[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UNIVERSITY OF DELAWARE]

The Bromination of Ethyl *p-t*-Butyl-*β*-cyano-*α*-hydroxycinnamate Intermediates

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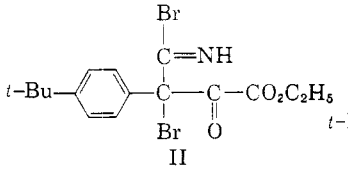
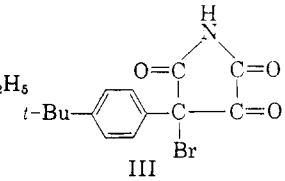
The bromination of ethyl *p-t*-butyl-*β*-cyano-*α*-hydroxycinnamate (I) in dry carbon tetrachloride gives an intermediate dibromide (II) and a monobromide (III) each of which is converted to *p-t*-butylphenylhydroxymaleimide by appropriate means. When the single reactive hydrogen in the enolic group of I is blocked by an ethyl group, the reaction with bromine does not take place and the ethyl ether of I is recovered unchanged. The experiments performed in the determination of the structure of the bromides are described and their significance is discussed.

Previous studies in this laboratory have indicated that bromine reacts with chloroform solutions of *β*-cyano-*α*-hydroxycinnamic esters in the presence of water to give *p*-bromoarylhydroxymaleimides. If the *para* position is blocked, cyclization occurs but bromine does not enter the ring.[1] If all *ortho* and *para* positions are substituted by methyl groups, an amide ester results in which the bromine is in the *alpha* position in the side chain. This is reminiscent of the similar behavior of ethyl cyanomethylpyruvate[2] and is a further indication that bromine first enters the side chain.

This work was undertaken for the purpose of the isolation and characterization of the intermediate reaction products in order to establish more definitely the course of the reaction. For this purpose we selected I, as it contains no easily displaceable hydrogen except that of the enolic group and this can be removed from the sphere of action by prior formation of the ether. Carefully purified carbon tetrachloride and dried reagents were used and the experiment was conducted under protection from outside moisture. The dibromide (II) precipitated relatively rapidly in a few hours and the monobromide (III) from the filtrate relatively slowly in a few weeks.



II



III

The dibromide was stable *in vacuo* over potassium hydroxide and phosphorus pentoxide for at least seven months and, therefore, does not seem to be a molecular complex. It was quite reactive toward either water or ethyl alcohol. Either reagent converted it to *p-t*-butylphenylhydroxymaleimide. It reacted with toluene to give benzyl bromide but upon standing with benzene free bromine was literated.

Hydrolysis of the dibromide in alcoholic potassium hydroxide gave *p-t*-butylphenylacetamide which was also formed by similar hydrolysis[1] of the hydroxymaleimide. Under these conditions it is probable that the hydrolysis proceeds through the intermediate formation of the hydroxymaleimide. On the other hand, if the dibromide were added to hot aqueous potassium hydroxide and the hydrolysis then completed, *p-t*-butylmandelic acid was the only identified product. This indicates the direct hydrolysis of the dibromide, that one of the bromine atoms is joined to the carbon *alpha* to the aromatic ring, and that both are capable of hydrolytic cleavage.

The dibromide is neither a molecular complex nor a simple addition product of bromine to the starting ester (I), as cyclohexene removed the bromine to give 1,2-dibromocyclohexane without regenerating the starting ester. It contains carbon-bromine bonds[3] as shown by infrared absorption bands at 17.5 and 18.2 μ with overtones at 8.8 and 9.2 μ.

The monobromide is considerably more stable than the dibromide, as it could be crystallized from carbon tetrachloride as well as chromatographed in chloroform solution. The bromine atom, however, is a reactive one which liberated iodine from a solution of sodium iodide in acetone and also gave an immediate precipitate with acidified alcoholic silver nitrate. The compound is not an enol, as it did not give the characteristic color with ferric chloride but when the solution was warmed a deep orange color developed. The almost white color of the monobromide is also in agreement with that of a series[4] of 1,4,4-trialkylpyrollidinetriones. The hydroxymaleimides are all colored yellow.

