tration. The filtrate was, reduced to about 2 ml. and cooled. A yield of 0.008 g. (57%) of colorless prisms melting at 220–223° was obtained.

Anal. Calcd. for $C_9H_{10}N_2O_5$: C, 47.78; H, 4.42; N, 12.39. Found: C, 47.70; H, 4.41; N, 11.89.

Acidic Hydrolysis of III.—A solution of 1 mg. of III in 3 ml. of 0.25 N sulfuric acid was refluxed for 3 hr. Water (2 ml.) was added, and the solution was treated with excess barium carbonate. After filtration the filtrate was taken to dryness *in vacuo*, and the residue was triturated with 8 ml. of hot ethanol. After removal of additional inorganic material, the solution was evaporated to dryness *in vacuo*, and the residue was dissolved in 3 drops of water. Ultraviolet absorption data were as follows: in water, λ_{max} 262 and 205 mμ, λ_{min} 230 mμ, ratio 260/230 mμ 4.8; in sodium hydroxide (0.1 N), λ_{max} 262 mμ, λ_{min} 241 mμ, ratio 260/280 mμ 2.9. Paper electrophoresis in borate buffer, pH 6.03, using Whatman 3MM paper for 2.3 hr. at 800 v. and 12–18 ma. gave only one spot (intense) of anodic migration 8.0 cm., which corresponded to 1-β-D-lyxofuranosyluracil, anodic migration 8.0 cm. Paper chromatography in a system of acetone–chloroform–water (5:1:1) showed one spot corresponding to that of 1-β-D-lyxofuranosyluracil, R_f 0.43.

2,3'-Anhydro-1-(2',5'-di-O-mesyl-β-D-lyxosyl)uracil (X).—A solution of 0.22 g. (0.46 mmole) of 1-(2',3',5'-tri-O-mesyl-β-D-arabinosyl)uracil (IX) and 0.25 g. (3.0 mmoles) of anhydrous sodium acetate in 25 ml. of dimethylformamide was heated at 100–104° for 30 min. Solvent was removed *in vacuo*, the residue was triturated with ether, the ether was decanted, and the residue was dried. Crystals, 0.12 g. (68%), were filtered after trituration with 2 ml. of cold water. In the ultraviolet region these possessed a maximum at 230 mμ and a shoulder at 245 mμ. Crystallization from 90% ethanol gave colorless needles melting at 219–221°, 225° eff.

Anal. Calcd. for $C_{11}H_{14}N_2O_9S_2$: C, 34.55; H, 3.69; N, 7.33; S, 16.75. Found: C, 35.00; H, 3.86; N, 7.35; S, 16.94.

1-(2',5'-Di-O-mesyl-β-D-lyxofuranosyl)uracil (XI).—A solution containing 0.07 g. (0.18 mmole) of X, 5 ml. of 1 N sulfuric acid, and 20 ml. of ethanol–water (1:1) was refluxed for 23 hr. Ultraviolet spectra indicated incomplete cleavage of the anhydro bond. After treatment with excess barium carbonate and filtering, the solution was taken to dryness *in vacuo*. Pale yellow crystals separated from a small amount of cold water. These melted at 219–221° with decomposition, and had an optical rotation, $[\alpha]^{25}D$ (acetone), of +57°. Ultraviolet absorption properties in water were λ_{max} 259 mμ, λ_{min} 228 mμ, ratio 260/230 mμ 4.11. The infrared spectrum was consistent with the expected product. The mother liquor showed (paper chromatog-

raphy with acetone–chloroform–water, 5:1:1) the presence not only of the desired product, but of starting material and a small amount of uracil. Due to the difficulty encountered in obtaining a sufficient amount of pure product, an elemental analysis was not obtained. The crude material was used in the synthesis of 1-(3',5'-epoxy-2'-O-mesyl-β-D-lyxosyl)uracil (VIII).

1-(3',5'-Epoxy-2'-O-mesyl-β-D-lyxosyl)uracil (VIII). Method A.—A solution of 47 mg. (0.12 mmole) of XI, containing 33% X (determined by paper chromatographic separation, elution, and ultraviolet absorption at 260 and 230 mμ) in 4 ml. of 0.1 N sodium hydroxide was stirred at 20–25° for 18 hr. After treatment with Dowex 50 (H$^+$) and neutralization of the solution with 1 drop of triethylamine, solvent was removed *in vacuo*. Crystallization occurred upon cooling a 90% ethanolic solution. Colorless needles, 14.5 mg. (41%), m.p. 177–178°, were collected. Crystallization from 60% ethanol gave colorless needles, 11.6 mg., m.p. 177–178°.

Anal. Calcd. for $C_{10}H_{12}N_2O_7S$: C, 39.47; H, 3.98; N, 9.21. Found: C, 39.07; H, 4.16; N, 9.31.

Method B.—A solution of 11.1 mg. (0.049 mmole) of V in 3 ml. of 0.2 N sodium hydroxide was allowed to stand at 23–25° for 17 hr. After removal of sodium ions with Dowex 50 (H$^+$) the acidic solution was neutralized with 1 drop of triethylamine. The mixture was evaporated to dryness *in vacuo* with added ethanol. Paper chromatography in a system of acetone–chloroform–water (5:1:1) gave only one spot migrating with a sample of 1-(3',5'-epoxy-β-D-lyxofuranosyl)uracil (III), R_f 0.71. The residue was dried well *in vacuo*, dissolved in 2 ml. of pyridine, and treated with 0.035 g. (0.30 mmole) of methanesulfonyl chloride in the cold. After standing at 4° overnight 1 drop of ethanol was added. After 30 min. the mixture was evaporated to dryness several times with ethanol, then dried. To the residue was added 3 drops of water. The mixture was allowed to stand 2 days at 23–25°. Needles, 3.5 mg. (32%), m.p. 165–175°, were collected. Crystallization from water gave colorless needles, m.p. 175–179°. A mixture of this sample and a sample prepared by method A, m.p. 176–179°, melted at 176.5–179°. Infrared and ultraviolet absorption spectra of samples prepared by the two methods were identical.

