from diene to monitor is vertical, the estimated "available" triplet energy of 42 kcal mol^{-1} for the relaxed ^{3}TMB* represents the energy gap between the latter and the corresponding vibrationally and torsionally excited S_0. The energy gain due to the twisting of the planar triplet can therefore not be estimated.

5. Conclusions

An application of the pulse radiolysis technique has allowed the first direct determinations of conjugated diene triplet lifetimes. The triplet state of cyclopentadiene has a natural lifetime of 1.7 μs in benzene. The establishment of energy-transfer equilibria between this triplet state and those of naphthalene and chrysene has yielded an accurate equilibrium triplet energy of 58.0 ± 0.2 kcal mol^{-1}, just below the singlet-triplet $\Delta E_{0,0}$ value of 58.3 kcal mol^{-1}. Thus, as might be anticipated on the basis of steric constraint, relaxation of the Franck-Condon triplet in solution is negligible. In contrast the triplet state of tetramethylbutadiene has a much shorter natural lifetime of 73 ns which presumably reflects the much greater degree of relaxation. In the absence of observation of energy-transfer equilibria it has only been possible to place its "available" triplet energy at approximately 42 kcal mol^{-1}. The energy transfer rate constant data for both dienes appear totally consistent with the participation of vertical processes only.

Work on related systems is in progress.[44]

Acknowledgment. We thank the Science Research Council and the Royal Society for financial support.

(42) As pointed out by a referee the above data are also inconsistent with the proposed quantum chain process for cis-trans isomerization of 1,3-dienes.[11c]

(43) The rate constants for quenching of pyrene, fluoranthene, and chrysene triplets by TMB appear to be somewhat larger than those for CPD. On the assumption that this is significant we have considered the possibility that it reflects a contribution from a low population of the s-cis form of TMB. This could have a significantly lower (~6-7 kcal mol^{-1}) Franck-Condon triplet energy, that of cyclohexa-1,3-diene being reported as 53.5[2] and 52.5[3] kcal mol^{-1}. However, steric interactions may well make the s-cis population totally insignificant and, as a referee has pointed out, some degree of nonverticality in the quenching process could account for this result.

(44) Since the submission of this manuscript we have observed what are almost certainly the triplet-triplet absorption spectra of CPD (λ_{max} 300 nm) and TMB (λ_{max} 290 nm) by pulse radiolysis of benzene solutions of these dienes. The lifetime of the CPD transient (1.6 μs, extrapolated to zero CPD concentration) compares well with that of ^{3}CPD* (1.7 μs) determined from the energy-transfer experiments. In the case of TMB the transient absorption is much weaker. This, coupled with the faster decay, has made kinetic analysis more difficult. An approximate lifetime of 50 ns (at 10^{-1} mol L^{-1} TMB) is to be compared with that for ^{3}TMB* of 71 ns calculated from the energy-transfer experiments.

Aryloxenium Ions. Generation from *N*-(Aryloxy)pyridinium Tetrafluoroborates and Reaction with Anisole and Benzonitrile[1]

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Abstract: *N*-(Aryloxy)pyridinium tetrafluoroborates (**4**) decompose thermally at 180-200 °C in anisole and benzonitrile to form products of intermolecular C-O-C and C-C bond formation. With anisole, diphenyl ethers (**5**) and hydroxybiphenyls (**6**) are formed; with benzonitrile, the main product is a benzoxazole (**14**). A homolytic process was ruled out by showing that none of these products were formed when perbenzoyl *p*-nitrophenyl carbonate (**18**) was decomposed in these solvents. The main products in this case were those of homolytic phenylation (and benzoyloxylation with anisole). A concerted S_N2-type heterolytic process was ruled out by showing that the nature of the substituent in the pyridine ring had no effect on the isomer ratios of **5** and **6** in the thermolysis of **4** (X = *p*-NO_2) in anisole. The results are explained in terms of a unimolecular heterolysis of **4** to give the pyridine and an aryloxenium ion **2** which now attacks solvent molecules. When an electron-withdrawing substituent is present in **2**, more C-O-C than C-C products are formed with anisole. When it is absent only products of C-C bond formation are found. PhO^+ is apparently electrophilic enough to attack anisole and give the four possible hydroxymethoxybiphenyls (**10-13**).

In recent years there has been considerable interest in the chemistry of phenoxenium ions,[3] particularly in connection with phenol oxidation in general[4b,5,6a,c,10,12] and biosynthetic-type oxidative coupling reactions in particular.[4a,10,11] The fact that oxenium ions are isoelectronic with carbenes and nitrenes adds

(1) For preliminary communications on some of this work, see: (a) Abramovitch, R. A.; Inbasekaran, M.; Kato, S. *J. Am. Chem. Soc.* **1973**, *95*, 5428; (b) Abramovitch, R. A.; Alvernhe, G.; Inbasekaran, M. N. *Tetrahedron Lett.* **1977**, 1113.

(2) To whom correspondence should be addressed at Clemson University.

(3) A variety of names have been used to describe the species ArO^+: phenoxonium ions,[4] phenoxylium ions,[5] aryloxy cations,[6] phenonium ions,[7] and aryloxenium ion.[7a,8,9] Of these, phenonium ion is quite unacceptable since it refers to a totally different, well-documented species. The "oxonium" ion terminology should be reserved for trisubstituted positively charged oxygen species R_3O^+. By analogy with positvely charged divalent nitrogen and trivalent carbon intermediates, a positively charged monovalent oxygen intermediate should have a name ending in "-enium", hence oxenium.

(4) (a) Barton, D. H. R. *Chem. Br.* **1967**, *3*, 330; (b) Hewgill, F. R. In "Free Radical Reactions", Vol. 10; Waters, W. A., Ed.; Butterworths: London, **1973**; Chapter 6, pp 167-204; (c) Anderson, R. A.; Dalgleish, D. T.; Nonhebel, D. C.; Pauson, P. L. *J. Chem. Res., Synop.* **1977**, 12; (d) Findlay, J. W.; Gupta, P.; Lewis, J. R. *J. Chem. Soc. C* **1969**, 2761.

(5) (a) Hewitt, D. G. *J. Chem. Soc. C* **1971**, 1750; (b) Chauhan, M.; Dean, F. M.; Hindley, K.; Robinson, M. *J. Chem. Soc., Chem. Comm.* **1971**, 1141.

(6) (a) Waters, W. A. *J. Chem. Soc. B* **1971**, 2026; (b) Haynes, C. G.; Turner, A. H.; Waters, W. A. *J. Chem. Soc.* **1956**, 2823; (c) Dimroth, K.; Umbach, W.; Thomas, H. *Chem. Ber.* **1967**, *100*, 132; (d) Adler, E.; Falkehag, I.; Smith, B. *Acta Chem. Scand.* **1962**, 529.

