The Reaction of Carbon Suboxide with Some Ketones. Formation and Structure of Pyrones from Acetylacetone, Benzoylacetone, Ethyl Acetoacetate, and Acetone

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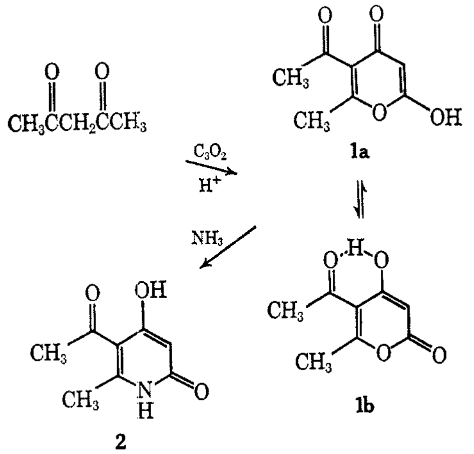
The reaction of carbon suboxide and benzaldehyde is reported to give the benzylidene ester of benzalmalonic acid,[1] whereas the reaction of carbon suboxide with some ketones produces pyronopyrone derivatives.[2,3] We now report on the reaction of carbon suboxide with several enolizable ketones.

The reaction of acetylacetone with C_3O_2 at 0–5° in the presence of sulfuric acid gave the 1:1 adduct, pyrone **1**, in 85% yield. The pyrone structure was based on spectral data and conversion of **1** into the corresponding pyridone (**2**).[4]



The ir spectrum of **1** in chloroform solution showed a hydrogen-bonded OH band at 3000 cm^{-1} and strong absorption at 1739 cm^{-1} due to the carbonyl stretch of α-pyrone.[5] The hydroxyl proton shifts in the nmr spectrum of **1** were relatively independent of the concentration and temperature (Tables I and II), and the molecular weight measurement by vapor pressure osmotic method using chloroform showed that **1** was monomeric in solution.

The ir spectrum in the solid phase (KBr disk) showed absorptions at 2600 cm^{-1} (strong hydrogen-bonded ν_{OH}) and at 1660 cm^{-1} ($\nu_{C=O}$ of γ-pyrone). These data suggest the γ-pyrone structure (**1a**) for the adduct in the solid state, whereas in the liquid phase this adduct may be present predominantly in the form of its tautomeric α-pyrone (**1b**).[6]

TABLE I

INFLUENCE OF CONCENTRATION[a]

Concn, %	OH shift, τ
0.7	−2.10
1.2	−2.10
3.3	−2.08
5.3	−1.97

[a] In $CDCl_3$ solution at 50°.

TABLE II

INFLUENCE OF TEMPERATURE[a]

Temp, °C	OH shift, τ
20	−2.10
50	−2.02

[a] In 1.9% $CDCl_3$ solution.

Two pyronopyrone isomers (**3**, mp 252–254°, and **4**, mp 226–228°) were produced by the reaction of carbon suboxide with benzoylacetone under similar conditions. The structure of these compounds were assigned by comparison with 7-substituted pyronopyrones as shown in Table III. The spectrum of **3** indicates conjugation between pyronopyrone ring and benzene ring. Thus, **3** and **4** can be assigned the structures 8-acetyl-4-hydroxy-7-phenyl-2H,5H-pyrono[3,2-*c*]pyrone and 8-benzoyl-4-hydroxy-7-methyl-2H,5H-pyrono[3,2-*c*]pyrone, respectively (Scheme I).

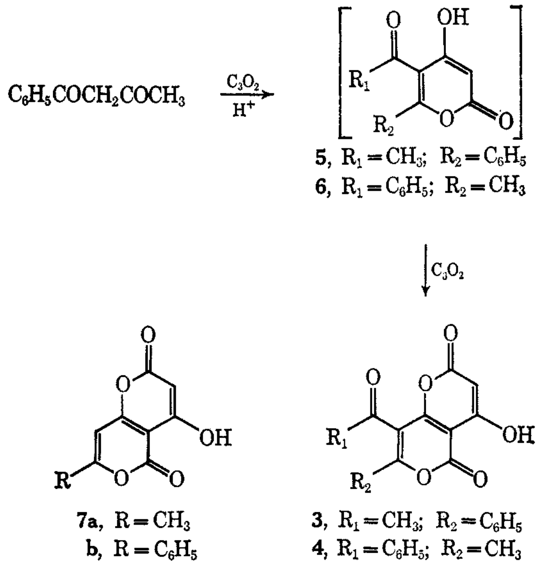
TABLE III

ULTRAVIOLET ABSORPTION MAXIMA

Compd	λ_{max}, mμ (log ε), in EtOH
3	245 (4.20), 278 (4.20), 357 (4.16)
4	255 (4.09), 315 (3.77)
7a[a]	270 (3.81), 330 (3.76)
7b[b]	219 (4.33), 247 (4.06) 280 (4.23), 363 (4.31)

