

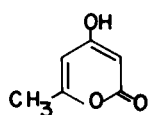
A Study of the Acylation of 4-Hydroxy-6-methyl-2-pyrone and 4-Hydroxy-6-phenyl-2-pyrone

E. Marcus, J. F. Stephen and J. K. Chan

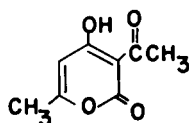
Research and Development Department, Union Carbide Corporation

The acylation of 4-hydroxy-6-methyl-2-pyrone (I) and 4-hydroxy-6-phenyl-2-pyrone (XXII) with aliphatic acid anhydrides, or with aliphatic acid chlorides in trifluoroacetic acid, has been found to produce first the corresponding ester, which then rearranges, partially or wholly, depending on the conditions and on the nature of the acyl moiety, to form the corresponding 3-acylpyrone. With aromatic acid chlorides in pyridine or in trifluoroacetic acid only the corresponding ester was obtained. These esters, however, could be rearranged to the corresponding 3-acylpyrones with aluminum chloride. Acetoacetylation of I and 4-hydroxycoumarin (XXIX) with diketene gave, in both cases, the *C*-acetoacetylated product.

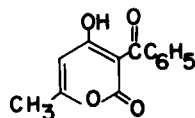
Acetylation of 4-hydroxy-6-methyl-2-pyrone (I) with acetic anhydride in the presence of either sulfuric acid, pyridine or sodium acetate to give dehydroacetic acid (II) has been known for a long time (1,2). More recently, Woods and Dix (3) acylated I with acetyl chloride and benzoyl chloride in trifluoroacetic acid and reported that they obtained II and the mono- and dibenzoylated derivatives III and IV, the latter compound being produced when two equivalents of benzoyl chloride were used.



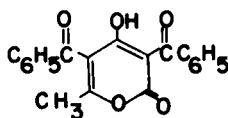
I



II



III



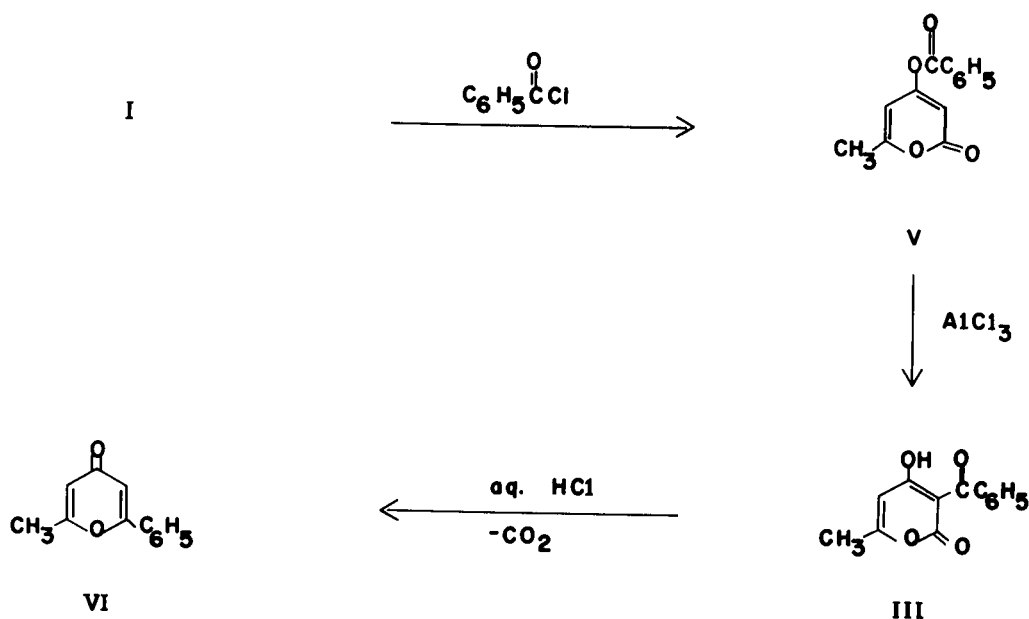
IV

We required a sample of III in connection with other studies and repeated the benzoylation of I under the same conditions as described by Woods and wish to report new observations on this reaction.

In our hands compound I reacted with one equivalent of benzoyl chloride in refluxing trifluoroacetic acid forming a crystalline compound (m.p. 87-89°) with molecular formula, C₁₃H₁₀O₄. Although Woods and Dix (3) had also obtained a compound of the same formula, their product melted much lower (m.p. 70-71°). Furthermore, our compound failed to give a positive enol test with ethanolic ferric chloride. Its infrared spectrum showed no absorption in the 3 to 4-μ region indicating the absence of a chelated hydroxyl group. The NMR spectrum exhibited peaks at 2.28, 6.14, 6.18, and multiplets at 7.33-7.80 and 8.00-8.33 δ with integrated area ratios corresponding to 3:1:1:5. It is not possible to reconcile these spectral data with structure III; however, the data can be accommodated by assigning structure V to the compound (Scheme I).

When V was treated with aluminum chloride at 100°, it underwent a Fries rearrangement to give III in 74% yield. Ester V could also be rearranged to III with difficulty upon prolonged heating in trifluoroacetic acid. Under these conditions, the rearrangement was accompanied by considerable degradation of V to triacetic acid lactone and benzoic acid.

