Photolysis of 1.—A solution of 0.026 g of 1 in 100 ml of dry ethyl ether was exposed to blue fluorescent light through a Corning 3-72 filter which removes all light of wavelength below 430 mμ. Under this condition of illumination, the sole product was 2.

Photolysis of 2.—An ether solution of 2, which was continuously flushed with nitrogen was exposed to the light of a high-pressure, water-cooled mercury arc which was filtered through Pyrex glass. An exposure time of 5 min reduced the 277-mμ absorption peak of 2 to less than one-quarter of its original value.

Registry No.—**1,** 6427-95-8; **2,** 15707-28-5; **4,** 15707-29-6; **5,** 15707-35-4; **6,** 15707-30-9; **7,** 15707-33-2; 2,3-dichloro-5,6-dimethyl-1,4-benzoquinone, 15707-31-0; 2-chloro-3-methoxy-1,4-naphthoquinone, 15007-32-1.

The Preparation of Certain Pyrylium Salts by Using Chalcone and Boron Trifluoride Etherate

J. A. VanAllan and G. A. Reynolds

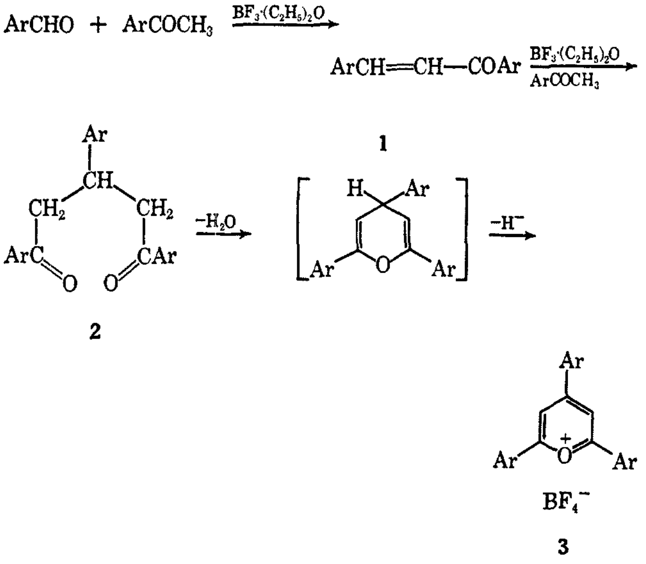
Research Laboratories, Eastman Kodak Company, Rochester, New York 14650

Received September 26, 1967

Some pyrylium salts were prepared from 1,5-diketones by using chalcone as a hydride-abstracting agent and boron trifluoride etherate as a cyclization medium. Under these conditions, 2-carbethoxy-1,3,5-triphenylpentane-1,5-dione (**9**) gave the 3-benzyl-2,4,6-triphenylpyrylium salt (**10**) rather than the expected 3-carbethoxy-2,4,6-triphenylpyrylium salt (**11**). An explanation for this result is proposed. Ethyl acetoacetate, chalcone, and boron trifluoride etherate gave 3-carbethoxy-2-methyl-4,6-diphenylpyrylium salt (**14**). Some 3-substituted 2,4,6-triphenylpyrylium salts were prepared from chalcone, α-substituted acetophenone derivatives, and boron trifluoride etherate.

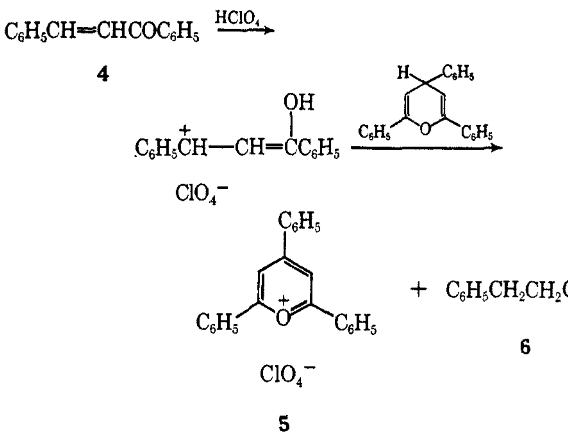
The most common preparative method for synthesizing 2,4,6-triarylpyrylium salts involves the condensation of 1 equiv of an aryl aldehyde and 2 equiv of an arylalkyl ketone in the presence of Lewis acids, strong mineral acids, or dehydrating agents such as polyphosphoric acid. We have found boron trifluoride etherate to be the most generally useful condensing agent for this synthesis. The reaction path is illustrated in Scheme I below. The 1,5-diketone **2** is an intermediate during the formation of **3**, since 1,5-diketones of this type readily yield **3** when treated with boron trifluoride etherate or perchloric acid. Inspection of the sequence shows that a dehydrogenation step is required to form **3**, and, since oxidizing agents are not usually present in the reaction medium, the nature of this dehydrogenation has long been a matter of conjecture.

