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Polar Radicals. 17.[1] On the Mechanism of Iodine Atom Transfer. A 9-I-2 Intermediate[2]

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Abstract: The atom-transfer reaction of iodine from an aryl iodide to a phenyl radical has been shown to proceed via a 9-I-2 intermediate. The relative kinetics of the reactions of the intermediate were investigated by studying its mode of decomposition upon formation from the reduction of a series of unsymmetrically substituted diaryliodonium salts. The iodonium salts were reduced by the electron-transfer reactions with several reagents: di-*tert*-butyl nitroxide, sodium 2,6-di-*tert*-butylphenylate, and sodium phenylate. The reduction by electron transfer of the iodonium salts by the latter reaction gives high yields of diaryl ethers. The mechanism for ether formation has been shown to proceed by two mechanistic pathways. For the diaryliodonium salts that have a *p*-cyano or *p*-nitro substituent, the ether is formed by a nucleophilic aromatic substitution; however, when the substituents were not strongly electron withdrawing, the mechanism resulting in ether formation involved electron transfer from the phenylate anion to the iodonium salt to form the phenoxy radical and a 9-I-2 intermediate. The intermediate decomposes to an aryl radical and an aryl iodide. The ether is formed from the efficient coupling of the aryl radical and the phenoxy radical.

The mechanism for the atom transfer of iodine from an aryl iodide to an aryl radical has been extensively studied.[4-8]

$$\mathrm{Ar}\cdot + \mathrm{Ar'I} \rightarrow \mathrm{ArI} + \mathrm{Ar'}\cdot$$

Three major mechanistic pathways have been considered.[4-8] The first pathway, aryl radical ipso addition and displacement of iodine (in a uni- or bimolecular sequence) to yield a new aryl iodide and a biaryl, could be ruled out since very little biaryl was formed. The second sequence involved the formation of a 9-I-2 intermediate followed by its decomposition to yield the new aryl iodide.

$$\mathrm{Ar}\cdot + \mathrm{Ar'I} \rightarrow \underset{\substack{\text{9-I-2}\\ \text{intermediate}}}{[\mathrm{Ar\text{-}\dot{I}\text{-}Ar'}]} \rightarrow \mathrm{ArI} + \mathrm{Ar'}\cdot$$

This mechanism was first recognized independently by Bunnett[4] and Cadogan[5] and was suggested as a feasible alternative possibility by Danen[6,7] to explain some irregularities in the kinetics of the atom-transfer reaction. The third mechanism considered, and the one favored by most workers,[4,5,7,8] involved direct atom abstraction.

$$\mathrm{Ar}\cdot + \mathrm{IAr'} \xrightarrow{\mathrm{Ar}\text{- - - -}\mathrm{I}\text{- - - -}\mathrm{A'}]^{\ddagger}\cdot} \mathrm{ArI} + \mathrm{Ar'}\cdot$$

The effect of a substituent on the relative rate of transfer of iodine from an aryl iodide to a phenyl radical was studied by Danen and Saunders.[6] The relative rectivities were determined competitively by generating phenyl radicals from the thermolysis (60 °C) of phenylazotriphenylmethane (PAT), in the presence of a series of meta- and para-substituted iodobenzenes, which were admixed with carbon tetrachloride (see Scheme I). A plot of log $(k_\mathrm{I}/k_\mathrm{Cl})$ (calculated from eq 1) vs. σ gave a good correlation,

$$k_\mathrm{I}/k_\mathrm{Cl} = ([\mathrm{PhI}]/[\mathrm{PhCl}])([\mathrm{CCl_4}]^0/[\mathrm{ArI}]^0) \qquad (1)$$

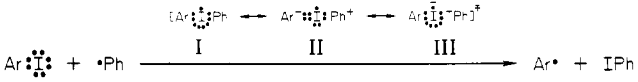
$r = 0.95$, and had a slope, ρ, of $+0.57$. The observation that electron-withdrawing substituents made the reaction more favorable (positive ρ value) indicates that a substantial contribution from charge-separated structures contributes to the transition state. Danen and Saunders[6] proposed that resonance structures II and III probably were representative of these canonical forms.

Scheme I

$$\mathrm{Ph{-}N{=}N{-}CPh_3} \xrightarrow[\Delta]{} \mathrm{Ph}\cdot + \cdot\mathrm{CPh_3} + \mathrm{N_2}$$

$$\mathrm{Ph}\cdot + \mathrm{IAr} \xrightarrow{k_\mathrm{I}} \mathrm{PhI} + \mathrm{Ar}\cdot$$

$$\mathrm{Ph}\cdot + \mathrm{CCl_4} \xrightarrow{k_\mathrm{Cl}} \mathrm{PhCl} + \cdot\mathrm{CCl_3}$$



Subsequent to this report it was pointed out that for a direct atom transfer, which was presumed a priori to be the mechanism of the reaction, the polarity of the important charge-separated contributors to the transition state would be expected to change from i to ii as the substituent was changed from an electron-withdrawing group to an electron-donating group.[8] The subsequent authors

$$[\underset{\text{i}}{\mathrm{Ar}^{\delta+}\text{–}\mathrm{I}\text{–}\mathrm{Ph}^{\delta-}} \leftrightarrow \underset{\text{ii}}{\mathrm{Ar}^{\delta-}\mathrm{I}\text{–}\mathrm{Ph}^{\delta+}}]^{\ddagger}\cdot$$

proposed a resonance structure for the transition state leading to abstraction, eq 2, which predicted a negative ρ for the reaction.[8]

$$[\mathrm{Ph}\cdot\dot{\mathrm{I}}\cdot\mathrm{Ar} \leftrightarrow (\mathrm{Ph}^{\delta+}\bar{\mathrm{I}}^{\,\delta+}\mathrm{Ar})\cdot] \qquad (2)$$

For rationalization of the positive ρ value observed by Danen, the effect of the substituent on the relative rate of reaction was proposed to be controlled by the change in bond dissociation energy (BDE) affected by the substituent on the aryl iodine bond.[8] Presumably electron-withdrawing groups weaken the carbon–halogen bond and electron-donating groups strengthen the bond. An explanation involving two opposing effects, polar and BDE's, may be necessary to explain the energetics of the reactions; however, in accepting this explanation one loses the ability to easily predict the structure–reactivity relationship.

Because of the possibility that the structure–reactivity relationship observed by Danen might also be compatible with the reversible formation of a 9-I-2 intermediate, the mechanism of the iodide atom transfer was reinvestigated.

Results and Discussion

Kinetic Analysis. Phenyl radicals were generated by the method of Danen[6] by the thermolysis of PAT at 60 °C for 18 h in a mixture of a substituted iodobenzene (ArI) and carbon tetrachloride. The competitive abstraction rate constants (Scheme I) were determined (using eq 1) for 20 substituted iodobenzenes. Included in this series were the 12 substrates reported previously.[6] A list of the relative reactivities obtained, and for comparison purposes the values obtained by Danen, is given in Table I. With

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(1) For part 16 of this series, see: D. D. Tanner, E. V. Blackburn, D. W. Reed, and B. P. Setiloane, *J. Org. Chem.*, **45**, 5183 (1980).

(2) For a complete description of this nomenclature, see: C. W. Perkins, J. C. Martin, A. J. Arduengo, W. Lau, A. Alegria, and J. K. Kochi, *J. Am. Chem. Soc.*, **102**, 7753 (1980).

