extracts were dried over calcium chloride and the solvent removed to leave an oily residue which, dissolved in 4 ml. of carbon tetrachloride, was added to a solution of 70 mg. of iodine in 10 ml. of carbon tetrachloride. After several minutes the iodine color had faded almost completely and another portion (50 mg.) of iodine in carbon tetrachloride (7 ml.) was added. The resulting slightly red-brown solution was concentrated at room temperature under a stream of nitrogen and the residue recrystallized from a small amount of carbon tetrachloride to give, in two crops, 294 mg. of diiodide **10**, m.p. 186–189°, identified by mixture m.p. with an authentic sample described above. Based on the amount of **3** and **4** consumed during the base treatment, the yield of spiro-dimer **9a**, isolated as diiodide **10**, was 33%.

The mother liquor from the recrystallization of diiodide **10** was washed with sodium thiosulfate solution and water and then evaporated to dryness. Trituration of the residue with ethanol, addition of the extracts to a solution of silver nitrate in 90% ethanol, filtration of the resulting hot mixture to remove silver iodide, and concentration of the filtrate gave 16.8 mg. of silver nitrate complex of paracyclophane **2** (3.3% yield based on the amount of monomers consumed).

Thermal Stabilities of Monomers 3 and 4.—A 0.02 *M* heptane solution of monomers **3** and **4** in a ratio of 64:36 was stored at 5° under nitrogen; the solution became cloudy after *ca.* 7 days as the formation of a colorless flocculent precipitate began. Quantitative determination of the monomer contents *via* Diels–Alder adducts showed that after 4 months 100% of the original amount of **3** but only 29% of **4** remained.

Refluxing a 0.024 *M* heptane solution of monomers **3** and **4** (ratio *ca.* 2:1) led to the recovery of 47% of the original amount; no precipitate was formed. Analysis of the solution after heating revealed that 33% of **3** and 94% of **4** had been consumed.

Attempted Acid-Catalyzed Isomerization of 3 and 4.—A heptane solution of 1.0 mmole of monomers **3** and **4** (ratio 71:29) was concentrated under reduced pressure at room temperature to one-twentieth of its original volume. The concentrate (2 ml.)

was added to a solution of 5 mg. of *p*-toluenesulfonic acid monohydrate in 10 ml. of chloroform. After refluxing under a nitrogen atmosphere for 5.5 hr., the clear and colorless solution was washed with 5% sodium bicarbonate solution and water, dried over anhydrous magnesium sulfate, and concentrated. The oily residue was dissolved in 50 ml. of *n*-heptane and added to a solution of 1.0 g. of maleic anhydride in 25 ml. of benzene to give 125 mg. of Diels–Alder adducts, equivalent to a recovery of 37% of the original amount of monomers. Quantitative infrared analysis of the adducts revealed the loss of 50% of **3** and 95% of **4**.

The mother liquor from the preparation of the Diels–Alder adducts was evaporated to dryness, the methanol extract of the residue diluted with water and extracted with heptane. The solvent was removed from the heptane solution, the residue dissolved in ethanol, and the resulting solution added to silver nitrate in 90% ethanol; the mixture remained clear, indicating the absence of paracyclophane **2**.

An aliquot (20 ml.) of the heptane layer from a dehydroiodination experiment and containing 0.37 mmole of monomers **3** and **4** (representing 70% of starting tetraiodide **1**) in a ratio of 71:29 was extracted with three 20-ml. portions of concentrated hydrochloric acid. The heptane layer was washed with water and dried over anhydrous magnesium sulfate. Examination of the Diels–Alder adduct from this solution revealed the complete destruction of monomer **4** in the acidic medium; however, 70% of the original amount of **3** was present. In the two-step procedure—dehydroiodination and acid treatment—a solution of monomer **3** free from **4** was obtained in 35% yield based on starting tetraiodide **1**.

The Synthesis and Decomposition of *o*-Iodosophenylacetic Acid[1]

BY J. E. LEFFLER, L. K. DYALL, AND P. W. INWARD

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o-Iodosophenylacetic acid, a cyclic derivative of trivalent iodine, is stable at room temperature but decomposes in solution at 80–100°. *o*-Iodomandelic acid is an intermediate in the decomposition; in acid or neutral solution it is rapidly oxidized by the starting material to *o*-iodobenzaldehyde. The initial attack on the active methylene group is catalyzed by protons and by a phosphate buffer component. In sulfate–bisulfate buffers there is a kinetic term corresponding to proton catalysis and a term apparently corresponding to a complex pre-equilibrium involving bisulfate. The latter term is of the form $[\mathrm{H^+}][\mathrm{SO_4^{-2}}]^{1/2}$.

Introduction

The decomposition of *o*-iodobenzoyl[2,3] and β-iodopropionyl[4] peroxides is accelerated by a concerted attack of the iodo group on an oxygen atom of the cleaving peroxide bond. No similar effect is observed in the decomposition of *o*-iodophenylacetyl peroxide.[5] In order to rule out the possibility that the *six-membered* iodine heterocycle required in the latter reaction might be of prohibitively high energy, we undertook the synthesis of compound I. Compound I proved to decompose only at much higher temperatures than *o*-iodophenylacetyl peroxide and to give quite different products.

The kinetics and mechanism of the decomposition of I are unusual in some respects. Although the reaction at first appears to be a straightforward acid- and base-catalyzed hydroxylation of the active methylene group, the expression for the pseudo-first-order rate constant in sulfate–bisulfate buffers contains a
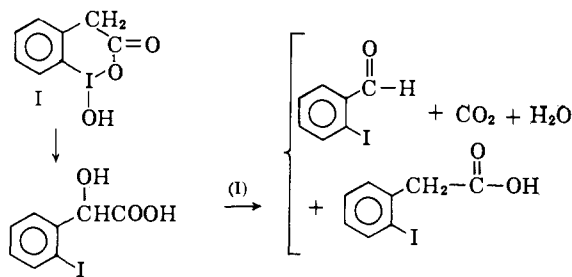
term of the form $[\mathrm{H^+}][\mathrm{SO_4^{-2}}]^{1/2}$, or its equivalent $[\mathrm{H_2SO_4}]^{1/2}$.[6]

Reaction Products.—The decomposition of *o*-iodosophenylacetic acid[7] (I) in water at 100° gives *o*-iodobenzaldehyde and *o*-iodophenylacetic acid. In 0.1 *M* sodium carbonate solution the major product is *o*-iodomandelic acid. In acidic or neutral aqueous solutions *o*-iodomandelic acid reacts rapidly with *o*-iodosophenylacetic acid to give *o*-iodobenzaldehyde and

(1) This research was part of an investigation into the decomposition mechanisms of trivalent iodine compounds. It was supported by a grant from the National Science Foundation.