Scheme I



Recently it was reported[1] that the conjugate acid of the intermediate chalcone serves as a hydride abstractor in the manner shown in Scheme II. Balaban proposed this reaction scheme on the basis of the improved yields of **5** that were obtained by the addition of chalcone (**4**) to 1,3,5-triphenylpentane-1,5-dione (**7**) in perchloric acid, and isolation of **6** from the reaction mixture.

Scheme II



We thought it of interest to investigate boron trifluoride etherate as a condensing agent and chalcone as a hydride abstractor in a synthetic procedure for pyrylium salts. The results obtained when **7** was allowed to react under a variety of conditions are summarized in Table I.

Procedure C (see Table I) was extended to include other 1,5-diketones, and in many cases excellent yields of pyrylium fluoroborates were obtained. For example, **8a** was obtained in 88% yield, **8b** in 93% yield and **8c** in 72% yield.

In some cases, however, this procedure led to un-

---

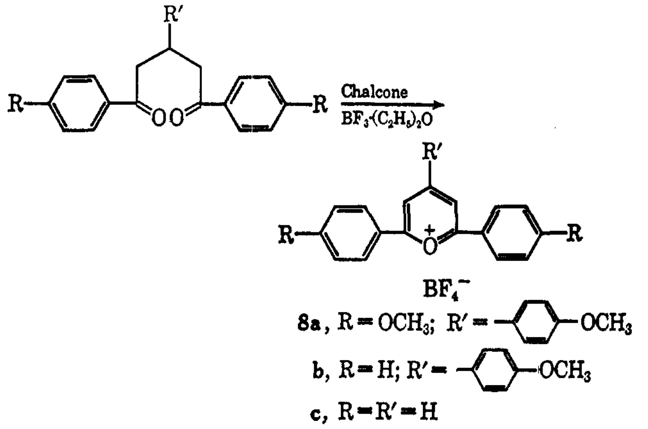
(1) A. T. Balaban, *Comp. Rend.*, **256**, 4239 (1963).

TABLE I

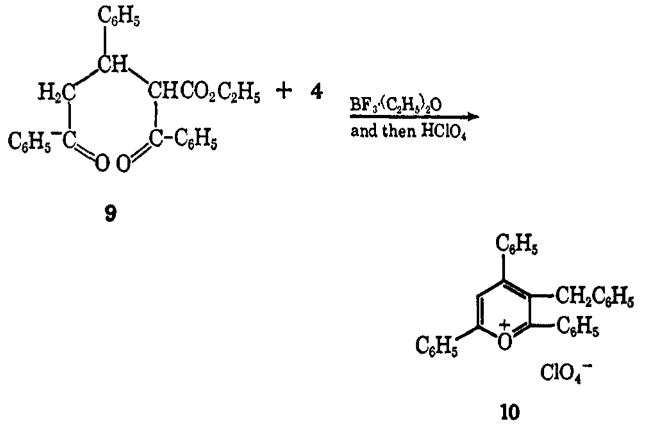
THE EFFECT OF VARYING REACTION CONDITIONS ON THE YIELD OF **5**

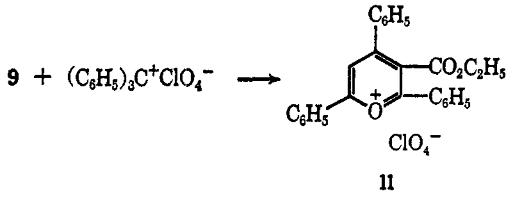
Procedure	Conditions Equivalents of **7**	Condensing agent	**4**	% yield of **5**
A	1	$2HClO_4$	1	75
B	1	$2HClO_4$	0	54
C	1	$8BF_3\cdot(C_2H_5)_2O$	1	96
D	1	$8BF_3\cdot(C_2H_5)_2O$	0.5	81
E	1	$8BF_3\cdot(C_2H_5)_2O$	0	59
F[a]	1	$8BF_3\cdot(C_2H_5)_2O$	0	63
G[b]	1	$(C_6H_5)_3C^+ClO_4^-$	0	86

[a] One-half equivalent of chloranil was present in the reaction mixture. [b] Siemiatycki and Fugnetto [*Bull. Soc. Chim. Fr.*, 538 (1961)] have shown that trityl perchlorate is a very useful condensing agent and hydride abstractor for preparing pyrylium salts from 1,5-diketones.

