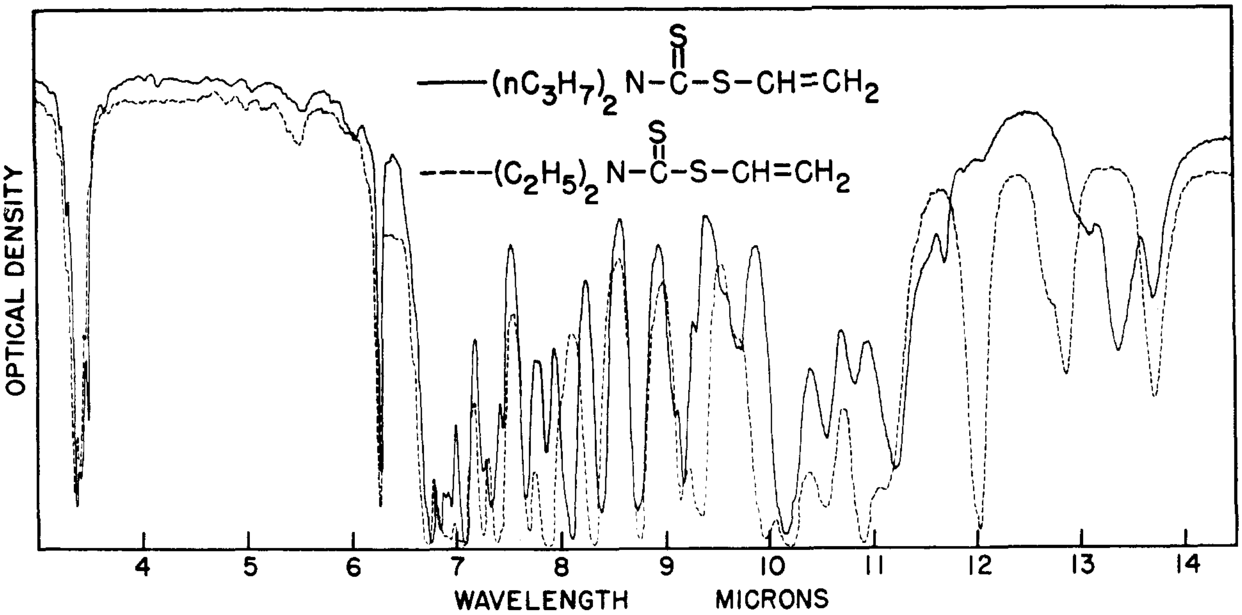

Figure 1

The infrared spectrum is very similar to that obtained for the *N,N*-diethyl analog (see Fig. 1).

Commercial-grade acetylene was purified according to a previously described procedure.[3] The amines were obtained from commercial sources and purified by distillation. The infrared spectra were determined on a Perkin-Elmer 21 double-beam spectrometer.

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[3] J. C. Sauer, *J. Am. Chem. Soc.*, **79**, 5314 (1957).

Reaction of 3-Phenyl-3-acetoxypropanoyl Chloride with Ethyl Sodioacetoacetate

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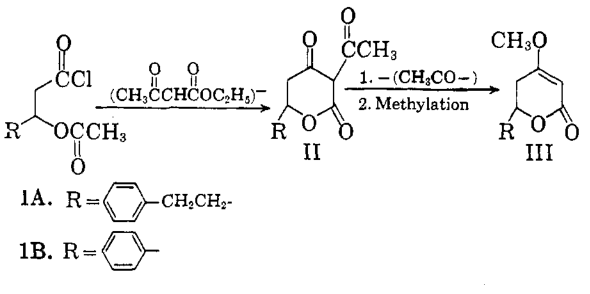
Anschütz[1] prepared 3-acetyl-4-hydroxycoumarin by treating acetylsalicyl chloride with sodioacetoacetic ester. This unique method of preparing β-ketolactones appeared promising as a method of preparing dihydrokavain, IIIA and the following reaction sequence was proposed:



The study of this synthetic route was undertaken using 3-phenyl-3-acetoxypropanoyl chloride, IB, as the model compound.

Two crystalline products were obtained from the reaction of ethyl sodioacetoacetate with 3-phenyl-3-acetoxypropanoyl chloride. Both products gave positive ferric chloride tests and were soluble in sodium hydroxide, but only one was soluble in sodium bicarbonate. On alkaline hydrolysis both compounds gave 3-phenyl-5-ketocaproic acid. The infrared spectrum of the sodium bicarbonate soluble material was in good agreement with the structure of 3-phenyl-4-carboethoxy-5-ketocaproic acid V; a 5.80 μ band being ascribed to the ester carbonyl groups (3-phenyl-5-ketocaproic acid has one sharp band 5.91 μ). This material had an ultraviolet absorption spectra of λ_{max}^{EtOH} 258 mμ, ε 336, however in alcoholic potassium hydroxide a shift to λ_{max} 283 mμ, ε 12,440 was observed after one hour.

