Syntheses and Structures of Acetylformoin and Its Related Compounds. III. Isobutyrylformoin*

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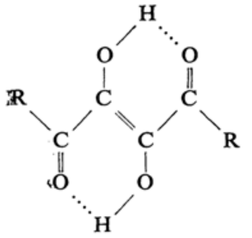
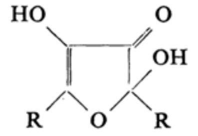
In previous papers, the chemistry of acetyl-[1], benzoyl-[1] and neopentoyl-formoin[2] was reported on. These formoins were synthesized by the acyloin condensation of methyl-, phenyl- and *t*-butyl-glyoxal; the possible structures for these formoins are I—III. The structures of acetyl-, benzoyl- and neopentoyl-formoin in the crystalline state were established as I ($R=CH_3$), II ($R=C_6H_5$) and II ($R=C(CH_3)_3$) respectively.

The present report is concerned with isobutyrylformoin, which was also synthesized by the acyloin condensation of isopropylglyoxal:

$$2\ (CH_3)_2CHCOCHO \rightarrow (CH_3)_2CHCOCH(OH)COCOCH(CH_2)_3$$



I



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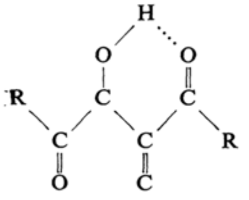
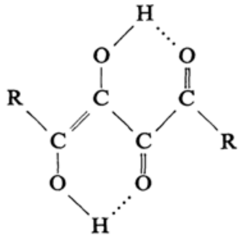
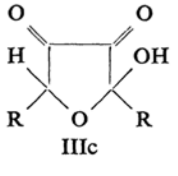


IIIa



IIIb



IIIc

Results and Discussion

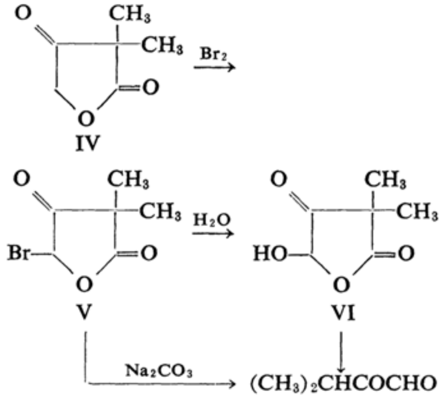
The Preparation of Isopropylglyoxal.—Conrad and Gast[3] first synthesized isopropylglyoxal by the following sequence of reactions:

$$CH_3COCH_2COOC_2H_5 \xrightarrow[Na]{CH_3I}$$

$$CH_3COC(CH_3)_2COOC_2H_5 \xrightarrow{Br_2}$$

$$BrCH_2COC(CH_3)_2COOC_2H_5 \xrightarrow{AcOK}$$

$$CH_3COOCH_2COC(CH_3)_2COOC_2H_5 \xrightarrow{H_2SO_4}$$



They obtained isopropylglyoxal by the decarboxylation of 5-oxy-3, 3-dimethyltetronic acid VI, which had been prepared by the hydrolysis of 5-bromo-3, 3-dimethyltetronic acid V. They isolated the latter compound as an oily products, but we found it a white solid melting at 52.5∼54°C. Reid, Fortenbaugh and Patterson[4] prepared isopropylglyoxal by the steam distillation of 5-bromo-3,3-dimethyltetronic acid V in a 20% yield. We are of opinion that the low yield may be due to the decomposition of isopropylglyoxal by hydrogen bromide, which is produced by the hydrolysis of V.

We succeeded in obtaining isopropylglyoxal directly from the bromide V by suspending it in an aqueous solution of enough amount of sodium carbonate to neutralize the acid produced and then by heating the entire mixture.

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[1] R. Goto, Y. Miyagi and H. Inokawa, This Bulletin, 36, 147 (1963).

[2] Y. Miyagi and R. Goto, ibid., 36, 650 (1963).

[3] M. Conrad and R. Gast, *Ber.*, 31, 2726 (1898).

[4] E. B. Reid, R. B. Fortenbaugh and H. R. Patterson, *J. Org. Chem.*, 15, 572 (1950).