(7) Finkbeiner, H.; Toothaker, A. T. *J. Org. Chem.* **1968**, *33*, 4347.

(8) Riecker, A. *Tetrahedron Lett.* **1969**, 2611.

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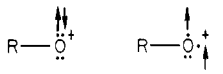
another dimension to the interest in these species. Thus, it is expected that free oxenium ions will exist in the singlet (**1a**) or triplet (**1b**) state, but no data are available on this subject. The



1a **1b**

observation of an ESR signal for **1b** in a frozen matrix will probably have to await the development of a convenient photochemical source of RO^+.

The oxidative coupling of phenols generally proceeds via aryloxy radicals,[10,11] but other mechanisms have been considered, including the following sequences:[4a]

$$ArOH + ArO^+ \rightarrow \text{dimer} + H^+ \quad (1)$$

$$ArO^- + ArO^+ \rightarrow \text{dimer} \quad (2)$$

In a very important paper, Waters[6a] discussed the effect of pH and the nature of the oxidizing agent on the course of phenol oxidation. He argued that since the oxidation of phenols to aryloxy radicals (eq 3) by one-electron acceptors, e.g., $Fe(CN)_6^{3-}$ is ac-

$$ArO^- \rightleftharpoons ArO\cdot + e \quad (3)$$

celerated by increasing the pH of the medium, and both ESR and flash photolysis studies have shown that phenols give radicals ArO· even in acidic solution,[13] then the known further oxidation (eq 4) of aryloxy radicals in strongly acidic solutions[8,14,15] should be

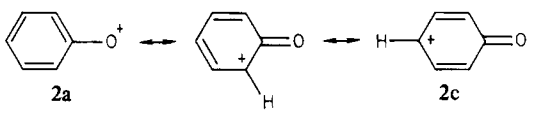
$$ArO\cdot \rightarrow ArO^+ + e \quad (4)$$

pH independent. Thus, plots of the critical oxidation potential for a given phenol against pH for equilibria 3 and 4 should cross and there should be an equipotential pH below which ArO· would be metastable with respect to ArO^+ and ArO^-. Under these conditions, ArO· should disproportionate (eq 5) rather than dimerize. At low pHs dimeric and other products would then arise

$$2ArO\cdot + H_3O^+ \rightarrow ArO^+ + ArOH + H_2O \quad (5)$$

by electrophilic aromatic substitution of ArO^+ upon ArOH (eq 1) rather than by radical coupling.

Further, Waters suggested that on the basis of the expected higher electron density on the oxygen atom than on the aromatic ring in PhO·, one would predict that such radicals would dimerize by C–O–C bond formation more than by C–C bond formation. On the other hand, the opposite should be true of phenoxenium ion **2** in which canonical structures b and particularly c should contribute more than a, leading to more C–C than C–O–C bond formation in reaction 1.



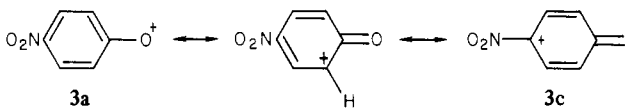
2a **2c**

2b

In view of our interest in the chemistry of the isoelectronic nitrene and carbene reactive intermediates, we felt that an unambiguous method of generating aryloxenium ions in solution was highly desirable to permit studies of their physical and chemical properties. Such a method would have to be different from a direct phenol oxidation to avoid possible ambiguities concerning alternate or competing radical mechanisms. The approach used here has been essentially an extension of the general thermal methods available for the generation of "enium" ions (eq 6). Here, X is

$$R_{n-1}E\text{-}X \longrightarrow R_{n-1}\text{-}E^+ + X^- \quad (6)$$

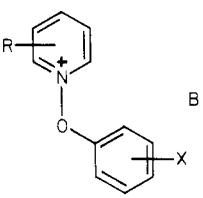
a good leaving group and n is the valency of the element E. If X is positively charged in the starting compound, neutral X will be eliminated, facilitating the reaction. Since, by analogy with phenylnitrene, it was expected[16] (incorrectly as it eventually turned out) that the phenoxenium ion PhO^+ itself might not be electrophilic enough to attack an aromatic nucleus, it was decided to introduce electron-withdrawing substituents into the aryl residue. In addition to increasing the electrophilicity of the oxenium ion, we expected these substituents to destabilize the positive charge delocalized into the aromatic nucleus (e.g., **3c**) and thus lead to increased amounts of intermolecular C–O–C bond formation relative to C–C bond formation.



3a **3c**

3b

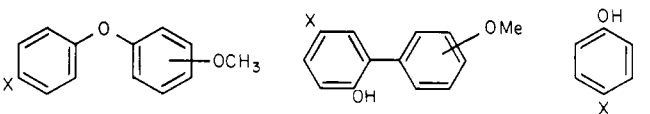
To that end, we studied the thermolysis of *N*-(aryloxy)-pyridinium tetrafluoroborates (**4**) in aromatic solvents. These



4

are readily available either by the reaction of pyridine 1-oxides with aryldiazonium tetrafluoroborates bearing electron-withdrawing substituents in the aryl residue[17] or from pyridine 1-oxides and iodonium salts.[18] We anticipated that heterolytic decomposition would occur, in the absence of external nucleophiles other than the aromatic substrate, via an S_N1 process, taking advantage of the leaving group ability of the pyridinium ion, thus generating an aryloxenium ion.

Thermolysis of *N*-(*p*-nitrophenoxy)pyridinium tetrafluoroborate (**4**, R = H; X = *p*-NO_2) in anisole at 180 °C for 5 h under dry nitrogen gave a mixture of 2- and 4-methoxy-4′-nitrodiphenyl ether (**5**, X = NO_2) (43.4%) (2′-:4′- = 29:71), 2-hydroxy-2′- and 4′-methoxy-5-nitrobiphenyl (**6**, X = NO_2) (9.2%) (2′-:4′- = 74:26), and *p*-nitrophenol (**7**, X = NO_2) (26.7%). At the time these

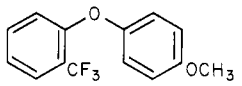


5 (*o*- and *p*-) **6** (*o*- and *p*-) **7**

results were originally communicated,[1] they represented the first example of intermolecular aromatic aryloxylation. *N*-(*p*-Cyanophenoxy)pyridinium tetrafluoroborate (**4**, R = H; X = *p*-CN) behaved similarly, yielding **5** (X = CN) (12.7%) (2-:4- = 45:55), **6** (X = CN) (13.6%) (2′-:4′- = 33:67), and **7** (X = CN), as did *N*-(*o*-(trifluoromethyl)phenoxy)pyridinium tetrafluoroborate

