*Syntheses and Structures of Acetylformoin and its Related Compounds. I**

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Acetylformoin (AF) and benzoylformoin (BF) are synthesized by the acyloin condensation of methyl- and phenyl-glyoxal respectively:

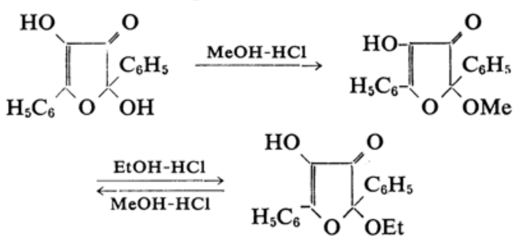
$$\text{R}=\text{CH}_3:\ \text{AF}$$

$$2\,\text{RCOCHO} \xrightarrow{\text{KCN}} \text{RCOCH(OH)COCOR}$$

$$\text{R}=\text{C}_6\text{H}_5:\ \text{BF}$$

The probable structures for these formoins are indicated by I—V in Fig. 1.

The structure of benzoylformoin has been investigated by earlier workers[1,2]. Benzoylformoin has two different kinds of hydroxyl groups, one of which is alkylated with an alcoholic solution of a mineral acid to give an *O*-alkyl derivative. *O*-Methyl derivative (methyl benzoylformoin) is converted to *O*-ethyl derivative (ethyl benzoylformoin) with ethanolic hydrogen chloride and vice versa with methanolic hydrogen chloride.



Blatt[2] stated that this type of etherification is characteristic of the glycosidic linkage and has suggested the cyclic structure VI for the

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* Partly presented at the 13th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1959.

[1] P. W. Abenius, *Ber.*, 25, 706 (1894).

[2] A. H. Blatt, *J. Am. Chem. Soc.*, 57, 1103 (1935); 58, 1894 (1936).

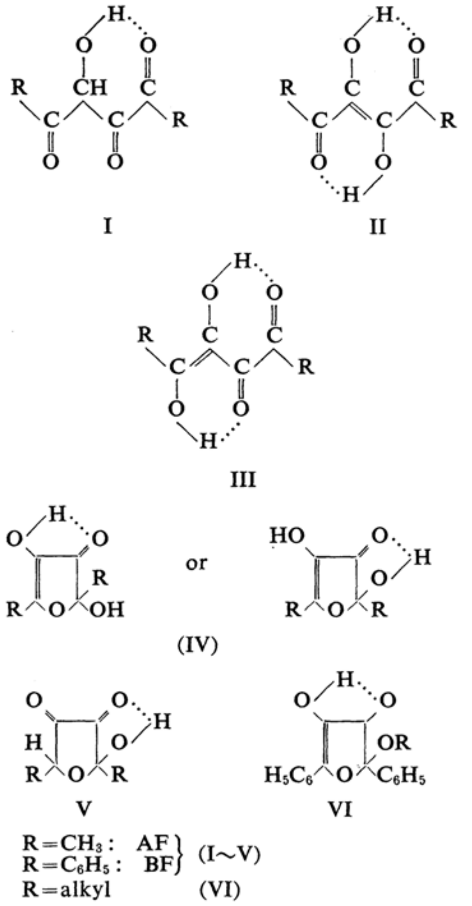

Fig. 1.

O-alkyl derivative. On this basis, he also proposed structure IV for benzoylformoin itself. On the other hand, it has been reported that the reaction with *o*-phenylenediamine and some other chemical behavior supported structure III. Blatt was of opinion that an equilibrium between III and IV occurred in solution. If this is the case, the formation of VI by the etherification can not be considered as an unequivocal evidence for the straightforward structure IV of benzoylformoin, since the equilibrium between the two tautomers could have been shifted due to the removal of IV by the etherification.

Acetylformoin was first synthesized by Nodzu and Kunichika[3] in our laboratory. More recently Steinbauer and Waldmann[4] studied the structure of acetylformoin. The reaction with *o*-phenylenediamine and methanolysis suggest an equilibrium between IV and III or II in solution.

