,7}; and (5) was catalytically reduced mainly to a saturated lactone,^{3c,d} VII (see below). In addition it is to be noted that the higher boiling lactone had the higher molar refraction, as would be expected because of its conjugation.⁸

In contrast to the above, the lower boiling lactone: (1) immediately decolorized bromine and had almost the theoretical iodine number; (2) gave a benzal derivative in over 90% yield; (3) immediately reduced ammoniacal silver nitrate; (4) gave a strong Legal test; and (5) was catalytically reduced to cyclohexylacetic acid in high yield. When the reduction of the lower boiling, $\Delta^{\beta,\gamma}$ -unsaturated, lactone was stopped after only one equivalent of hydrogen had been absorbed, half of the original lactone was isolated unchanged and half had been converted into cyclohexylacetic acid. This indicates that catalytic reduction does not proceed through the saturated lactone stage. It is interesting to note that in this reduction a carbon-oxygen bond is hydrogen-

(6) Thiele and Straus, *Ann.*, **319**, 155 (1901); reference 3b; and Bull., "Biochemistry of the Lipids," John Wiley and Sons, Inc., New York, N. Y., 1937, p. 86.

(7) See Fieser, "The Chemistry of Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1st ed., 1936, p. 265.

(8) Leermakers and Weissberger in Gilman's "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 2nd ed., Vol. II, p. 1736.

olyzed in preference to the saturation of a carbon-carbon double bond.

It was also shown that each of the two pure isomers IV and V is converted into the same equilibrium mixture of the two (about 7% of IV and 93% of V) by refluxing in alcohol containing piperidine. This isomerization undoubtedly is initiated by an acid-base reaction of the lactone with piperidine. The anion thus formed resonates but favors a conjugated structure which, on reaction with the piperidinium ion, yields the $\Delta^{\alpha,\beta}$ -unsaturated lactone. The failure of aniline to effect this isomerization (see Experimental Part) is explained by assuming that aniline is too weak a base to initiate the acid-base reaction. Finally, it was noted that

of the two lactones, IV is hydrolyzed to the keto-acid, III, more rapidly than V.

The saturated lactone, VII, obtained on catalytic reduction of the $\Delta^{\alpha,\beta}$ -unsaturated lactone, V, proved to be isomeric with the lactone, I. Attempted isolation of a stable hydroxy-acid by hydrolysis of VII, in direct contrast to the results obtained with I, was entirely unsuccessful. Addition of the quantitative amount of hydrochloric acid at 0° to a solution of the sodium salt resulting from the treatment of VII with alkali produced an acid which was spontaneously relactonized to form VII.

On the other hand, the hydroxy acid II, formed by the hydrolysis of I, was stable even in boiling water; relactonization to I was effected only by several hours of refluxing in dilute acid solution or by heating at 200°.

On the basis of the stability of II and the difficulty of ring formation required by its lactonization, it was assigned the structure of *trans*-cyclohexanol-2-acetic acid, and the corresponding lactone, I, then became the lactone of *trans*-cyclohexanol-2-acetic acid. Similarly VII, because of the ease of lactonization of the corresponding hydroxy-acid, was formulated as the lactone of *cis*-cyclohexanol-2-acetic acid.

Catalytic hydrogenation of the keto-acid, cyclohexanone-2-acetic acid, III, produced a mixture consisting mainly of the lactone of *cis*-cyclohexanol-2-acetic acid, VII, with small amounts of *trans*-cyclohexanol-2-acetic acid, II. Physical constants of the *cis*-lactone precluded the possibility that it might be identical with the lactone reported by Coffey.⁵

Formation of the lactone of *trans*-cyclohexanol-2-acetic acid upon decarboxylation of the lactone of cyclohexanol-2-malonic acid, which, in turn,

resulted from hydrolysis of the product of reaction of cyclohexene oxide with sodium malonic ester, substantiates the view⁹ that the reaction of the latter compound with olefin oxides proceeds with Walden inversion about one of the carbon atoms to which the oxygen is attached.

