

CIS-TRANS ISOMERISM OF  $\gamma$ -LACTONES  
AND  
SOME ASPECTS OF ACENAPHTHENONE  
CHEMISTRY

by

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Hugh J. Campbell

CIS-TRANS ISOMERISM OF  $\delta$ -LACTONES AND SOME  
ASPECTS OF ACENAPHTHENONE CHEMISTRYABSTRACT

The lactones of cyclohexanol-2-acetic acid and cyclohexanol-2- $\alpha$ -propionic acid have been prepared by two different procedures. The method involving cyclohexene oxide as a starting point was known to yield a lactone of the trans configuration. This investigation has shown that an alternate synthesis through a Reformatsky reaction yielded the corresponding cis lactone. A set of derivatives have been prepared and spectroscopic data presented for each isomer. In particular, the first overtone of the carbonyl stretching frequency has been identified at 2.8 microns using the Beckmann D.K. spectrophotometer.

In the second part of this work a number of the condensation reactions of acenaphthenone with aromatic aldehydes have undergone investigation. Two products with distinctly different melting points are often obtained from the same reactants. This may be due to genuine cis-trans isomerism, as seems to be the case for the o-nitrobenzalacenaphthenones, or merely to various polymorphic forms, as in the case of the p-anisalacenaphthenones. A number of near infra red spectra (2.0 - 2.85  $\mu$ ) of acenaphthenone and related compounds are also presented.

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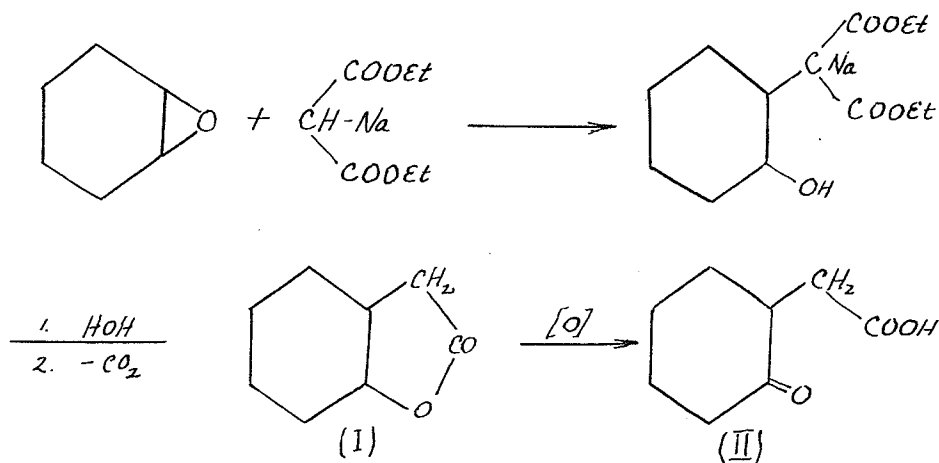
PART I

CIS - TRANS ISOMERISM OF  $\delta$ -LACTONES

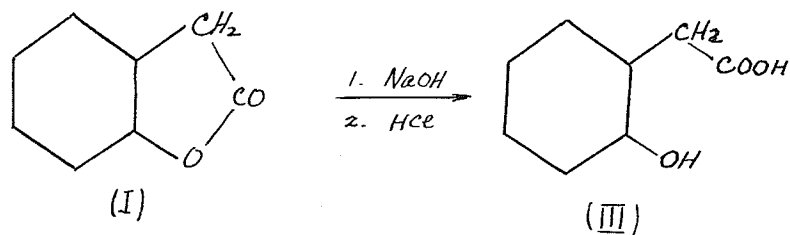


## INTRODUCTION

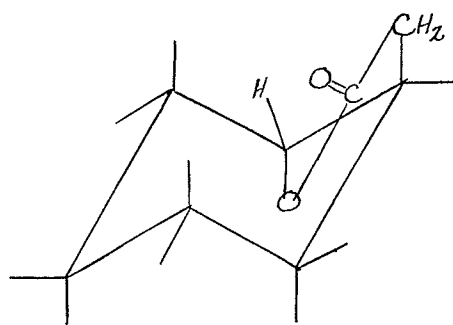
The lactone of cyclohexanol-2-acetic acid (I) was first prepared by Coffey (12) by the hydrolysis and decarboxylation of the product resulting from the condensation of cyclohexene oxide and the sodio derivative of malonic ester. Later workers (24, 25) oxidized this lactone to cyclohexanone-2-acetic acid (II).



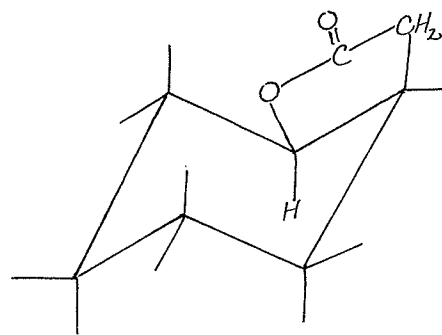
Newman and Van der Werf (25), by catalytic hydrogenation of the keto acid (II), obtained a lactone isomeric with (I). They noted that while Coffey's lactone (I) yielded a hydroxy acid (III), this new isomeric lactone failed to do so.



Apparently the acyl-oxygen fission of the isomeric lactone occurred readily enough, but upon acidification the ring closed to regenerate the original lactone. The hydroxy acid (III) proved to be quite stable, resistant to relactonization even in boiling water. Upon this basis these investigators assigned the trans configuration (Ia) to Coffey's lactone and the cis configuration (Ib) to their isomeric lactone.

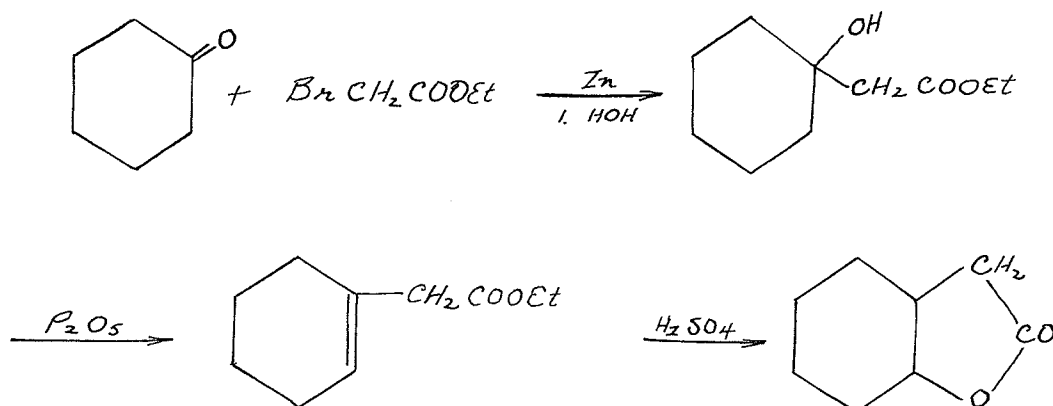


(Ia) "trans"



(Ib) "cis"

By a Reformatsky reaction followed by dehydration and hydrolysis Stachiw<sup>+</sup> (28) has obtained one of these lactones.



+ The method of Stachiw is a repetition and improvement of that of MacFarlane(8) carried out in these laboratories in 1942.

At first, this Reformatsky lactone was thought to be identical with that of Coffey. However, Moir (private communication, 1948) claimed that it had been inadequately characterized in view of the fact that both cis and trans isomers were known to exist.

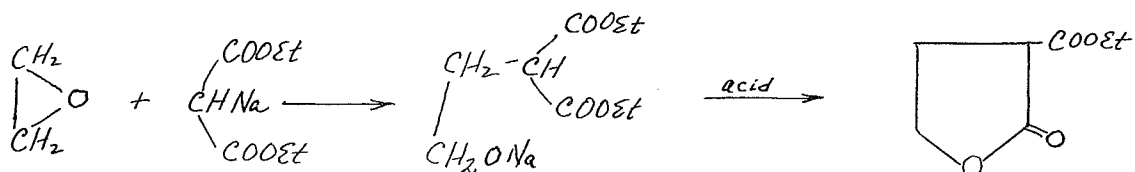
The present work has undertaken an investigation of the configuration of this Reformatsky lactone and a careful comparison of it with the Coffey lactone. The results show that Moir's point was well taken. This Reformatsky product is of the cis configuration, not trans as previously supposed. Derivatives and infra red spectra are among the confirmatory evidence presented in this work.

The geometric isomers of the  $\gamma$ -lactones of cyclohexanol-2- $\alpha$ -propionic acid have been prepared and characterized. As before, the cyclohexene oxide condensation yielded the trans isomer and the Reformatsky reaction, the cis form.

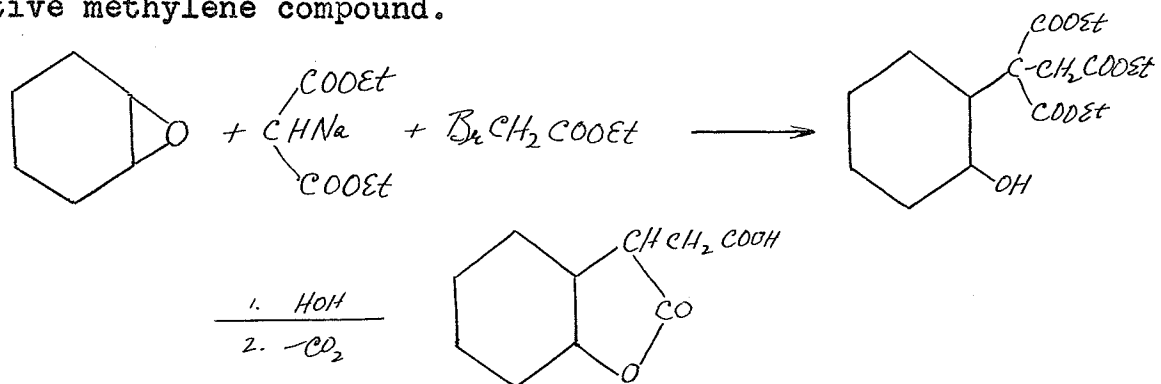
## LITERATURE SURVEY

Cyclohexene Oxide Condensations

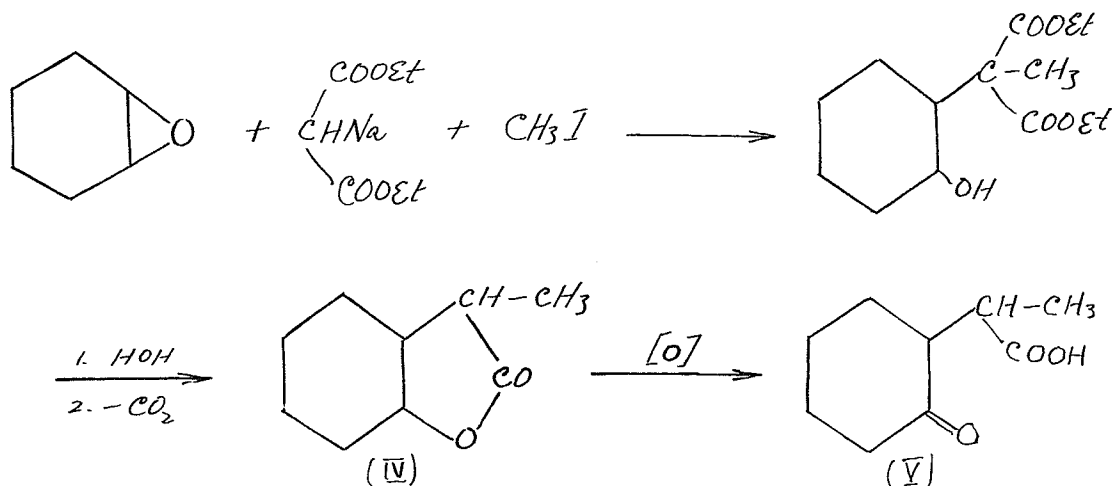
The cyclohexene oxide - sodio malonic ester condensation was suggested to Coffey (see Introduction) by the previous work of Traube and Lehmann (30, 31) with ethylene oxide .



Kendall and associates (17, 18) extended the work of Coffey, performing the condensation in the presence of a halo-ester, thus substituting the second hydrogen of the active methylene compound.

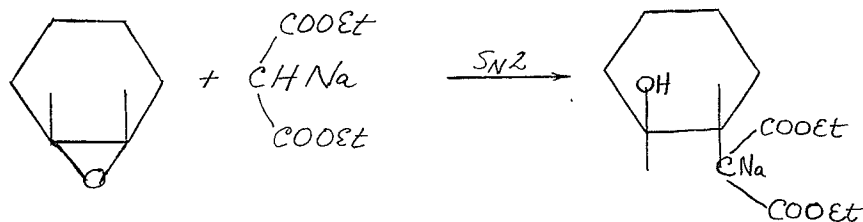


McRae, Charlesworth and Alexander (24) developed these condensations further, using an alkyl halide in place of the  $\alpha$ -halo-ester. With methyl iodide, the  $\delta$ -lactone of cyclohexanol-2- $\alpha$ -propionic acid (IV) was obtained. This lactone was then oxidized by either bromine- magnesium hydroxide, or cold permanganate, to the keto acid (V).



Linstead and Meade (19) have demonstrated that two five - membered rings could be fused together (ortho) only in a cis configuration. The trans form, except in one or two cases, was far too unstable to exist because of the prohibitive strain involved. A five and a six membered ring, however, can undergo fusion resulting in a trans configuration; the ring strain, although considerable, is not critical.

Grigsby, Hind, Chanley and Westheimer (16) have discussed the reactions of olefin oxides with sodio-malonic ester as a normal displacement reaction which should proceed by  $S_N2$  inversion about one of the carbon atoms to which the oxygen is attached. For the case considered below, this may be envisaged as a nucleophilic attack of the sodio-ester directed against the "back" side (relative to the epoxide oxygen) of either of the carbon atoms involved. The subsequent shift of the displaced hydrogen atom and the fission of a carbon - oxygen bond results in the inverted configuration.



If the stereochemical configuration of this addition product remains fixed and trans, then, precluding any alkyl-oxygen fission, the following intermediates will also be trans.

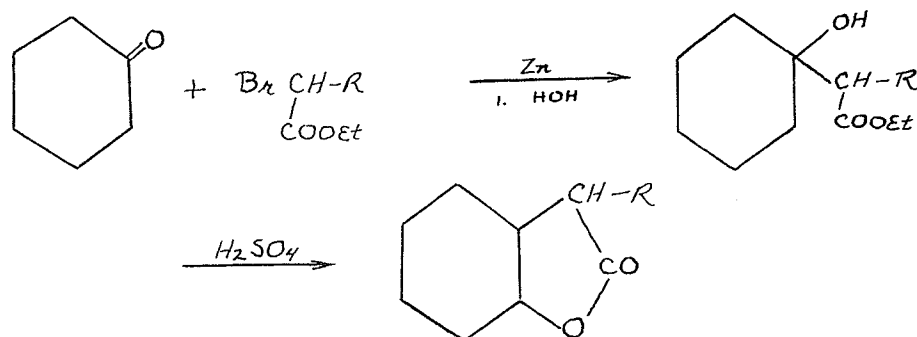


That hydrolysis and relactonization do not involve any change in configuration was indicated by the work of Newman and Van der Werf (see page 8). These investigators found that the catalytically - produced isomeric cis lactone could not be converted into the trans isomer even under the most rigorous conditions.

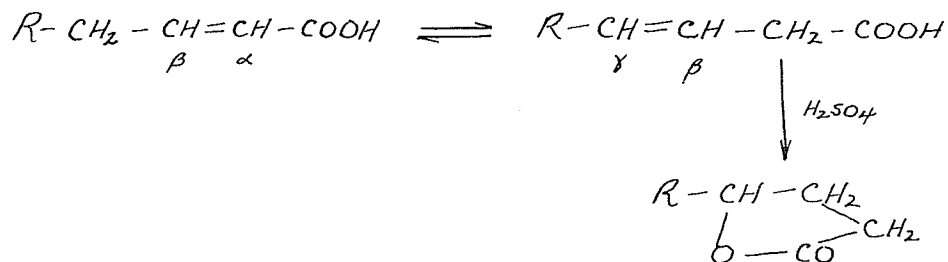
In conclusion, therefore, it appears that all such lactones prepared by olefin oxide condensations, and cyclohexene oxide in particular, will have the same trans configuration. Furthermore, opening or closing of the lactone ring does not alter the initial configuration. This means, of course, that acyl-oxygen fission alone is operative; never alkyl-oxygen fission.

### Reformatsky Synthesis of $\delta$ -Lactones

$\alpha$ -(1-cyclohexanol) esters were synthesized by Wallach and coworkers (32, 33, 34) and by Auwers and Ellinger (1). Boehringer and Sohn (4) applied "Fittig's conditions" (14) using excess 50% aqueous sulphuric acid to these hydroxy esters, converting them to the corresponding lactones. This method was further investigated by MacFarlane (8, 22).



