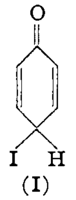
their interpretation of the kinetics of the iodination of phenol by solutions of iodine-triiodide ion in water. They concluded that the mechanism of the reaction probably involved attack of I^+ (or H_2OI^+) and acyl hypoiodite (or catalysis of HOI by a general acid HA) upon phenoxide ion. Grovenstein and Henderson[9] have pointed out that the kinetic results available do not exclude a rapid and reversible attack of iodine molecule upon phenoxide ion followed by a slow loss of proton to the solvent or to a general base A^- conjugate to the buffer acid HA.

In order to elucidate further the mechanism of the iodination of phenol, 2,4,6-trideuterophenol was prepared after the general procedure of Ingold[10] and co-workers. After two equilibrations of phenol with heavy water, a product which is estimated to be at least 99% 2,4,6-trideuterophenol was obtained. This phenol undergoes iodination at one fourth the rate of ordinary phenol. Thus in a typical experiment at 25° at initial concentrations of 0.0080 *M* in phenol and 0.00196 *M* in iodine, in aqueous solvent which was 0.500 *M* in acetic acid, 0.050 *M* in sodium acetate, 0.230 *M* in sodium perchlorate, and 0.020 *M* in sodium iodide, the initial apparent second order rate constants (calculated in terms of stoichiometric concentrations of phenol and iodine) were 1.21×10^{-3} l. mole^{-1} sec.$^{-1}$ for ordinary phenol and 3.05×10^{-4} l. mole^{-1} sec.$^{-1}$ for 2,4,6-trideuterophenol. These data give k_H/k_D 3.97. In related runs but in dilute perchloric acid in place of the acetate buffer, isotope effects of similar magnitude were obtained.

The present case, as far as we are aware, constitutes the first example of a hydrogen isotope effect during electrophilic aromatic halogenation. The only other known cases of hydrogen isotope effects during electrophilic aromatic substitution seem to be sulfonation[1,11] (k_H/k_T = 1.8), cyclodehydration[12] of 2-anilino-pent-2-ene-4-one (k_H/k_D = 1.5), and the reactions[4] of some diazonium ions upon hindered 2-naphthol-6,8-disulfonic acid (k_H/k_D = 3.6–6.6). Our present example shows that a phenol need not necessarily be hindered to give an isotope effect. We think it is significant that for the four types of electrophilic substitution reactions for which hydrogen isotope effects are known, three, including the present, involve reactions of phenols or aromatic amines. These are just the types of compounds which would be expected to give the most stable reactive intermediates, thus (I) for iodination of phenol. Substances analogous to (I) have indeed been isolated from reactions of 2,4,6-trisubstituted phenols.[13] General evidence, therefore, favors (I) as an intermediate in the iodination of phenol. On this basis, in order to account for both the kinetic evidence and isotope effect, intermediate (I) must, under the kinetic conditions which have been studied,[7,8] be transformed back to reactants considerably faster than into the final products, *i.e.*, (I) must be essentially at equilibrium with the reactants. From such kinetic data, therefore, the nature of the iodinating agent for phenol *cannot be specified*. We hope to be able to find conditions in which intermediates such as (I) from phenols are formed in the rate-determining step; only under such conditions, at best, can the nature of the iodinating agent be ascertained by reaction kinetics. Meanwhile we are investigating the generality of isotope effects during electrophilic halogenation of phenols and related compounds.



(I)

---

[9] E. Grovenstein, Jr., and U. V. Henderson, Jr., THIS JOURNAL. 569 (1956).

[10] C. K. Ingold, C. G. Raisin and C. L. Wilson, *J. Chem. Soc.*, 1637 (1936); A. P. Best and C. L. Wilson, *ibid.*, **28** (1938).

[11] U. Berglund-Larsson and L. Melander, *Arkiv Kemi*, **6**, 219 (1953).

[12] T. G. Bonner and J. M. Wilkins, *J. Chem. Soc.*, 2358 (1955).

[13] Thus see G. M. Coppinger and T. W. Campbell, THIS JOURNAL, **75**, 734 (1953); L. E. Forman and W. C. Sears, *ibid.*, **76**, 4977 (1954); J. A. Price, *ibid.*, **77**, 5436 (1955).