SCHEME I



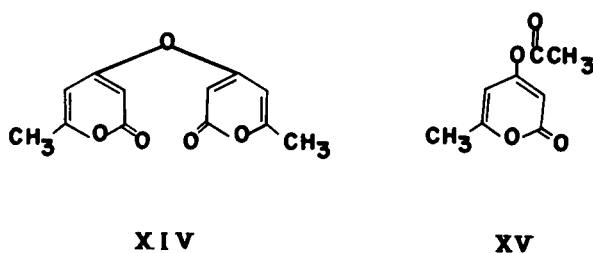
III melted at $108-110^\circ$, not at $70-71^\circ$ as had been reported by Woods and Dix (3), and gave an orange color with ethanolic ferric chloride solution. Its infrared spectrum (potassium bromide) showed broad weak absorption in the $4\text{-}\mu$ region indicating a chelated hydroxyl group; it also displayed carbonyl absorption at $5.74\ \mu$ due to the lactone and benzoyl carbonyl groups. Its NMR spectrum exhibited peaks at 2.26 and 6.00, a multiplet at 7.32-7.80, and a peak at 15.9 δ . The integrated area ratios corresponded to 3:1:5:1. The structure was further substantiated by converting III to 2-methyl-6-phenyl-4-pyrone (VI) with concentrated hydrochloric acid. The hydrochloric acid-catalyzed decarboxylation and rearrangement of 3-acyl-4-hydroxy-6-methyl-2-pyrone to 2-substituted-6-methyl-4-pyrone is well-known (4-8).

Benzoylation of I with two or three equivalents of benzoyl chloride in trifluoroacetic acid produced only V and benzoic acid (from hydrolysis of the benzoyl chloride). No dibenzoylated derivative (IV) could be detected.

A number of esters of I (VII to XI) were prepared and are summarized in Table I. Compounds V, VII, and VIII were most conveniently prepared by acylating I with the appropriate acid chloride in pyridine at 0° . Surprisingly, only a very poor yield of X was obtained when acylation of I with 2-naphthoyl chloride was attempted in pyridine. A somewhat better yield was obtained when the acylation was conducted in refluxing trifluoroacetic acid. Compounds VII and VIII were readily rearranged to the corresponding


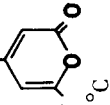
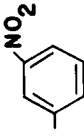
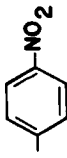
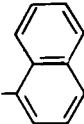
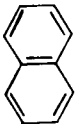
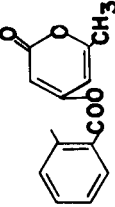



C-benzoylated derivatives, XII and XIII (Table II), respectively, with aluminum chloride, while treatment of IX and X with aluminum chloride under similar conditions gave unidentified products.

Next we investigated the acylation of I with selected aliphatic acid anhydrides and acyl chlorides. Collie (1) acylated I with an excess of acetic anhydride in the presence of a catalytic amount of sulfuric acid and obtained II. On the other hand, Dieckmann and Breest (2) treated I with acetic anhydride in the presence of a trace of acetyl chloride and obtained, after distillation of the reaction mixture, an oil to which they assigned structure XIV.



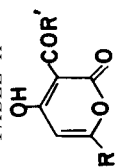
We re-examined both reactions and found that Collie's procedure gave II in good yield while the Dieckmann acylation procedure gave, on crystallization of the residue remaining after removal of excess acetic anhydride, II and XV. Structure XV was supported by elemental and spectral analyses. Compound XV could also be obtained in good

TABLE I

Compound	R	R'	Yield, %	M.P. °C	OCOR'	Method	Recryst. Solvent	Formula	Anal.	C%	H%	N%
V	CH ₃		84	87-89		A	Ethanol	C ₁₃ H ₁₀ O ₄	Calcd.: Found:	67.82 67.70	4.38 4.35	
VII	CH ₃		88	143-144		A	Ethanol	C ₁₃ H ₉ NO ₆	Calcd.: Found:	56.73 56.52	3.30 3.35	5.09 5.04
VIII	CH ₃		83	177-180		A	Toluene	C ₁₃ H ₉ NO ₆	Calcd.: Found:	56.73 56.66	3.30 3.15	5.09 4.95
IX (d)	CH ₃		67	117-119		B (b)	Methanol	C ₁₇ H ₁₂ O ₄	Calcd.: Found:	72.85 71.96	4.32 4.29	
X	CH ₃		28	128-129		B	Benzene	C ₁₇ H ₁₂ O ₄	Calcd.: Found:	72.85 72.83	4.32 4.26	
XI	CH ₃		53	149-151		B (b)	Methanol	C ₂₀ H ₁₆ O ₈	Calcd.: Found:	62.50 62.87	4.20 3.95	
XX	CH ₃	C(CH ₃) ₃	89 41	34-36		A B	Heptane	C ₁₁ H ₁₄ O ₄	Calcd.: Found:	62.84 62.82	6.71 6.77	
XVIII (a,c)	CH ₃	CF ₃	70	B.P. 97°/4 mm.		C	---	---	---	---	---	
XXIII		CH ₃	20	79-83		C	Benzene-cyclohexane	C ₁₃ H ₁₀ O ₄	Calcd.: Found:	67.82 68.10	4.38 4.27	
XXVI			62	115-116		A	Ethanol	C ₁₈ H ₁₂ O ₄	Calcd.: Found:	73.96 73.97	4.14 4.28	
XV	CH ₃	CH ₃	71	42-45		—	Toluene-hexane	C ₈ H ₈ O ₄	Calcd.: Found:	57.14 57.35	4.80 4.76	

(a) In the preparation of this compound, general Method C was followed; however, after reflux, excess anhydride was evaporated under reduced pressure and the acylated product was isolated by distillation. (b) General Method B was followed but the reaction was carried out in toluene as solvent. (c) This compound was very unstable to air, an attempt to obtain elemental analyses was not made. (d) Several attempts to obtain a better carbon analysis for this compound failed; however, its structure was firmly supported by spectral analyses.