The monobromide by hydrolysis in aqueous potassium hydroxide gave *p-t*-butylmandelic acid as well as oxalic acid. This indicates that the bromine atom is at a position *alpha* to the aromatic nucleus. The products of this hydrolysis indicate especially that the monobromide is 4-bromo-4-

(1) Glenn S. Skinner, Jules A. Gladner, and Richard F. Heitmiller, *J. Am. Chem. Soc.*, **73**, 2230 (1951).

(2) W. Wislicenus and W. Silberstein, *Ber.*, **43**, 1834 (1910).

(3) L. A. Henderson, thesis, University of Delaware, 1951.

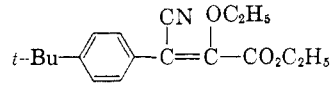
(4) G. S. Skinner and R. E. Ludwig, *J. Am. Chem. Soc.*, **78**, 4656 (1956).

p-t-butylphenylpyrrolidinetrione (III). In this connection, if the bromine atom were replaced with hydrogen, *p-t*-butylphenylhydroxymaleimide was formed. This reaction was carried out in excellent yield by heating the dibromide with toluene to form also benzyl bromide.

The assigned structure of the monobromide is further supported by the infrared[5] spectrum which shows a band at 3.16 μ that is attributed to the N–H bond. Bands arising from the carbonyl functions are also present at 5.52, 5.58, and 5.83 μ. This splitting to form a doublet at 5.52 and 5.84 μ probably results from the two carbonyl functions involved in the imide structure.

One of the bromine atoms in the dibromide also must be in the *alpha* position to the aromatic nucleus as the dibromide, in a separate experiment under identical conditions, was converted to this monobromide. This conclusion is further supported by the fact that aqueous alkaline hydrolysis of the dibromide gave the identical *p-t*-butylmandelic acid.

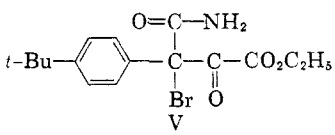
The above behavior of the dibromide and its relation to the monobromide indicate very strongly that the two bromine atoms are vicinal. The formation of a debromination product different from the original ester can be explained by the loss and readdition of hydrogen bromide to the nitrile function. As support for this interpretation of the reaction may be cited the fact that the ethyl ether



IV

(IV) of the starting ester did not react with bromine in anhydrous carbon tetrachloride although it was converted to *p-t*-butylphenylethoxymaleimide by hydrochloric acid in alcohol. The ether contains no reactive hydrogen to form hydrogen bromide. This explains why the ether did not react with bromine under these conditions.

Bromine did not react with *p-t*-butylphenylhydroxymaleimide to give the monobromide. Its formation most likely proceeds through the partially hydrolyzed dibromide (V), which has not been isolated in this case. The water necessary for this reaction may have become slowly available through the ground glass joints or, more likely, by oxidation, as the dibromide was converted to the hydroxymaleimide by ethanol as well as by water.



V

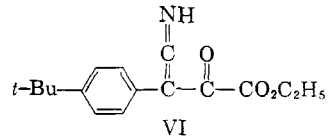
The debrominated product from the reaction of the dibromide with cyclohexene is not a simple dimerization product of a ketenimine but a compound which also requires water for its formation. Its analysis and molecular weight indicate that it is derived from two molecules of the starting ester and that the molecular formula is $C_{30}H_{36}O_7N_2$. This bimolecular compound on hydrolysis with aqueous potassium hydroxide ultimately yielded only *p-t*-butylphenylacetic acid. Reaction with hot 30% sulfuric acid gave one mole of *p-t*-butylphenylhydroxymaleimide and some *p-t*-butylphenylpyruvic acid also. The distillate contained ammonia and gave a positive iodoform test. The reaction of the bimolecular compound with alcoholic hydrochloric acid gave more than one mole of *p-t*-butylphenylhydroxymaleimide. In addition there was obtained a small amount of the ethyl ether of the hydroxymaleimide.

As the bimolecular compound was formed in spite of careful exclusion of water in the reaction of cyclohexene with the dibromide, the water needed for partial reaction must have arisen within the medium. This necessity for water is borne out by the fact that the addition of a very small amount of water to the filtrate, from the bimolecular compound, yielded more of it in considerable amount.

