of the bromoaniline was recovered. The alkaline solution was acidified to congo red with 20% hydrochloric acid but there was no precipitation of a β-amino acid.

Second Experiment.—Propiolactone (7.2 g.) was added dropwise to a solution of 18 g. of sodium benzenesulfonate in 100 ml. of water at 10°. The clear solution was stirred at 0–10° for 2 hours and then at 26° overnight. Then a solution of 17.2 g. of bromoaniline in 100 ml. of acetone was added to this slightly acidic solution. The clear solution was stirred at 26° for 2 hours after which time the acetone was removed under diminished pressure. With processing similar to the above there was recovered 16.6 g. (91%) of bromoaniline and there was formed no β-amino acid.

N-2-Carboxyethyl-N-*p*-bromophenyl-*p*-toluenesulfonamide.—Propiolactone (10.8 g.) was added dropwise and with stirring during five minutes to a solution of 35.9 g. of *p*-toluenesulfone-(*p*-bromoanilide), m.p. 143–146°, in 200 ml. of water containing 5.6 g. of sodium hydroxide. The turbid solution clarified immediately with evolution of heat. Stirring was continued for an hour and then the mixture was kept at 25° overnight. After acidification (HCl) the resulting precipitate was extracted with benzene. The organic layer was then extracted with aqueous sodium bicarbonate. The cloudy alkaline extract (A) was washed with ether to clarify it and the ether extract was combined with the benzene layer. The organic layer was dried, solvent removed and the remaining light tan oil was stirred with aqueous sodium bicarbonate (B). The insoluble solid (25.14 g.) was collected, m.p. 137–142°. This was the original starting material. Its recovery was 59.5%.

Extract A was acidified (HCl) to give 12.65 g. of a white solid. From the alkaline washing (B), another 1.6 g. of product was secured: total 14.25 g., m.p. 127–131°. This is a 100% yield, based on the unrecovered sulfonanilide. It was recrystallized four times from aqueous methanol to give colorless prisms of m.p. 133–134°.

The same compound was prepared from N-*p*-bromophenyl-β-alanine[1] (11.6 g.) and *p*-toluenesulfonyl chloride (9.1 g.) dissolved in 30 ml. of dry pyridine and 150 ml. of benzene. After 3 hours of refluxing and conventional processing operations there was isolated 9 g. of crystalline product, m.p. 134–135°, after crystallization from ether-hexane. The mixture of this with that obtained above melted at 133–135°.

Anal. Calcd. for $C_{16}H_{16}BrNO_4S$: N, 3.52. Found: N, 3.39.

N-2-Carboxyethyl-N-*p*-nitrophenyl-*p*-toluenesulfonamide.—A solution of 56.4 g. of *p*-toluenesulfone-(*p*-nitroanilide) (m.p. 189°), 500 ml. of water and 7.8 g. of sodium hydroxide was warmed to about 50°. To it was added 14.0 g. of propiolactone dropwise with stirring during 5 minutes. When about half of the lactone was added a yellow precipitate began to separate from the clear red-brown solution. The mixture was stirred at this temperature for 1.5 hours and then set at 25° overnight. Processing followed the method given above for the *p*-bromo analog. There was a 77% recovery (43.5 g., m.p. 185–186°) of starting nitroanilide. The desired product originally appeared as a yellow sticky gum on acidification of the alkaline solution. It slowly solidified to give 11.5 g. of the product. This is a 93% yield, based on the nitroanilide which reacted. One recrystallization from aqueous methanol (Norit) gave yellow, sandy crystals of m.p. 147–151°, weight 9.5 g. After 4 crystallizations from aqueous methanol and vacuum drying for 3 hours over phosphorus pentoxide the substance appeared in colorless needles melting at 150–151°.

Anal. Calcd. for $C_{16}H_{16}N_2O_6S$: N, 7.68. Found: N, 7.61.

N-*p*-Thiocyanophenyl-β-alanine.—A solution of 0.04 mole each of propiolactone and *p*-thiocyanoaniline[2] in 60 ml. of acetone was refluxed for 3 hours. After distillation of solvent, the residue was worked up as usual[1] to give 1.95 g. (32% recovery) of the thiocyanoaniline and 5.6 g. (61% yield) of a product melting at 156–158°. After 2 recrystallizations from aqueous methanol a pure sample melted at 159–160°.

Anal. Calcd. for $C_{10}H_{10}N_2O_2S$: C, 54.0; H, 4.50; N, 12.6. Found: C, 54.0; H, 4.53; N, 12.4.