(9) Endo, Y.; Shudo, K.; Okamoto, T. *J. Am. Chem. Soc.* **1977**, *99*, 7721.
(10) McDonald, P. D.; Hamilton, G. A. In "Oxidation in Organic Chemistry", Part B; Trahanovsky, W. S., Ed.; Academic Press: New York, 1973; Chapter II, pp 97–133.
(11) Taylor, W. I.; Battersby, A. R. "Oxidative Coupling of Phenols"; Marcel Dekker: New York, 1967.
(12) Mihailović, M. L. J.; Čeković, Z. In "The Chemistry of the Hydroxyl Group", Part 1; Patai, S., Ed.; Wiley-Interscience: New York, 1971; Chapter 10, p 505.
(13) Land, E. J.; Porter, G.; Strachan, E. *Trans. Faraday Soc.* **1961**, *57*, 1885.
(14) Steuber, F. W.; Dimroth, K. *Chem. Ber.* **1966**, *99*, 258.
(15) Suttie, A. B. *Tetrahedron Lett.* **1969**, 953.
(16) Abramovitch, R. A.; Challand, S. R.; Scriven, E. F. V. *J. Org. Chem.* **1972**, *37*, 2705.
(17) (a) Abramovitch, R. A.; Kato, S.; Singer, G. M. *J. Am. Chem. Soc.* **1971**, *93*, 3074; (b) Abramovitch, R. A.; Inbasekaran, M. N.; Kato, S.; Singer, G. M. *J. Org. Chem.* **1976**, *41*, 1717.
(18) Abramovitch, R. A.; Inbasekaran, M. N. *Tetrahedron Lett.* **1977**, 1109.

(**4**, R = H; X = *o*-CF_3), which gives **8** (18%) (no ortho isomer detected) and **9** (8%) (isomers not resolved).



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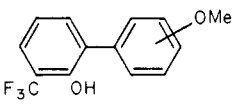
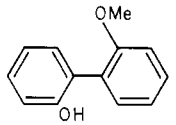


9

It was not necessary for an electron-withdrawing function to be present in the aryloxy group to observe intermolecular attack on anisole. Thus, when 4-methoxy-1-phenoxypyridinium tetrafluoroborate (**4**; R = 4-OMe; X = H) was thermolyzed in anisole at 180–190 °C for 8 h, all the possible hydroxymethoxybiphenyls that could be formed were: 2-hydroxy-2′-methoxy- (**10**) (19.2%), 2-hydroxy-4′-methoxy- (**11**) (14.6%), 4-hydroxy-2′-methoxy- (**12**) (18.8%), and 4-hydroxy-4′-methoxybiphenyl (**13**) (12.4%). No



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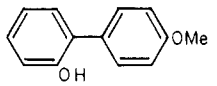

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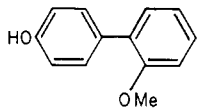

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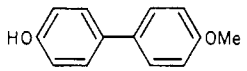
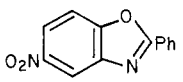


13

phenol or methoxydiphenyl ethers were detected, though in an earlier run (by a different co-author) which could not be reproduced later phenol (2.1%), **13** (21.5%), and 2- and 4-methoxybiphenyl ether (7.8%) (2-:4- = 41:59) (identified by comparison with authentic samples) were isolated.

Thermolysis of **4** (R = H, X = *p*-NO_2) in benzonitrile led to an interesting array of products, the main ones being 5-nitro-2-phenylbenzoxazole (**14**) (35%) and phenol (28%), together with *p*-nitrophenyl benzoate (13%) and small amounts of *p*-nitrophenoxyamine (**15**) and benzamide.



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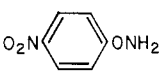
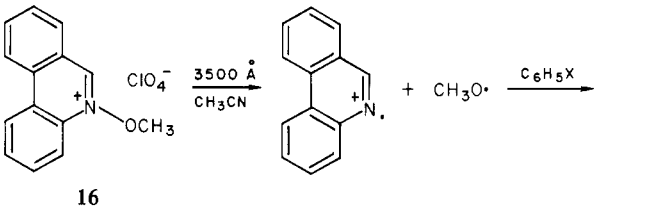


15

At least three possible mechanisms can be envisioned to account for this novel intermolecular aryloxylation. (i) Homolytic N–O bond fission would give ArO· and the pyridinium radical cation $C_5H_5N^{+}\cdot$. ArO· would then add to Ar′H to form σ complexes from which ArOAr′, Ar′-ArOH, and ArOH would result by hydrogen abstraction by $C_5H_5N^{+}\cdot$. Such a process has, indeed, been reported by Mee et al.[19] in the photolysis of *N*-methoxyphenanthridinium perchlorate (**16**) in aromatic solvents. Methoxyl radicals were thought to be generated which then attacked the aromatic solvent to give the substituted anisoles (**17**) in low yield together with phenanthridine (80%), methanol, and formaldehyde dimethyl acetal. The isomer distribution in **17** was quite consistent with attack by a free radical. Other convincing evidence (bibenzyl formation in toluene, polymerization of acrylonitrile) for the formation of radicals in this reaction was also presented. (ii) Heterolytic N–O cleavage would give pyridine and an aryloxenium ion ArO^{+}. The latter, by analogy with carbenes and nitrenes, could exist either as a singlet ($Ar\ddot{O}^{+}$) or a triplet ($Ar\dot{O}\cdot^{+}$). The former could attack Ar′H as do other electrophilic reagents, while the latter (probably the ground state) would abstract hydrogen to give $ArO^{+}H_2 \rightarrow ArOH + H^{+}$. (ArOH could also arise by a competing process leading to ArO· as indicated above.) (iii) A concerted nucleophilic attack by Ar′H upon the developing positive charge on the *N*-(aryloxy) function simultaneous with the departure of pyridine could occur, so that a "free" aryloxenium ion was not



16

17, X = H, CN, CH_3, OMe

formed. An alternative one-electron transfer from the substrate to the pyridinium salt is conceivable with electron-rich substrates but not with benzonitrile.

The results obtained with benzonitrile as the solvent and substrate speak against the radical pathway since, in contrast to the results obtained with **16**, no attack of the aromatic nucleus was observed that resulted in C–O–C bond formation and no diphenyl ethers were detected. In order to distinguish definitively between mechanism i on the one hand and ii and iii on the other, an unambiguous source of *p*-nitrophenoxy radicals in aromatic solvents was sought. An attempt was made to oxidize *p*-nitrophenol in anisole with silver carbonate on Celite,[20] but only starting phenol was recovered. The use of thallium trifluoroacetate in the oxidative coupling of phenols[21] prompted us to oxidize *p*-nitrophenol with this reagent in the presence of anisole (20 °C, 20 h; 155 °C, 20 h). A complex mixture of six products was detected by gas chromatography, but no diphenyl ethers **5** (X = NO_2) or biphenyls (**6**, X = NO_2) were detected, and the mixture was not analyzed further at this time.