(2) J. E. Leffler, R. D. Faulkner, and C. C. Petropoulos, *J. Am. Chem. Soc.*, **80**, 5435 (1958).

(3) W. Honsberg and J. E. Leffler, *J. Org. Chem.*, **26**, 733 (1961).

(4) J. E. Leffler and J. S. West, *ibid.*, **27**, 4191 (1962).

(5) J. E. Leffler and A. F. Wilson, *ibid.*, **25**, 424 (1960).

(6) A kinetic term proportional to $[\mathrm{H_2SeO_3}]^{1/2}$ has been noted in the selenious acid oxidation of 1,2-dibenzoylethane in acetic acid: J. P. Schaefer, *J. Am. Chem. Soc.*, **84**, 713 (1962).

(7) This substance, like *o*-iodosobenzoic acid, exists in the cyclic form. It has a K_A of 5.1 × 10⁻⁷ in water at 95°, ionic strength 0.096. In contrast, K_A for *o*-iodophenylacetic acid under the same conditions is 1.23 × 10⁻⁴.
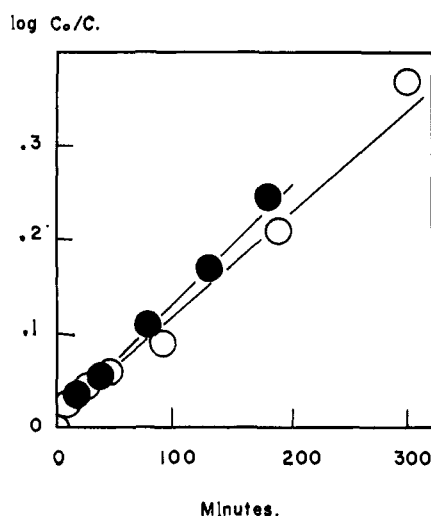
Fig. 1.—Salt effect in water: O, decomposition of o-iodoso-phenylacetic acid in water at 100°, C_0 = 0.0102 M; ●, decomposition in 0.14 M KClO₄, C_0 = 0.010 M.

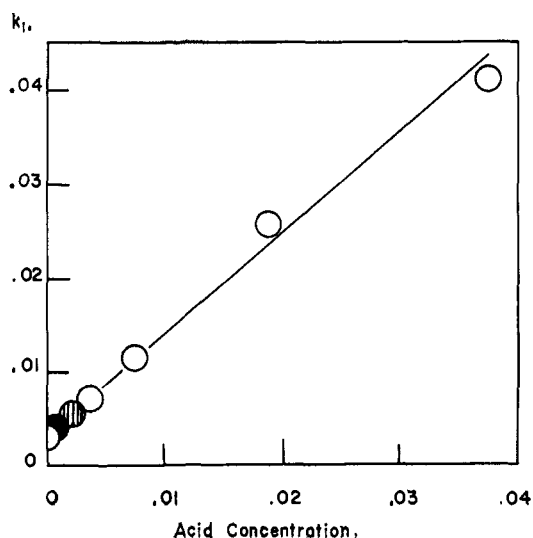

Fig. 2.—Proton catalysis: O, HClO₄; ●, picric acid; ⦰, protons from 0.04 M o-iodophenylacetic acid.

o-iodophenylacetic acid. In acetic anhydride the major product is o-iodoacetylmandelic acid.

Free radicals are produced in rather low yields in aqueous media as indicated by the polymerization of acrylonitrile. The maximum yield of polymer is obtained in the absence of added acid or base. The organic radicals that seem most likely to be formed in the uncatalyzed decomposition of I are o-iodophenyl-acetyl and o-iodobenzyl. However, the decomposition of I in water gave none of the easily isolable o-iododibenzyl and o-iodobenzyl alcohol or ester observed in the free radical decomposition of o-iodophenylacetyl peroxide.[5] It was also demonstrated that o-iodobenzyl alcohol is only slowly and incompletely oxidized by I in water at 100°. It is therefore not a precursor of the o-iodobenzaldehyde.

Kinetics.—In water the first-order rate constants at 100° (Table I) are insensitive to changes in initial concentration and to degassing, particularly for initial concentrations near 0.01 M. Unless otherwise noted, we have used this initial concentration and have not degassed. The salt effect in water is also small (Fig. 1).

The Effect of Hydrogen Ion.—Catalysis by hydrogen ions in water at 100° and μ = 0.14 (KClO₄) follows rate law 1 as shown in Fig. 2 and 3. o-Iodophenylacetic

$$k_1 \text{ (min.}^{-1}) = 3.10 \times 10^{-3} + 1.05[\text{H}^+] \qquad (1)$$
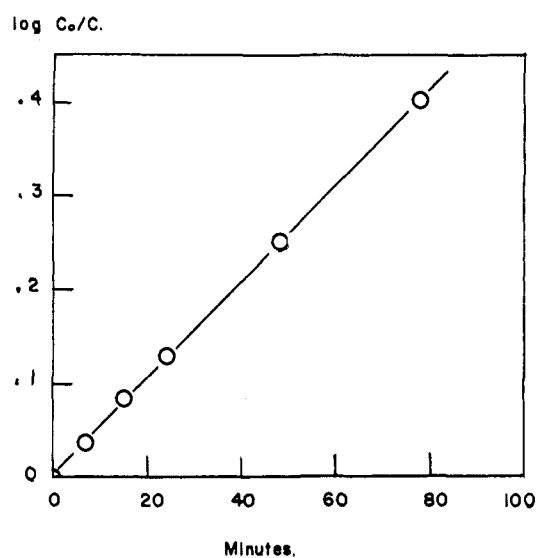