Ozonation of 2,5-Diphenylfuran[1]

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Ozonations of 2,5-diphenylfuran (Ib) in both participating and nonparticipating solvents are described. The percentages of 1,2-bond-cleavage products [1,2-dibenzoylethylene (VIIb) or ozonolysis products thereof] and of 2,3-bond-cleavage products [β-benzoyloxycinnamaldehyde (IXb) or peroxidic precursors or decomposition and ozonolysis products thereof] have been accurately determined. Both the type of solvent and the reaction temperature affect the competition between the two types of reactions involved. General mechanisms are proposed to account for the competitive reactions which occur during ozonation of furans.

Wibaut and co-workers[3–5] were the first[3] to report the ozonation of furans and pyrroles to give not only

(1) For a preliminary report on a part of this work, see P. S. Bailey and H. O. Colomb, Jr., *J. Am. Chem. Soc.*, **79**, 4238 (1957).

(2) To whom inquiries should be directed.

(3) (a) J. P. Wibaut and A. R. Guljé, *Koninkl. Ned. Akad. Wetenschap., Proc., Ser. B.*, **54**, 330 (1951); (b) J. P. Wibaut, *Ind. chim. belge*, **20**, 3 (1955); (c) J. P. Wibaut, *J. chim. phys.*, **53**, 143 (1956); (d) J. P. Wibaut, *Advan. Chem. Ser.*, **21**, 153 (1959).

(4) B. P. Jibben and J. P. Wibaut, *Rec. trav. chim.*, **79**, 342 (1960).

(5) (a) J. P. Wibaut, *Chimia* (Aarau), **11**, 321 (1957); (b) J. P. Wibaut, *Festschr. Arthur Stoll*, 249 (1957); (c) J. P. Wibaut, *Koninkl. Ned. Akad. Wetenschap., Verslag Gewone Vergader. Afdel. Nat.*, **71**, 141 (1962).

the expected ozonolysis products, but also products resulting from cleavage of bonds other than the double bonds of the classical valence structures (*e.g.*, methyl-glyoxal, Xa, from 2,5-dimethylfuran, Ia).

In 1957 we published a preliminary report on the ozonation of 2,5-diphenylfuran (Ib, in methanol–acetone solvent) to give a 12% yield of *cis*-1,2-dibenzoylethylene (VIIb), with 1 mole equiv. of ozone, or a 14% yield of phenylglyoxal (Xb) with 2 mole equiv. of ozone.[1] We suggested that (1) VIIb was produced *via* a 1,4-
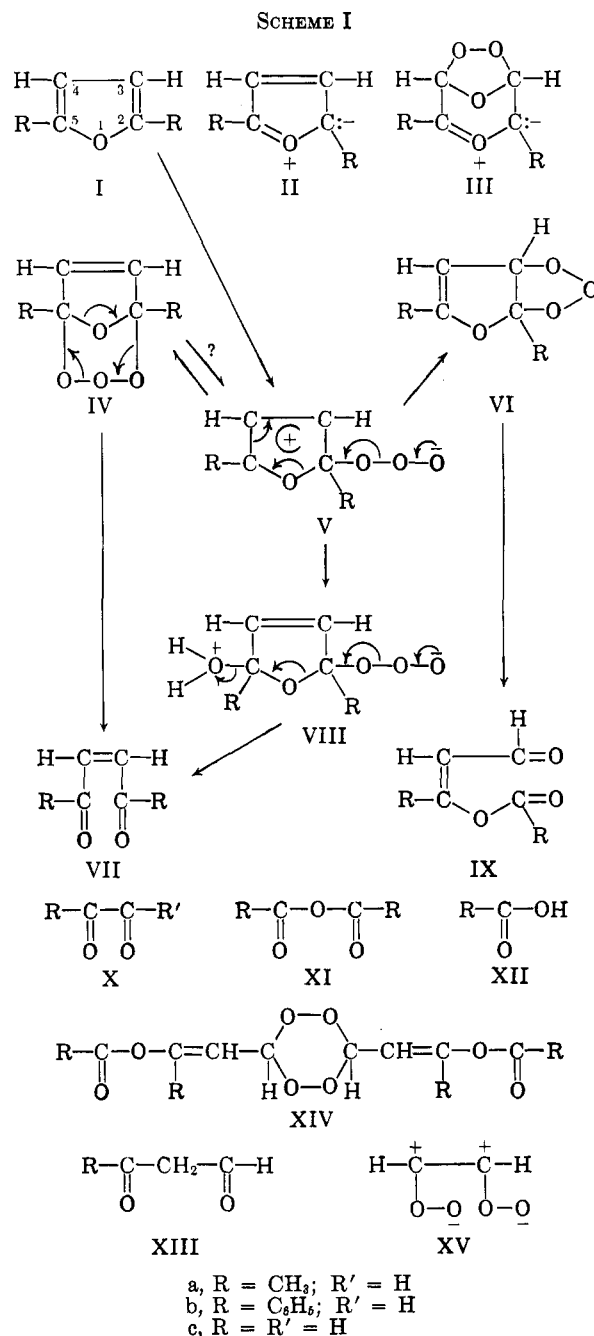
addition of ozone to the reactive furan diene system[6] (*e.g.*, Ib → IVb → VIIb + O$_2$), (2) phenylglyoxal (Xb) resulted from further ozonation of VIIb, and (3) Wibaut's[3-5] results involved a similar reaction mechanism. Since then, Lutz and Dien[8] have correctly suggested that *cis*-1,2-dibenzoylethylene (VIIb) could just as well have resulted from an electrophilic attack of ozone on Ib to give a σ-complex (Vb, which may or may not be in equilibrium with IVb), followed by loss of molecular oxygen.