[a] T. Money, I. H. Qureshi, G. B. Webster, and A. I. Scott, *J. Amer. Chem. Soc.*, **87**, 3004 (1965). [b] J. L. Douglas and T. Money, *Can. J. Chem.*, **45**, 1990 (1967).

SCHEME I



5, $R_1 = CH_3$; $R_2 = C_6H_5$
6, $R_1 = C_6H_5$; $R_2 = CH_3$

7a, $R = CH_3$
b, $R = C_6H_5$

3, $R_1 = CH_3$; $R_2 = C_6H_5$
4, $R_1 = C_6H_5$; $R_2 = CH_3$

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(1) H. Hopff and G. Hegar, *Helv. Chim. Acta*, **44**, 2016 (1961).

(2) E. Ziegler and H. Biemann, *Monatsh. Chem.*, **93**, 34 (1962).

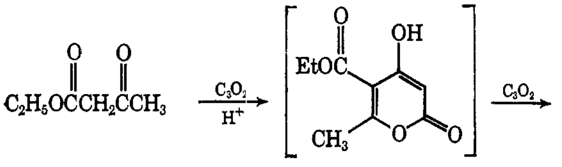
(3) F. Haadetzky and E. Ziegler, *ibid.*, **97**, 398 (1966).

(4) M. A. Butt and Y. A. Elvidge, *J. Chem. Soc.*, 4483 (1963).

(5) D. Herbst, W. B. Moro, O. R. Gottlieb, and C. Djerassi, *J. Amer. Chem. Soc.*, **81**, 2427 (1959).

(6) Butt and Elvidge[4] discussed the structure of **1** and concluded that it was **1a** on the basis of the nmr ($CDCl_3$) and ir (Nujol); however, their treatment may be inadequate because our observation suggests that the structure of **1** in liquid phase is different from that in the solid.

The reaction of carbon suboxide with ethyl acetoacetate gave the pyronopyrone **9** in a 70% yield. The assignment of **9** is based on uv, ir, and nmr data.



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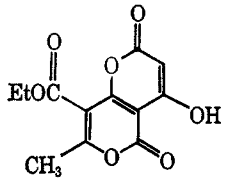

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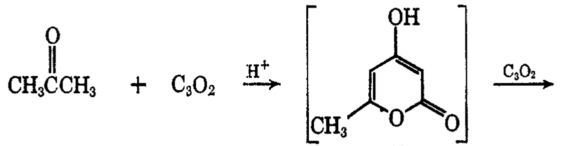
The reaction of acetone with carbon suboxide gave pyronopyrone **11** in 8% yield; the corresponding pyrone **10** was not obtained.



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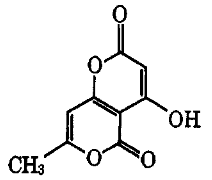

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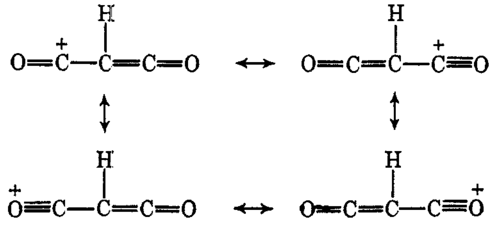
Although the β-diketones in our experiments were present in significant amounts of their enol form in the reaction mixture,[7] the reaction did not take place without sulfuric acid; a catalytic amount of acid caused the reaction smoothly at room temperature. This suggests that the active species in these reactions may be a protonated carbon suboxide molecule, stabilized by resonance, and that cyclization to form the pyrone ring includes the reaction of enolic β-diketones with protonated carbon suboxide.

$$O{=}C{=}C{=}C{=}O + H^+ \longrightarrow$$



The fact that the reaction of acetylacetone gave pyrone and the reaction of the other ketones afforded pyronopyrones under similar conditions suggests that the pyrone (**1b**) may be stabilized by the intramolecular hydrogen bond between 4-hydroxyl and 5-acetyl groups, and may be less reactive toward carbon suboxide than the other intermediates (**5**, **6**, **8**, and **10**). In the cases of **5** and **6**, the intramolecular hydrogen bonding may be unfavorable owing to steric interaction between phenyl and acetyl groups, so that further reaction with carbon suboxide can proceed to yield pyronopyrone. In the case of intermediate **10** from the reaction of acetone, there is no stabilization by hydrogen bonding so that pyronopyrone formation can occur; steric interaction may also interfere with intramolecular hydrogen bonding in intermediate **8** in the reaction with acetoacetic ester.