An independent synthesis of 3-phenyl-4-carbethoxy-5-ketocaproic acid, V, was undertaken and on mixed melting point with the sodium bicarbonate soluble product no depression was observed. The infrared spectrum of the sodium bicarbonate insoluble product differed greatly from V, however

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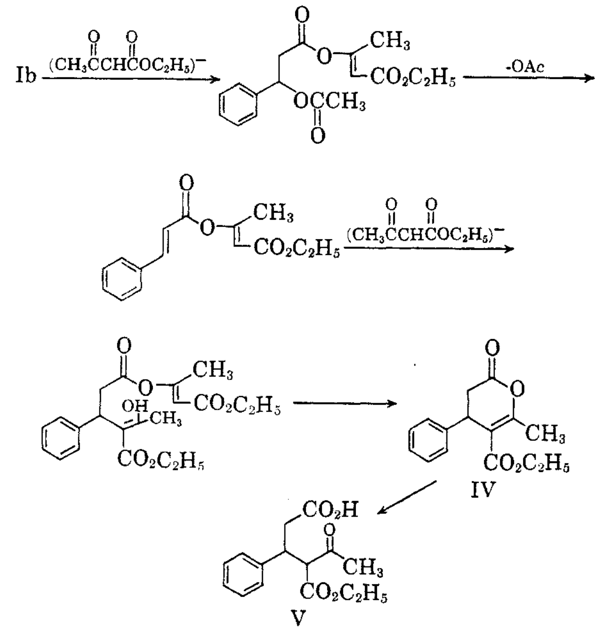
[1] R. Anschütz, *Ann.*, **367**, 193 (1909).

the difference in molecular formulas was one molecule of water. The infrared spectrum suggested an enol lactone structure and 4-phenyl-5-carboethoxy-6-methyl 3,4-dihydro-2-pyrone, IV, was commensurate with the analytical data. Additional evidence for the enol lactone structure was obtained from the ultraviolet spectrum, λ_{max}^{EtOH} 240, ϵ 8,883. The absorption maxima was immediately shifted to 283 mμ in alcoholic potassium hydroxide and after one hour the molecular extinction coefficient was 12,160 which is in agreement with that found when 3-phenyl-4-carbethoxy-5-ketocaproic acid, V, was treated with base.

The enol lactone, IV, was prepared from 3-phenyl-4-carbethoxy-5-ketocaproic acid by treating it with acetic anhydride and anhydrous sodium acetate. The formation of these two products, IV and V, can be rationalized in the following manner:



EXPERIMENTAL

3-Phenyl-3-hydroxypropanoic acid. The method of Hauser and Breslow[2] was used to prepare ethyl 3-phenyl-3-hydroxypropanoate. From 83.5 g. (0.50 mole) ethyl bromoacetate, 65.0 g. (0.61 mole) benzaldehyde, and 40.0 g. (0.60 g.-atom) zinc was obtained 101.0 g. of crude hydroxyester. On hydrolysis 58.8 g. (70.7%) of 3-phenyl-3-hydroxypropanoic acid, m.p. 96–97° (lit. m.p. 100°) was isolated.

3-Phenyl-3-acetoxypropanoic acid. To 6.0 g. (0.0361 mole) 3-hydroxy-3-hydroxypropanoic acid was added 17.8 g. (0.175 mole) acetic anhydride. The mixture was heated and stirred constantly at 90° for 2 hr. Water was added to the cooled reaction mixture. The solution was concentrated and cooled until crystallization occurred. This material was chromatographed on a silicic acid–chloroform column. The first fraction eluted was cinnamic acid. Further elution gave 3.29 g. (43.8%) of 3 phenyl-3-acetoxypropanoic acid, m.p. 102–104; neutral equivalent: calcd. 208.3; found 211.4. λ_{max}^{EtOH} 258 mμ, ϵ 242.

3-Phenyl-3-acetoxypropanoyl chloride. 3-Phenyl-3-acetoxypropanoic acid was heated at 70° with a two-fold excess of thionyl chloride for 0.5 hour. The excess thionyl chloride was removed *in vacuo*. Anhydrous ether was added and the evaporation procedure repeated twice. The resulting acid chloride, $\lambda_{max}^{Et_2O}$ mμ, ϵ 960, formed a *p*-bromoanilide, m.p. 145.2–147.2.

Anal. Calcd. for $C_{17}H_{16}O_3$ NBr: C, 56.37; H, 4.45. Found: C, 56.51; H, 4.06.