(3) B. P. Setiloane, Postdoctoral Fellow, University of Alberta, 1981–1982.

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

(5) D. L. Brydon and J. I. Cadogan, *Chem. Commun.*, 744 (1966); *J. Chem. Soc. C*, 819 (1968).

(6) W. C. Danen and D. G. Saunders, *J. Am. Chem. Soc.*, **91**, 5924 (1969).

(7) W. C. Danen, "Methods in Free-Radical Chemistry", Vol. 5, Chapter 1, E. S. Huyser, Ed., Marcell Dekker, New York, 1974.

(8) W. H. Davis, Jr., J. H. Gleaton, and W. A. Pryor, *J. Org. Chem.*, **42**, 7 (1979).

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Table I. Relative Reactivities (k_I/k_{Cl}) for Iodine Abstraction from Substituted Iodobenzenes (XC_6H_4I, 1.5 M) by the Phenyl Radical at 60 °C[a]

substituent X	$[CCl_4]^0/[XC_6H_4I]^0$	$[PhI]/[PhCl]^b$	$\log (k_I/k_{Cl})^b$	$\log (k_I/k_{Cl}^-)^d$	σ^e
m-NO_2	7.00	6.07	1.63 ± 0.01 (3)	1.67	0.71
p-NO_2	80.9 (17.06)[f]	0.297 (1.45)[f]	1.36 ± 0.01 (7)	1.54	0.81
p-CN	15.3	2.15	1.52 ± 0.00 (3)	1.51	0.70
m-Br	6.93	4.69	1.51 ± 0.00 (3)	1.53	0.37
m-$COCH_3$	7.00	3.82	1.43 ± 0.04 (3)	1.44	0.36
p-Br	7.07	3.02	1.33 ± 0.00 (2)	1.32	0.26
m-OCH_3	6.46	3.36	1.33 ± 0.00 (2)	1.32	0.10
m-CH_3	6.71	2.92	1.29 ± 0.00 (2)	1.23	−0.06
p-C_6H_5	7.02	1.92	1.14 ± 0.02 (4)	1.14	0.05
p-CH_3	7.03	1.90	1.13 ± 0.00 (4)	1.11	−0.14
p-OCH_3	7.00	1.43	1.00 ± 0.00 (3)	0.98	−0.12
m-CN	6.91	5.51	1.58 ± 0.01 (2)		0.62
p-CHO	7.05	3.97	1.45 ± 0.00 (2)		0.47
m-CF_3	7.00	3.99	1.45 ± 0.00 (3)		0.46
m-CHO	7.00	3.99	1.44 ± 0.01 (3)		0.41
m-CO_2CH_3	7.00	3.57	1.40 ± 0.00 (3)		0.35
p-CO_2CH_3	7.02	2.72	1.28 ± 0.01 (3)		0.44
p-$COCH_3$	7.00	2.60	1.26 ± 0.00 (3)		0.47
m-NH_2	7.00	2.52	1.25 ± 0.01 (2)		−0.09
p-NH_2	6.99	1.18	0.92 ± 0.01 (6)		−0.30

[a] In this work the [PAT] was 0.2 M. [b] Calculated from the area of the ratios determined from GLPC analysis and corrected by determining a calibration factor with using known amounts of authentic materials. [c] The errors indicated correspond to average deviation from the mean, while the numbers given in parentheses are the number of individual experiments. [d] Values previously reported, see ref 6. [e] The σ values used were taken from the recommended best values: O. Exner, "Correlation Analysis in Chemistry", N. B. Chapman and J. Shorter, eds., Plenum Press, London, 1978. [f] Solvent CCl_4 was diluted with benzene 1:1 (v:v) for added solubility. The values with and without benzene were within the experimental error shown.

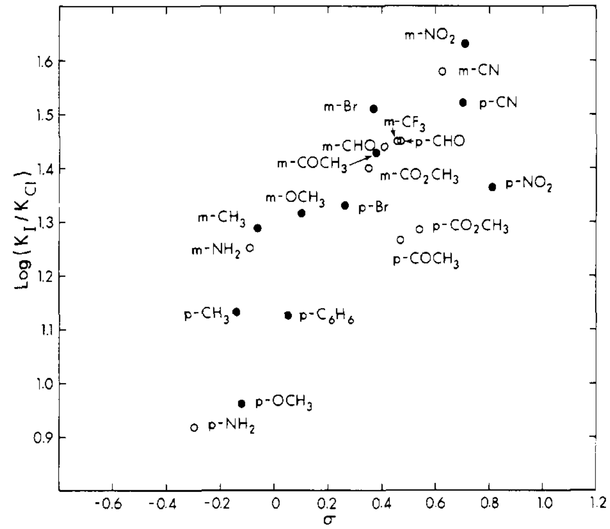


Figure 1. Plot of log (k_I/k_{Cl}) at 60 °C vs. Hammett σ constants (see data in Table I). Closed circles (●) are the redetermined values previously reported in ref 6. Open circles (○) have not been previously measured.

the exception of the value obtained for the reaction of p-nitroiodobenzene, the relative rates previously reported[6] and those obtained in this study agreed within experimental error, ±2%. When a plot of log (k_I/k_{Cl}) was made for the values obtained for the entire series of substituted iodobenzenes investigated (see Table I and Figure 1), the Hammett correlation was unsatisfactory ($\rho = 0.474$, $r = 0.820$, $S_\rho = 0.108$).

Originally Danen[6] had observed that the Hammett plot for the abstraction reaction appeared to be nominally divided into two groups of substituents. Although he made a single correlation, he noted that two better correlations could be obtained by grouping the meta and the para substituents separately. On this basis he suggested the alternative explanation that a 9-I-2 intermediate could account for the deviation of the relative rates obtained for the reactions of the para-substituted iodobenzenes. No such grouping of the reactivities for the meta- and para-substituted aryl iodides was observed in our study (see Figure 1); however, it was evident that the lack of correlation indicated a mechanism more complex than direct abstraction.

It is clear that, for a reaction with such a small substituent constant, if an intermediate is involved in the reaction pathway, it must be formed reversibly. A scheme based on a reversibly formed intermediate is shown in Scheme II. A kinetic expression for the relative formation of iodobenzene and chlorobenzene from the competitive reaction of phenyl radicals with an aryl iodide and carbon tetrachloride can be derived by using scheme II (see eq 3). In this scheme the ratio of observed rate constants de-

$$\frac{[PhI]}{[PhCl]}\,\frac{[CCl_4]}{[ArI]} = \frac{k_I}{k_{Cl}}\left(\frac{1}{k_2/k_{-1} + 1}\right) \tag{3}$$

termined, $(k_I/k_{Cl})_{obsd}$, is a more complex expression (see eq 4).

$$(k_I/k_{Cl})_{obsd} = \frac{k_I}{k_{Cl}}\left(\frac{1}{k_2/k_{-1} + 1}\right) \tag{4}$$

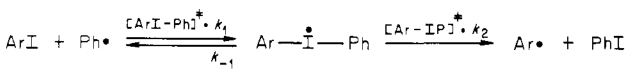
Any Hammett linear free-energy correlation in this type of complex mechanism will follow a substituent dependence for the three individual processes, the combination of which may not show a linear correlation.