Dodonov and Waters[22] have established that the thermal decomposition of perbenzoyl aryl carbonates in benzene proceeds by homolysis of the O–O bond, leading to benzoyloxy and aryloxy radicals and to CO_2. From the high recovery of benzoic acid they concluded that $PhCO_2\cdot$ acts mainly as a dehydrogenator of ArO· or its condensation products and that little decomposition of $PhCO_2\cdot$ occurred in this case. Any phenyl radicals formed gave rise to biphenyl with solvent benzene. ArO· radicals gave mainly polymers of low molecular weight (30% yield).

We have synthesized perbenzoyl *p*-nitrophenyl carbonate (**18**) (percent peroxide, 99.12) from *p*-nitrophenyl chloroformate (**19**)[23] and peroxybenzoic acid in methylene chloride containing pyridine at −15 °C (eq 7). Its thermolysis in anisole at 180 °C led to the

$$\underset{\textbf{19}}{p\text{-}O_2NC_6H_4OCOCl} + C_6H_5CO_3H \xrightarrow{C_5H_5N} \underset{\textbf{18}}{p\text{-}NO_2C_6H_4OCOOOCOPh} \quad (7)$$

formation of **7** (X = NO_2) (60%), benzoic acid (20%), *o*- and *p*-anisyl benzoates (**19**) (15.1%; *o*-:*p*- = 3.2:1), and the three possible methoxybiphenyls (**20**) (29.8%; *o*-:*m*-:*p*- = 7.5:1:1.4) together with oligomeric or polymeric material (14%), presumably arising from the *p*-nitrophenoxy radicals.[22] No nitrodiphenyl ethers or nitrohydroxybiphenyls were detected, indicating that a different reactive intermediate was formed here than in the thermolysis of *N*-(*p*-nitrophenoxy)pyridinium tetrafluoroborate (**4**, R = H; X = *p*-NO_2). The ratio of methoxybiphenyls obtained is similar to (but not identical with; the ratio varies slightly with temperature) that reported[24] for the free-radical phenylation of anisole, using

(19) Mee, J. D.; Heseltine, D. W.; Taylor, E. C. *J. Am. Chem. Soc.* **1970**, *92*, 5915.

(20) Balogh, V.; Fetizon, M.; Golfier, M. *J. Org. Chem.* **1971**, *36*, 1339.

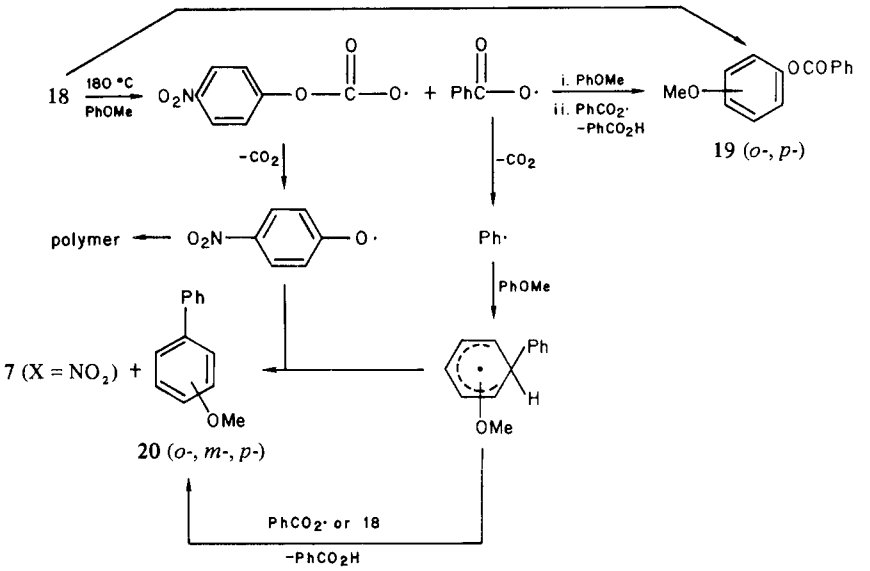
(21) Schwartz, M. A.; Rose, B. F.; Vishnuvajjala, B. *J. Am. Chem. Soc.* **1973**, *95*, 612.

(22) Dodonov, V. A.; Waters, W. A. *J. Chem. Soc.* **1965**, 2459.

(23) Zabik, J.; Schuetz, R. D. *J. Org. Chem.* **1967**, *32*, 300.

(24) (a) Morrison, R. T.; Cazes, J.; Samkoff, N.; Howe, C. A. *J. Am. Chem. Soc.* **1962**, *84*, 4152; (b) Lynch, B. M.; Moore, R. B. *Can. J. Chem.* **1962**, *40*, 1461.

Scheme I

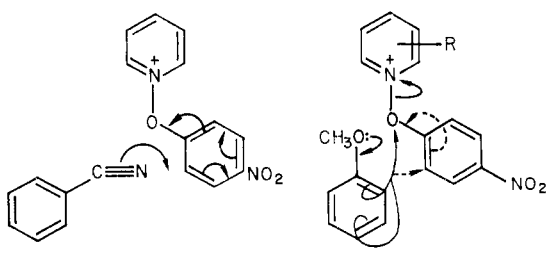


benzoyl peroxide as the source of radicals. Small quantities of esters are known to result from attack by benzoyloxy radicals on many aromatic substrates and they constitute some of the main products in the reaction of benzoyl peroxide with naphthalene.[25] Appreciable yields of methoxyphenyl benzoates are formed in the decomposition of $(PhCO_2)_2$ in anisole,[24b] with more ortho than para isomer being formed and no meta isomer. Consequently, our results are clearly consistant with the expected formation of benzoyloxy, and thence phenyl, radicals in the thermolysis of **18** and also the concurrent formation of the desired *p*-nitrophenoxy radicals.

Thermolysis of **18** in benzonitrile at 180 °C gave *p*-nitrophenol (**7**) (62%), benzoic acid (25.3%), and the three cyanobiphenyls (**21**) (18.5%) but no 5-nitro-2-phenylbenzoxazole (**14**). The isomer ratio of the cyanobiphenyls (2-:3-:4- = 60.3:9.9:29.8) is in excellent agreement with that reported (60:10:30) in the homolytic phenylation of benzonitrile with benzoyl peroxide at 80 °C.[26]

The above results can be accounted for as illustrated in Schemes I and II. It should be pointed out that **19** could also arise by the induced decomposition of the starting peroxide[24b] and that the high ortho/para ratio could result from initial complexing at anisole oxygen followed by intramolecular rearrangement, as previously suggested. Some free benzoyloxy radicals must be formed, however, to account for the formation of Ph· in at least 30% yield.

Having ruled out a free-radical mechanism to account for the formation of the products from **4**, a decision between possibilities ii and iii needs to be made. Again, the reaction with benzonitrile argues against a concerted process iii since one would not expect nucleophilic participation by the relatively poor nucleophilic nitrile nitrogen in an S_N2' displacement leading to **14** in a concerted mechanism (**22**).