Fig. 3.—Decomposition of o-iodosophenylacetic acid in water at 100°, μ = 0.14 (KClO₄), [HClO₄] = 7.53 × 10⁻³ M, C_0 = 0.010 M, not degassed.
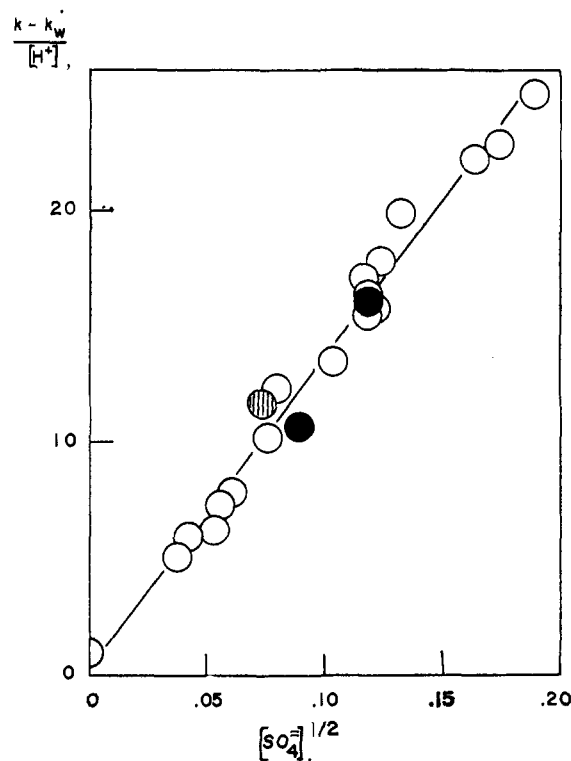

Fig. 4.—The effect of sulfate ion in acidic solutions: ●, degassed; ⦰, picric acid added.

acid and picric acid (a potential trap for free radicals) have no effect other than that expected from their dissociation into hydrogen ions.

The Effect of Sulfate Ion.—In a series of sodium bisulfate–sodium sulfate solutions ranging in bisulfate ion concentration from 0.004 to 0.04 M, in sulfate ion concentration from 0.0015 to 0.035 M, and in hydrogen ion concentration from 6.7 × 10⁻⁵ to 2.7 × 10⁻³ M, the first-order rate constant is given by eq. 2

$$k_1 = k_w + k_p[\text{H}^+] + k_a[\text{H}^+][\text{SO}_4^{-2}]^{1/2} \qquad (2)$$

The fit of the data of Table III to this equation, using the k_w and k_p values from eq. 1 is shown by the plot of $(k_1 - k_w)/[\text{H}^+]$ vs. $[\text{SO}_4^{-2}]^{1/2}$ in Fig. 4. A typical run is shown in Fig. 5. The effect of sodium sulfate on the rates in water without added acid or base (Table II)
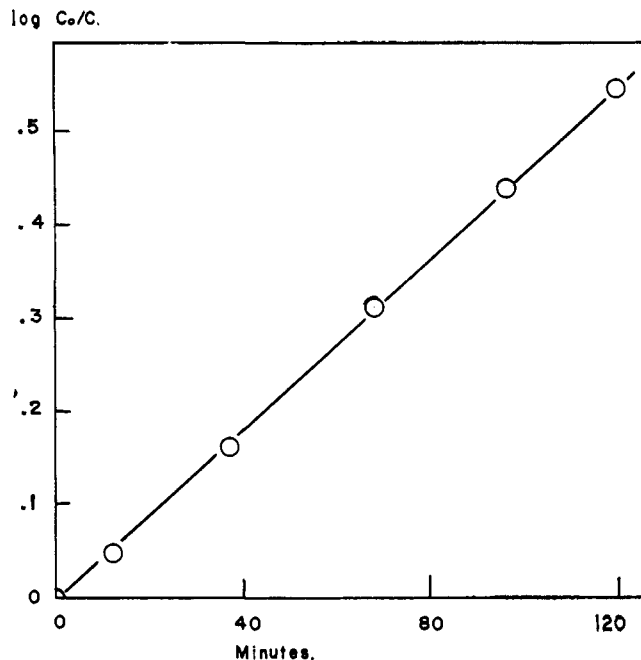
log C₀/C.

Fig. 5.—A run with $[HSO_4^-] = 20 \times 10^{-3} M$, $[SO_4^{-2}] = 5.74 \times 10^{-3} M$, and ionic strength $= 0.14$ (KClO₄).

is large compared to that of potassium perchlorate at the same ionic strength but is consistent with the rate enhancement predicted by eq. 2, the protons being supplied by the o-iodophenylacetic acid formed in the reaction. In *alkaline* solutions the effects of sodium sulfate and potassium perchlorate at equal ionic strengths are identical.

TABLE I

CONCENTRATION EFFECTS IN WATER[a] AT 100°

Init. concn., mole/l.	Rate constant, min.⁻¹ × 10⁴	
	Oxygen present	Degassed
0.0058	3.04	2.98
.0062	. .	2.96
.0102	2.93	2.95
		2.87[b]
.0150	3.64	3.40[b]
.0180	4.09	3.69
.0203	4.57	3.53
	4.61	
.0255	4.58	4.08
	4.45	

[a] No added salts. [b] In water specially treated to ensure low copper ion content. Copper ion catalyzes the free radical decomposition of diphenyliodonium hydroxide.[8,9]

TABLE II

EFFECT OF Na₂SO₄ IN WATER AT 100°[a]

[Na₂SO₄], M	Rate constant, min.⁻¹ × 10⁴
0	2.93
0.015	3.36
.0207	3.53
.066	3.97

[a] The initial concentration of o-iodosophenylacetic acid was 0.01 M; not degassed, no added bisulfate or acid.

Kinetics in Alkaline Solutions.—In 0.033 M Na₂CO₃ solution the decomposition of I is too fast for accurate measurement and apparently strongly autocatalytic. In a solution 0.010 M in I, 0.011 M in Na₂CO₃, and $\mu = 0.063$, k_1 is 16×10^{-3} min.⁻¹. In Na₂HPO₄–NaH₂PO₄ buffers the rates are slightly greater than first order.

(8) M. C. Caserio, D. L. Glusker, and J. D. Roberts, *J. Am. Chem. Soc.*, **81**, 336 (1959).