The polarity of the two transition states for the decomposition reactions of the intermediate should determine the response of the reaction to the substituent. The reaction which involves the formation of a phenyl radical, rate constant k_{-1}, and its microscopic reverse, rate constant k_1, will have the same response to a substituent (Scheme II).

The Intermediate. The observed kinetics (Scheme II) for the atom-transfer reactions could be evaluated if the rate constants, or their ratios, k_{-1} and k_2, were known. In principle, the ratio k_2/k_{-1} could be determined (see eq 5) from an analysis of the products obtained from the decomposition of the 9-I-2 intermediate generated from the reduction of the appropriate diaryliodonium salt (Scheme III).

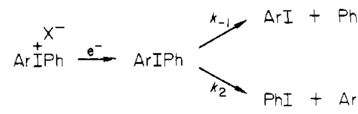
An attempt to generate the intermediate electrochemically proved unsuccessful, since the reduction process was found to depend upon the surface of the electrode (mercury or platinum). However, several chemical reductions were developed, which allowed the evaluation of the relative rates of decomposition of the intermediate.

Scheme II



$$ArI + Ph\bullet \xrightleftharpoons[k_{-1}]{[ArI\text{-}Ph]^{\ddagger}\cdot\, k_1} Ar{-}\overset{\bullet}{I}{-}Ph \xrightarrow{[Ar\text{-}IP]^{\ddagger}\cdot\, k_2} Ar\bullet + PhI$$

Scheme III



$$[PhI]/[ArI] = k_2/k_{-1} \tag{5}$$

Scheme IV

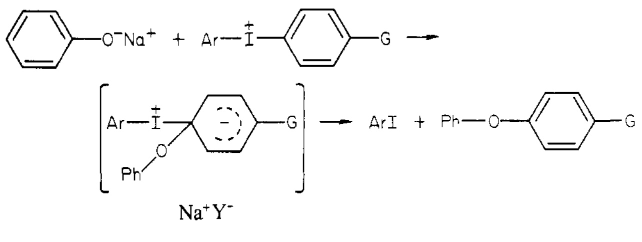


Table II. Products from the Reaction of Diaryliodonium Salts with Sodium Phenoxide, 60 °C, and the Relative Rates of Decomposition of the 9-I-2 Intermediate, C_6H_5-I-C_6H_4Y

	reactants,[a] mmol × 10^2	products,[b] mmol × 10^2						yield, %			
Y	PhI^+ArX^-	PhI	C_6H_4YI	PhOPh	PhOAr[c]	C_6H_6	C_6H_5Y	iodides	ether	benzenes	k_2/k_{-1}
p-NO_2	10.0	8.37	0.070	tr	7.95	ND	ND	84.5	79.5	ND	119
	10.0	8.38	0.065	tr	7.96	ND	ND	84.5	79.6	ND	128
p-CN	10.0	9.14	0.123	0.0831	8.61	ND	ND	92.6	87.0	ND	74.1
	9.88	9.00	0.145	0.0987	8.64	ND	ND	91.5	87.4	ND	90.9
m-NO_2	10.0	8.56	0.844	0.309	7.98			94.0	79.83		10.4
	25.0	21.0	2.16	1.73	19.0	1.44	0.918	94.2	84.35	9.43	10.1
p-Br	10.0	4.87	3.35	2.89	4.53			82.2	74.2		1.45
	10.0	4.89	3.38	2.91	4.58			82.7	74.8		1.45
	27.0	13.6	8.98	7.85	12.4	0.62	1.30	99.2	89.9	8.46	1.51
m-CHO	9.98	5.89	1.78	0.886				76.75			3.30
	9.98	5.82	1.69	0.883				75.12			3.43
p-CH_3	9.85	1.51	5.13	4.82	1.40			67.4	63.2		0.294
	9.85	1.39	4.61	4.61	1.27			61.0	59.7		0.302
	29.7	6.85	22.3	20.9	5.87	1.43	1.33	99.1	90.3	9.29	0.328
	29.7	7.21	22.0	19.8	6.59	1.50	1.49	98.2	88.9	10.1	0.320
m-CH_3	7.57	2.78	4.74	4.65	2.35			99.3	92.0		0.589
	7.57	1.84	3.05	2.97	1.31			64.6	56.5		0.602
m-CN	10.0	7.92	1.11	0.426	7.34			90.3	77.6		7.20
	10.0	7.82	1.09	0.736	7.29			89.1	80.3		7.16
p-OCH_3	10.0	0.513	5.52	5.60				60.3			0.092
	9.98	0.606	6.56	6.65				71.7			0.092
m-Br	10.0	4.69	1.57	0.889	3.46			62.6	43.5	2.99	
	10.0	4.82	1.64	0.961	4.03			64.6	49.6	2.94	
	20.3	14.9	5.08	4.73	12.4	0.82	1.37	98.4	84.4	10.8	2.98
m-CF_3	10.0	4.40	1.07	0.505	3.35			54.7	38.5		4.11
	10.0	4.61	1.14	0.509	3.70			57.5	42.1		4.04
	10.0	6.92	1.48	1.01	4.78			84.0	59.9		4.68
m-OCH_3	21.5	8.82	10.8	9.16	6.95	1.02	1.21	91.4	75.9	10.4	0.814
	17.2	7.32	8.98	7.21	5.85	0.893	0.935	94.8	76.0	10.6	0.815

[a] The anions, X^-, used were those listed in the Experimental Section. [b] ND, not detectable. [c] The values that are omitted were done so since the authentic ethers were unavailable for calibration.

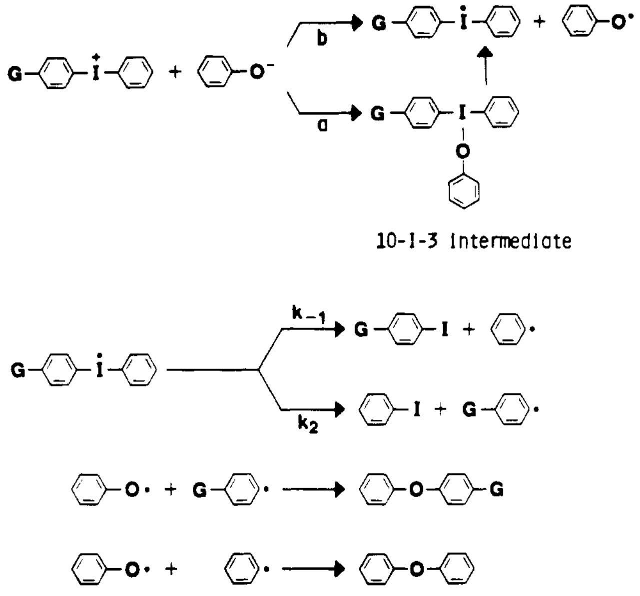
The syntheses of diaryl ethers from diaryliodonium salts and the sodium salt of a phenylate anion have been reported.[9] Although the reaction was proposed to proceed via nucleophilic aromatic substitution (see Scheme IV), the substitution does not require activation by electron-withdrawing substituents.

A survey of the literature on the decomposition (i.e., reactions) of diaryliodonium salts suggests an alternative mechanism for diaryl ether formation (see Scheme V). Both of the pathways a and b leading to the formation of the 9-I-2 intermediate (see Scheme V) have been described as alternative reaction sequences leading to the formation of aryl radicals.