Since it was known that "Fittig's conditions" were applicable primarily to  $\beta, \delta$ -unsaturated acids, the foregoing reaction probably involves dehydration of the hydroxy ester to a  $\beta, \delta$ -unsaturated intermediate prior to lactonization. Linstead and associates (5, 6, 20, 21) demonstrated that  $\alpha, \beta$ -unsaturated acids could also be lactonized in this way because of the operation of a tautomeric shift to  $\beta, \delta$ -unsaturation.



Stachiw<sup>+</sup> (28) found that if the hydroxy ester obtained from the Reformatsky reaction were first dehydrated with phosphorus pentoxide in a separate step, the application of "Fittig's conditions" to the  $\beta, \delta$ -unsaturated ester yielded a purer, more easily isolable lactone product. It was the identification of the  $\delta$ -lactone of cyclohexanol-2-acetic acid, synthesized in this way, that Moir<sup>+</sup> (see Introduction) criticized. The analysis and boiling point of this product were such that it was considered identical with Coffey's lactone, consequently, no further work had been done.

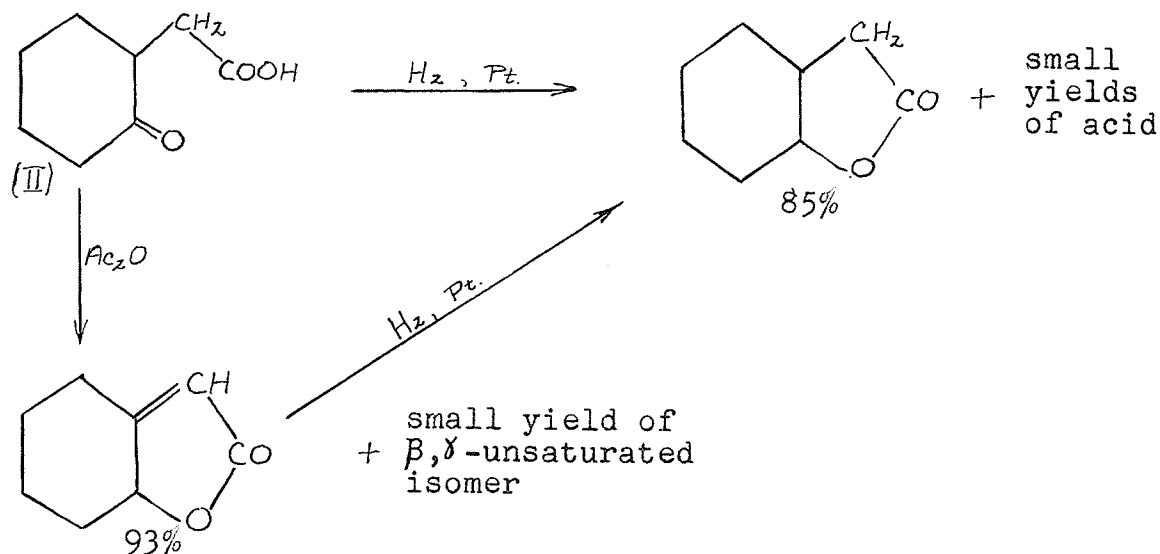
#### Cis-trans $\delta$ -Lactone Pairs

The keto acid, cyclohexanone-2-acetic (II), was prepared previously by Chuang and Ma (11), Chatterjee (10), and Ghosh (15). McRae, Charlesworth and Alexander (24) found that the bromine-magnesium hydroxide oxidation of Coffey's lactone (I) yielded the keto acid (II) in a much purer state. An identical product of comparable purity was obtained by Newman and Van der Werf (25) who used chromic trioxide in acetic acid to oxidize the free hydroxy acid (III, see Introduction).

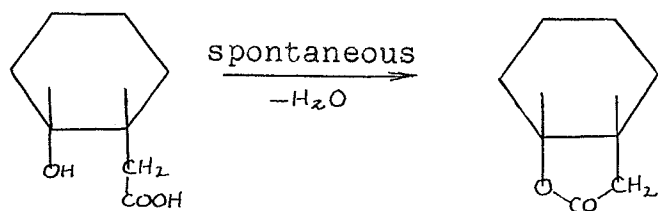
It was from this keto acid (II) that Newman and Van der Werf discovered methods whereby a new isomer of cyclohexanol-2-acetic acid was obtained.

+ See foot note on Page 2

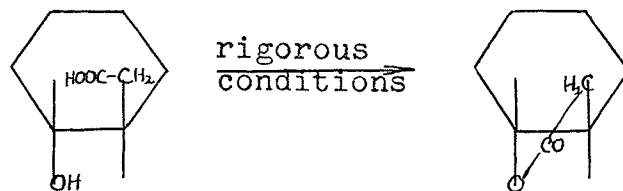




This isomeric lactone yielded a transient hydroxy acid which spontaneously relactonized. Apparently this was due to the proximity of the hydroxyl and carboxylate groups and to the relative ease of cis ring formation.



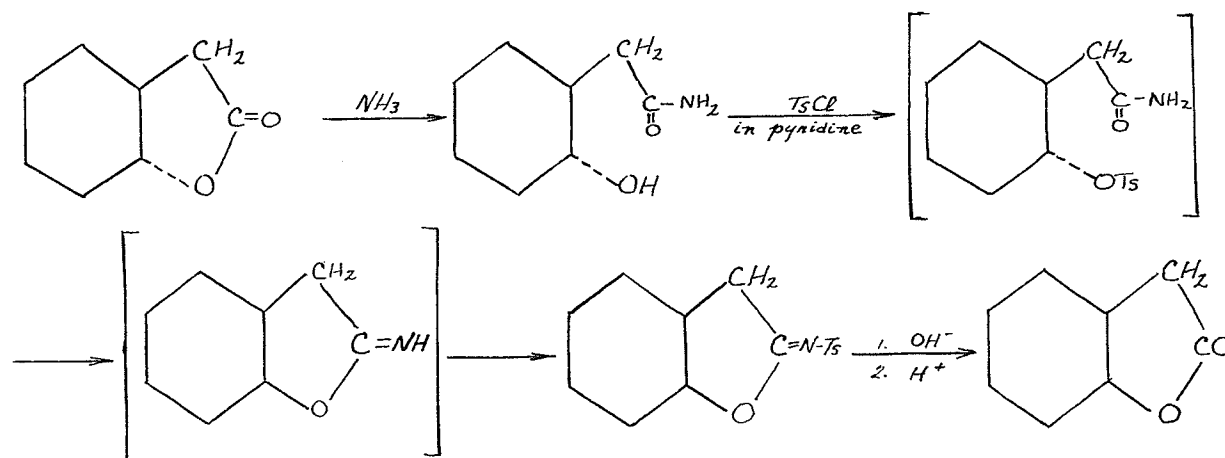
On the other hand, the trans hydroxy acid was quite stable, undergoing relactonization only when refluxed for several hours in dilute acid, or direct heating at 200° C.



The reluctance to lactonize in this case was ascribed to the relative difficulty of trans ring formation.

As has been mentioned previously, these authors assigned the cis configuration to their new isomer, and the trans configuration to Coffey's lactone. Slight variations in the physical constants of the two isomeric lactones were also detected.

In a recent paper Brewster and Kucera (7) have reported the conversion of the trans isomer to the cis isomer.



The essential feature is an internal nucleophilic displacement of the tosylate group by the carbonyl oxygen atom of the neighboring amide group thereby effecting an inversion of configuration. The authors had originally thought that tosylation of the trans hydroxy acid would yield the cis lactone by displacement of the tosylate group by the neighboring carboxylate group. This had proven fruitless however.

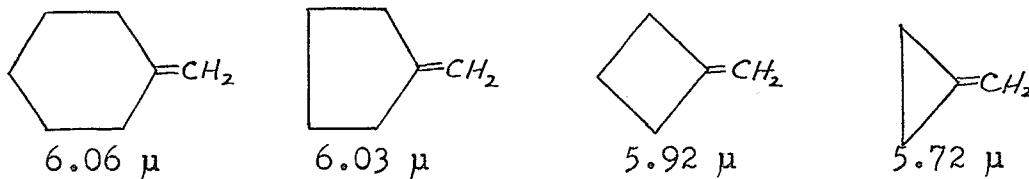
Brewster and Kucera have also prepared the cis and trans amides and N-benzylamides. Newman and Van der Werf had been unable to obtain any derivative of the cis lactone.

<u>Derivative</u>	<u>"trans"</u>	<u>"cis"</u>
hydroxy acid	105-106°	----
amide	150-151°	120-121°
N-benzylamide	141-142°	97-98°

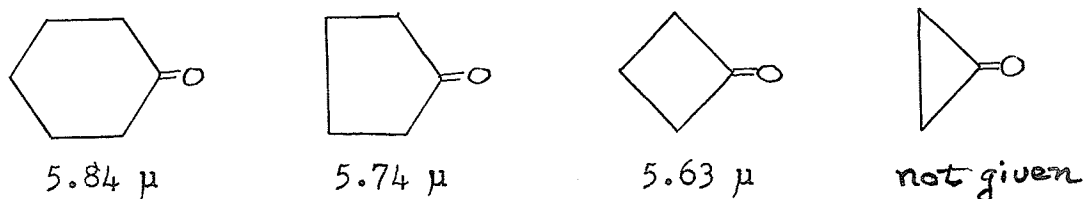
### Infra Red Spectra

Rasmussen and Brattain (26) give 5.65  $\mu$  as the characteristic frequency of the carbonyl stretching vibration of a simple five - membered lactone ring. Whereas, according to Berson (3) a six - membered lactone ring, being unperturbed by strain, absorbs at 5.75  $\mu$ , the same as for open chain esters.

It is a well known fact that ring strain raises the stretching frequency of an exocyclic double bond (27, 29, 35).



Bartlett and Stiles (2) give the following absorption frequencies for cyclic ketones (2.5% in Carbon tetrachloride).



In agreement with the foregoing, Brewster and Kucera reported that the position of the carbonyl stretching absorption of the relatively unstrained cis-cyclohexanol-2-acetic acid lactone was at 5.70  $\mu$ , while that of the more strained trans isomer was displaced towards a shorter frequency, viz, 5.62  $\mu$ .

Marion, Ramsay and Jones (23) have remarked that since carbonyl groups produce intense absorption bands in the 5620 - 6170  $\text{cm}^{-1}$  region, one might expect to observe weak overtone bands at approximately twice this frequency, viz, 2800 - 3080  $\text{cm}^{-1}$ . They add that, although such overtone bands overlap the OH and NH stretching band region, no cases have yet arisen in which there was any confusion .

## DISCUSSION OF RESULTS

Characterization of the Reformatsky - Fittig Lactones

The following points of similarity have been established as existing between the Reformatsky - Fittig produced lactone of cyclohexanol-2-acetic acid and the cis lactone of Newman and Van der Werf.

1. Neither lactone yields a stable hydroxy acid.
2. Their densities (20°) are virtually identical, viz, 1.0921 and 1.0923 respectively.
3. The infra red spectra (in the range 2.2 - 2.85  $\mu$ ) are very similar, whereas that of the trans lactone differs markedly.
4. Both lactones yield identical hydrazides (m.p. 140 - 141°), and N-benzylamides (m.p. 97 - 98°). On the other hand, the melting points of the corresponding derivatives of the trans lactone are respectively, 167.5° and 141 - 142°.

Thus, it may be definitely concluded that the Reformatsky - Fittig lactone and the cis lactone of Newman and Van der Werf are completely identical.

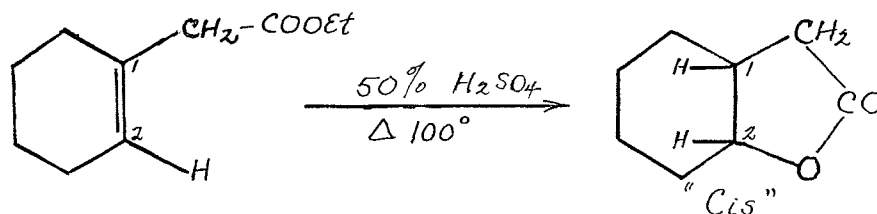
The  $\delta$ -lactones of cyclohexanol-2- $\alpha$ -propionic acid, although treated less thoroughly, also appear to fit into the above scheme.

1. No hydroxy acid is obtainable from the Reformatsky - Fittig lactone.

2. Both this Reformatsky lactone and the catalytically-produced product give similar spectra, the most intense peaks occurring at 2812  $\mu$ , as compared to the 2819  $\mu$  peak exhibited by the trans lactone.

3. The trans lactone yields a hydrazide melting at 190 - 191 $^{\circ}$  whereas the Reformatsky - Fittig hydrazide melts at 136 - 137 $^{\circ}$ .

Mechanism of Lactonization by Fittig's Conditions



Very little can be said definitely about the actual mechanism since it is not known upon which of the carbon atoms ( $\text{C}_1$  or  $\text{C}_2$ ) the initial attack occurs. Even the nature of the attacking species, whether it is water in the first instance or  $\text{OSO}_2\text{OH}^-$  followed by water, is in doubt.

All that can be said is that a trans type of addition occurs at the double bond which results, before lactonization, in a hydroxyl group on C<sub>2</sub> cis to the carbethoxyl or carboxyl group.

An interesting possibility might be realized by changing the nature of the hydrolysis. If cold, concentrated sulphuric acid were used followed by water, the milder hydrolysis might conceivably lead to a cis type of addition and the formation of the trans lactone.

### Interpretation of Spectra

The lactones investigated in this work all exhibited prominent absorption bands at approximately  $2.8 \mu$ . Similar bands were reported by Rasmussen and Brattain (26) for  $\gamma$ -valerolactone,  $\beta, \delta$ -angelica lactone,  $\alpha$ -acetyl- $\gamma$ -butyrolactone, and  $\delta$ -valerolactone. Since this region of the infra red is that in which free hydroxyl groups produce their fundamental stretching vibrations, these authors ascribed their  $2.8 \mu$  bands to the presence of adventitious water or other hydroxylic impurities.

The present work has shown that Rasmussen and Brattain were definitely in error regarding the interpretation of the  $2.8 \mu$  bands.  $\gamma$ -valerolactone has been taken as a case in point. The product used was an Eastman practical grade, consequently it would be expected to contain a significant amount of water. The absorption curves of this lactone (fig. 4) prove fairly conclusively that it is not the  $2.8 \mu$  band but rather a second and less prominent band at  $2.71 \mu$  that is ascribable to adventitious water. It was the relative height of this second band that was increased when the solvent was changed from dry carbon tetrachloride to carbon tetrachloride saturated with water. The position of the  $2.8 \mu$  (more exactly,  $2812 \text{ m}\mu$ ) peak remained unaffected, raised only the 3 - 4% indicated by the wet carbon tetrachloride base line.



Another interesting feature is that the peak for water alone in carbon tetrachloride occurs at 2696  $\text{m}\mu$  whereas when the lactone is present this peak is always shifted to 2710  $\text{m}\mu$ . Indeed, all the lactones investigated in this work exhibited a peak at this position. This seems to indicate that when adventitious water is present it bonds itself in some way with the lactone molecule resulting in a shift of the hydroxyl peak to a slightly lower frequency.

The band at 2.8  $\mu$  is exactly where one would expect the first overtone of the fundamental stretching carbonyl frequency (5.6  $\mu$ ) to be. Furthermore, in view of the shift reported by Brewster and Kucera — 5.62 to 5.70  $\mu$  in going from trans to cis cyclohexanol-2-acetic lactone — it would be expected that a roughly comparable shift should be shown by these 2.8  $\mu$  bands if they actually are the first overtones as postulated. Such a shift, although apparently much less pronounced, was indeed observed.

fig. 1, lactone of cis-cyclohexanol-2-acetic acid ....2808  $\text{m}\mu$   
 " " trans " " " " ....2802 "

fig. 3, lactone of cis-cyclohexanol-2- -propionic acid..2819  $\text{m}\mu$   
 " " trans " " " " ..2812 "

In each case the carbonyl shift bears out the more strained condition of the trans configuration.

Since the relative strain experienced by the lactone ring is alone responsible for the perturbation of the carbonyl vibration it was predicated that butyrolactone (fig. 5) should exhibit its carbonyl overtone band at exactly the same position as that of cis-cyclohexanol-2-acetic lactone. The prediction was completely validated when it was found that the butyrolactone band was positioned at exactly the same wavelength as that of the cis lactone, viz, 2808  $\mu$ .

Another point that can readily be adduced from these spectra is that although the butyrolactone used was a reagent grade Eastman product, it exhibited just as prominent a 2.71  $\mu$  peak as the practical grade  $\gamma$ -valerolactone. The fact that adventitious water appears to be bonded to the lactone molecule (perhaps as a hydrogen bond to the carbonyl oxygen) would indicate that the last traces of water are very difficult to remove. Even though the cyclohexanol lactones were redistilled many times during the course of this work, the 2.71  $\mu$  peaks could not be eliminated completely, although they were successively reduced in size. In a completely anhydrous sample this 2.71  $\mu$  peak should be absent. If this peak were found to follow a Beer's law plot upon addition of small increments of water, this might provide a convenient and accurate method for the determination of trace quantities of water in an organic compound.