TABLE II



Compound	R	R'	Yield, %	M.P. °C	Method	Recryst. Solvent	Formula	Anal.	C%	H%	N%
III	CH ₃		73	108-110	D	Methanol	C ₁₃ H ₁₀ O ₄	Calcd.: 67.82 Found: 67.83	4.38 4.36		
XII	CH ₃		78	185-187	D	Isopropanol	C ₁₃ H ₉ NO ₆	Calcd.: 56.73 Found: 56.43	3.30 3.11	5.09 4.99	
XIII	CH ₃		82	249-250	D	Acetic Acid	C ₁₃ H ₉ NO ₆	Calcd.: 56.73 Found: 56.76	3.30 3.29	5.09 5.07	
XVI	CH ₃	CH ₂ CH ₃	62	105-107	C	Methanol	C ₉ H ₁₀ O ₄	Calcd.: 59.33 Found: 59.56	5.53 5.55		
XVII	CH ₃	CH ₂ CH ₂ CH ₃	60	57-59	C	Methanol	C ₁₀ H ₁₂ O ₄	Calcd.: 61.21 Found: 61.26	6.17 6.15		
XIX	CH ₃	CH(CH ₃) ₂	56	75-77	B	Methanol	C ₁₀ H ₁₂ O ₄	Calcd.: 61.21 Found: 61.00	6.17 6.15		
XXI	CH ₃	C(CH ₃) ₃	3	87-90	B	Heptane	C ₁₁ H ₁₄ O ₄	Calcd.: 62.84 Found: 62.64	6.71 6.60		
XXIV		CH ₃	82 55	169-171	D C	Ethyl Acetate	C ₁₃ H ₁₀ O ₄	Calcd.: 67.82 Found: 68.00	4.38 4.31		
XXV		CH ₂ CH ₃	86	155.5- 156.5	C	Benzene	C ₁₄ H ₁₂ O ₄	Calcd.: 68.84 Found: 69.11	4.95 4.95		
XXVII			40	169-172	D	Acetone	---	---	---	---	
XXVIII	CH ₃	CH ₂ COCH ₃	82	107-109	-	Cyclohexane	C ₁₀ H ₁₀ O ₅	Calcd.: 57.14 Found: 57.01	4.80 4.71		
XXX			86	130-133	-	Toluene	C ₁₃ H ₁₀ O ₅	Calcd.: 63.41 Found: 63.65	4.09 4.33		

TABLE III
Nuclear Magnetic Resonance and Infrared Absorption Data

Compound	δ , ppm	Multiplicity	Assignment	Absorption Peaks, μ
V (a)	2.28	(S)	CH ₃ (6)	5.77, 5.83, 6.10, 6.34, 6.88,
	6.14	(M)	H (5)	7.23, 8.19, 8.6, 9.5, 9.74,
	6.18	(S)	H (3)	13.94, 14.35
	7.33-7.8 and 8.0-8.33	(M)	Aromatic	
VII	2.32	(S)	CH ₃ (6)	5.75, 6.05, 6.2, 6.3, 8.0,
	6.05-6.25	(M)	H (3) and H (5)	8.2, 8.66, 9.45
	7.74, 8.33-8.65	(S) (M)	Aromatic	
	8.85-8.97	(M)		
VIII (a)	2.26	(S)	CH ₃ (6)	5.73, 5.83, 6.1, 6.2, 6.3,
	6.05	(M)	H (5)	7.95, 8.23, 8.6, 8.75, 9.3
	6.16	(D)	H (3)	
	8.32	(S)	Aromatic	
IX	2.28	(S)	CH ₃ (6)	5.7, 5.79, 6.07, 6.62, 6.93,
	6.05-6.25	(M)	H (3) and H (5)	7.21, 8.08, 8.25, 8.41, 8.72,
	7.25-8.7	(M)	Aromatic	9.05
X (a)	2.30	(S)	CH ₃ (6)	5.74, 5.85, 6.1, 6.25, 6.4,
	6.15	(M)	H (5)	7.9, 8.2, 8.46, 8.62, 8.84,
	6.23	(D)	H (3)	9.4
	7.4-8.2 and 8.73	(M)	Aromatic	
XI	2.3	(S)	2 x CH ₃ (6)	5.72, 5.81, 6.1, 6.35, 7.94,
	6.19	(S)	2H (3) and 2H (5)	8.23, 8.57, 9.24, 11.62,
	7.65-8.1	(M)	Aromatic	13.72
XX	1.3	(S)	COC(CH ₃) ₃	5.68, 5.78, 6.1, 6.3, 7.85,
	2.26	(S)	CH ₃ (6)	8.2, 9.2
	6.0	(S)	H (3) and H (5)	
XVIII (a)	2.33	(S)	CH ₃ (6)	5.52, 5.7, 6.08, 6.3, 8.1,
	6.17	(S)	H (3) and H (5)	8.4-8.8, 9.0-9.1
XXIII	2.3	(S)	CH ₃ (OCOCH ₃)	5.62, 5.83, 6.11, 6.34, 6.45,
	6.12(D), 6.54 (D)		H (3) and H (5)	6.68, 7.96, 8.35, 8.63, 9.35
	7.25-7.52 and 7.56-7.90	(M)	Aromatic	
XXVI	6.12 (D), 6.73 (D)		H (3) and H (5)	5.75, 5.82, 6.1, 6.25, 6.34, 6.4,
	7.22-7.95, 7.95-8.23	(M)	Aromatic	6.69, 8.0, 8.54, 9.25, 9.35
XV	2.27	(S)	CH ₃ (6) and OCOCH ₃	5.65, 5.75, 6.05, 6.33, 8.32,
	6.0 (M), 6.05 (D)		H (5) and H (3)	9.85
XVI	1.16	(T)	CH ₃ (COCH ₂ CH ₃)	3.74-5.37, 5.81, 6.10, 6.20,
	2.28	(D)	CH ₃ (6)	6.43, 6.88, 7.22, 8.09, 10.0, 11.69
	3.13	(Q)	CH ₂ (COCH ₂ CH ₃)	
	5.98	(D)	H (5)	
	16.73 (S broad)		OH (4, chelated OH)	
XVII	0.98	(T)	CH ₃ (COCH ₂ CH ₂ CH ₃)	3.85-5.16, 5.83, 6.06, 6.19,
	1.6	(M)	CH ₂ (COCH ₂ CH ₂ CH ₃)	6.4, 6.81, 8.06, 10.03
	2.24	(S)	CH ₃ (6)	
	3.05	(T)	CH ₂ (COCH ₂ CH ₂ CH ₃)	
	5.87	(M)	H (5)	
XIX	1.17	(D)	CH ₃ (CH(CH ₃) ₂)	4.0, 5.8, 6.09, 6.2, 6.4, 8.1
	2.26	(D)	CH ₃ (6)	
	3.95	(M, 7 lines)	H (CH(CH ₃) ₂)	
	5.95	(Q)	H (5)	

