proton quartet, $J_{1ax,2ax}$ = 9 Hz, $J_{1ax,2eq}$ = 3 Hz, H-1), 5.26 (one-proton broad singlet, H-4), 5.78 (one-proton octet, $J_{5,6}$ = 6 Hz, $J_{5,4}$ = 1 Hz, H-5), 6.75 (three-proton singlet, C-3 OMe), 7.9, 7.95 (three-proton singlets, C-1 and C-4 OAc's), 8.9 (three-proton singlet, C-3 Me), 8.9 (three-proton doublet, J = 6 Hz, C-5 Me).

Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.5; H, 7.7. Found: C, 55.8; H, 7.9.

6-Chloro-9-(4′-*O*-acetyl-2′,6′-dideoxy-3′-*C*-methyl-3′-*O*-methyl-β-L-*xylo*-hexopyranosyl)purine (3).—An intimate mixture of compound **2** (24 mg), 6-chloropurine (16 mg, 1.1 equiv), and a trace of *p*-toluenesulfonic acid was heated at 100° (oil bath temperature) for 5 min. The dark brown solid residue was extracted with two 10-ml portions of hot ethyl acetate and the extracts were concentrated to a viscous syrup after treatment with carbon. Tlc showed the presence of eight components, the major one having R_f 0.13. Preparative tlc afforded 3.8 mg (12%) of nucleoside **3** as a homogeneous glass: R_f 0.13 (tlc); $[\alpha]_D$ +10° (*c* 0.4, EtOAc), $[\alpha]_{365}$ +50° (*c* 0.4, EtOAc); uv max (EtOH) 208 mμ (ε 13,000), 264 (11,000); ir (film) 5.75 (OAc), 6.3, 6.4, 6.7 μ (purine ring); nmr ($CDCl_3$) τ 1.23, 1.62 (one-proton singlets, H-8 and H-2), 4.15 (one-proton quartet, $J_{1'ax,2'ax}$ = 8 Hz, $J_{1'ax,2'eq}$ = 4.5 Hz, H-1′), 5.05 (one-proton broad singlet, H-4′), 5.70 (one-proton multiplet, H-5′), 6.60 (three-proton singlet, C-3′ OMe), 7.76 (three-proton singlet, C-4′ OAc), 8.74 (three-proton singlet, C-3′ Me), 8.8 (three-proton doublet, J = 6 Hz, C-5′ Me).

Anal. Calcd for $C_{15}H_{19}O_4N_4Cl$: C, 51.0; H, 5.4; N, 15.8. Found: C, 51.3; H, 6.0; N, 15.4.

Registry No.—2, 7308-86-3; **3**, 18339-01-0.

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The Reactions of 3-Hydroxyflavanone with Carbonyl Reagents

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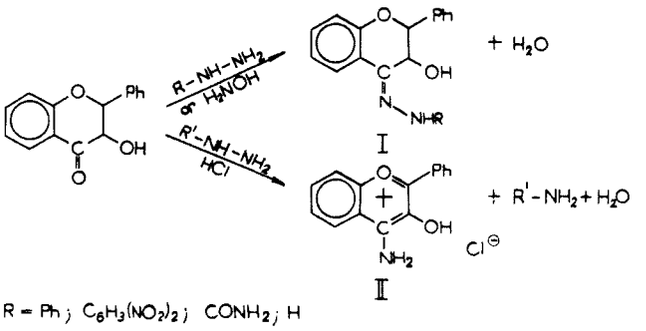
An extension of the study on the carbonyl reactions of flavanone[1] has shown that 3-hydroxyflavanone with *p*-tosylhydrazine gives, by an anomalous reaction, 3-hydroxy-4-aminoflavylium chloride.[2]

The present study is aimed at establishing the conditions leading to the formation of the true carbonyl derivatives I of 3-hydroxyflavanone, or of the flavylium salt II.

Examples from the literature[3] and our additional experiments have revealed that the normal carbonyl derivatives I can be prepared by reacting 3-hydroxyflavanone with hydrazine, a substituted hydrazine, or hydroxylamine.

The use of an acid hydrazide invariably results in the formation of the flavylium salt II (Scheme I).

SCHEME I[a]



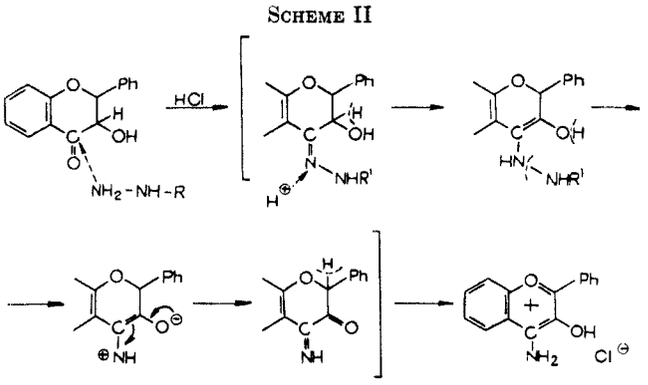
R = Ph; $C_6H_3(NO_2)_2$; $CONH_2$; H

R′ = $SO_2C_6H_4CH_3$; $SO_2C_6H_4Br$; $COC_6H_4NO_2$; COPh; $COCH_3$

[a] In the case of hydroxylamine NHR stands for OH.

