Radical-Induced Deiodination of Aryl Iodides in Alkaline Methanol[1]

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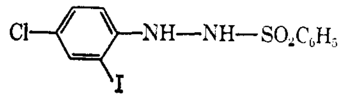
Abstract: *m*-Chloroiodobenzene is cleaved to chlorobenzene and iodide ion when exposed to the combination of a source of reactive radicals and a high concentration of sodium methoxide in methanol. Effective radical sources include 1-phenyl-2-benzenesulfonhydrazide (**3**) (with atmospheric oxygen), peroxydisulfate ion, benzenediazonium ion, phenylazotriphenylmethane, and azobisisobutyronitrile. The chlorobenzene formed in CH_3OD solution is substantially free of deuterium and *m*-chlorobiphenyl is formed in a benzene-rich solvent; the intermediacy of *m*-chlorophenyl radicals is indicated. Nitrobenzene, even in small amount, largely inhibits deiodination. The cyclic mechanism of eq 6–11 is proposed. Its unique features are formation of $\cdot CH_2O^-$ from $\cdot CH_2OH$ in an acid–base reaction and electron transfer from $\cdot CH_2O^-$ to the aryl iodide, with concomitant or subsequent ejection of iodide ion and formation of aryl radical.

The reaction of 1-(2-iodo-4-chlorophenyl)-2-benzenesulfonhydrazide (**1**) with sodium methoxide in methanol was found to produce chlorobenzene, an unexpected product, in addition to *m*-chloroiodobenzene and other products which were anticipated.[4] Happer, who performed that experiment, obtained evidence that the chlorobenzene resulted from deiodination of the *m*-chloroiodobenzene under the conditions of the reaction. Moreover, his experiments suggested that for deiodination to occur, it was necessary to provide both a high concentration of sodium methoxide and a 1-aryl-2-benzenesulfonhydrazide. Thus, *m*-chloroiodobenzene underwent deiodination on treatment with 1-(*o*-chlorophenyl)-2-*p*-toluenesulfonhydrazide in 2 *M* methanolic sodium methoxide, but not in the alcoholic base alone or with benzenesulfonamide in alcoholic base.



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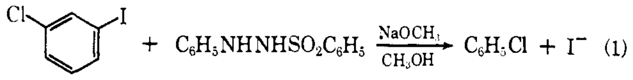
Hydrazide-Induced Deiodinations. Our investigation of the deiodination reaction therefore began with the system *m*-chloroiodobenzene (**2**)–phenyl-2-benzenesulfonhydrazide (**3**)–sodium methoxide–methanol. A series of experiments was performed to reveal the effects of several variables. In these experiments, 240 mg (0.001 mole) of *m*-chloroiodobenzene was treated with other reagents in the molar proportions indicated in Table I, in a total solvent volume of 20 ml, and under other conditions as noted. The results of these experiments are listed in Table I.



$$\mathbf{2} + C_6H_5NHNHSO_2C_6H_5 \xrightarrow[CH_3OH]{NaOCH_3} C_6H_5Cl + I^- \quad (1)$$

2 **3**

Table I. Deiodination of *m*-Chloroiodobenzene Induced by 1-Phenyl-2-benzenesulfonhydrazide[a]

Run no.	Moles of **3** per mole of **2**	Moles of $C_6H_5NO_2$ per mole of **2**	[$NaOCH_3$], *M*	Unreacted **2**, %	Product yields,[g] % C_6H_5Cl	C_6H_5I	I^-
1[b]	0	0	2.03	83	0.5	0	1
2[b]	1	0	0	95	0	0	0
3[b]	1	0	2.03	80	22	*e*	22
4[c]	1	0	2.03	38	41	*e*	43
5[d]	1	0	2.03	35	55	*e*	55
6	1	0	2.03	0	94	10	87
7	0.50	0	2.03	42	57	7	53
8	0.25	0	2.03	53	48	7	41
9	0.10	0	2.03	63	39	3	37
10	1	10.0	2.03	84	15	15	0
11	1	1.0	2.16	86	17	12	4
12	1	0.50	2.16	78	22	15	6
13	1	0.25	2.16	74	23	14	11
14	1	0.125	2.16	63	31	14	19
15	1	0.050	2.16	58	38	13	30
16	1	0	2.16	16	86	11	75
17	1	0	1.08	37	59	17	46
18	1	0	0.54	59	36	20	23
19	1	0	0.27	64	32	22	16
20[f]	1	0	2.16	70	30	5	26

[a] Unless otherwise noted, the reactions were carried out under air at ~23° for 1 day. [b] Reaction carried out at reflux temperature for 1 hr. [c] Reaction time 2 days at 0°. [d] Reaction time 2 hr. [e] Not determined. [f] Reaction carried out under nitrogen. [g] All yields are based on the amount of *m*-C_6H_4ClI provided.

It is noteworthy that sodium methoxide alone effects scarcely any deiodination (run 1), that no iodide ion is released by the hydrazide in the absence of base (run 2), and that higher yields of chlorobenzene and iodide ion were obtained at room temperature (*ca.* 23°) than at reflux or at 0° (runs 3–6). As to the stoichiometry of the process, the yields of deiodination products fall as the molar ratio of hydrazide to aryl iodide is progressively diminished, but not in direct proportion (runs 6–9). In run 9, only 0.1 mole of hydrazide was furnished per mole of *m*-chloroiodobenzene, but nearly 40% of the substrate was cleaved to chlorobenzene and iodide ion. Thus, some reactive species is regenerated in the course of the reaction.