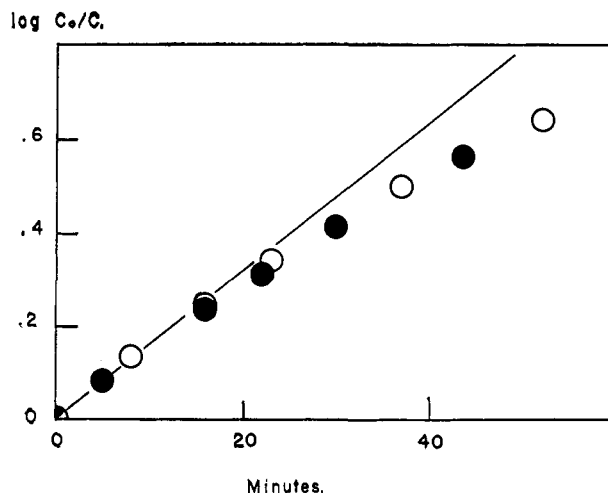(9) F. M. Beringer, E. M. Gindler, M. Rapoport, and R. J. Taylor, *ibid.*, **81**, 351 (1959).

log C₀/C.

Fig. 6.—Decomposition in a solution initially 0.0249 M in NaH₂PO₄ and 0.0051 M in Na₂HPO₄ at $\mu = 0.14$: O, ionic strength made up using Na₂SO₄; ●, ionic strength made up using KClO₄.

The deviation from first-order kinetics is considerable in certain buffers and just noticeable in the others, as shown in Fig. 6 and 7. The buffers for which curvature is pronounced are in general the more acidic ones, but the buffer concentration must be fairly high as well. Figure 6 also illustrates the precise equivalence of the KClO₄ and Na₂SO₄ salt effects in a $H_2PO_4^-/HPO_4^{-2}$ buffer.

TABLE III

RATES IN BISULFATE– ULFATE SOLUTIONS

Rate constant, k,[a] min.⁻¹ × 10³	[HSO₄⁻],[c] g. ion l.⁻¹ × 10³	[SO₄⁻²],[c] g. ion l.⁻¹ × 10³	[H⁺], g. ion l.⁻¹ × 10³	Ionic strength[b]
13.82	40.63	10.8	0.794	0.14
10.55	19.97	5.74	.73	.14
7.92	9.71	3.15	.65	.14
5.69	3.63	1.51	.51	.11
13.0	40.03	13.93	.607	.135[d]
12.9	40.03	13.93	.607	.135
12.37	39.8	13.95	.602	.14
5.64	3.61	1.77	.429	.14
10.36	45.92	30.45	.318	.14
10.04	40.00	27.00	.313	.14
8.68	22.80	15.4	.313	.14
8.43	20.15	13.6	.312	.14
6.68	8.84	6.43	.290	.14
6.52	7.83	5.63	.294	.13
6.98	8.20	5.25	.33	.13[e]
4.88	3.91	2.95	.280	.14
8.43	36.16	35.5	.215	.14
7.36	18.04	17.80	.214	.14
4.66	3.45	3.72	.196	.14

[a] Initial concentration of I was 0.01 M. The runs were not degassed; temperature 100°. [b] The ionic strength was adjusted by addition of KClO₄. [c] These concentrations correspond to the added NaHSO₄ and Na₂SO₄ corrected for the equilibrium $HSO_4^- \rightleftarrows H^+ + SO_4^{-2}$ using the constant $K_{100} = 2.11 \times 10^{-4}$ at ionic strength = 0.14: H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Corp., New York, N. Y., 1958; M. H. Lietzke, R. H. Stoughton, and T. F. Young, *J. Phys. Chem.*, **65**, 2247 (1961). [d] Degassed run. [e] Run with picric acid (5.82 × 10⁻⁴ mole/l.) added.

The first-order rate constants (Table IV) are related to the concentration of $[H_2PO_4^-]$ as shown in Fig. 8. For six runs of marked curvature the value used is an estimated *initial* first-order rate constant. There is no correlation of k_1 with hydrogen ion concentration within the range 5×10^{-10} to 9×10^{-9} M covered by the
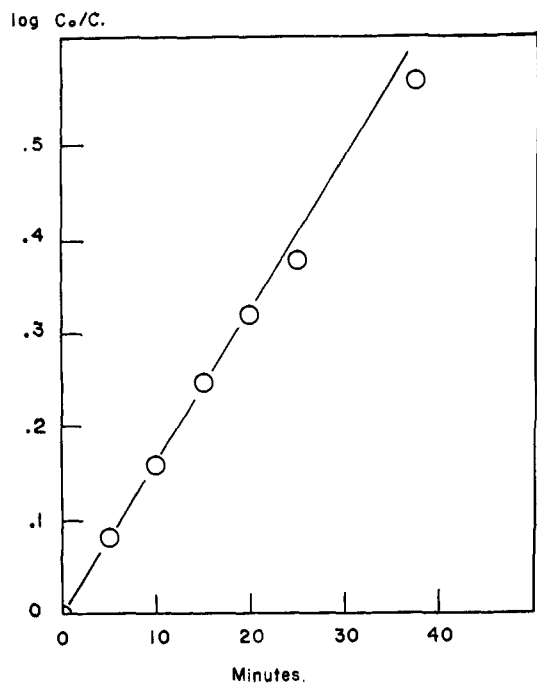
Fig. 7.—Decomposition in a solution initially 0.0205 M in NaH$_2$PO$_4$ and 0.032 M in Na$_2$HPO$_4$. Ionic strength was adjusted with Na$_2$SO$_4$ to 0.195.

buffers. Compound I exists almost entirely as its conjugate base in these media and its neutralization by the buffer has been taken into account in calculating