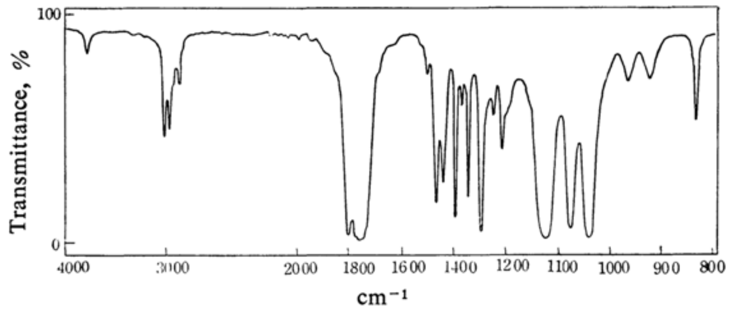

Fig. 1. Infrared spectrum of 3,3-dimethyltetronic acid (IV) in carbon tetrachloride.

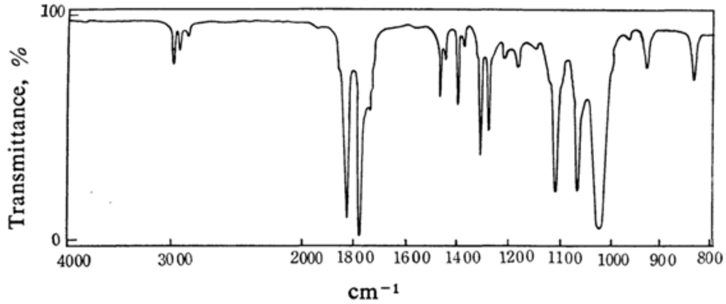

Fig. 2. Infrared spectrum of 5-bromo-3,3-dimethyltetronic acid (V) in carbon tetrachloride.

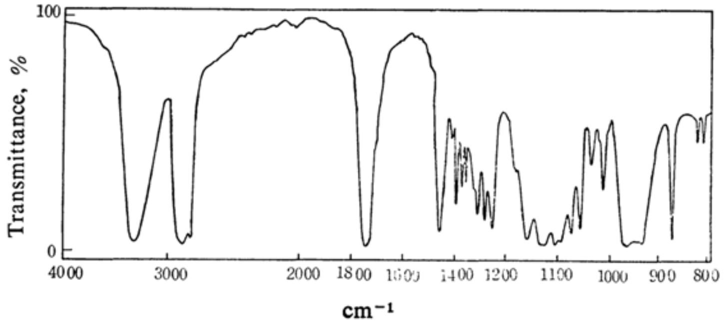

Fig. 3. Infrared spectrum of 5-oxy-3,3-dimethyltetronic acid (VI) in Nujol.

Figures 1, 2 and 3 show the infrared spectra of compounds IV, V and VI respectively. Compound IV shows a broad band of the C=O stretching absorption between 1740 and 1810 cm^{-1} in carbon tetrachloride. Similarly, compound VI absorbs at 1740∼1770 cm^{-1} in Nujol. These broad bands may be overlapping bands of ring ketones and γ-lactones; five-membered ketones are said to absorb at around 1750 cm^{-1} 5-7), and γ-lactones absorb at around 1770 cm^{-1} 8,9). The C=O stretching absorption band of compound VI arises at 1760∼1800 cm^{-1} in tetrahydrofuran. Compound V shows two separated bands, at 1825 and 1773 cm^{-1}. The absorption bands of α-bromoketones are usually shifted to a higher frequency by about 20 cm^{-1}. Thus, in compound V, the absorption band of the ring ketone may be considered to arise at a higher frequency, 1825 cm^{-1}, separated from the lactone band at 1773 cm^{-1}.

Isobutyrylformoin.—The reaction product of isopropylglyoxal with sodium cyainde is a white solid, which was proved by elementary analysis and by molecular weight determination to be a condensation product of the two molecules of isopropylglyoxal.

The infrared absorption bands of isobutyrylformoin in the regions of C=O, C=C and OH stretching absorption are listed in Table I. The

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5) R. N. Jones, V. Z. Williams, M. J. Whalen and K. Dobriner, *J. Am. Chem. Soc.*, **70**, 2024 (1948).

