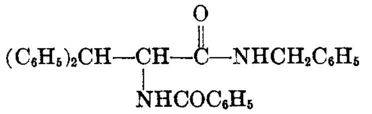
$\gamma$-lactones,[3b] and >C=N absorption[3a] at 1650 cm.$^{-1}$, IV shows strong absorption at 1810 cm.$^{-1}$ and 1645 cm.$^{-1}$ The latter bands are almost identical with those observed for the 4-isopropyl analog[3a] and this shift of carbonyl absorption is consistent with removal of the conjugation created by attachment of an exocyclic double bond in the 4-position, as in I. It has also been shown that the frequency of the >C=N stretching mode is not appreciably affected by changes in the 4-position of these oxazolones.[3a]

The ultraviolet spectrum further supports structure IV. The intense maximum observed with I at 360 m$\mu$ has been attributed to the $C_6H_5CH{=}C{-}N{=}C{-}C_6H_5$ chromophore.[4] The disappearance of this maximum in IV is evidence that this chromophore is absent, whereas the presence of $\lambda_{max}^{EtOH}$ 245 m$\mu$ ($\epsilon$ 5450) is characteristic of the $N$-benzylidene group, $-N{=}\underset{|}{C}{-}C_6H_5$.[5] The end absorption observed is also typical of such oxazolones.[5]

Saturated azlactones are generally very susceptible to hydrolysis and particularly to aminolysis.[6] However, IV was stable to a boiling water-acetone mixture, but reacted readily with benzylamine to form the 2-benzamidobenzylamide, VI, in nearly quantitative yield. The formation of an amide has at times been the sole evidence of the presence of an oxazolone and benzylamine is used for determining the proportion of oxazolone in a mixture ("azlactone equivalent").[7]



$$(C_6H_5)_2CH{-}\underset{\displaystyle NHCOC_6H_5}{\underset{|}{CH}}{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}NHCH_2C_6H_5$$

VI

In contrast to these results, I reacts with phenylmagnesium bromide by ring opening followed by 1,2-addition to give the tertiary alcohol.[8] Results of similar studies on the structurally related $\alpha$-benzylidene-$\gamma$-phenyl-$\Delta$ $\beta,\gamma$-butenolide will be reported in a forthcoming paper and compared with those observed with the oxazolone.

## EXPERIMENTAL[9]

*Reaction of 2-phenyl-4-benzylidene-5(4H)-oxazolone* (I) *with benzene.* In a 1-l., round-bottom flask, fitted with a mechanical stirrer, dropping funnel, and reflux condenser, were placed 9.5 g. (0.072 mole) of anhydrous aluminum chloride in 125 ml. of dry, thiophene-free benzene. The mixture was cooled to 10° and stirred for 1 hr. To this solution was added dropwise with stirring a solution containing 6 g. (0.024 mole) of 2-phenyl-4-benzylidene-5(4*H*)oxazolone in 125 ml. dry benzene, the temperature being maintained at 10–20° during the addition. The mixture turned brick red. When all of the oxazolone had been added, the mixture was stirred for an additional 3 hr. at room temperature. The complex was decomposed with 250 ml. dilute (1:15) HCl and two clear layers were obtained. The benzene layer was separated, the aqueous layer extracted with benzene, and the combined benzene extracts washed with dilute HCl, then with water until neutral to litmus. Benzene was removed by evaporation on a steam bath to give a yellow oil which was dissolved in ether and on addition of petroleum ether formed a light yellow precipitate. The product was recrystallized from 95% ethanol to give 4.8 g. (62%) of light yellow crystals, m.p. 158–159°.

*Anal.* Calcd. for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.24; N, 4.28. Found: C, 80.87; H, 5.23; N, 4.25.

*Reaction of 2-phenyl-4-diphenylmethyl-5(4H)-oxazolone* (IV) *with benzylamine.* A mixture of 1.96 g. (0.006 mole) of oxazolone in 10 ml. dry benzene and 0.64 g. (0.06 mole) of benzylamine was heated under reflux for 30 min. On cooling, white crystals separated, which were washed with petroleum ether and recrystallized from 85% ethanol ($H_2O$ as diluent) to give 2.4 g. (92%) of VI, m.p. 260–261°.