TABLE IV

DECOMPOSITION OF o-IODOSOPHENYLACETIC ACID[a] IN PHOSPHATE BUFFERS

10^3k, min.$^{-1}$	[H$_2$-PO$_4$$^-$],[b] M	[H-PO$_4$$^{-2}$],[b] M	μ^c	10^3k, min.$^{-1}$	[H$_2$-PO$_4$$^{-2}$],[b] M	[H-PO$_4$$^{-2}$],[b] M	μ^c
55[d]	0.040	0.020	0.120				
45[d]	.0309	.0111		37[h]	0.0237	0.0180	
35[d]	.0249	.0051		33	.0198	.0100	
35[d,e]	.0178	.00025		28	.0158	.00207	
38[d]	.0249	.0051	.140	39	.0250	.0350	0.150
38[d,f]	.0249	.0051		38.5	.0250	.0350	
49	.0370	.030	0.147	36	.0205	.0215	
45	.0370	.030		33	.0175	.0125	
34	.0235	.010		31	.0144	.0036	
32	.0180	.00209		39	.0250	.0500	0.195
4.36[g]	.0298	.000	0.0298	37	.0205	.0320	
26[f]	.010	.020	0.140	34	.0175	.0200	
42	.0295	.0300		31	.0144	.0081	
35	.0237	.0180		43	.0281	.0625	0.235

[a] Initial concentration 0.01 M, not degassed, 100°. [b] Except where noted the concentration of H$_2$PO$_4$$^-$ listed is equal to the nominal concentration plus a 0.01 M contribution from the neutralization of I. Similarly, the concentration of HPO$_4$$^{-2}$ listed is the nominal concentration minus 0.01 M. [c] Ionic strength adjusted by addition of Na$_2$SO$_4$ unless otherwise noted. [d] Initial value only. [e] In this run the extent of conversion of I to its conjugate base is estimated to be 87%; in the other runs 99 to 100%. [f] Ionic strength adjusted by addition of KClO$_4$. [g] Run in acid buffer component only. [h] Containing 6.8 × 10^{-4} M picrate ion.

the actual H$_2$PO$_4$$^-$ and HPO$_4$$^{-2}$ concentrations.[10] The equation for the line of Fig. 8 is

$$k_1 \text{ (min.}^{-1}) = 17 \times 10^{-3} + 0.88[\text{H}_2\text{PO}_4^-] \qquad (3)$$

The intercept is close to the value 16 × 10^{-3} min.$^{-1}$ observed for k_1 in 0.011 M Na$_2$CO$_3$. The rate constant in a typical phosphate buffer was not affected by 6.8 × 10^{-4} M picrate ion.

(10) A run in the acid buffer component only (Table IV) gave a rate only about 50% higher than that in water. In the absence of the basic buffer component, I is not appreciably ionized to its conjugate base.
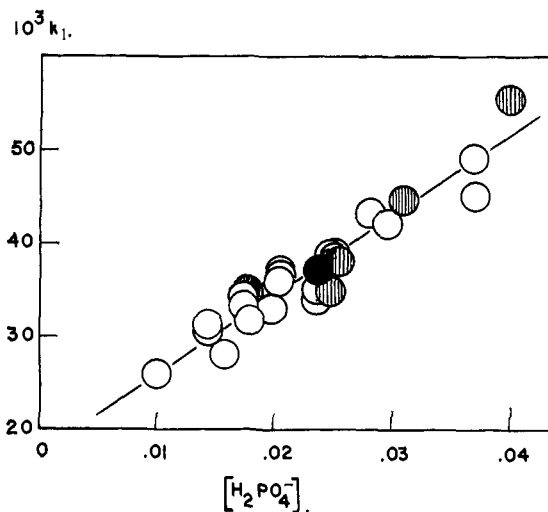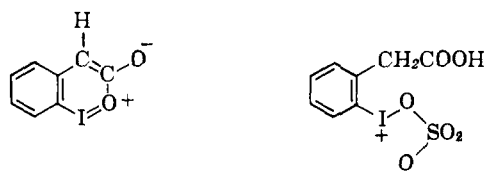

Fig. 8.—Correlation of k_1 with [H$_2$PO$_4$$^-$] in phosphate buffers: solid point, picric acid added; shaded points, estimates of initial rate constant.

Discussion

Except in water without added catalyst, the yield of radicals as measured by acrylonitrile polymerization is negligible, and even in water the reaction products do not support the hypothesis that the free radical reaction is anything more than a minor side reaction. The lack of any appreciable inhibition by oxygen or picric acid also favors a nonradical mechanism.

The water and hydrogen ion-catalyzed reactions are probably analogous in mechanism to the intermolecular oxidation of active methylene compounds by a reagent such as bromine. However, the observed rate constant in acid solution is twice that of the initial step, since o-iodomandelic acid rapidly reduces a second molecule of I under these conditions. The reaction in phosphate buffers is probably a base-catalyzed enolization. The data will not permit a distinction between mechanisms involving the reaction of un-ionized I with hydroxide and HPO$_4$$^{-2}$ ions $vs.$ the reaction of the conjugate base of I with water and H$_2$PO$_4$$^-$ ion.

Equation 2 for the kinetics in sulfate–bisulfate buffer contains a term of the form $k[\text{H}^+][\text{SO}_4^{-2}]^{1/2}$. Although it would be tempting to explain this term by means of a radical chain process,[11] the yield of polymerized acrylonitrile is well below 1%, much less than that in water alone. Some of the runs in these buffers show a very short induction period usually concealed by the time needed to attain the bath temperature. An induction period and half-order kinetics can be explained by a pre-equilibrium step leading to two species in equal concentration, one of which undergoes the rate-determining reaction. One such mechanism involves the species shown below. The first of these would have to react with water to give o-iodomandelic acid,

which must then rapidly reduce the second to o-iodophenylacetic acid.

(11) SO$_4$$^-$ has been suggested as an intermediate in the oxidation of organic compounds and the polymerization of vinyl monomers by persulfate in water: P. D. Bartlett and J. D. Cotman, Jr., $J. Am. Chem. Soc.$, 71, 1419 (1949); R. G. R. Bacon and R. W. Bott, $Chem. Ind.$ (London), 1285 (1953).