More than one mole of *p-t*-butylphenylacetic acid was obtained on alkaline hydrolysis, which indicates that both moieties of the bimolecular compound must be capable of hydrolysis to this acid. The reaction with 30% sulfuric acid gives a strong indication that one part of the molecule was furnished by *p-t*-butylphenylhydroxymaleimide. This must be joined to another part which is capable of acid hydrolysis to *p-t*-butylphenylpyruvic acid. The amount of this acid under identical conditions from the hydroxymaleimide was far less.

The reaction of the bimolecular compound with hydrogen chloride in ethanol to give more than one mole of the hydroxymaleimide shows that both parts of the molecule were converted to *p-t*-butylphenylhydroxymaleimide. The fact that *p-t*-butylphenylethoxymaleimide also was isolated while none was obtained from the hydroxymaleimide under identical conditions shows that only the other part of the molecule is capable of yielding this ether.

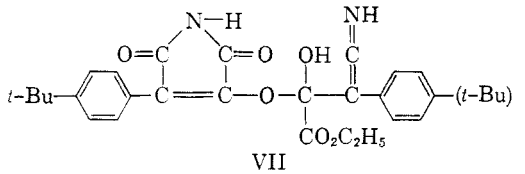
The starting ester is converted to the hydroxymaleimide by bromine with free access of water.[1] Although we apparently have failed in our efforts to keep all moisture from the reaction mixture during the debromination with cyclohexene, we have succeeded in preventing complete conversion of the intermediate to the hydroxymaleimide. The initial debrominated intermediate, we believe,



VI

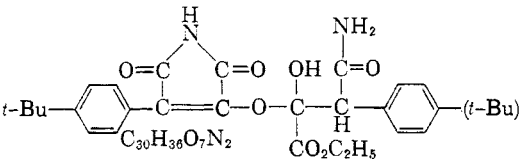
(5) Consultation with Dr. H. C. Beachell.

is the ketenimine VI. The formation of the bimolecular compound can be explained by its partial conversion in the presence of insufficient water to the hydroxymaleimide, which adds to more of the ketenimine to give VII. This then may react with water to precipitate the less soluble bimolecular



VII

compound VIII. Although it is unstable near its



VIII

melting point, the substance is quite stable in the lower temperature ranges and is easily purified by crystallization from ethanol.

EXPERIMENTAL

Bromination of ethyl p-t-butyl-β-cyano-α-hydroxycinnamate in dry carbon tetrachloride. The bromination was conducted in an Ace Glass Mini Lab set up to provide for addition of reagents, stirring, exclusion of atmospheric moisture and filtration. Dry bromine (4.5 cc.; 1.2 mole) was added in one portion to a stirred solution of 13.8 g. (0.066 mole) of the ester in 45 cc. of dried and distilled carbon tetrachloride. In 6–7 min. brick-red crystals began to separate. After 24 hr. the brick-red solid was filtered on the sintered glass plate and washed with three 40-cc. portions and one 60-cc. portion of carbon tetrachloride. As soon as the excess liquid had been removed, the flask containing the brick-red solid was placed *in vacuo* over potassium hydroxide and phosphorus pentoxide. If the transfer were not rapid, the brick-red solid became tinged with yellow. After standing *in vacuo* for 1–2 weeks, it assumed a permanent tan-orange color, m.p. 156.5–157.5° dec.

Anal. Calcd. for $C_{16}H_{19}O_3NBr_2$: C, 44.36; H, 4.42; N, 3.23; Br, 36.90. Found: C, 44.0; H, 4.0; N, 3.4; Br, 35.1.

Trituration of the dibromide with water gave *p*-*t*-butylphenylhydroxymaleimide,[1] m.p. 249–250°. Crystallization of the dibromide from ethanol also gave the identical hydroxymaleimide.

Reaction of the dibromide with alcoholic potassium hydroxide. The dibromide (2.5 g.; 0.0058 mole) was added to a refluxing mixture of 20 cc. of ethanol and 3 cc. of 40% potassium hydroxide solution. A yellow solid formed immediately. Heating was continued for 28 hr. during which 9 cc. of water and 4–5 pellets of potassium hydroxide were added. The solution was cooled and the white precipitate was filtered and washed with 2:1 ethanol-water to give 0.9 g. of potassium oxalate. The residue from the evaporation of the filtrate gave a white solid soluble in ether that after two recrystallizations from benzene-ligroin had a melting point of 125.5–127° which was not depressed by an authentic sample of *p*-*t*-butylphenylacetamide, m.p. 126–127°. The above basic solution upon acidification gave a viscous oil which could not be induced to crystallize.