SCHOOL OF CHEMISTRY ERLING GROVENSTEIN, JR.
GEORGIA INSTITUTE OF TECHNOLOGY
ATLANTA, GEORGIA DONALD C. KILBY

RECEIVED APRIL 24, 1957

DETECTION OF FREE RADICAL INTERMEDIATES IN THE ACTION OF OXIDATION INHIBITORS

Sir:

Aromatic amines and phenolic compounds which inhibit oxidation have been presumed to act through the removal of hydrogen from the hydroxyl or amino group:

$$\mathrm{ArXH} + \mathrm{RO_2}\cdot \longrightarrow \mathrm{ArX}\cdot + \mathrm{RO_2H}$$
$$(\mathrm{ArX}\cdot \longrightarrow \text{inactive products})$$
$$k_1 \qquad (1)$$

Recent investigations have brought alternative proposals for the terminating reaction involving these inhibitors. Kooyman and Bickel[1] now suggest two consecutive reactions, both of which terminate oxidation chains

$$\mathrm{ArXH} + \mathrm{RO_2}\cdot \longrightarrow \mathrm{ArX}\cdot + \mathrm{RO_2H}\ k_{1a} \qquad (1a)$$
$$\mathrm{ArX}\cdot + \mathrm{RO_2}\cdot \longrightarrow \text{Stable product}\ k'_{1a} \qquad (1'a)$$

In (1'a) the product is either an adduct or the result of a second hydrogen abstraction.

Boozer, Hammond, *et al.*,[2,3] suggest two consecutive reactions

$$\mathrm{RO_2}\cdot + \mathrm{ArXH} \rightleftharpoons (\mathrm{RO_2ArXH})\cdot K_{1b} \qquad (1b)$$
$$(\mathrm{RO_2ArXH})\cdot + \mathrm{RO_2}\cdot \longrightarrow \text{inactive products},\ k'_{1b} \qquad (1'b)$$

the first of which is reversible and leads to an equilibrium concentration of a radical complex.

Kinetic analysis of the course of an oxidation inhibition period, when the inhibitor acts by the Kooyman and Bickel processes, gives

$$[\mathrm{ArX}\cdot] = \frac{1}{k_c - 1}[\mathrm{ArXH}]\left\{1 - \left(\frac{[\mathrm{ArXH}]}{[\mathrm{ArXH}]_0}\right)^{k_c - 1}\right\} \qquad (2)$$

for the concentration of the intermediate radical, where $[\mathrm{ArXH}]_0$ is the concentration of inhibitor

---

[1] A. F. Bickel and E. C. Kooyman, *J. Chem. Soc.*, 2215–2221 (1956).

[2] C. E. Boozer, G. S. Hammond, C. E. Hamilton and J. N. Sen, THIS JOURNAL, **77**, 3233–3237 (1955).

[3] G. S. Hammond, C. E. Boozer, C. E. Hamilton and J. N. Sen, *ibid.*, **77**, 3238–3243 (1955).

at the beginning of the inhibition period and $k_c = k'_{1a}/k_{1a}$.[4]

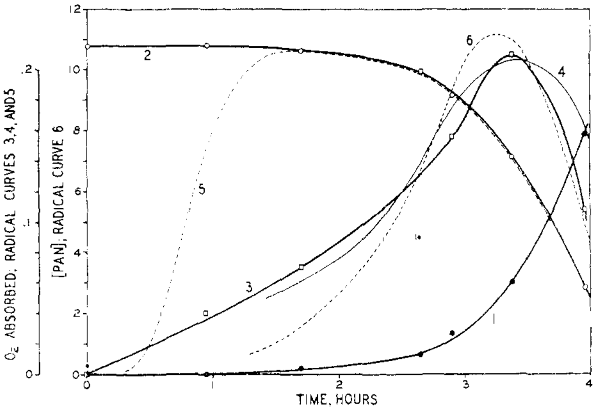
The Boozer and Hammond inhibition processes give

$$[(RO_2ArXH)\cdot] = \left(\frac{K_{1b}}{k'_{1b}}\right)^{1/2} [ArXH]^{1/2} (k_i + k_4[RO_2H])^{1/2} \qquad (3)$$

during the inhibition period, where $(k_i + k_4[RO_2H]) = -d[ArXH]/dt$.

We have followed the concentration of a radical formed during the oxidation at 171° of octadecene, inhibited with phenyl-α-naphthylamine (PAN) at 0.0108 *M* initial concentration. The radical concentration was determined by electron paramagnetic resonance measurements[5] made upon samples withdrawn during the course of the oxidation reaction and immediately frozen in liquid nitrogen. The half-life of the radicals at 25° was estimated to be about 30 hours. No radicals were detected in the unoxidized sample, in the inhibitor by itself, or in octadecene oxidized in the absence of inhibitor.

The results of our measurements are shown in the accompanying figure. The radical concentrations observed during the course of the reaction agree approximately with those predicted by the Boozer and Hammond reactions (Equation 2) for $K_{1b}/k'_{1b} = 1.1 \times 10^{-6}$ hour.