The reaction of 3-phenyl-3-propanoyl chloride and ethyl sodioacetoacetate. To 4.0 g. (0.0307 mole) ethyl acetoacetate in 200 ml. of ether was added 0.667 g. (0.029 g.-atom) sodium. The reaction mixture was allowed to stir until the sodium metal was completely consumed. To the suspension of ethyl sodioacetate was added an ether solution of 3-phenyl-3-acetoxypropanoyl chloride prepared from 1.781 g. (0.00856 mole) 3 phenyl-3-acetoxypropanoic acid. After addition was complete the mixture was refluxed 18 hr. The reaction mixture was decomposed with dilute hydrochloric acid and the ether solution washed with water and dried over magnesium sulfate. The ether was removed and the remaining liquid carefully chromatographed on a silicic acid–chloroform column. Two crystalline fractions were obtained. The first and more plentiful, 4-phenyl-5-carboethoxy-6-methyl-3,4-dihydro-2-pyrone, was recrystallized from high boiling petroleum ether, m.p. 83.0–84.0°. λ_{max}^{EtOH} 240 mμ, ϵ 8.883. The λ_{max} was immediately shifted to 283 mμ in 0.382*N* ethanolic potassium hydroxide, the ϵ value having a hyperchromic shift to 12,160 in 1 hr. in base.

Anal. Calcd. for $C_{15}H_{16}O_4$: C, 69.21; H, 6.06. Found: C, 69.21, 69.52; H, 6.32, 6.17.

The second crystalline fraction, 3-phenyl-4-carboethoxy-5-ketocaproic acid, was recrystallized from carbon tetrachloride–chloroform, m.p. 128.0–130.6°; neutral equivalent: calcd. 278; found 266; λ_{max}^{EtOH} 258 mμ, ϵ 336, in 0.382*N* ethanolic potassium hydroxide λ_{max} was immediately shifted to 283 mμ, ϵ 12,440 after 1 hr. in base.

Anal. Calcd. for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.74, 64.86; H, 6.43, 6.52.

Hydrolysis of 4-phenyl-5-carboethoxy-6-methyl-3,4-dihydro-2-pyrone. To 10 ml. of 0.191*N* potassium hydroxide was added 0.123 g. (0.473 Millimole) of 4-phenyl-5-carboethoxy-6-methyl-3,4-dihydro-2-pyrone. The mixture was refluxed for 3 hr. After concentration, the mixture was acidified and extracted with several portions of ether. The ether extracts yielded 0.095 g. (97.5%) of 3-phenyl-5-ketocaproic acid, m.p. 84.1–85.3° from benzene/pet. ether (lit. m.p. 85°) neutral equivalent: calcd. 207, found 212. 3-Phenyl-5-ketocaproic acid semicarbazone, m.p. 166.0–168.0° from water (lit. m.p. 171.5°).[3] Final identification was obtained by converting the semicarbazone to its methyl ester (diazomethane) m.p. 122.0–125.0° (lit. m.p. 121–124°).[4] A mixed melting point with authentic sample gave no depression of melting point.

3-Phenyl 4-carbethoxy-5-ketocaproic acid. Approximately 100 mg. of freshly cut sodium, 10.7 g. (0.066 mole) methyl cinnamate, and 8.6 g. (0.066 mole) ethyl acetoacetate were heated at 100° with stirring for 6 hr. The mixture was dissolved in ether and decomposed with dilute hydrochloric acid. The dried organic phase was distilled *in vacuo* to remove the starting material (61% of methyl cinnamate was recovered). The residue was dissolved in ether and extracted with three 15-ml. portions of 5% sodium hydroxide. Acidification of the alkaline phase, followed by ether extraction, yielded an oil which slowly crystallized when dissolved in warm *n*-butyl ether. The small quantity of 3-phenyl-4-carbethoxy-5-ketocaproic acid thus obtained was recrystallized from *n*-butyl ether, m.p. 123.0–124.0°. Mixed melt with previously isolated material gave no depression.

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(2) C. R. Hauser and D. Breslow, *Org. Syntheses*, **Coll. Vol. III**, 408.

(3) M. Qudrate-I-Khada, *J. Indian Chem. Soc.*, **8**, 215 (1931).

(4) S. M. McElvain, E. Degginger, and J. Behiam, *J. Am. Chem. Soc.*, **76**, 5736 (1954).

4-Phenyl-5-carboethoxy-6-methyl-3,4-dihydro-2-pyrone. A trace of anhydrous sodium acetate, 6.0 ml. of acetic anhydride, and 0.057 g. (0.205 millimole) 3-phenyl-4-carboethoxy-5-ketocaproic acid were refluxed for 4 hr. under an atmosphere of dry nitrogen. After removal of the acetic anhydride the residue was dissolved in 25 ml. of ether and washed with 2–10 portions of water. The dried ether solution on evaporation yielded 0.051 g. (95.6%) of crystalline 4-phenyl-5-carboethoxy-6-methyl-3,4-dihydro-2-pyrone, m.p. 81.0–81.3 from high boiling petroleum ether.