N,N-Bis-(trichlorophenyl)-β-alanine.—Dry chlorine gas was bubbled for an hour into a cold solution (10°) of 4.9 g. of N,N-diphenyl-β-alanine[3] in 50 ml. of chloroform. The solution was then washed with water and shaken with 10% sodium hydroxide solution to cause separation of 2.75 g. of sodium salt. This salt was treated with dilute hydrochloric acid to form 1.4 g. of colorless prisms of m.p. 168–168.5°. After two recrystallizations from methanol a pure sample, m.p. 169.5–170°, resulted. That it contained chlorine was proved by sodium fusion. It was insoluble in dilute acid or base or in boiling water; however, it was soluble in hot methanol or in boiling sodium hydroxide solution.

Anal. Calcd. for $C_{15}H_9Cl_6NO_2$: C, 40.2; H, 2.01; N, 3.13. Found: C, 40.5; N, 2.07; N, 3.21.

2,3-Dibromopropiono-*p*-toluidide.—A solution of 4.2 g. of bromine in 30 ml. of acetic acid was added dropwise during 15 minutes into a warm (90°) solution of 4.2 g. of acrylo-*p*-toluidide in 70 ml. of glacial acetic acid. The clear solution, light yellow in color, was heated at 100° for an hour and with stirring. It was maintained at room temperature overnight. Dilution with water yielded 7.7 g. (87.5%) of product, m.p. 147–149°. Two recrystallizations from benzene-hexane and two from aqueous acetone gave rise to white needles of m.p. 152°.

Anal. Calcd. for $C_{10}H_{11}Br_2NO$: C, 37.4; H, 3.43; N, 4.36. Found: C, 37.35; H, 3.68; N, 4.41.

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[2] H. P. Kaufmann and W. Oehring, *Ber.*, **59**, 187 (1926).

[3] T. L. Gresham and collaborators, THIS JOURNAL, **73**, 3168 (1951).

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Carboxy β-Lactones

BY CHARLES D. HURD AND SHIN HAYAO

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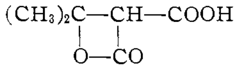
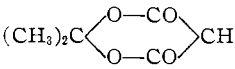
An extensive series of recent papers by Vul'fson deals[1] with the formation of β-lactones by reaction of aldehydes or ketones with malonic acid under dehydrating conditions. He used either malonic acetic anhydride, $CH_2(COOCOCH_3)_2$, or a mixture of malonic acid, acetic anhydride and a trace of sulfuric acid. The structure given for the product of reaction with acetone as the ketone is I. Since this is a β-lactone our interest in this field prompted us to investigate these claims. If the compounds



$$\begin{array}{l}(CH_3)_2C{-}CH{-}COOH \\ \quad\;\;\;\, | \qquad | \\ \quad\;\;\; O{-}CO\end{array}$$

I



II

were indeed β-lactones then they should react chemically in the manner of propiolactone[2a] or of β-isovalerolactone.[2b] The synthesis in question actually was discovered in 1908 by Meldrum[3] who used acetone, malonic acid, acetic anhydride and sulfuric acid, and it was he who assigned structure I to it. He found that the compound was acidic and that if it was heated with aniline it yielded acetone, carbon dioxide and acetanilide.

Meldrum's work was extended by Ott,[4] by Michael and Ross,[5] and it has been considered acceptable in recent reviews.[6] The interpretation was ques-

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[1] N. S. Vul'fson and M. M. Shemyakin, *J. Gen. Chem.* (*U.S.S.R*), **13**, 436, 448 (1943); Vul'fson, *ibid.*, **20**, 425, 435, 595, 600, 603 (1950).

[2] (a) C. D. Hurd and S. Hayao, THIS JOURNAL, **74**, 5889 (1952); (b) T. L. Gresham, J. E. Jansen, F. W. Shaver and W. L. Beears, *ibid.*, **76**, 486 (1954).

[3] A. N. Meldrum, *J. Chem. Soc.*, **93**, 598 (1908).

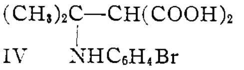
[4] E. Ott, *Ann.*, **401**, 159 (1913).

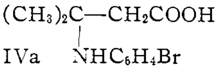
[5] A. Michael and J. Ross, THIS JOURNAL, **55**, 3684 (1933).

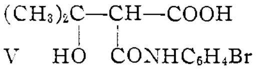
[6] W. E. Hanford and J. C. Sauer in "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 108.