The authors have tried to determine the structure of benzoyl- and acetyl-formoin by the spectrophotometric method.

Results and Discussion

The spectral data obtained by the authors are listed in Tables I and II.

The Structure of Acetylformoin. — Acetylformoin was examined as a solid state in Nujol and as a solution in chloroform. The spectrum of acetylformoin in Nujol is very similar to that of the chloroform solution immediately after dissolving, except that in solution there appears another absorption band of weak intensity, at 1710 cm^{-1}. In both cases, there is an intense absorption at 1620 cm^{-1}. In the chloroform solution, immediately after dissolving a very weak broad absorption band, extending from 2800 cm^{-1} to beyond 3600 cm^{-1}, is observed. In Nujol, acetylformoin shows no distinct absorption over 3000 cm^{-1}, but a weak, broad absorption on both sides of the sides of the strong absorption of Nujol at 2800∼3000 cm^{-1}.*

A part of structure II, $-C(OH)=\underset{|}{C}-CO-$, is the enol form of a β-diketone and constitutes the so-called "conjugate chelation". In enolic β-diketones, the C=O stretching absorption band is found to be widely shifted close to 1600 cm^{-1}, with a great enhancement of its intensity, and the OH stretching absorption band becomes very weak and broad. This phenomenon was first reported by Rasmussen, Tunnicliff and Brattain[5], who attributed the anomalies to resonance structures:

$$\begin{matrix} OH\cdots\cdots O & & {}^{+}OH\cdots\cdots O^{-} \\ | \qquad\quad \| & \longleftrightarrow & \| \qquad\quad | \\ -C{=}\underset{|}{C}{-}C- & & -C{-}\underset{|}{C}{=}C- \end{matrix}$$

This chelation has been termed "conjugate chelation" to distinguish it from the normal hydrogen bonding. Similar observations have been reported for acetylacetone[5,6], benzoylacetone[6], dibenzoylmethane[5,6], α-acetyltetronic acid[7] and many other compounds[8].

Exactly the same type of anomalies was observed with the spectra of acetylformoin: there arise a C=O stretching absorption band at a very low wave number, 1620 cm^{-1}, and a

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3) R. Nodzu and S. Kunichika, This Bulletin, **15**, 211 (1940).

4) E. Steinbauer and E. Waldmann, *Monat.*, **89**, 570 (1958).

* The spectum of acetylformoin in hexachlorobutadiene mull also shows this broad absorption band. In this case, however, there arises an additional absorption at 1710 cm^{-1}, as in the chloroform solution. It might be considered that acetylformoin partly dissolves in hexachlorobutadiene. On this point more details are under investigation.

5) R. S. Rasmussen, D. D. Tunnicliff and R. B. Brattain, *J. Am. Chem. Soc.*, **71**, 1068 (1949).

6) S. Batos, D. Hadži and G. Rossmy, *Trans. Faraday Soc.*, **52**, 464 (1956).

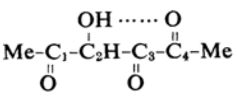
7) L. A. Duncanson, *J. Chem. Soc.*, **1953** 1207.

8) L. J. Bellamy, "Infrared Spectra of Complex Molecules", Methuen, London (1958), pp. 104, 142.

weak, broad band of the OH stretching absorption. In structure II, enediol $-C(OH)=C(OH)-$ serves to form conjugate chelation on both sides of the carbonyl group; therefore a stronger chelation may be expected.

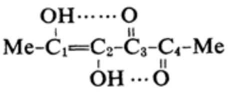
In enolic β-diketones, the C=C stretching absorption can not be observed. Rasmussen[5] stated that this is to be accounted for by its being hidden by the very strong C=O band or by its being shifted out of the double-bond region because of its loss of a double-bond character. Furthermore, it is not too difficult to comprehend the disappearance of the C=C stretching absorption band of acetylformoin when due attention is paid to the fact that C=C is fully and symmetrically substituted.