Experimental Section

Preparation of Carbon Suboxide.—Carbon suboxide was prepared by the pyrolysis[8] of diacetyltartaric anhydride at about 700° and trapped at −78° in a bath of Dry Ice–methanol, and purified by distillation from trap to trap. The identification of carbon suboxide was established by preparation of malonanilide by the reaction of carbon suboxide with aniline.

5-Acetyl-2-hydroxy-6-methyl-4-pyrone (1a).—To a solution of carbon suboxide (0.48 g, 0.007 mol) in dry ether (100 ml) were added slowly acetylacetone (7.0 g, 0.07 mol) and concentrated sulfuric acid (0.02 ml) at −78°. The reaction mixture was maintained at 0–5° for 8 days. Solids (1.0 g, 85%) were separated on a filter and recrystallization from ethyl acetate yielded compound 1a: mp 156–157°; ν_{max}^{KBr} 2600 (-OH), 1695 (C=O), 1660 (C=O), 1600 (C=C), and 1549 cm^{-1} (C=C); $\nu_{max}^{CHCl_3}$ 3000 (-OH), 1739 (C=O), 1660 (C=O) and 1525 cm^{-1} (C=C); λ_{max}^{EtOH} 225 mμ (log ε 4.0) and 261 (3.91); nmr (CDCl$_3$) τ 7.39 (s, 3, CH$_3$), 7.32 (s, 3, CH$_3$), 4.47 (unresolved, 1, CH=C), and −1.90 (s, 1, OH). The molecular weight was found to be 167 (CHCl$_3$, osmotic method) (calcd for $C_8H_8O_4$, 168.1).

Anal. Calcd for $C_8H_8O_4$: C, 57.14; H, 4.80. Found: C, 57.47; H, 4.88.

5-Acetyl-4-hydroxy-6-methyl-2-pyridone (2).—In a 50-ml autoclave were placed the pyrone (1a, 1.0 g) and aqueous ammonia (20 ml, *d* 0.9). The autoclave was heated to 70° and maintained at 70° for 6 hr and at 20° for 3 days. The solvent was evaporated and the residue was triturated with ether. Recrystallization from ethanol yielded compound 2: mp 284–286° dec; yield 0.5 g.

Anal. Calcd for $C_8H_9O_3N$: C, 57.48; H, 5.43; N, 8.38. Found: C, 57.41; H, 5.71; N, 8.40.

8-Acetyl-4-hydroxy-7-phenyl-2H,5H-pyrono[3.2-c]pyrone (3) **and 8-Benzoyl-4-hydroxy-7-methyl-2H,5H-pyrono[3,2-c]pyrone** (4).—To a solution of carbon suboxide (2.2 g, 0.032 mol) in absolute ether (130 ml) were added at −78° benzoylacetone (7.9 g, 0.049 mol) and concentrated sulfuric acid (0.05 ml). The reaction mixture was maintained at 0–5° for 1 day, and then the solids were filtered and recrystallization from benzene gave compound 3: mp 252–254°; yield 0.55 g (12%); ν_{max}^{KBr} 1750 [-C(=O)O-, α-pyrone], 1690 [-C(=O)O-, α-pyrone], 1640 cm^{-1} (C=O); λ_{max}^{EtOH} 245 mμ (log ε 4.20), 278 (4.20), 357 (4.16); enolic OH group (by FeCl$_3$ test). The molecular weight was found to be 285 (CHCl$_3$, osmotic method) (calcd for $C_{16}H_{10}O_6$, 298.

Anal. Calcd for $C_{16}H_{10}O_6$: C, 64.43; H, 3.08. Found: C, 64.32; H, 3.27.