The decomposition of diaryliodonium salts in *n*-propyl alcohol carried out in the presence of metallic tellurium was reported to yield diaryltellurium. The mechanism of the reaction was proposed to involve the formation of phenyl radicals and their subsequent capture by tellurium to form the organometallic.[10] The reaction of diaryliodonium salts with neutralized (sodium carbonate) aqueous solutions of thiols (thiophenol, thioglycolic acid) yielded thio ethers or thioesters. The phenyl radicals, presumably intermediates in the reaction, could be scavenged by tellurium to form the diaryltellurium.[11]

The base-promoted phenylation of pyridine had been suggested[12] to involve phenyl radicals generated from the homolysis of a 10-I-3 intermediate, $(C_6H_5)_2IOH$. The same intermediate was proposed to be involved in hydrolysis of diaryliodonium salts.[13,14] During the investigation of the hydrolysis reaction, it was noted that the direction of cleavage of unsymmetrically substituted diaryliodonium salts did not proceed in a manner consistent with an S_NAr mechanism.[14]

Scheme V



The phenylation of enolate anions by diphenyliodonium salts has been reported.[15] These reactions have been proposed to proceed by a homolytic pathway that involves the generation of the phenyl radicals by electron transfer from the enolate anion to the diaryliodonium salt with subsequent decomposition of the

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(9) (a) F. M. Beringer, A. Brierley, M. Drexler, E. M. Grindler, and C. C. Lumpkin, *J. Am. Chem. Soc.*, **75**, 2708 (1953); (b) F. M. Beringer and E. M. Grindler, *ibid.*, **77**, 3203 (1955); (c) J. R. Growder, E. E. Glover, M. F. Grundon, and H. X. Kaempfen, *J. Chem. Soc.*, 4578 (1963).

(10) R. B. Sandin, F. T. McClure, and F. Irwin, *J. Am. Chem. Soc.*, **61**, 2944 (1939).

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(13) F. M. Beringer, E. M. Gindler, M. Rapoport, and R. J. Taylor, *J. Am. Chem. Soc.*, **81**, 351 (1959).

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

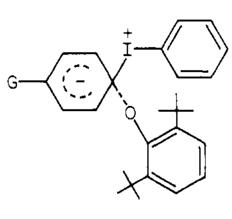
(15) (a) F. M. Beringer, S. A. Galton, and S. J. Huang, *J. Am. Chem. Soc.*, **84**, 2819 (1962). (b) F. M. Beringer and P. S. Forgione, *Tetrahedron*, **19**, 739 (1963).

9-I-2 intermediate. The coupling products of the radicals formed were consistent with the mechanism, as were the products from phenyl radical abstraction from the alcoholic solvents used.

A number of unsymmetrically substituted iodonium salts were synthesized and were allowed to react with aqueous solutions of sodium phenoxide (60 °C). An analysis of the product mixtures showed that besides unreacted starting materials an almost equimolar amount of aryl iodide and diaryl ether had been formed. The iodides were formed in slightly higher yields than the ethers, but accompanying the ether formation were small amounts of benzene and substituted benzenes (see Table II). Assuming the mechanism depicted in Scheme V, the relative ratios of rate constants, k_2/k_{-1}, were calculated from the relative amounts of iodobenzenes formed (see eq 5). Regardless of the extent of reaction, the relative rate ratios remained constant. For a mechanism that involved the formation of diaryl ethers from the coupling of aryl and phenoxy radicals (see Scheme V), the high yield of ethers suggests that ether formation results from the coupling of geminately formed radical pairs. Consistent with this mechanism, however, was the observation that benzenes appeared to be formed at the expense of the diaryl ethers (see Table II), presumably from the reaction of cage-escaped radicals.

Examination of the ratios of k_2/k_{-1} values calculated for the reaction of the series of diaryliodonium salts (see Table II) suggests that the series of substituents forms a group of reactions governed by inductive effects with the exception that the reaction of *p*-cyano- and *p*-nitrodiphenyliodonium chloride appeared to give much higher values than anticipated. The high values obtained for the reactions of diaryliodonium salts containing strongly electron-withdrawing groups suggest the possibility that these substrates are able to stabilize the transition state leading to the formation of the S_NAr intermediate (see Scheme IV) and that they react with phenoxide anion to give the unsymmetrically substituted ether not only by electron transfer but also by the nucleophilic aromatic-substitution mechanism originally proposed.[9] In support of the nonhomolytic pathway, it is noted that the reactions of the substrates that proceeded primarily via nucleophilic aromatic substitution, the *p*-nitro- and *p*-cyano-substituted diaryliodonium salts, also did not yield detectable amounts of benzene, as did the reactions that utilized the homolytic pathway (see Table II).

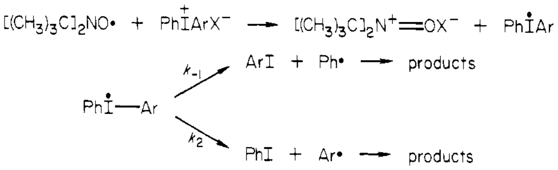
It was assumed that the reactions that proceeded by the homolytic pathway would show the same ratio of rate constants, k_2/k_{-1}, for the decomposition of the intermediate formed by electron transfer with a hindered phenolate anion, 2,6-di-*tert*-butylphenolate, as were found for the reaction of phenolate anion. However, if the reaction proceeded by a combination of both mechanistic pathways, the S_NAr reaction would be sterically retarded by the hindered phenol (see eq 6) and the ratio of decomposition rates, k_2/k_{-1}, would be different.



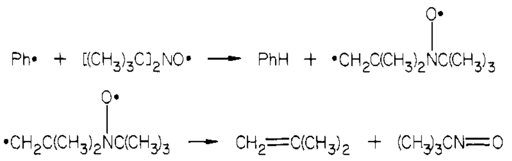
(6)

When the iodonium salts were allowed to react with the sodium salt of 2,6-di-*tert*-butylphenol, more complex mixtures of products were obtained; however, an analysis of the ratio of products iodobenzene/aryl iodide allowed the determination of k_2/k_{-1} (see eq 5). A comparison of relative rate constants obtained for the reaction of both phenolates is shown in Table III. In agreement with the assumptions concerning steric effects, the reactions run with the hindered phenol gave the same relative rate ratios for the diaryliodonium salts with electron-donating or moderate electron withdrawing substituents, but for the reactions of the iodonium salts with strongly electron withdrawing groups, *p*-nitro or *p*-cyano, the ratio of k_2/k_{-1} changed significantly (see Table III). The k_2/k_{-1} values obtained from the reactions with the hindered phenols presumably represent the results obtained subsequent to electron transfer. For a further probe of the assumption that the relative rates, k_2/k_{-1}, are solely resultant from the reductive decomposition of the iodonium salts, another method for the reduction of the iodonium salts involving electron transfer was available to test the mechanism for reduction. Electron-transfer reactions with the stable free radical di-*tert*-butyl nitroxide as the reagent have been reported by Tedder.[16]

Scheme VI



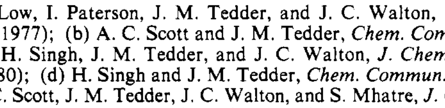
Scheme VII



The reagent radical has been used as an electron-transfer agent for the reduction of stable acceptors or reactive intermediate radicals and cations, which function as acceptors. The use of di-*tert*-butyl nitroxide as a reducing agent for the diaryliodonium salts is analogous to the reduction of aryldiazonium salts recently published by Tedder.[16e] Similarly, a scheme can be devised for the generation of the 9-I-2 intermediate from a diaryliodonium salt (see Scheme VI).