The addition of excess nitrobenzene blocks deiodination (run 10). As the molar ratio of nitrobenzene

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[1] Based in part on the Sc.B. Thesis of C. C. W., June 1966. Research supported in part by the National Science Foundation.

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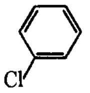
[4] J. F. Bunnett, D. A. R. Happer, M. Patsch, C. Pyun, and H. Takayama, *J. Am. Chem. Soc.*, **88**, 5250 (1966).

is reduced, deiodination makes a weak appearance (runs 10–15). But even when only 0.05 mole of nitrobenzene is present per mole of aryl iodide or hydrazide, the yield of deiodination products is reduced from about 90% to about 30% (*cf.* runs 6 and 15).

In most of the experiments of Table I, iodobenzene was obtained in small yield (usually about 15%) as a by-product. We speculated that the iodobenzene arose from the following sequence of reactions: cleavage of **3**, by methoxide ion, to form phenyldiimide ion (**4**);[5–7] air oxidation to phenylazo radical (**5**), which splits spontaneously to form phenyl radical and N_2;[8] and capture of iodine from **2** by phenyl radical (eq 4).

$$\mathbf{3} + OCH_3^- \longrightarrow \underset{\mathbf{4}}{C_6H_5N{=}N{:}^-} + C_6H_5SO_2^- \qquad (2)$$

$$\mathbf{4} + O_2 \longrightarrow \underset{\mathbf{5}}{C_6H_5N{=}N\cdot} \longrightarrow C_6H_5\cdot + N_2 \qquad (3)$$

$C_6H_5\cdot \;+\; \mathbf{2} \;\longrightarrow\; C_6H_5I \;+$  (4)

Inasmuch as the literature contained no indication that aryl radicals could abstract iodine from aryl iodides, the question was probed experimentally and the postulated abstraction was indeed found to occur, with ease.[9] Simultaneously, the iodine capture reaction was discovered by Brydon and Cadogan.[10]

The formation of iodobenzene was not blocked by addition of nitrobenzene (run 10) or by reducing the sodium methoxide concentration to a low level (run 19). Thus deiodination and iodine atom abstraction are fundamentally different processes. However, in the absence of sodium methoxide, iodobenzene failed to form just as deiodination failed to occur (run 2). This suggests that both deiodination and formation of iodobenzene have some early step in common.

All but the last run in Table I were performed in an air atmosphere. Under nitrogen, the yields of deiodination products and of iodobenzene were considerably less than they were under air (*cf.* runs 16 and 20). This suggests that both reactions require oxygen, at least in small amounts.

We hypothesize that phenyl radical, formed by reactions 2 and 3, is a common intermediate in both deiodination induced by **3** and in formation of iodobenzene.

Peroxydisulfate-Induced Deiodinations. If phenyl radical plays a key role in deiodinations induced by **3**, other reactive radicals might serve equally well. Peroxydisulfate ion is known to undergo thermal homolytic scission into two sulfate radical anions (eq 5).[11]

$$S_2O_8^{2-} \longrightarrow 2SO_4\cdot^- \qquad (5)$$

As shown in Table II, peroxydisulfate induces deiodination of *m*-chloroiodobenzene about as well as **3** does.

In Table II it is noteworthy that the combination of peroxydisulfate, in amount equivalent to *m*-chloroiodobenzene, and 2.2 *M* sodium methoxide effects quantitative deiodination (run 23). However, deiodination scarcely occurs in the absence of the radical source (run 21) and utterly fails in the absence of sodium methoxide (run 22). Inasmuch as the base is not required to generate radicals from peroxydisulfate ion (*cf.* eq 5), it is evident that high alkalinity is requisite for the deiodination process. This same conclusion can be inferred from runs 16–19, Table I.

Table II. Deiodination of *m*-Chloroiodobenzene Induced by Potassium Peroxydisulfate[a]

Run no.	Moles of $S_2O_8^{2-}$ per mole of **2**	Moles of $C_6H_5NO_2$ per mole of **2**	[NaOCH$_3$], *M*	Unreacted **2**, %	Product yields,[b] % C_6H_5-Cl	Product yields,[b] % I^-
21[c]	0	0	2.16	99	2	2
22	0.5	0	0	100	0	0
23	0.5	0	2.16	0	100	100
24[d]	0.25	0	2.16	59	41	41
25	0.25	0	2.16	11	85	86
26	0.125	0	2.16	43	57	52
27	0.050	0	2.16	55	47	46
28	0.125	0.25	2.16	100	0	1.5

[a] Unless otherwise noted, the reactions were carried out under nitrogen at reflux temperature for 1 day. [b] Yields are based on the amount of *m*-C_6H_4ClI provided. [c] Reaction time 16 hr. [d] Reaction carried out under air.

As the molar ratio of peroxydisulfate to *m*-chloroiodobenzene is reduced (runs 23 and 25–27), the yield of deiodination products also is reduced but not in proportion. When the maximum supply of radicals is only one-tenth the number of aryl iodide molecules, the yield of deiodination products (based on the aryl iodide) is still about 46%. The similarity of results between runs 9 and 27 is to be noted. In both series, the nonstoichiometric character of the reaction is evident.

A further similarity with the experience of Table I is the fact that nitrobenzene also blocks peroxydisulfate-induced deiodination (run 28).

All the reactions of Table II except run 24 were performed under nitrogen. Run 24 was carried out under air and the deiodination yield is distinctly lower than in a comparable run under nitrogen (run 25). With peroxydisulfate, oxygen is not required to generate radicals; evidently oxygen interferes with the deiodination process proper.