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Infrared Spectra of Some Cyclic Anhydrides

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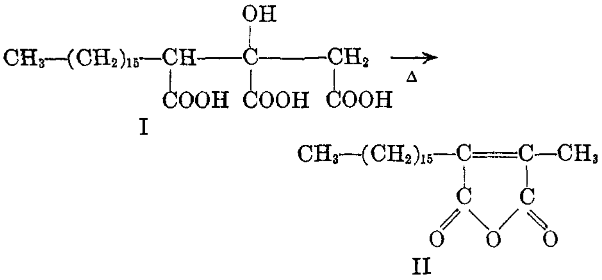
The infrared spectrum of an acid anhydride is characterized by a doublet in the 1750–1850 cm.$^{-1}$ region[2] and this doublet most likely arises from their coupling between the carbonyl vibrations in inphase and out of phase modes.[3] In general, the 2 bands fall into characteristic regions: The open chain or relatively unstrained cyclic glutaric anhydrides possess the doublet in the 1740–1760 cm.$^{-1}$ and 1800–1825 cm.$^{-1}$ regions, and the more strained cyclic succinic anhydrides possess the doublet in the 1770–1790 cm.$^{-1}$ and 1850–1870 cm.$^{-1}$ regions. Furthermore, when this latter series of compounds possesses a conjugated olefinic linkage, the bands shift 20–40 cm.$^{-1}$ towards lower frequency. As has been pointed out by Bellamy,[2] this latter shift places conjugated strained anhydrides in the same region of absorption as unstrained saturated anhydrides and makes structural diagnosis on the basis of infrared absorptions somewhat indefinite.

Jones[3] has called attention to the fact that the two bands need not be of equal intensity, but little attention has been paid to the intensity relationship of the two bands in anhydride absorption. Listed in Table I are the results of a limited study of this feature of the spectrum. It is apparent that the intensity features of the bands are of useful diagnostic value. The ratio of the intensities is expressed in terms of optical density (R = D low frequency band/D high frequency band) and, except for the acyclic materials, this rough measure of intensity is a fair approximation of the more exact integrated intensity values.

As seen from the data in Table I, the intensities of the two bands do not differ greatly in the acyclic anhydrides. In the unstrained glutaric anhydride, the intensity of the lower frequency band remains about the same, but the intensity of the higher band is greatly diminished and the ratio of intensities increases. In all of the succinic anhydrides, the intensity of the lower frequency band is greater and the intensity of the other band remains about the same order of magnitude as in glutaric anhydride. The ratio of intensities in the succinic series of all of the materials is about the same. For the maleic anhydrides, smaller changes in both bands are found, but the ratio of the intensities increases.

The most striking case is that of methyl hexadecylmaleic anhydride (II), the last entry in the table. This material is a degradation product of the fungal metabolite *agaric acid*, 2-hexadecylcitric acid (I).[4]



$$CH_3-(CH_2)_{15}-\underset{COOH}{CH}-\overset{OH}{\underset{COOH}{C}}-\underset{COOH}{CH_2}\xrightarrow{\Delta}$$

I

II

The high value of 11.1 for relative band intensities makes it imperitive to utilize a very concentrated solution for, otherwise, only the 1757 cm.$^{-1}$ band is seen and the presence of a lactone grouping might be indicated. In the case of the two disubstituted maleic anhydrides, a third band of very low intensity lies about 30 cm.$^{-1}$ higher than the 1808–1812 cm.$^{-1}$ band; perhaps this band is concerned with the anhydride absorption and accounts for the low intensity of the higher frequency band. However, on the basis of the intensity ratio of the maleic anhydrides, a clear differentiation can be made between them and the unstrained cyclic anhydrides absorbing in the same region.

In the succinic and maleic anhydride series, the different effect of substitution is of interest. The band positions in the succinic anhydride series are practically independent of substitution, even though the anhydride is part of a highly strained ring system such as cyclopropane and cyclobutane. Such is not the case in the maleic anhydride series, for the less intense bands shift about 30 cm.$^{-1}$ to lower frequency.

As mentioned above, the doublet in the anhydride absorption most likely arises from coupling between carbonyl vibrations. In cyclic anhydrides, the constraint produced by ring closure should increase the angle between the two carbonyl groups, approaching as a limit a colinear arrangement. As this limit is approached, there would be a progressive decrease in intensity of the phase motion because of

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(1) United States Rubber Company Fellow in Chemistry, 1957–1958.

(2) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, J. Wiley and Sons, Inc., New York, 1956, p. 110.

(3) R. N. Jones and C. Sandor, *Techniques of Organic Chemistry*, A. Weissberger, Editor, Interscience Publishing Co., Inc., New York, 1956, Vol. IX, p. 495.

(4) H. Thoms and F. Vogelsang, *Ann.*, **357**, 145 (1907).