# *Syntheses and Structures of Acetylformoin and its Related Compounds. II. Neopentoylformoin**

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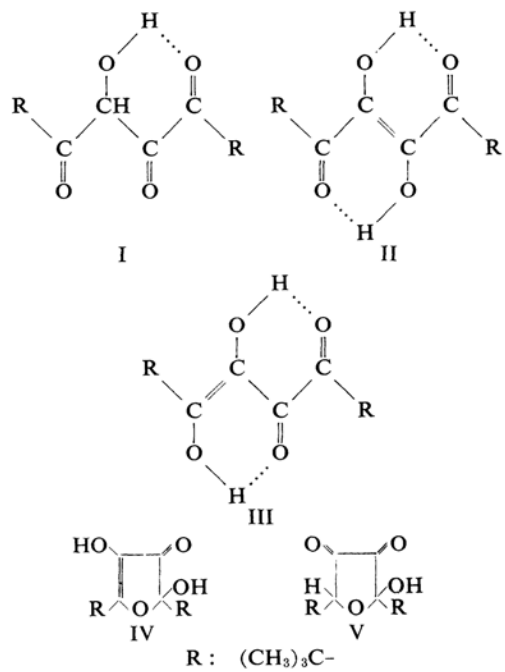
It is well known that the condensation of ketoaldehydes in the presence of alkali cyanide yields formoins:

$$2\ \mathrm{RCOCHO} \xrightarrow{CN^-} \mathrm{RCOCH(OH)COCOR}$$

Condensation products of phenyl-[1], *p*-methoxyphenyl-[2], *p*-chlorophenyl-[3], *p*-bromophenyl-[3], mesitoyl-[4] and methylglyoxal[5,6] have been reported. Benzoylformoin was synthesized by Abenius[7] in a totally different way.

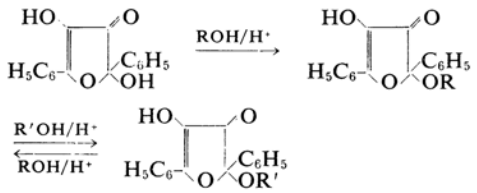
For these formoins, the following five structures are possible. Structure IV was suggested for benzoylformoin on the basis of the fact



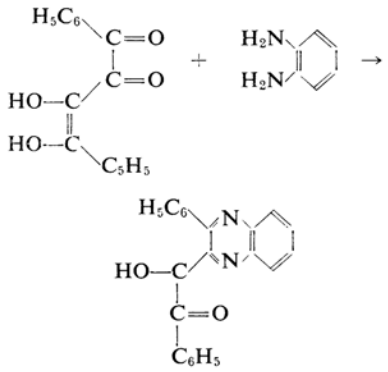

* Presented in part at the 13th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1960.

1) R. Goto, Y. Miyagi and H. Inokawa, This Bulletin, **36**, 147 (1963).
2) P. Karrer and A. v. Segesser, *Helv. Chim. Acta*, **18**, 273 (1935).
3) P. Karrer and C. Musante, ibid., **18**, 1140 (1935).
4) A. R. Gray and R. C. Fuson, *J. Am. Chem. Soc.*, **56**, 1367 (1934).
5) R. Nodzu and S. Kunichika, This Bulletin, **15**, 211 (1940).
6) E. Steinbauer and E. Waldman, *Monat.*, **89**, 569 (1958).
7) P. W. Abenius and H. G. Söderbaum, *Ber.*, **24**, 3033 (1891); **25**, 3468 (1892); P. W. Abenius, ibid., **27**, 706 (1894).

that it undergoes alcoholysis with an alcoholic solution of an acid to give an alkoxy compound[8]. This fact, however, can not afford a straight foreward deduction of structure IV



for benzoylformoin itself. The formation of a quinoxaline derivative suggested structure III.



On these bases, an equilibrium between III and IV in solution was proposed[8].

Steinbauer and Waldman[6] also studied the reaction of acetylformoin with *o*-phenyleneamine:

In a previous paper[1], the authors reported that the crystal of acetylformoin has the enediol structure II (R=$CH_3$) while that of benzoylformoin does the furanone structure IV (R=$C_6H_5$). In the present paper, the structure of neopentoylformoin and its properties are being reported.