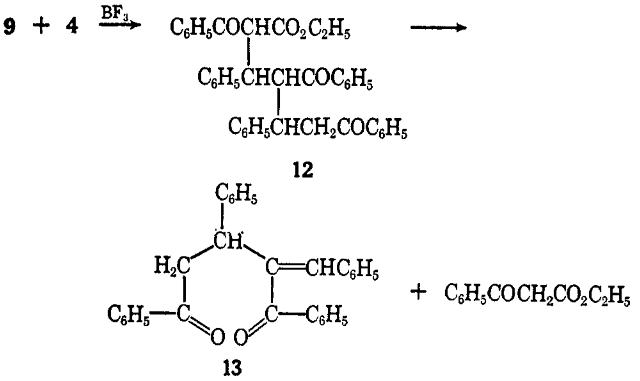


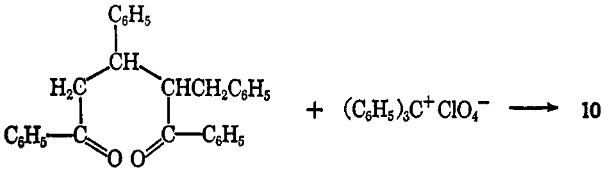
expected results. For example, the substituted 1,5-diketone **9** in the presence of **4** and boron trifluoride etherate gave 3-benzyl-2,4,6-triphenylpyrylium fluoroborate (isolated as the perchlorate salt **10**) rather than the expected 3-carbethoxy derivative **11**, and **9** with trityl perchlorate gave **11**. A rationale for the formation of **10** is that **9** adds to chalcone (**4**) under the influence of boron trifluoride, to give **12** which, in turn, eliminates ethyl benzoylacetate by a reverse Michael reaction to form **13** which is cyclized to **10**. This sequence of reactions is illustrated in Scheme III. The fact that the adduct of chalcone and dimethyl malonate reacts with a further equivalent of chalcone to give **10** is substantiating evidence for the mechanism just proposed for the formation of **10** from **4** and **9**, since it shows that the exact nature of the group that is eliminated in the reverse Michael step is not important. The structural proof for the pyrylium salt **10** follows from its synthesis from 2-benzyl-1,3,5-triphenylpentane-1,5-dione and trityl perchlorate.



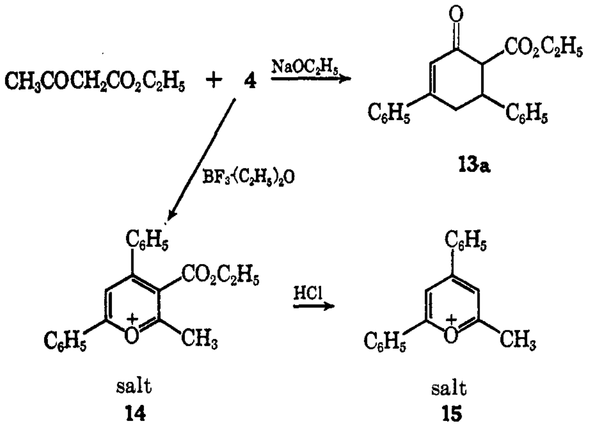


SCHEME III





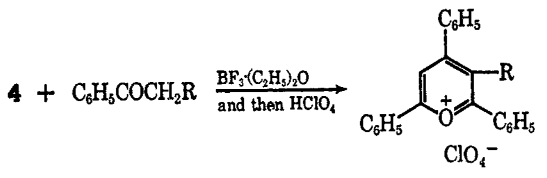
Attempts to treat chalcone with ethyl acetoacetate gave interesting results. It had been shown[2] that basic reaction conditions gave the cyclohexenone **13a**, but we found that the acidic catalyst, boron trifluoride etherate, gave the pyrylium salt **14**. Acid hydrolysis of **14** yielded 2-methyl-4,6-diphenylpyrylium salt (**15**), indicating that the 3-carbethoxy group of the pyrylium salt is readily hydrolyzed and decarboxylated.