6) E. J. Hartwell, R. E. Richards and H. W. Thompson, *J. Chem. Soc.*, **1948**, 1436.

7) J. F. Grove and H. A. Willis, ibid., **1951**, 883.

8) R. S. Rasmussen and R. Brattain, *J. Am. Chem. Soc.*, **71**, 1073 (1949).

9) D. H. Whiffen and H. W. Thompson, *J. Chem. Soc.*, **1946**, 1005.

TABLE I. INFRARED ABSORPTION BANDS, cm^{-1}

Formoin	Phase					
Benzoyl-	Nujol	3500	3270	1685	1608	1595
Neopentoyl-	Nujol	3330	3180	1690	1605	
Isobutyryl-	Nujol	3340	3100	1690	1598	
	Tetrahydrofuran	3290		1705	1635	
	Chloroform	weak and broad 3700∼2600		1635		
Acetyl-	Nujol Chloroform	weak and broad 3600∼2800		1625		

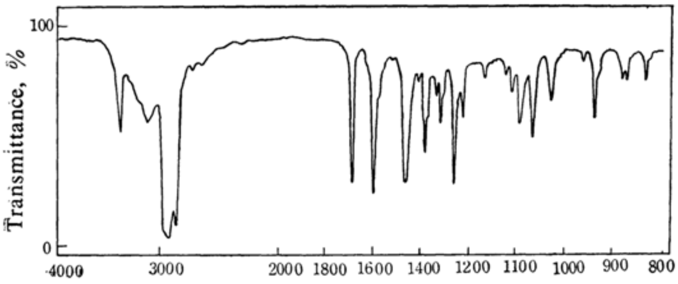


Fig. 4. Infrared spectrum of isobutyrylformoin in Nujol.

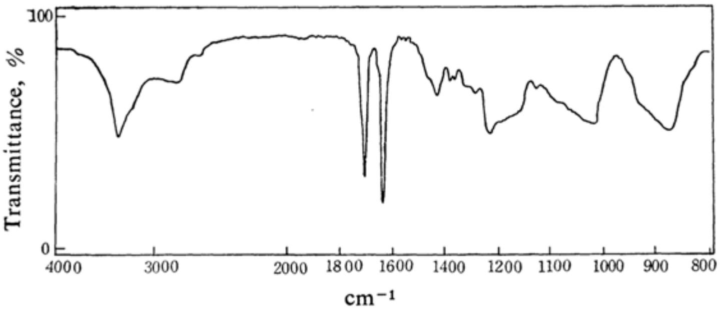


Fig. 5. Infrared spectrum of isobutyrylformoin in tetrahydrofuran.

infrared spectrum of isobutyrylformoin in Nujol (Fig. 4) is very similar to those of benzoylformoin and neopentoylformoin, the structures of which were both established as II ($R=C_6H_5$ and CMe_3)[1,2]. Thus, the structure of isobutyrylformoin also seems to be II ($R=CHMe_2$). The absorption band at 1598 cm^{-1} and that at 1690 cm^{-1} are attributable to the C=C and C=O stretching absorption respectively. This assignment seems probable, in spite of the lack of spectral data on furanones, because conjugated ketones usually absorb at 1690∼1680 cm^{-1}, and olefinic linkages do at around 1600 cm^{-1}.

The spectrum in tetrahydrofuran (Fig. 5) resembles that in Nujol, except that the former shows only one band of the OH stretching absorption at 3290 cm^{-1}, while the latter shows two bands, at 3340 and 3100 cm^{-1}. Therefore, isobutyrylformoin may be considered to have structure II in tetrahydrofuran. The difference in the hydroxyl bands between the solid state and the solution does not suggest that isobutyrylformoin would have a structure other than II in tetrahydrofuran, because the position of the OH stretching absorption band is easily shifted with the strength of hydrogen bondings, which may be different in the solid state and in the solution. Moreover, the spectrum can not be explained on the basis of structures I, IIIa, IIIb and IIIc for reasons similar to those discussed in a previous paper[1].