The other structures, I, III, IV and V, are excluded for the following reasons.



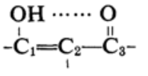
$$\mathrm{Me{-}\underset{\underset{O}{\|}}{C_1}{-}\overset{\overset{OH\cdots\cdots}{|}}{C_2}H{-}\underset{\underset{O}{\|}}{C_3}{-}\overset{\overset{O}{\|}}{C_4}{-}Me}$$

As for structure I, there are three kinds of carbonyl groups: $C_1=O$ is a normal carbonyl group; $C_3=O$ is a carbonyl group in α-diketone, and $C_4=O$ is a hydrogen-bonded carbonyl group. Therefore, their absorption may be expected to split. Among them, the absorption band of $C_4=O$ is expected to arise at the lowest wave number because of the hydrogen bonding, but the so wide shift over to 1620 cm^{-1} as observed can not be expected with the simple hydrogn bonding, which would produce somewhat sharper bands of the OH stretching absorption.



$$\mathrm{Me{-}\overset{\overset{OH\cdots\cdots}{|}}{C_1}{=}\underset{\underset{OH\cdots}{|}}{C_2}{-}\overset{\overset{O}{\|}}{C_3}{-}\underset{\underset{O}{\|}}{C_4}{-}Me}$$

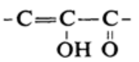
As for structure III, the band at 1620 cm^{-1} is attributable to $C_3=O$ because a part of the structure,



$$\mathrm{{-}\overset{\overset{OH\cdots\cdots}{|}}{C_1}{=}\underset{|}{C_2}{-}\overset{\overset{O}{\|}}{C_3}{-}}$$

constitutes the conjugate chelation and can result in a large shift, as been observed. $C_4=O$, however, is simply* a hydrogen-bonded carbonyl group, and its absorption band will arise at a higher wave number, probably close to 1700 cm^{-1}. Since the hydroxyl group attatched to C_2 forms only a simple* hydrogen bonding on $C_1=O$, there should appear some distinct bands of the OH stretching absorption.

As for structure IV, the value, 1620 cm^{-1}, is too low for the carbonyl group of IV, which is the enol form of α-diketone.



$$\mathrm{{-}C{=}\underset{\underset{OH}{|}}{C}{-}\underset{\underset{O}{\|}}{C}{-}}$$

In such enolic α-diketones as phenylbenzylglyoxal $C_6H_5COCOCH_2C_6H_5$, no anomalies arising in enolic β-diketones are observed, and the C=O stretching absorption arises at the position of normal conjugated ketones, around 1670 cm^{-1}[9]. Moreover, in structure IV, the bands of the C=C and C=O stretching absorption may be expected to separate, and weak, broad band of OH stretching absorption can not be explained with structure IV.

As for structure V, the C=O stretching absorption may be expected to arise at a much higher wave number because the α-diketones in 5-membered ring system absorb at 1760∼1776 cm^{-1}[10]. In structure V, some distinct bands of OH stretching absorption may be expected to arise.

The absorption band at 1710 cm^{-1}, which is observed in the chloroform solution immediately after dissolving, becomes stronger when the solution is left standing; at the same time there arise very weak but distinct absorption bands at 3600, 3340, 2970, 2880 and 1763 cm^{-1}. Therefore, in the chloroform solution acetylformoin seems to change to another structure than II, but the identity of this new structure has not yet been determined.