Although Wibaut[3,5,9] suggested a mechanism similar to this for the ozonation of pyrroles to products other than those expected from ozonolysis of the classical valence structures, he and Jibben[4] rejected such a mechanism for the analogous ozonation of alkyl-substituted furans in solvents such as chloroform (non-participating solvents[11,12]) on the basis that only 1.6 rather than 2.0 mole equiv. of ozone was required to complete the ozonation. Instead, they made the unlikely suggestion that, although normal ozonolysis of furans requires 2 mole equiv. of ozone, products such as methylglyoxal (Xa), from Ia, result from the attack of 1 mole equiv. of ozone on canonical structures such as IIa, to give ozonides such as IIIa, which cleave directly to the substituted glyoxal (*e.g.*, IIIa → 2Xa).

In the present paper we report ozonations of 2,5-diphenylfuran (Ib) in both participating[12] and non-participating solvents, cite further evidence for the mechanism involving V, and suggest how this mechanism can be reconciled with the results of Jibben and Wibaut.[4]

Ozonation of 2,5-diphenylfuran (Ib) with 1 mole equiv. of ozone was quantitative in all of the solvents tried, and all of the starting material appeared to be consumed. The products of the reaction were *cis*-1,2-dibenzoylethylene (VIIb, from 1,2-bond cleavage) and peroxidic precursors (and/or decomposition products thereof) of β-benzoyloxycinnamaldehyde (IXb, from 2,3-bond cleavage). These, apparently, are less reactive toward ozone than is the starting furan (Ib) and do not react appreciably with ozone until all of Ib is consumed. Active oxygen determinations on the reaction mixtures showed 0.8 equiv. from ozonation in methylene chloride at 25°, and 0.75 equiv. from ozonation in glacial acetic acid at 10°. (See Scheme I.)

When the ozonation was allowed to proceed further, essentially quantitative absorption occurred until 1.3–1.8 mole equiv. of ozone had been absorbed, after which absorption continued, with some ozone passing into the trap, until at least 2.0 mole equiv. of ozone had reacted with Ib. From such reactions the 1,2-bond-cleavage products should be phenylglyoxal (Xb) and/or peroxides which should reduce to Xb,[12] and the 2,3-bond-cleavage products should be glyoxal (Xc) and benzoic anhydride (XIb, or benzoic acid, XIIb), and/or

(6) 1,4-*Additions of ozone occur with the anthracene ring system.*[7]

(7) (a) R. E. Erickson, P. S. Bailey, and J. C. Davis, Jr., *Tetrahedron*, **18**, 389 (1962); (b) P. S. Bailey, P. Kolsaker, B. Sinha, J. B. Ashton, F. Dobinson, and J. E. Batterbee, *J. Org. Chem.* **29**, 1400 (1964).

(8) R. E. Lutz and C. K. Dien, *ibid.*, **23**, 1861 (1958).

(9) He, however, showed the central atom of the ozone molecule making the electrophilic attack. Not only is this unlikely on the basis of the structure of the ozone molecule,[10, 11] but it is difficult to rationalize the loss of molecular oxygen from such a complex.

(10) J. Meinwald, *Chem. Ber.*, **88**, 1889 (1955).

(11) P. S. Bailey, *Chem. Rev.*, **58**, 925 (1958).

(12) P. S. Bailey, S. B. Mainthia, and C. J. Abshire, *J. Am. Chem. Soc.*, **82**, 6136 (1960).

SCHEME I

a, R = CH$_3$; R' = H
b, R = C$_6$H$_5$; R' = H
c, R = R' = H

peroxides which should reduce to these. Benzoic acid (XIIb) could also come from rearrangement of peroxides which should yield phenylglyoxal (Xb) upon reduction.[12,13] The products from ozonation of Ib with approximately 2 mole equiv. of ozone in the presence of methanol, followed by a reductive work-up, were phenylglyoxal (Xb), in about the same yield that dibenzoylethylene (VIIb) was obtained from 1 mole equiv. of ozone experiments in methanol, and benzoic acid (XIIb) in good yield. Similar ozonations of Ib in carbon tetrachloride or methylene chloride gave only benzoic anhydride (XIb) and/or benzoic acid (XIIb). In one instance (methylene chloride) a 22% yield (0.44 mole equiv.) of benzoic acid was extracted with sodium bicarbonate. The rest of the material was shown by its infrared spectrum to be largely benzoic anhydride. These differences are to be ex-

(13) (a) P. S. Bailey and S. S. Bath, *ibid.*, **79**, 3120 (1957); (b) P. S. Bailey and Y. G. Chang, *J. Org. Chem.*, **27**, 1192 (1962).