*Anal.* Calcd. for $C_{29}H_{26}N_2O_2$: N, 6.45. Found: N, 6.57.

*Spectral measurements and analyses.* Infrared spectra were obtained on a Perkin-Elmer 21 spectrophotometer and Perkin-Elmer "Infracord." The samples were examined either as Nujol mulls or by use of a KBr disk.

Ultraviolet spectra were measured in 95% ethanol using a Beckman DK-2 spectrophotometer.

The elemental analyses were carried out by Micro-Tech Laboratories, Skokie, Ill.

*Acknowledgment.* The authors are grateful to the Research Corp. for financial support of this work.

DEPARTMENT OF CHEMISTRY
ILLINOIS INSTITUTE OF TECHNOLOGY
CHICAGO 16, ILL.

---

(4) D. A. Bassi, V. Deulofeu, and F. A. F. Ortega, *J. Am. Chem. Soc.*, **75**, 171 (1953).

(5) R. B. Woodward, A. Neuberger, and N. R. Trenner, in *The Chemistry of Penicillin*, Princeton University Press, Princeton, N. J., 1949, p. 429.

(6) (a) H. E. Carter in *Org. Reactions*, III, 215 (1946). (b) E. Baltazzi, *Quart. Revs.* IX, No. 2 (1955), p. 160.

(7) J. W. Cornforth in *The Chemistry of Penicillin*, Princeton University Press, Princeton, N. J., 1949, p. 735.

(8) (a) R. Filler and J. D. Wismar, *J. Org. Chem.* **22**, 853 (1957). (b) A. Mustafa and A. H. E. Harhash, *J. Org. Chem.* **21**, 575 (1956).

(9) Melting points were determined on a Fisher-Johns block and are not corrected.

---

## 8-(2-Methoxyethoxy)caffeine

CARL TABB BAHNER, JOSEPH A. DIPAOLO, AND HELEN JONES

*Received June 17, 1958*

Kihlman[1] has reported. that 8-ethoxycaffeine produced structural chromosomal changes in the root tips. This and closely related compounds have been studied at the Roswell Park Memorial Institute as possible anti-cancer agents. 8-(2-Methoxyethoxy)caffeine was prepared from 8-chlorocaffeine and sodium 2-methoxyethoxide by the general method of Huston and Allen.[2] The crude product, obtained in 80% yield, was recrystallized twice from hot water and once from carbon tetrachloride; m.p. 98.5–99.5° (Fisher-Johns melting

---

(1) B. Kihlman, *Exptl. Cell Research* **1**, 135 (1950).

(2) R. C. Huston and W. F. Allen, *J. Am. Chem. Soc.*, **56**, 1356 (1934).

point apparatus); ultraviolet absorption maximum 279mμ.[3]

*Anal.* Calcd. for $C_{11}H_{16}N_4O_4$: C,49.24; H, 6.02; N, 20.89. Found C, 49.02; H, 6.04; N, 21.09.[4]

When S-180 bearing animals were treated with 125 mg./kg. or 500 mg./kg., tumor growth appeared inhibited about 15%. This compound was not effective in prolonging the survival time of mice that had received injections of Ehrlich ascites cells, Krebs-2 ascites cells, or L-1210 cells.

ROSWELL PARK MEMORIAL INSTITUTE
BUFFALO, N. Y.
CARSON-NEWMAN COLLEGE
JEFFERSON CITY, TENN.

---

(3) The ultraviolet absorption peak was determined by Mr. Oakley Crawford.

(4) Analyses by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

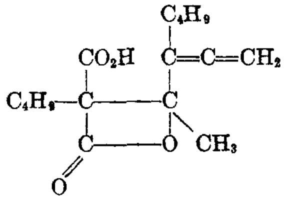
---

## Reinvestigation of the Structure of the "Dimeric" Acid Found in the Carbonation Products of the Grignard Reagent Formed from 1-Bromo-2-heptyne

JOHN H. WOTIZ,[1] JOSEPH S. MATTHEWS,[2] AND HOWARD E. MERRILL[3]

*Received June 23, 1958*

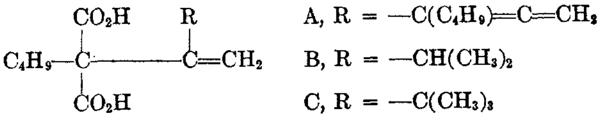
It was reported[4] that the "dimeric" acid found in the carbonation products of the Grignard reagent formed from 1-bromo-2-heptyne is the β-lactonic acid (I)



I

The structure assignment was based on degradation studies, catalytic hydrogenation studies in which two moles of hydrogen were absorbed, and especially in the fact that the "dimeric" acid titrated as a monobasic acid.