Reaction of the dibromide with aqueous potassium hydroxide. To a stirred hot solution of 1.7 g. of potassium hydroxide in 20 cc. of water was added 1.5 g. (0.0035 mole) of the dibromide. Immediately there was formed a yellow solid which gradually changed to an oil that remained after refluxing 2 hr. Alcohol (6.5 cc.) was added and the heating was continued for 36 hr. The solution was extracted with ether to remove a drop or two of a dark oil. The acid from the aqueous layer amounted to 0.8 g. of a brown oil which after long standing deposited crystals that were filtered and washed with pentane. Two recrystallizations from benzene gave 0.025 g. of *p*-*t*-butylmandelic acid, m.p. 149–150°, lit.,[6] m.p. 149.5–150°. Ammonia and oxalic acid also were formed in the hydrolysis.

Reaction of the dibromide with toluene. The dibromide (0.50 g.) was allowed to stand 5 months in an all-glass container with 5 cc. of dry toluene. The products isolated were *p*-*t*-butylhydroxymaleimide (0.22 g.) and ammonium bromide (0.02 g.) from the precipitate and from the toluene free bromine and 0.1 g. of a lachrymator which was identified as benzyl bromide by conversion to benzyl β-naphthyl ether, m.p. 100–101°.

Reaction of the dibromide in benzene. The dibromide (0.9 g.) in an all glass container with 9 cc. of dry benzene dissociated bromine almost immediately. After 3 days the solid (0.23 g.) was filtered and identified as the hydroxymaleimide, m.p. 248–250°. The red liquid distillate of bromine and benzene required 4–5 drops of cyclohexene for decolorization. A reddish tar (0.25 g.) remained in the residue.

Reaction of cyclohexene with the dibromide. For this purpose the dibromide was prepared from 9.1 g. (0.033 mole) of the starting ester. When the precipitation appeared complete (6 hr.) the red dibromide was filtered and washed in the Mini Lab with three 9-cc. portions of dry carbon tetrachloride. Then 13 cc. of carbon tetrachloride was stirred into a smooth paste. Cyclohexene (5 cc.) freshly distilled from sodium in a nitrogen atmosphere was added at once with good stirring. The temperature rose to 30–35° and solution was complete in 1 min. except for a minute amount of solid dispersed in the light wine-colored liquid. The precipitation of a yellow solid began in 5 min. and was essentially complete in 15 min. After standing 45 min. longer, the product was filtered and washed with 8-cc. portions of carbon tetrachloride. It was crystallized from ethanol to yield 1.1 g. of yellow fibrous material which began to darken at 210° and melted at 220–222° dec.

The mother liquor, from which the yellow solid precipitated, was shaken with 1 cc. of water. Within 1 min. a yellow solid started to separate. The mixture was allowed to stand 3 hr. after which the yellow solid was filtered and washed well with carbon tetrachloride. Crystallization from ethanol gave 0.7 g. more of the identical compound, m.p. 220–222° dec.

Anal. Calcd. for $C_{30}H_{36}O_7N_2$: C, 67.16; H, 6.75; N, 5.22. Found: C, 67.22; H, 6.77; N, 5.24.

The above carbon tetrachloride mother liquor which had been treated with water was distilled under diminished pressure to give 2 g. of 1,2-dibromocyclohexane, n_D^{25} 1.5507,

Wt. of Compound	Wt. of Camphor	Molality	$-\Delta t$	M.W.
0.0162	0.0697	0.433	18.2	507
0.0303	0.1400	0.403	17.0	505
0.0106	0.0602	0.328	12.4	564
0.0100	0.0712	0.288	11.1	553
0.0104	0.0846	0.229	8.7	560
0.0132	0.1609	0.153	6.6	490
				Av. 530
Calcd. for $C_{30}H_{36}O_7N_2$				537

(6) J. L. Riebsomer, J. Irvine, and R. Andrews, *J. Am. Chem. Soc.*, **60**, 1015 (1938).

lit.,[7] n_D 1.5507, b.p. 50.5–52° (0.2 mm.). There remained 0.6 g. of a reddish oil.