Experimental

o-Iodophenylacetic acid was prepared by the method of Leffler and Wilson[6] and also by a preferred method of catalytically hydrogenating *o*-nitrophenylacetic acid in the presence of HCl, followed by a Sandmeyer reaction of the resulting aminoacid hydrochloride. The yield of material melting at 113–114° was 46%.

o-Iodosophenylacetic Acid.—Dry chlorine was passed over the surface of a solution of *o*-iodophenylacetic acid (4 g.) in anhydrous chloroform (50 ml.) until no further precipitation occurred. The *o*-iodophenylacetic acid dichloride was collected, air-dried, and then stirred with saturated sodium bicarbonate solution for 5 min. The colorless material so obtained was washed thoroughly with distilled water and recrystallized in small portions by adding the solid (*ca*. 1 g.) to boiling water (100 ml.), stirring for 30 sec., filtering rapidly, and cooling by plunging into an ice bath. Pure *o*-iodosophenylacetic acid (m.p. 130° but dependent on rate of heating) was thus obtained. The infrared spectrum (Nujol) showed strong bands at 2420 and 751 cm.$^{-1}$ and medium bands at 1600, 1345, 1160, 935, and 725 cm.$^{-1}$. The acid dissociation constant at 95° and ionic strength 0.096 is 5.1×10^{-7}.

Anal. Calcd. for $C_8H_7O_3I$: C, 34.57; H, 2.52; I, 45.65; equiv. wt., 139. Found: C, 34.34; H, 2.86; I, 45.18; equiv. wt. (iodometric), 137.5, 138.

Methyl *o*-Iodomandelate.—The bisulfite adduct of *o*-iodobenzaldehyde (15 g.) was stirred with a solution of sodium cyanide (14 g.) in water (75 ml.) for 10 min. The cyanohydrin was collected, dried *in vacuo*, and dissolved in methanol (100 ml.). This solution was cooled in an ice bath, saturated with dry hydrogen chloride gas (*ca* 2.5 hr.), and boiled under reflux for 6 hr. The volume of the solution was reduced to 40 ml. by distillation and water (200 ml.) added, precipitating an oil, which was extracted into ether. This extract, after being washed with saturated sodium bisulfite solution (30 ml.) and water (50 ml.) and dried over anhydrous magnesium sulfate, yielded a viscous oil (6 g.) which after purification by chromatography on Florisil and subsequent recrystallization from hexane–benzene gave white needles, m.p. 71–73° (2.5 g.). Further recrystallization gave pure methyl *o*-iodomandelate, m.p. 74–75°.

Anal. Calcd. for $C_9H_9O_3I$: C, 37.01; H, 3.11. Found: C, 37.23; H, 2.67.

o-**Iodomandelic Acid.**—Methyl *o*-iodomandelate (1.7 g.) was stirred with a warm (50°) solution of sodium hydroxide (2 g.) in water (50 ml.) until completely dissolved (*ca*. 10 min.). The solution was then cooled, acidified, and extracted with ether (5 × 20 ml.). The ether extract was dried over anhydrous magnesium sulfate and evaporated to dryness, giving a residue (1.5 g.) which after three recrystallizations from benzene–hexane gave pure *o*-iodomandelic acid (m.p. 107–108°). The analysis indicated that the acid contained 1 molecule of benzene of crystallization.

Anal. Calcd. for $C_{14}H_{13}O_3I$: C, 45.94; H, 3.65. Found: C 45.94; H 3.25.

Decomposition of *o*-Iodosophenylacetic Acid in Water at 100°.—*o*-Iodosophenylacetic acid (1.60 g., 0.00576 mole) was suspended in distilled water and nitrogen bubbled through the mixture for 30 min. It was then boiled under reflux for 12 hr., the gases evolved being swept through a condenser into an alkaline barium chloride trap which was protected from the atmosphere by a sodium hydroxide trap. The yield of barium carbonate was 0.46 g. The reaction mixture was cooled and extracted with chloroform. After separation of the acidic and neutral products by extraction with sodium bicarbonate solution, two products were obtained. The first was an acid (0.62 g.) shown by m.p. (115°) and mixture m.p. to be *o*-iodophenylacetic acid and the second, a viscous oil (0.29 g.) shown by its infrared spectrum to be largely *o*-iodobenzaldehyde. The aldehyde gave a 2,4-dinitrophenylhydrazone, m.p. 214–215°, mixture m.p. with an authentic sample 214.5–215.5°. The yields after correction for aliquots of solution removed for titration (moles of product/mole of I) were: CO_2, 0.45; *o*-iodophenylacetic acid, 0.46; and *o*-iodobenzaldehyde (0.22).

o-**Iodobenzaldehyde 2,4-Dinitrophenylhydrazone.**—Prepared in the usual way from the aldehyde in ethanol with a trace of HCl, the 2,4-dinitrophenylhydrazone is pale orange, m.p. 216–217°. It may be recrystallized from acetone (prisms) or from acetone–ethanol (needles).

Anal. Found: C, 37.94; H, 2.59. Calcd.: C, 37.9; H, 2.21.

Decomposition of *o*-Iodosophenylacetic Acid in 0.1 *N* Sulfuric Acid.—The procedure used for the isolation and identification of the products was exactly as described for the decomposition in water, and the corrected yields (moles of product/mole of I) were: CO_2, 0.32; *o*-iodophenylacetic acid, 0.48; and *o*-iodobenzaldehyde, 0.15.

Decomposition of *o*-Iodosophenylacetic Acid in 0.1 *M* K₂CO₃ Solution.—*o*-Iodosophenylacetic acid (0.55 g.) was dissolved in 0.1 *M* K₂CO₃ solution (100 ml.) and boiled under reflux for 30

min. The solution was extracted with chloroform (3 × 25 ml.), acidified, and subjected to continuous ether extraction for 48 hr. The chloroform extract yielded an oil (0.01 g.) having an infrared spectrum almost identical with that of *o*-iodobenzaldehyde. The ether extract yielded a solid residue (0.55 g.) which after trituration with a small volume of benzene–pentane melted at 85–90°. After one recrystallization from benzene, a colorless crystalline compound was obtained (0.245 g., m.p. 106–107°) which was identified as *o*-iodomandelic acid by mixture m.p. with an authentic sample and similarly *via* the methyl ester. From the crystallization residues a semisolid was obtained by trituration with carbon disulfide and evaporation of the resulting solution. Further trituration with hexane gave a crystalline solid (0.01 g., m.p. 110°,) the infrared spectrum of which was identical with *o*-iodophenylacetic acid. The yields of products (moles of product/mole of I) were: *o*-iodomandelic acid, 0.45; *o*-iodophenylacetic acid, 0.02; *o*-iodobenzaldehyde, 0.02.

