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Syntheses and Structures of Acetylformoin and Related Compounds. VI. Substituent Effects

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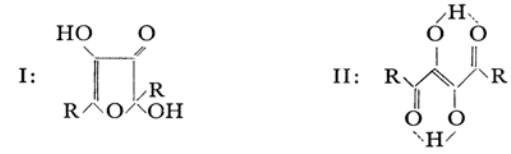
In the presence of cyanide ions, an α-ketoaldehyde dimerizes to give an acylformoin. The tautomerism of this compound was studied. It was found that the tautomerism between I and II is affected by the solvents and by the substituents. In proton-accepting solvents (EtOH, THF), I predominates. In ethanol-free chloroform, II is dominant for almost all substituents. In ethanol-containing chloroform, some acylformoins exist as I, while the others exist as II. The former case is observed when R=*t*-Bu and *p*-X-C_6H_4 (X=H, *t*-Bu, Cl, and Br); the latter case, when R=Me, *i*-Pr, and *p*-Me-C_6H_4. In the former case, ethanol reacts slowly with I to give an *O*-ethyl derivative (III). When R=2,4,6-Me_3-C_6H_2, II predominates in all states. When R=*p*-Cl-C_6H_4 and *p*-Br-C_6H_4, I and II were isolated as crylstals. The solvent effects are interpreted in terms of the hydrogen-bonding interactions of I with basic and hydroxylic solvents.



By a self-condensation similar to the benzoin condensation, an α-ketoaldehyde (an alkyl- or aryl-glyoxal) gives an acylformoin (Eq. (1)). Although five tautomers are possible for such compounds, only two tautomers, 2,5-dialkyl (or diaryl)-2,4-dihydroxyfuranone-3 (I) and *trans*-1,2-diacyl (or diaroyl)-1,2-dihydroxyethylene (II), have been found to exist for various acylformoins.[1] I and II have quite different spectral properties; these properties are summarized in Table 1. This paper will be concerned with the tautomerism of some homologues of benzoylformoins. Some detailed studies of chloroform solutions of acylformaoins will also be reported. Table 2 summarizes the spectral results.

1) a) R. Goto, Y. Miyagi and H. Inokawa, This Bulletin, **36**, 147 (1963). b) Y. Miyagi and R. Goto, *ibid.*, **36**, 650. c) Y. Miyagi and R. Goto, *ibid.*, **36**, 921. d) Y. Miyagi, *ibid.*, **37**, 12 (1964). e) S. Kimura, Y. Miyagi and R. Goto, *ibid.*, **39**, 1333 (1966). f) The references in a—e.

TABLE 1. SPECTRAL CHARACTERISTICS

Tautomer	State	IR absorption bands (cm^{-1}) ν_{OH}	$\nu_{C=O}$	$\nu_{C=C}$	UV absorption bands R in Eq. (1)	λ_{max}(mμ)
I	Solid state	Two bands 3600—3200	1695	1620	Aliphatic	305—310
	Solution	One bond (distinct but broad) 3500—3200	1705	1625	Aryl	355—360(C_2H_5OH) 370($CHCl_3$-C_2H_5OH)*
II	Solid state	broad and weak	1620	—	Aliphatic	355—360
	Solution	broad and weak	1630	—	Aryl	390—410

* Eisters stated[6] that the ultraviolet absorption in chloroform containing ethanol shows up at 355 mμ. In our measurements, however, it arises at 370 mμ.

TABLE 2. SPECTRAL RESULTS

Formoin	R in Eq.(1)	ν_{max}, cm^{-1} Solid state (Nujol)	Solution in THF	λ_{max}, mμ (ε_{max}) C_2H_5OH	$CHCl_3$-C_2H_5OH*	$CHCl_3$* (C_2H_5OH free)	CCl_4*
p-Bromobenzoyl-	*p*-Br-C_6H_4	red cryst. 1580	3240	358(17700)	370	410	415
		yellow cryst. 3180, 3440	1700	350(14800)			
		1690	1625	238(14800)		300	305
		1605, 1585	1580				
p-Chlorobenzoyl-	*p*-Cl-C_6H_4	red cryst. 1549	3200	360(15000)	373	410	420
		yellow cryst. 3500, 3200	1710				
		1700	1630	247(14000)		300	300
		1617, 1595	1600				
p-Anisoyl-	*p*-MeO-C_6H_4	1590	3260				415
			1703	355(19000)			
			1623	225(17200)	—	—	320
			1608				
Mesitoyl-	2,4,6-Me_3-C_6H_2	1615	1620	380(13300)	383	383	383