That conclusion obviously requires that the lactone of cyclohexanol-2-malonic acid likewise possessed the *trans*-configuration. Evidence that the decarboxylation of the malonic acid lactone did not involve a change in configuration was offered by the fact that the lactone, VII, of *cis*-cyclohexanol-2-acetic acid could be recovered unchanged after being heated at 200° for twenty-four hours. In fact, all attempts to convert the *cis*-lactone into its *trans*-isomer under a variety of conditions resulted in complete recovery of the unchanged *cis*-form. The assignment of *cis* and *trans* configurations to these two lactones assumes that in hydrolysis and relactonization no Walden inversion occurs.

In the reaction of cyclohexene oxide with malonic ester⁵ a carbethoxylactone is first formed. This product is saponified with sodium hydroxide and the free acid liberated with mineral acid. However, the lactone of *trans*-cyclohexanol-2-malonic acid is obtained. This fact is somewhat surprising in view of the remarkable stability of *trans*-cyclohexanol-2-acetic acid, II.

Experimental^{10,11,12}

2-Chlorocyclohexanol.—After an extended investigation of various methods for the preparation of this compound, we finally adopted a modification of that of Detoeuf¹³ which, in our opinion, is much superior to that of Coleman and Johnstone.¹⁴

A typical run was carried out as follows. Into a mechanically stirred, ice-cooled mixture of 300 cc. of water, 360 g. (6 moles) of urea, and 300 g. (3 moles) of reprecipitated chalk in a 3-liter flask, chlorine gas was passed through the glass stirrer¹⁵ until a gain in weight of 275 g. had occurred. About one hour was required, the rate at which the chlorine was admitted being limited only by the efficiency of the cooling. Addition of much excess chlorine above the amount specified is to be avoided as it results in the formation of a solid product which exploded in one case after filtration.

The mixture was transferred to a 5-liter flask, 1000 cc. of ice-cold water, 1200 g. of ice, 230 cc. of glacial acetic acid, and 395 g. (4.7 moles) of cyclohexene were added, and mechanical stirring begun. If noticeable warming occurred after the ice had melted, additional ice was added. Stirring was continued until no top layer of cyclohexene

remained and a heavy oil had settled to the bottom (two to four hours required). The mixture was then saturated with salt, steam distilled, and the distillate extracted with ether. After the combined ether extracts had been washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate, the solvent was removed. On distillation of the residue, 478 g. (74% of the theoretical amount based on cyclohexene) of 2-chlorocyclohexanol, b. p. 85–86° at 17 mm., was obtained.

Lactone of *trans*-Cyclohexanol-2-acetic Acid, I.—In a typical run, 45.5 g. (1.98 moles) of sodium was dissolved in 1460 cc. of absolute alcohol¹⁶ contained in a 5-liter, 3-necked flask fitted with condenser, thermometer, mercury-seal stirrer, and nitrogen inlet tube. After 292 cc. (308 g., 1.91 moles) of diethyl malonate had been run in with stirring, the mixture was cooled to a little below 20°, just above the point at which the material began to solidify, and maintained there while 177 g. (1.82 moles) of cyclohexene oxide¹⁷ was added dropwise. No noticeable reaction ensued until the mixture was warmed slowly to 70° on a steam-bath and maintained at that temperature for fifteen minutes, after which time it suddenly went solid. Stirring was stopped and the reaction mixture was kept at 70° for three hours. Warm water (800 cc.) was added, and, after all the solid had dissolved, 163 g. (2.9 moles) of solid potassium hydroxide was added cautiously. The resulting solution was heated with stirring and the alcohol removed using a take-off condenser. After 2000 cc. of distillate had been collected, a like volume of water was added and the process repeated. After cooling, the solution was acidified with 420 cc. of sulfuric acid (2:1); the product was isolated by ether extraction and decarboxylated by heating to 185°. A small amount of acetic acid distilled and was tapped off from time to time. After one and one-quarter hours, the reaction was complete as noted by a cessation of carbon dioxide evolution. The temperature was then raised rapidly to 205° and the reaction stopped. Distillation under reduced pressure from the same flask gave 195 g. (77%) of the colorless lactone of cyclohexanol-2-acetic acid, I, b. p. 118–119° at 6 mm., 131–132° at 11.5–12 mm.

Lactone of *trans*-Cyclohexanol-2-malonic Acid.—In the preceding synthesis, the residue obtained prior to decarboxylation crystallized if cooled in an ice-bath. Recrystallized three times from boiling water, the product separated in large hexagonal crystals, m. p. 114.5–117.0°.