TABLE III (Continued)

XXI (a)	1.37	(S)	CH ₃ (C(CH ₃) ₃)	3.7-4.6, 5.8, 6.02, 6.22, 6.45,
	2.25	(D)	CH ₃ (6)	7.15, 7.28, 8.55
	5.90	(S)	H (5)	
	17.00	(S)	OH (4, chelated)	
III (a)	2.22	(D)	CH ₃ (6)	3.8-5.3, 5.74, 6.12, 6.39, 7.34,
	5.95	(D)	H (5)	7.85, 10.03, 12.91, 14.17
	7.32-7.65	(M)	Aromatic	
	15.90	(S)	OH (4, chelated)	
XII (a,b)	2.34	(S)	CH ₃ (6)	3.6-4.3, 5.79, 6.08, 6.23, 6.35,
	6.09	(S)	H (5)	6.45, 6.53, 8.0
	7.89 (T), 8.13-8.65	(M)	Aromatic	
XIII (a)	2.33	(S)	CH ₃ (6)	4.3, 5.83, 6.1, 6.3, 6.43, 6.6,
	6.09	(S)	H (5)	8.02
	7.75 and 8.33 (AB pattern)		Aromatic	
XXIV	2.69	(S)	CH ₃ (COCH ₃)	3.9, 4.3, 4.7, 5.88, 6.15-6.2,
	6.51	(S)	H (5)	6.3, 6.45, 6.75, 8.02
	7.33-7.60 and 7.73-7.96	(M)	Aromatic	
	16.54	(S)	OH (4, chelated)	
XXV	1.19	(T)	CH ₃ (COCH ₂ CH ₃)	3.7-4.08, 5.85, 6.2, 6.45, 6.66,
	3.15	(Q)	CH ₂ (COCH ₂ CH ₃)	8.09
	6.53	(S)	H (5)	
	7.33-7.67 and 7.70-7.95	(M)	Aromatic	
XXVIII	2.14	(S)	CH ₃ (COCH ₂ COCH ₃)	3.7-4.1, 5.88, 6.15, 6.35, 6.5,
	4.1	(S)	CH ₂ (COCH ₂ COCH ₃)	7.41, 8.1, 10.58, 11.95
	2.3	(S)	CH ₃ (6)	
	5.96	(M)	H (5)	
	16.23	(S)	OH (4, chelated)	
XXX	2.3	(S)	CH ₃ (COCH ₂ COCH ₃)	3.6-4.7, 5.86, 6.18, 6.48, 7.17
	4.1	(S)	CH ₂ (COCH ₂ COCH ₃)	7.66, 7.88, 8.32, 9.8, 10.1 10.97,
	7.1-7.45 and 7.9-8.2	(M)	Aromatic	12.14

Spectra were determined with a Varian A-60 spectrometer in 5-10% solution in CDCl₃ using tetramethylsilane as internal reference. (a) This spectrum was determined with a Varian HA-100 spectrometer. (b) Spectrum recorded in dimethylformamide. S = singlet, D = doublet, M = multiplet, T = triplet, Q = quartet.

yield by heating I and one equivalent of acetic anhydride in toluene containing a catalytic amount of either sulfuric acid, *p*-toluenesulfonic acid or pyridine; it also could be made from I and acetic anhydride in dilute aqueous sodium hydroxide by the Chattaway procedure (9). Compound XV was readily rearranged to II with aluminum chloride as well as by further refluxing in acetic anhydride containing sulfuric acid or by refluxing in trifluoroacetic acid. In contrast to the rearrangement of 4-benzoyloxy-6-methyl-2-pyrone (V) to 3-benzoyl-4-hydroxy-6-methyl-2-pyrone (III) in trifluoroacetic acid which was accompanied by considerable degradation of the ester, the rearrangement of XV in trifluoroacetic acid proceeded smoothly to give dehydroacetic acid (II) in high yield. Very little ester cleavage was observed.