The extinction coefficients of the 2.8  $\mu$  peaks of the cyclohexanol lactones were found to average about 5 units,

whereas that of butyrolactone and  $\gamma$ -valerolactone were 3 - 4 units. A much more complete spectrum (2 - 15  $\mu$ ) was taken of the cis and trans lactones of cyclohexanol-2-acetic acid on the Perkin - Elmer Model 21 spectrophotometer. Since the smallest gasket available was .25 mm. the 5.6  $\mu$  peak for the pure liquid went off scale. Consequently no estimation of its extinction coefficient could be obtained. Other workers have reported that the value for this 5.6  $\mu$  carbonyl band is usually within a range of 300 to 1300 units. Consequently it may be seen how much weaker these first overtones appear to be.

The remainder of the bands from 2.6 - 2.3  $\mu$  are less pronounced and rather more detailed. They are very probably due to overtone carbon - hydrogen vibrations from the cyclic  $\text{CH}_2$  groups in both the cyclohexane and lactone rings.

#### Hydrolyses of the $\gamma$ -Lactones

Fig. 6 shows the relative rates of hydrolysis of the two pairs of lactones investigated in this work. It had been hoped that the cis and trans lactones of cyclohexanol-2-acetic acid would have shown markedly different hydrolysis curves — the cis being much slower to hydrolyze than the trans. Apparently however, the ease of ring opening is not very different in this case. For the cis and trans cyclohexanol-2- $\alpha$ -propionic lactones however, there seems to be much more pronounced difference. The trans lactones in both instances hydrolyze at an almost identical rate.

TABLE OF PHYSICAL CONSTANTS OF  $\delta$ -LACTONES

	$\delta$ -lactone of cyclohexanol-2-acetic acid			$\delta$ -lactone of cyclohexanol-2- $\alpha$ -propionic acid		
	cyclohexene oxide product(trans)	Reformatsky product (cis)	cis, according to Newman	cyclohexene oxide product(trans)	Reformatsky product(cis)	catalytically produced product (cis)
b.p.	131-132/12 mm.	129-130/13	128-128.5/10	125-128/10	131-134/11	132-135/13
$D_4^{20}$	1.0859	1.0921	1.0923	1.0519	1.0589	
$n_D^{20}$	1.4752	1.4784	1.4773	1.4719	1.4756	1.4751
$M_R$	36.36	36.36	36.30	41.04	41.04	
$M_R$ (calc)	36.398			41.016		
position of C=O overtone in $\mu$ .	2802	2808	2808	2812	2819	2819