Mixtures of aqueous solutions of diaryliodonium salts (2 × 10^{-2} M) and di-*tert*-butyl nitroxide (1 × 10^{-2} M) were allowed to react thermally (60 °C) or were further catalyzed by light (60 °C, Pyrex, 500-W incandexcent bulb). An analysis of the ratio of [PhI]/[ArI] formed in the di-*tert*-butyl nitroxide reductions of a series of iodonium salts allowed the calculation (see eq 5) of k_2/k_{-1}. The photoinitiated reactions proceeded to a greater extent than the thermal reaction, presumably by a photostimulated electron-transfer process; however, the relative rate constants, k_2/k_{-1}, obtained from both types of reaction were the same, within the experimental limitations reported. A comparison of these values to those obtained for the reactions of the two phenylate salts is listed in Table III. Within experimental error the k_2/k_{-1} values obtained for the nitroxide reductions are the same as those obtained for the homolytic reactions of the phenylate or 2,6-di-*tert*-butylphenylate anions. The nitroxide reduction of the diazonium salts was reported to produce phenyl radicals, which were found to yield a complex mixture of products.[16c] One of the proposed routes leading to the formation of benzene was phenyl radical abstraction from the solvent di-*tert*-butyl nitroxide. The new radical underwent fragmentation to yield isobutylene and 2-methyl-2-nitrosopropane (see Scheme VII).

The nitroso compound functions as a spin trap, and its subsequent reaction with a phenyl radical yielded the stable radical phenyl *tert*-butyl nitroxide, eq 7. A series of EPR spectra taken



$$Ph\cdot + (CH_3)_3CN{=}O \longrightarrow Ph\overset{O\cdot}{N}C(CH_3)_3 \quad (7)$$

during the course of the reaction showed the spectrum of the phenyl *tert*-butyl nitroxide superimposed upon the spectrum of the di-*tert*-butyl nitroxide.[16c] When the photoinitiated reduction of diphenyliodonium chloride was carried out with di-*tert*-butyl

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[16] (a) H. Low, I. Paterson, J. M. Tedder, and J. C. Walton, *Chem. Commun.*, 171 (1977); (b) A. C. Scott and J. M. Tedder, *Chem. Commun.*, 64 (1979); (c) H. Singh, J. M. Tedder, and J. C. Walton, *J. Chem. Res. Synop.*, 300 (1980); (d) H. Singh and J. M. Tedder, *Chem. Commun.*, 1095 (1980); (e) A. C. Scott, J. M. Tedder, J. C. Walton, and S. Mhatre, *J. Chem. Soc., Perkin Trans. 2*, 260 (1980); (f) H. Singh and J. M. Tedder, *Chem. Commun.*, 70 (1981); (g) H. Singh, J. M. Tedder, and J. C. Walton, *J. Chem. Soc., Perkin Trans. 2*, 1259 (1980).

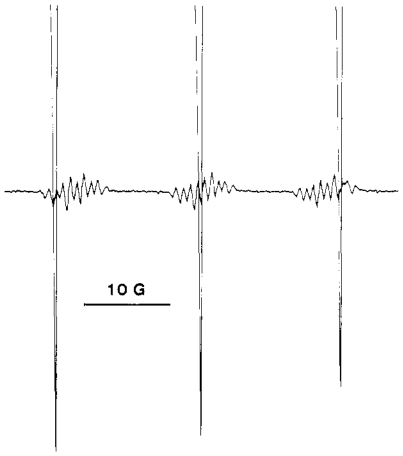


Figure 2. EPR spectrum of phenyl *tert*-butyl nitroxide obtained after irradiation of a mixture of diphenyliodonium chloride and di-*tert*-butyl nitroxide. The spectrum is superimposed upon the partial spectrum of the mixture before irradiation.

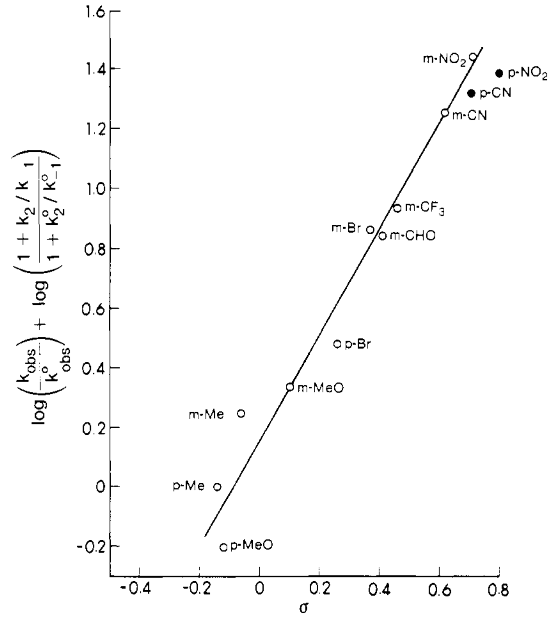


Figure 3. A plot of log $(k_1/k_1^{0\circ})$ vs. σ for the reduction of diaryliodonium salts with phenolate anion, open circles (○), and with 2,4-di-*tert*-butylphenolate anion, closed circles (●).

nitroxide in the cavity of the EPR spectrometer, the strong spectrum of the di-*tert*-butyl nitroxide was replaced by the less intense, but persistent, spectrum of phenyl *tert*-butyl nitroxide (see Figure 2).

Mechanistic Conclusions concerning the Iodine-Transfer Reaction. The mechanistic process depicted in Scheme II could be shown to be consistent with the kinetics observed for the iodine-transfer reaction, eq 4, since a plot of the log of the relative rates of addition of the phenyl radical to the aryl iodide, log $(k_1/k_{\rm Cl})$ vs. σ, was linear (see Figure 3), while a similar plot for log $(k_{\rm I}/k_{\rm Cl})$ (see Figure 1) did not give a satisfactory linear correlation. The values for $k_1/k_{\rm Cl}$ were calculated from the data given in Tables I–III by using eq 3. The Hammett treatment for phenyl radical addition to the series of aryl iodides gave an excellent correlation (ρ = 1.63, r = 0.983, S_ρ = 0.97) when the relative rate data, k_2/k_{-1}, from the phenolate reductions of the substituted iodonium salts and the values obtained from the reductions by 2,6-di-*tert*-butylphenolate anion of the *p*-cyano- and *p*-nitro-substituted salts were used to calculate $k_1/k_{\rm Cl}$ (see Figure 3). Since the log $(k_1/k_{\rm Cl})$ vs. σ plot showed a positive slope, both the addition process, rate constant k_1, and its reverse reaction, rate constant k_{-1}, are favored by electron-withdrawing substituents. It was experimentally observed that the decomposition of the 9-I-2 intermediate to yield aryl radicals, rate constant k_2, was likewise favored by electron-withdrawing substituents (see Table III). The major polar contributing structures involved in the iodine-transfer reaction import a net polarity on the transition states involved, as indicated in Scheme VIII. The energy diagrams for the phenyl radical abstraction of iodine from *p*-nitroiodobenzene and from 4-iodoanisol can be seen in Figure 4.