The preparation of 3-substituted 2,4,6-triphenylpyrylium salts by the reaction of chalcone (**4**) with acetophenone derivatives in the presence of boron trifluoride etherate is quite general, and **16a**, **b**, **c**, **d**, and **e** were synthesized in this manner.

---

[2] E. Knoevenagel and H. Schmidt, *Ann.*, **281**, 58 (1894).



16a, $R = CH_3$
b, $R = C_2H_5$
c, $R = C_4H_9$
d, $R = C_6H_5$
e, $R = OCOCH_3$

Experimental Section

2,4,6-Triphenylpyrylium Salts (Table I). Procedure A.—A mixture of 6.6 g (0.02 mol) of **7**,[3] 4.2 g of chalcone (**4**), and 6 g of 70% perchloric acid was heated on the steam bath for 1 hr. The mixture was diluted with 20 ml of alcohol and chilled, and the solid was collected and recrystallized from acetic acid to give 6.2 g (75% yield) of 2,4,6-triphenylpyrylium perchlorate, mp 293–295°.

Procedure B.—A mixture of 6.6 g (0.02 mol) of **7** and 6 g of 70% perchloric acid was heated on the steam bath for 1 hr, and the product was isolated and purified as described for procedure A.

Procedure C.—A mixture of 0.02 mol of **4** and **7** in 25 ml of boron trifluoride etherate was heated for 2 hr on the steam bath, cooled, and diluted with ether. The solid was collected and recrystallized from ethanol to give 7.6 g (96% yield) of the fluoroborate salt, mp 252–253°.

Procedure D.—The reaction was carried out as described for procedure C, except that 0.01 mol of **4** was used.

Procedure E was the same as procedure C except that no chalcone was used.

Procedure F was the same as procedure E but included 0.01 mol of chloranil in the reaction mixture.

Procedure G.[4]—A mixture of 0.02 mol of **7**, 0.02 mol of trityl perchlorate, and 50 ml of acetic acid was refluxed for 30 min, and, after the mixture had cooled, the product was collected.

2,4,6-Tri(4-methoxyphenyl)pyrylium Fluoroborate (8a).—A mixture of 8.4 g (0.02 mol) of 1,3,5-tri(4-methoxyphenyl)-1,5-pentanedione,[5] 4.2 g (0.02 mol) of chalcone, and 24 ml of boron trifluoride etherate was heated on the steam bath for 2 hr, cooled, and diluted with ether; the solid was collected and recrystallized from acetonitrile to yield 8.6 g (88% yield) of **8a**, mp 346–347° (lit.[6] mp 345–347°).

4-(4-Methoxyphenyl)2,6-diphenylpyrylium Fluoroborate (8b).—The procedure described for the preparation of **8a** was used, except that anisylidenebisacetophenone[7] was employed as the diketone. The yield of **8b** was 7.9 g (93%), mp 238–240° (from a mixture of ethanol and acetonitrile).

Anal. Calcd for $C_{24}H_{19}BF_4O_2$: C, 67.6; H, 4.5. Found: C, 67.9; H, 4.7.

A sample of **8a** was converted into the perchlorate salt which melted at 260° (lit.[8] mp 257–259°).

2,6-Diphenylpyrylium Fluoroborate (8c).—The procedure described for the preparation of **8a** was used with 1,3-dibenzoylpropane[9] as the diketone to yield 4.6 g (72%) of **8c**, mp 206–207°. The product was dissolved in hot acetic acid, 2 ml of 70% perchloric acid was added to the solution, and, after the solution had cooled, the 2,6-diphenylpyrylium perchlorate was collected, mp 224–225° (lit.[4] mp 226°).

3-Benzyl-2,4,6-triphenylpyrylium Perchlorate (10).—A mixture of 7.5 g (0.02 mol) of the diketone **9**,[10] 4.2 g of **4**, and 25 ml of boron trifluoride etherate was heated on the steam bath for 4 hr and then poured into a mixture of 75 ml of ethanol and 5 ml of 70% perchloric acid. The mixture was chilled and the product was collected and recrystallized from acetic acid to yield 4.7 g of **10**, mp 241°. The ultraviolet spectrum in acetonitrile solution showed peaks at λ 273 mμ (ε 15,600) and 383 mμ (ε 21,800).