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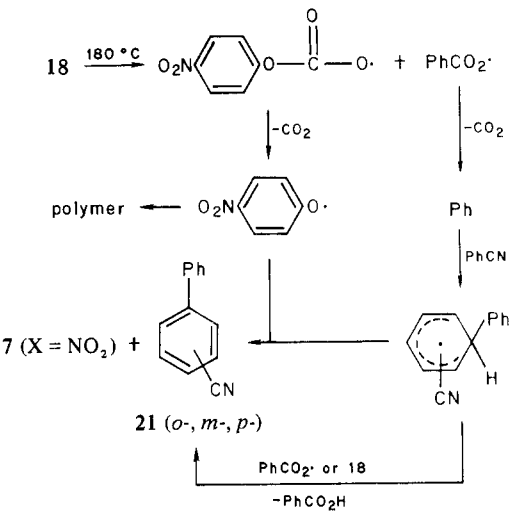
Although a kinetic study would have been the most appropriate tool with which to distinguish between mechanism ii and iii, it

(25) Davies, D. I.; Hey, D. H.; Williams, G. H. *J. Chem. Soc.* **1958**, 1878.

Scheme II



was not carried out owing to the initial heterogeneity of the reaction mixture. Instead, the effect of substituents in the pyridine ring of *N*-(*p*-nitrophenoxy)pyridinium tetrafluoroborates (**4**, X = *p*-NO_2) on the isomer ratios of **5** (X = NO_2) and **6** (X = NO_2) in the substitution of anisole under otherwise identical conditions was studied quantitatively. In a stepwise process, once singlet *p*-$NO_2C_6H_4O^+$ is formed, the ratio of products formed by its attack on anisole will be independent of the nature of the substituent in the pyridine ring, provided that formation of the σ complex is the rate-determining step in the substitution process and there is no selective removal of individual σ complexes or products. In a concerted process (**23**) the substituent in the pyridine ring will influence the leaving group ability of that moiety and hence the electrophilicity of the oxygen or the ortho carbon atoms undergoing attack, resulting in a probable change in the isomer ratios of substitution products.

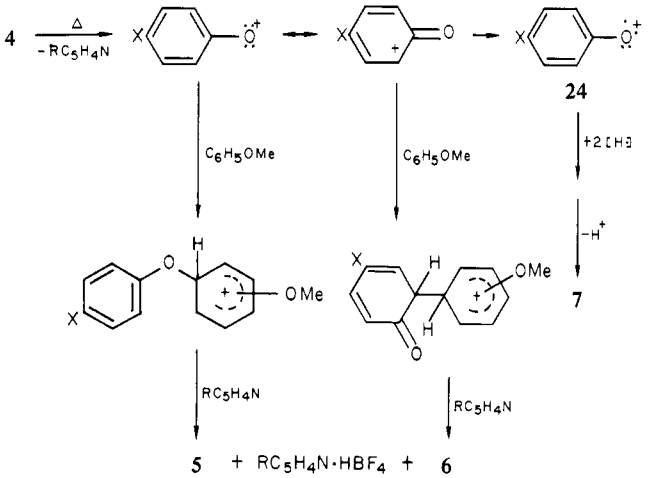
Table I summarizes the results obtained. As can be seen, the ortho:para ratio of the methoxydiphenyl ethers (**5**, X = NO_2) remains relatively constant at 28:72 (±2) for all substituents in the pyridine ring expect R = 4-Cl. While we have no explanation for the anomalous behavior of the latter compound, we suspect that selective removal of one of the σ complexes may be occurring, perhaps by a reaction involving the very reactive electrophile 4-chloropyridine (or its salt). The ortho:para ratio of hydroxybiphenyls (**6**, X = NO_2) is constant at 75:25 within experimental error in all cases, except that when X = 2-OH the yield of **6** was too low to be determined. In this case, the yield of the major

Table I. Yields and Isomer Ratios of Products in the Thermolysis of 4 (X = p-NO_2) in Anisole[a]

R	% 5[b]	o-5:p-5[c]	% 6[b]	o-6:p-6[c]	7
H	43.4	29:71	9.2	74:26	26.7
4-Me	42.5	28.72	8.5	77:23	27.2
4-OMe	43.0	30:70	8.0	76:24	26.0
4-Ph	44.7	26:74	9.3	75:25	25.4
4-Cl	57.4	37:63	10.5	77:23	5.0
3-CO_2Me	53.2	28:72	10.9	76:24	3.6
2-OH[d]	5.1	29:71			17.8

[a] Degassed. Reaction conditions: 5 h at 180 °C under dry N_2. [b] Isolated yields based on the amount of 4 used. [c] Determined by gas chromatography. [d] Thermolysis at 154 °C for 5 h. The starting material was prepared from 1-(p-nitrophenoxy)-2(1H)-pyridone and 1 equiv of CF_3SO_3H.

Scheme III[a]



[a] X = 4-NO_2, 4-CN, 2-CF_3.

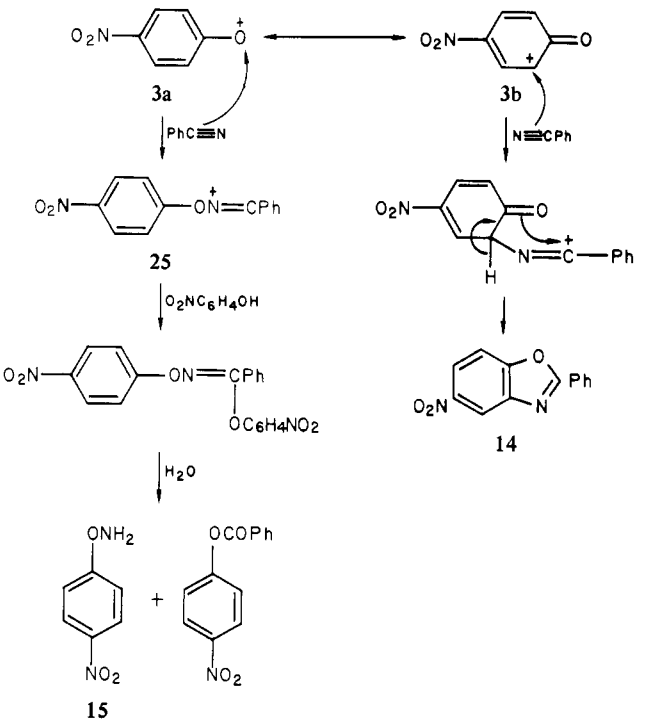
product **5** (C–O–C bond formation) was also considerably lower than usual. To the extent that starting 1-(p-nitrophenoxy)-2-(1H)-pyridine is protonated at the carbonyl oxygen by CF_3SO_3H, one would then expect the resulting 2-hydroxypyridinium salt to undergo normal heterolysis leading to **5** and **6**. A lower thermolysis temperature was used in this case so that decomposition may have been incomplete as well.