In the light of the recent findings that highly substituted malonic acids titrate as monobasic acids in 50% alcohol,[5] the structure of the "dimeric" acid was reinvestigated. We are now favoring the structure IIA, butyl [1-(3-hepta-1,2-dienyl)vinyl]-malonic acid.



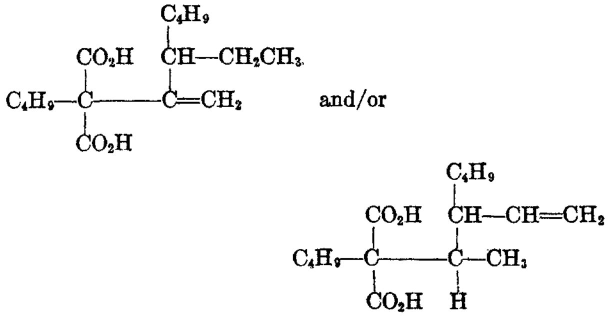
$$C_4H_9-C(CO_2H)_2-C(R)=CH_2 \qquad \begin{array}{l} A,\ R = -C(C_4H_9)=C=CH_2 \\ B,\ R = -CH(CH_3)_2 \\ C,\ R = -C(CH_3)_3 \end{array}$$

II

The $K_1$ to $K_2$ ratio in IIA of 7,760,000 is very high which indicates a highly branched malonic acid. However, it is not as high as in IIB, 28,000,000, or IIC, 57,600,000.[5] The ionization of the acid could be affected in parts by the electronic and electrostatic effects of the unsaturation in R.

It was previously reported[4] that in the presence of Adams' catalyst the "dimeric" acid absorbs hydrogen to the extent of 100% of theory calculated for two double bonds. Additional hydrogenation studies, using a different and more "active" lot of Adams' catalyst, have now shown that the "dimeric" acid absorbs hydrogen to the extent of 100% of theory calculated for three double bonds. In fact, there was no sharp decrease in the rate of the hydrogen uptake after the addition of two moles of hydrogen.

The infrared spectrum of IIA has a single band near 1920 cm.$^{-1}$ characteristic of the allenic linkage,[6] a single, sharp carbonyl band near 1740, and bands near 1635 and 900 cm.$^{-1}$ characteristic of $-\overset{|}{C}=CH_2$. When the hydrogenation is interrupted after the addition of two moles of hydrogen, the product is III.



and/or

III

The infrared spectrum of III shows the presence of the 1635 and 900 cm.$^{-1}$ bands and the absence of the 1920 cm.$^{-1}$ band. All three bands are absent after the uptake of three moles of hydrogen.

Quantitative esterification of IIA and of the hydrogenated products of IIA, also favors the substituted malonic acid structure. When IIA reacted with diazomethane, two moles of nitrogen, per mole of acid, were liberated and the distilled product analyzed for the dimethyl ester. However, its infrared spectrum indicated that a molecular rearrangement had taken place since the characteristic

---

(1) Research Center, Diamond Alkali Company, Painesville, Ohio.

(2) Gulf Research, Pittsburgh, Pa.

(3) Abstracted from a portion of the Ph.D. dissertation of H.E.M., present address, Esso, Baton Rouge, La.

(4) J. H. Wotiz and J. S. Matthews, *J. Org. Chem.*, **20**, 155 (1955).

(5) J. H. Wotiz and H. E. Merrill, *J. Am. Chem. Soc.*, **80**, 866 (1958).

(6) J. H. Wotiz and D. E. Mancuso, *J. Org. Chem.*, **22**, 207 (1957).