Anal.^a Calcd. for C₉H₁₂O₄: C, 58.7; H, 6.6; neut. equiv., 184. Found: C, 58.7; H, 6.6; neut. equiv., 186 (av.).

***trans*-Cyclohexanol-2-acetic Acid, II.**—To a mixture of 140 g. (1 mole) of the lactone, I, and 700 cc. of water there was added 40 g. (1 mole) of solid sodium hydroxide. Heating due to the dissolving of the alkali was sufficient to bring the lactone into solution in a few minutes. Cooled in an ice-bath, the solution was made just acid to litmus with concentrated hydrochloric acid. *trans*-Cyclohexanol-2-acetic acid (155.4 g., 98%) settled in colorless leaflets, m. p. 103.2–106.1°. A sample recrystallized from ether melted at 105.8–106.6°.

Anal.^b Calcd. for C₉H₁₄O₃: C, 60.7; H, 8.9; neut. equiv., 158. Found: C, 60.6, 60.5; H, 9.1, 9.2; neut. eq., 159 (av.).

Lactonization of II.—A series of experiments revealed that the conditions just sufficient to effect complete lactonization of II were: (1) heating at 200° for three hours, (2) heating at 150° for three hours under 20 mm. pressure, or (3) refluxing for four hours in a water-alcohol solution 0.25 *N* with respect to hydrochloric acid.

Titration of a sample of the acid which had been kept in

(9) Grigsby, Hind, Chanley and Westheimer, *THIS JOURNAL*, **64**, 2808 (1942).

(10) All melting points corrected.

(11) Boiling points uncorrected.

(12) Analyses marked *a* by David Mowry, *b* by Sterling Olsen, *c* by Arlington Laboratories, *d* by C. A. V. W.

(13) Detoeuf, *Bull. soc. chim.*, **31**, 176 (1922); see, also, McRae Charlesworth and Alexander, *Can. J. Research*, **21B**, 1 (1943).

(14) Gilman, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932, pp. 151–153.

(15) The stirrer shaft terminated at the top as the bearing tube of a mercury seal so that the mercury cup revolved with the stirrer. Chlorine was admitted into the stirrer shaft by means of a stationary tube fitted over the inner bearing tube (top of the stirrer shaft) and extending at least 8 cm. below the surface of the mercury. The stirrer was revolved by means of a belt and pulley; smooth operation was obtained by use of two ball bearing mountings.

(16) Obtained by dehydration of commercial "absolute" alcohol according to the method of Manske, *THIS JOURNAL*, **53**, 1108 (1931).

(17) Obtained in the early stages of the investigation through the courtesy of the E. I. du Pont de Nemours and Company and Van Ameringen-Haebler Co., and later by preparation from 2-chlorocyclohexanol according to the method of Osterberg, ref. 14, pp. 179–180.

a desiccator over sulfuric acid for one year indicated that only 14% lactonization had occurred.

Cyclohexanone-2-acetic Acid, III.—In the best experiment, 434 cc. of a chromic acid solution¹⁸ containing 0.048 g. of available oxygen per cc. was added dropwise with stirring over the course of two hours at 25–30° to a solution of 200 g. of II in 700 cc. of glacial acetic acid. Stirring was continued at room temperature for an additional thirty hours at the end of which time sodium bisulfite was added to destroy excess chromic acid. Solvent (700 cc.) was removed under diminished pressure, an equal volume of water added, and the process repeated. The mixture was then diluted to 1000 cc. and submitted to continuous ether extraction for three days. The product remaining after removal of the ether was distilled through a Podbielniak type column to yield 26 g. of recovered lactone, II, b. p. 118–119° at 6 mm., and 107 g. (62% based on II reacted) of crystalline cyclohexanone-2-acetic acid, b. p. 161° at 6 mm. Recrystallization from petroleum ether, b. p. 80–90°, gave 102 g. of a pure product as long slender needles, m. p. 72.6–74.0°.

Anal.^a Calcd. for C₈H₁₂O₃: C, 61.5; H, 7.4. Found: C, 61.5; H, 7.7.

The semicarbazone, thick needles from absolute alcohol, melted at 197.4–198.5° with decomposition.

Anal.^a Calcd. for C₉H₁₃O₃N₂: N, 19.7. Found: N, 19.9.