Anal. Calcd for $C_{30}H_{23}ClO_5$: C, 72.2; H, 4.6; Cl, 7.1. Found: C, 72.2; H, 4.8; Cl, 7.2.

Compound **10** was also prepared by heating 4.8 g (0.025 mol) of ethyl benzoylacetate, 10.4 g (0.50 mol) of **4**, and 30 ml of boron trifluoride etherate on the steam bath for 4 hr. The product was isolated as just described and was obtained in 6.2-g yield.

Compound **10** was also prepared from 17 g of the adduct of **4** and dimethyl malonate, 4,4-dicarbomethoxy-3-phenylpropiophenone,[11] 10 g of **4**, and 30 ml of boron trifluoride etherate. The reaction was carried out as already described, to yield 12 g of **10**.

A mixture of 0.015 mol of 2-benzyl-1,3,5-triphenylpentane-1,5-dione and trityl perchlorate in 35 ml of acetic acid was refluxed for 15 min and cooled; the solid was collected and recrystallized from acetic acid to yield 4 g of **10**.

3-Carbethoxy-2,4,6-triphenylpyrylium Perchlorate (11).—A mixture of 12 g (0.03 mol) of **9**, 10.8 g (0.032 mol) of trityl perchlorate, and 75 ml of acetic acid was refluxed for 5 min, cooled, and diluted with a large volume of ether; the solid that separated was collected. The solid was recrystallized from acetic acid to yield 6.2 g of **11**, mp 235°. The ultraviolet spectrum in acetonitrile showed peaks at λ 235 mμ (ε 13,900), 275 (16,800), 351 (27,200) and 398 (24,000).

Anal. Calcd for $C_{26}H_{21}ClO_7$: C, 65.0; H, 4.4; Cl, 7.4. Found: C, 65.3; H, 4.4; Cl, 7.7.

3-Carbethoxy-2-methyl-4,6-diphenylpyrylium Perchlorate (14).—A solution of 10.4 g (0.05 mol) of **4**, 6.5 g (0.05 mol) of ethyl acetoacetate, and 40 ml of boron trifluoride etherate was heated on the steam bath for 5 hr. The reaction mixture was poured into 30 ml of ethanol and 9 ml of 70% perchloric acid and chilled. The solid was collected and recrystallized from acetic acid to yield 4.6 g of **14**, mp 178°. The ultraviolet spectrum in acetonitrile showed peaks at λ 257 mμ (ε 14,600) and 376 mμ (ε 25,500).

Anal. Calcd for $C_{21}H_{19}ClO_7$: C, 60.2; H, 4.6; Cl, 8.5. Found: C, 60.5; H, 4.7; Cl, 8.4.

2-Methyl-4,6-diphenylpyrylium Perchlorate (15).—A solution of 2 g of **14** in 20 ml of acetic acid and 12 ml of concentrated hydrochloric acid was refluxed for 2 hr. The mixture was cooled and the solid was collected and recrystallized from acetic acid to give 0.8 g of **15**, mp 205°. The product showed an infrared absorption curve which was identical with that of an authentic sample of **15**.[12]

The general procedure employed for the preparation of **16a**, **b**, **c**, **d**, and **e** was the following. A solution of 10.4 g (0.1 mol) of **4**, 0.05 mol of the acetophenone derivative, and 35 ml of boron trifluoride etherate was heated on the steam bath for 2 hr, cooled, and poured into 35 ml of methanol and 10 ml of 70% perchloric acid. The mixture was chilled and the solid was collected and recrystallized from the appropriate solvent.

3-Methyl-2,4,6-triphenylpyrylium Perchlorate (16a). From Propiophenone.—The product was obtained in 13-g yield (62%), mp 236°. The ultraviolet spectrum in acetonitrile showed peaks at λ 229 mμ (ε 14,700), 272 (17,300), 340 (17,900), and 386 (23,200).

Anal. Calcd for $C_{24}H_{19}ClO_5$: C, 68.3; H, 4.5. Found: C, 68.2; H, 4.7.

3-Ethyl-2,4,6-triphenylpyrylium Perchlorate (16b). From Butyrophenone.—This compound was obtained in 13-g (60%) yield, mp 180° (from acetonitrile). The ultraviolet spectrum in acetonitrile showed peaks at λ 248 mμ (ε 10,300), 271 (13,200), ~350 (16,000), and 380 (21,000).