Deiodinations Induced by Other Radical Sources. If only a reactive radical is needed to induce deiodination, in the presence of methoxide ion, other radical sources should also be effective. Experiments summarized in Table III show that this expectation is fulfilled.

$C_6H_5N_2^+BF_4^-$
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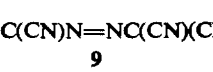
$C_6H_5\overset{\overset{\displaystyle O}{\|}}{C}N{=}NC_6H_6$
7

$(C_6H_5)_3CN{=}NC_6H_5$
8

$(CH_3)_2C(CN)N{=}NC(CN)(CH_3)_2$
9

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(5) R. W. Hoffmann, *Chem. Ber.*, **98**, 222 (1965).

(6) J. F. Bunnett and D. A. R. Happer, *J. Org. Chem.*, **31**, 2369 (1966).

(7) E. M. Kosower and P. C. Huang, *J. Am. Chem. Soc.*, **87**, 4645 (1965).

(8) S. G. Cohen and J. Nicholson, *ibid.*, **86**, 3892 (1964); **88**, 2247 (1966); *J. Org. Chem.*, **30**, 1162 (1965).

(9) J. F. Bunnett and C. C. Wamser, *J. Am. Chem. Soc.*, **88**, 5534 (1966).

(10) D. L. Brydon and J. I. G. Cadogan, *Chem. Commun.*, 744 (1966).

(11) J. O. Edwards, A. R. Gallopo, and J. E. McIsaac, *J. Am. Chem. Soc.*, **88**, 3891 (1966).

Table III. Deiodination of *m*-Chloroiodobenzene Induced by Diverse Reagents

Run no.	Reagent	Moles of reagent per mole of **2**	[NaOCH$_3$], *M*	Atm	Temp, °C	Time	Unreacted **2**, %	Product yields,[a] %		
								C$_6$H$_5$Cl	C$_6$H$_5$I	I$^-$
29	**6**	1	2.03	Air	*Ca.* 23[c]	2 hr	13	90	*b*	*b*
30	**7**	1	2.16	Air	*Ca.* 23	1 day	59	28	*b*	22
31	**7**	1	2.16	N$_2$	*Ca.* 23	1 day	75	6	1	5
32	**8**	0.74	2.16	Air	Reflux	1 day	0	100	0	100
33	**8**	0.74	0	Air	Reflux	1 day	88	12	12	0
34	**9**	0.50	2.16	N$_2$	Reflux	1 day	0	80	0	98

[a] Yields are based on the amount of *m*-C_6H_4ClI provided. [b] Not determined. [c] Room temperature, approximately 23°.

Decomposition of benzenediazonium ion in alkaline methanol was interpreted by DeTar and Turetzky[12] as a radical reaction. Their interpretation is supported by recent experiments in our laboratories.[13] Accordingly it is consistent that benzenediazonium fluoroborate (**6**) was effective in inducing deiodination (run 29).

Cohen and Nicholson[8] have shown that phenyl radicals are produced upon decomposition of benzoylphenyldiimide (**7**) in methanolic sodium methoxide. Presumably phenyldiimide anion is the immediate product from **7** and methoxide ion and oxidation is required to generate phenyl radical and nitrogen. It is therefore not unexpected that deiodination occurs with **7** and sodium methoxide under air (run 30) but to a lesser extent when precautions were taken to exclude oxygen (run 31). In runs 30 and 31, methyl benzoate was formed only to the extent of about 30%. Coupled with the relatively low efficiency of **7** in inducing deiodination, this implies that side reactions of reactive intermediates with **7** occurred to a large extent.[8]

Phenylazotriphenylmethane (**8**) undergoes homolytic scission to form phenyl radical, triphenylmethyl radical, and nitrogen.[14] In accord with experience described above, it very effectively induces deiodination in the presence of 2.2 *M* sodium methoxide (run 32), but not in its absence (run 33). It is curious that no iodobenzene was detected in run 32.

Azobisisobutyronitrile is widely employed as a radical source. In the presence of 2.2 *M* sodium methoxide, it also induces efficient deiodination (run 34).

Evidence for the Intermediacy of *m*-Chlorophenyl Radicals. It was conceivable that, in the formation of chlorobenzene from *m*-chloroiodobenzene, either *m*-chlorophenyl radical or *m*-chlorophenyl anion was an intermediate. These possibilities could be distinguished by performing the deiodination in methanol-O-*d* solution.[13,15] If the radical were the precursor of chlorobenzene, ordinary chlorobenzene ought to be formed because a radical can more readily abstract hydrogen from carbon of CH_3OD than deuterium from oxygen.[16] But the anion intermediate would capture the more acidic hydrogen isotope, namely, the deuterium, forming *m*-C_6H_4DCl.

The experiment was performed twice, once with hydrazide **3** as radical source (run 35, Table IV) and once with peroxydisulfate (run 36). In each case the total yield of chlorobenzene was high and it was predominantly free of deuterium. The intermediacy of *m*-chlorophenyl radicals is indicated. In each case, a small percentage of C_6H_4DCl was detected by mass spectrometry. It is not clear whether a small fraction of the reaction occurs *via* aryl anion intermediates or whether the deuterium is introduced by some other means.

Another test for the intermediacy of radicals is to perform deiodination in a solvent rich in benzene.[8,13] If *m*-chlorophenyl radicals are extant in the system, they ought to arylate the benzene, forming *m*-chlorobiphenyl. This product was indeed formed, with both hydrazide **3** (run 37) and diazonium salt **6** as radical sources (run 38).