## Results and Discussion

Neopentoylformoin is prepared by the action of an alkali cyanide on an aqueous alcoholic solution of *t*-butylglyoxal. The chemical behaviors of neopentoylformoin are rather like those of benzoylformoin[8]. Neopentoylformoin suffers methanolysis with methanolic hydrogen chloride to give a mono-*O*-methyl derivative and ethanolysis with ethanolic hydrogen chloride to give a mono-*O*-ethyl derivative. Furthermore, the mono-*O*-methyl derivative is converted to the *O*-ethyl derivative and vice

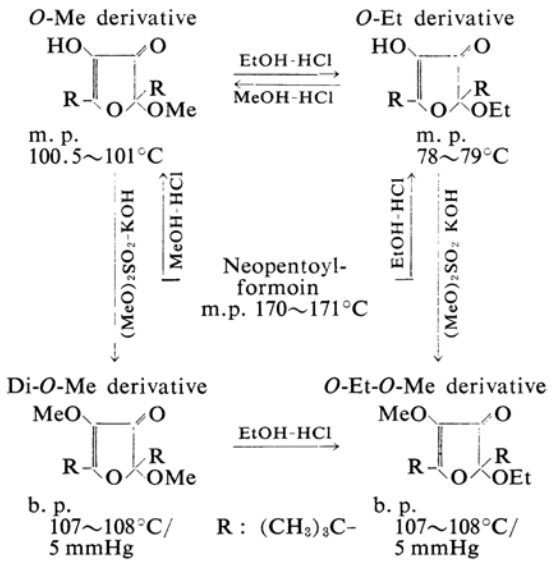
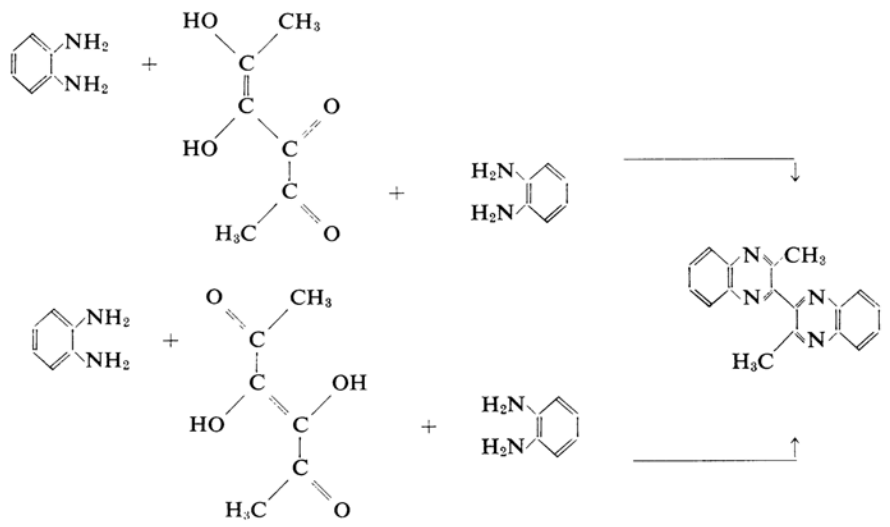


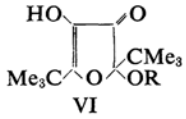

Fig. 1



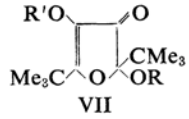
8) A. H. Blatt, *J. Am. Chem. Soc.*, **57**, 1103 (1935); **58**, 1894 (1936).

versa. Another methoxy group was introduced into the *O*-alkyl derivatives by the methylation with dimethyl sulfate or methyl iodide. It was also tried to convert the di-*O*-methyl derivative to an *O*-ethyl-*O*-methyl derivative, ethanolic hydrogen chloride being used as reagent. Though the boiling point of the product is the same as that of the starting di-*O*-methyl derivative, the completion of the conversion was proved by the fact that the alkoxyl group content and elementary analysis coincided quite well with the values calculated for the *O*-ethyl-*O*-methyl derivative.

This sequence of reactions may be illustrated as in Fig. 1, since the etherification with an alcoholic solution of an acid is characteristic of the glycosidic linkage. Therefore, the structure of the mono-*O*-alkyl derivatives and that of the di-*O*-alkyl derivatives are established as VI, 2, 5-di-*t*-butyl-2-alkoxy-4-oxy-furanone-3 and VII, 2, 5-di-*t*-butyl-2, 4-dialkoxy-furanone-3, respectively.




VI




VII

The above sequence of reactions, however, can not suggest structure IV for neopentoylformoin itself, because the equilibrium could be shifted to produce VI in the presence of acids:

$$\text{III} \rightleftharpoons \text{IV} \xrightarrow{H^+} \text{VI}$$

The structure of neopentoylformoin must be determined by another method.