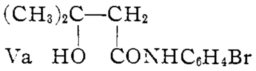
tioned in 1948, however, by Davidson and Bernhard[7] who established that the compound was in fact not I but II, namely, isopropylidene malonate. This is an acylal, not a lactone. Many of Vul'fson's papers have appeared since Davidson and Bernhard's article, but there is no mention of it in any of his work. Corey[8] has described the pyridine-catalyzed condensation of II with mesitylenecarboxaldehyde to yield isopropylidene (2,4,6-trimethylbenzylidene)-malonate.

Our synthesis of this compound followed Meldrum's procedure. As a β-lactone it should react[2] with p-bromoaniline to yield IV (or IVa by subsequent decarboxylation) but neither compound was found. If the β-lactone cleaved in the alternative way, then V or Va would result but these compounds also were not found.


IV $\mathrm{(CH_3)_2\underset{\displaystyle NHC_6H_4Br}{\underset{|}{C}}{-}CH(COOH)_2}$


IVa $\mathrm{(CH_3)_2\underset{\displaystyle NHC_6H_4Br}{\underset{|}{C}}{-}CH_2COOH}$

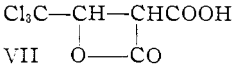

V $\mathrm{(CH_3)_2\underset{\displaystyle HO}{\underset{|}{C}}{-}\underset{\displaystyle CONHC_6H_4Br}{\underset{|}{CH}}{-}COOH}$

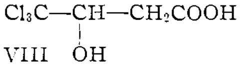

Va $\mathrm{(CH_3)_2\underset{\displaystyle HO}{\underset{|}{C}}{-}\underset{\displaystyle CONHC_6H_4Br}{\underset{|}{CH_2}}}$

Instead, the product formed when acetonitrile was used as solvent was N-p-bromophenylmalonamic acid (VI): $\mathrm{BrC_6H_4NH_2 + II \rightarrow \underset{VI}{BrC_6H_4NHCOCH_2COOH} + (CH_3)_2CO}$. If Meldrum had performed his experiment with aniline in acetonitrile solvent, then he would undoubtedly have found N-phenylmalonamic acid instead of acetanilide.

Several analogous compounds for which β-lactone structures have been claimed presumably also have structures like II. Some of these are the reaction products of methylmalonic acid with acetone,[3] or of malonic acid with diisopropyl ketone,[9] cyclopentanone, cyclohexanone,[1,9] m-nitrobenzaldehyde.[1]

Another reaction claimed by Vul'fson and Shemyakin[10] to yield β-lactones is that of bromoacetaldehyde or chloral hydrate with malonic acid in a medium of acetic acid containing a trace of piperidine. For the chloral reaction they claimed structure VII, whereas earlier investigators[9,11] regarded the substance as a β-hydroxy acid VIII.


VII $\mathrm{Cl_3C{-}\underset{\displaystyle O}{\underset{|}{CH}}{-}\underset{\displaystyle CO}{\underset{|}{CH}}COOH}$


VIII $\mathrm{Cl_3C{-}\underset{\displaystyle OH}{\underset{|}{CH}}{-}CH_2COOH}$

We also investigated this reaction and obtained no support for the lactone structure. Analysis agreed with VIII, not VII. Furthermore, the product did not react with p-bromoaniline in boiling acetonitrile or with ethyl p-aminobenzoate in boiling acetone, procedures which resulted in smooth reactions with propiolactone.[2] The reactants were recovered almost completely.

Experimental

Isopropylidene malonate, colorless needles of m.p. 93–94°, was prepared according to directions in the literature.[7]

Reaction with p-Bromoaniline.—A solution of 3.3 g. of isopropylidene malonate and 3.95 g. of p-bromoaniline in 50 ml. of acetonitrile was refluxed for 3 hours. Then the solvent was evaporated to leave 4.8 g. of a tan solid. This was insoluble in dilute hydrochloric acid, but was soluble in aqueous sodium carbonate with evolution of carbon dioxide. It was dissolved in sodium carbonate solution. A trace of insoluble matter was filtered off and the clear filtrate was made acidic with 20% hydrochloric acid. The white precipitate was crystallized once from aqueous methanol to give colorless, shiny plates of m.p. 159–160° dec. It depressed the m.p. of p-bromoacetanilide (m.p. 164–166°) to 130–131° dec. The substance was N-p-bromophenylmalonamic acid, $\mathrm{BrC_6H_4NHCOCH_2COOH}$.