* Intensities of absorption bands were not determined because of low solubility or technique of vacuum sealed cell (see: experimental parts).

$$2RCOCHO \xrightarrow{CN^-} RCOCH(OH)COCOR \quad (1)$$

I II

p-Chloro- and p-Bromo-benzoylformoin. *p*-Chloro- and *p*-bromo-benzoylformoins (R=*p*-Cl-C_6H_4 and *p*-Br-C_6H_4 respectively, in Eq. (1)), were first reported by Karrer and his co-workers.[2] They carried out the condensation in an aqueous alcoholic solution containing potassium cyanide and obtained red crystals by recrystallizing the reaction products from hot benzene in both cases. Following their method, the present authors found that the addition of water to a reaction solution precipitates yellow crystals, which can then be recrystallized from ethanol. When a hot benzene solution of yellow crystals is allowed to stand, at first red crystals and then yellow crystals precipitate. After a prolonged heating of the benzene solution, only the red crystals precipitate. The red crystals of both acylformoins do not change their color on heating and melt sharply at their melting points. On the other hand, the yellow crystals of both acylformoins gradually turn red on heating and melt at a temperatures slightly lower than the melting point of the corresponding red crystals. Thus, the melting points proper to the yellow crystals can not be observed. The yellow crystals have IR spectral characteristics of I, while the red crystals have those of II, in both cases.

p-Anisoylformoin and Mesitoylformoin. The syntheses of *p*-anisoylformoin[3] and mesitoylformoin[4] (R=*p*-MeO-C_6H_4 and 2,4,6-Me_3-C_6H_2 in Eq. (1) respectively) have been reported in the literature. In these cases, the present authors could not isolate the two tautomers as crystals. Both acylformoins are red crystals and show IR

2) P. Karrer and C. Musante, *Helv. Chim. Acta*, **18**, 1140 (1935).

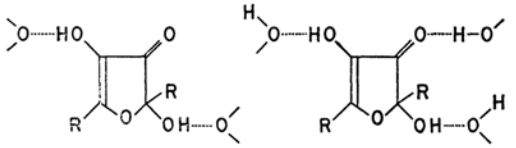
3) P. Karrer and A. v. Segesser, *ibid.*, **18**, 273 (1935).

4) A. R. Gray and R. C. Fuson, *J. Am. Chem. Soc.*, **56**, 1367 (1934).

spectra characteristic of II.

Tautomers in Tetrahydrofuran and Ethanol. Solutions of the three acylformoins other than mesitoylformoin in tetrahydrofuran or ethanol show the IR and UV spectra characteristic of I. It has been reported that I arises also in these solutions of other acylformoins, and it has been suggested that proton-accepting solvents might stabilize I by a solvation such as that depicted in Fig. 1, so that I can be predominant in these solvents.[1d]

Unlike the others, however, mesitoylformoin does not show any tautomerism and exists as II in chloroform and also in tetrahydrofuran.

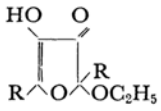


(A) (B)

Fig. 1. Solvation by ethers (A) and alcohols (B).

Tautomers in Chloroform. Since benzoyl-, *t*-butylbenzoyl-, and neopentoyl-formoins are easily oxidized in chloroform, the UV spectra of the solutions were measured in vacuum-sealed cells. Solutions of these acylformoins in ethanol-containing chloroform[5] show the UV spectra characteristic of I.

However, Eistert isolated an *O*-ethyl derivative (III, $R=C_6H_5$) by refluxing an ethanol-chloroform solution of benzoylformoin.[6] III ($R=C_6H_5$) shows the same UV spectra as that of II ($R=C_6H_5$).



III

He suggested that benzoylformoin reacts with ethanol to give III ($R=C_6H_5$) in ethanol-containing chloroform. The spectrum observed in our experiments could, therefore, be due to III and not to I.

The following facts suggest, however, that the absorption of the ethanol-containing chloroform solution is not always caused by III. In a vacuum-sealed cell, a solution of neopentoylformoin in ethanol-containing chloroform shows an absorption at 310 mμ characteristic of I or III. After the solution has stood overnight, the intensity of this absorption does not change. When the cell is then opened to the atmosphere, the intensity decreases gradually, as has been reported previously[1d] (Fig. 2). However, when the cell is opened immediately after sealing, the 310 mμ band decreases rapidly and disappears after two hours. Since I may be more easily oxidized than III, these facts suggest the predominance of I immediately after dissolution and the subsequent predominance of III after the solution has been allowed to stand overnight. This means that I reacts slowly with ethanol to give III.[7]