We conclude that, at least for the most part, *m*-chlorophenyl radicals are precursors to the chlorobenzene formed in deiodination.

Experiments with Other Substrates. Deiodination of iodobenzene was attempted under conditions otherwise identical with those of run 23 (Table II). Only 19% of iodide ion and 12% of benzene were detected and 73% of the iodobenzene was unconsumed.[17] Iodobenzene is considerably less susceptible to deiodination than its *m*-chloro derivative.

Again under the conditions of run 23, debromination of *p*-bromochlorobenzene was attempted. Neither bromide ion nor chlorobenzene nor bromobenzene was detected as a product; the *p*-bromochlorobenzene was determined by quantitative glpc to be virtually unaffected. Earlier Happer, using 1-(*o*-chlorophenyl)-2-*p*-toluenesulfonhydrazide to induce dehalogenation, was unable to detect debromination of *m*-bromochlorobenzene or *p*-bromobenzotrifluoride. Debromination thus fails to occur under conditions which are conducive to deiodination.

Deiodination of *o*-bromoiodobenzene was effected under the conditions of run 6 (Table I). The products identified were iodide ion (94%), bromobenzene (100%), and iodobenzene (5%). With respect to experiences described above, these are normal products. It is significant that no trace of anisole was detectable. Were *o*-bromophenyl anion precursor to the bromobenzene formed, about 10% of it ought to have lost bromide ion, forming benzyne and thence anisole.[6] This is further evidence against the intermediacy of phenyl anions in this type of dehalogenation.

Reaction Mechanism. A satisfactory reaction mechanism must account for the effectiveness of radicals

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[12] D. F. DeTar and M. N. Turetzky, *J. Am. Chem. Soc.*, **78**, 3925, 3928 (1956).

[13] J. F. Bunnett and H. Takayama, unpublished experiments.

[14] R. Huisgen and H. Nakaten, *Ann.*, **586**, 70 (1954).

[15] J. F. Bunnett, D. A. R. Happer, and H. Takayama, *Chem. Commun.*, 367 (1966).

[16] C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p 480.

[17] A similar experiment, but using 1-(*o*-chlorophenyl)-2-*p*-toluenesulfonhydrazide to induce dehalogenation, was earlier performed by D. A. R. Happer, with similar results.

Table IV. Deiodination of *m*-Chloroiodobenzene in Special Solvents

Run no.	Radical source	Moles of radical source per mole of **2**	[$NaOCH_3$], *M*	Solvent	Atm	Temp, °C	Time, days	Products, %
35	**3**	1.0	2	CH_3OD	Air	*Ca.* 23	2	I^-, 100 C_6H_5I, 3 C_6H_5Cl, 91 C_6H_4DCl, 5
36	$S_2O_8^{2-}$	0.5	2	CH_3OD	N_2	Reflux	1	I^-, 93 C_6H_5Cl, 84 C_6H_4DCl, 12
37	**3**	1.0	1.36	67% CH_3OH 33% C_6H_6	Air	*Ca.* 23	2	I^-, 75 C_6H_5Cl, 72 C_6H_5I, 8 $(C_6H_5)_2$, 9 *m*-ClC_6H_4-C_6H_5, 13
38	**6**	1.0	1.36	67% CH_8OH 33% C_6H_6	Air	*Ca.* 23	1	I^-, 35 C_6H_5Cl, 38 C_6H_5I, 14 $(C_6H_5)_2$, 9 *m*-ClC_6H_4-C_6H_6, 9
39	$S_2O_8^{2-}$	0.5	0.5[a]	$(CH_3)_2CHOH$	N_2	Reflux	1	I^-, 20 C_6H_5Cl, 80
40	$S_2O_8^{2-}$	0.2	0.2[b]	$(CH_3)_3COH$	N_2	Reflux	1	I^-, 0.7 *c*

[a] Sodium isopropoxide. [b] Potassium *t*-butoxide. [c] A mere trace of chlorobenzene was formed; approximately 100% *m*-C_6H_4ClI unconsumed.

in inducing deiodination, for the nonstoichiometric character of the reaction in respect to the radical source, for the requirement of high methoxide ion concentration, and for the blocking effect of nitrobenzene, and it must specify an aryl radical as precursor to the deiodinated aromatic product.

For a while, a mechanism involving radical abstraction of iodine[9,10] as its key step was considered. In that mechanism, the initial radical abstracted hydrogen from methanol to form $\cdot CH_2OH$ which in turn abstracted iodine from *m*-chloroiodobenzene, forming iodomethanol (ICH_2OH) and *m*-chlorophenyl radical. Spontaneous breakup of the former afforded iodide ion and formaldehyde (observed products), while the latter abstracted hydrogen from methanol to produce chlorobenzene and regenerate $\cdot CH_2OH$, which started the cycle again. However, this mechanism had to be rejected because it does not account for the requirement of high sodium methoxide concentration nor for the blocking of deiodination by addition of nitrobenzene. Radical capture of iodine is not interfered with by nitrobenzene (*cf.* run 10, Table I).