Anal. Calcd for $C_{25}H_{21}ClO_5$: C, 67.2; H, 5.0. Found: C, 67.2; H, 4.8.

3-*n*-Butyl-2,4,6-triphenylpyrylium Perchlorate (16c). From Hexanophenone.—The product was obtained in 9-g yield (39%), mp 201° (from a mixture of acetonitrile and ether). The ultraviolet spectrum in acetonitrile showed peaks at λ 232 mμ (ε 16,500), 275 (9500), 332 (14,300), and 382 (11,200).

Anal. Calcd for $C_{27}H_{25}ClO_5$: C, 70.0; H, 5.4. Found: C, 69.9; H, 5.1.

2,3,4,6-Tetraphenylpyrylium Perchlorate (16d). From Desoxybenzoin.—The yield of product was 11.7 g, mp 261° (from acetic

---

(3) St. V. Kostanecki and G. Rossbach, *Ber.*, **29**, 1488 (1896).

(4) See Table I, footnote *b*.

(5) W. Schneider and G. Gramms, *ibid.*, **69**, 2543 (1936).

(6) W. C. Dovey and R. Robinson, *J. Chem. Soc.*, 1389 (1935).

(7) W. Dilthey and R. Taucher, *Ber.*, **53**, 255 (1920).

(8) W. Dilthey, G. F. Frode, and H. Koenen, *J. Prakt. Chem.*, **114**, 153 (1926).

(9) F. R. Japp and A. C. Michie, *J. Chem. Soc.*, **79**, 1017 (1901).

(10) R. Connor and D. Andrews, *J. Amer. Chem. Soc.*, **56**. 2713 (1934).

(11) E. P. Kohler, *Amer. Chem. J.*, **46**, 482 (1911).

(12) W. Schneider and F. Seebach, *Ber.*, **54**, 2289 (1921).

acid) (lit.[13] mp 261°). The ultraviolet spectrum in acetonitrile showed peaks at λ 276 mμ (ϵ 16,400) and 386 mμ (23,100).

3-Acetoxy-2,4,6-triphenylpyrylium perchlorate (16e) was obtained in 7.6-g yield, mp 230° (lit.[14] mp 230°).

Registry No.—Chalcone, 94-41-7; boron trifluoride etherate, 109-63-7; **5**, 1484-88-4; **8a**, 75696-46-5; **8b**, 15696-47-6; **8c**, 15696-48-7; **10**, 15707-55-8; **11**, 15707-56-9; **14**, 15707-57-0; **15**, 7654-52-6; **16a**, 3558-70-1; **16b**, 15707-60-5; **16c**, 15707-61-6; **16d**, 3558-71-2; **16e**, 15893-40-0.

---

[13] W. D. Dilthey and T. Bottler, *Ber.*, **52**, 2046 (1919).

[14] G. Suld and C. C. Price, *J. Amer. Chem. Soc.*, **83**, 1770 (1961).

Hydrolytic Dimerization of Ethyl 5-Amino-2-furoate[1]

GEORGE M. KLEIN,[2a] JAMES P. HEOTIS,[2a] AND JERROLD MEINWALD[2b]

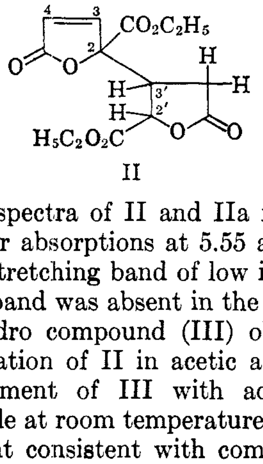
Chemistry Division, The Norwich Pharmacal Company, Norwich, New York, and Department of Chemistry, Cornell University, Ithaca, New York

Received August 30, 1967

The acid hydrolysis of ethyl 5-amino-2-furoate (I) is shown to produce two stereoisomers of diethyl [(2,2′,3′,4′,5,5′-hexahydro-5,5′-dioxo)-2,3′-bifuran]-2,2′-dicarboxylate (II and IIa). A possible mechanism for this hydrolytic dimerization is proposed.

