BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 42 3233—3237 (1969)

The Reaction of Carbon Suboxide with Alicyclic Diketones and with Phenols. Formation and Structure of Pyrone Derivatives

Akira Omori, Noboru Sonoda, Yuzo Uchida and Shigeru Tsutsumi

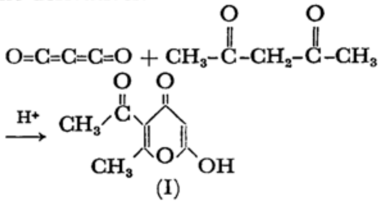
Department of Chemical Technology, Faculty of Engineering, Osaka University, Suita, Osaka

(Received April 7, 1969)

The reactions of carbon suboxide with alicyclic diketones and with phenols were found to give various pyrone derivatives. From the reaction of 5,5-dimethyl-1,3-cyclohexanedione, 4-hydroxy-7,7-dimethyl-5,6,7,8-tetrahydro-2*H*-benzo[*b*]pyran-2,5-dione (II) was produced in the presence of a sulfuric acid catalyst. However, the reaction with 1,2-cyclohexanedione gave the malonic acid diester (III), and the formation of corresponding pyrone was not observed. The reaction of phenols with carbon suboxide gave only esters of malonic acid in the presence of the sulfuric acid catalyst, whereas cyclization to coumarin derivatives occurred on the presence of aluminum trichloride, in addition to the formation of the esters. The structure of the pyrone derivatives and the possible reaction mechanism were discussed.

The reaction of carbonyl compounds with carbon suboxide has been reported by several workers.[1–3] The reaction between carbon suboxide and benzaldehyde was reported to give the benzalmalonic acid benzylidenester,[1] whereas the reaction of carbon suboxide with some ketones produced dipyrone derivatives.[2,3]

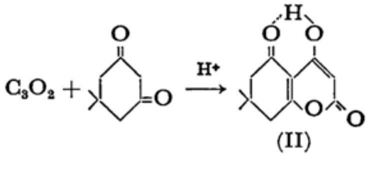
In a recent publication,[4] we have reported the reaction of carbon suboxide with acetylacetone in the presence of a sulfuric acid catalyst to produce 3-acetyl-6-hydroxy-2-methyl-4-pyrone (I), (1) while the reaction with aliphatic-1,3-diketones affords dipyrone derivatives.


(I) (1)

In the present paper, we wish to report on the reaction for the formation of various pyrone derivatives by the reaction of carbon suboxide with alicyclic diketones and with phenols, which have an ene-ol functional group$(\rangle C{=}\overset{OH}{\overset{|}{C}}{-})$ in their molecular structure.

Results and Discussion

Reaction of Cyclohexanedione Derivatives. Pyrone (II) was prepared in a 44% yield by the reaction of carbon suboxide with 5,5-dimethyl-1,3-cyclohexanedione at 0—5°C in the presence of a catalytic amount of sulfuric acid (2). However, by the reaction with 1,2-cyclohexanedione, only the malonic acid diester (III) was isolated in a 41% yield under similar conditions (3). In the reaction of 1,4-cyclohexanedione, the dione was recovered almost completely.


(II) (2)

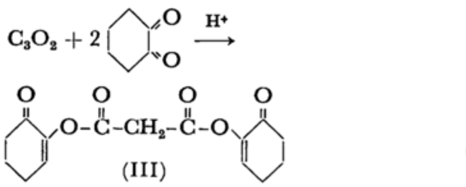
---

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

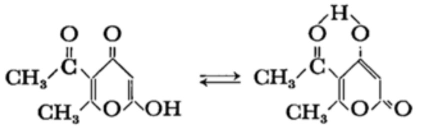
[2] E. Ziegler and H. Bieman, *Monatsh. Chem.*, **93**, 34 (1962).

[3] F. Haadetzky and E. Ziegler, *Monatsh. Chem.*, **97**, 398 (1966).

[4] A. Omori, N. Sonoda, S. Okano and S. Tsutsumi, *Tetrahedron Letters*, **1968**, 3647.