The Structure of Benzoylformoin.—Benzoylformoin absorbs at 3500, 3210, 1685, 1608 and 1595 cm^{-1}. An *O*-alkyl derivative, ethyl benzoylformoin (EBF), absorbs at 3270, 1688, 1605 and 1595 cm^{-1}. Structure IV seems to be most compatible with these observations. The reasons are as follows: first of all, in the region of C=O and C=C stretching absorption, the spectrum of benzoylformoin is very similar to that of ethyl benzoylformoin, the structure of which was established to be VI, as mentioned above. The band at 1685 cm^{-1} may be assigned to the carbonyl group, and those at 1608 and 1595 cm^{-1}, to the phenyl and olefin groups. These assignments seem to be appropriate, since enolic α-diketones absorb at around 1670 cm^{-1}[9], as mentioned above in the discussion of acetylformoin. When one of the hydroxyl groups of benzoylformoin is ethylated there occurs an accompanying change in the spectrum: benzoylformoin shows two bands of OH stretching absorption, while ethyl benzoylformoin shows one of OH stretching absorption.

Structures I, II, III and V are excluded for the following reasons.

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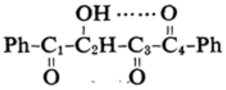
* Here "simple" or "simply" means hydrogen bondinigs without any involvement in the conjugate chelation.

[9] R. P. Barnes and G. E. Pinkney, *J. Am. Chem. Soc.*, **75**, 479 (1953).

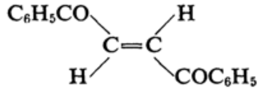
[10] K. Alder, H. K. Schäfer, H. Esser, H. Krieger and R. Reubke, *Ann.*, **593**, 23 (1955).



$$\mathrm{Ph{-}\underset{\underset{O}{\|}}{C_1}{-}\overset{\overset{OH\cdots\cdots}{|}}{C_2}H{-}\underset{\underset{O}{\|}}{C_3}{-}\overset{\overset{O}{\|}}{C_4}{-}Ph}$$

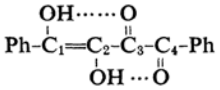
As for structure I, the C=O stretching absorption bands will probably split, because C_4=O is conjugated and hydrogen-bonded, C_3=O is the carbonyl group in α-diketone, and C_1=O is conjugated but not hydrogen-bonded. Above all, the absorption band of C_3=O will arise at around 1710 cm^{-1} 5).

As for structure II, a model compound of II, *trans*-dibenzoylethylene VII, absorbs at 1635 cm^{-1}. The C=O stretching absorption band of structure II may be shifted to a lower wave number than 1635 cm^{-1} by its conjugate chelation*. Furthermore, two distinct bands of OH stretching absorption can not be explained with structure II.



VII

As for structure III, there are two kinds of carbonyl groups: C_4=O is conjugated and simply hydrogen-bonded, while C_3=O is a carbonyl group involved in the conjugate chelation*. Hence, the following assignment



$$\mathrm{Ph{-}\overset{\overset{OH\cdots\cdots}{|}}{C_1}{=}\underset{\underset{OH\cdots}{|}}{C_2}{-}\overset{\overset{O}{\|}}{C_3}{-}\underset{\underset{O}{\|}}{C_4}{-}Ph}$$

is possible: the absorption band at 1685 cm^{-1} is attributed to C_4=O, and the bands at 1605 and 1595 cm^{-1} are attributed to the overlapping bands of C_3=O and C=C stretching absorptions. If this be the case, the bands at 1605 and 1595 cm^{-1} would have been stronger than the bands at 1685 cm^{-1}, because the band of C_3=O is that of the conjugate chelation, which should have a much stronger intensity and because, moreover, this band of C_3=O is overlapped with the C=C stretching absorption band to enhance the intensity. The intensities of the band at 1685 cm^{-1} and the bands at 1605 and 1595 cm^{-1}, however, are almost equal. Furthermore, the hydroxyl group attatched to C_1 constitutes a conjugate chelation, but the absorption bands of benzoylformoin in the region of the OH stretching absorption are not so weak and broad as that of the conjugate chelation.

As for structure V, structure V is expected to show its C=O stretching absorption bands at a higher wave number, over 1760 cm^{-1}, as mentioned above in the discussion of acetylformoin.