Presumably, I is the primary product of the reaction leading to II; it is the electron-withdrawing character of the substituent attached to the N atom of the carbonyl reagent and the pH of the reaction medium which decide whether I is isolable as such, or eliminates $R'NH_2$ to become converted into II. The yields of II are higher as the electrophilic character of R′ is increased. The role of I as an intermediate is confirmed by conversion of the isolated normal carbonyl derivatives (including the oxime) into the aminocyanidin salt by boiling them in alcoholic hydrochloric acid. For further evidence, 3-hydroxyflavanone tosylhydrazone (I, R = $SO_2C_6H_4CH_3$) was prepared by tosylation in alkaline medium. This compound is converted into II in hot alcoholic HCl, in quantitative yield. It is reasonable to suppose the reaction mechanism given in Scheme II.

SCHEME II



The necessity of the presence of an enolizable 3-OH group is shown by the experimental evidence that while 3-acetoxyflavanone N-monoacetylhydrazone gives mainly 3-hydroxyflavanone on treatment with alcoholic HCl, the 3-hydroxy derivative is converted into II in 63% yield.

A continuation of this work is in progress concerning the carbonyl reactions of C_5-substituted 3-hydroxyflavanones.

Experimental Section

All melting points were determined on a Kofler block and are uncorrected. The compounds were checked for purity by tlc;

(1) F. Kállay, G. Janzsó, and I. Koczor, *Tetrahedron*, **23**, 4317 (1967).
(2) G. Janzsó, F. Kállay, and I. Koczor, *ibid.*, **22**, 2909 (1966).
(3) R. Bognár, M. Rákosi, H. Fletcher, E. M. Philbin, and T. S. Wheeler, *ibid.*, **19**, 391 (1963).

their ir and nmr spect were recorded as a means of identification or evidence of structure.

3-Hydroxyflavanone 2,4-Dinitrophenylhydrazone [I, R = $C_6H_3(NO_2)_2$].—A solution of 3-hydroxyflavanone (0.5 g, 2.08 mmol) in EtOH (40 ml) was mixed with 2,4-dinitrophenylhydrazine (0.42 g, 2.12 mmol) in EtOH (60 ml). HCl (1 ml) was added, and the red solution was refluxed for 3 hr. The red needles were filtered off after cooling (786 mg, 90.1%), mp 257° (unchanged on recrystallization from dioxane). *Anal.* Calcd for $C_{21}H_{16}O_6N_4$ (420.39): C, 60.0; H, 3.83; O, 22.81; N, 13.34. Found: C, 59.97; H, 4.08; O, 22.57; N, 13.24.

3-Hydroxyflavanone Hydrazone (I, R = H).—A solution of 3-hydroxyflavanone (5.0 g, 0.0208 mol) in pyridine (100 ml) was mixed with a solution of hydrazine monohydrochloride (10 g, 0.146 mol) in 50% aqueous pyridine (100 ml). Standing for 20 hr at room temperature gave a deposit of small yellow crystals (by-product 3-hydroxyflavanone azine), which were removed by filtration, and the mother liquor was poured into ice–water (800 ml). The pale yellow precipitate (4.0 g, mp 138–140°) was dissolved in hot EtOH (80 ml), filtered, and mixed with hot water (85 ml). Cooling gave glistening prisms (3.49 g, 65.9%); mp 147°. *Anal.* Calcd for $C_{15}H_{14}O_2N_2$ (254.29): C, 70.99; H, 5.54; O, 12.56; N, 11.02. Found: C, 70.82; H, 5.68; O, 12.39; N, 11.21.

3-Hydroxyflavanone Azine.—The azine, obtained above as a by-product, could be prepared in good yields by boiling a solution of 3-hydroxyflavanone and hydrazine monohydrochloride in 50% aqueous pyridine for 3 hr, mp 199–200°. *Anal.* Calcd for $C_{30}H_{24}O_4N_2$ (476.53): C, 75.71; H, 5.07; O, 13.45; N, 5.89. Found: C, 75.67; H, 5.11; O, 13.60; N, 5.92.