The mechanism of eq 6–11 is compatible with the facts known to us. Reaction 6 has ample precedent.[16,18]

$$R\cdot + CH_3OH \longrightarrow RH + \cdot CH_2OH \qquad (6)$$

$$\cdot CH_2OH + CH_3O^- \rightleftarrows CH_3OH + \cdot CH_2O^- \qquad (7)$$

$$\cdot CH_2O^- + ArI \longrightarrow CH_2O + [ArI]\cdot^- \qquad (8)$$

$$[ArI]\cdot^- \longrightarrow Ar\cdot + I^- \qquad (9)$$

$$Ar\cdot + CH_3OH \longrightarrow ArH + \cdot CH_2OH \qquad (10)$$

$$\text{termination reactions} \qquad (11)$$

Reaction 7 is an acid–base reaction;[19] the species $\cdot CH_2O^-$, can be described as formaldehyde radical anion or ketyl anion.[20] The pK_a of diphenylhydroxymethyl radical, $(C_6H_5)_2\dot{C}OH$, has been estimated as 9.2 by Porter and Wilkinson.[21] This radical is several pK units more acidic than its "parent," benzhydrol, from which it can be derived by removal of a hydrogen atom. It is probable that α-hydroxyalkyl radicals in general are stronger acids than the parent alcohols.[22,23] The equilibrium of reaction 7 therefore probably lies well to the right.

Reaction 8 is an electron-transfer reaction. The formaldehyde radical anion should be an effective electron donor to a suitable acceptor. Aryl iodides are known to accept electrons with considerable ease. They are, for example, exceptionally reactive with the hydrated electron.[24] Electron acceptance is concerted with or followed by expulsion of iodide ion, which generates an aryl radical.[25] The unusual ease of electron acceptance by aryl iodides, as compared to other benzene derivatives, is thought to stem from the capability of iodine to accept the electron directly in one of its atomic orbitals; the electron may not need to enter a π-antibonding orbital, as is necessary with most aromatic compounds.[26]

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(18) M. C. R. Symons, *J. Chem. Soc.*, 277 (1959); W. T. Dixon and R. O. C. Norman, *ibid.*, 3119 (1963).

(19) Equation 7 can also be viewed as a hydrogen atom exchange equilibrium. The distinction is not relevant to this discussion, since the position of an equilibrium depends only on the initial and final states.

(20) Conceivably, the extra electron could be resident in an sp^3 orbital, as suggested by the formula $\cdot CH_2O^-$, or in an antibonding π orbital of formaldehyde.

(21) G. Porter and F. Wilkinson, *Trans. Faraday Soc.*, 57, 1686 (1961).

(22) R. Stewart, "Oxidation Mechanisms," W. A. Benjamin, Inc., New York, N. Y., 1964, p 66.

(23) W. V. Sherman, *J. Am. Chem. Soc.*, **89**, 1302 (1967).

(24) M. Anbar and E. J. Hart, *ibid.*, **86**, 5633 (1964).

(25) M. Anbar, M. Bobtelsky, and M. Mantel, unpublished work quoted by M. Anbar in E. J. Hart, "The Solvated Electron," Advances in Chemistry Series, No. 50, American Chemical Society, Washington, D. C., 1965, p 55.

(26) An unlikely variation on reaction 8 would be release of an electron from $\cdot CH_2O^-$ to solvent, forming formaldehyde and solvated electron, which then supplied the electron to the aryl iodide.

Polarographic reduction of aryl iodides is a two-electron process, but it is believed that transfer of the first electron is rate determining and that scission of the C–I bond is concerted with it.[27] Thus reaction 9 may not be an independent step, but rather concerted with reaction 8.

Reaction 10 is straightforward and similar to reaction 6. It completes a cycle which starts with reaction 7. The cycle accounts for the nonstoichiometric or catalytic character of the over-all process.

The termination reactions (11) involve interaction of radical species. They are discussed below.

Nitrobenzene blocks deiodination, in our view, by accepting electrons from $\cdot CH_2O^-$ more readily than *m*-chloroiodobenzene accepts them.[28] Moreover, the nitrobenzene radical anion or radicals derived from it may accumulate in the system and act as scavengers for the radicals which propagate the chain. In other researches, the blocking of a reaction by addition of a superior electron acceptor has been taken to support a mechanism involving electron transfer.[29]

The fact that *m*-chloroiodobenzene is more rapidly deiodinated than iodobenzene is also consistent with the mechanism of eq 6–11. The chlorine substituent increases the efficiency of electron transfer.[24,28] When it is absent, other reactions of $\cdot CH_2O^-$ or $\cdot CH_2OH$ have more opportunity to occur.

The inhibitory effect of oxygen (*cf.* runs 24 and 25, Table II) is also compatible with a radical chain mechanism.

The proposed mechanism should be capable of generalization to embrace primary and secondary alcohols, but not tertiary alcohols. In fact, deiodination does occur in isopropyl alcohol (run 39, Table IV) but it fails in *t*-butyl alcohol (run 40).

The Termination Reactions (11). We have not isolated or detected any termination products and therefore cannot judge from that type of evidence what termination step is the most important.

However, one feature of the data suggests that combination of two hydroxymethyl radicals to form ethylene glycol, or of $\cdot CH_2OH$ with $\cdot CH_2O^-$, is the predominant termination step. This is the fact that a high concentration of sodium methoxide is necessary to obtain optimum deiodination yields (*cf.* runs 16–19, Table I). If $\cdot CH_2OH$ is a substantially stronger acid than CH_3OH,[22,23] relatively low methoxide concentrations suffice to convert most of the $\cdot CH_2OH$ into $\cdot CH_2O^-$. The beneficial effect of high sodium methoxide concentration is therefore not primarily that it increases the supply of the electron transfer reagent.