Molecular weight of the compound $C_{30}H_{36}O_7N_2$. The following relatively low melting solvents were unsuited because of lack of solubility: borneol, camphene, naphthalene, phenanthrene, tribromophenol, and triphenylmethane. The initial melting with camphor had to be done as rapidly as possible, as in some cases the samples on recooling and remelting gave still lower melting points.

Basic hydrolysis of the compound $C_{30}H_{36}O_7N_2$. A mixture of 0.50 g. of the substance, 1.0 g. potassium hydroxide, 10 cc. of water and 5 cc. of ethanol was refluxed for 21 hr. Ammonia was evolved. The colorless solution was evaporated to half its volume and acidified to give 0.33 g. of solid which from petroleum ether (b.p. 00–00°) melted at 79–80°. Admixture with an authentic sample of *p-t*-butylphenylacetic acid showed no depression in the melting point. The aqueous filtrate gave a positive test for oxalate ion.

Hydrolysis of $C_{30}H_{36}O_7N_2$ *with 30% sulfuric acid.* A mixture of 1.0 g. of the substance and 25 cc. of 30% sulfuric acid was refluxed for 48 hr. The yellow solid (0.83 g.), filtered and washed at room temperature, was heated with 20 cc. of ligroin containing 1 cc. of benzene and filtered hot, then washed several times with hot ligroin to give 0.58 g. which from toluene gave 0.46 g. of *p-t*-butylphenylhydroxymaleimide, m.p. 248.5–250°.

From the ligroin filtrate there was obtained 0.08 g. of solid which from benzene gave 0.06 g. of white crystals, m.p. 164–165°. Likewise from the above toluene filtrate there was obtained 0.05 g., m.p. 164–165°. Mixed with an authentic sample of *p-t*-butylphenylpyruvic acid the melting point was unchanged. The infrared spectra were also identical. It was further identified by oxidation[8] with hydrogen peroxide to *p-t*-butylphenylacetic acid, m.p. 79–80°, yield 82%.

The original acid filtrate afforded a distillate which gave the iodoform reaction. The residue gave tests for ammonia and oxalate ion.

When 0.50 g. of *p-t*-butylphenylhydroxymaleimide was refluxed similarly with 30% sulfuric acid there was obtained 0.36 g. of the unchanged maleimide, m.p. 248–250°, and 0.046 g. of material, m.p. 156–161°. The melting point of the recrystallized product was 160–162°, mixed with the sample, m.p. 164–165°, the melting point was 160–162°.

Reaction of the substance $C_{30}H_{36}O_7N_2$ *with hydrogen chloride in ethanol.* Hydrogen chloride was passed into a mixture of 1.0 g. (0.19 mole) of the substance, 30 cc. of ethanol, and 0.05 cc. of hydrochloric acid (s.g. 1.18) for 1 hr. The resulting solution was heated on the steam bath for 3 hr. After standing overnight it was concentrated under diminished pressure to half its volume to give 0.42 g. of yellow crystals. Further concentration gave 0.25 g. The combined product was washed with a little benzene and crystallized from toluene, yield 0.50 g., m.p. 248–250°. Ammonium chloride (0.05 g.) was filtered from the hot toluene solution.

The above benzene washings were evaporated to an oil which crystallized when warmed with ligroin. Recrystallization from benzene gave 0.09 g., m.p. 128–131°, which then yielded 0.08 g., m.p. 130–132°. This melting point was not depressed by authentic *p-t*-butylphenylethoxymaleimide. The filtrate gave 0.23 g. of a light yellow oil which would not crystallize.

When *p-t*-butylphenylhydroxymaleimide was treated in the same way with ethanolic hydrochloric acid 89% of the starting material was recovered and there was no *p-t*-butylphenylethoxymaleimide. The only other products were 0.01 g. of ammonium chloride and 0.07 g. of an uncrystallizable oil.