3-Hydroxyflavanone Benzaldazine.—A solution of the hydrazone in EtOH gave with benzaldehyde pale yellow needles (71.6%), mp 177°. *Anal.* Calcd for $C_{22}H_{18}O_2N_2$ (342.38): C, 77.20; H, 5.28; O, 9.34; N, 8.19. Found: C, 77.17; H, 5.59; O, 9.25; N, 8.12.

3-Acetoxyflavanone Monoacetylhydrazone.—I (R = H) was acetylated with Ac_2O–Py at room temperature, and the product recrystallized from EtOH, yield 70.2%, mp 205–206°. *Anal.* Calcd for $C_{19}H_{18}O_4N_2$ (338.36): C, 67.40; H, 5.36; O, 18.90; N, 8.28. CH_3CO, 25.43. Found: C, 67.86; H, 5.57; O, 18.85; N, 8.54; CH_3CO, 25.43.

Ir analysis showed bands at 1683 (C=O of N-acetyl) and 1720 cm^{-1} (C=O of O-acetyl).

3-Hydroxyflavanone monoacetylhydrazone (I, R = $COCH_3$) was prepared by selective hydrolysis of the former compound. 3-Acetoxyflavanone monoacetylhydrazone (0.5 g) was dissolved in hot 90% aqueous MeOH (100 ml); $KHCO_3$ (0.5 g) was added, and the mixture refluxed for 3 hr. About half of the solvent was evaporated and the residue mixed with hot water (150 ml). Standing at room temperature for 24 hr gave pale yellow plates (320 mg, 73%) which were recrystallized from 96% EtOH to give 208 mg, mp 212°. *Anal.* Calcd for $C_{17}H_{16}O_3N_2$ (296.33): C, 68.99; H, 5.44; O, 16.20; N, 9.45; CH_3CO, 14.53. Found: C, 69.04; H, 5.54; O, 16.69; N, 9.53; CH_3CO, 13.51.

Ir analysis showed a band at 1645 cm^{-1} (C=O of N-acetyl).

3-Hydroxyflavanone Tosylhydrazone (I, R = $SO_2C_6H_4CH_3$).—A suspension of 3-hydroxyflavanone hydrazone (2.0 g, 7.85 mmol) in benzene (360 ml) was mixed with pyridine (1.2 ml, 15.6 mmol) and *p*-toluenesulfonic anhydride (5.1 g, 15.6 mmol; mp 124°). A red solution was obtained which was allowed to stand 1 hr at room temperature. The 3-hydroxyflavanone azine which deposited was removed by filtration, and the benzene solution was extracted with four 100-ml portions of water. The benzene layer was evaporated under reduced pressure to dryness, and the residue rubbed with petroleum ether (bp 30–60°) to give a powder (3.21 g), which was repeatedly recrystallized from EtOH to obtain a white microcrystalline product (602 mg), mp 184° dec. *Anal.* Calcd for $C_{22}H_{20}O_4N_2S$ (408.48): C, 64.75; H, 4.92; O, 15.69; N, 6.66; S, 7.84. Found: C, 64.52; H, 5.21; O, 15.30; N, 6.86; S, 7.99.

3-Hydroxy-4-aminoflavylium Chloride (II). A. From 3-Hydroxyflavanone Oxime.—The oxime (200 mg) was refluxed for 5 hr in EtOH (25 ml) containing HCl (0.4 ml). Cooling gave a pale yellow crystalline product (86 mg, 40.3%), mp 258°, which was identical with II prepared by any of the methods described below.

B. From 3-Hydroxyflavanone Monoacetylhydrazone.—I (R = $COCH_3$, 100 mg) in EtOH (25 ml) was refluxed for 5 hr in the presence of HCl (0.5 ml). The solution was diluted with *n*-hexane and chilled to obtain II (57.2 mg, 62.3%), mp 258–260°.

C. From 3-Hydroxyflavanone Tosylhydrazone.—I (R = $SO_2C_6H_4CH_3$, 400 mg) was treated as described in B to obtain II (248 mg, 92%), mp 258–260°.

D. From 3-Hydroxyflavanone and an Acid Hydrazide.—The procedure described[2] for *p*-tosylhydrazine could be applied to the preparation of II using *p*-bromobenzenesulfonylhydrazine, *p*-nitrobenzoylhydrazine, benzoylhydrazine, and monoacetylhydrazine. The yields were between 50 and 70%.

Registry No.—I [R = $C_6H_3(NO_2)_2$], 18500-74-8; I (R = H), 18500-75-9; I (R = $COCH_3$), 18500-76-0; I (R = $SO_2C_6H_4CH_3$), 18500-77-1; II, 4281-27-0; 3-hydroxyflavanone, 1621-55-2; 3-hydroxyflavanone azine, 18500-72-6; 3-hydroxyflavanone benzaldazine, 18500-73-7; 3-acetoxyflavanone monoacetylhydrazone, 18540-93-7.

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