On the other hand, the concentration of neutral hydroxymethyl radicals is appreciably reduced by increasing sodium methoxide concentration to a high level. If combination of two hydroxymethyl radicals is the predominant termination step and activity coefficient effects are neglected, a tenfold increase in sodium methoxide concentration (for example, from 0.2 to 2.0 *M*) will cause a 100-fold decrease in termination rate. The same change in base concentration would retard reaction of $\cdot CH_2O^-$ with $\cdot CH_2OH$ by a factor of 10. Increasing the methoxide concentration beyond, say, 0.1 *M* would not retard termination through reaction of two $\cdot CH_2O^-$ radical anions with each other, but the reaction between two radical anions is likely to be very slow for electrostatic and entropic reasons. If so, the postulate of predominant termination by reaction of $\cdot CH_2OH$ with $\cdot CH_2OH$ or $\cdot CH_2O^-$ accounts for the beneficial effect of high sodium methoxide concentrations. Independent confirmation of the postulated termination step would be desirable.

Related Reactions. The unique features of the proposed mechanism are the acid–base reaction of hydroxymethyl radical (eq 7) and the postulate that formaldehyde radical anion acts as an electron donor to aryl iodides (eq 8). We have been unable to discover prior mention of $\cdot CH_2O^-$ in the literature.

Ketyls from ketones are of course well known. The acetaldehyde radical anion has been judged to be formed on photolysis of nitrobenzene in alkaline ethanol, and then to donate an electron to nitrobenzene.[30]

A mechanism similar to that of eq 6–11 has recently been proposed by Sherman[23] for the radical-induced decomposition of nitrous oxide in alkaline 2-propanol. An important intermediate in his mechanism was the acetone radical anion, $(CH_3)\dot{C}{-}O^-$.

Beringer and Forgione[31] observed formation of benzene and iodide ion, the latter an unexpected product, in systems containing iodobenzene and radical sources with sodium alkoxides in the corresponding alcohols. It is probable that formation of iodide ion in their system represents the reaction with which the present paper is concerned.

If formaldehyde radical anion is indeed a key intermediate in the reactions we have described, it or its homolog, the acetaldehyde radical anion, is likely to be involved in other reductions which occur in alkaline methanol or ethanol, respectively. Certain reductions which occur on prolonged refluxing with alcoholic alkoxides come to mind, such as that of 2,4,6-trichloroiodobenzene to 1,3,5-trichlorobenzene[32] and of 2,4,6-tribromobenzophenone to 4-bromobenzhydrol.[33] In these cases radical formation probably depends on reactions involving atmospheric oxygen and thus is slow. The formaldehyde radical anion may also be involved in the reduction of nitrobenzene to azoxybenzene in hot alkaline methanol. The facts that there is an induction period and that azoxybenzene formation is retarded by oxygen[34] are consistent with a radical mechanism.

Experimental Section

Materials. Methanol (Baker and Adamson reagent grade) was purified by distillation from magnesium turnings, according to the method of Fieser.[35] Methanolic sodium methoxide was prepared

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[27] G. Rigatti in "Advances in Polarography," Vol. 3, I. S. Longmuir, Ed., Pergamon Press, Ltd., London, England, 1960, p 904.

[28] The polarographic half-wave reduction potentials of relevant species are formaldehyde, −1.71 v; iodobenzene, −1.62 v; *m*-chloroiodobenzene, −1.45 v; nitrobenzene, −0.83 v. It is probable that the rate of electron transfer from one species to another is greater the greater the difference in their reduction potentials. L. Meites, "Polarographic Techniques," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1965, Appendix C.

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[32] C. L. Jackson and F. H. Gazzolo, *Am. Chem. J.*, 22, 52 (1899).

[33] P. J. Montagne, *Rec. Trav. Chim.*, 27, 327 (1908).

[34] Y. Ogata and J. Mibae, *J. Org. Chem.*, 27, 2048 (1962).

[35] L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., New York, N. Y., 1957, p 289.

from clean sodium and methanol and kept in a reservoir under a soda-lime tube. Stock solutions were made up approximately 2 *M* and were standardized at least three times against potassium hydrogen phthalate, using phenolphthalein indicator. Methanol-O-*d* (CH_3OD) was generously provided by Dr. Hiroaki Takayama, who prepared it from deuterium oxide (D_2O) and dimethylcarbonate, according to the procedure of Streitwieser, *et al.*[36] Infrared spectra were taken of the samples just before use. The ratio of the areas of the O–H stretching band (3350 cm^{-1}) to the O–D stretching band (2500 cm^{-1}) was never more than about 5%. Isopropyl alcohol was purified by distillation through a 2-ft Vigreux column at 82°. The distillate was about 80% frozen in liquid nitrogen, the unfrozen material decanted away, and the solid retained. Potassium *t*-butoxide (0.2 *N*) in *t*-butyl alcohol was generously provided by Miss Rae R. Victor. Benzene was Fisher Certified reagent grade. Bromobenzene was from Eastman Kodak Co. and was shown to be pure by gas–liquid partition chromatography. A 4-ft column packed with 10% SE-30 on Chromosorb P was used with a column temperature of 90°. Iodobenzene from commercial sources was found unsuitable for use because of a major impurity, obvious in both its gas–liquid partition chromatogram and its infrared spectrum. Iodobenzene was prepared by diazotization of aniline and treatment with aqueous potassium iodide, according to the method of Lucas and Kennedy.[37] The product, bp 186–187°, was pure by gas–liquid partition chromatography under the conditions just described and gave an infrared spectrum identical with that published by the National Bureau of Standards.[38] Nitrobenzene was Fisher Certified Reagent Grade. *m*-Chloroiodobenzene was from Eastman Kodak Co. and was shown to be pure by gas–liquid partition chromatography under the conditions previously described. *o*-Bromoiodobenzene and *p*-bromochlorobenzene were from Eastman Kodak Co.