FIGURE I

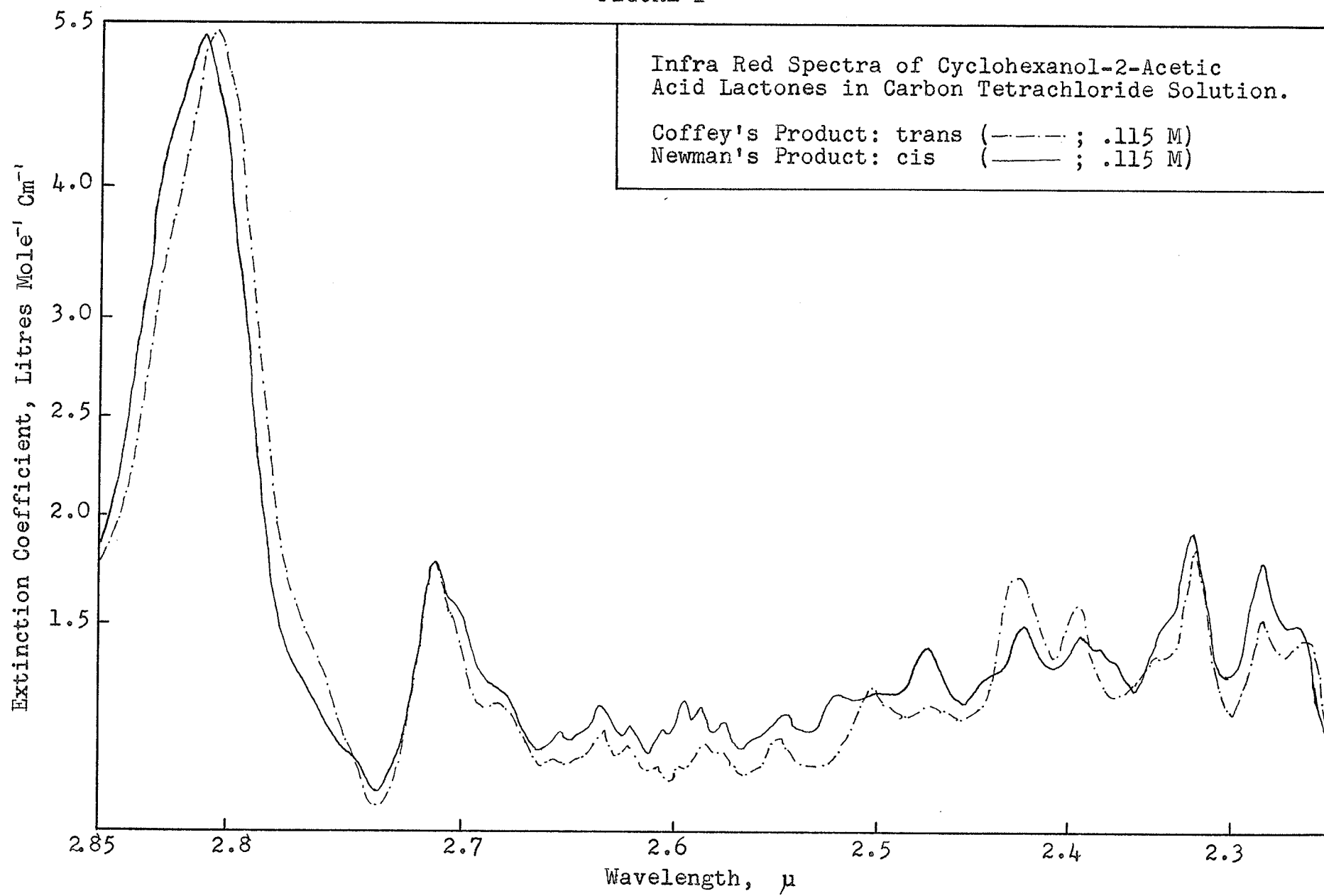


FIGURE 2

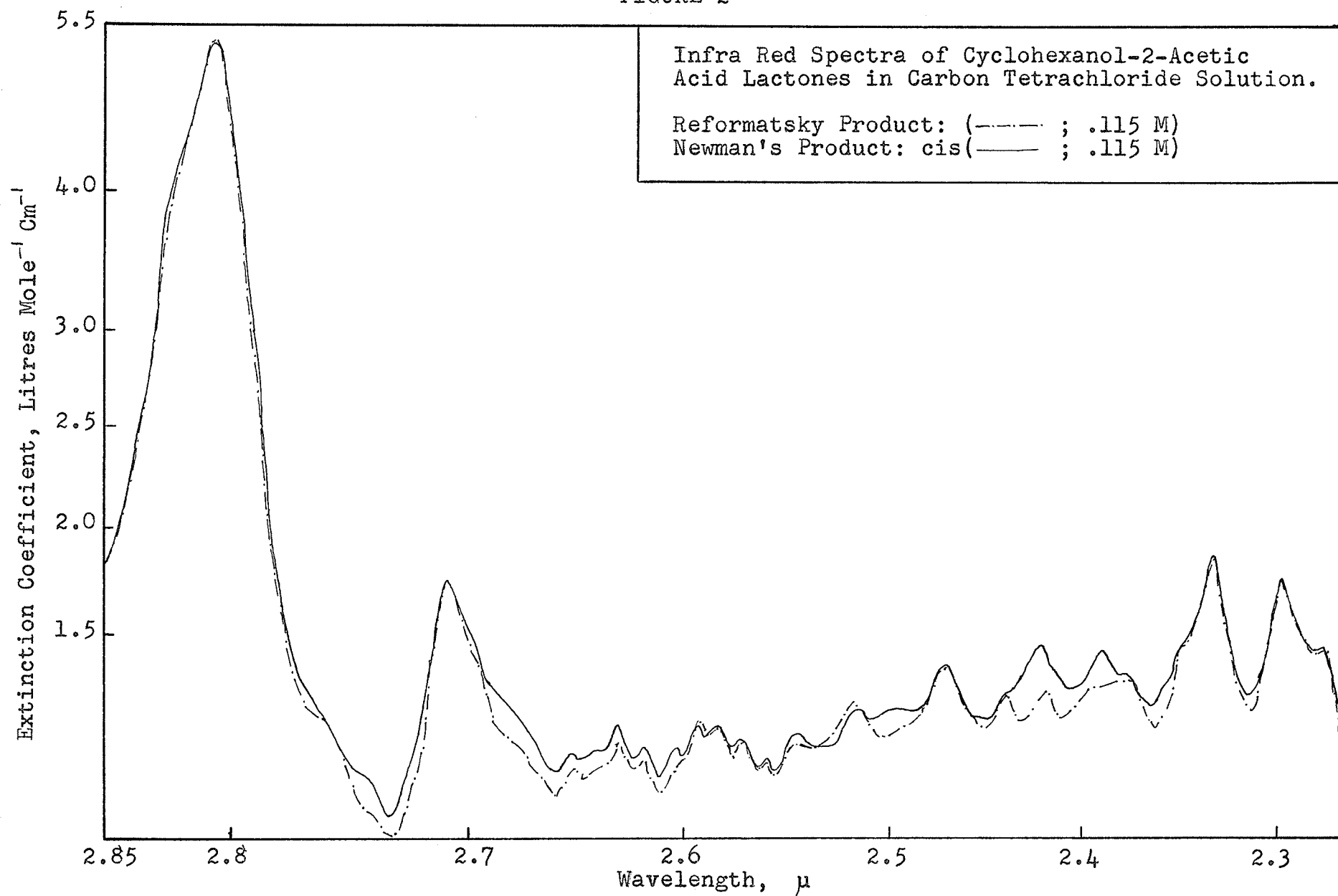


FIGURE 3

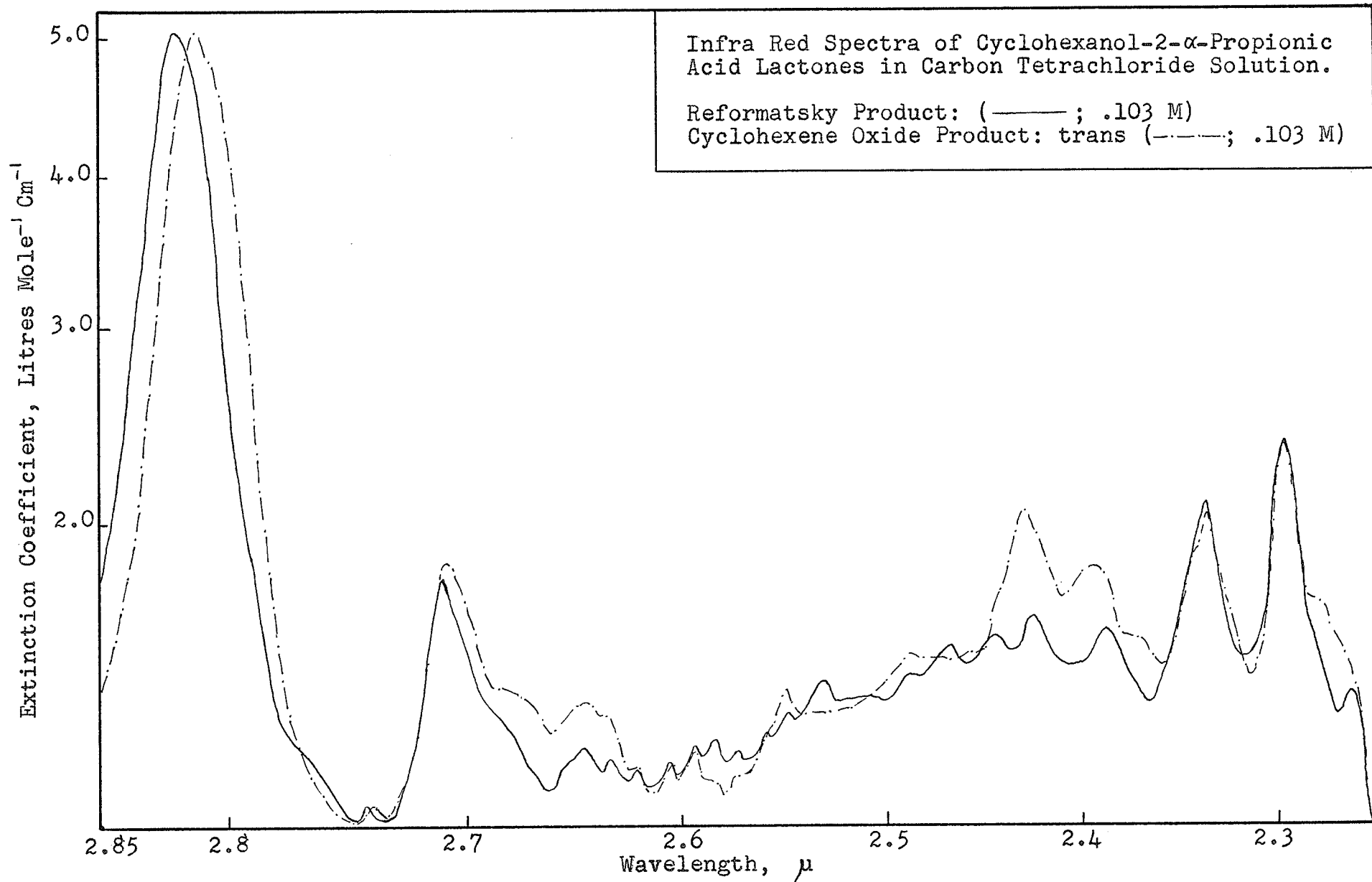


FIGURE 4

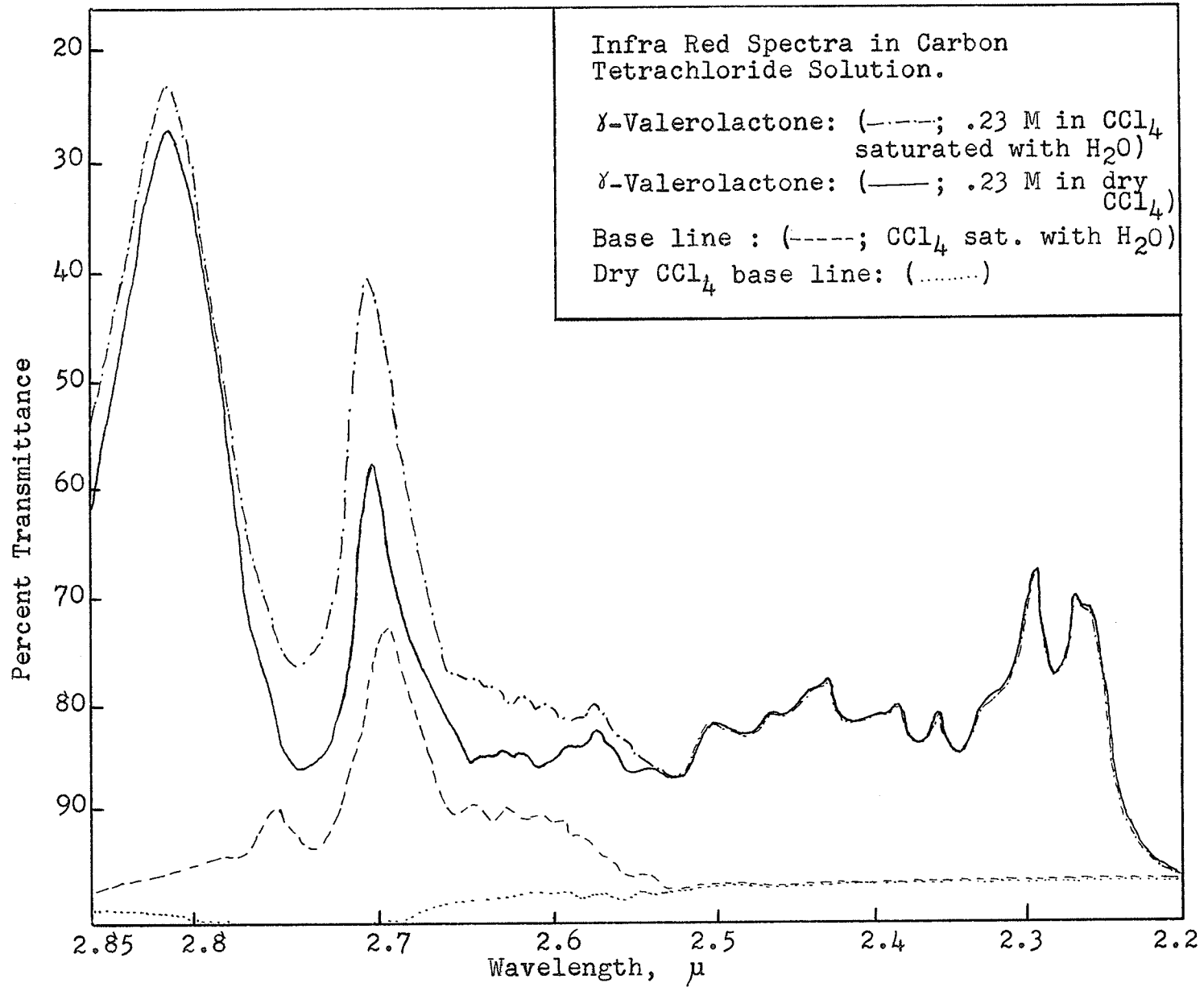




FIGURE 5

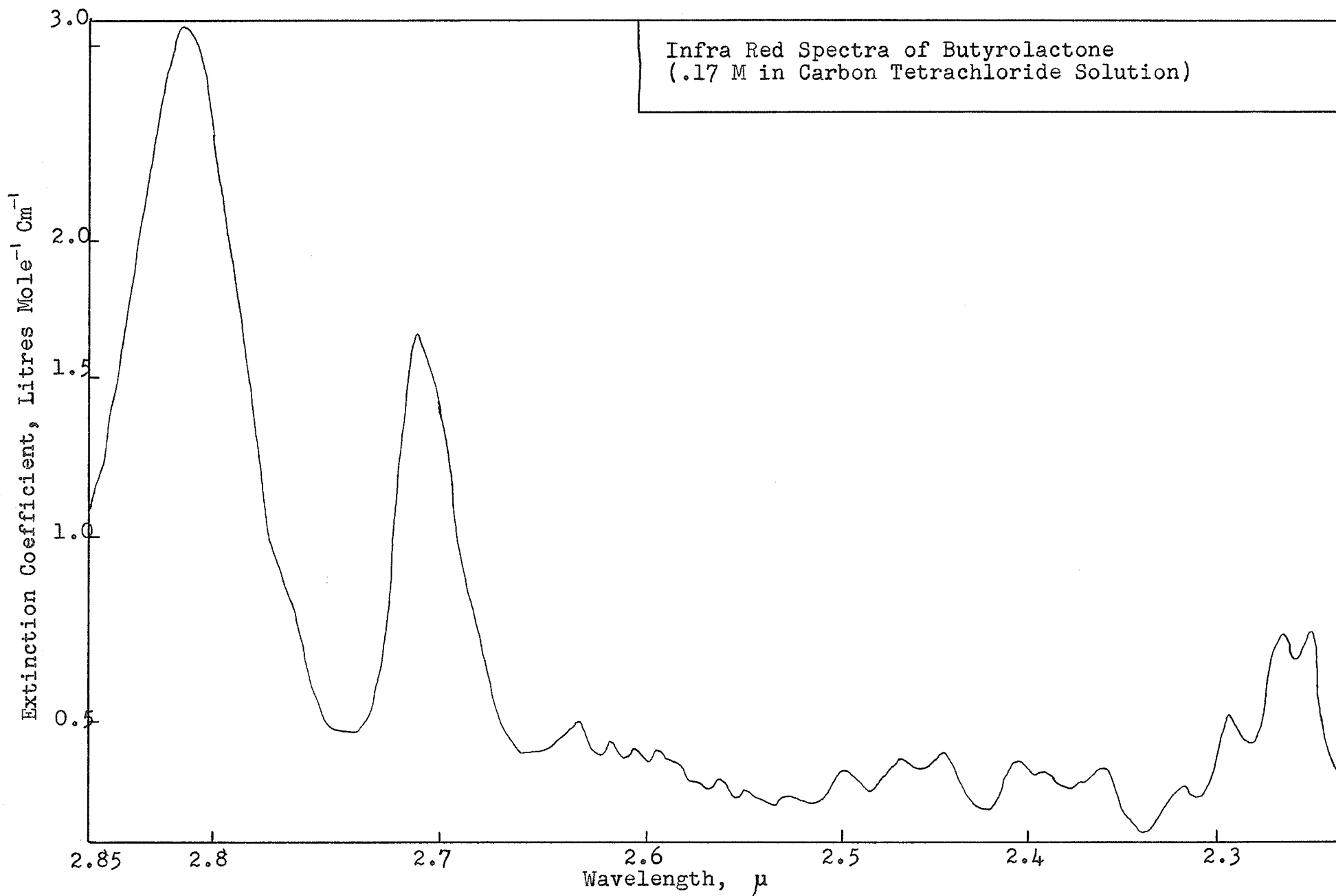
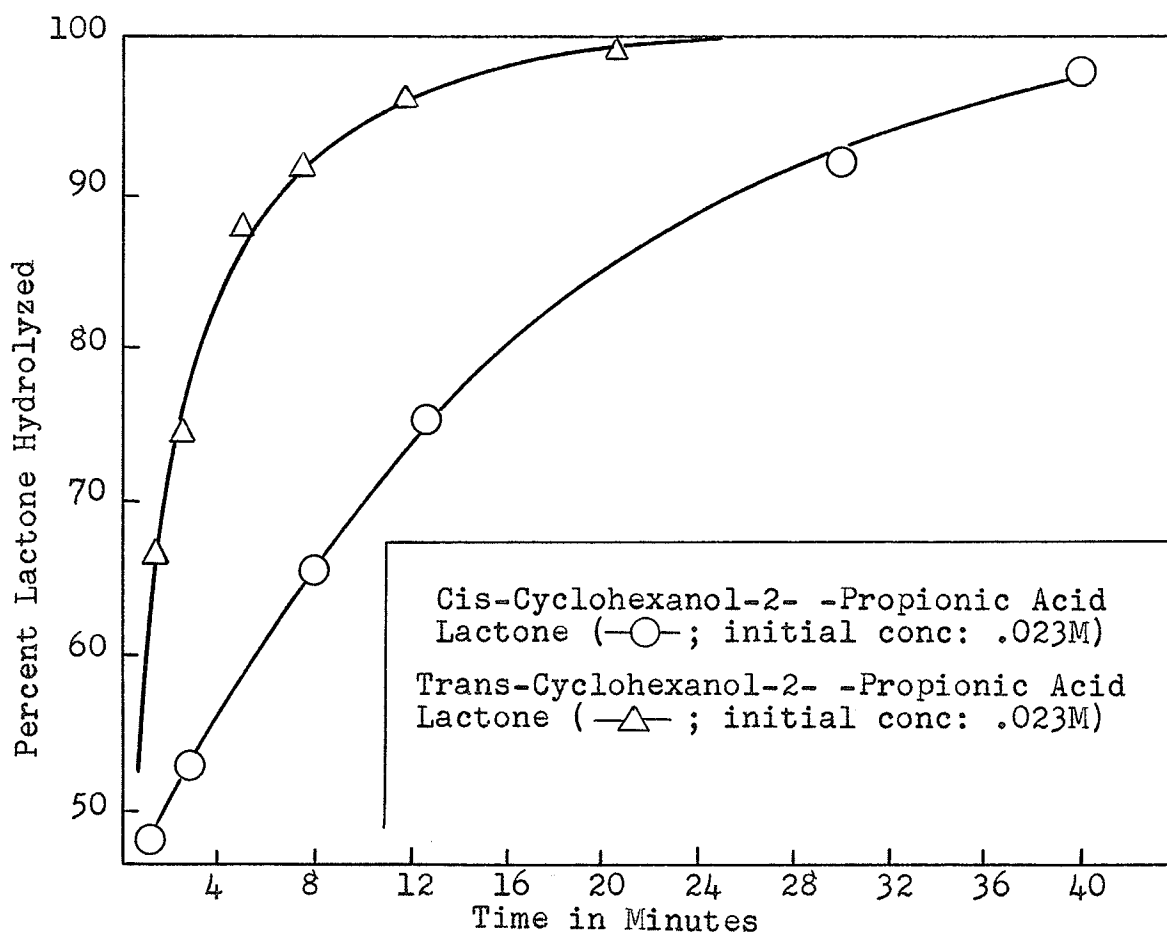
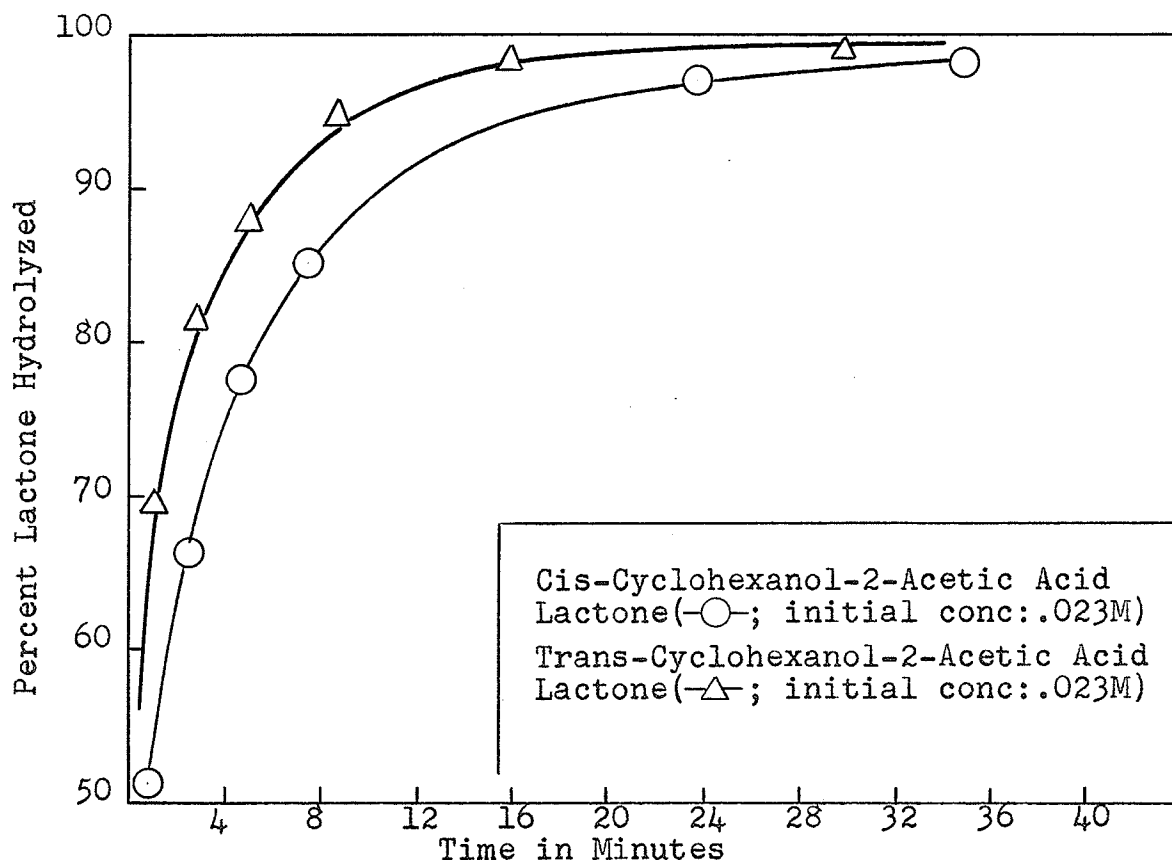


FIGURE 6. Rates of Hydrolysis of Cis - Trans  $\gamma$ -Lactones by .0765 N Sodium Hydroxide Solution at 20°C.



## EXPERIMENTAL

Preparation of the  $\gamma$ -Lactones of Cyclohexanol-2-Acetic Acid (I)

(a) Coffey's method (trans isomer)

Sodium (15 gm.) was dissolved in absolute alcohol (270 ml.) in a one litre flask. Malonic ester (102 gm.) was added and the mixture cooled below 20°. Cyclohexene oxide (60 gm.) was added and the contents shaken until a clear solution resulted. Upon heating at 70° for an hour solidification of the sodium compounds occurred. Water was then added to dissolve the solid mass and the mixture refluxed for an hour. The alcohol was distilled off under a partial vacuum. The volume of the solution was further reduced to about 300 ml. and the residue acidified with 10N sulphuric acid. The oily layer which separated was extracted repeatedly with ether. The oil obtained after evaporation of the ether was heated slowly in an oil bath up to 200° where a vigorous evolution of carbon dioxide occurred. The residue was then distilled under reduced pressure, the fraction boiling between 128 - 132°/15mm. being collected. The yield was 50 gm. or 60% of theory. Further distillation gave a product of b.p. 131 -132°/12mm.,  $n_D^{20}$  1.4752;  $D_4^{20}$  1.0859.



(b) Reformatsky - Fittig method (cis isomer)

The procedure given by Stachiw (28) was followed.

Freshly distilled cyclohexanone (59 gm.), zinc dust (39 gm.) and dry benzene (250 ml.) were placed in a two-litre, three necked flask equipped with a stirrer and a condenser. Ethyl bromoacetate (100 gm.), containing a trace of iodine, was placed in a dropping funnel and inserted in the third neck. The solution was heated to boiling whereupon some 15 gm. of the ester was added to initiate the reaction. Once the reaction had commenced the heating was discontinued. The solution was then stirred while the remainder of the ester was added at a rate such that moderate refluxing was maintained. The reaction mixture was refluxed for half an hour after all the ester had been added, and then cooled. The mixture was acidified with dilute cold sulphuric acid (150 ml.), stirred for a time and transferred to a separatory funnel. The benzene layer was washed with water and with dilute sodium carbonate and dried with calcium chloride. After removal of the benzene the ethyl-(1-cyclohexanol) acetate boiling at 110 - 120°/12mm. was collected. The yield of 80 gm. was approximately 70% of theory.

Dehydration was then carried out by dissolving the hydroxy ester (80 gm.) in dry benzene (240 ml.) to which phosphorus pentoxide (64 gm.) was added. This was refluxed on a water bath for three hours after which the benzene

solution was decanted. The solid residue yielded a further quantity of solution. After removal of the benzene by distillation the ethyl cyclohexene-1-acetate boiling at 100 - 102°/15mm. was collected. The yield was 48 gm. or 68% of theory.

In the final step this  $\beta, \delta$  -unsaturated ester was converted to the corresponding  $\gamma$ -lactone through the application of "Fittig's conditions". The ester (48 gm.) and 50% (by volume) sulphuric acid (300 ml.) were placed in a one-litre two-necked flask equipped with a stirrer and a condenser. The mixture was heated on a water bath until the oily layer disappeared, a time of about an hour. During this time the formation of a considerable amount of green scum was observed. The solution was cooled and extracted repeatedly with ether. The combined extract was washed with sodium carbonate solution and dried over potassium carbonate. Distillation yielded a colorless liquid boiling at 129 - 130°/13mm. The main impurity was probably the unlactonized ester. After several redistillations the physical constants were:  $n_D^{20}$  1.4784;  $D_4^{20}$  1.0921. Newman and Van der Werf (25) give:  $n_D^{20}$  1.4773 and  $D_4^{20}$  1.0923 for their isomeric cis lactone.

Preparation of  $\delta$ -Lactones of Cyclohexanol-2- $\alpha$ -Propionic Lactone (IV)

(a) Cyclohexene oxide method (trans isomer)

This lactone was apparently first prepared by MacFarlane although it is described only in a paper by McRae, Charlesworth and Alexander (24). The method was similar to that used by Kendall, Osterberg and MacKenzie (17).

Sodium (10.5 gm.), absolute ethanol (180 ml.), malonic ester (73 gm.) and cyclohexene oxide (44 gm.) were reacted in the manner previously described. As much of the alcohol as possible was removed under reduced pressure and the solid cake broken up into small pieces. To a benzene (500 ml.) suspension of the above product, methyl iodide (64 gm.) was added and the mixture refluxed for twenty hours. The benzene was then removed by distillation and sufficient water and alcohol added to clear the solution. Saponification was carried out using 5N sodium hydroxide (100 ml.) and refluxing for two hours. Upon acidification with 10N sulphuric acid an oil material appeared which solidified into a white mass upon standing. A small amount of this material was set aside for characterization, the remainder of which was heated in an oil bath up to 210° where decarboxylation occurred. Distillation yielded a colorless oil (35 gm., 52% of theory) boiling at 125 - 128°/11mm.,  $n_D^{20}$  1.4719;  $D_4^{20}$  1.0519. Found: C, 70.15; H, 9.27%. Calc. for C<sub>9</sub>H<sub>14</sub>O<sub>2</sub>: C, 70.1; H, 9.15%.

## (b) Reformatsky-Fittig method (cis isomer)

The method given by Stachiw (28) was repeated and almost identical yields obtained. Cyclohexanone (54 gm.) and ethyl  $\alpha$ -bromopropionate (100 gm.) reacted as previously described. After dehydration and lactonization the product (34 gm.) distilled at 131 - 134<sup>o</sup>/11mm.,  $n_D^{20}$  1.4756;  $D_4^{20}$  1.0589. Found: C, 69.89; H, 9.04%.

Preparation of the  $\gamma$ -Lactone of Cyclohexanol Methyl Malonic Acid

This solid material was isolated prior to the decarboxylation step in the foregoing cyclohexene oxide synthesis of (IV). After recrystallization from benzene - ligroin, white crystals were obtained of melting point 151 - 152<sup>o</sup>. Found: C, 60.98; H, 7.22%; equivalent weight, 198.0. Calc. for  $C_{10}H_{14}O_4$ : C, 60.6; H, 7.12%; equivalent weight, 198.2.

This acid is analogous to the lactone of cyclohexanol malonic acid (m.p. 121 - 122<sup>o</sup>) obtained in a similar manner by Kendall and associates (17, 18).