The results clearly support a stepwise heterolytic process (mechanism ii) for the thermal decomposition of **4** leading to a 4-nitrophenyloxenium ion, which then attacks the solvent anisole (Scheme III) or benzonitrile (Scheme IV). Formation of the p-nitrophenol (**7**) could arise either from the singlet oxenium ion (**3**) dropping to the triplet (**24**) and the latter then abstracting hydrogen from appropriate donor molecules to give **7** or from some competing homolytic N–O bond fission. That **15** and p-nitrophenyl benzoate could indeed arise during workup by the pathway shown in Scheme IV involving attack of the oxenium ion at the nitrile nitrogen was shown by treating authentic nitrilium ion **25** [prepared in situ (eq 8) from p-nitrophenyl benzohydroxamate and thionyl chloride and then adding antimony pentachloride] in benzonitrile with p-nitrophenol. Addition of cold aqueous sodium bicarbonate gave **15** (70%) and p-nitrophenyl benzoate (60%):

$$p\text{-}O_2NC_6H_4ONHCOPh + SOCl_2 \rightarrow p\text{-}O_2NC_6H_4ON{=}C(Cl)Ph \xrightarrow{SbCl_5} \mathbf{25}\cdot SbCl_6^- \quad (8)$$

It is interesting to note that Waters' prediction[6a] concerning the predominance of C–C bond formation in reactions of **2** with aromatic substrates is fully borne out by our experiments to date. Thus, in the absence of an electron-withdrawing substituent in the aryloxenium ion, **2** reacts with anisole to give only products of C–C bond formation (**10**–**13**), whereas, as we anticipated, an electron-withdrawing substituent results in more C–O–C than C–C products being formed with that substrate. Clearly also, unlike phenylnitrene, phenyloxenium ion *is* electrophilic enough to attack a moderately activated aromatic nucleus.

Scheme IV



Experimental Section

Melting points are uncorrected. IR spectra were determined on Perkin Elmer 257, 357 or Beckman Acculab 3 instruments and NMR spectra on a Varian Associates HA-100 or a Hitachi Perkin-Elmer R20B spectrometer using tetramethylsilane as internal standard. The mass spectra were determined on a CEC 21-104 or Hitachi Perkin-Elmer RMU-6M spectrometer and UV spectra on a Cary 14 spectrophotometer. Gas chromatographic analyses were carried out on a Varian Aerograph 1700 gas chromatograph using helium as a carrier gas.

Reagents and solvents were usually reagent grade and were fractionally distilled or recrystallized before use. Drying of organic extracts was effected with calcium chloride, magnesium sulfate, or molecular sieves (Davidson, Type 4A, grade 514, 8–12 mesh). Light petroleum refers to the fraction bp 30–60 °C unless otherwise stated. Basic alumina for column chromatography was Alcoa (F-20) and neutral alumina was prepared by taking this basic alumina, boiling it with distilled water, neutralizing with acetic acid, rinsing with a large volume of distilled water, and activated by heating at 375 °C for 12 h, followed by cooling it in a vacuum desiccator. Dry, oxygen-free nitrogen was obtained by passing commercial grade nitrogen through a train consisting of a basic solution of pyrogallol, then sulfuric acid, and finally anhydrous calcium chloride. Yields in the thermolyses are based on the amount of pyridinium salt or of peroxycarbonate used.

***N*-(Aryloxy)pyridinium Tetrafluoroborates.** Except as discussed below the preparation of these salts has already been described.[7b]

3-(Carbomethoxy)-1-(*p*-nitrophenoxy)pyridinium Tetrafluoroborate. To a solution of 3-(carbomethoxy)pyridine 1-oxide (1.8 g) in freshly distilled sulfolane (4 g) at 80 °C was added p-nitrobenzenediazonium tetrafluoroborate (2.37 g) in portions over 15 min with vigorous stirring. The reaction mixture was stirred at 80 °C for 2 h and cooled. Evaporation of the solvent and trituration of the residue with anhydrous ether (3 × 15 mL), benzene (15 mL), and methanol (5 mL) gave a yellow solid (2 g, 55%): mp 120–123 °C. Recrystallization from acetonitrile–ether (2:1, v/v, 15 mL) yielded yellow prisms of the tetrafluoroborate: mp 126–127 °C; IR (KBr) 1735, 1520, 1350, 1100 cm^{-1}; NMR (Me_2SO-d_6) δ 10.44 (d, 1, $J_{2,4}$ = 1.5 Hz, H_2), 9.94 (d, 1, $J_{5,6}$ = 6.2 Hz, H_6), 9.30 (dd, 1, $J_{4,5}$ = 7.8 Hz, $J_{2,4}$ = 1.5 Hz, H_4), 8.68–8.20 (m, 3, H_5 and H_m), 7.45 (d, 2, $J_{o,m}$ = 9.5 Hz, H_o), 4.03 (s, 3, CO_2CH_3); mass spectrum, m/e 322 (M^+ · − 2HF), 274 (M^+ · − HBF_4), 138 ($O_2NC_6H_4O^+$ ·), 137 ($C_5H_4NCO_2Me^+$ ·). Anal. Calcd for $C_{13}H_{11}BF_4N_2O_5$: C, 43.09; H, 3.04. Found: C, 43.20; H, 3.10.

4-Methoxy-1-phenoxypyridinium Tetrafluoroborate. A solution of diphenyliodonium tetrafluoroborate (1.472 g) and 4-methoxypyridine 1-oxide (0.56 g) in acetonitrile was heated under reflux for 40 min. The

solvent was evaporated to dryness and the residue was triturated with $CHCl_3$–ether (1:3, v/v, 20 mL) at 0 °C. The colorless crystals were filtered (1.06 g, 94.7%) to give the tetrafluoroborate: mp 122–122.5 °C (from absolute EtOH); IR (KBr) 1120–1000 cm^{-1} (BF_4^-); λ_{max}(MeCN) 249 μm; NMR (CF_3CO_2H); NMR δ 8.8 (d, 2, $J_{2,3}$ = 7.5 Hz, H_2), 7.64 (d, 2, $J_{2,3}$ = 7.5 Hz, H_3), 7.49 (m, 3, H_{m+p}), 7.06 (dd, 2, $J_{o,m}$ = 7.6 Hz, $J_{o,p}$ = 1.4 Hz, H_o), 4.28 (s, 3, OCH_3); mass spectrum, *m/e* (rel intensity) 289 ($M^{+\cdot}$, 5), 202 ($M^{+\cdot} - BF_4$, 5), 201 ($M^{+\cdot} - HBF_4$, 10). Anal. Calcd for $C_{12}H_{12}BF_4NO_2$: C, 49.83; H, 4.15. Found: C, 49.76; H, 4.18.