1-Benzenesulfonyl-2-phenylhydrazide was prepared from benzenesulfonyl chloride and phenylhydrazine in pyridine solution, according to the method of Bradshaw and Lambert.[39] The preparation from benzenesulfonyl chloride and excess phenylhydrazine in ether solution, after Fischer,[40] was equally effective. The product, recrystallized from absolute ethanol, was isolated as tiny white needles and had mp 157–159° (lit.[41] mp 164.5°) with evolution of gas.

Benzenediazonium fluoroborate was prepared by the diazotization of aniline hydrochloride, followed by treatment with aqueous fluoroboric acid, according to the method of Flood.[42] The product was isolated as a pale green powder, mp 125° dec (lit.[43] mp 121–122° dec).

Benzoyl phenyldiimide was prepared by oxidation of 1-benzoyl-2-phenylhydrazide by yellow mercuric oxide. The 1-benzoyl-2-phenylhydrazide precursor was prepared from benzoyl chloride and phenylhydrazine in pyridine solution. The synthesis is described by Cohen and Nicholson.[8] The product was isolated as an orange solid and kept constantly refrigerated, since it melted at room temperature (lit.[8] mp 28°).

Phenylazotriphenylmethane was prepared by oxidation of 1-triphenylmethyl-2-phenylhydrazine by potassium ferricyanide, according to the method of Wieland, vom Hove, and Börner.[44] The 1-triphenylmethyl-2-phenylhydrazine precursor was prepared from triphenylmethyl chloride and excess phenylhydrazine in ether solution, according to the method of Gomberg.[45] The final product was isolated as yellow needles, mp 119° dec (lit.[46] mp 110–112° dec).

Potassium peroxydisulfate was Baker and Adamson Reagent Special Grade. Azobisisobutyronitrile was from Aldrich Chemical Co. 1,2,3,4-Tetrahydrophthalazine reagent was generously provided by Professor E. Schmitz of the Deutsche Akademie der Wissenschaften zu Berlin, in a private communication to the senior author. Authentic samples used in product identifications were from the following sources. Chlorobenzene was from Eastman Kodak Co., shown to be pure by gas–liquid partition chromatography under the conditions previously described. Biphenyl was a sample available in the laboratory, recrystallized twice, mp 69.5–70.5°. *m*-Chlorobiphenyl, prepared from *m*-chloroaniline by a Gomberg reaction, was generously provided by Dr. Hiroaki Takayama.

General Reaction Procedure. A typical reaction was run in a 50-ml round-bottom flask equipped with magnetic stirrer, reflux condenser, and soda-lime tube. The compound serving as the radical source was weighed out accurately on a tared piece of glazed paper and transferred to the flask. The aryl iodide was weighed in a tared 5-ml beaker and transferred quantitatively to the flask by rinsings with a known amount of methanol. Any additional reagents, such as nitrobenzene, were added at this point. The sodium methoxide solution was added and the net concentration calculated. Reactions involving 1-benzenesulfonyl-2-phenylhydrazide typically became deep red upon addition of the base, the solid dissolved slowly in the base, and eventually the solution was pale yellow. In reactions involving potassium peroxydisulfate, crystals of potassium peroxydisulfate dissolve extremely slowly. Upon completion of the reaction, a finely divided white powder was present, presumably sulfate salts. All reactions of peroxydisulfate were protected from light by a complete aluminum foil covering.

Reactions with other radical sources and other solvents were run similarly. All reactions were worked up and analyzed as follows.

An accurately known amount of an internal standard, generally bromobenzene, was dissolved in the reaction solution. The solution was poured into 100 ml of distilled water and extracted twice with 20-ml portions of pentane. The pentane extracts were combined and dried over anhydrous magnesium sulfate. The aqueous solution was diluted to 250 ml in a volumetric flask.

Iodide ion yields were determined by potentiometric titrations of 50-ml aliquots of the aqueous reaction solution with 0.02 *N* silver nitrate solution, previously standardized against potassium iodide solutions. The solutions to be titrated were made distinctly acid by addition of 3 *M* nitric acid solution.

The organic products of the reaction were observed by gas–liquid partition chromatography of the pentane solution. The instrument used was an F & M Model 500, with thermal conductivity detector. The column most appropriate was a 4 ft × 0.25 in. aluminum column packed with 10% SE-30 on Chromosorb P. Separation was most effective at 60°, with a helium flow of about 60 ml/min. Typically, about 250 μl of the pentane solution was injected and the peaks observed, in order of increasing retention times, were pentane, benzene, chlorobenzene, bromobenzene, iodobenzene, nitrobenzene, and *m*-chloroiodobenzene. In the reactions which involve biphenyls as products, biphenyl and then *m*-chlorobiphenyl were observed as the last peaks. To speed some of the later peaks, the temperature was usually raised to 100° after the nitrobenzene peak and to 150° after the *m*-chloroiodobenzene peak. This allows all the peaks to be well shaped and still well separated.

Yields of all products were derived by comparison of peak areas with the peak area of the internal standard. Standardizations were made in the form of calculated molar response factors. These were determined for each individual product by analysis of an accurately known mixture of the product in question and the internal standard, chromatographed under conditions close to those encountered in a typical reaction analysis.