Preparation of trans- Cyclohexanol-2-Acetic Acid.

## (a) Newman and Van der Werf's method

Solid sodium hydroxide (.6 gm.) was added to a mixture of the trans lactone (2 gm.) and water (10 ml.). After solution was complete the mixture was cooled and made just acid to litmus with concentrated hydrochloric acid. Trans cyclohexanol-2-acetic acid settled in white flakes. After recrystallization from a benzene - ligroin solvent, the melting point was

105 - 106° and the equivalent weight 159 (calc. 158).

(b) Coffey's method

The trans lactone was boiled with excess alcoholic potassium hydroxide. The resulting potassium salt was filtered off and treated with dry hydrogen chloride in absolute ether. The viscous oil which separated gradually solidified when kept in the ice box for several weeks. Repeated recrystallizations from benzene - ligroin failed to elevate its melting point of 97 - 102°. The equivalent weight was 180 indicating that the acid was impure, probably contaminated by unchanged lactone. This acid exhibited a rather pronounced tendency to relactonize in aqueous solution, a fact that led Newman and Van der Werf to claim that Coffey's material was not identical to theirs. It seems more reasonable however, to view the instability of Coffey's product as resulting merely from its impurity. A mixed melting point of the two products in question revealed no pronounced depression.

Preparation of trans-Cyclohexanol-2- $\alpha$ -Propionic Acid

The method of Newman and Van der Werf as previously outlined was used to obtain a white crystalline acid which, after recrystallization from water melted at 110°. Found: C, 63.0; H, 9.16%; equivalent weight, 173.5. Calc. for C<sub>9</sub>H<sub>16</sub>O<sub>3</sub>: C, 62.8; H, 9.31%; equivalent weight, 172.2.



Attempted Preparation of the Lactone of Cyclohexanol-2-Isovaleric Acid by the Cyclohexene Oxide Method

It was hoped that an isopropyl group could be substituted in a manner comparable to that described for methyl iodide. Accordingly, a benzene suspension of the sodio addition product was refluxed with isopropyl bromide for a period of twenty-four hours. Failure to obtain the desired product can probably be attributed to steric hindrance.

Preparation of Cyclohexanone-2-Acetic Acid (II)

The method used was that of McRae, Charlesworth and Alexander (24). Cyclohexanol-2-acetic lactone (14 gm.) was dissolved in 5N sodium hydroxide solution (75 ml.) in a 500 cc. flask equipped with a stirrer, and the mixture heated to boiling. A hot solution of magnesium sulfate (44 gm. of the heptahydrate in 35 ml. of water) was slowly run into the vigorously stirred solution. The mixture was then cooled to below 10° in an ice bath and bromine (5.5 gm.) slowly added over a period of two hours. The yellow color of the bromine was rapidly dissipated at first; more slowly towards the end of the oxidation. A fresh supply of ice was packed around the flask which was left overnight. The solution was then acidified with 10N sulphuric acid and reduced in volume as much as possible by distillation. The resulting layer of brown oil was extracted with ether and dried over sodium sulphate. After removal of the ether crystallization of the residue occurred upon standing in the ice box for one or two

days. After two recrystallizations from benzene - ligroin and charcoal, the white keto acid was obtained melting at 73 - 74°. The yield was 5.5 gm. representing 35% of theory.

#### Preparation of Cyclohexanone-2- $\alpha$ -Propionic Acid (V)

The lactone of cyclohexanol-2- $\alpha$ -propionic acid (IV) was oxidized by bromine - magnesium hydroxide in the manner described for the preceding preparation. After recrystallization, the melting point was 133 - 135°.

#### Preparation of cis-Cyclohexanol-2-Acetic Acid Lactone by Catalytic Hydrogenation of (II)

The method described by Newman and Van der Werf (25) was repeated. The keto acid cyclohexanone-2-acetic (2.5 gm.) was dissolved in ethanol (50 ml.), placed in a thoroughly cleaned pressure bottle with platinum oxide (.15 gm.) added, and shaken in a Parr apparatus at forty pounds pressure for three hours. The hydrogenation appeared to be virtually complete within one hour. Most of the alcohol was then removed by distillation and the residue washed with a small quantity of dilute sodium hydroxide solution to convert the acidic impurities into the corresponding salt. The neutral portion was then immediately extracted with ether and after removal of which, the cis lactone (1.9 gm.) was isolated and purified by distillation. The boiling point was comparable to that reported by Newman and Van der Werf: 128 128.5°/10-11mm.

Because of the small quantity of product some difficulty was experienced in removing the last traces of impurity. The sodium hydroxide treatment could not be prolonged because of the consequent hydrolysis. Nevertheless, the infra red spectra of this and the Reformatsky lactone proved identical.

#### Catalytic Hydrogenation of Cyclohexanone-2- $\alpha$ -Propionic Acid (V)

The method described above was applied to the methyl - substituted keto acid. The product, boiling point 132 - 135°/13 mm., although difficult to purify, gave a spectrum which was practically identical with that of the Reformatsky - Fittig lactone.

#### Relative Rates of Hydrolysis of the cis-trans $\gamma$ -Lactones

The technique used was adapted from that described by Kendall, Osterberg and MacKenzie (17) for the determination of the rate of ring opening of a  $\gamma$ -lactone. The hydrolysis was found to be too rapid for measurement at temperatures above 20°. Even at 20° the half-time is of the order of one minute.

The lactone (1/200 mole) was dissolved in ethanol (25 ml.) and introduced into a flask containing .086N sodium hydroxide solution (200 ml.) thermostated at 20°. At periodic intervals 20 ml. portions were withdrawn with a pipette and run into hydrochloric acid (20 ml., .0896N). The excess acid was then

titrated with standard alkali and the hydrolysis rate plotted graphically (fig. 6).

#### Preparation of Hydrazone Derivatives

The method described by Coffey (12) was used. A 10% solution of the lactone in alcohol was boiled with hydrazine (95%). Upon cooling, the hydrazone separated and was recrystallized from water.

Trans cyclohexanol-2-acetic acid lactone yielded a hydrazone melting at  $167.5^{\circ}$ ; identical to that reported by Coffey.

The Reformatsky - Fittig lactone and the Newman cis lactone both gave a hydrazone which, when recrystallized from benzene - ligroin, melted at  $140 - 141^{\circ}$ . Found: N, 16.12%. Calc. for  $C_8H_{16}O_2N_2$ : N, 16.26%. This derivative was far more soluble in both polar and organic solvents than the corresponding trans derivative.

The hydrazones of cyclohexanol-2- $\alpha$ -propionic acid lactone were also prepared. The trans compound gave a derivative which when recrystallized from water, melted at  $191 - 192^{\circ}$ . Found: N, 14.76%. Calc. for  $C_9H_{18}O_2N_2$ : N, 15.04%.

The Reformatsky - Fittig lactone yielded a derivative which, after two recrystallizations from benzene - ligroin, melted at 136 - 137°. Found: N, 15.15%. Calc: 15.04%.

Preparation of the N-Benzylamide of cis-Cyclohexanol-2-Acetic Acid Lactone

The method used was that of Dermer and King (13). The Reformatsky - Fittig lactone (1 gm.) was refluxed with benzylamine (3 ml.) in the presence of ammonium chloride (.1 gm.). The amide, when recrystallized from benzene - ligroin, melted at 97 - 98°. Brewster and Kucera (7) reported an identical melting point for the N-benzylamide prepared from Newman and Van der Werf's cis lactone.

Notes on the Infra Red Spectra

The spectra presented in this work were obtained using the Beckmann D.K. recording spectrophotometer. The wavelength region investigated was a small portion of the near infra red, 2.2 - 2.85  $\mu$ .

Since it was impossible to find two corex cells which matched in the 2.8  $\mu$  region, a pair of quartz cells were used instead. The 100% line obtained with these cells did not deviate more than 3 - 4% on either side.

The lactone samples were weighted directly into the cell and a measured amount of the solvent carbon tetrachloride added.

After investigating several chart speeds, it was found that none of the finer detail was omitted if the chart speed was set at 10 in./min. and the time constant at .6 sec.

## SUMMARY

1. This investigation has demonstrated that the lactone of cyclohexanol-2-acetic acid made by the Reformatsky - Fittig method is identical to the cis isomer characterized by Newman and Van der Werf.
2. Cis - trans isomerism also appears to be exhibited by the Reformatsky - Fittig and cyclohexene oxide produced lactones of cyclohexanol-2- $\alpha$ -propionic acid, respectively.
3. One of the interesting features is that, in both cases, the cis lactones will not yield stable hydroxy acids.
4. Rates of hydrolysis of both pairs of lactones have been determined and plotted. It was seen that for the cyclohexanol-2-acetic acid lactones the cis isomer underwent ring opening only slightly less rapidly than the trans isomer. The difference was far more notable in the cyclohexanol-2- $\alpha$ -propionic acid lactone case.
5. Hydrazides of both these cis - trans pairs have been prepared, the melting points of the cis derivatives being about 30 - 40° lower than the corresponding trans derivatives.
6. The isolation and characterization of two hitherto unreported acids has been accomplished:
  - (i) cyclohexanol-2- $\alpha$ -propionic acid; m.p. 110 - 111°.
  - (ii)  $\delta$ -lactone of methyl malonic acid; m.p. 151 - 152°.

7. These cis - trans lactone pairs have been investigated in the 2.3 - 2.85  $\mu$  region of the infra red.

8. The first overtone bands of the fundamental carbonyl stretching frequency have been identified as appearing at 2802 - 2819  $m\mu$  on the basis of observed peak shifts consistent with expected strain present in a five - membered trans lactone ring.

9. The peak at 2710  $m\mu$  present in all lactones investigated has been ascribed to adventitious water on the basis of its marked elevation upon the addition of a trace of water.

10. In conclusion, it has been suggested that the Reformatsky - Fittig method will probably yield cis lactones exclusively, whereas the cyclohexene oxide method involving as it does, an initial trans addition, will inevitably yield trans lactones.

## RECOMMENDATIONS FOR FUTURE WORK

1. The various higher homologues of these lactones could be investigated along lines similar to those presented in this work. Cyclohexene oxide condensations could perhaps be made to work with ethyl iodide etc.

2. An attempt should be made to repeat the work of Boehringer and Sohn, or more particularly, that of MacFarlane, in which the lactone of cyclohexanol-2-acetic acid was presumably synthesized directly from the hydroxy-ester using either sulphuric or hydrochloric acid. The product would likely prove to be the cis lactone, but in view of the different conditions employed, this should be verified.

3. Variations of Fittig's conditions should be tried in order to see if the trans lactone could ever be obtained. In particular, it was suggested (page 15) that the  $\beta, \delta$ -unsaturated ester might be treated with cold, concentrated sulphuric acid followed by gradual addition of water.

4. Catalytic hydrogenations of keto acids could be further investigated, following the work of Newman and Van der Werf.



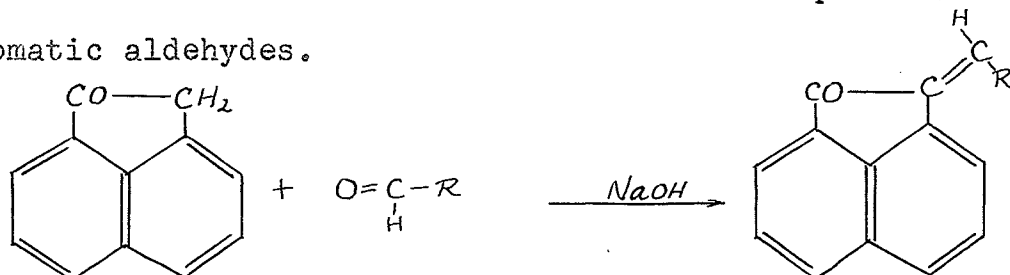
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## INTRODUCTION

Sircar and Gopalan (18, 19) and de Fazi (7) investigated Claisen - Schmidt condensations between acenaphthenone and aromatic aldehydes.



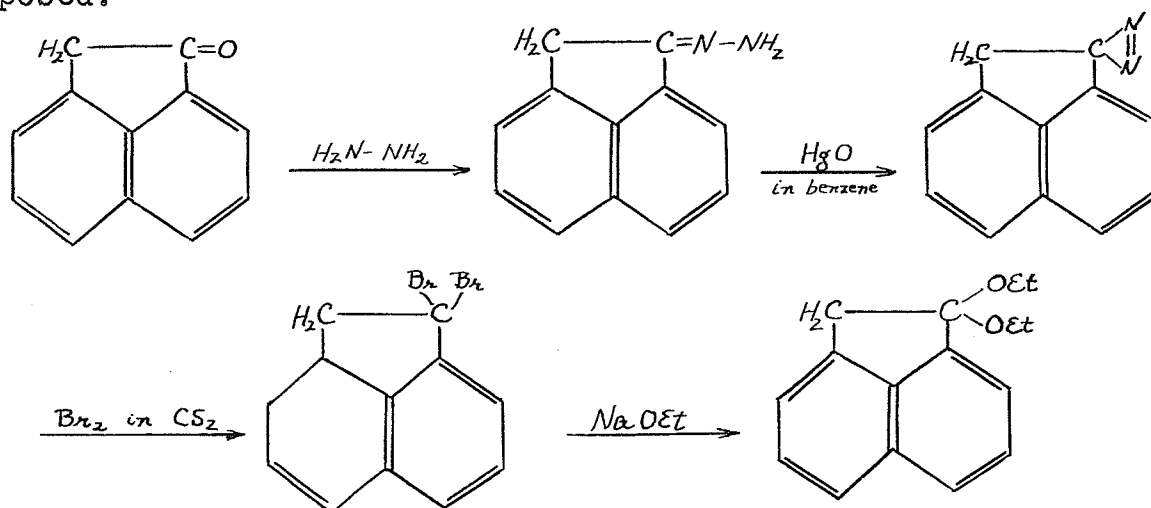
In many cases these authors reported different condensation products resulting from the same aldehyde. Stachiw (21) observed that isomerism might possibly account for this. Acid as well as alkaline conditions were utilized by Stachiw in an attempt to isolate two products, but only for the case of *o*-nitrobenzaldehyde was he successful. Attempts to convert the lower melting to the higher melting product failed.

In the present work ultraviolet absorption spectra of these two *o*-nitrobenzalacenaphthenones were taken. The curves varied significantly indicating that the products might well be geometric isomers. Two products were also obtained from anisaldehyde but these appear to be merely different polymorphic forms because their spectra proved identical. A further number of acid condensations uncovered no additional pairs.

Elston (9) failed to obtain a crystalline product when

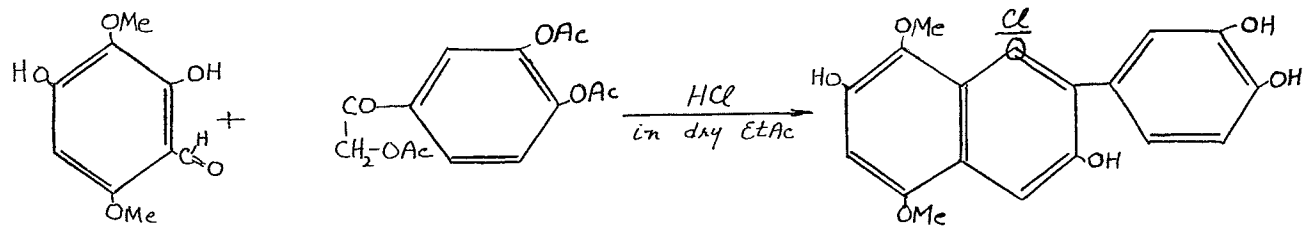
phloroglucinaldehyde was condensed with acenaphthenone. He suggested that pyrylium salt formation might be effected with the use of 2-O-benzoylphloroglucinaldehyde rather than the unprotected aldehyde which apparently underwent self-condensation. This was tried in the present work and met with success.

Attempts to prepare the diethyl ketals of acenaphthenone and fluorenone by the orthoformate method failed. An alternate synthesis of the acenaphthenone ketal along lines similar to a method developed by Staudinger (22) for fluorenone was proposed.



The hydrazone was obtained satisfactorily, but the diazo - compound appeared to be impure probably by virtue of its instability. The next step was attempted but due to lack of time the product has not been characterized.

Finally, a synthesis of the anthocyanidin, gossypetinidin chloride, commenced several years ago by Borkowski (3), has been advanced one further stage.



The remaining demethylation step has yet to be carried out.

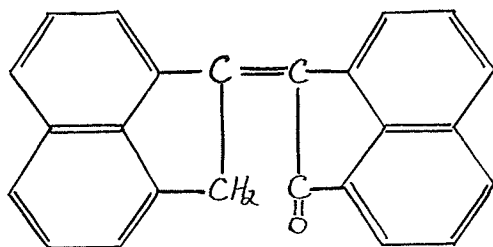
## LITERATURE SURVEY

Condensation Reactions of Acenaphthenone with Aromatic Aldehydes

## (a) Under Alkaline Conditions

The method of de Fazi (7) involved the use of 50% aqueous sodium hydroxide whereas that of Sircar and Gopalan (18, 19) was with 10% alcoholic potassium hydroxide. In view of the apparently minor change of conditions it was rather surprising that these authors should report products of different melting points for condensations involving the following aldehydes: both o- and p-nitrobenzaldehyde, o-hydroxybenzaldehyde, anisaldehyde, and cinnamaldehyde. Elsevier's Encyclopedia (8) has given a complete table of melting points both for the aforementioned aldehydes and also for those for which only one product has been reported.