The spectrum of isobutyrylformoin in chloroform (Fig. 6) is remarkably different from those in tetrahydrofuran and Nujol; it is, however, very similar to that of acetylformoin in chloroform or Nujol. There is only a broad, weak absorption band extending from 2600 cm^{-1}

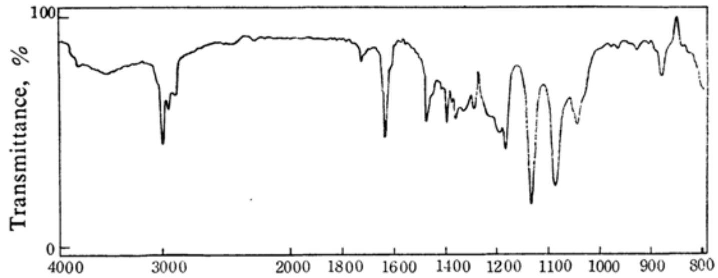
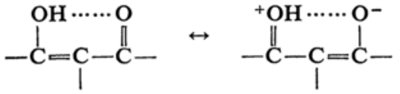


Fig. 6. Infrared spectrum of isobutyrylformoin in chloroform.

beyond over 3700 cm^{-1} instead of distinct bands at 3340 and 3100 cm^{-1} in Nujol or at 3290 cm^{-1} in tetrahydrofuran. The C=O stretching absorption band is widely shifted to 1635 cm^{-1}. This type of spectra has been said to be characteristic of the enol form of β-diketones and has been attributed to the resonance structures[10]:



$$\begin{array}{c}\text{OH}\cdots\cdots\text{O}\\ |\qquad\ \ \|\\ -\text{C}=\text{C}-\text{C}-\\ |\end{array} \leftrightarrow \begin{array}{c}{}^{+}\text{OH}\cdots\cdots\text{O}^{-}\\ \|\qquad\ \ |\\ -\text{C}-\text{C}=\text{C}-\\ |\end{array}$$

Structure I (R=CHMe$_2$) is most compatible with these observations, as in the case of acetylformoin. Any further explanation and exclusion of the other structures, II, IIIa, IIIb and IIIc, would be the same as have been given in a previous paper[1].

A similar tendency is observed in the ultraviolet absorption spectra. In tetrahydrofuran, the absorption maximum is attained at 305 mμ with $\varepsilon_{\max}$, 7350. On the other hand, in chloroform it is shifted to 360 mμ, with a great enhancement of its intensity ($\varepsilon_{\max}$=14200). Thus, the absorption at 360 mμ is attributable to the enediol structure I and that at 305 mμ, to the furanone structure II.

Experimental

Ethyl α,α-Dimethylacetoacetate. — This compound was prepared by the method of Marshall and Cannon[11]; 51%; b. p. 96~98°C/40 mmHg; n_D^{25} 1.4180.

Found: C, 60.99; H, 8.96. Calcd. for $C_8H_{11}O_3$: C, 60.74; H, 8.92%.

Ethyl γ-Bromo-α,α-dimethylacetoacetate.—This compound was prepared by the method of Conrad and Gast[3,12]: 70%; b. p. 109~111°C/10 mmHg; n_D^{25} 1.4682.

Found: C, 40.62; H, 5.50; Br, 33.68. Calcd. for $C_8H_{13}O_3Br$: C, 40.55; H, 5.49; Br, 33.42%.

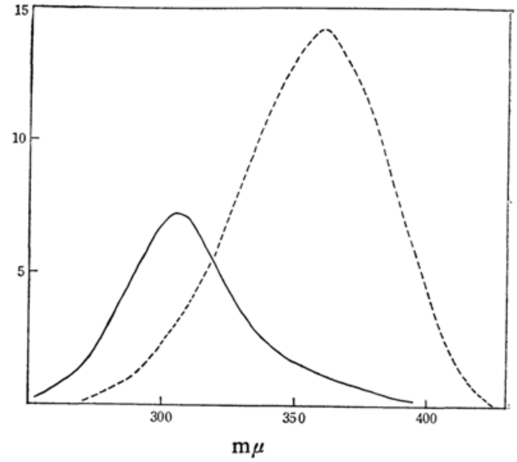


Fig. 7. Ultraviolet spectra of isobutyrylformoin: —— in tetrahydrofuran; ---- in chloroform.