An additional 0.34 g (7%) of compound 4, mp 226–228°, was obtained by repeated crystallization from the mother liquor. The infrared spectrum of 4 showed ν_{max}^{KBr} 1750 [-C(=O)O-, α-pyrone], 1702 [-C(=O)O-, α-pyrone], 1670 cm^{-1} (C=O). The ultraviolet spectrum of 4 showed λ_{max}^{EtOH} 255 mμ (log ε 4.09), 315 (3.77). The nmr spectrum of 4 (in CDCl$_3$) showed τ 2.5 (m) Ph, 4.5 (s) C=CH, 7.7 (s) CH$_3$. 4 had an enolic OH group (by FeCl$_3$ test). The molecular weight was found to be 290 (CHCl$_3$, osmotic method) (calcd for $C_{16}H_{10}O_6$, 298).

Anal. Calcd for $C_{16}H_{10}O_6$: C, 64.43; H, 3.08. Found: C, 64.53; H, 3.37.

8-Ethoxycarbonyl-4-hydroxy-7-methyl-2H,5H-pyrono[3,2-c]-pyrone (9).—To a solution of carbon suboxide (1.1 g, 0.016 mol)

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(7) E. S. Gould in "Mechanism and Structure in Organic Chemistry," Holt-Dryden, New York, N. Y., 1959, p 376.

(8) E. Ott, *Ber.*, **47**, 2388 (1914).

in dry ether (100 ml) were added ethyl acetoacetate (10 g, 0.077 mol) and concentrated sulfuric acid (0.02 ml) at −78 . The reaction mixture was maintained at 0–5° for 10 days. The crystals (1.5 g, 70%) were isolated, and recrystallization from ethyl acetate gave compound 7: mp 142–143°; ν_{max}^{KBr} 1763 (C═O), 1700 (C═O), 1689 cm^{-1} (C═O); λ_{max}^{EtOH} 268 mμ (log ε 4.05), 329 (3.74); nmr ($CDCl_3$) τ 8.57 (t, 3, $-CH_2CH_3$), 7.42 (s, 3, $-CH_3$), 5.54 (q, 2, $-CH_2CH_3$), 4.35 (s, 1, C═CH–); enolic –OH group (by $FeCl_3$ test). The molecular weight was found to be 280 ($CHCl_3$, osmotic method) (calcd for $C_{12}H_{10}O_7$, 266).

Anal. Calcd for $C_{12}H_{10}O_7$: C, 54.14; H, 3.79. Found: C, 53.89; H, 3.94.

4-Hydroxy-7-methyl-2H,5H-pyrono[3,2-*c*]pyrone (11).—In a 200-ml autoclave were placed acetone (40.7 g, 0.72 mol), carbon suboxide (8.7 g, 0.12 mol), dry ether (110 ml), and concentrated sulfuric acid (0.3 ml). The autoclave was maintained at 20° for 14 days, and heated to 60° for 1 day. The resinoid was separated on a filter, and 1.0 g (8%) of solid was extracted with ether from the resinoid. The recrystallization from ethyl acetate gave compound **8**: mp 225°; ν_{max}^{KBr} 1762 (C═O), 1695 (C═O), 1638 cm^{-1} (C═O); λ_{max}^{EtOH} 271 mμ (log ε 4.17), 330 (3.93); nmr ($CDCl_3$) τ 7.60 (s, 3, CH_3), 4.50 (s, 1, C═CH), 3.78 (s, 1, C═CH). The molecular weight found to be 180 (Rast method) (calcd for $C_9H_6O_5$, 194.1).

Anal. Calcd for $C_9H_6O_5$: C, 55.68; H, 3.14. Found: C, 55.81; H, 3.04.

Registry No.—Carbon suboxide, 12076-43-6; acetylacetone, 123-54-6; benzoylacetone, 93-91-4; ethyl acetoacetate, 141-97-9; acetone, 67-6-41; **1a,** 19926-37-5; **2,** 1198-08-9; **3,** 17313-47-2; **4,** 19926-40-0; **9,** 19926-41-1; **11,** 4860-88-2.

Novel Formation of the Benzil from 2-(Dimethylaminomethyl)benzaldehyde under Benzoin Condensation Conditions[1]

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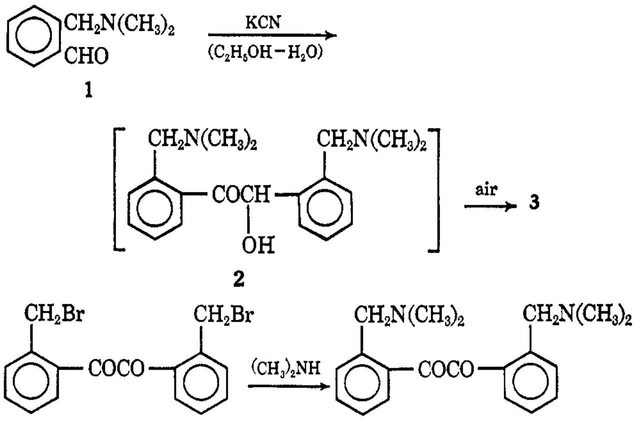
Although many examples of the benzoin condensation of an aromatic aldehyde by an alkali cyanide in ethanol-water have been reported,[2] none appears to have been accompanied by oxidation to form the benzil instead of the benzoin. In fact, subsequent conversion of the benzoin into the benzil has generally been effected by moderate or strong oxidizing agents.[3]