(3)

The pyrone structure of II was confirmed by a study of infrared, ultraviolet, and NMR spectra. The ultraviolet spectrum of II showed two bands, at 232 mμ (log ε, 4.27) and 270 mμ (log ε, 4.13), which were closely similar to those of 5-acetyl-4-hydroxy-6-methyl-2-pyrone (Ia) [225 mμ (log ε, 4.00) and 261 mμ (log ε, 3.91)],[4] characteristic absorptions of the pyrone ring. The infrared spectrum of II in both KBr and a chloroform solution showed a band at 3000 cm^{-1} which suggested the presence of hydrogen bonding, and one at 1742 cm^{-1} due to the carbonyl stretch of α-pyrone. However, the infrared spectrum[4] of I in KBr showed bands at 2600 cm^{-1} (strong hydrogen-bonded ν-OH) and at 1660 cm^{-1} (νC=O of γ-pyrone), but in a chloroform solution they were at 3000 cm^{-1} (hydrogen-bonded ν-OH) and 1739 cm^{-1} (νC=O of α-pyrone). Therefore, I is considered to have a γ-pyrone structure (I) in the solid phase and α-pyrone structure (Ia) in the liquid phase.


(I) (Ia)

Additionally, the hydroxy proton shifts of the NMR spectrum of II in a deuteriochloroform solution were independent of the concentration, as is shown in Table 1.

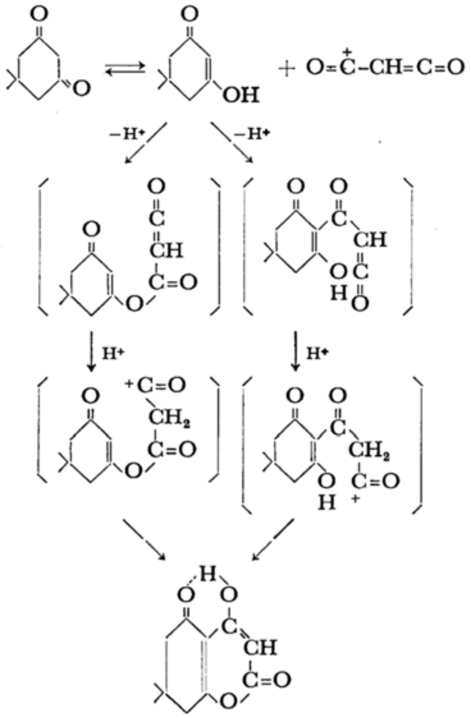
TABLE 1. INFLUENCE OF CONCENTRTION ON OH SHIFTS*

Concentration	τ Value of OH-proton
1.1%	−1.58
2.5	−1.60
4.5	−1.62

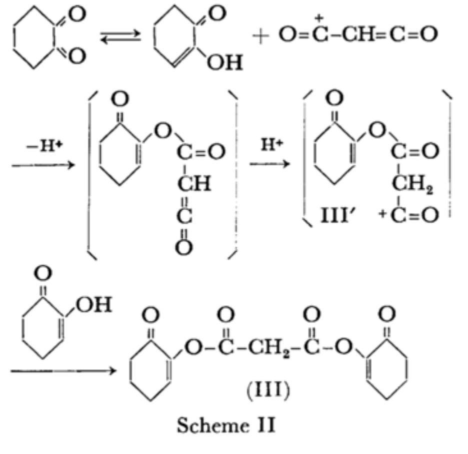
* In CDCl$_3$ Solution at 25°C.

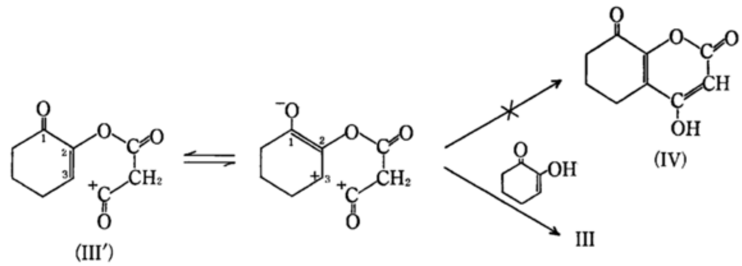
In contrast with the pyrone (I) from acetylacetone, this evidence suggested the α-pyrone structure for the pyrone (II), which had a strong intramolecular hydrogen bond, in both the solid phase and the liquid phase. The structure of III was established by analyses of the infrared, ultraviolet, and NMR spectra. The ultraviolet spectrum of III showed bands at 230 mμ (log ε, 4.27) and 304 mμ (log ε, 2.57) which were similar to the characteristic absorption bands reported for α,β-unsaturated ketone. The infrared and NMR spectra were consistent with those of the malonic acid diester (III).