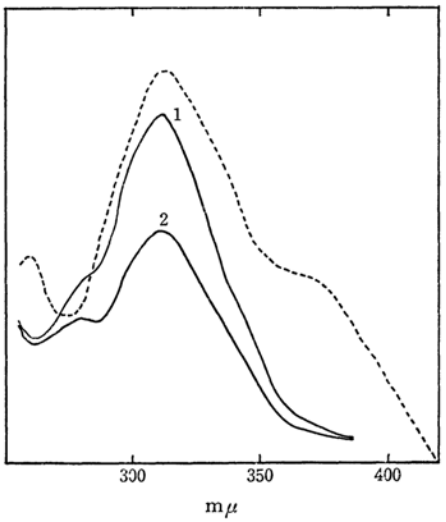


Fig. 2. Ultraviolet spectra of neopentoylformoin in vacuum-sealed cells: ——1, in ethanol-containing chloroform, ——2, 2 hr after breaking seal of a cell after standing overnight an ethanol-containing chloroform solution; ---- in ethanol-free chloroform.

The spectrum of neopentoylformoin in ethanol-free chloroform[8] (Fig. 2) shows its main absorption at 311 mμ, with a shoulder at about 370 mμ, indicating a mixture of I (the major component) and II (the minor component). It may be concluded that, in the case of neopentoylformoin, I predominates even in this solvent where stabilization by solvation by ethanol is absent. An ethanol-containing chloroform solution of acetylformoin shows an absorption band characteristic of II at 355 mμ; this band gradually decreases in an open cell. When measured in a vacuum-sealed cell, however, the spectrum did not change on standing. This means that acetylformoin does not react with ethanol in chloroform, since, if this were the case, an absorption would arise at about 310 mμ on standing.

5) As the ethanol-containing chloroform, we used spectro-grad chloroform (Dotite) containing ethanol as a stabilizer (the ethanol content was about 0.5%).

6) B. Eistert, private communication. We are indebted to him for informing us of his observations prior to publication.

7) There is a possibility that this etherification is catalyzed by a trace amount of hydrogen chloride present as an impurity.

8) Ethanol-free chloroform was prepared by shaking spectro-grade chloroform with sulfuric acid, washing it with water, drying, and distilling.

As has been briefly mentioned in a previous paper[1e], *p*-*t*-butylbenzoylformoin behaves interestingly. In a vacuum-sealed cell, the λ_{max} value of its ethanol-containing chloroform solution is 371 mμ. However, an ethanol-free chloroform solution shows an absorption at about 380 mμ immediately after dissolution; this absorption maximum shifts to 405 mμ in about five minutes (Fig. 3). These facts mean that this acylformoin exists as I immediately after dissolution, but is rapidly converted to II in this solvent. The fact that I exists in ethanol-containing chloroform, while II exists in ethanol-free chloroform, can be explained in terms of the solvation of I by ethanol, as is shown in Fig. 1.

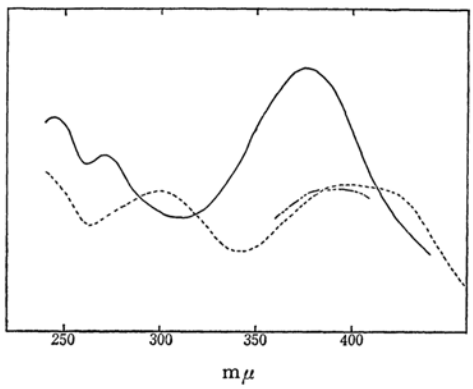


Fig. 3. UV spectra of *p*-*t*-butylbenzoylformoin in vacuum-sealed cells: ——— immediately after dissolving in ethanol-free chloroform; ---- about five minutes after dissolving in ethanol-free chloroform; —— in ethanol-containing chloroform.

p-Toluylformoin shows an absorption at 380 mμ, with a should around 410 mμ in ethanol-containing chloroform (Fig. 4). On the other hand, in ethanol-free chloroform the only absorption maximum is at 405 mμ. Thus, II seems to exist in ethanol-free chloroform and an equilibrium

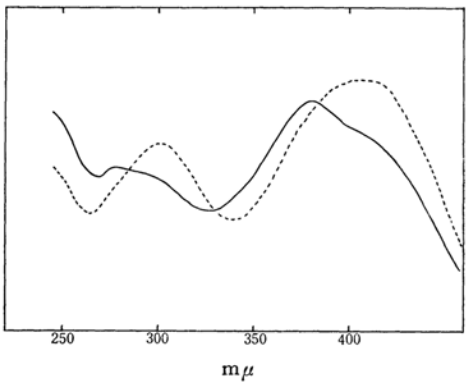


Fig. 4. UV spectra of *p*-toluylformoin in vacuum-sealed cells: —— in ethanol-containing chloroform; ---- in ethanol-free chloroform.