Identification of Products. Various products from these reactions were isolated by preparative gas–liquid partition chromatography. The column found most effective was a 4.5 ft × 0.375 in. aluminum column packed with 17% Carbowax 200M on Chromosorb P, using a helium flow of about 100 ml/min. The pentane reaction solution was concentrated to about 1 ml, all of which was injected. Collections were made in "U" tubes cooled in Dry Ice–isopropyl alcohol. The resulting samples were then analyzed for melting point, infrared spectrum, and/or mass spectrum, as described below.

From reaction 37, chlorobenzene, iodobenzene, biphenyl, and *m*-chlorobiphenyl were isolated. Chlorobenzene and iodobenzene were identified by their infrared spectra, which were in excellent agreement with spectra of authentic samples and spectra published by the National Bureau of Standards.[38] Biphenyl was identified by its infrared spectrum, in excellent agreement with the spectrum

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of an authentic sample, and its melting point of 67–68°. *m*-Chlorobiphenyl was identified by its infrared spectrum, in excellent agreement with that of an authentic sample.

Formaldehyde was detected in 45% yield from a reaction run identically with reaction 6. Formaldehyde was isolated by precipitation of its derivative with 1,2,3,4-tetrahydrophthalazine, as described by Schmitz and Ohme.[47] The derivative, 1,2,4,5-bis(*o*-xylylen)hexahydro-*sym*-tetrazine, was recrystallized from chlorobenzene and had mp 278–282° dec (lit.[47] mp 265–270° dec).

Chlorobenzene was isolated from reactions 35 and 36. In these cases, the extent of deuteration was calculated from mass spectrographic data. The normal parent peak was compared with the next higher peak, taking into account a correction factor for the natural abundance of carbon-13.

Note Added in Proof. Recently at the California Institute of Technology, with the cooperation of Dr. Steven Weiner, C. C. W. prepared a solution of 0.002 mole of *o*-chlorobenzene and 0.001 mole of 9 in 20 ml of 2-propanol saturated with sodium 2-propoxide. This solution was irradiated in the cavity of an esr spectrometer. Irradiation stimulated gas evolution and iodide ion was produced, but no esr signal was obtained.

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The Deamination of Optically Active Neopentylamine-1-*d*

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Abstract: (+)-(*R*)-Neopentylamine-1-*d* (I) underwent deamination in acetic acid to give (−)-(*R*)-2-methyl-1-butene-3-*d* (II) and the corresponding deuterated *t*-amyl acetate which was converted to II of the same optical purity by pyrolysis. The mechanistic implications of the high degree of stereospecificity observed are discussed.

There are few reactions of organic chemistry which have been more extensively examined than the deamination of primary amines, yet basic problems remain unresolved and obvious experiments require attention. We were struck by the fact that in no case had the stereochemistry of migration to primary carbon been investigated in this reaction. Sanderson and Mosher[1] have carried out the deoxidation of optically active neopentyl-1-*d* alcohol and have determined the stereochemistry of methyl migration but have suggested a mechanism different from that usually assumed for deaminations. The stereochemistry of substitution has been investigated in the deamination of *n*-butylamine-1-*d*[2] but no method for determining the stereochemistry of the competing hydrogen migration in such a case has yet been devised.

To be sure, many examples of deamination of optically active secondary carbinyl primary amines have been reported[3,4] and these usually show the low stereospecificity expected for relatively free carbonium ions. This would seem to demonstrate that even though product stability is of minimal importance in decomposition of alkyldiazonium salts, its influence is felt to the extent that reactions of primary alkylcarbinyl primary amines are more stereospecific than those of the corresponding secondary carbinylamines. The study of the stereochemistry of the deamination of optically active primary alkylcarbinylamines thus represents an upper limit on the stereospecificity which can be expected in deamination reactions for nonconformational reasons. Migration to give a tertiary carbonium ion should maximize such increases in migration rate as may be derived from the stability of the migration product and one might predict that methyl migration in the deamination of neopentylamine would show close to the maximum stereospecificity possible for loss of nitrogen from a diazonium salt.

Results and Discussion

(+)-(*R*)-Neopentylamine-1-*d* (I) of 93.5%[5] optical purity was treated with *n*-butyl nitrite in acetic acid to give a mixture of (−)-(*R*)-2-methyl-1-butene-3-*d* (II), 2-methyl-2-butene-3-*d* of 58% isotopic purity, (−)-(*R*)-1,1-dimethyl-1-propyl-3-*d* acetate (III), and a trace of neopentyl acetate. The optical rotation observed for II was $\alpha^{3}\text{D}$ −0.64 ± 0.05°. Pyrolysis of III at 500° gave II with $\alpha^{3}\text{D}$ −0.56 ± 0.03° and $\alpha^{20}\text{D}$ −0.52 ± 0.03°. Correction of these values for isotopic and optical impurities in the starting material gives a best value of $\alpha^{20}\text{D}$ −0.57° or 85% of the maximum rotation for the enantiomeric form of this compound as determined by Sanderson and Mosher.[1] It should be noted, however, that these authors found $\alpha^{23}\text{D}$ +0.61 ± 0.01° in an earlier experiment which is nearly within the experimental error of our value. The deuterium content of the starting amine was 98.5% of one atom of D but had been reduced to 96% in II, which could indicate exchange *via* diazoneopentane in the manner suggested by Friedman[6] and this would be accompanied by some racemization. It seems safe to

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