Two pathways for the formation of the pyrone (II) may be worthy of consideration. The first of these may be C-acylation of the enol of dione with protonated carbon suboxide; the alternative pathway may involve the O-acylation as the initial step (Scheme I). However, in the case of 1,2-cyclohexanedione, the formation of the diester(III) of malonic acid indicates that O-acylation occurred preferentially (Scheme II). Therefore, in the case of 1,3-cyclohexanedione, the reaction path may also include O-acylation mainly rather than C-acylation.

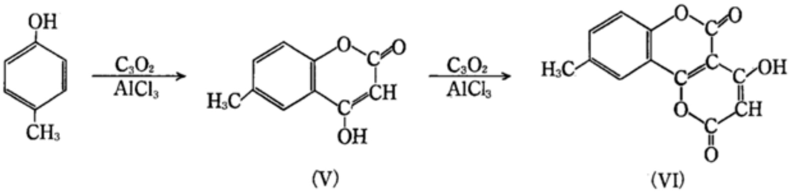

(II)

Scheme I


Scheme II



(4)



(5)

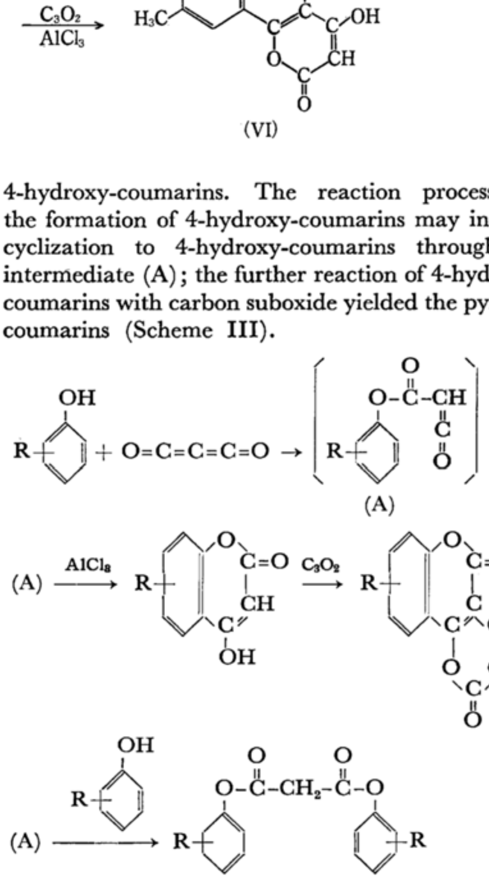
To account for the formation of pyrone(II), a reaction process is proposed which involves an electrophilic attack on the C-2 position by the acyl cation (Scheme I). In the case of the reaction with 1,2-dione, the presence of an electron-withdrawing carbonyl group at the C-1 position in the intermediate (III′) would deactivate the C-3 position toward electrophilic attack (4); consequently, the cyclization to pyrone (IV) is not likely.

Reaction of Phenols. The reaction of carbon suboxide with phenols in the presence of a sulfuric acid catalyst gave only diphenyl malonate derivatives, and no cyclization to coumarin derivatives was observed. However, it was confirmed that, in the presence of aluminum trichloride, the reaction of phenols produced coumarins to some extent at low temperatures. In the case of *p*-cresol, 4-hydroxy-6-methyl-coumarin (V) was obtained in an 8.5% yield in tetrachloroethane plus traces of 4-hydroxy-9-methyl-2*H*,5*H*-pyrano[3,2-*c*]benzo[*b*]-pyran-2,5-dione (VI) and di-*p*-tolyl malonate (5).