<div align="center">

Table I

Ozonations of 2,5-Diphenylfuran (Ib)[a] with 1 Mole Equiv. of Ozone[b]

</div>

Expt.	Solvent	Temp., °C.	O₂ evolved[c]	VIIb[c,d]	XIIb[c]	Work-up[e]
				—————% yield—————		
1	CH_2Cl_2	−78	4	3	26	A
2	CH_2Cl_2	−40	5	5	f	A
3	CH_2Cl_2	−20	9	8[d]	27	A
4	CH_2Cl_2	−20	b	7	25	A
5	CH_2Cl_2	0	10	f	f	f
6	CH_2Cl_2	25	11	10[d]	33	A
7	CCl_4	15–20	b	10[d]	f	E
8	CH_2Cl_2–CH_3OH (1:1)	−70	2	3[d]	f	D
9	CH_2Cl_2–CH_3OH (1:1)	−20	b	12[d]	43–66[g]	D, F
10	CH_3OH	−20	b	11–14	45–57[h]	C, G
11	CH_3OH–HOH (9:1)	−20	b	14	59	C
12	gl. HOAc	10	b	12	56	B
13	gl. HOAc[i]	10	11	11	55	B
14	gl. HOAc	25	b	18	68	B
15	gl. HOAc	25	20	21	71	C
16	HOAc–HOH (9:1)	0	24	25	56	C
17	HOAc–HOH (9:1)	25	b	31	63	B
18	HOAc–HOH (9:1)	25	18–21[j]	32–33[j]	104[k]	C
19	88% formic acid	25	b	33	32	B
20	Acetone–aqueous HCl[l]	−20	b	15[d]	81	H

[a] All 10–20 mmoles of Ib that was employed was consumed in these experiments. [b] Ozone–nitrogen[14,15] rather than ozone–oxygen mixtures were used, except in expt. 4, 7, 9–12, 14, 17, 19, and 20, and absorption was quantitative. [c] Mole per cent based on Ib or ozone reacting. [d] In expt. 3, 6–9, and 20 the *trans* isomer was produced because the acidic reaction mixture was allowed to stand (often times with iodine present, after reduction with iodide). In expt. 19, part of the product (2%) was *trans*. In all other experiments the product was the pure *cis* isomer. [e] See Experimental section for work-up procedures. [f] Not determined. In expt. 5 only the oxygen yield was determined. [g] The higher yield of benzoic acid was from work-up procedure F. [h] The higher benzoic acid yield was obtained by work-up procedure G. [i] From similar experiments using a 1:1 mixture of methylene chloride–glacial acetic acid at 10°, the molecular oxygen yield was 5% and the yield of VIIb was 6%. The benzoic acid yield was 55%. [j] Result of several experiments. [k] Determined in a separate, identical experiment, except that ozone–oxygen was used. [l] Acetone, 9 parts, and 1 part concentrated hydrochloric acid.

pected since ozonolysis of *trans*-1,2-dibenzoylethylene in methanol, followed by a reductive work-up, gave a good yield of phenylglyoxal (Xb), and ozonolysis of the same compound in carbon tetrachloride gave largely benzoic acid regardless of work-up procedure[12]; presumably the same is true with the *cis* isomer (VIIb).

Whereas ozonations of Ib with 1 mole equiv. of ozone from ozone–nitrogen mixtures[14,15] generally gave molecular oxygen yields[15] equal to those of the 1,2-bond-cleavage product (VIIb), ozonations with 2 mole equiv. of ozone in both methylene chloride and 90% acetic acid solvents gave additional quantities of molecular oxygen, equal to approximately 0.45 mole/mole of peroxidic precursors of IXb reacting. We believe this due to decomposition of a diozonide, or other peroxidic equivalents of zwitterion XVb,[11] thus accounting, also, for the nonisolation of glyoxal (Xc) or equivalents thereof.

The most significant results were from the 1 mole equiv. of ozone experiments. Table I shows the yields of the 1,2-bond-cleavage product (VIIb) and one of the 2,3-bond-cleavage products, benzoic acid (XIIb), from ozonations in several different solvents. Assuming that the benzoic acid comes entirely from hydrolysis of peroxidic precursors of IXb, the combined VIIb and XIIb yields should total 100%. When the ozonation was carried out in 90% acetic acid, this was very nearly true, even with a mild work-up (expt. 17). The same was true in expt. 20, where hydrochloric acid was present in the solvent. With methyl-

(14) G. A. Cook, A. D. Kiffer, C. V. Klumpp, A. H. Malik, and L. A. Spence, *Advan. Chem. Ser.*, **21**, 44 (1959).

(15) P. S. Bailey and A. M. Reader, *Chem. Ind.* (London), 1063 (1961).

ene chloride solvent and essentially the same work-up procedure the benzoic acid yields were only 25–33% (expt. 1, 3, 4, and 6), except in one instance where the reaction mixture was allowed to stand in the presence of acetic acid overnight, in which case the benzoic acid yield was 55% and the combined yields of VIIb and XIIb totaled about 67%. Thus, some hydrolysis of peroxidic precursors of IXb occurs during work-up of the reaction mixtures, and, probably, also during the ozonation, as suggested by the sodium bicarbonate extraction of 0.44 mole equiv. of benzoic acid from a 2 mole equiv. of ozone experiment in methylene chloride. Such hydrolyses would also be expected to occur with alkylfuran intermediates such as IXa, especially during the slow ozonations necessary with ozone obtained electronically.[4] This would result in substances such as XIIIa, with no double bonds remaining, and the utilization of less than 2 mole equiv. of ozone by the alkylfurans.' This, certainly, is a much more satisfactory explanation for the results of Jibben and Wibaut[4] than their highly improbably mechanism involving III.