Anal. Calcd. for $\mathrm{C_9H_8BrNO_3}$: neut. equiv., 258. Found: neut. equiv., 256.

Reaction of Chloral and Malonic Acid.—A solution of 16.5 g. of chloral hydrate, 10.4 g. of malonic acid and 5 ml. of piperidine in 50 ml. of glacial acetic acid was kept at 20° for 12 hours, then was heated at 100° for 2 hours, after which time it was poured into 50 ml. of 10% sulfuric acid. The clear solution was extracted with ether, the ether layer dried over sodium sulfate, and the ether evaporated under diminished pressure. The remaining sirup was treated with cold benzene to give 16.0 g. (77%) of a colorless solid of m.p. 116°. It was twice crystallized from benzene–pentane to give white crystals of m.p. 116–116.5° (softening at 110°). Analysis confirmed $\mathrm{C_4H_6Cl_3O_3}$, hence the substance is 4,4,4-trichloro-3-hydroxybutyric acid (VIII).

Anal. (by Mrs. C. White). Calcd. for $\mathrm{C_5H_3Cl_3O_4}$: . C, 25.53; H, 1.28. Calcd. for $\mathrm{C_4H_5Cl_3O_3}$: C, 23.13; H, 2.41. Found: C, 23.30; H, 2.46.

Non-reaction of VIII with p-Bromoaniline or with Ethyl p-Aminobenzoate.—A solution of 5.7 g. of p-bromoaniline and 7.8 g. of VIII in 100 ml. of acetonitrile was refluxed for 3 hours. After removal of solvent the remaining dark brown sirup was treated with aqueous sodium carbonate and the insoluble sirup was extracted with ether. The ether extract was shaken with dilute hydrochloric acid and then the organic layer was made basic with aqueous sodium carbonate to leave a dark brown oil, weight 5.4 g. (95% recovery of the amine). This was benzoylated to yield benzo-p-bromoanilide, m.p. 198–199°; mixed m.p. with an authentic specimen of m.p. 200–202° was 200–202°.

Similarly, after 3 hours of refluxing of a mixture of 5.7 g. of VIII, 3.6 g. of ethyl p-aminobenzoate and 100 ml. of acetone and removal of the acetone there remained a colorless oil. The latter was treated with 50 ml. of cold water (filtrate A) to give 3.5 g. of light tan solid. The latter was treated with aqueous sodium carbonate, collected and washed with water; yield 3.0 g., which is 84% recovery of the amino ester. It melted at 85–87°, and the mixed m.p. with ethyl p-aminobenzoate was undepressed. Filtrate A was extracted with ether and the ethereal layer was dried over sodium sulfate. After removal of the ether there remained a tan amorphous solid; yield 5.3 g., or 93% recovery of VIII. The latter was crystallized once from benzene–pentane to give needles of m.p. 116–117°. The mixture of this and the original VIII was not depressed in m.p. Its neutral equivalent was 207.3, compared to the calculated 207.5 for $\mathrm{C_4H_5Cl_3O_3}$.

Reaction of Benzaldehyde and Malonic Acid.—To a suspension of 20.8 g. of malonic acid in a mixture of 21.2 g. of benzaldehyde and 100 ml. of glacial acetic acid was added 10 ml. of piperidine. This caused the solid to dissolve exothermically to give a light yellow solution. The latter was kept at 25° for 4 hours, then at 100° for 2 hours ($\mathrm{CO_2}$ evolved). The mixture was poured into 100 ml. of 10% sulfuric acid to give 7.1 g. of white precipitate. After 3 crystallizations there resulted 5.0 g. of colorless, shiny prisms of m.p. 130–131°. This was cinnamic acid. Its neutralization equivalent was 148.0 against a calculated 148.0.

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[7] D. Davidson and S. A. Bernhard, THIS JOURNAL, **70**, 3426 (1948).

[8] E. J. Corey, *ibid.*, **74**, 5897 (1952).

[9] O. Doebner and L. Segelitz, *Ber.*, **38**, 2733 (1905).

[10] N. S. Vul'fson and M. M. Shemyakin, *Compt. rend. acad. sci., U.R.S.S.*, **29**, 206 (1940); Shemyakin and Vul'fson, *ibid.*, **30**, 812 (1941); *C. A.*, **35**, 3968 (1941); **37**, 610 (1943).

[11] K. G. Thurnlackh, *Monatsh.*, **12**, 556 (1891); K. von Auwers and M. Schmidt, *Ber.*, **46**, 487 (1913).