The structure of V and VI was confirmed by comparison with an authentic sample or by analyses of the infrared and ultraviolet spectral data. The ultraviolet spectrum of VI showed two bands, at 261 mμ (log ε, 4.16) and 351 mμ (log ε, 4.02), which were closely similar to those reported for 4-hydroxy-7-methyl-2*H*,5*H*-pyrano[3,2-*c*]pyran-2,5-dione[4] [270 mμ (log ε, 3.81) and 330 mμ (log ε, 3.76)], while the infrared spectrum of VI showed bands at 3150 cm^{-1} (–OH), 1745, 1695 cm^{-1} (C=O of lactone, and 1520 cm^{-1} (C=C of dipyrone).

m-Cresol reacted with carbon suboxide to give two isomers, 4-hydroxy-7-methyl-coumarin (VII) and 4-hydroxy-5-methyl-coumarin (VIII); the ratio of the two isomers was determined by the ultraviolet spectrum analysis. The results obtained by the reaction of phenols are shown in Table 2.

The table shows that tetrachloroethane is a better solvent than nitrobenzene for the formation of 4-hydroxy-coumarins. The reaction process for the formation of 4-hydroxy-coumarins may include cyclization to 4-hydroxy-coumarins through an intermediate (A); the further reaction of 4-hydroxy-coumarins with carbon suboxide yielded the pyrono-coumarins (Scheme III).



Scheme III

Experimental

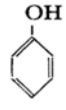
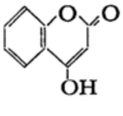
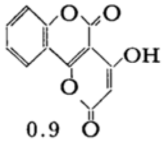
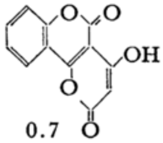
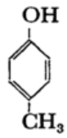
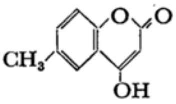
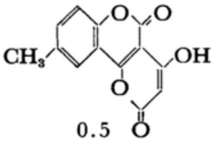
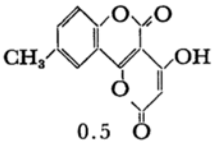
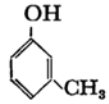
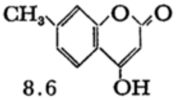
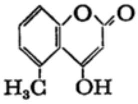
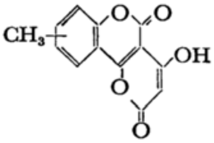
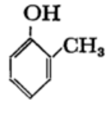
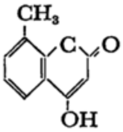
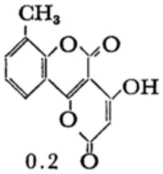
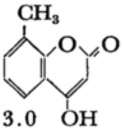
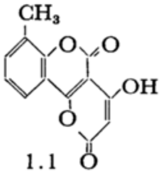
Preparation of Carbon Suboxide. Carbon suboxide was prepared by the pyrolysis[5] of diacetyltartaric anhydride at about 700°C; it was trapped at −78°C in a bath of dry ice-methanol and purified by distillation from trap to trap. The identification of carbon suboxide was established by the preparation of malonanilide by the reaction of carbon suboxide with aniline.

4-Hydroxy-7,7-dimethyl-5,6,7,8-tetrahydro-2*H*-benzo[*b*]pyran-2,5-dione (II). To a solution of carbon suboxide (1.65 g, 0.024 mol) in dry ether (60 m*l*)

---

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

TABLE 2

Reactant	Solvent	Product (Yield* %)		
		Coumarin		Diester
	$CHCl_2CHCl_2$	 0.2	0.9 	28
	$C_6H_5NO_2$		0.7 	36
	$CHCl_2CHCl_2$	 8.4	0.5 	16
	$C_6H_5NO_2$		0.5 	31
	$CHCl_2CHCl_2$	8.6  5.7 	 0.5	34
	$C_6H_5NO_2$	——		35
	$CHCl_2CHCl_2$	 8.6	0.2 	18
	$C_6H_5NO_2$	 3.0 1.1	1.1 	22

* The yield was based on used phenol or cresol.