Decomposition of *o*-Iodosophenylacetic Acid in Acetic Anhydride.—*o*-Iodosophenylacetic acid (0.52 g.) was dissolved in acetic anhydride (50 ml.) by stirring vigorously at 80°. A portion (20 ml.) of this solution was heated at 90° for 90 min. and solvent removed by distillation under reduced pressure. Separation into acidic and neutral components gave as main product an acid oil (0.3 g.), which on heating with dilute potassium hydroxide solution, acidification, extraction with ether, and recrystallization of the product from benzene–hexane, gave colorless crystals, m.p. 104.5–106.5°, shown by mixture m.p. and comparison of infrared spectra to be identical with authentic *o*-iodomandelic acid. The original oil on recrystallization from benzene–hexane gave a solid, m.p. 113–115°. The spectrum of this compound in carbon tetrachloride had peaks at 1750 and 1730 cm.$^{-1}$ indicating that it is probably the acetate of *o*-iodomandelic acid.

The rate of decomposition of *o*-iodosophenylacetic acid is about the same at 80° in undegassed acetic anhydride or in acetonitrile as it is in water at 100°.

Polymerization Tests.—The presence or absence of free radicals. in the reaction mixtures was determined by their ability to polymerize acrylonitrile. Freshly distilled acrylonitrile (1 ml.) was added to a suspension of *o*-iodosophenylacetic acid (14 mg.) in water (5 ml.). The mixture was degassed by alternate freezing and thawing at 5×10^{-3} mm. and the ampoule sealed. The ampoule was heated to 100° for 2 min. and shaken thoroughly to effect solution and then maintained at 100° for one half-life of the decomposition reaction. The polymer was then collected, dried, and weighed.

Wt. iodoso acid, mg.	Medium	Wt. of polymer, g[t]
14.3	Water	0.392
14.6	0.072 *M* H₂SO₄	.004
13.6	0.04 *M* NaHSO₄,	
	0.027 *M* Na₂SO₄	.043[a]
13.9	0.036 *M* Na₂CO₃	.01

[a] From 0.5 ml. of acrylonitrile.

o-**Iodosophenylacetic Acid and *o*-Iodomandelic Acid.**—*o*-Iodosophenylacetic acid (0.100 g., 3.6×10^{-4} mole) and *o*-iodomandelic acid (0.100 g., 2.8×10^{-4} mole) were dissolved in water (20 ml.) at 100° and maintained at this temperature for 2 hr. Separation of acidic and neutral components in the usual manner gave a white solid acid (0.102 g., m.p. 92–96°) the infrared spectrum of which was almost identical with that of *o*-iodophenylacetic acid and lacked the strong absorption at 1082 cm.$^{-1}$ characteristic of *o*-iodomandelic acid. The neutral component was an oil (0.06 g.), infrared spectrum identical with that of *o*-iodobenzaldehyde.

The rate of the reaction between equivalent amounts of *o*-iodomandelic acid and *o*-iodosophenylacetic acid (0.01 *M* in each) was measured in an experiment similar to the other kinetic experiments. In water and in a solution buffered at pH 7, the half-life was approximately 2 min. This showed that in both of these media the rate of this reaction was fast compared with the rate of the decomposition of *o*-iodosophenylacetic acid alone.

o-**Iodobenzyl Alcohol and *o*-Iodosophenylacetic Acid.**—*o*-iodobenzyl alcohol (32 mg., 1.38×10^{-4} mole) and *o*-iodosophenylacetic acid (77 mg., 2.8×10^{-4} mole) were dissolved in water (25 ml.) at 100° and maintained at that temperature for 5 hr. After cooling, a test for oxidizing power of the solution indicated that not all the *o*-iodosophenylacetic acid had been consumed. The solution was then extracted with ether and the product separated into neutral and acidic fractions. The acidic material (61 mg.) was recrystallized from hexane to give colorless needles, m.p. 116°, undepressed on admixture with authentic *o*-iodophenylacetic acid. The neutral portion was an oily solid (57 mg.) which after sublimation and recrystallization of the sublimate from hexane gave *o*-iodobenzyl alcohol (10 mg.), m.p. 89°, undepressed on admixture with an authentic sample. The infrared spectra of residues from the sublimation and the crystal-

lization showed features characteristic of both o-iodobenzyl alcohol and o-iodobenzaldehyde.

Kinetic Procedure.—Runs were performed using sealed ampoules surrounded by steam in equilibrium with water at atmospheric pressure. Temperature variation during a run was ±0.05°.

Nondegassed Runs.—o-Iodosophenylacetic acid (14 mg.) was accurately weighed into each ampoule and the appropriate solution added by pipet. The ampoule was then sealed.

Degassed Runs.—The ampoules were filled as described above and the suspension was then frozen in liquid air. The ampoules were evacuated (5–10 × 10⁻³ mm.) and allowed to thaw gradually, and after three of these cycles they were sealed and allowed to stand at room temperature for 10 min. (shielded in case of explosion).

The ampoules were then placed in a steam bath for 2 to 3 min., shaken vigorously to effect solution, and replaced. After 5 or 10 min. the first ampoule was removed for titration, and this was

taken as zero time. At appropriate intervals, ampoules were withdrawn, plunged into ice water, and then frozen in a Dry Ice–acetone bath. The ampoule was then opened and the contents dissolved in water to which 2 N sulfuric acid had been added. Solid potassium iodide (0.2 g.) was then added and the liberated iodine titrated against standard 0.01 N or 0.02 N sodium thiosulfate solution using starch indicator.

pK_a **Values.**—pK_a values were obtained by titration of the acids against standard sodium hydroxide solution in an atmosphere of nitrogen. Sodium sulfate was added to the solution to bring the ionic strength to ca. 0.1 at half-equivalence. The change in pH was followed using a Beckman model G pH meter and pK_a values calculated from a number of points on the titration curve using the Henderson equation.

The Syntheses of Cyclopenta[c]thiapyran and 2-Phenyl-2-pyrindine[1–3]

By Arthur G. Anderson, Jr., William F. Harrison,[4] and Robert Gordon Anderson

The syntheses of the compounds in the title, which are iso-π-electronic with azulene and the first simple π-excessive[6] heterocyclic analogs of a nonalternant aromatic hydrocarbon, is described. Certain physical properties, e.g., the visible and ultraviolet absorption spectra, of these substances were found to be similar to those of azulene. The n.m.r. and infrared spectra of the new substances are reported.