A number of nitrofurans have acquired considerable importance as chemotherapeutic agents.[3] In connection with biochemical studies concerning the metabolism of nitrofurans,[4,5] alkaline and acid hydrolyses of ethyl 5-amino-2-furoate (I) were investigated. The alkaline hydrolysis of I to give α-ketoglutaramic acid has been reported.[6] We now wish to report on a strikingly different reaction observed when I is treated with acid.

In aqueous–alcoholic hydrochloric acid at room temperature, I was found to undergo a rapid reaction resulting in the formation of the crystalline dilactone (II) as the major product. A higher melting isomer (IIa) was obtained simultaneously in low yield. The evidence for the structural assignments is presented.



II

The infrared spectra of II and IIa revealed intense lactone and ester absorptions at 5.55 and 5.73 μ, with a double-bond stretching band of low intensity at 6.25 μ. The 6.25-μ band was absent in the spectrum of the crystalline dihydro compound (III) obtained by catalytic hydrogenation of II in acetic acid over Adams catalyst. Treatment of III with aqueous–alcoholic sodium hydroxide at room temperature gave a saponification equivalent consistent with complete hydrolysis of the lactone and ester groups of III. The high value of the saponification equivalent of II may be due to incomplete hydrolysis of the unsaturated lactonic ester portion of II. The nmr spectrum of II is shown in Figure 1a. The pair of doublets at τ 2.51, and 3.62 may be attributed to the protons on the α,β-unsaturated carbonyl system of II. The doublet at τ 5.12 may be assigned to the proton on the oxygen-bearing carbon at 2′. The simple splitting pattern of the 2′ proton, as well as mechanistic considerations, suggest monosubstitution at C-3′. The 3′ and 4′ protons appear as complex multiplets centered at τ 6.50 and 7.50, respectively. The characteristic ethyl quartet and triplet are shown at 5.71 and 8.67. The nmr spectra of II and IIa are very similar and, since structure II contains three asymmetric centers, it is reasonable to assume that these two compounds are diastereoisomers. Both show a 4-cps coupling constant for the doublet at τ 5.12 (5.42 for IIa) indicating that both have a *trans* relationship between the 2′ and 3′ protons.[7] It would appear, therefore, that the two dilactones differ by their configuration at C-2.

Ultraviolet absorption studies of the reaction of I in aqueous–alcoholic hydrochloric acid show rapid disappearance of I and suggest the formation of an intermediate, which is converted into the final products at a slower rate. Hydrolysis of the amine group during the hydrolytic dimerization of I was determined by liberation of ammonia. The biphasic nature of this hydrolysis suggests the formation of the partially hydrolyzed intermediate V or VI, either of which could be formed *via* the reaction mechanism shown in Scheme I.

Dimerization of I may be considered to proceed *via* a nucleophilic addition of C-2 in one aminofuran molecule to the electrophilic site at C-3 of another. Hydrolysis of the 5′-amino or the 5-imino group of the initially formed intermediate (IV) would lead to V or VI. When the reaction is stopped at a time when most of I has disappeared and only about half the total ammonia has been liberated (2 min), a chloroform extract of the reaction mixture shows nmr signals at τ 3.12 and 3.59 (Figure 1b) which may be assigned to the protons on the α,β-unsaturated imino system of V. When the extracted material was hydrolyzed in the presence of deuterium oxide, II was formed without deuterium substitution. This observation supports the hypothesis that the hydrolytic dimerization of I proceeds *via* V rather than VI, since hydrolysis of the 5′-amino group of VI would result in deuterium substitution at C-4′.

Hydrolytic dimerization of I in a deuterated system results in a mixture of deuterated forms of II (Figure

---

[1] A preliminary report of this work has been presented at the 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March 1966.

[2] (a) The Norwich Pharmacal Co.; (b) Cornell University.

[3] H. E. Paul and M. F Paul in "Experimental Chemotherapy," Vol. II, R. J. Schnitzer and F. Hawking, Ed., Academic Press Inc., New York, N. Y., 1964, p 307.

[4] H. E. Paul, V. R. Ells, F. Kopko, and R. C. Bender, *J. Med. Pharm. Chem.*, **2**, 563 (1960).

[5] J. Olivard, S. Valenti, and J. A. Buzard, *ibid.*, **5**, 524 (1962).

[6] G. M. Klein, J. P. Heotis, and J. A. Buzard, *J. Biol. Chem.*, **238**, 1625 (1963).

[7] H. Conroy, *Advan. Org. Chem.*, **2**, 311 (1960).