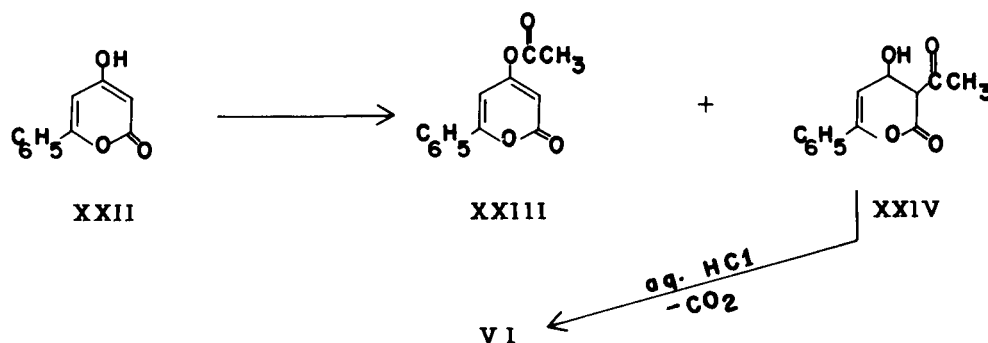
Acylation of I with propionic anhydride and butyric

anhydride proceeded readily in the presence of a catalytic amount of sulfuric acid to produce the corresponding *C*-acylated pyrones, XVI and XVII (Table II). With trifluoroacetic anhydride and sulfuric acid as catalyst, I gave the *O*-acylated compound, XVIII (Table I), an unstable liquid which hydrolyzed rapidly on exposure to air.

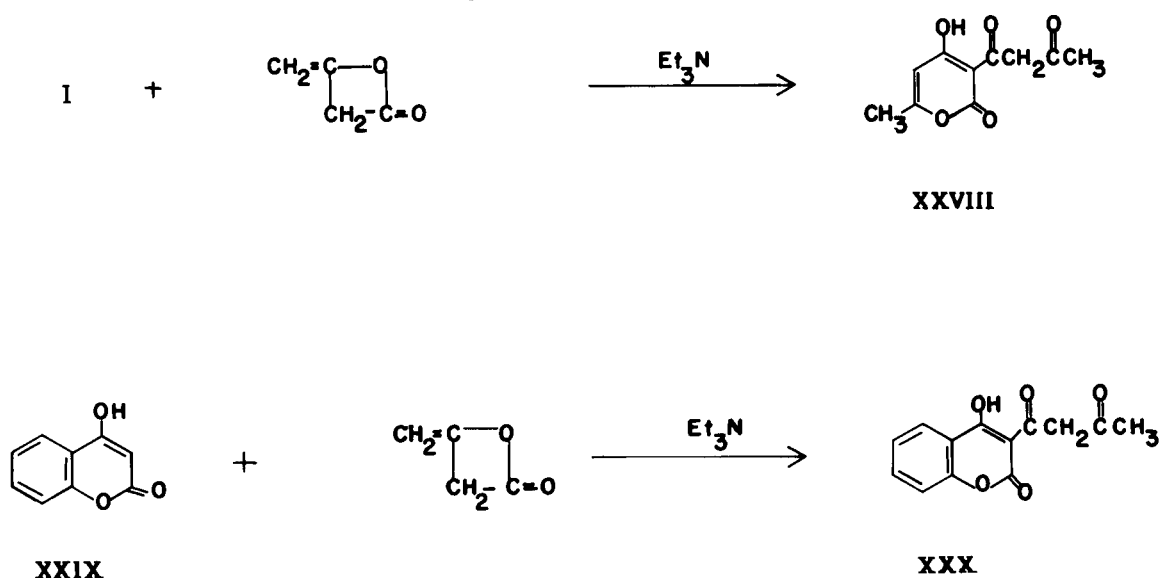
I was also acylated with propionyl chloride and isobutyryl chloride in trifluoroacetic acid to afford the *C*-acylated pyrones XVI and XIX. With pivalyl chloride, under similar conditions, a mixture of the *O*- and *C*-acylated products XX and XXI was obtained. When I was reacted with pivalyl chloride in pyridine, exclusive *O*-acylation was observed.

We also made a brief study of the acylation of 4-hydroxy-6-phenyl-2-pyrone (XXII) with acetic anhydride, propionic anhydride, and benzoyl chloride. With

SCHEME 2



SCHEME 3



an excess of acetic anhydride in the presence of a catalytic amount of sulfuric acid, a mixture of the *O*- and *C*-acylated pyrones XXIII and XXIV was obtained. The yields were 20 and 55%, respectively (Scheme 2). Structures XXIII and XXIV were supported by elemental and spectral analyses. Structure XXIV was further substantiated when this compound was converted to VI with hydrochloric acid. On heating XXIII with aluminum chloride or in acetic anhydride containing a small amount of sulfuric acid, XXIV was obtained. Treatment of XXII with propionic anhydride in the presence of a catalytic amount of sulfuric acid gave the *C*-acylated product XXV in good yield, while benzoylation of XXII with benzoyl chloride in pyridine yielded only the *O*-benzoylated product XXVI. Isomerization of XXVI with aluminum

chloride gave XXVII, which was identified by comparison of its infrared spectrum and melting point with those of an authentic sample of XXVII (9).