Ethyl γ-Acetoxy-α,α-dimethylacetoacetate. — This compound was also prepared by the method of Conrad and Ggast[3,12]: 55%; b. p. 91~92°C/1 mmHg; n_D^{25} 1.4339.

Found: C, 55.32; H, 7.22. Calcd. for $C_{10}H_{21}O_5$: C, 55.54; H, 7.46%.

3,3-Dimethyltetronic Acid.—This compound was prepared by the method of Cannon and Jones[12]: 70%; b. p. 70~72°C/3 mmHg; n_D^{25} 1.4475.

Found: C, 56.30; H, 6.52. Calcd. for $C_6H_8O_3$: C, 56.24; H, 6.29%.

5-Bromo-3,3-dimethyltetronic Acid.—A solution of 16 g. of 3,3-dimethyltetronic acid in 30 ml. of carbon tetrachloride was warmed at 60°C, and then 20 g. of bromine was added with stirring. The solvent was evaporated off under reduced pressure. Upon the cooling with ice-water, all the residue was solidified. The product was washed with cold water, dried in vacuo over potassium hydroxide, and recrystallized from ether; 92%; m. p. 52.5~54°C (decomp.).

Found: C, 34.75; H, 3.68; Br, 42.02. Calcd. for $C_6H_7O_3Br$: C, 34.78; H, 3.38; Br, 41.88%.

5-Oxy-3,3-dimethyltetronic Acid[3].—A suspension of 5-bromo-3,3-dimethyltetronic acid in water was stored in a refrigerator for over a month. The solid product was recrystallized from methanol; m. p. 137°C.

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[10] R. S. Rasmussen, D. D. Tunnicliff and R. B. Brattain, *J. Am. Chem. Soc.*, **71**, 1068 (1949); L. J. Bellamy, "Infrared Spectra of Complex Molecules", Methuen, London (1958), pp. 104, 142.

[11] R. J. Marshall and W. N. Cannon, *J. Org. Chem.*, **21**, 245 (1956).

[12] W. N. Cannon and R. G. Jones, ibid., **23**, 126 (1958).

Found: C, 49.89; H, 5.72. Calcd. for $C_6H_8O_4$: C, 50.00; H, 5.60%.

Isopropylglyoxal. — Five grams of pulverized 5-bromo-3,3-dimethyltetronic acid was suspended in an aqueous solution of 1.3 g. of sodium carbonate in 50 ml. of water. The entire mixture was whirled. The evolusion of carbon dioxide began immediately, and after about half an hour the characteristic odor of isopropylglyoxal could be smelled. The entire mixture was stored in a refrigerator. After a few hours, most of the solid disappeared, but after standing overnight many white needles were deposited. The entire mixture was then gradually heated to 90°C. The needles dissolved in the solution, and a steady evolution of gas took place. After its end, the solution was cooled with ice-water. The long white needles which were deposited were collected by filtration. The purification was effected by vacuum sublimation; yield, 85%; m. p. 95~96.5°C.

Found: C, 59.80; H, 8.07. Calcd. for $C_5H_8O_2$: C, 60.00; H, 8.00%.

Isobutyrylformoin.—Into a solution of 4.5 g. of isopropylglyoxal in 150 ml. of 90% aqueous alcohol, a solution of 0.2 g. sodium cyanide in 5 ml. of water was added under a nitrogen stream. The entire solution was then cooled at 0°C for about twenty minutes. After the addition of a few drops of phosphoric acid, the solvent was evaporated off under reduced pressure. The faint-colored crystals which appeared were washed with about 50 ml. of cold water, then dissolved in a minimum amount of alcohol and crystallized by the addition of water: yield, 68%; m. p. 88~93°C.

Found: C, 59.78; H, 7.75; mol. wt. (Rast), 186. Calcd. for $C_{10}H_{16}O_4$: C, 60.00; H, 8.00%; mol. wt., 200.

Spectra. — The infrared spectra were recorded with a Koken model DS-301 spectrophotometer. The ultraviolet spectra were recorded with a Shimadzu model QR-50 spectrophotometer.

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