Other "bond-attack" products isolated from the 1 mole equiv. ozonations of Ib were (1) 5–20% yields of dimeric peroxide XIVb from ozonation in methylene chloride followed by a nonreductive work-up and (2) about a 30% yield of acylal XVI from ozonation in either methylene chloride or glacial acetic acid followed by reduction with sodium iodide in acetic acid. Evidence for structure XIVb was elemental analyses, molecular weight, a peroxidic test with iodide ion in hot acetic acid, hydrolysis to benzoic acid, and infrared and n.m.r. spectra. The infrared spectrum showed a vinyl ester carbonyl band shifted to slightly

higher wave length (5.75) by the phenyl substituent at the α carbon atom, peroxy bands at 9.3–9.5, a carbon–carbon double bond band at 6.01, and no band for aldehydic hydrogen at 3.6–3.7 or for an α,β-unsaturated aldehyde at 5.9–6.0 μ (as would be found had the zwitterion formed at C-2 during ozonolytic cleavage of the 2,3-bond of Ib). Along with XIVb, monomeric and/or polymeric ozonides are probably produced in nonparticipating solvents.

Elemental analyses for the acylal fit either structure XVI or XVII. Both the infrared and n.m.r. spectra favor structure XVI, which could be produced from XIVb, an ozonide, XVIIIb, or even XIXb, by the following reactions, not necessarily in the order listed: (1) reduction, (2) acylal formation, (3) hydrolysis of the benzoyloxy group, (4) ketonization.

The infrared spectrum shows a typical benzoyl carbonyl band at 5.95, typical ester carbonyl bands

at 5.7–5.75 μ, but no aldehydic hydrogen band. The n.m.r. spectrum accounts for all protons; the band of one of these is too far upfield for an aldehydic proton, but is reasonably situated for the proton on the carbon atom of XVI to which the acetoxy groups are attached.

The 1,2-dibenzoylethylene produced was always the cis isomer (VIIb), except in cases where an acidic reaction mixture was allowed to stand for a period of time, in which case either the more stable[16] trans isomer or a mixture of the cis and trans isomers was obtained. The cis-dibenzoylethylene (VIIb) was produced directly, rather than via a peroxidic precursor, since it precipitated upon addition of water to the reaction mixture (in the case of methanol or acetic acid solvents). The yield of VIIb was the same, within experimental error, whether an ozone–oxygen or an ozone–nitrogen[14,15] mixture was used (cf. expt. 3, 4, 12–15, 17, and 18, Table I).

One mole of molecular oxygen was evolved per mole of VIIb produced in the ozone–nitrogen experiments (expt. 1–3, 6, 8, 13, 15, and 16), except in the case of 90% acetic acid solvent at 25° (expt. 18). We believe that in this case the molecular oxygen yield was low owing to reaction of some oxygen, as it was produced, with compounds in the reaction mixture, such as XIIIb. In 90% acetic acid the peroxidic 2,3-bond-cleavage product from the 1 mole equiv. ozonation is probably XVIIIa or, less likely, XIXa. At 25° it is quite likely that these substances would undergo loss of hydrogen

(16) L. P. Kuhn, R. E. Lutz, and C. R. Bauer, J. Am. Chem. Soc., 72, 5058 (1950).

peroxide and hydrolysis (not necessarily in the order named) to give XIIIb, which could then undergo peroxide-catalyzed autoxidation (using up some of the molecular oxygen yield of expt. 18) to give peroxides (e.g., XX) which could decompose to benzoic acid (XIIb). Evidence for this proposal is first, XIIIb does oxidize to XIIb in the presence of hydrogen peroxide. Second, the molecular oxygen yields coincided with the yields of VIIb in the cases of ozonations at 25° in methylene chloride (expt. 6) and glacial acetic acid (expt. 15), where the peroxidic intermediate (an ozonide, XIVb, XVIIIb or XIXb) can not split out hydrogen peroxide, or otherwise readily afford XIIIb. The yields of molecular oxygen and VIIb also coincided in expt. 16 (ozonation in 90% acetic acid at 0°) where the reaction temperature, apparently, was too low for appreciable hydrolysis of IXb (or XVIIIa or XIXa) or oxidation of XIIIb to occur. Third, when an ozonation in 90% acetic acid at 25° was worked up by addition of water followed by refluxing, the yield of benzoic acid increased (probably from decomposition of XX) to 104% (expt. 18, footnote k), whereas the yields of VIIb and benzoic acid together normally should not exceed 100%. A similar work-up of a glacial acetic acid reaction mixture gave no excess benzoic acid (expt. 15). Fourth, no greater yield of VIIb was obtained in expt. 17 than in expt. 18, indicating that attack by molecular oxygen on Ib is not the reason for the increased yields of VIIb in 90% acetic acid at 25°; neither did hydrogen peroxide in acetic acid oxidize Ib at 25°. Thus we believe that the yields of VIIb in expt. 17 and 18, rather than the molecular oxygen yield in expt. 18, represent the true extent to which 1,2-bond cleavage by ozone occurs with Ib under the conditions employed.