Finally, we investigated the acetoacetylation of I and 4-hydroxycoumarin (XXIX) in benzene containing a catalytic amount of triethylamine. In both cases, the products formed were found to be the corresponding *C*-acylated derivatives, XXVIII and XXX. The yields were 82 and 86%, respectively. No *O*-substituted products could be detected (Scheme 3).

Although no detailed mechanistic studies have been conducted, it appears that the acylation of I and XXII with aliphatic acid anhydrides in the presence of sulfuric acid proceeds through the intermediate formation of the ester. The formation of an intermediate ester is confirmed

by the following observations: (a) Treatment of I with an excess of acetic anhydride containing sulfuric acid yielded II; (b) compound XV rearranged in acetic anhydride containing sulfuric acid under the conditions of the above mentioned reaction to yield II; (c) the reaction of I with an equivalent amount of acetic anhydride containing sulfuric acid yielded XV.

4-Acetoxy-6-phenyl-2-pyrone (XXIII), which was isolated along with 3-acetyl-4-hydroxy-6-phenyl-2-pyrone (XXIV) from the reaction mixture of XXII and acetic anhydride containing sulfuric acid, was shown to be an intermediate by being converted, on further treatment with acetic anhydride containing sulfuric acid, to XXIV. Furthermore, the ester XVIII was observed as the sole product in the reaction of I with trifluoroacetic anhydride containing a catalytic amount of sulfuric acid. The inertness of XVIII to rearrangement is presumably due to the strong electron withdrawing effect of the trifluoromethyl group, which makes the heterolysis of the acyl-oxygen bond difficult.

The acylation of I with aliphatic acid chlorides in trifluoroacetic acid also appears to produce first the ester which is then converted to the corresponding 3-acylpyrone. Actually, the ester was isolated along with the 3-acylpyrone from the reaction involving I and pivalyl chloride.

Similarly, acylation of I with aromatic acid chlorides in trifluoroacetic acid affords the ester. As was mentioned earlier, 4-benzoyloxy-6-methyl-2-pyrone (V) was found to rearrange with difficulty to 3-benzoyl-4-hydroxy-6-methyl-2-pyrone (III) in refluxing trifluoroacetic acid, while 4-acetoxy-6-methyl-2-pyrone (XV) underwent facile rearrangement to II under similar conditions. The resistance of V to rearrangement in trifluoroacetic acid is presumably due to the electron withdrawing effect of the aromatic ring, which makes cleavage of the acyl-oxygen bond difficult. Steric hindrance is also probably a contributing factor.

EXPERIMENTAL

All melting points are uncorrected and were taken on a Mel-Temp Capillary melting point apparatus. Infrared spectra were determined with Baird-Atomic Models AB-2 and 4-55 and Perkin-Elmer Model 21 spectrometers using potassium bromide pellets of the compounds. Elemental analyses were performed by the Analytical Department of the Union Carbide Corporation, South Charleston, West Virginia. Dehydroacetic acid (II) was the commercial product of Union Carbide Corporation. Dehydrobenzoylactic acid (XXVII) was prepared by the sodium hydrogen carbonate-catalyzed self-condensation of ethyl benzoylacetate as described in the literature (10). Compound I was obtained by deacetylating II as described by Collie (11). Compound XXII was prepared by debenzoylating dehydrobenzoylactic acid by the method of Arndt (10).

Reaction of 4-Hydroxy-6-methyl-2-pyrone (I) with Benzoyl Chloride in Trifluoroacetic Acid.

The procedure used in this experiment was the same as that described by Woods and Dix (3). A mixture of I (11.4 g., 0.1 mole), benzoyl chloride (14.1 g., 0.1 mole), and trifluoroacetic acid (20 ml.) was refluxed until hydrogen chloride evolution ceased. The mixture was then poured into 100 ml. of water and chilled. The solid formed was recovered by filtration. Recrystallization of this solid from ethanol gave 5.2 g. of a white solid, m.p. 87-89°. The compound was identified as V by spectral and elemental analyses. No product with a melting point of 70-71° could be isolated. Only unchanged starting material (I) and some benzoic acid were found in the filtrates.

4-Benzoyloxy-6-methyl-2-pyrone (V). The following procedure illustrates the general Method A.

Benzoyl chloride (145 g., 1.03 moles) was added dropwise over a period of 14 minutes to a stirred solution of I (126 g., 1.0 mole) in 750 ml. of pyridine at 0°. After the addition was completed the mixture was stirred at room temperature for 1 hour and then allowed to stand overnight. The mixture was poured into 3 l. of 10% hydrochloric acid, and the solid which separated was collected by suction filtration. Crystallization of this material from ethanol afforded 192.7 g. (84%) of V, m.p. 87-89°.

3-Isobutyryl-4-hydroxy-6-methyl-2-pyrone (XIX). The following procedure illustrates the general Method B.

A mixture of I (12.6 g., 0.1 mole) and isobutyryl chloride (11.7 g., 0.11 mole) in 30 ml. of trifluoroacetic acid was heated at a bath temperature of 85° for 1 hour and then at 125° for 3 hours. The hot solution was poured into 100 ml. of water, and the oil which separated solidified on cooling. Filtration gave 10.9 g. (56%) of XIX, m.p. 70-73°. An analytical sample was recrystallized from methanol, m.p. 75-77°. Evaporation of the aqueous filtrate above gave 5.2 g. of unchanged I, m.p. 184-186°.