Oxidation of octadecene inhibited by 0.108 *M* phenyl-α-naphthylamine (PAN), at 171°: 1, oxygen consumed (moles/liter); 2, [PAN], $M \times 10^3$; 3, observed radical, $M \times 10^4$; 4, calculated radical ($M \times 10^4$), Equation 3, $K_{1b}/k'_{1b} = 1.1 \times 10^{-6}$; 5, calculated radical, Equation 2, $k_c = 500$; 6, calculated radical, Equation 2, $k_c = 7$.

The Kooyman and Bickel reactions, however, require either that the peak radical concentration be 50 times that observed (Curve 6), if the peak is to occur at the time in the reaction at which it is observed to occur, or that the peak occurs much earlier in the reaction and that the shape of the curve (Curve 5) be quite different from that observed, if the observed peak radical concentration is to be matched.

The great stability of the radical at room temperature argues somewhat against the Boozer and Hammond mechanism, because if the radical is formed reversibly, radical decay by $RO_2\cdot + RO_2\cdot$ is possible.

The inhibitor decay curve measured by a fluorescence method and the oxygen absorption curve are acceptable by both mechanisms.

Reaction (1) can also provide the radical concentrations observed if it is assumed that the radical product is destroyed rapidly by some oxidation product, perhaps peroxide, which rises to high concentration near the end of the inhibition period.

Attempts were made to measure concentrations of radicals formed during inhibition periods in octadecene at 171° where the inhibitors were 4-amino-3-pentadecylphenol, di-*t*-butyl-*p*-cresol, and *t*-butylcatechol. No radicals were found. The experiments are being continued at lower temperatures in the hope that increased radical stability will permit detection.

We are indebed to Dr. R. H. Sands and to Varian Associates of Palo Alto, California, for the electron paramagnetic resonance measurements.

CALIFORNIA RESEARCH CORPORATION O. L. HARLE
RICHMOND, CALIFORNIA J. R. THOMAS

RECEIVED APRIL 4, 1957

---

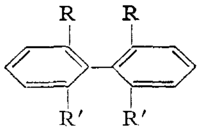
[4] Papers 22 (O. L. Harle and J. R. Thomas) and 23 (O. L. Harle) presented at the General Session of the Petroleum Division of the ACS, April 7-12, 1957; kinetic analyses available in Petroleum Division Preprints.

[5] J. E. Wertz, *Chem. Rev.*, **55**, 829-955 (1955).

THE ABSOLUTE CONFIGURATION OF 6,6'-DINITRO-2,2'-DIPHENIC ACID AND 6,6'-DIMETHYL-2,2'-BIPHENYLDIAMINE

Sir:

Kuhn and Rometsch have assigned[1] the R-configuration to (−)-Ia as a result of calculations based on a theoretical model.[2] We have now obtained evidence directly at variance with the above conclusion.



I

Ia, R = CH_3, R' = NH_2
b, R = COOH, R' = NO_2
c, R = $COOCH_3$, R' = NO_2
d, R = CH_2OH, R' = NO_2
e, R = CH_2Br, R' = NO_2
f, R = CH_3, R' = NO_2

Esterification of (−)-Ib[3] (m.p. 230–233°, $[\alpha]^{23}D$ −125° (MeOH)) gave (−)-Ic (m.p. 141–142°, $[\alpha]^{28}D$ −113° (EtOAc)); found: C, 53.6; H, 3.2, N, 8.2), which was reduced to (−)-Id (m.p. 120–121°, $[\alpha]^{20}D$ −65° (EtOAc)); found: C, 55.5; H, 3.7; N, 9.1) with $LiAlH_4$–$AlCl_3$. Conversion to (−)-Ie (m.p. 172–173°, $[\alpha]^{32}D$ −8.9 (THF)); found: C, 39.3; H, 2.1; N, 6.7) was followed by ring-closure to the iminonitrile (m.p. 295–300° dec., $[\alpha]^{28}D$ +837° (pyridine); found: C, 60.1; H, 3.7; N, 17.4). Hydrolysis gave DNDBCH-6-one[4] (m.p. 227–229°, $[\alpha]^{25}D$ +218° (EtOAc); found: C, 61.0; H, 3.8; N, 9.5). Since (+)-DNDBCH-6-one has the S-configuration,[4] the absolute configuration of (−)-Ib is thus established. Ib is of historical interest: it is the first compound[5] known to owe its optical activity to restricted rotation about a single bond.

---

[1] W. Kuhn and R. Rometsch, *Helv. Chim. Acta*, **27**, 1346 (1944).

[2] Reviewed by W. Kuhn, *Z. Elektrochem.*, **56**, 506 (1952).

[3] A. W. Ingersoll and J. R. Little, THIS JOURNAL, **56**, 2123 (1934).

[4] K. Mislow and P. Newman, *ibid.*, **79**, 1769 (1957).

[5] G. H. Christie and J. Kenner, *J. Chem. Soc.*, 614 (1922).