Isolation of the monobromide (III). The carbon tetrachloride filtrate from the precipitate of dibromide (II) obtained from 19.0 g. of the ester (I) was quickly poured into a flask equipped with a tightly fitting glass stopper and allowed to stand in the closed flask. Red crystals slowly separated. At the end of 4 months the precipitate was filtered and washed with dry carbon tetrachloride until the washings from the yellow solid were colorless, weight 4.9 g., m.p. 145–150° dec.

This was chromatographed on a $1^1/_8$ in. column using 25 g. of silicic acid for 1.5 g. Elution was performed with chloroform. The upper narrow bright yellow band gave 1.8 g. of *p-t*-butylphenylhydroxymaleimide and the lower broad almost white band gave 2.8 g. of III, m.p. 163–165°. The ethanol solution of III made acid with nitric acid gave an immediate precipitate with silver nitrate. It also liberated iodine from an acetone solution of sodium iodide. Tribromophenol was used as the cryoscopic solvent.

Anal. Calcd. for $C_{14}H_{14}BrNO_3$: C, 51.9; H, 4.4; Br, 24.7; N, 4.3; Mol. Wt., 324. Found: C, 51.2; H, 4.5; Br, 25.3; N, 4.2; Mol. Wt., 320 ± 20.

The filtrate from the above 4.9 g., after removal of the solvent under diminished pressure, left 12.2 g. of reddish glassy material that could not be crystallized.

The monobromide also was obtained in poor yield by allowing the crystalline dibromide to stand 3 months in a closed system with carbon tetrachloride and a slight excess of bromine.

Hydrolysis of the monobromide. A solution of 0.70 g. of the monobromo compound in 10 cc. of water containing 1.0 g. of potassium hydroxide was obtained by heating 15–20 min. After refluxing 6.5 hr. the cooled solution was filtered. The reddish filtrate was extracted with ether to remove a slight amount of tar. The basic solution gave an oily solid acid which was collected with ether and crystallized from benzene-ligroin to give 0.18 g., m.p. 144–147°. This on crystallization from benzene gave 0.16 g. of *p-t*-butylmandelic acid, m.p. 149–150° identical with that obtained from the dibromide.

Reaction of the monobromide with toluene. The monobromide (0.52 g.) was covered with 4 cc. of dry toluene and heated 13 hr. at 95–100° protected from moisture. The yellow crystalline material was recrystallized from toluene to give 0.38 g. (97%) of *p-t*-butylphenylhydroxymaleimide, m.p. 249–250°.

Removal of the toluene under diminished pressure gave 0.25 g. of residual lachrymatory oil which reacted with β-naphthol in hot alcoholic sodium hydroxide to give, after crystallization from alcohol, 0.15 g. of benzyl β-naphthyl ether, m.p. 100–101°, identical with an authentic sample.

Ethyl p-t-butyl-β-cyano-α-ethoxycinnamate. A cold dry solution of 3.28 g. of diazoethane[9] in 150 cc. of ether was slowly poured into a well-swirled ice-cold solution of 16.0 g. of ethyl *p-t*-butyl-β-cyano-α-hydroxycinnamate in 50 cc. of ether. After standing overnight the ether was removed from the reddish solution and the residue was distilled, yield of light yellow product, 14.3 g., b.p. 153–153.5° (0.10 mm.); m.p. 41–43°; d_4^{24} 1.0389; n_D^{25} 1.5315.

Anal. Calcd. for $C_{18}H_{23}O_3N$: C, 71.73; H, 7.69; N, 4.65. Found: C, 71.72; H, 7.55; N, 4.79.

p-t-Butylphenylethoxymaleimide. Hydrogen chloride was passed into a mixture of 10 cc. of ethanol and 0.26 cc. of water for 35 min. Then 4.3 g. of ethyl *p-t*-butyl-β-cyano-α-ethoxycinnamate in 8 cc. of ethanol was added and the passage of hydrogen chloride was continued for 1 hr. Next day the mass of crystals was filtered and washed with dilute alcohol, yield, 3.2 g. Recrystallization from ligroin gave 2.8 g. of yellow crystals, m.p. 133–134°.

Anal. Calcd. for $C_{16}H_{19}O_3N$: C, 70.31; H, 7.01; N, 5.13. Found: C, 70.28; H, 7.06; N, 5.12.