γ-Lactone, IV, of (2-Hydroxy-1-cyclohexen-1-yl)-acetic Acid and γ-Lactone, V, of (2-Hydroxycyclohexylidene)-acetic Acid.—The acetic acid formed on refluxing a solution of 249 g. of II, 5 g. of fused sodium acetate and 600 cc. of acetic anhydride was distilled from a packed column during three hours. The remaining acetic anhydride was removed under reduced pressure and the crude product vacuum distilled to give 208.8 g. (95%) of a mixture of the isomeric lactones.

This was fractionated under vacuum in a heated column packed (30 inches) with Berl saddles and equipped with a total reflux partial take-off head to yield 19 g. (8.6%) of pure IV (b. p. 133.5–134.0° at 20 mm., 117° at 6 mm.; *n*_D²⁰ 1.4903; *d*₄²⁰ 1.1148; *M*R_D calcd., 35.93; obsd., 35.85); 120 g. (54.5%) of pure V, (b. p. 160.5 at 20 mm.; 136 at 6 mm.; *n*_D²⁰ 1.5064; *d*₄²⁰ 1.1194; *M*R_D calcd., 35.93; obsd., 36.69; *M*R exalt. 0.76); and 28 g. of an intermediate fraction.

A time temperature cooling curve for IV showed a long flat at –37.4° and for V, at 31.2°.

*Anal.*¹⁹ Calcd. for C₈H₁₀O₂: C, 69.5; H, 7.3. Found^d for IV: C, 69.3; H, 7.4. Found^e for V: C, 69.4, 69.4; H, 7.4, 7.2.

Properties of IV and V.—A solution of 2.00 g. of the unsaturated lactone, IV, dissolved in 20 cc. of absolute ethanol to which 2 drops of piperidine had been added was refluxed for ten hours on a water-bath. The solvent was then removed completely under vacuum and the residue distilled from a small specially constructed Claisen flask. The index of refraction (1.5053 at 35°) of the distillate (1.74 g.) corresponded to that of a synthetic mixture containing 7% of IV and 93% of V. Hydrolysis of the distillate yielded the quantitative amount of III.

Under identical treatment, V gave 1.66 g. of a similar mixture (*n*_D²⁰ 1.5049).

A 5% solution of bromine in carbon tetrachloride was immediately decolorized when added dropwise to one drop of IV, but was unaffected by V even upon long standing. Similarly, V gave an iodine number of zero when tested by the method of Wijs.²⁰ Lactone IV gave an average value of 164 (calcd. for C₈H₁₀O₂, 183) when the titration was carried to the point at which the dark blue color first faded to a light purple. The latter color could not be discharged

completely by further addition of great excess of sodium thiosulfate, due, no doubt, to the instability of the halogenated lactone.

Addition of 1 drop of ammoniacal silver nitrate (1 *M*) solution to 4 cc. of a 0.2% solution of IV in water, gave an immediate blue-black finely divided precipitate of silver; under identical conditions, V gave a negative test even upon standing for several days.

The Legal test served to distinguish most sharply between the unsaturated lactones when applied as follows: to 1 cc. of a 10% solution of the lactone in pyridine there was added 2 drops of a saturated sodium nitroprusside solution followed by 1 drop of 10% sodium hydroxide solution. Under these conditions, IV gave an immediate blood-red color which persisted for several minutes, finally fading to a dark brown, and then to dark purple upon acidification with dilute hydrochloric acid. No color change could be observed in the case of V until the solution was acidified, when a light yellow coloration resulted. Tests using potassium ferricyanide were inconclusive.

To 0.50 g. of IV dissolved in 8 cc. of absolute alcohol was added 0.40 g. of benzaldehyde and 1 drop of aniline. The solution was maintained at 50° for forty-eight hours. Upon cooling, fine light-yellow needles (0.76 g.) of the benzal derivative were formed. A sample recrystallized from absolute alcohol sintered at 165.2° and melted at 167.2–168.0°. When treated in an identical fashion, V gave no crystalline derivative.

Anal.^d Calcd. for C₁₅H₁₄O₂: C, 79.6; H, 6.2. Found: C, 79.5, 79.5; H, 6.2, 6.3.