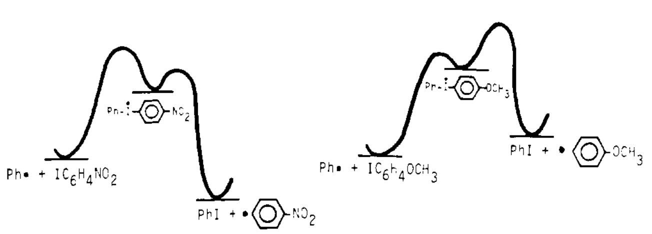
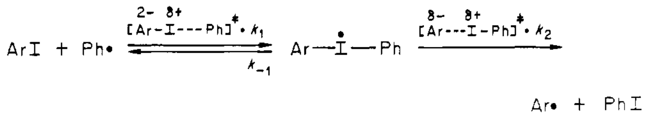


Figure 4.

Scheme VIII



For the abstraction reactions from electronegatively substituted aryl iodides, the rate-determining step in the reaction is the addition of the phenyl radical to the aryl iodide, while during abstraction reactions from an aryl iodide substituted with an electron-donating group the formation of the aryl radical is the rate-determining step.

The observations concerning the substituent effects governing the reactions with rate constants k_1, k_{-1}, or k_2 indicate that aryl substituents facilitate the processes in Scheme VIII by stabilization of a negative charge on carbon relative to iodine. The effect of this stabilization will be less evident when the attacking radical is the *p*-nitrophenyl radical generated from the decomposition of NAT. The replacement of the phenyl radical by a *p*-nitrophenyl radical would no doubt diminish if not reverse the polarity imparted to the two transition states involved in iodine atom transfer, and one would predict for these reactions a ρ very close to zero, if a correlation is obtained at all. In accord with this prediction, preliminary results from a series of reactions carried out with *p*-nitrophenyl radicals show a ρ value of zero.[17]

Experimental Section

Materials. Unless otherwise stated the substituted iodobenzenes were commercially available materials, whose physical constants and GLC purity were determined before use. When necessary the materials were purified in the manner stated below. *p*-Iodonitrobenzene (Aldrich Chemical Co.) was recrystallized from ethanol and sublimed, mp 172–173 °C (lit.[18] mp 174 °C).

m-Iodonitrobenzene (Aldrich Chemical Co.) was recrystallized from ethanol, mp 36–37 °C (lit.[19] mp 38.5 °C).

p-Iodoaniline (Aldrich Chemical Co.) was dissolved in a 1:1 carbon tetrachloride–diethyl ether mixture, washed with an aqueous sodium thiosulfate solution and then water, and extracted into 10% hydrochloric acid. The mixture was neutralized with a sodium hydroxide solution and extracted with ether. After the mixture was dried, the ether was removed by distillation and the resulting product was recrystallized from hexane, mp 62–63.5 °C (lit.[20] mp 61–63 °C).

p-Iodobiphenyl (Terochem Laboratories, Ltd.) was recrystallized from ethanol, followed by sublimation, mp 113.5–114 °C (lit.[21] mp 114 °C).

p-Iodoacetophenone was prepared by the literature method[22] from *p*-aminoacetophenone, mp 84–85 °C (lit.[22] mp 85 °C). Anal. Calcd for C_8H_8IO: C, 39.05; H, 2.87. Found: C, 38.98; H, 2.86.

m-Iodoacetophenone was prepared from *m*-aminoacetophenone by the literature route;[23] bp 128.5 °C (8 mm), $n^{20}{}_{\rm D}$ 1.6286 (lit.[23] bp 117 °C (4

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(17) Unpublished results from this laboratory.
(18) P. J. Montagne, *Ber. Dtsch. Chem. Ges.* **51**, 1489 (1918).
(19) P. Brenans, *Bull. Soc. Chim. Fr.*, **15**, 381 (1914).
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Table III. A Comparison of the Relative Rates of Decomposition, k_2/k_{-1}, for the Intermediate Formed from the Reaction of Diaryliodonium Salts (PhIC$_6$H$_4$Y) with the Phenolate Anion (PhO$^-$), 2,6-Di-*tert*-butylphenolate Anion (ArO$^-$), and Di-*tert*-butyl Nitroxide ((t-Bu)$_2$NO·)

		reactants, mmol × 10^2	products, mmol × 10^2		
Y	reagent	ArI$^+$Ph	ArI	PhI	k_2/k_{-1}[a]
p-CH$_3$	PhO$^-$	*b*	*b*	*b*	0.298 ± 0.04 (4)
	ArO$^-$	10.0	4.62	1.41	0.305
	ArO$^-$	9.88	5.75	1.78	0.310
	(t-Bu)$_2$NO·	10.0	0.440	0.151	0.343
	(t-Bu)$_2$NO·	10.0	0.601	0.210	0.344
	(t-Bu)$_2$NO·, $h\nu$	10.1	2.49	0.824	0.331
	(t-Bu)$_2$NO·, $h\nu$	10.0	3.43	1.14	0.333
m-NO$_2$	PhO$^-$	*b*	*b*	*b*	10.2 ± 0.02 (2)
	ArO$^-$	15.0	0.110	1.09	9.91
	ArO$^-$	21.1	1.37	13.6	9.93
	(t-Bu)$_2$NO·, $h\nu$	13.0	0.829	8.22	9.92
	(t-Bu)$_2$NO·, $h\nu$	10.0	0.552	5.45	9.87
m-CH$_3$	PhO$^-$	*b*	*b*	*b*	0.596 ± 0.014 (2)
	ArO$^-$	10.0	4.07	2.42	0.595
	ArO$^-$	9.69	4.48	2.62	0.586
	(t-Bu)$_2$NO·, $h\nu$	11.0	4.33	2.57	0.593
	(t-Bu)$_2$NO·, $h\nu$	10.1	4.76	2.55	0.537
m-CH$_3$O	PhO$^-$	*b*	*b*	*b*	0.815 ± 0.001 (2)
	ArO$^-$	10.0	2.73	2.20	0.806
	ArO$^-$	15.0	6.35	5.15	0.811
	(t-Bu)$_2$NO·, $h\nu$	10.6	3.15	3.07	0.974
	(t-Bu)$_2$NO·, $h\nu$	9.30	4.18	4.12	0.986
p-Br	PhO$^-$	*b*	*b*	*b*	1.47 ± 0.02 (3)
	ArO$^-$	9.90	2.96	4.33	1.46
	ArO$^-$	10.0	1.85	2.76	1.49
	(t-Bu)$_2$NO·, $h\nu$	10.0	1.81	2.49	1.38
	(t-Bu)$_2$NO·, $h\nu$	10.0	4.87	6.67	1.37
m-CHO	PhO$^-$	*b*	*b*	*b*	3.36 ± 0.06 (2)
	ArO$^-$	10.0	1.47	4.59	3.12
	ArO$^-$	13.0	2.13	7.03	3.30
	(t-Bu)$_2$NO·, $h\nu$	10.0	2.07	6.23	3.01
	(t-Bu)$_2$NO·, $h\nu$	10.0	1.41	4.19	2.98
m-CN	PhO$^-$	*b*	*b*	*b*	7.18 ± 0.13 (2)
	ArO$^-$	10.0	0.914	6.59	7.21
	ArO$^-$	10.0	0.615	4.38	7.13
	(t-Bu)$_2$NO·, $h\nu$	13.0	1.13	7.86	6.96
	(t-Bu)$_2$NO·, $h\nu$	10.1	1.01	6.99	6.92
m-Br$^-$	PhO$^-$	*b*	*b*	*b*	2.97 ± 0.03 (3)
	ArO$^-$	12.0	2.22	6.68	3.01
	ArO$^-$	10.1	2.06	6.24	3.06
	(t-Bu)$_2$NO·, $h\nu$	10.0	1.55	4.45	2.87
	(t-Bu)$_2$NO·, $h\nu$	9.89	1.53	4.37	2.86
m-CF$_3$	PhO$^-$	*b*	*b*	*b*	4.28 ± 0.16 (3)
	ArO$^-$	11.0	1.53	6.59	4.31
	ArO$^-$	10.1	1.37	5.83	4.26
	(t-Bu)$_2$NO·, $h\nu$	20.0	2.99	13.0	4.35
	(t-Bu)$_2$NO·, $h\nu$	14.0	1.46	6.14	4.21
p-MeO	PhO$^-$	*b*	*b*	*b*	0.0927 ± 0.001 (2)
	ArO$^-$	10.0	4.61	0.435	0.0944
	ArO$^-$	10.0	6.66	0.633	0.0950
	(t-Bu)$_2$NO·, $h\nu$	23.0	10.9	1.09	0.0999
	(t-Bu)$_2$NO·, $h\nu$	10.0	4.76	0.543	0.114
p-CN	PhO$^-$	*b*	*b*	*b*	82.5 ± 8.4 (2)
	ArO$^-$	23.1	1.88	17.1	9.09
	ArO$^-$	10.0	0.668	6.13	9.18
	(t-Bu)$_2$NO·, $h\nu$	16.1	1.02	8.98	8.80
	(t-Bu)$_2$NO·, $h\nu$	10.0	0.498	4.50	9.03
	(t-Bu)$_2$NO·	10.0	0.0404	0.359	8.89
p-NO$_2$	PhO$^-$	*b*	*b*	*b*	123 ± 5.0 (2)
	ArO$^-$	10.0	0.446	7.18	16.1
	ArO$^-$	10.0	0.494	8.01	16.2
	(t-Bu)$_2$NO·, $h\nu$	10.0	0.379	5.98	15.8
	(t-Bu)$_2$NO·, $h\nu$	10.0	0.235	3.78	16.1