and THF (75 m*l*), 5,5-dimethyl-1,3-cyclohexanedione (3.75 g, 0.024 mol) and conc. sulfuric acid (0.02 m*l*) were added at −78°C. The reaction mixture was maintained at 0—5°C for 7 days. The solids (2.4 g, 44%) were then separated on a filter; subsequent recrystallization from ethyl acetate gave the compound II; mp 138—139°C; ν_{max} (KBr and $CHCl_3$) 3000 (broad ν-OH), 1742 (C=O), 1670 (C=O), 1570 (C=C) cm^{-1}; λ_{max}^{EtOH} 232 (log ε, 4.27), 270 (log ε, 4.13) mμ: NMR ($CDCl_3$) τ 8.81 (s, 6H, $-CH_3$), 7.52 (s, 2H, $-CH_2-$), 7.28 (s, 2H, $-CH_2-$), 4.49 (s, H, $>C=CH-$); enolic −OH group (by $FeCl_3$ test). Found: C, 63.66; H, 5.90%; mol wt ($CHCl_3$ osmotic method), 203. Calcd for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81; mol wt, 208.2.

Bis(6-oxo-1-cyclohexenyl) Malonate (III). To a solution of carbon suboxide (1.2 g, 0.018 mol) in dry ether (100 m*l*), 1,2-cyclohexanedione (4.2 g, 0.038 mol) and conc. sulfuric acid (0.05 m*l* were added at −78°C. The reaction mixture was maintained at 25°C for 1 day. The solids (2.1 g, 41%) were then separated on a filter; subsequent recrystallization from ethanol gave the compound II; mp 80—81°C; ν_{max}^{KBr} 1760 (C=O), 1685 (C=O), 1650 (C=C) cm^{-1}; λ_{max}^{EtOH} 230 (log ε, 4.27), 304 (log ε, 2.57) mμ; NMR ($CDCl_3$) τ 7.9 (m, 4H, $-CH_2-$), 7.5 (m, 8H, $-CH_2-$), 6.3 (s, 2H, $-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-$), 3.4 (t, 2H, $-CH=C\langle$). Found: C, 62.40; H, 5.34%; mol wt (benzene cryoscopic method), 298. Calcd for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52%; mol wt, 292.

4-Hydroxy-coumarin and 4-Hydroxy-*2H*,*5H*-pyrano[3,2-*c*]benzo[*b*]-pyran-2,5-dione. To a solution of phenol (6.1 g, 0.06 mol) in tetrachloroethane (130 m*l*) we added a solution of carbon suboxide (4.4 g, 0.06 mol) in carbon disulfide (20 m*l*) at −44°C under nitrogen; then a solution of $AlCl_3$ (17.3 g, 0.12 mol) in tetrachloroethane (140 m*l*) was stirred into this reaction mixture drop by drop over a period of 2 hr. The reaction mixture was maintained at −44—−30°C for 9 hr, at 0°C for 10 hr, and at 25°C for 12 hr, and was then poured into ice water. A solid thus deposited was extracted with a saturated sodium bicarbonate solution, and the solution was acidified. From the non-soluble materials thus separated were isolated ethanol-soluble crystals and non-soluble crystals. The recrystallization of the former from ethanol gave 4-hydroxy-coumarin (0.02 g, 0.2%); mp 203—205°C. From ethanol-nonsoluble crystals, 4-hydroxy-*2H*,*5H*-pyrano[3,2-*c*]benzo-[*b*]pyran-2,5-dione (0.13 g, 0.9%) was isolated by crystallization from acetone; mp 241—243°C (decomp.); ν_{max}^{KBr} 3250 (−OH), 1750 (C=O), 1695 (C=O), 1550 (C=C) cm^{-1}: λ_{max}^{EtOH} 260.5 (log ε, 4.19), 339 (log ε, 4.03) mμ; enolic −OH group (by $FeCl_3$ test). Found: C, 62.52; H, 2.71%. Calcd for $C_{12}H_6O_5$: C, 62.62; H, 2.63%. From the tetrachloroethane layer, diphenyl malonate (164—168°C/3.5 mmHg) was obtained; yield 2.3 g (28%).