3-Acetyl-4-hydroxy-6-phenyl-2-pyrone (XXIV) and 4-Acetoxy-6-phenyl-2-pyrone (XXIII). The following procedure illustrates the general Method C.

A solution of XXII (41.4 g., 0.22 mole) in 145 ml. of acetic anhydride containing 12 drops of concentrated sulfuric acid was heated under reflux for 1 hour and then poured while hot into 1300 ml. of water. The solid which formed was collected by filtration to give 43.7 g., m.p. 136-146°. Recrystallization from ethyl acetate gave 25.5 g. of XXIV, m.p. 168-170°. Evaporation of the ethyl acetate mother liquor afforded 17.9 g. of a pale yellow solid, m.p. 68-110°. This was dissolved in 150 ml. of benzene and the solution was washed with 100 ml. of 10% sodium carbonate solution. The benzene layer was separated, dried over magnesium sulfate and concentrated *in vacuo* to give 14.2 g. of a solid, m.p. 75-80°. Recrystallization of this material from benzene-cyclohexane mixture gave 10.1 g. (19.95%) of XXIII, m.p. 77-80°. Acidification of the carbonate solution furnished 3.6 g. of solid, which upon recrystallization from ethyl acetate gave 2.5 g. of XXIV, m.p. 169-171°. The combined yield of XXIV was 55.3%.

The original aqueous filtrate on standing deposited 3.7 g. of unchanged XXII, m.p. 239-243° dec.

Conversion of 4-Acetoxy-6-phenyl-2-pyrone (XXIII) to 3-Acetyl-4-hydroxy-6-phenyl-2-pyrone (XXIV) in Acetic Anhydride.

A solution of 4-acetoxy-6-phenyl-2-pyrone (1 g.) in 5 ml. of acetic anhydride containing a catalytic amount of sulfuric acid was refluxed for 1 hour. The mixture was poured into excess water, and the solid which precipitated was collected. Recrystallization from ethyl acetate furnished 0.7 g. (70%) of 3-acetyl-4-hydroxy-6-

phenyl-2-pyrone. The mixed melting point with authentic 3-acetyl-4-hydroxy-6-phenyl-2-pyrone was 169-171°.

3-Benzoyl-4-hydroxy-6-methyl-2-pyrone (III). The following procedure illustrates general Method D.

A mixture of finely powdered V (167 g., 0.73 mole) and anhydrous aluminum chloride (668 g.) was heated at 100° for 2.5 hours. The resulting complex was decomposed with ice and dilute hydrochloric acid, and the solid which separated was collected by filtration and extracted with dilute aqueous sodium carbonate solution. Acidification of the carbonate solution and recrystallization of the yellow solid thus obtained from methanol afforded 122 g. (73%) of III, m.p. 108-110°.

Rearrangement of 4-Benzoyloxy-6-methyl-2-pyrone (V) to 3-Benzoyl-4-hydroxy-6-methyl-2-pyrone (III).

A solution of V (10 g., 0.043 mole) in 30 ml. of trifluoroacetic acid was refluxed for 16 hours. The mixture was poured into 200 ml. of water. After chilling in ice for several hours the precipitate was collected by filtration, and the filtrate was evaporated to dryness *in vacuo* to give a second crop. The combined crude solid (6.7 g.) was mixed with 5% sodium bicarbonate solution (2 x 100 ml.), and the insoluble solid was collected by filtration. Recrystallization of this solid from ethanol afforded unchanged V, 1.91 g., m.p. 84-86°. Acidification of the bicarbonate solution furnished 2.00 g. of solid, m.p. 100-118°, which was collected by filtration. The infrared spectrum (potassium bromide disc) indicated that this material consisted of a mixture of benzoic acid and a compound which displayed absorption bands at 5.7, 6.1, 6.4, 6.45, 11.1, 11.87, 12.0 and 12.95 μ . The nmr spectrum (deuteriochloroform) showed a doublet at δ 2.19 (CH₃), a doublet at 5.73 (=CHC=O), a complex multiplet pattern at 7.28-7.65, a multiplet pattern at 8.00-8.23 (aromatic protons) and a broad peak at 15.15 (OH); it was consistent with a mixture containing 93 mole % of benzoic acid and 7 mole % of 3-benzoyl-4-hydroxy-6-methyl-2-pyrone. No attempt was made to resolve the mixture. Evaporation of the aqueous filtrate above to about one half of its original volume resulted in the separation of 1.6 g. of material, m.p. 114-170°. Analysis of this material by infrared spectroscopy indicated that it consisted of a mixture of triacetic acid lactone and benzoic acid.

4-Acetoxy-6-methyl-2-pyrone (XV).

(a) A solution of I (12.6 g., 0.1 mole), acetic anhydride (10.5 g., 0.1 mole) and 2 drops of concentrated sulfuric acid in 100 ml. of toluene was heated in a flask equipped with a 6-inch glass-packed column topped with a stillhead. The mixture was heated for 1 hour, acetic acid being removed azeotropically as it was formed. Addition of hexane to the cold toluene solution resulted in the separation of 11.9 g. (71%) of XV, m.p. 42-45°. Recrystallization from a toluene-hexane mixture did not change the melting point.