[a] Average values obtained for two or more independent experiments. The values in parentheses are the number of independent experiments. [b] See Table II.

mm), $n^{20}{}_D$ 1.6220). Anal. Calcd for C$_8$H$_8$IO: C, 39.05; H, 2.87. Found: C, 38.96; H, 2.87.

p-Iodobenzaldehyde was prepared from p-iodobenzonitrile following the procedure of Bowen and Wilkinson,[24] mp 77.5–78 °C (lit.[25] mp 78 °C).

m-Iodobenzaldehyde (ICN Pharmaceuticals, Inc.) was recrystallized from hexane followed by sublimation, mp 56–57 °C (lit.[26] mp 57 °C).

p-Iodoanisole (Eastman Chemical Co.) was purified by sublimation, mp 51–52 °C (lit.[27] mp 51–52 °C).

Methyl p-iodobenzoate was prepared by the literature route[28] and purified by recrystallization from diethyl ether followed by sublimation, mp 114 °C (lit.[28] mp 114 °C).

Methyl m-iodobenzoate was prepared by the literature route[29] and purified by recrystallization from ethanol followed by sublimation, mp 48.5–49 °C (lit.[29] mp 54–55 °C). Anal. Calcd for C$_8$H$_7$IO$_2$: C, 36.67; H, 2.69. Found: C, 36.61; H, 2.67.

p-Iodobenzonitrile (Eastman Chemical Co.) was purified by sublimation, mp 127–127.5 °C (lit.[30] mp 127 °C).

m-Iodobenzonitrile was prepared from m-iodobenzaldehyde following the literature route,[31] mp 39.5 °C (lit.[31] mp 39 °C).

m-Iodobenzotrifluoride (ICN Pharmaceuticals, Inc.), bp 183–185 °C (10 mm) (lit.[32] mp 186 °C); p-bromoiodobenzene (Eastman Chemical Co.), mp 91–92 °C (lit.[33] mp 92 °C); m-bromoiodobenzene (CPL Chemical Co.), bp 118–119 °C (8 mm) (lit.[34] mp 120 °C (8 mm)); p-iodotoluene (Eastman Chemical Co.), mp 36–37 °C (lit.[35] mp 36–37 °C); m-iodotoluene (Aldrich Chemical Co.), bp 80–82 °C (10 mm), $n^{20}{}_D$ 1.6040 (lit.[36] $n^{20}{}_D$ 1.6053); and m-iodoanisole (ICN Pharmaceuticals, Inc.), bp 123 °C (14 mm) (lit.[37] mp 123 °C (14 mm)) were used without further purification.

p-Methyldiphenyliodonium chloride was prepared by the method of Willgerodt,[38] mp 189–190 °C (lit.[38] mp 193 °C). Anal. Calcd for C$_{13}$H$_{12}$ClI: C, 47.09; H, 3.64. Found: C, 46.90; H, 3.58.

m-Methyldiphenyliodonium chloride was prepared from m-methyliodobenzene (20 g, 0.085 mol) by the method developed by Beringer[40] for similar iodonium salts. The method gave the required product (15 g, 0.045 mol, 53%), mp 211–212 °C (lit.[39] mp 213 °C). Anal. Calcd for C$_{13}$H$_{12}$ClI: C, 47.09; H, 3.64. Found: C, 47.26; H, 3.80.

m-Cyanodiphenyliodonium iodide, mp 183 °C (lit.[40] mp 184–185 °C); m-nitrodiphenyliodonium bromide, mp 169–171 °C (lit.[40] mp 171–172 °C); p-bromodiphenyliodonium bromide, mp 173–174 °C (lit.[40] mp 175

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°C); and *p*-methoxydiphenyliodonium bromide, mp 183–184 °C (lit.[40] mp 185 °C) were all prepared by the method reported by Beringer.[40]

m-Bromodiphenyliodonium iodide was prepared from the reaction of *m*-bromoiodobenzene dichloride (6 g, 0.017 mol) with diphenylmercury (10 g, 0.028 mol) to give the required product (6 g, 0.012 mol, 74%), mp 133–134 °C (lit.[41] mp 133–134 °C). Anal. Calcd for $C_{12}H_9BrI_2$: C, 29.60; H, 1.86. Found: C, 29.52; H, 1.86.

m-Methoxydiphenyliodonium iodide was prepared from the reaction of *m*-methoxyiodobenzene dichloride (8 g, 0.026 mol) and diphenylmercury (8.6 g, 0.026 mol) to give the required product (6.1 g, 0.014 mol, 53%), mp 164–165 °C (lit.[40] mp 166 °C).

3-Formyldiphenyliodonium iodide was prepared from the reaction of 3-formyliodobenzene dichloride (10 g, 0.023 mol) with diphenylmercury (15 g, 0.042 mol) to give the product (10 g, 0.020 mol, 87%), mp 142–142.5 °C. Anal. Calcd for $C_{13}H_{10}I_2O$: C, 35.81; H, 2.31. Found: C, 35.68; H, 2.29.

m-(Trifluoromethyl)diphenyliodonium iodide was prepared from the reaction of the corresponding iodobenzene dichloride (5 g, 0.015 mol) with diphenylmercury (10 g, 0.025 mol) to give the product (6 g, 0.013 mol, 86%), mp 159–161 °C. Anal. Calcd for $C_{13}H_9F_3I_2$: C, 32.80; H, 1.91. Found: C, 32.77; H, 1.90.