1-(*o*-(Trifluoromethyl)phenoxy)pyridinium Tetrafluoroborate. Prepared from *o*-(trifluoromethyl)benzenediazonium tetrafluoroborate (2.6 g) and pyridine 1-oxide (1.05 g) in sulfolane (3 mL) at room temperature (3 h), it was obtained (2.66 g, 81%) as colorless needles: mp 169–171 °C (from MeOH); mass spectrum, *m/e* (rel intensity) 180 (56), 160 (52), 132 (84), 79 (100), 52 (92). Anal. Calcd for $C_{12}H_9BF_4NO$: C, 44.07; H, 2.78. Found: C, 44.22; H, 2.88.

Thermolysis of *N*-(*p*-Nitrophenoxy)pyridinium Salts (4, X = *p*-NO_2) in Anisole. General Procedure for the Quantitative Analyses of the Products and Isomer Ratios. A mixture of the *N*-(*p*-nitrophenoxy)-substituted pyridinium tetrafluoroborate (0.001 mol) and anisole (10 mL) was thoroughly degassed and heated at 180 °C for 5 h in a Fischer–Porter tube. Anisole was removed under vacuum and the residue was digested with hot chloroform (2 × 50 mL). The chloroform solution was extracted with saturated aqueous $NaHCO_3$ solution (3 × 40 mL) to remove *p*-nitrophenol and then with 10% aqueous NaOH to remove the hydroxybiphenyls. The dried ($MgSO_4$) $CHCl_3$ extracts were evaporated, and the residue was chromatographed on a column of silica gel (2.2 × 20 cm). Elution with benzene–light petroleum (bp 30–60 °C) (4:1, v/v) gave a mixture of 2- and 4-methoxy-4′-nitrodiphenyl ether [NMR ($CDCl_3$) δ 8.2 (d, 2, J_o = 9 Hz), 7.2–6.8 (m, 6, 3.82 (OCH_3), 3.75 (OCH_3)]. Quantitative analysis was carried out on the isolated hydroxybiphenyls (following acidification of the basic extract) and of the diphenyl ethers, using a 6 ft × $^3/_{16}$ in. 10% SE-30 on Gas-Chrom Q column and a He flow rate of 50 mL/min. The diphenyl ethers were resolved at a column temperature of 200 °C (isothermal), using Ph_2O as the internal standard (retention time, 240 s). Under these conditions the ortho isomer had a t_R of 945 s, the para 1210 s. The same column was used for the hydroxybiphenyls but the temperature of the column was programmed from 240 to 280 °C at 4 °C min^{-1}. Retention times (s): Ph_2O, 190; ortho, 1120; para, 1560. The individual products were collected from the GC and their infrared spectra compared with those of authentic samples (see below). The quantitative data are summarized in Table I.

2-, 3-, and 4-Methoxy-4′-nitrodiphenyl Ether (*o*-, *m*-, and *p*-5, X = NO_2). These were prepared from the appropriate methoxyphenol and *p*-bromonitrobenzene according to the literature.[27] 2-Isomer: mp 102–103 °C (lit.[27] mp 104–105 °C); 3-isomer: mp 85 °C (lit.[27] mp 88 °C); 4-isomer: mp 111–112 °C (lit.[27] mp 111 °C).

2-Hydroxy-2′-methoxy-5-nitrobiphenyl (*o*-6, X = NO_2). This compound was identical (mp, IR, NMR, mass spectrum) with a sample prepared as in the literature: mp 133–135 °C (lit.[28] mp 133–135 °C).

2-Hydroxy-4′-methoxy-5-nitrobiphenyl (*p*-6; X = NO_2). 2-Bromo-4-nitrophenyl acetate[29] (2.6 g), *p*-bromoanisole (1.87 g), and freshly prepared copper powder (2.52 g) were mixed in a Fischer–Porter tube, and the mixture was degassed and heated at 180 °C for 24 h. The mixture was cooled, heated with hot $CHCl_3$ (500 mL) for 5 h, and filtered and the solution was dried ($MgSO_4$) and evaporated. The black residue was chromatographed on a silica gel column. Elution with chloroform gave the desired biphenyl (98 mg, 4%): mp 145 °C; IR (KBr) 3280 (br), 1520, 1330 cm^{-1}. Anal. Calcd for $C_{13}H_{11}NO_4$: C, 63.67; H, 4.52. Found: C, 63.58; H, 4.51.

4′-Cyano-2- (and 4-) methoxydiphenyl Ether (5, X = CN). Authentic samples were prepared by literature methods. 2-Isomer: mp 93 °C (lit.[30] mp 93–94 °C); 4-isomer: mp 108–109 °C (lit.[31] mp 109 °C).

5-Cyano-2-hydroxy-2′-methoxybiphenyl (*o*-6, X = CN). 2-Bromo-4-cyanophenyl acetate (2.39 g), *o*-bromoanisole (1.86 g), and freshly precipitated copper powder (2.52 g) were heated in a Fischer–Porter tube at 220 °C for 2.5 h. Workup as with the nitro compound above and preparative TLC on silica gel using benzene as the developer gave the 2′-methoxybiphenyl (0.27 g, 12%): mp 82–84 °C (from $CHCl_3$–*n*-hexane). Anal. Calcd for $C_{14}H_{11}NO_2$: C, 74.67; H, 4.89. Found: C, 74.63; H, 4.94.

5-Cyano-2-hydroxy-4′-methoxybiphenyl (*p*-6, X = CN). This was prepared in 25% yield in the same way but with *p*-bromoanisole: mp 96–98 °C (from *n*-hexane). Anal. Found: C, 74.52; H, 4.93.

Thermolysis of *N*-(*p*-Cyanophenoxy)pyridinium Tetrafluoroborate in Anisole. A mixture of *N*-(*p*-cyanophenoxy)pyridinium tetrafluoroborate (0.568 g) and anisole (10 mL) was degassed and heated as above at 200 °C for 24 h. The excess anisole was distilled off under reduced pressure and the residue was extracted with $CHCl_3$ (20 mL). The $CHCl_3$ solution was washed with 10% aqueous NaOH (3 × 2 mL), dried ($MgSO_4$), and evaporated. The residue was chromatographed on a column of silica gel (60–200 mesh) (2.4 × 24 cm). Elution with benzene gave an oil which crystallized from ethanol to give a mixture of diphenyl ethers (0.056 g, 12.7%): mp 95–100 °C. This was resolved by GLC on a 6 ft × $^3/_{16}$ in 20% SE-30 on Gas-Chrom Q column at 190 °C with a He flow rate of 55 mL/min to give 4′-cyano-2-methoxybiphenyl ether (t_R, 360 s) and 4′-cyano-4-methoxydiphenyl ether (t_R, 410 s), identical (IR) with authentic samples. The ortho:para ratio was 45:55. The alkaline extracts were acidified and extracted with $CHCl_3$, and the extracts were dried ($MgSO_4$), evaporated, and chromatographed as before on silica gel. Elution with benzene gave a mixture of the isomeric hydroxybiphenyls (0.060 g, 13.6%): mp 90–93 °C; IR (KBr) 3400, 2240 cm^{-1}. Elution with $CHCl_3$ gave *p*-cyanophenol (0.064 g, 24%): mp 110–111 °C, identical with authentic material. The hydroxybiphenyls were resolved on the same GLC column as the ethers under the same conditions to give 5-cyano-2-hydroxy-2′-methoxybiphenyl and 5-cyano-2-hydroxy-4′-methoxybiphenyl [identical (IR) with authentic samples] in the ratio of 33:67.