(b) Compound XV was also prepared by the Chattaway procedure (9). To a solution of triacetic acid lactone (23.3 g., 0.185 mole) in 10% sodium hydroxide solution (100 ml.) was added crushed ice (100 g.) and acetic anhydride (60 ml.). The mixture was shaken vigorously for several minutes, and the oil which separated was extracted with benzene. The dried (magnesium sulfate) benzene solution was evaporated under reduced pressure, and the oil was crystallized from a toluene-hexane mixture to give 25.2 g. (81%) of XV, m.p. 43-46°.

Conversion of 4-Acetoxy-6-methyl-2-pyrone (XV) to Dehydroacetic Acid (II) in Trifluoroacetic Acid.

A solution of 4-acetoxy-6-methyl-2-pyrone (10 g., 0.06 mole) in 30 ml. of trifluoroacetic acid was heated under reflux for 15.5 hours. The mixture was poured into 200 ml. of water. The precipitated dehydroacetic acid, 8.6 g. (86%), m.p. 110-114°, was collected by filtration. A mixture melting point with an authentic sample of dehydroacetic acid was undepressed. The filtrate was evaporated to dryness under reduced pressure; the residue thus obtained was recrystallized from water using charcoal to give 1 g. of triacetic acid lactone, melting point and mixed melting point with authentic triacetic acid lactone, 185-188°.

Conversion of 4-Acetoxy-6-methyl-2-pyrone (XV) to Dehydroacetic Acid (II) in Acetic Anhydride.

A solution of 4-acetoxy-6-methyl-2-pyrone (7.2 g., 0.043 mole) in 21.6 ml. of acetic anhydride containing a small amount of sulfuric acid was heated under reflux for 1 hour. The mixture was poured into water, and the solid which separated was collected by filtration. Crystallization of this material from methanol using charcoal gave 5 g. (69.4%) of dehydroacetic acid, m.p. 110-112°.

3-Acetoacetyl-4-hydroxy-6-methyl-2-pyrone (XXVIII).

Diketene (106.4 g., 1.3 moles) was added to a mixture of I (140 g., 1.1 moles) and benzene (900 ml.) containing 3 g. of triethylamine over a period of 25 minutes at 80°. The mixture was further refluxed for 1.5 hours. On cooling 192.3 g. (82%) of XXVIII, m.p. 106-109°, crystallized from solution. Recrystallization from cyclohexane raised the melting point to 107-109° (lit. m.p. 117°) (12).

3-Acetoacetyl-4-hydroxycoumarin (XXX).

A mixture of XXIX (8.1 g., 0.05 mole), triethylamine (0.15 g.) and benzene (50 ml.) was refluxed while adding diketene (4.5 g., 0.053 mole) over a 25-minute period. After the addition the mixture was refluxed for an additional 1.5 hours. The solid which separated on cooling was collected by filtration giving 10.6 g. (86%) of XXX, m.p. 130-133°. Recrystallization from toluene raised the melting point to 135-136° (lit. m.p. 134°) (13).

Rearrangement of 3-Benzoyl-4-hydroxy-6-methyl-2-pyrone (III) to 2-Methyl-6-phenyl-4-pyrone (VI) with Hydrochloric Acid.

Finely powdered III (1 g.) was suspended in 28 ml. of concentrated hydrochloric acid, and the mixture was refluxed for 5 hours. After cooling the solution was poured into 40 ml. of water. The solution was then neutralized with 30% sodium hydroxide solution. On standing 0.8 g. of solid, m.p. 44-47°, separated. This material was collected and dissolved in benzene. Evaporation of the benzene gave a crystalline residue which was recrystallized from heptane to give 0.5 g. of VI, m.p. 85-87°, (lit. m.p. 85-87°) (14).

VI was also obtained when XXIV was treated with concentrated hydrochloric acid.

Acknowledgment.

Thanks are extended to Messrs. C. B. Strow and H. L. Joyce of the Union Carbide Corporation for interpretations of NMR and infrared data.

REFERENCES

- (1) J. N. Collie, *J. Chem. Soc.*, 77, 976 (1900).
- (2) W. Dieckmann and F. Breest, *Ber.*, 37, 3388 (1904).
- (3) L. L. Woods and P. A. Dix, *J. Org. Chem.*, 26, 2588 (1961).
- (4) J. N. Collie, *J. Chem. Soc.*, 59, 619 (1891).
- (5) F. Feist, *Ber.*, 25, 1067 (1892).

- (6) J. N. Collie and T. Tickle, *J. Chem. Soc.*, **75**, 710 (1899).
(7) F. Arndt and P. Nachtwey, *Ber.*, **57**, 1491 (1924).
(8) R. H. Wiley, C. J. Jarboe and H. G. Ellert, *J. Am. Chem. Soc.*, **77**, 5102 (1955).
(9) F. D. Chattaway, *J. Chem. Soc.*, 2495 (1931).
(10) F. Arndt, B. Eistert, H. Scholz and E. Aron, *Ber.*, **69**, 2373 (1936).
(11) J. N. Collie, *J. Chem. Soc.*, **59**, 607 (1891).
(12) P. F. G. Prail and A. L. Whitear, *Proc. Chem. Soc.*, **112**, (1961).
(13) A. Mustafa, O. H. Hsihmat, S. M. A. D. Zayed and A. H. Nawar, *Tetrahedron*, **19**, 1831 (1963).
(14) R. J. Light and C. R. Hauser, *J. Org. Chem.*, **25**, 542 (1960).

Received November 9, 1968

South Charleston,
West Virginia 25303