The demonstration of aromatic character in the azulene molecule[6] led us to the consideration of analogous structures, among which were heterocycles wherein (a) one or more carbons in either the 5- or 7-ring would be replaced by a corresponding number of nitrogens to form molecules related to azulene as pyridine, pyrimidine, etc., are related to benzene[7]; (b) two adjacent carbons in the 7-ring would be replaced by a nitrogen or sulfur to form molecules related to azulene as pyrrole and thiophene are related to benzene.[8] In compounds of the first type there are the same number of π-electrons as ring atoms and the term π-equivalent may be used to describe this condition.[9] Compounds of the second type have more π-electrons than ring

atoms and may be called π-excessive.[9] The first known examples of the latter were methyl nor-harmine and harmine, isolated by Sir Robert Robinson and co-workers more than forty years ago.[10a] A number of related pyrindole derivatives are known.[10b] At the inception of the present studies and prior to the preliminary report[3] no mention of the preparation of a simple, unsubstituted π-excessive heteroanalog of azulene was found in the literature,[11] and a comparison of the properties of such compounds with those of azulene seemed of interest. These structures would have a different ring size and shape in addition to the presence of the heteroatom and yet still be nonalternant, and it was the expectation that a comparison of the properties of these molecules with those of azulene would provide data useful in the theroetical interpretation of the role of the heteroatom in π-excessive heteroaromatic compounds in general.

Syntheses.—A synthetic route (Fig. 1 and 2) wherein the heteroatom was introduced in the last step prior to the introduction of the unsaturation was chosen because it was direct, uncomplicated, and, more important, permitted the formation of the saturated bicyclic sulfur, nitrogen, and oxygen molecules from the same intermediates. The Dieckmann condensation of diethyl adipate to form 1 (83–89%) was effected with a sodium hydride dispersion and the product was transformed into the cyano ester 2 in ca. 70% yield via the method of

(1) Supported in part by a contract with the Office of Ordnance Research and a grant from the National Science Foundation.

(2) From the Ph.D. theses of William F. Harrison and Robert G. Anderson.

(3) A portion of this work was reported in preliminary communications: A. G. Anderson, Jr., W. F. Harrison, R. G. Anderson, and A. G. Osborne, J. Am. Chem. Soc., 81, 1255 (1959); A. G. Anderson, Jr., and W. F. Harrison, Tetrahedron Letters, 2, 11 (1960).

(4) Standard Oil of California Fellow, summer, 1958; National Science Foundation Predoctoral Fellow, 1959–1960.

(5) A. Albert, "Heterocyclic Chemistry. An Introduction," Essential Books, Fair Lawn, N. J., 1959.

(6) A. G. Anderson, Jr., J. A. Nelson, and J. J. Tazuma, J. Am. Chem. Soc., 75, 4980 (1953). For a general review and discussion see E. Heilbronner, "Non-benzenoid Aromatic Compounds," ed. by D. Ginsburg, Interscience Publishers, Inc., New York, N. Y., 1959, Chapt. V.

(7) The first example of this type, 1-azabenz[b]azulene, was prepared in our laboratories: A. G. Anderson, Jr., and J. J. Tazuma, J. Am. Chem. Soc., 74, 3455 (1952). 1-Aza-, 1,3-diaza-, and 1,2,3-triazaazulene were subsequently prepared and studied by T. Nozoe. For reference see T. Nozoe, "Non-Benzenoid Aromatic Compounds," ed. by D. Ginsburg, Interscience Publishers, Inc., New York, N. Y., 1959, Chapt. VII, and W. Keller-Shierlein and E. Heilbronner, ibid., Chapt. VI. K. Hafner and M. Kreuder, Angew. Chem., 73, 657 (1961), have more recently prepared 5-azaazulene.

(8) Structures of this type (including 9 and 12) were first proposed in our laboratories during a discussion between A. G. A. and Allan G. Osborne and we acknowledge with thanks the contribution of the latter to the initial considerations which resulted in the present work.

(9) A. Albert, ref. 5, uses the terms π-deficient and π-excessive for the two types of simple heterocycles derived from benzenoid aromatic compounds to reflect the relative deficiency or excess, respectively, of π-electrons on the ring carbons. As these situations might not obtain in all cases of heterocycles derived from other aromatic systems, we prefer the use of the terms π-equivalent and π-excessive to describe only the relative numbers of π-electrons and ring atoms.

(10) (a) W. H. Perkin, Jr., and R. Robinson, J. Chem. Soc., 115, 921 (1919); W. O. Kermack, W. H. Perkin, Jr., and R. Robinson, ibid., 1877 (1922); (b) See for example R. H. F. Manske and H. L. Holmes, "The Alkaloids," Vol. II, Academic Press, Inc., New York, N. Y., 1952, Chapt. 13; E. Gellert, R.-Hamet, and E. Schlittler, Helv. Chim. Acta, 34, 642 (1951); R. A. Abramovitch, K. A. H. Adams, and A. D. Notation, Can. J. Chem., 38, 2152 (1960); L. Paoloni, ibid., 40, 1717 (1962).

(11) In recent years descriptions of a number of benz-derivatives of such structures have appeared. For leading references see D. Leaver, J. Smolinz, and W. H. Stafford, J. Chem. Soc., 740 (1962); W. Treibs and J. Beger, Ann., 652, 192, 204, 212 (1962); W. Treibs, W. Schroth, H. Lichtmann, and G. Fischer, Ann., 642, 97 (1961); M. Los and W. H. Stafford, J. Chem. Soc., 1680 (1959); W. Triebs and G. Kempter, Ber., 92, 601 (1959); G. V. Boyd, J. Chem. Soc., 55 (1959); G. V. Boyd, ibid., 1978 (1958); M. Los, J. P. Saxema, and W. H. Stafford, Proc. Chem. Soc., 352 (1957).

Subsequent to the completion of our work R. Mayer and J. Franke, Tetrahedron Letters, 9, 289 (1961), reported the preparation of the isomeric cyclopenta[b]thiapyran.