(7) S. Winstein, *J. Am. Chem. Soc.*, **64**, 2792 (1942).

(8) R. B. Wagner and H. D. Zook, *Synthetic Organic Chemistry*, John Wiley and Sons, New York, p. 422 (1953).

(9) A. L. Wilds and A. L. Meader, *J. Org. Chem.*, **13**, 763 (1948).

Nonformation of a dibromide from ethyl p-t-butyl-β-cyano-α-ethoxycinnamate. Dry bromine (1.0 cc.) was added dropwise with stirring to a solution of 5.1 g. of the ester in 20 cc. cc. of carbon tetrachloride protected from moisture in the Mini Lab. After standing 7 days there was no evidence of reaction. The mixture was distilled under diminished pressure to give 4.3 g. of starting material, b.p. 156–159° (0.26 mm.); n_D^{25} 1.5320. No bromide could be isolated.

NEWARK, DEL.

[CONTRIBUTION FROM LABORATORY OF CHEMISTRY, RAMNARAIN RUIA COLLEGE, UNIVERSITY OF BOMBAY]

β-Arylglutaconic Acids. IV.[1] Synthesis of Crotono- and Valerolactones of β-Arylglutaconic and Glutaric Acids

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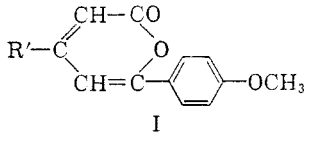
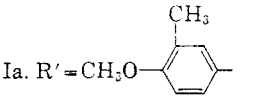
Through the condensation of β-arylglutaconic anhydrides with phenolic ethers in the presence of anhydrous aluminum chloride, a series of β-aryl-γ-benzoylcrotonic acids and their lactones were prepared. In addition, a general method for the synthesis of β,γ-substituted benzoylbutyric acids has been developed. These acids after reduction and lactonization gave the corresponding β,δ-substituted valerolactones. The crotono- and valerolactones are being tested for their anthelmintic activity and for their perfumery properties.

Though the relationship between chemical constitution and anthelmintic effect has not been fully elucidated, a number of the anthelmintics have been found which possess a lactonic group.[3] A detailed study by Rosenmund[4] and Nargund[5] has indicated that some arylbutyrolactones possess good anthelmintic effect. Moreover, unsaturation in the lactone ring has been shown to enhance the anthelmintic activity.[6]

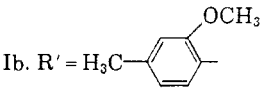
These findings have led us to prepare a number of unsaturated lactones with different aryl substituents (Type I) for testing their anthelmintic effects.



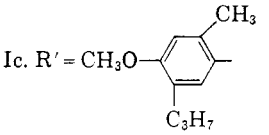
I



Ia. R′ = CH_3O



Ib. R′ = H_3C



Ic. R′ = CH_3O

Since 1926, the chemistry of lactones has assumed a great importance in the field of perfumery. Many naturally occurring lactones and their synthetic substitutes have been extensively studied in the light of their perfumery values.[7–9] The variation in odor of lactone has been studied as a function of the substituents attached to the lactone and, accordingly, a series of α and γ-substituted γ-butyrolactones were prepared.[10] Even the variation in intensity of odor with increase in the size of the lactonic ring was studied.[11] However, as yet, no definite relationship between the structure of a lactone and the intensity of its odor has been determined. It was therefore thought interesting to study the lactones (I) from the perfumery value point of view and attempt to gain some knowledge concerning the relationship between structure and odor intensity.

In the present work, condensation of (1) β-(4-methoxy-3-methylphenyl)-, (2) β-(2-methoxy-4-methylphenyl)- and (3) β-(4-methoxy-2-methyl-5-isopropylphenyl(glutaconic anhydrides in nitrobenzene with an equimolar quantity of anisole in the presence of anhydrous aluminum chloride was effected following the observation of Bhave.[12] From this reaction, two distinct products were isolated. The predominant product (80% yield) was a neutral compound and by analogy with

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(1) (a) Prior publications, *J. Org. Chem.*, **24**, 520 (1959); (b) *J. Org. Chem.*, **24**, 2055 (1959); (c) *J. Org. Chem.*, in press.

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