The data of infrared spectra are listed in Table I.

Table I. Absorption bands of infrared spectra ($cm^{-1}$)

| Neopentoyl-formoin | Mono-*O*-Me deriv. | | Di-*O*-Me deriv. | Benzoyl-formoin |
|---|---|---|---|---|
| Nujol | Nujol | $CCl_4$ soln. | $CCl_4$ soln. | Nujol |
| 3330 | 3310 | 3290 | — | 3500 |
| 3180 | — | — | — | 3210 |
| 1690 | 1690 | 1693 | 1705 | 1688 |
| 1600 | 1600 | 1610 | 1615 | 1605 |
| | | | | 1595 |

Neopentoylformoin and the mono-*O*-methyl derivative were examined as a solid state in Nujol*, then the latter and the di-*O*-methyl derivative as the solution in carbon tetrachloride.

In the regions of the C=O and C=C stretching absorption, there are found very little changes between the spectrum of neopentoylformoin and those of derivatives: neopentoylformoin and the mono-*O*-methyl derivative absorb at 1690 and 1600 $cm^{-1}$; the latter compound shows similar spectra both in Nujol and in solution; in the di-*O*-methyl derivative, the corresponding absorption bands arise at 1705 and 1615 $cm^{-1}$.

Since the spectrum of neopentoylformoin is very similar to those of its derivatives**, structure IV, 2, 5-di-*t*-butyl-2, 4-dioxy-furanone-3, may be assigned to neopentoylformoin. This assignment is further supported by the fact that the spectrum of neopentoylformoin is very similar to that of benzoylformoin, the structure of which was established as IV ($R=C_6H_5$)[1].

The absorption band at 1690 $cm^{-1}$ and that at 1600 $cm^{-1}$ may be assigned to the C=O and C=C stretching absorption, respectively. Other structures I, II, III and V seem to be unreasonable on the basis of similar reasons as seen in a previous paper[1].

In the region of the OH stretching absorption, neopentoylformoin shows two distinct bands at 3330 and 3180 $cm^{-1}$ in Nujol. The mono-*O*-methyl derivative shows a distinct band at 3310 $cm^{-1}$ in Nujol and broad one at 3290 $cm^{-1}$ in solution. With *O*-alkylation there occurs a similar change of the spectra of neopentoylformoin and benzoylformoin in Nujol: both formoins show two OH stretching absorption bands while their mono-*O*-alkyl derivatives do only one of the OH stretching absorption. However, nothing conclusive can be deduced from these data of the OH stretching absorption bands, since the OH stretching absorption bands are easily shifted by the strength of hydrogen bondings.

On melting the color of neopentoylformoin turned to red. It is very interesting benzoylformoin changes its color from yellow to red on melting. Blatt considered, without striking evidence, that the reddish distillate of benzoylformoin was enediol II. The authors are also of opinion that the structure of melted neopentoylformoin is an enediol, II or III. However no evidece has been found.

## Experimental

**Synthesis of Neopentoylformoin.**—In 100 ml. of 70% aqueous alcohol, *t*-butylglyoxal hydrate[9] (4 g.) was dissolved. The solution was cooled to 0°C. To this solution, a solution of 0.25 g. of sodium cyanide in 10 ml. of 50% aqueous alcohol was added with stirring. The solution immediately colored yellow. After stirring for 30 min.,

* Neopentoylformoin is insoluble in carbon tetrachloride or other desirable solvents for the spectrophotometric measurement.

** The structures of the derivatives are established as VI and VII, as mentioned above.

9) R. C. Fuson, H. Gray and J. J. Gouza, *J. Am. Chem. Soc.*, **61**, 1937 (1939).

alcohol was evaporated under reduced pressure. White crystals were collected by filtration and washed with water and dried in vacuo over phosphorus pentoxide. Yield, 2.3 g. (73%). Recrystallization was effected from isopropanol. Yield, 1 8 g. (56%). M. p. 170~171°C. Insoluble in ordinary organic solvent except alcohols.

Found: C, 63.04; H, 8.86; mol. wt. (Rast) 219. Calcd. for $C_{12}H_{10}O_4$: C, 63.16; H, 8.77%; mol. wt., 228.

When a crude glyoxal monomer[9] was used, the procedure was the same except for purification; crude formoin was dissolved in a minimum amount of alcohol and precipitated with addition of water.