Elston (9) encountered further irregularities when attempting some additional alkaline condensations. For example, naphthalic acid was obtained when m-methoxybenzaldehyde was used, and from m-tolualdehyde a product was obtained which was later characterized by Stachiw (21) as naphthalic anhydride. Elston also found that attempted condensations with aliphatic aldehydes, such as propionaldehyde and n- butyraldehyde, yielded only the acenaphthenone self-condensation product, biacenone.



Stachiw found that biacenone resulted from an attempted alkaline condensation even with p-tolualdehyde. He suggested that since the five - membered ring in acenaphthenone is likely under some strain, any condensation which does not stabilize the ring will be suppressed in favor of ring opening to naphthalic acid (or its anhydride) or self-condensation product, biacenone. These findings are in agreement with the work of Graebe and Jequier (12) who reported that even at room temperature acenaphthenone underwent self-condensation in an alcoholic sodium hydroxide solution. Graebe and Gfeller (11) reported the formation of naphthalic acid in a boiling solution of alkali and acenaphthenone.

(b) Under Acid Conditions

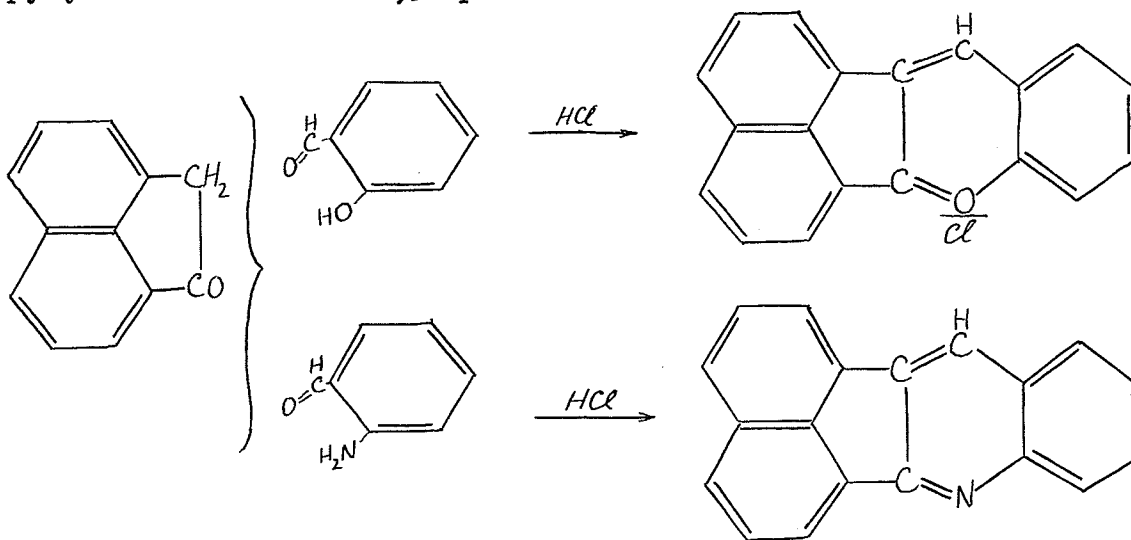
Stachiw attempted to repeat the work of de Fazi and the Indian workers but had obtained one product alone where two had been reported. He therefore initiated the use of gaseous hydrogen chloride as a condensing agent hoping to obtain at least some of these pairs. The acid condensation was found to work well, but only in the case of o-nitrobenzaldehyde was a product obtained which was different from that resulting from the alkaline conditions, the former melting at 163 - 165°, and the latter at 242 - 244°. Assuming that these were stereoisomers and that the lower melting was of the cis configuration an attempt was made to effect a conversion to the higher melting, presumably more stable trans form. All the standard

methods — irradiation with ultraviolet light, refluxing with iodine as a catalyst, refluxing with palladium on charcoal, heating above the melting point — failed to produce any change.

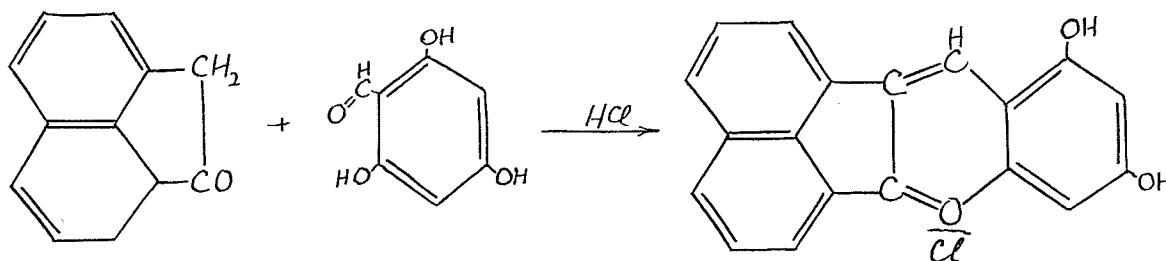
This entire problem has been reviewed and some new condensation products reported in a recent paper by Charlesworth, Campbell, Conn, Elston and Stachiw (4).

### (c) Pirylium Salt Formation

Sircar and Gopalan (17, 18) demonstrated that, under acid conditions, ring closure occurred when the aldehyde used contained either a hydroxy or an amino group in the ortho position. The resulting products were, respectively, 2,3-pirylium salts and 2,3-quinoline derivatives.



Elston (9) attempted to extend this to phloroglucin-aldehyde hoping to obtain the pyrylium salt.

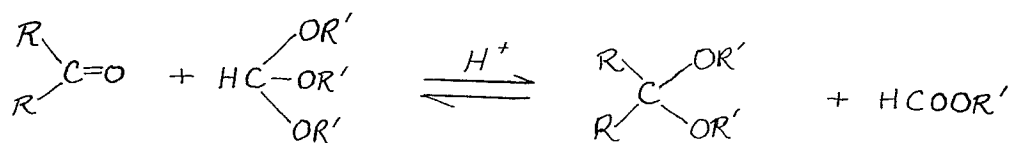




Apparently however, the aldehyde underwent some sort of polymerization because he obtained only an amorphous, red substance. The same result issued from a blank run with the aldehyde alone.

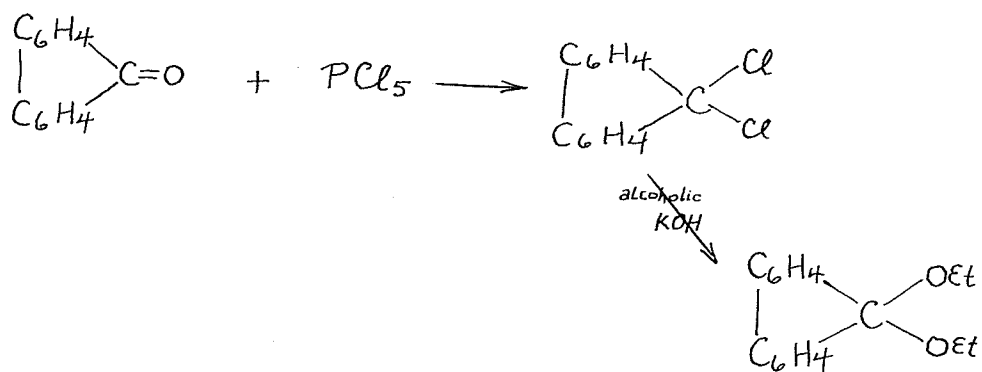
### Formation of Ketals from Ketones

Ketones cannot be induced to form ketals in the manner that aldehydes form acetals, that is, from simple alcohols plus an acid catalyst. Claisen (5), therefore, developed a new method involving the use of orthoformic esters and acid catalysts.



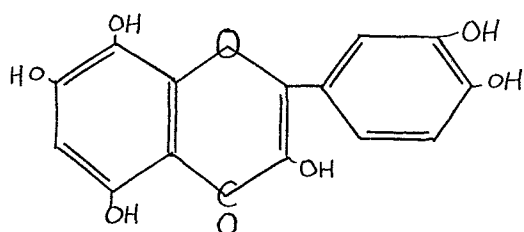
In cases where this method is not usable Helferich and Hausen (13) developed an alternate procedure involving the use of esters of orthosilicic acid in place of the orthoformate.

An entirely different method was employed by Smedley (20) to obtain the diethyl ketal of fluorenone.



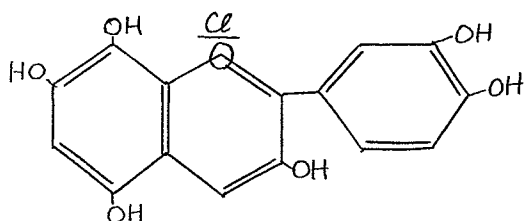
Miscellaneous: Gossypetinidin Chloride

The flavonol, gossypetin (isolated in 1899 by Perkin from flowers of the Indian cotton plant) was obtained synthetically by Robinson (2).



gossypetin

Synthesis of the corresponding anthocyanidin, gossypetinidin chloride has, however, not yet been reported in the literature.



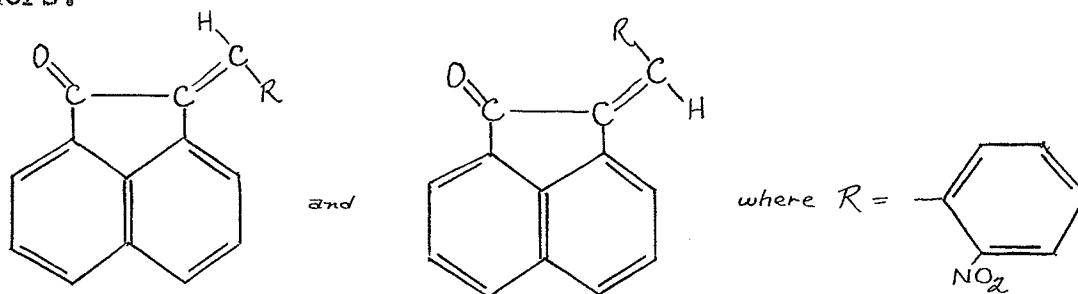
gossypetinidin  
chloride

Borkowski (3) undertook its synthesis but due to lack of time proceeded only as far as the preparation of the intermediate aldehydic and acetoxy-acetophenone fragments.

## DISCUSSION OF RESULTS

Ultraviolet Spectra of Acenaphthenone Condensation Products  
(figs. 7 & 8)

The ultraviolet absorption spectra of the two o-nitro-benzalacenaphthenones demonstrate that there exists a definite structural difference between them (fig. 8). While both have the same sort of peak at 231 - 232 m $\mu$ , the peak at 281 - 282 m $\mu$  exhibited by the lower melting (163 - 165 $^{\circ}$ ) product is not shown by the higher melting (242 - 244 $^{\circ}$ ) product. This appears to substantiate Stachiw's view that these are actual cis - trans isomers.



The problem of definite characterization still remains however. Stachiw, assuming the lower melting to be the less stable cis isomer, was unsuccessful in attempts to convert it to the higher melting trans form. Corresponding treatment of the higher melting product, although not attempted, seems even less likely to be rewarding. In view of the fact that product formation seems to occur more rapidly under acid than under alkaline conditions, one would expect that the former should yield the less stable kinetically - controlled product whereas from the latter the more stable thermodynamically -

controlled product should result. If melting points are any criterion of stability then this appears to be consistent since the lower melting results from the acid condensation and the higher from the alkaline.

A search of the literature failed to provide any means whereby the difference in spectra might be interpreted as indicative of either cis or trans configuration. The only possibility encountered offering even a modicum of hope was a technique described by Schriener, Fuson and Curtin (16). It involves the comparative use of model compounds, that is, the use of relatively simple substances of known configuration which differ from the unknown in a way that should not affect the absorbing unit. In this case one of the closest compounds conceivable would be o-nitrobenzalacetophenone. This compound is reported by Cromwell and Setterquist (6) to have an ultra-violet maximum at 262 m $\mu$  with an extinction coefficient of  $1.756 \times 10^4$  units. This information does not appear to have too much relevance to the case in point however, since 281 - 282 m $\mu$  is the position of the peak of interest here. Furthermore, the foregoing authors do not specify the configuration of this acetophenone product, and even its synthesis is referred to unpublished work.

The absorption spectra for both 96 - 98° and 126 - 127° melting p-methoxybenzalacenaphthenones proved to be exactly identical (fig. 7). Ostensibly, this indicates that no unique structural difference other than mere polymorphism obtains

between these two products. If this is so then it should be possible to convert at least the lower melting compound to the higher by nothing more drastic than changing the recrystallizing solvent. It was gratifying therefore, to find that changing the solvent from glacial acetic acid to an acetone - water solution, the 96 - 98° product was transformed to the 126 - 127° product.

Since this is the case for the two p-methoxybenzaldehyde products it is entirely possible that some of the other pairs reported by de Fazi and the Indian workers — especially those whose melting points are only some 30 - 40° apart — may also be polymorphic crystalline forms. This includes the p-nitrobenzaldehydes (203 and 240°), the o-hydroxybenzaldehydes (168 and 187°). In the only apparently genuine isomeric case so far established, the o-nitrobenzaldehydes, the melting points are 80° apart.

A good deal more work is indicated in order to determine exactly what causes the variability in the products obtained. A good example of this vagarious behavior is provided by the previously mentioned p-methoxybenzaldehydes. De Fazi reported the 96 - 98° product, the Indian workers the 126 - 127° product, Stachiw, repeating the work of both investigators, obtained only the 96 - 98° product, and in the present work only the 126 - 127° product was isolated. Perhaps temperature, rate of addition of alkali, nature of solvent, etc., are critical factors.

Infra Red Spectra of Acenaphthenone Derivatives (figs. 9 - 14)

By comparison of the infra red spectra of acenaphthenone, acenaphthene and acenaphthylene, in the C-H overtone region, 2.85 - 2.1  $\mu$ , it was hoped that sufficient points of similarity would be found such that any pronounced differences might be ascribed to the change of structure (figs. 9, 10 & 11). This hope proved illusory however. Aside from broad generalizations nothing very definite can be said. One interesting point however, is that the enol form of acenaphthenone must be almost negligible since there is virtually no peak at all at 2.77  $\mu$ , and what there is can probably be ascribed to hydroxylic impurities. Regarding acenaphthylene, since the five - membered ring may now undergo resonance with the naphthalene nucleus, it may be observed that there is a general ironing out of sharp peaks in favor of a more even, less abrupt distribution.

Acenaphthenol was found to exhibit its O-H stretching vibration at 2771  $\text{cm}^{-1}$  with an extinction coefficient of approximately 53 units (fig. 12). This compares very closely to that for cyclohexanol at 2762  $\text{cm}^{-1}$  and an extinction coefficient of 50 units, as given by Weissberger and West (23).

The spectra of naphthalene and  $\alpha$ -methyl-naphthalene were also compared. It was very surprising to observe the complete absence of any similarity at all.

TABLE OF CONDENSATION PRODUCTS FROM  
ACENAPHTHENONE AND AROMATIC ALDEHYDES

Aldehyde	Melting Point	
	Literature	Found
o-nitrobenzaldehyde	241 - 243° (7)	242 - 244°
	157° (18)	163 - 165°
p-methoxybenzaldehyde (anisal)	95 - 98° (7)	95 - 96°
	126 - 127° (19)	126 - 127°
piperonal	159 - 160° (7)	158 - 159°
m-hydroxybenzaldehyde	191 - 192° (19)	192 - 194°
m-methoxybenzaldehyde	————	122 - 124°
p-methylbenzaldehyde	————	131 - 132°

The literature melting points in the above table are those quoted by Elsevier (8) and, without exception, are for alkaline condensations. Whereas, the second column quotes melting points found for products resulting from both acid and alkaline condensations performed in this work.

All melting points determined in the course of this investigation have been corrected.