It is apparent from Table I that both solvent and temperature effects are operative in regard to the proportions of 1,2-bond- and 2,3-bond-cleavage products obtained from ozonation of Ib. Comparisons of expt. 1–6, 8 and 9, 12 or 13 and 14 or 15, and 16 and 18 show definite, though small, temperature effects with methylene chloride, methanol, and the acetic acid solvents; expt. 6, 15 and 18 prove definite solvent effects, as do also to a lesser degree expt. 3 and 9–11. Unfortunately, it was impossible to compare methanol with the acetic acid solvents at the same temperature, since at temperatures much above −20° methanol reacted with ozone at the expense of Ib, and the acetic acid solvents freeze at 0–5°. Also, although a methylene chloride–methanol mixture apparently has the same effect as methanol as a solvent (cf. expt. 9 and 10), the same is not true in regard to acetic acid vs. methylene chloride–acetic acid mixtures as solvents (the yields of VIIb were much lower in the case of the latter; cf. expt. 13, footnote i). It seems likely, however, that the nucleophilic solvents methanol and water (from 90% acetic acid) would give similar results f they could be compared at the same temperature, since the yield of VIIb was essentially the same from methanol at −20° as it was from glacial acetic acid at 10° (expt. 9–13, showing that the more nucleophilic methanol is superior to acetic acid) and since there is a definite temperature effect with both glacial and 90% acetic acids (expt. 12–18, indicating that the temperature effect should continue also with methanol).

A comparison of expt. 10, 11, and 20 shows that it is the nucleophilicity rather than the acidity or polarity of the solvent that is important. Thus, it appears that the ratio of 1,2-bond- to 2,3-bond-cleavage products increases as both the reaction temperature and the nucleophilicity of the solvent increases.

We, therefore, propose the following mechanisms for the ozonation of 2,5-diphenylfuran (Ib) and furans in general. Two types of initial ozone attack occur. One is an electrophilic attack at a reactive α-position, to give σ-complex V. The other is an attack on the 2,3-bond to give VI, either through a four-center reaction, or, more likely via a π-complex.[12] Whereas VI can afford only 2,3-bond-cleavage products, V can yield either 2,3-bond-cleavage products (through completion of a 1,2-addition to give VI) or 1,2-bond-cleavage products, by loss of molecular oxygen to give VII. The latter would occur, as shown in V, to produce the double bond at the same time that ring cleavage occurs, thus giving the cis isomer. As the reaction temperature increases, the tendency for V to lose molecular oxygen rather than to cyclize to VI should increase, thus leading to increased yields of VII. As the nucleophilicity of the solvent increases, there should be an increasing stabilization (of the type shown in VIII) of the σ-complex. This should not only lower the activation energy for σ-complex formation and allow it to compete more favorably with initial formation of VI, but also should increase the tendency for the σ-complex (VIII) to lose oxygen (and the solvent molecule) and produce VII, rather than to cyclize to VI. This same effect of nucleophilic solvents appears to be a factor in the ozonation of 9,10-dibromoanthracene.[17] Probably, also, polarization of ozone by the more polar solvents, increasing the ease of reaction to give V rather than VI, plays a minor role.

Experimental

The ozonation set-up and procedures are described in earlier publications.[7b,13a,15] Solvents were pure and anhydrous, unless otherwise stated. 2,5-Diphenylfuran (Ib) was prepared by the standard procedure,[18] and melted sharply at 90°.

Ozonations of 2,5-Diphenylfuran (Ib) with 1 Mole Equiv. of Ozone.—In most experiments a solution of 2.2 g. (10 mmoles) of Ib in 100 ml. of the solvent was treated with either an ozone–oxygen (ca. 3% ozone) or an ozone–nitrogen[14,15] stream containing 10 mmoles of ozone; ozone absorption by the reaction mixture was quantitative. When an ozone–nitrogen mixture was used the molecular oxygen yield was usually determined, by procedures previously described.[7b,15] Several different work-up procedures were employed. These are described below and the results are listed in Table I.

Work-Up Procedure A.—The solvent was removed under reduced pressure and the residue was dissolved in about 50 ml. of 95% ethanol. The solution was poured into a solution of 5 g. of sodium iodide in 10 ml. of glacial acetic acid. After at least an hour, the liberated iodine was reduced with sodium thiosulfate solution, and the resulting solution or mixture was extracted three times with 75-ml. portions of ether. The ether extract was extracted with several 100-ml. portions of saturated sodium bicarbonate solution, after which it was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was crystallized from 95% ethanol, giving crude 1,2-dibenzoylethylene (VIIb) (cis, m.p. ca. 120–125°; trans, ca. 101–107°); recrystallized from 95% ethanol (cis, m.p. 134–135°;

(17) P. Kolsaker, P. S. Bailey, F. Dobinson, and B. Kumar, J. Org. Chem., 29, 1409 (1964).

(18) R. E. Lutz and R. J. Rowlett, Jr., J. Am. Chem. Soc., 70, 1359 (1948).

trans, 110–111°). The dibenzoylethylene was usually cis, unless the acetic acid–iodide reduction mixture was allowed to stand for several hours or overnight. Infrared spectra showed the crude products to be almost pure; recovery from recrystallization was high, but, for exactness, small corrections in yield were made with the cis compound, based on the determined solubility of the pure compound in 95% ethanol at the ice-bath temperature. The bicarbonate extract was acidified with hydrochloric acid and extracted with ether. The ether extract was dried and evaporated, yielding crude benzoic acid (XIIb), m.p. ca. 110–112°; recrystallization from 50 ml. of water gave m.p. 121–122°; corrections in yield were made based on the determined solubility of pure benzoic acid in water at the ice-bath temperature.