**Mono-*O*-methyl Derivative.**—In about 10 ml. of 12% methanolic hydrogen chloride, 2 g. of neopentoylformoin was dissolved. After standing overnight at room temperature, alcohol and acid were evaporated under reduced pressure. The residue, dried in vacuo over potassium hydroxide, was washed quickly with cold water and dried in vacuo over phosphorus pentoxide. M. p. 100.5~101°C.

Found: C, 64.64; H, 9.25; MeO, 12.75. Calcd. for $C_{13}H_{22}O_4$: C, 64.64; H, 9.07; MeO, 12.81%.

**Mono-*O*-ethyl Derivative.**—The procedure was the same as in methanolysis. M. p. 77~78°C.

Found: C, 65.41; H, 9.43. Calcd. for $C_{14}H_{24}O_4$: C, 65.52; H, 9.38.

**Di-*O*-methyl Derivative.**—*Method A.*—In 20 ml. of water containing 1 g. of potassium hydroxide, mono-*O*-methyl derivative (4 g.) was dissolved. The solution was brilliant yellow. Into this solution, 2 g. of dimethyl sulfate was added during 30 min. with stirring, and stirring was continued for additional 30 min. After addition of 0.5 g. of potassium hydroxide, the dropping of 1 g. of dimethyl sulfate was continued during 30 min. and then the solution was stirred for additional 30 min. at 50°C. During the reaction, the yellow color of the solution was diminished and colorless oil separated. The whole solution was extracted with carbon tetrachloride. The extract was dried over anhydrous sodium sulfate. The solvent was evaporated and the residue of colorless liquid was distilled under reduced pressure. Fraction boiling at 107~108°C/5 mmHg was collected. Yield, 2.3 g. (53%).

Found: C, 65.51; H, 9.40; MeO, 24.12. Calcd. for $C_{14}H_{24}O_4$: C, 65.52; H, 9.38; MeO, 24.22%.

*Method B.*—In 30 ml. of absolute methanol containing 0.6 g. of sodium, mono-*O*-derivative (3.6 g.) was dissolved. The solution colored yellow. After addition of 20 g. of methyl iodide, the solution was refluxed for 4 hr. During this period, the color of solution was diminished as in method A. The solution was stood overnight at room temperature. After the addition of 10 ml. of water, methanol was evaporated under reduced pressure. The residue was extracted with ether. The extract was dried over anhydrous sodium sulfate. Ether was evaporated off. The residue of pale yellow liquid was distilled under reduced pressure. Fraction boiling at 107~108°C/5 mmHg was collected. Yield, 2.1 g. (58%).

Found: C, 65.51; H, 9.40%.

The infrared spectrum of the product in carbon tetrachloride solution was coincident with that of the product obtained in the method A even in details.

***O*-Ethyl-*O*-methyl Derivative.**—This compound was prepared as in the method A and boiling at 107~108°C/5 mmHg.

Found: C, 66.74; H, 9.41; RO, 27.94. Calcd. for $C_{15}H_{26}O_4$: C, 66.66; H, 9.63; RO, 28.14%.

**The Conversion of the Mono-*O*-methyl Derivative to the Mono-*O*-ethyl Derivative and Vice Versa.**—About 0.1 g. of mono-*O*-methyl derivative was dissolved in 1 ml. of 8% ethanolic hydrogen chloride and the procedure was the same as above. M. p. 78~79°C. Mixed melting point with the authentic *O*-ethyl derivative showed not any depression. The procedure was the same in the case of the conversion of the *O*-ethyl derivative to the *O*-methyl derivative. M. p. 100~101°C. Not any depression of the melting point was observed at a mixed melting point.

**The Conversion of the Di-*O*-methyl Derivative to the *O*-Ethyl-*O*-methyl Derivative.**—A solution of 3 g. of di-*O*-methyl derivative in 15 ml. of 12% ethanolic hydrogen chloride was stood overnight at room temperature. The solvent and the acid were evaporated under reduced pressure and evaporation was repeated with addition of absolute ethanol and the residue of liquid was dissolved in carbon tetrachloride. The solution was washed with cold water, then dried over anhydrous sodium sulfate. Removal of the solvent, followed by distillation, gave 2.2 g. of liquid; boiling at 105~109°C/5 mmHg.

Found: C, 66.65; H, 9.36; RO, 28.01%.

**Spectra and Alkoxy Group.**—The infrared spectra were recorded with a Koken model DS-301 spectrophotometer.

The alkoxy group content was determined by the method of Hoffman and Wolfrom[10].

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10) D. O. Hoffman and M. L. Wolfrom, *Anal. Chem.*, 19, 225 (1947).