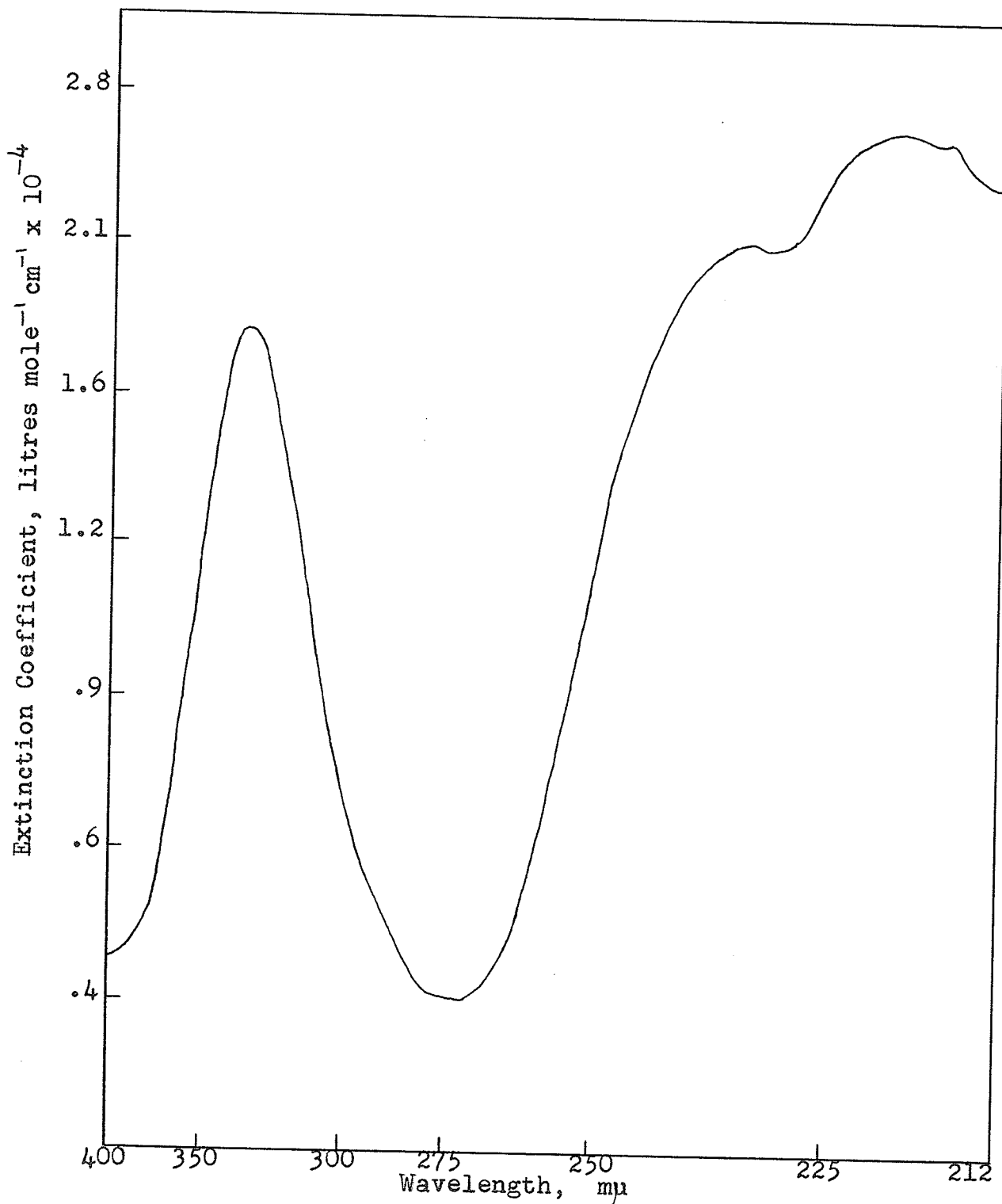


Fig. 7. Ultraviolet Absorption Spectrum of both p-methoxybenzalacenaphthenones (m.p. 96 - 98° and 126 - 127°).



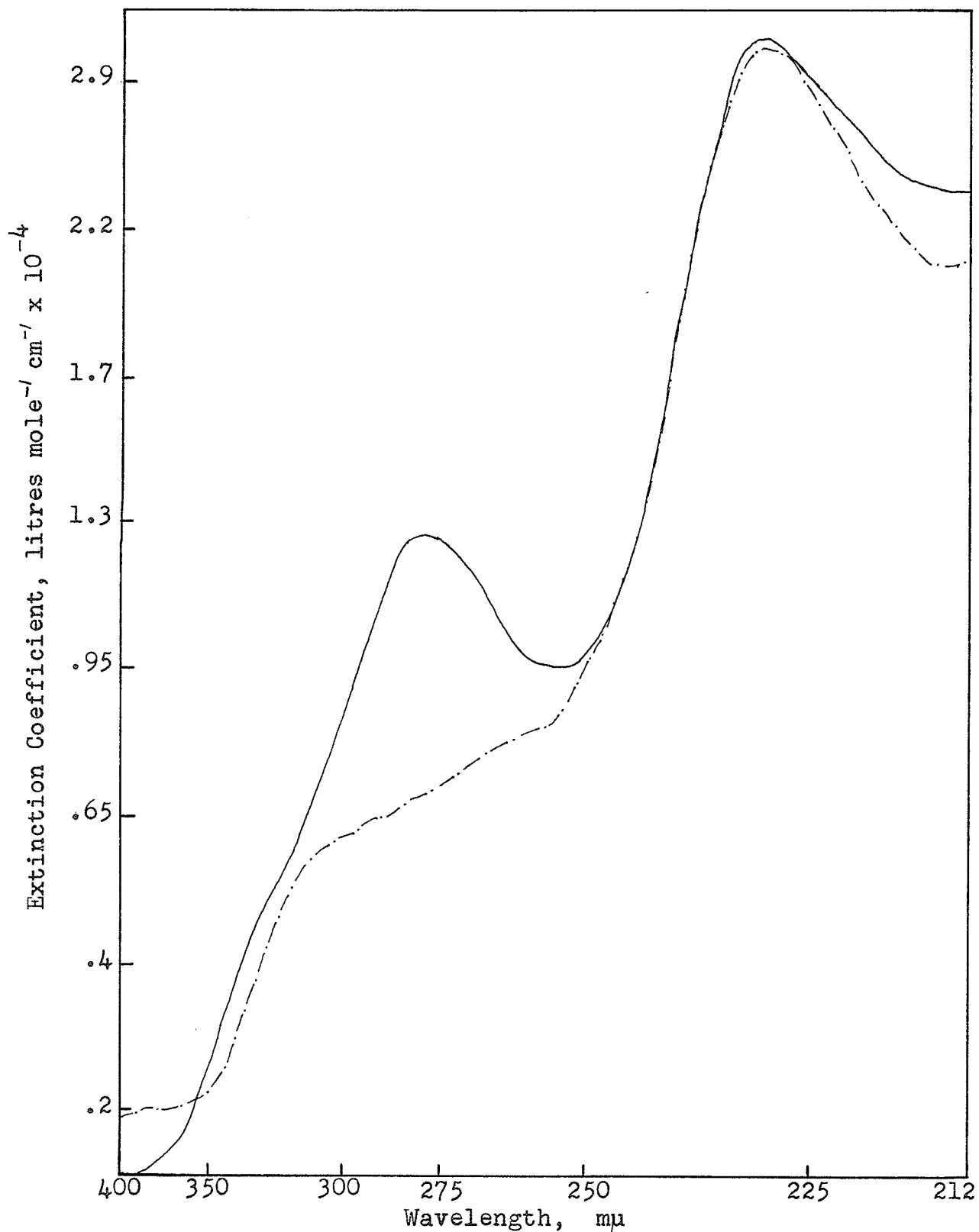
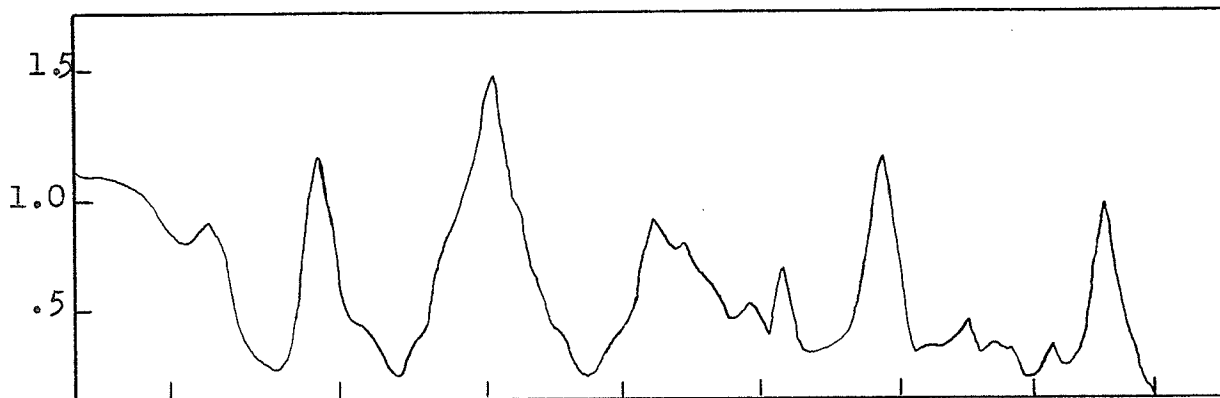
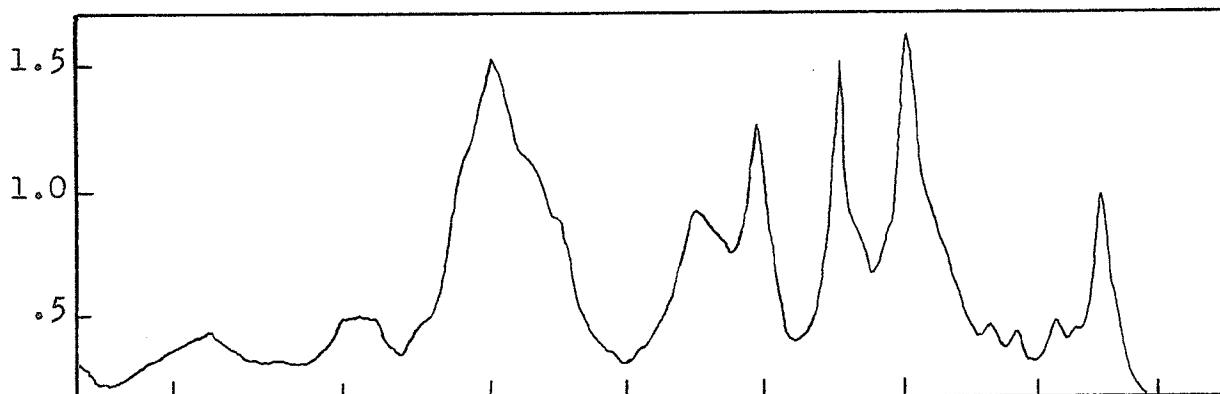
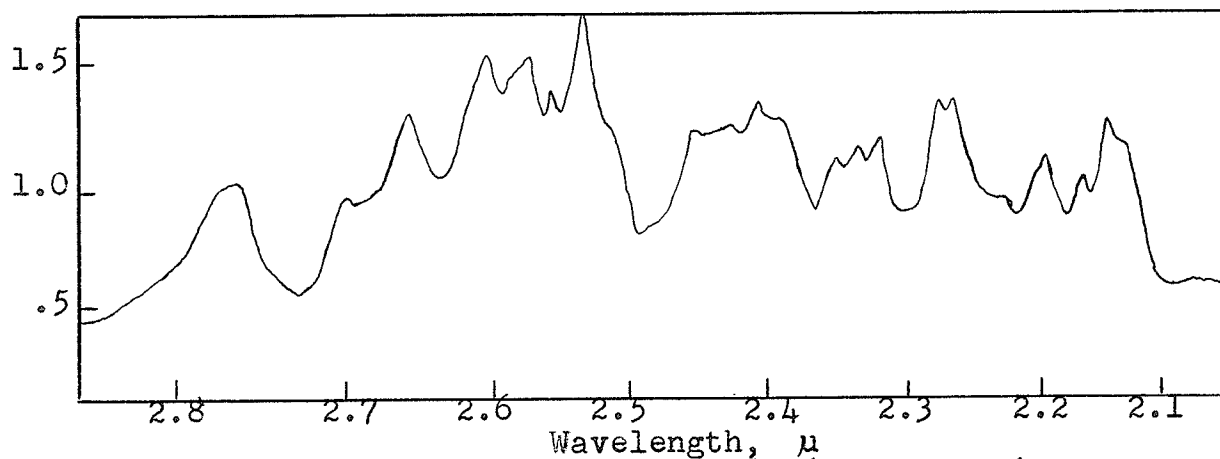


Fig. 8. Ultraviolet Absorption Spectra of the two  
 Isomeric *o*-Nitrobenzalacenaphthenones.  
 Conc:  $2.4 \times 10^{-5}$  M in Ethanol.  
 Alkaline Condensation: yellow needles,  
 m.p.  $242-244^{\circ}$  (— · — · —)  
 Acid Condensation: yellow needles,  
 m.p.  $163-165^{\circ}$  (—)

## INFRA RED SPECTRA

Fig. 9 Acenaphthenone (.16 M in CCl<sub>4</sub>)Extinction Coefficient, litres mole<sup>-1</sup> cm<sup>-1</sup>Fig. 10 Acenaphthene (.17 M in CCl<sub>4</sub>)Extinction Coefficient, litres mole<sup>-1</sup> cm<sup>-1</sup>Fig. 11 Acenaphthylene (.16 M in CCl<sub>4</sub>)

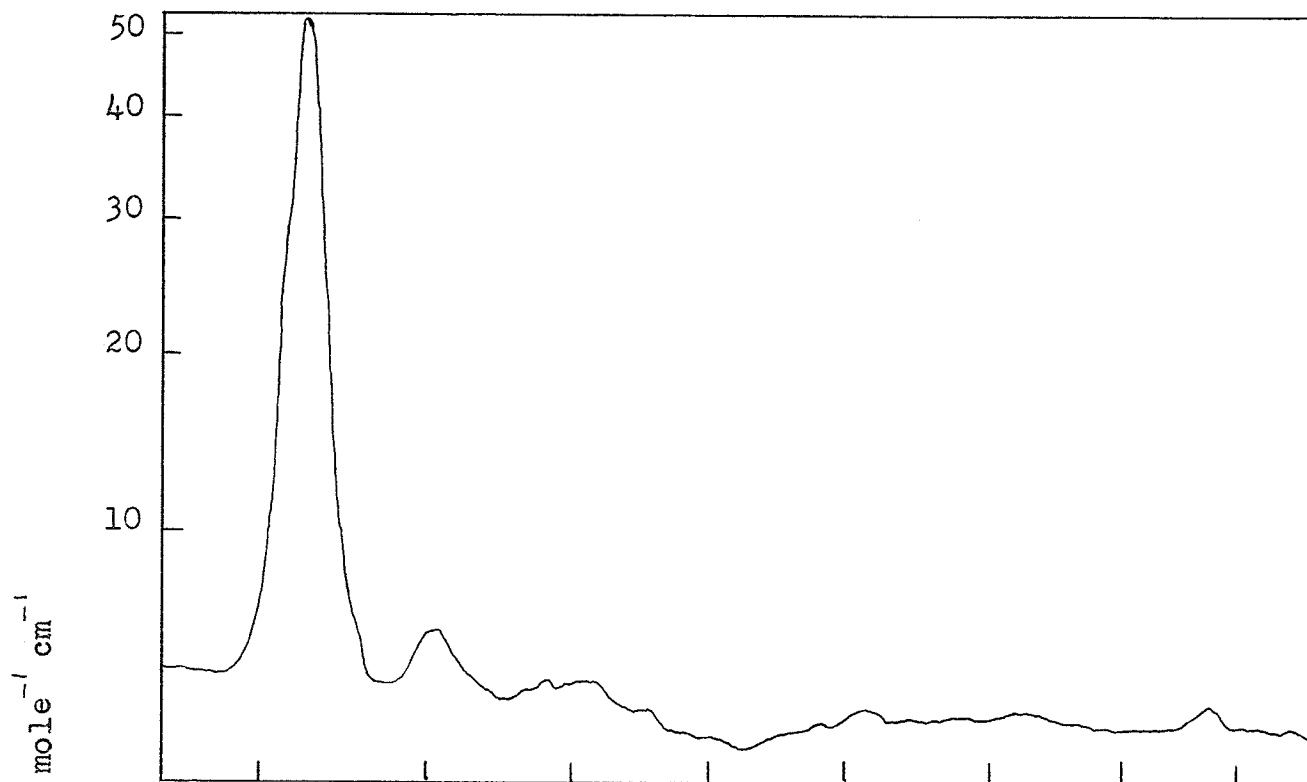


Fig. 12 Acenaphthenol (.0133 M in  $\text{CCl}_4$ )

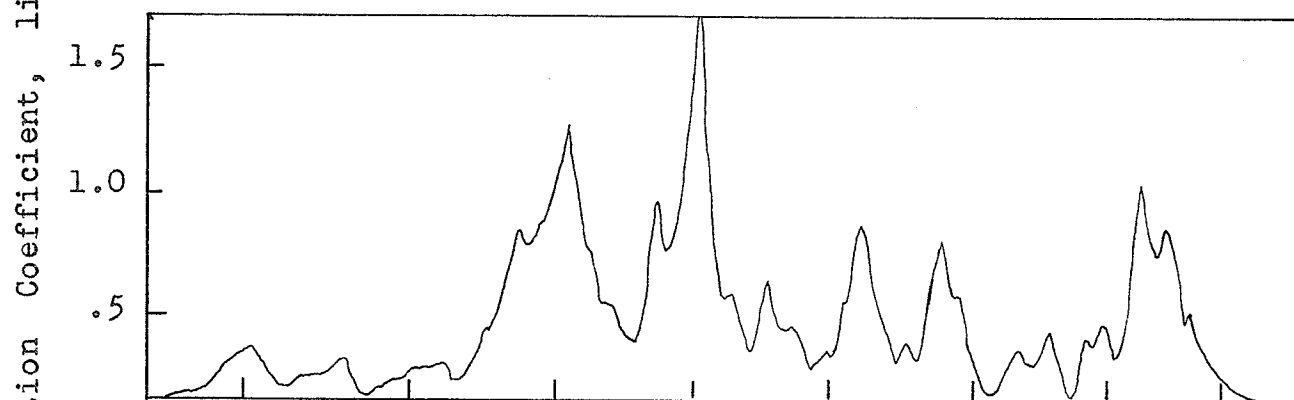


Fig. 13 Naphthalene (.16 M in  $\text{CCl}_4$ )