TABLE I. ABSORPTION BANDS OF AF (cm^{-1})

Nujol	$CHCl_3$ solution*	$CHCl_3$ solution**
Weak and broad 3600～2800	Weak and broad 3600～2800	3600 vw 3340 w 2970 w 2880 w
	1710 w	1763 m 1707 s
1620 s	1625 s	1620 s

* 10^{-1} M. immediately after dissolying
** 10^{-1} M. 43 hr. after dissolving
vw: very weak, w: weak,
m: medium, s: strong

TABLE II. ABSORPTION BANDS OF BF AND EBF (cm^{-1})

BF (Nujol)	EBF (Nujol)
3500 m	
3210 m	3270 m
1685 s	1688 s
1608 s	1605 s
1595 w	1595 w

Benzoylformoin is so scarcely soluble in carbon tetrachloride or other desirable solvents for the spectrophotometric measurement that the spectrum of benzoylformoin in solution could not be observed.

More details are under investigation.

Experimental

Synthesis of Acetylformoin3,4).—The freshly distilled monomer of methylglyoxal was dissolved in cold water (pH value: 2.4) and the solution was stored in a refrigerator overnight. The condensation was effectd according to Steinbauer's method4), i.e., under a nitrogen stream, a pH-meter being used. An aqueous solution of sodium cyanide (molar ratio to methyl glyoxal: 0.08), previously cooled to 0°C, was added through a dropping funnel to the aqueous methylglyoxal solution; then the pH value rose to 9.5. The temperature of the reaction mixture did not rise above 2°C under cooling with ice-water, though Steinbauer and Waldman stated that it rose up to 5°C under cooling. Sodium bicarbonate was added to keep the pH value of the solution between 7～8. When the aqueous methylglyoxal solution was used soon after dissolving, the pH value did not decrease below 8 even though considerable amount of sodium bicarbonate was added. After 30 min., condensation was stopped by adding phosphoric acid (pH: 5.0). The procedure thereafter was as usual. The solution was concentrated to a syrup, and alcohol was added to it. Inorganic salt was filtered off. The filtrate was concentrated to a syrup which was dissolved in ether, and the inorganic salt was filtered off again. The filtrate was dried over sodium sulfate. The syrup obtained by concentrating the ethereal solution was distilled under a vacuum. The yield was about 10%. The purification was effected by vacuum sublimation at 30～35°C, resulting in yellow crystals, m. p., 82～83°C.

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* As for the conjugate chelation, see the discussion for acetylformoin.

Synthesis of Benzoylformoin. — Phenylglyoxal hydrate (1 g., m. p. 81°C) was dissolved in 35 cc. of water, with slight warming if it was necessary. To this solution was added a solution of 0.04 g. of potasium cyanide (molar ratio to phenylglyoxal hydrate: 0.08) in 10 cc. of water. Immediately the mixture of solution was colored yellow, and crystalline benzoylformoin began to precipitate. After 3 hr, the solution was neutralized with hydrochloric acid. Benzoylformoin was collected by filtration. The yield was about 85%. The recrystallisation was effected from aqueous ethanol. Yellow crystals, m. p., 186～188°C.

Synthesis of Ethyl Benzoylformoin[2].—Benzoylformoin was dissolved in a minimum amount of about 10% ethanolic hydrogen chloride. Ethyl benzoylformoin was deposited when the solution was left standing at room temperature overnight. It was decanted off from the mother liquor, dried in vacuo over potassium hydroxide, and recrystallized from ethanol. The yield was about 90%. Yellow crystals; m. p., 214°C.

Synthesis of *trans*-Dibenzoylethylene. — This was prepared from fumaryl chloride and benzene by the method of Conant and Lutz[11]. Yellow crystals; m. p., 109～110°C.

Spectra. — The infrared spectra were recorded with a Koken model DS-301 spectrophotometer (double-beam type).

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[11] J. B. Conant and R. E. Lutz, *J. Am. Chem. Soc.*, **45**, 1303 (1923).