To a solution of 2.0 g. of sodium hydroxide in 30 cc. of water was added 5.0 g. of IV. The mixture was refluxed for five minutes, made just acid with concentrated hydrochloric acid, and seeded with a crystal of cyclohexanone-2-acetic acid. After cooling, 4.7 g. of cyclohexanone-2-acetic acid, m. p. 72.1–74.0°, was obtained. No depression of the m. p. was observed when the product was mixed with an authentic sample of cyclohexanone-2-acetic acid.

Similarly treated, 5.0 g. of V gave the greatest amount (4.6 g.) of the keto-acid when refluxing in basic solution was continued for fifty minutes.

Catalytic Hydrogenation of IV.—Exactly 1.00 g. of IV was dissolved in 50 cc. of absolute alcohol and 0.1 g. of freshly prepared platinum oxide added. Hydrogenation with shaking, at atmospheric pressure, proceeded uniformly over the course of forty minutes: total hydrogen uptake, 420 cc.; calcd. for 2 moles, 411 cc.

The catalyst was removed by filtration and the alcoholic solution titrated with 0.1709 *N* sodium hydroxide using phenolphthalein as an indicator: required, 41.4 cc.; calcd. for 1 mole, 42.4 cc.

The reduction described above was repeated but stopped after absorption of one equivalent (218 cc.) of hydrogen. After removal of the catalyst, the solution was titrated as above: required, 20.7 cc.; calcd. for 0.5 mole, 21.2 cc.

The alcohol was then removed at the take-off and the residue taken up in ether. Following the removal of ether, the residue was refluxed with standard base and back titrated with standard acid: additional base required, 20.2 cc.

Pressure hydrogenation (45 lb.) of 4.0 g. of IV dissolved in 50 cc. of absolute ethanol in the presence of 0.1 g. of catalyst was complete in fifteen minutes. The product was separated into neutral and acid fractions. No neutral material was obtained, but the acid fraction yielded 3.71 g. of a colorless liquid, b. p. 119° at 6 mm., which crystallized in colorless needles, melting at 27.2°. No depression in melting point was observed for the free acid or its amide, m. p. 167.5–168.6°, with authentic samples prepared by the hydrogenation of phenylacetic acid.²¹

Catalytic Hydrogenation of V.—Exactly 1.00 g. of the Δ^{α,β}-unsaturated lactone, V, was dissolved in 50 cc. of ethanol and hydrogenated at atmospheric pressure in the presence of 0.1 g. of platinum oxide. Almost three hours was required for complete reaction: total hydrogen uptake, 241 cc.; calcd. for 1 mole, 217 cc.

(18) Cook, Hewett and Lawrence, *J. Chem. Soc.*, 71 (1936).

(19) Due to the pronounced hygroscopic nature of IV and V, satisfactory analyses were obtained only when run immediately following vacuum distillation of the lactones under rigorously anhydrous conditions.

(20) Wijs, *Ber.*, 31, 750 (1898).

(21) Wallach, *Ann.*, 358, 297 (1907).

Titration of the filtered alcoholic solution required 5.10 cc. of 0.1709 *N* base, corresponding to 11.9% acid formation.

Hydrogenation under 45 lb. pressure of 94 g. of V, dissolved in 600 cc. of ethanol with 0.7 g. of catalyst added, was complete in two hours. In the titration of the catalyst-free filtrate, 78.56 cc. of 1.004 *N* base was required, indicating 11.3% reduction to cyclohexylacetic acid. Following separation of the product into neutral and acid fractions, the latter was distilled and 10.6 g. (11.0%) of cyclohexylacetic acid, identified as above, obtained.

From the neutral fraction there was obtained by distillation under reduced pressure 81.0 g. (85.0%) of the lactone, VII, of *cis*-cyclohexanol-2-acetic acid, b. p. 128–128.5° at 10–11 mm., 112° at 6 mm.; n_D^{20} 1.4773; d_4^{20} 1.0923; *M*R_D calcd., 36.40; obsd., 36.20. This product showed a long flat at 14.8° in a time-temperature cooling curve.

Corresponding constants for the *trans*-lactone, I, are: n_D^{15} 1.4798, n_D^{20} 1.4777; $d_4^{12.8}$ 1.0926, d_4^{20} 1.0860; *M*R_D obsd., 36.43. The time-temperature cooling curve showed a long flat at -1.2°.