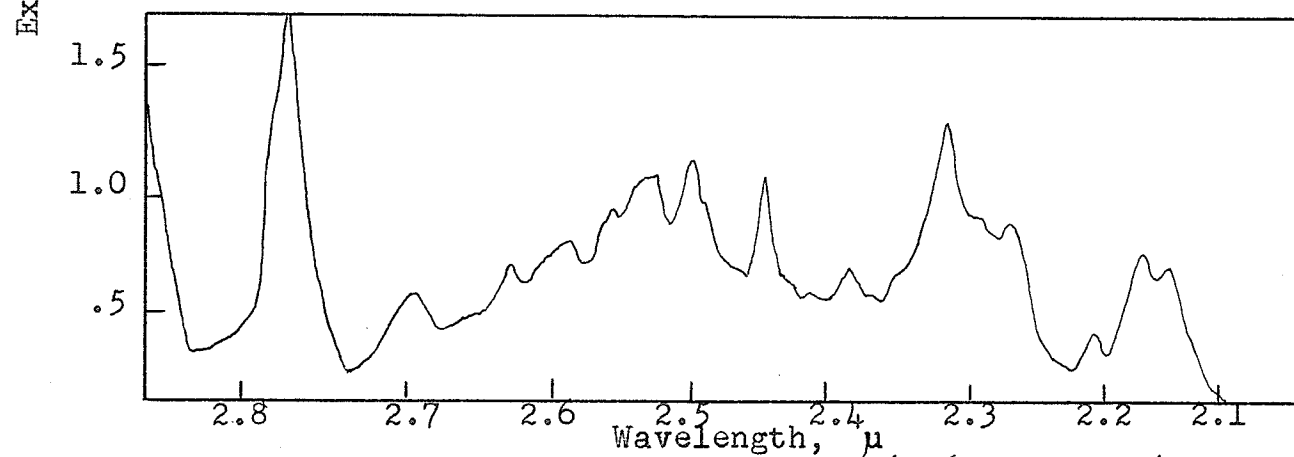


Fig. 14 Methyl Naphthalene (.16 M in  $\text{CCl}_4$ )

## EXPERIMENTAL

Preparation of Acenaphthenone

Acenaphthenone was prepared by the method of Fieser and Cason (10). Acenaphthene (technical grade) was oxidized with lead tetracetate. Alkaline hydrolysis of this acetate yielded acenaphthenol which, upon chromic oxide oxidation gave acenaphthenone. Purification of the ketone was effected through a steam distillation and a recrystallization from acetone (m.p. 121° C).

Acid Condensation of Acenaphthenone with Piperonal

Acenaphthenone (1 gm.) and piperonal (.9 gm.) were dissolved in glacial acetic acid (25 ml.). Dry hydrogen chloride gas was passed into the solution for half an hour during which time an orange - red material precipitated. Two recrystallizations from glacial acetic acid yielded a yellow powder melting at 158 - 159°. Elsevier (8) gives 160° as the melting point of the alkaline condensation product obtained by de Fazi. The two products are therefore, undoubtedly identical.

Acid Condensation of Acenaphthenone with m-Hydroxybenzaldehyde

The acid condensation gave a product of melting point 192 - 194°, as compared to 191 - 192° for the alkaline condensation product. No further investigation was indicated since the two are ostensibly the same.

Acid Condensation of Acenaphthenone with m-Methoxybenzaldehyde

Elston (9) had attempted the alkaline condensation but obtained only biacenone. The acid condensation performed in this work, after two recrystallizations from acetone - ethanol yielded a product melting at 122 - 124°. Found: C, 83.1; H, 4.93%. Calc. for C<sub>20</sub>H<sub>14</sub>O<sub>2</sub>: C, 83.8; H, 4.93%.

Acid Condensation of Acenaphthenone with p-Methylbenzaldehyde  
(p-Tolualdehyde)

Stachiw (21) reported that biacenone resulted from the alkaline condensation. In this work, the acid condensation was found to yield a product which, after two recrystallizations from glacial acetic acid, melted at 130 - 131°. Found: C, 88.75; H, 5.14%. Calc. for C<sub>20</sub>H<sub>14</sub>O: C, 88.8; H, 5.22%.

Acid Condensation of Acenaphthenone with p-Methoxybenzaldehyde  
(Anisaldehyde)

Stachiw had been unable to isolate any product under acid conditions. This condensation was repeated. After half an hour of the hydrogen chloride treatment the solution had become deep red in color but no precipitate was observed. This was apparently due merely to its solubility because when a little water was added and the solution frozen in the ice box, the yellow condensation product was readily obtained. Two recrystallizations from acetone - ethanol yielded a product melting at 126 - 127°, a melting point identical to that reported by Sircar and Gopalan for their product (page 55).

Both types of alkaline condensation were also performed, the 126 - 127° melting product being obtained in each case. Stachiw, on the other hand, reported that the 96 - 98° melting product resulted from both condensations. Obviously there appears to be a great deal of variability involved.

A small amount of Stachiw's 96 - 98° product (crystallized from glacial acetic acid) was available. A portion of this was melted and then allowed to solidify, whereupon the melting point was found to be 123 - 125°. The remainder of the lower melting product was recrystallized from an acetone - water solvent. The melting point was again raised to 125 - 126°. A mixed melting point of this and the above acid condensation product revealed no depression.

#### Attempted Acid Condensation of Acenaphthenone with Aliphatic Aldehydes

Both acetaldehyde and propionaldehyde were tried without success. Biacenone (m.p. 262°) was isolated in each case. This parallels the results Elston (9) obtained for propionaldehyde and n-butyraldehyde under alkaline conditions.

#### Attempted Acid Condensation of Acenaphthenone with Furfural

A dark brown material resulted from this reaction. It was, in all likelihood, a resin - type of polymerization product, and therefore, no further investigation was carried out.

### Acid Condensation of Acenaphthenone with Veratric Aldehyde

Apparently a mixture resulted from this condensation because, after a fractional recrystallization from glacial acetic acid two crystalline species were obtained: yellow crystals, m.p. 127 - 128°; orange crystals, m.p. 141 - 142°. Time did not permit further investigation.

### Preparation of Phloroglucinaldehyde

Phloroglucinaldehyde was prepared by the Adams and Levine (1) modification of the Gattermann synthesis of hydroxy aldehydes. In particular, the directions followed were those supplied by Elston (9). A 95% yield was obtained.

### Preparation of 2-O-Benzoylphloroglucinaldehyde

The method used was that of Robertson and Robinson (15) who had found that this O-benzoyl - derivative was by far the best way to introduce phloroglucinaldehyde in all syntheses leading to pyrylium salts of the anthocyanidin type.

Phloroglucinaldehyde (5.2 gm.) was added to a solution (cooled to 10°) of potassium hydroxide (1.7 gm.) in water (150 ml.). The mixture was cooled to -5°C, part of the potassium derivative separating in glistening plates. Benzoyl chloride (2.35 gm.) was then introduced in three portions with vigorous shaking which was continued until the odor of the chloride had almost disappeared. The mixture was then stirred

for half an hour with an excess of aqueous sodium bicarbonate and the solid collected, washed, and again triturated with aqueous bicarbonate. The crude product was then dissolved in hot ethanol (100 ml.), charcoal added, and the filtered solution poured into water (400 ml.). The emulsion quickly resolved itself into white hair - fine needles (5 gm.), which become pink at 155°, brick red at 195° and melt at 198 - 200° into a dark red liquid.

Acid Condensation of Acenaphthenone with 2-O-Benzoylphloroglucinaldehyde

Elston (9) performed a blank run with the unprotected phloroglucinaldehyde alone and found that self - condensation resulted. In the present work a blank run with the O-benzoyl derivative demonstrated that no undesirable condensation now occurred.

Acenaphthenone (1 gm.) and 2-O-benzoylphloroglucinaldehyde <sup>(1.55 gm.)</sup> were dissolved in anhydrous ethyl acetate (5 ml.) and a little glacial acetic acid (to effect complete solution of the aldehyde). Dry hydrogen chloride gas was passed into the mixture for an hour. The solution, which had become deep red in color, was placed in an ice box for 4 to 5 days. A red powdery material separated which melted at 140 - 141°. Upon recrystallization from absolute ethanol saturated with gaseous hydrogen chloride, the product became much darker in color. The analysis for acenaphthylene-1',2'; 2,3,5 -benzoyloxy- 7-



hydroxybenzopyrylium chloride was found to fit a 1.5 hydrate best. Found: C, 68.3, H, 4.00; Cl, 7.29; loss at 110° in vacuo over phosphoric anhydride 6.45%. Calc. for  $C_{26}H_{15}O_4Cl \cdot 1.5 H_2O$ : C, 68.9; H, 3.98; Cl, 7.84;  $H_2O$ , 5.97%.

Attempted Preparation of Diethyl Ketals of Fluorenone and Acenaphthenone by the Orthoformate Method

The general method as given by Claisen (5) was used.

The aldehyde or ketone (1 mole) <sup>portion</sup> was mixed with the orthoester (1.1 mole), absolute ethanol (3 moles) and a few decigrams of catalyst. The liquid was boiled for about 10 minutes or allowed to remain at room temperature for a longer interval. The mixture was then diluted with ether and sufficient ammonium hydroxide added to neutralize the solution if an acid catalyst were used. The ethereal solution was then dried and carefully fractionated. One important consideration is that the acids used as catalysts promote not only the product formation but also the hydrolysis back to reactants. Consequently an increase in quantity of catalyst, or prolongation of boiling may decrease the yield markedly.

All attempts to make fluorenone diethyl ketal using ethyl orthoformate failed, the unchanged ketone being recovered in every case. The various catalysts tried were: hydrochloric acid, ammonium chloride, p-toluenesulfonic acid, boron trifluoride, and methylamine hydrochloride. Acenaphthenone on the other hand was found to yield biacenone in an alcoholic

acid solution when refluxed for 2 - 3 minutes or after 1 - 2 hours standing at room temperature.

An attempt to prepare the dichloro compound of acenaphthenone using phosphorus pentachloride along the lines described by Smedley (20) for fluorenone proved far too drastic for acenaphthenone and, as expected, a dark brown tar was the outcome.

The method of Helferich and Hausen (13) in which orthosilicic esters are used was also tried without success.

#### Preparation of the Semicarbazone of Acenaphthenone

Acenaphthenone (1 gm.), semicarbazide hydrochloride (1 gm.) and sodium acetate (1.5 gm.) were dissolved in ethanol (10 ml.). The solution was heated on a water bath for 1 - 2 minutes whereupon a bright yellow precipitate appeared. After two recrystallizations from ethanol (charcoal) a white fluffy solid was obtained melting at  $241 - 243^{\circ}$  (with decomp.). Found: N, 18.64%. Calc. for  $C_{13}H_{11}ON_3$ : N, 18.66%.

#### Preparation of the Hydrazone of Acenaphthenone

Acenaphthenone (1 gm.) was dissolved in ethanol (10 ml.) and excess hydrazine (95%) added. The solution was heated on a water bath for 10 minutes, then cooled in the ice box. The crude yellow hydrazone, when recrystallized from ethanol (charcoal), melted at  $116 - 118^{\circ}$ . Found: N, 15.03%. Calc. for  $C_{12}H_{10}N_2$ : N, 15.37%.

### Preparation of Diazoacenaphthene

The method used was that described in Organic Syntheses (14).

Acenaphthenone hydrazone (10 gm.) was mixed in a mortar with mercuric oxide (25 gm.). The mixture was placed in a bottle with anhydrous sodium carbonate (5 gm.) and dry ether (70 ml.). Cold, saturated alcoholic potassium hydroxide (2 ml.) was added to act as a catalyst. The mixture was then shaken vigorously for 10 minutes, during which time its color turned from orange to brown - black. The solution was then filtered and the residue washed several times with ether. The combined ethereal extract was then evaporated on a water bath at 40°. The yellow crystalline material which separated was recrystallized twice from ethanol (charcoal) and each time dark brown crystals were deposited along with a larger quantity of yellow - brown needles. This latter substance turned brown at 85 - 100°, softened at 105° and melted with decomposition at 107 - 112°. Found: N, 13.81%. Calc. for C<sub>12</sub>H<sub>8</sub>N<sub>2</sub>: N, 15.55%. If this is actually the desired diazo - compound then the analysis indicates that its loss of nitrogen has been fairly appreciable.

### Attempted Preparation of 1,1-Dibromoacenaphthene

The method that Staudinger and Gaule (22) used to prepare 9,9-dibromofluorene from the corresponding diazo-compound was followed.

The previously prepared impure diazoacenaphthene (2.5 gm.) was dissolved in carbon disulfide (100 ml.) and, with external

cooling applied to the solution, bromine (1.3 gm.) was added dropwise. The immediate formation of a dark precipitate was observed. The solvent was then evaporated off and a dark brown material isolated. Time was not available for further investigation of this product.

#### Preparation of Methoxygossypetinidin Chloride

The method described by Baker, Nodzu, and Robinson (2) was utilized by Borkowski (3) to prepare 2,5-dimethoxyresorcinol. Using the Adams and Levine modification of the Gattermann reaction Borkowski had then converted this to the aldehyde, 2,4-dihydroxy-3,6-dimethoxybenzaldehyde. As a derivative he prepared the oxime which, after recrystallization from water, melted at 182°. Found: N, 6.53%. Calc. for  $C_9H_{10}O_5N$ : N, 6.57%.

Borkowski had also prepared a quantity of  $\omega$ :3,4-triacetoxyacetophenone, but due to lack of time had been unable to attempt the proposed condensation. In the present work, this condensation has been effected, using the products left by Borkowski.

The aldehyde (.5 gm.) and the acetoxy compound (.75 gm.) were dissolved in ethyl acetate (10 ml.) and a little glacial acetic acid. Dry hydrogen chloride gas was passed through the solution for two hours during which time it turned an intense purple color. After four days in the ice box dark purple crystals were filtered off. This product was recrystallized

from ethanol saturated with hydrogen chloride gas. Upon heating up to 250° no distinct melting point was ascertained. When tested with an aqueous sodium carbonate solution a bright green color resulted. Upon heating at 110° in vacuo over phosphorus pentoxide for two hours, a 9.08% loss in weight was observed. This redried material proved hygroscopic. Found: C, 55.74; H, 4.18; Cl, 8.80; methoxyl, 16.24%. Calc. for  $C_{17}H_{15}O_7Cl$ : C, 55.70; H, 4.12; Cl, 9.66; methoxyl, 16.90%.

It is usually found that these anthocyanidins experience a loss of chloride and therefore a low analysis is not unexpected.

## SUMMARY

1. The ultraviolet absorption spectra of the two o-nitrobenzalacenaphthenones indicate that there exists a definite structural difference, and that therefore they might well be genuine cis - trans isomers.

2. On the other hand, it has been shown conclusively that the lower melting p-methoxybenzalacenaphthenone is merely a polymorphic form of the more stable higher melting product.

3. Two new acenaphthenone condensation products, under acid conditions, have been reported:

(i) m-methoxybenzalacenaphthenone, m.p. 122 - 124°

(ii) p-methylbenzalacenaphthenone, m.p. 131 - 132°

4. Following Elston's suggestion, phloroglucinaldehyde, in the form of its mono-oxybenzoyl derivative was condensed (under acid conditions) with acenaphthenone to yield the pyrylium salt.

5. All attempts to prepare the diethyl ketals of acenaphthenone and fluorenone by the orthoformate method failed, the former giving biacenone and the latter being recovered unchanged.

6. Two previously unreported derivatives of acenaphthenone have been prepared:

(i) semicarbazone, m.p. 241 - 243°

(ii) hydrazone, m.p. 116 - 118°

7. Diazoacenaphthene was prepared but was apparently rather unstable. That this material experienced a nitrogen loss was indicated by a low (1.7%) nitrogen analysis.

8. Methoxygossypetinidin chloride was prepared from products left by Borkowski.

## RECOMMENDATIONS FOR FUTURE WORK

1. Further investigations are in order regarding the other condensation products for which two melting points are reported, in order to determine which are merely polymorphic modifications.
2. The problem of reproducibility should be investigated by introducing slight variations into the reaction conditions for alkaline condensations.
3. The condensation product of veratric aldehyde and acenaphthenone which appears to have yielded a mixture requires further work.
4. Some attempt should be made to characterize the o-nitrobenzalacenaphthenones by means of the method of model compounds (page 52).
5. Dizaocacenaphthene should be investigated further and an attempt made to obtain it in a purer form.
6. The uncharacterized bromination product of the diazo - compound requires investigation.
7. The final demethylation step of the gossypetinidin chloride synthesis remains to be carried out.



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