Work-up procedure B was used only when the ozonation solvent was miscible with water. The ozonation mixture was diluted to turbidity with water and cooled at 10° for several hours or overnight. Filtration gave crude cis-dibenzoylethylene (VIIb) which was purified as described in procedure A. The filtrate was reduced with sodium iodide and worked up for benzoic acid as described in procedure A.

Work-up procedure C was similar to that of B except that, after the isolation of VIIb, the filtrate was refluxed until it gave a negative iodide test for active oxygen, after which it was worked up as in procedure A to give benzoic acid and a small amount of tar (neutral layer).

Work-Up Procedure D.—The ozonation mixture was poured into a solution of 5 g. of sodium iodide and 10 ml. of glacial acetic acid. After at least an hour, the released iodine was reduced with sodium thiosulfate solution and the nonmiscible ozonation solvent was removed by distillation. The remainder of the work-up was the same as procedure A.

Work-Up Procedure E.—The reaction mixture was evaporated and the residue was taken up in 95% ethanol as in procedure A. The ethanol solution was cooled in the freezer overnight. Filtration then yielded trans-1,2-dibenzoylethylene. In this case the reaction mixture was not worked up immediately, thus accounting for isomerization of cis (VIIb) to trans.

Work-up procedure F was like procedure D except that the filtrate from which the crude dibenzoylethylene was obtained was evaporated and the residue was hydrolyzed with potassium hydroxide to give additional benzoic acid (XIId).

Work-up procedure G was identical to procedure B, except that a catalytic hydrogenation (palladium on barium carbonate) was used rather than reduction by iodide ion.

Work-up procedure H was like procedure B except that the filtrate from which dibenzoylethylene was obtained was simply extracted with ether to obtain benzoic acid (XIId).

Benzoylacetaldehyde Diacetylacylal (XVI).—The ozonation of Ib was carried out in methylene chloride at 25°; the work-up was essentially procedure D. In one case the iodide reduction was carried out under nitrogen and the titration with 0.1 N sodium thiosulfate showed 80% active oxygen. In another case the acetic acid–sodium iodide reduction mixture was allowed to stand overnight. The benzoic acid yield in this case was 55%, which was considerably higher than usual (expt. 1–6, Table I). The filtrate from which the dibenzoylethylene was removed in procedure D was diluted with water to turbidity, cooled overnight in the refrigerator, and filtered to give a 32% yield of crude XVI melting at 50–55°. Recrystallization from benzene–ether raised the melting point to 80°.

Anal. Calcd. for $C_{13}H_{14}O_5$: C, 62.4; H, 5.6; mol. wt., 250. Found: C, 62.2; H, 5.7; mol. wt. (osmometer), 245.

The n.m.r. spectrum (carbon tetrachloride) had a sharp peak at τ 8.0 (acetyl), a doublet centered on 6.62 with $J = 6$ c.p.s. (—CH$_2$—), a triplet centered on 2.97 with $J = 6$ c.p.s. [—CH-(OAc)$_2$], and unresolved multiplet centered on 2.3 (aromatic). The relative areas were 6, 2, 1, and 5, respectively.

The infrared spectrum of the crude acylal showed it to be almost pure in spite of its low melting point; much is lost, however, during recrystallization. In some experiments the crude acylal was obtained as an oil in as high as 50% yield; the infrared spectrum showed it to be almost pure XVI. The acylal was also obtained in a similar fashion after ozonation of Ib in glacial acetic acid at 10° (a careful active oxygen determination on the reaction mixture in one case gave 75%). It did not appear to be present in 90% acetic acid ozonation mixtures, however, as indicated by infrared spectra of the oils obtained, instead. Probably this oil is a mixture of decomposition products of IXb and XIIIb.

When the acylal (XVI) was heated at 175° until it decomposed, and the product was analyzed by v.p.c., only one peak, identical with that for pure acetophenone, was obtained.

Dimeric β-Benzoyloxycinnamaldehyde Peroxide (XIVb).—The ozonation of Ib was carried out in methylene chloride and worked up essentially by procedure A. Instead of immediately reducing the ethanol solution (or suspension) of the residue left by evaporation of the ozonation mixture, it was cooled in the refrigerator overnight, to give 5–20% yields of the peroxide, melting at 155–165°; recrystallized from ethanol, m.p. 170°. The filtrate was then reduced as in procedure A. The peroxide gave a weak active oxygen test with iodide ion in hot acetic acid, as is typical of such dimeric peroxides.

Anal. Calcd. for $C_{32}H_{24}O_8$: C, 71.6; H, 4.5; mol. wt., 536. Found: C, 71.6; H, 4.5; mol. wt., 527.

The infrared spectrum showed strong bands at 5.75, 9.3–9.5, and 6.01 μ.

Hydrolysis of 0.3 g. of XIVb with 10 ml. of 10% potassium hydroxide over the steam bath gave, after acidification, extraction with ether, and evaporation of the ether extract, a 62% yield of benzoic acid (XIIb); identification was by infrared spectrum.