Anal.^d Calcd. for C₈H₁₆O₂: C, 68.6; H, 8.6. Found for VII: C, 68.2, 68.4; H, 8.7, 8.6. For I: C, 68.4, 68.4; H, 8.5, 8.6.

Hydrolysis of the *cis*-Lactone, VII.—Exactly 5.0 g. of VII was added to a solution of 1.5 g. of sodium hydroxide in 10 cc. of water and the mixture refluxed until all of the lactone had dissolved. The solution was cooled in an ice-bath and 3.2 cc. of concentrated hydrochloric acid was added. A colorless liquid immediately oiled out; attempts at its crystallization either by cooling for long periods or by seeding with *trans*-cyclohexanol-2-acetic acid were unsuccessful. The mixture was finally extracted with ether; distillation of the residue after removal of the solvent resulted in the recovery of 4.6 g. of VII.

Attempted *cis-trans* Isomerization. Both the *cis*-lactone and the *trans*-lactone were recovered unchanged after treatment under any of the following conditions: (1) heated at 200° for twenty-four hours; (2) refluxed in pyridine for eight hours; (3) exposed to sunlight or ultraviolet light for seven days.

Ammonolysis of the Saturated Lactones.—A solution containing 0.50 g. of the *trans*-lactone in 5 cc. of ethanol saturated with ammonia gas was heated at 90° for ten hours in a sealed tube. Removal of the solvent under reduced pressure left 0.52 g. of the amide of *trans*-cyclohexanol-2-acetic acid. A sample recrystallized from acetone-water formed clusters of white needles which melted at 151.0–152.4°, in agreement with the value reported by Coffey⁶ for the amide formed from his lactone. Similarly treated, the *cis*-lactone was recovered unchanged.

Catalytic Hydrogenation of Cyclohexanone-2-acetic Acid.—In a typical run, 2.5 g. of the keto-acid dissolved in 50 cc. of ethanol was placed in a pressure bottle, thor-

oughly cleaned by steaming, 0.15 g. of freshly prepared platinum oxide added, and the material shaken in a Parr apparatus at 40 lb. pressure. Hydrogen absorption was complete in three hours. From the neutral fraction there was isolated 1.9 g. (84%) of the lactone, VII, of *cis*-cyclohexanol-2-acetic acid, and from the acid fraction, 0.2 g. (8%) of *trans*-cyclohexanol-2-acetic acid, II. Under the same experimental conditions, the *trans*-lactone, I, was recovered unchanged.

Summary

1. A method for the synthesis from cyclohexene of a new pair of isomeric unsaturated lactones, the γ -lactone of (2-hydroxy-1-cyclohexen-1-yl) acetic acid and the γ -lactone of (2-hydroxy-cyclohexylidene)-acetic acid is described. The former, the $\Delta^{\beta,\gamma}$ -unsaturated lactone, may be distinguished from its $\Delta^{\alpha,\beta}$ -unsaturated isomer on the basis of the following behavior and properties: it is the lower boiling and less refractive of the two isomers and is more easily oxidized and hydrolyzed in alkaline solution; it adds bromine readily, gives approximately the calculated iodine number, condenses with benzaldehyde, and is quantitatively hydrogenated to cyclohexylacetic acid. The $\Delta^{\alpha,\beta}$ -unsaturated lactone, on the other hand, fails to add bromine, and has an iodine number of zero, does not condense with benzaldehyde, and, upon catalytic hydrogenation, yields mainly the *cis*-saturated lactone with only a small amount of cyclohexylacetic acid.

2. Synthesis of a pair of saturated lactones, the lactone of *trans*-cyclohexanol-2-acetic acid and the lactone of *cis*-cyclohexanol-2-acetic acid is described. The *trans* configuration was assigned on the basis of the fact that on hydrolysis a stable hydroxy acid is formed whereas it was found impossible to isolate the hydroxy acid from the lactone designated as *cis*. The two lactones may be distinguished easily by the fact that the *trans* form is easily ammonolyzed to yield a crystalline amide, designated as the *trans* amide.

3. Evidence is presented to substantiate the view that the reaction of malonic ester with olefin oxides proceeds with Walden inversion about one of the carbon atoms of the oxide ring.

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RECEIVED OCTOBER 7, 1944