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.

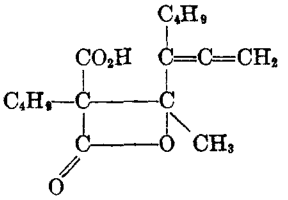
[4] Analyses by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

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

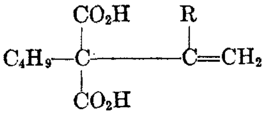
It was reported[4] that the "dimeric" acid found in the carbonation products of the Grignard reagent formed from 1-bromo-2-heptyne is the β-lactonic acid (I)



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.



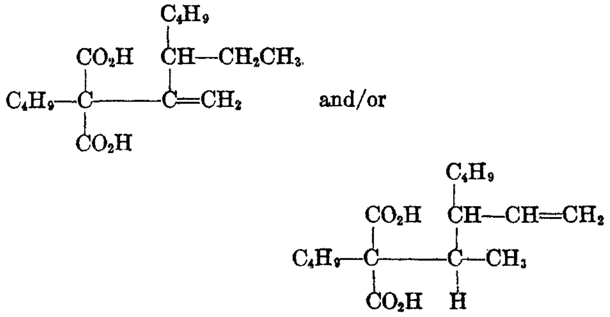
A, R = $-C(C_4H_9)=C=CH_2$
B, R = $-CH(CH_3)_2$
C, R = $-C(CH_3)_3$

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.



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.

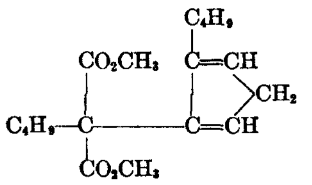
[3] Abstracted from a portion of the Ph.D. dissertation of H.E.M., present address, Esso, Baton Rouge, La.

[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).

allene absorption at 1920 cm.$^{-1}$ and the terminal methylene group absorption bands near 1635 and 900 cm.$^{-1}$, were absent. Two new, strong and sharp absorption bands at 1620 and 1670 cm.$^{-1}$ were found which we attribute to the presence of conjugated double bonds of a cyclopentadienyl ring in IV.



IV

The presence of the cyclopentadienyl ring is also favored by the fact that IV reacted with maleic anhydride and that a highly red-colored product (substituted fulvene) was obtained when IV was condensed with benzaldehyde.

The half esterification of IIA yielded an acid which contained all the characteristic bands of IIA. The carbonyl group absorption region showed two absorption bands at 1725 and 1680 cm.$^{-1}$, due to the ester and acid linkages.

The esterification of III also yielded two moles of nitrogen and the product contained a terminal methylene group as evidenced by the bands at 1625 and 910 cm.$^{-1}$ The half esterification of III produced a monobasic acid with two different carbonyl groups (bands at 1725 and 1690 cm.$^{-1}$) and a terminal methylene group (1630 and 912 cm.$^{-1}$).

Hydrogenation studies have shown the presence of three double bonds, esterification with diazomethane the presence of two carboxy groups, and the titration studies are in accord with the behavior of other highly branched malonic acids.[5] On that basis we are assigning the dimeric acid to have the structure IIA, a structure previously considered[4] but not adopted.

EXPERIMENTAL

IIA. The preparation was previously described,[4] m.p. 99–100°: The esterification was carried out by treating 0.7043 g. (0.00251 mole) of IIA with 0.00595 mole of diazomethane in ether. The volume of evolved nitrogen was 119 ml. (S.T.P.), 105% of theory based on two acid groups. The product distilled at 178° at 17 mm.

Anal. Calcd. for $C_{18}H_{28}O_4$: C, 70.1; H, 9.1. Found: C, 70.1; H, 9.1.

The distillate gave a deep red colored solution when treated with benzaldehyde in the presence of sodium ethoxide. When refluxed with a saturated solution of maleic anhydride in toluene, a white crystalline solid separated.

The half esterification was carried out by treating 0.3769 g. (0.001345 mole) of IIA with 0.00159 mole of diazomethane dissolved in ether. The evolved nitrogen, 31.5 ml. (S.T.P.), was 52% of theory based on two acid groups. The ether was evaporated and the crude residue had a neutralization equivalent of 304.

Anal. Calcd. for $C_{17}H_{28}O_4$: neut. equiv. 294.

III. The preparation was previously described.[4] The dimethyl ester was prepared by treating 0.6672 g. (0.00235 mole) of III with an excess of diazomethane. The volume of nitrogen was 102 ml. (S.T.P.) which is 97% of theory based on two acid groups. Upon the evaporation of the ether, the product boiled at 132–134° at 4 mm.

Anal. Calcd. for $C_{18}H_{32}O_4$: C, 69.2; H, 10.2. Found: C, 70.6; H, 9.7.

The monomethyl ester was prepared as previously described.[4]

Anal. Calcd. for $C_{17}H_3O_4$: neut. equiv. 298. Found: neut. equiv. 296.

In the complete hydrogenation of IIA, 0.0812 g. (0.00029 mole) of IIA absorbed 19.7 ml. (S.T.P.) of hydrogen in 100 min. when an "active" lot of platinum oxide catalyst (0.0077 g.) was used. After the removal of the acetic acid solvent, the residue was crystallized from petroleum ether, m.p. 104–105°.

Anal. Calcd. for $C_{16}H_{30}O_4$: C, 67.1; H, 10.5; mol. wt. 286. Found: C, 66.0; H, 10.1; mol. wt. 304 (titration), 277 (cryoscopic).

CONTRIBUTION NO. 1030 FROM THE DEPARTMENT OF CHEMISTRY,
UNIVERSITY OF PITTSBURGH
PITTSBURGH 13, PA.

Ammajin, a New Constituent of *Ammi Majus* (L.)

NICOLAS A. STARKOWSKY AND NASRY BADRAN

Received May 26, 1958

The fruits of the umbelliferous plant *Ammi majus* (L.) which grows freely in the Nile Delta have been used for centuries as a remedy for leukoderma (vitiligo). The active constituents responsible for the photodynamic properties of this Egyptian plant have been identified with the furocoumarins xanthotoxin, bergapten and imperatorin.[1] Recently, there was an increase of interest in the physiologically active furocoumarins because of the development of the psoralen (furocoumarin) treatment of pigmentation diseases[2a] and alopecia areata,[2b] and the discovery of the effect of these photosensitizing agents on skin carcinogenesis.[2c]

As many plants containing free furocoumarins have, among their other constituents, glycosidic compounds whose aglucones are related coumarins, it was worth studying the glycoside fraction of the fruits of *Ammi majus* (L.) and isolating such compounds. It has been reported in the literature that the fruits of this plant contain about 1% of an amorphous glucosidal principle,[3] but until now no

---

(1) I. R. Fahmy, H. Abu-Shady, A. Schönberg, and A. Sina, *Nature*, **160**, 468 (1947); I. R. Fahmy and H. Abu-Shady, *Quart. J. Pharm. and Pharmacol.* **20**, 281 (1947); *Quart. J. Pharm. and Pharmol.* 21, 499 (1948).

(2) (a) Comp. E. Sidi, J. Bourgeois-Spinasse, and P. Planat, *Dyschromies et Vitiligo*, Expansion scientifique française, Paris, France, 1957; (b) E. Sidi and J. Bourgeois-Spinasse, *Presse med.*, **63**, 458 (1955); (c) M. A. O'Neal and A. C. Griffin, *Cancer Research* 17, 911 (1957).

(3) I. R. Fahmy and M. A. El Keiy, *Rep. Pharm. Soc. Egypt*, **3**, 72 (1931).