4-Hydroxy-6-methyl-coumarin (V) and 4-Hydroxy-9-methyl-*2H*,*5H*-pyrano[3,2-*c*]benzo[*b*]pyran-2,5-dione (VI). To a solution of *p*-cresol (8.7 g, 0.08 mol) in tetrachloroethane (150 m*l*) there was added a solution of carbon suboxide (5.5 g, 0.08 mol) in carbon disulfide (20 m*l*) at −44°C under nitrogen; a solution of $AlCl_3$ (21.6 g, 0.16 mol) in tetrachloroethane (130 m*l*) was then stirred into this reaction mixture drop by drop over a period of 2 hr. By treating the reaction mixture as has been described above for the case of phenol, 4-hydroxy-6-methyl-coumarin (V) (1.2 g, 8.4%; mp 247—249°C) and VI (0.1 g, 0.5%; mp 241—243°C (decomp.)) were obtained; ν_{max}^{KBr} 3160 (OH), 1740 (C=O), 1695 (C=O), 1570 (C=C) cm^{-1}; λ_{max}^{EtOH} 261(log ε, 4.16), 351 (log ε, 4.02) mμ. Found: C, 63.90; H, 3.25%. Calcd for $C_{13}H_8O_5$: C, 63.94; H, 3.30%. From a similar organic layer, 1.87 g (16%) of di-*p*-tolyl malonate (181—185°C/3.0 mmHg) was obtained.

4-Hydroxy-8-methyl-coumarin and 4-Hydroxy-7-methyl-*2H*,*5H*-pyrano[3,2-*c*]benzo[*b*]pyran-2,5-dione. To a solution of *o*-cresol (7.0 g, 0.06 mol) in tetrachloroethane (150 m*l*) there was a solution of carbon suboxide (4.4 g, 0.06 mol)in carbon disulfide (20 m*l*) at −44°C under nitrogen; then a solution of $AlCl_3$ (17.3 g, 0.12 mol) in tetrachloroethane (130 m*l*) was stirred into this reaction mixture drop by drop over a period of 2 hr. By treating the reaction mixture as has been described above for the case of phenol, 4-hydroxy-8-methyl-coumarin (0.98 g, 8.6%; mp 231—233°C) and 4-hydroxy-7-methyl-*2H*,*5H*-pyrano[3,2-*c*]-benzo[*b*]pyran-2,5-dione (0.04 g, 0.2%; mp 229—231°C) were obtained; ν_{max}^{KBr} 3220 (−OH), 1740 (C=O), 1715 (C=O), 1570 (C=C) cm^{-1}; λ_{max}^{EtOH} 264 (log ε, 4.23), 348 (log ε, 4.05); Found: C, 64.46; H, 3.19%. Calcd for $C_{13}H_8O_5$: C, 63.94; H, 3.30%. From a similar organic layer, 1.66 g (18%) of di-*o*-tolyl malonate (180—190°C/4.5 mmHg) were obtained.

4-Hydroxy-7-methyl-coumarin (VII) and 4-Hydroxy-5-methyl coumarin (VIII) and 4-Hydroxy-8-methyl- or 4-Hydroxy-10-methyl-*2H*,*5H*-pyrano-[3,2-*c*]benzo[*b*]pyran-2,5-dione (IX). To a solution of *m*-cresol (8.7 g, 0.08 mol) in tetrachloroethane (150 m*l*) there was added a solution of carbon suboxide (5.5 g, 0.08 mol) in carbon disulfide (20 m*l*) at −44°C under nitrogen; then a solution of $AlCl_3$ (21.6 g, 0.16 mol) in tetrachloroethane (170 m*l*) was stirred into this reaction mixture drop by drop over a period of 2 hr. By treating the reaction mixture as has been described above for phenol, VII (1.2 g, 8.6%; mp 214—216°C) and VIII (0.8 g, 5.7%; mp 221—223°C) were obtained. The ratio of the two isomers was determined by the UV spectrum analysis. IX (0.1 g, 0.5%.) was obtained in addition to the two isomers; mp 218—220°C; ν_{max}^{KBr} 3090 (−OH), 1755 (C=O), 1690 (C=O), 1565 (C=C)cm^{-1}; λ_{max}^{EtOH} 266 (log ε, 4.15), 339 (log ε, 4.10) mμ. Found: C, 64.22; H, 3.33%. Calcd for $C_{13}H_8O_5$: C, 63.94; H, 3.30%. From a similar organic layer, 3.91 g (34%) of di-*m*-tolyl malonate (180°C/4.0 mmHg) were obtained.