mixture of I (the major component) and II (the minor component) in ethanol-containing chloroform.

p-Chloro- and *p*-bromo-benzoylformoins are not easily oxidized in chloroform. Their UV sepctra can be measured in open cells. These acylformoins show absorption bands at 370 mμ in ethanol-containing chloroform and at 410 mμ in ethanol-free chloroform and in carbon tetrachloride.

p-Anisoylformoin shows an absorption at 410 mμ in carbon tetrachloride, but a broad band around 350—400 mμ in chloroform. Nothing conclusive has been obtained regarding the latter solution.

Discussion

The tautomeric behavior of the acylformoin is summarized in Table 3.

In tetrahydrofuran and ethanol, all the acylformoins studied except mesitoylformoin exist as I, presumably solvated as depicted in Fig. 1. Although some acylformoins are easily oxidized

Table 3. Tautomers of acylformoins

Formoin	Ref.	R in Eq. (1)	Solid state	Solution in		
				THF, C_2H_5OH	$CHCl_3$-C_2H_5OH	$CHCl_3, CCl_4$
Acetyl-	1a	Me	II	I	II	II
Isobutyryl-	1c	Me_2CH-	I	I	II	II
Neopentoyl-	1b	Me_3C-	I	I	I	I+II (I>II)
p-*t*-Butylbenzoyl	1e	*p*-Me_3C-C_6H_4	I	I	I	II
Benzoyl-	1a,d	C_6H_5	I	I	I	II
p-Chlorobenzoyl-	2	*p*-Cl-C_6H_4	I,II	I	I	II
p-Bromobenzoyl-	2	*p*-Br-C_6H_4	I,II	I	I	II
p-Anisoyl-	3	*p*-Me O-C_6H_4	II	I	I	II
p-Toluyl-	1e	*p*-Me-C_6H_4	I	I	I+II (I>II)	II
Mesitoyl-	4	2,4,6-Me_3-C_6H_2	II	II	II	II

in chloroform, they are rather stable to oxidation in these solvents.

In most cases, I predominates in ethanol-containing chloroform, while II is dominant in ethanol-free chloroform or carbon tetrachloride. Since I is solvated by ethanol in the former solvent, it may be considered that II is more stable than I in the absence of solvation by ethanol. However, as for neopentoylformoin, I is more stable than II, even in the absence of ethanol and its accompanying solvation.

It may be feasible to consider that the stability of II is affected by the substituent, R. For acetyl-, isobutyryl- and *p*-toluyl-formoins, II may be considered to be more stable than for the other acylformoins. For the first two, II exists as a sole component, even in ethanol-containing chloroform. For the third, II is observed as one component of an equilibrium mixture. Consequently, for the above three acylformoins II is present in ethanol-containing chloroform, while other acylformoins exist as I in this solvent. In the case of neopentoylformoin, in which the R is *t*-butyl, II is unstable, as has been mentioned above.

Mesitoylformoin exists as II in all states.

In the case of *p*-chloro- and *p*-bromo-benzoylformoins, the stability of II presumably becomes comparable with that of I and the isolation of both tautomers is possible.

From the above considerations, it may be suggested that hyperconjugation is effective in stabilizing II. However, nothing confirmative has yet been obtained.

Experimental

Acylformoins. The following four acylformoins were prepared in the same way. A solution of sodium cyanide (0.2 g) in 20 m*l* of 50% aqueous ethanol was added to a solution of a glyoxal hydrate (5 g) in 50 m*l* of ethanol. After standing for 3 hr in an ice-cold bath, the solution was poured into cold water. The precipitated crystals were collected by filtration.

p-Bromobenzoylformoin. Yellow crystals, recrystallized from ethanol; on heating began to turn red at around 80°C and melted at 178—184°C. Red crystals, recrystallized from benzene; mp 195°C.

p-Chlorobenzoylformoin. Yellow crystals, recrystallized from ethanol; on heating, began to tunr red at around 145°C and melted at 181—182°C. Red crystals, recrystallized from benzene; mp 181—182°C.

p-Anisoylformoin. Red crystals, recrystallized from ethanol; mp 145—146°C (lit.,[3] 151°C).

Mesitoylformoin. Red crystals, recrystallized from ethanol; mp 188—189°C.

Technique of Vacuum-sealed Cell; explained in experimental part of Reference 1d; the absorption intensities in Figs. 2—4 are arbitrary.