Ozonation of 2,5-Diphenylfuran (Ib) with 2 Mole Equiv. of Ozone.—The ozonation was carried out as described for the 1 mole equiv. experiments. Ozone absorption was quantitative in all solvents until about 1.3–1.8 mole equiv. of ozone had reacted, depending largely on the rate of ozonation. From then on, some ozone passed into the trap, but, if ozonation was continued, 2.0–2.7 mole equiv. of ozone actually reacted with Ib (total amount passed minus trap). The following are examples.

A. Ozonation with ozone–nitrogen in 90% acetic acid at 25° resulted in absorption of essentially 2 mole equiv. of ozone and the release of 0.52 mole equiv. of molecular oxygen. Reduction of the reaction mixture with sodium iodide under nitrogen, and determination of the released iodine with standard 0.1 N thiosulfate, showed 1.1 equiv. of active oxygen. With a similar ozonation in methylene chloride solution at −20°, 0.52 mole equiv. of molecular oxygen also was released. The low active oxygen yield is consistent with the fact that excess oxygen is evolved in the 2 mole equiv. ozonations.

B. Ozonation in Methylene Chloride–Methanol (1:1).—The ozonation was carried out at −20° and 1.8 mole equiv. of ozone was absorbed. The work-up procedure was the same as procedure D above through the sodium bicarbonate extraction, from which benzoic acid was obtained. After the sodium bicarbonate extraction, the ether layer was extracted three times with 20-ml. of 30% sodium hydroxide solution. When the sodium hydroxide extract was acidified and cooled, more benzoic acid was obtained. Extraction of the filtrate with four 30-ml. portions of ether, and evaporation of the ether extract (after drying over anhydrous sodium sulfate) gave an oil which crystallized from benzene to give *dl*-mandelic acid. Evaporation of the benzene filtrate and recrystallization of the residue from benzene-petroleum ether (b.p. 40–60°) gave additional mandelic acid. The total benzoic acid yield was 20% (m.p. 121–122°) and the total mandelic acid yield was 13% (m.p. 118–120°), each based on an expected 2 mole equiv., and each identified by a mixture melting point with an authentic sample. The mandelic acid yield represents the yield of phenylglyoxal (Xb), which is converted to mandelic acid with strong base.[12]

C. Ozonation in Methanol–Acetone (1:1).—The reaction was carried out at about −40°; 2.7 mole equiv. of ozone reacted with Ib. The reaction mixture was hydrogenated over palladium on barium carbonate (1.4 mole equiv. of hydrogen reacted), after which it was filtered (to remove catalyst) and evaporated. The residue was treated with 100 ml. of water at the reflux temperature for 30 min., after which the resulting

mixture was extracted eight times with 20-ml. portions of petroleum ether (b.p. 40–60°). Evaporation of the water layer, extraction of the residue with acetone, and evaporation of the acetone extract gave a 13% yield (based on an expected 2 mole equiv.) of phenylglyoxal (Xb), identified as the *p*-nitrophenylhydrazone (m.p. and m.m.p., with an authentic sample, 310°).[19] Evaporation of the petroleum ether extracts, extraction of the residue with 5% sodium hydroxide solution, and acidification of the basic extract gave a 74% yield of benzoic acid (m.p. 121–122°), based on an expected 2 mole equiv.

D. Ozonation in Carbon Tetrachloride.—The reaction was carried out at 0° and 1.7 mole equiv. of ozone reacted. The reaction mixture was catalytically hydrogenated as in the preceding experiment, and then filtered and evaporated. The residue was dissolved in ether and extracted twice with sodium bicarbonate solution. Acidification of the bicarbonate layer gave a 51% yield of benzoic acid (m.p. 121–122°) based on an expected 2 mole equiv. The ether layer was evaporated and the residue was distilled at 150–170°. This material was shown to be at least 88% benzoic anhydride by hydrolysis to benzoic acid; this represents, at least, a 38% yield of benzoic anhydride (XIb).

E. Ozonation in Methylene Chloride.—After absorption of 2 mole equiv. of ozone by Ib in methylene chloride at −40°, the reaction mixture was evaporated and the residue was hydrolyzed with excess 2 *M* potassium hydroxide in methanol. The solution was evaporated and the residue was taken up in water and acidified. An essentially quantitative yield (based on an expected 2 mole equiv.) of benzoic acid melting at 120–121° was obtained (see discussion section concerning reactions of the 1,2-bond-cleavage product VIIb with ozone). In another experiment, the ozonation mixture was stirred with an equal volume of sodium bicarbonate solution for 30 min. Separation and acidification of the bicarbonate layer gave a 22% yield of benzoic acid (m.p. 121–122°) based on the expected 2 mole equiv. An infrared spectrum of the methylene chloride layer showed it to contain largely benzoic anhydride.

Attempted oxidation of 2,5-diphenylfuran (Ib) by hydrogen peroxide (10 mmoles of Ib, 90 ml. of glacial acetic acid, 4 ml. of 30% hydrogen peroxide, and 6 ml. of water) at room temperature for 1 hr. under nitrogen failed. Dilution of the reaction mixture with water gave a 98% recovery of pure Ib.

Oxidation of benzoylacetaldehyde (XIIIb, 0.5 g., prepared by the method of Allan, Forman, and Ritchie[20]) with 3 ml. of 30% hydrogen peroxide in 20 ml. of glacial acetic acid at 100° for 1 hr. gave a 23% yield of benzoic acid; identification was by infrared spectrum. The reaction mixture was worked up by dilution with a large volume of water, extraction with ether, extraction of the ether extract with sodium bicarbonate solution, acidification of the bicarbonate layer, extraction with ether, and evaporation of the ether layer.

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