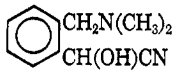
We have found that 2-(dimethylaminomethyl)benzaldehyde (**1**) undergoes the benzoin condensation under the usual conditions to form directly 2,2′-bis-(dimethylaminomethyl)benzil (**3**) in about 50% yield. Presumably diaminobenzoin **2** was an intermediate which was oxidized by air. The starting compound **1** was prepared from the reaction of the lithium derivative of benzyldimethylamine with N,N-dimethylformamide and from the Grignard reagent of 2-bromobenzyldimethylamine and triethyl orthoformate. The first method is the one of choice. The diaminobenzil **3** was independently synthesized from 2,2′-dimethylbenzil through the dibromo derivative **4** (see Experimental Section).



4 **3**

The structure of the diaminobenzil **3** was supported by analysis and absorption spectra. The infrared spectrum showed a carbonyl peak at 5.98 μ but no hydroxyl peak. The nmr spectrum showed the methyl protons and methylene protons as singlets and an aromatic proton multiplet in the ratio 12:4:8. The mass spectrum showed the highest peak at *m/e* 324, with the base peak at *m/e* 162, and a reasonably intense peak at *m/e* 58 [$(CH_3)_2N^+{=}CH_2$] as might be expected for a benzil[4a] and for a benzyldimethylamine.[4b]

That diaminobenzoin **2** was an intermediate was supported by effecting the reaction under nitrogen in the absence of air. The resulting crude product evidently consisted of mainly **2** as indicated by its nmr spectrum, which also showed the presence of very little **3**. Some of the cyanohydrin **5** may have been present. Recrystallization of this crude product from hot ethanol afforded diaminobenzil **3** in almost quantitative yield.



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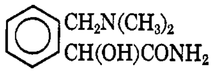

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In addition to the yellow diaminobenzil **3**, there was isolated from the reaction mixture a white solid which was shown by high resolution mass spectrometry and elemental analysis to have the elemental composition $C_{11}N_{16}N_2O_2$. Its infrared and nmr spectra are consistent with hydroxyaminoamide **6**, which would be the partial hydrolysis product of the cyanohydrin **5**. Cyanohydrins are known to be intermediates in the benzoin condensation[5] but formation of a hydroxyamide such as **6** as a by-product appears not to have been reported previously. As might be expected, the methylene group of **6** showed geminal coupling, having an AB pattern in its nmr spectrum which is characteristic of methylene groups *ortho* to an asymmetric center.[6]

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(1) Supported by Public Health Service Grant No. CA-04455 from the National Cancer Institute.

(2) (a) W. S. Ide and J. S. Buck, *Org. Reactions*, **4**, 60 (1948); (b) C. D. Shacklett and H. A. Smith, *J. Amer. Chem. Soc.*, **75**, 2655 (1953).

(3) (a) R. Adams and C. S. Marvel, *Org. Syn.*, **1**, 25 (1921); (b) J. van Alphen, *Rec. Trav. Chim. Pays-Bas*, **48**, 1112 (1929); (c) B. Klein, *J. Amer. Chem. Soc.*, **63**, 1474 (1941); (d) A. I. Vogel, "A Textbook of Practical Organic Chemistry," 3rd ed, Longmans, Green and Co., London, England, 1957, p 715; (e) H. T. Clarke and E. E. Dreger, *Org. Syn.*, **6**, 6 (1926); (f) E. Fischer, *Ann. Chem.*, **211**, 214 (footnote) (1882).

(4) (a) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day Inc., San Francisco, Calif., 1967, p 138; (b) pp 297–309.

(5) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, pp 394–397.

(6) J. C. Randall, R. L. Vaulx, M. E. Hobbs, and C. R. Hauser, *J. Org. Chem.*, **30**, 2035 (1965); J. C. Randall, J. J. McKleskey, III, P. Smith, and M. E. Hobbs, *J. Amer. Chem. Soc.*, **86**, 3229 (1964).