Phenylazotriphenylmethane (Eastman Organic Chemicals) was sublimed before use, mp 109–111 °C (lit.[42] mp 109–111 °C).

Phenol (Aldrich Chemical Co.), bp 180–182 °C (lit.[43] mp 181 °C); 2,6-di-*tert*-butylphenol (Aldrich Chemical Co.), mp 68 °C (lit.[44] mp 69.4 °C); and di-*tert*-butyl nitroxide (Eastman Organic Chemicals), bp 74–75 °C (35 mm) (lit.[45] mp 73–75 °C (35 mm)) were distilled before use.

Procedure for the Reaction of Aryl Iodides with PAT. Mixtures of an aryl iodide (14.8 mmol), carbon tetrachloride (10.4 mmol), and phenylazotriphenylmethane (PAT) (2.1×10^{-1} mmol) were placed in Pyrex ampules that were degassed, sealed, and thermostated at 60 ± 0.1 °C for 18 h. The reaction mixtures were cooled (−80 °C), the ampules opened, and the samples subjected to analysis by GLC (with either a $^1/_8$ in. × 10 ft, 20% FFAP on Chromosorb PAW 60–80 mesh stainless steel column or a $^1/_8$ in. × 20 ft, 3% OV-101 on Chromosorb WAW/DMCS 80–100 mesh stainless steel column). The relative concentrations of products were calculated from the integrated (HP 5840A integrator) GLC area ratios of the products by using a calibration factor determined from known mixtures of authentic materials.

Reaction of Iodonium Salts with Sodium Phenoxide and Sodium 2,6-Di-*tert*-butylphenoxide. Aqueous solutions of the iodonium salts (5×10^{-4} M) and the appropriate sodium phenoxide (5×10^{-4} M), prepared by mixing equimolar amounts of sodium hydroxide and the phenol, were placed in Pyrex ampules that were degassed, sealed, and thermostated at 60.0 ± 1 °C for 36–100 h, depending on a given substrate's proclivity to reaction.

The ampules were cooled (−80 °C) and opened, and the product mixture was dissolved in acetonitrile containing standard amounts of 1,2,4,5-tetramethylbenzene.

Quantitative analysis of the reaction mixtures was carried out by HPLC with a Perkin-Elmer Series 2 chromatograph fitted with a Waters RCM-100 Radical-Pak compressor and a C_{18} reverse-phase radial-Pak compressor and a C_{18} reverse-phase radial-pak column or a C_8 reverse-phase radial-pak column, with a 50:50 water to acetonitrile solvent mixture. A Perkin-Elmer LC-55B UV detector was used. The relative concentrations of products were calculated from the integrated (HP 3380A integrator) area ratios to the products with use of a calibration factor determined from known mixtures of authentic materials.

Reaction of Iodonium Salts with Di-*tert*-butyl Nitroxide. Aqueous solutions of the iodonium salt (0.2 M) and di-*tert*-butyl nitroxide (0.1 M) were placed in Pyrex ampules that were degassed, sealed, and thermostated at 60 ± 0.1 °C for periods ranging from 18 to 60 h. For reactions requiring light, a 500-W incandescent lamp was used to irradiate the reaction mixtures.

The ampules were cooled (−80 °C) and opened, and the mixture was dissolved in acetonitrile containing standard amounts of 1,2,4,5-tetramethylbenzene. The relative concentrations of products were calculated from the integrated (HP 3380A integrator) area ratios of the products and standard with use of a calibration factor determined from known mixtures of authentic materials.

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Registry No. *m*-$O_2NC_6H_4I$, 645-00-1; *p*-$O_2NC_6H_4I$, 636-98-6; *p*-NCC_6H_4I, 3058-39-7; *m*-BrC_6H_4I, 591-18-4; *m*-$CH_3COC_6H_4I$, 14452-30-3; *p*-BrC_6H_4I, 589-87-7; *m*-$CH_3OC_6H_4I$, 766-85-8; *m*-$CH_3C_6H_4I$, 625-95-6; *p*-$C_6H_5C_6H_4I$, 1591-31-7; *p*-$CH_3C_6H_4I$, 624-31-7; *p*-$CH_3OC_6H_4I$, 696-62-8; *m*-NCC_6H_4I, 69113-59-3; *p*-$OHCC_6H_4I$, 15164-44-0; *m*-$F_3CC_6H_4I$, 401-81-0; *m*-$OHCC_6H_4I$, 696-41-3; *m*-$CH_3OCOC_6H_4I$, 618-91-7; *p*-$CH_3OCOC_6H_4I$, 619-44-3; *p*-$CH_3COC_6H_4I$, 13329-40-3; *m*-$H_2NC_6H_4I$, 626-01-7; *p*-$H_2NC_6H_4I$, 540-37-4; *p*-$CH_3C_6H_4I^+Ph\cdot Cl^-$, 56530-34-8; *m*-$O_2NC_6H_4I^+Ph\cdot Br^-$, 23351-89-5; *m*-$CH_3C_6H_4I^+Ph\cdot Cl^-$, 81447-67-8; *m*-$CH_3OC_6H_4I^+Ph\cdot I^-$, 81447-68-9; *p*-$BrC_6H_4I^+Ph\cdot Br^-$, 59696-27-4; *m*-$OHCC_6H_4I^+Ph\cdot I^-$, 81447-69-0; *m*-$NCC_6H_4I^+Ph\cdot I^-$, 81447-70-3; *m*-$BrC_6H_4I^+Ph\cdot I^-$, 81447-71-7; *m*-$F_3CC_6H_4I^+Ph\cdot I^-$, 81447-72-5; *p*-$CH_3OC_6H_4I^+Ph\cdot Br^-$, 2665-61-4; *p*-$NCC_6H_4I^+Ph$, 81447-73-6; *p*-$O_2NC_6H_4I^+Ph$, 46734-23-0; phenyl radical, 2396-01-2; sodium 2,6-di-*tert*-butylphenoxide, 7175-96-4; sodium phenoxide, 139-02-6; di-*tert*-butyl nitroxide, 2406-25-9.

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Stereoselective, Biogenetically Patterned Synthesis of (±)-Aplysistatin

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Abstract: A synthesis of (±)-aplysistatin (**1**) from geraniol is described, in which the key step is a biogenetically modeled cyclization of **24** to **26**. Methyl (*E*)-homogeranylacetate (**5c**) was converted to the tetronic acid **10c** via chloroacetylation of the derived ketene acetal **7c**, and **10c** was sulfenylated and reduced to give **24**. Cyclization of the latter with mercuric trifluoroacetate, followed by brominative substitution of mercury, yielded **26** with high stereoselectivity. Oxidation of **26** and thermal elimination of the sulfoxide **28** gave (±)-**1**.

The isolation of aplysistatin (**1**) by Pettit et al. from the sea hare *Aplysia angasi* brought to light a novel, brominated sesquiterpene skeleton (aplysistane) containing an oxepane ring.[2] Interest in **1** was further heightened by the report that it shows significant inhibition of murine lymphocytic leukemia, with a T/C of 175 at 400 mg/kg in the National Cancer Institute's P-388 screen.[3]

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