Thermolysis of *N*-(*o*-(Trifluoromethyl)phenoxy)pyridinium Tetrafluoroborate in Anisole. The tetrafluoroborate (0.654 g) and anisole (20 mL) (degassed) were heated at 180 °C for 4 h as above. Excess anisole was distilled under vacuum [50–52 °C (~1.5 mm)] and the residue digested with hot $CHCl_3$. The insoluble portion was filtered (0.120 g) and recrystallized from MeOH to give pyridinium tetrafluoroborate: mp 217–219 °C. The chloroform extract was treated with 10% NaOH solution (3 × 60 mL), and the aqueous layer was acidified with HCl (50 mL) and extracted with ether (3 × 60 mL). The extracts were dried ($CaCl_2$) and evaporated, and the residue was chromatographed on a column of silica gel (1 × 10 cm). Elution with benzene–chloroform (3:7, v/v) gave hydroxybiphenyl(s) as a yellow oil (0.043 g, 8%): bp 144–146 °C (2 mm); IR (NaCl) 3400 (OH), 1130 cm^{-1} (CF); NMR (CCl_4) δ 7.65–6.75 (m, 7 H), 6.2 (s, OH, exchangeable), 3.73 (s, 3 H, OCH_3); mass spectrum, *m/e* 268 ($M^{+\cdot}$), 253 ($M^{+\cdot} - CH_3$), 249 ($M^{+\cdot} - F$), 248 ($M^{+\cdot} - HF$), 233 ($M^{+\cdot} - CH_3 - HF$). Anal. Calcd for $C_{14}H_{11}F_3O_2$: C, 62.70; H, 4.11. Found: C, 62.54; H, 4.19.

The original chloroform extract was washed with water, dried, and evaporated to give an oily residue which was chromatographed on a column of silica gel (2.4 × 20 cm). Elution with methylene chloride gave a dark-yellow oil (0.14 g, 26%), which was purified further by distillation [bp 130–132 °C (2.5 mm)] to give 1-methoxy-4-(*o*-(trifluoromethyl)-phenoxy)benzene (0.098 g, 18%): IR (NaCl) 1130 cm^{-1} (CF_3); NMR (CCl_4) δ 7.65 (d, 1, J_o = 8 Hz), 7.25 (t, 1, J_o = 8 Hz), 7.05–6.70 (m, 6), 3.70 (s, 3, OCH_3; mass spectrum, *m/e* 268 ($M^{+\cdot}$), 253 ($M^{+\cdot} - CH_3$), 233 ($M^{+\cdot} - HF - CH_3$). Anal. Calcd for $C_{14}H_{11}F_3O_2$: C, 62.70; H, 4.11. Found: C, 62.93; H, 4.25.

Thermolysis of 4-Methoxy-1-phenoxypyridinium Tetrafluoroborate in Anisole. A mixture of 4-methoxy-1-phenoxypyridinium tetrafluoroborate (1.16 g, 0.004 mol) and anisole (20 mL) was degassed and heated at 180–190 °C for 8 h. The excess anisole was evaporated and the residue was extracted to give a light oil (700 mg) which was analyzed by gas chromatography on a 10% SE-30 on Chromosorb Q (8 ft × $^1/_8$ in.) column and a nitrogen flow rate of 30 mL/min. The column temperature was held at 160 °C for 5 min and then raised at the rate of 30 °C/min to 180 °C and held there for another 5 min. Four products with retention times of 3.8, 5.4, 6.6, and 8.5 min, respectively, were collected and shown to be: (i) 2-hydroxy-2′-methoxybiphenyl (**10**) (19.2%): mp 73–74 °C (lit.[32] mp 73–74 °C); NMR δ 4.00 (OCH_3), 7.1–7.6 (ArH); (ii) 2-hydroxy-4′-methoxybiphenyl (**11**) (14.6%): mp 65–66 °C (lit.[33] mp 65–65.5 °C); NMR V 3.97 (OCH_3), 7.0–7.7 (ArH); (iii) 4-hydroxy-2′-methoxybiphenyl (**12**) (18.8%): mp 112–114 °C (lit.[34] mp 113–114 °C); NMR δ 3.92 (OCH_3), 7.0–7.7 (ArH); (iv) 4-hydroxy-4′-methoxybiphenyl (**13**) (12.4%): mp 180–181 °C (lit.[35] mp 183 °C); NMR δ 3.94 (OMe), 7.0–7.7 (ArH). All these products were identical with authentic samples. No phenol or methoxydiphenyl ethers were detected.

In an earlier run, phenol (2.1%) (isolated and analyzed as phenyl benzoate), 4-hydroxy-4′-methoxybiphenyl (21.5%), and a mixture of 2-

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and 4-methoxydiphenyl ether (7.8%) were obtained. The latter were resolved on a 6 ft × $^3/_{16}$ in. 20% SE-30 on Gas-Chrom Q column at 230 °C (benzoic acid as internal standard) to give the 2-:4- isomer ratio as 41:59 (comparison with authentic samples). The results of this earlier run could not be reproduced.

Thermolysis of 1-(*p*-Nitrophenoxy)pyridinium Tetrafluoroborate in Benzonitrile. A mixture of 1-(*p*-nitrophenoxy)pyridinium tetrafluoroborate (0.76 g, 0.0025 mol) and benzonitrile (10 mL) was degassed and heated at 180 °C in a Fischer–Porter tube for 72 h. Excess benzonitrile was removed under vacuum and the residue was digested with boiling chloroform (2 × 5 mL). The chloroform solution was extracted with a saturated solution of sodium bicarbonate (3 × 50 mL). The bicarbonate extracts were acidified and extracted with ether (2 × 100 mL) to remove *p*-nitrophenol (0.092 g, 26.5%): mp 112–113 °C; IR spectrum identical with that of an authentic sample.

A portion of the chloroform solution was evaporated and the residue was analyzed by GLC (15% SE-30 on Chromosorb Q; column temperature, 260 °C; He flow rate, 50 mL min^{-1}). Four peaks with retention times of 100, 160, 780, and 1120 s were observed and were tentatively identified as benzamide, *p*-nitrophenoxyamine, *p*-nitrophenyl benzoate, and 5-nitro-2-phenylbenzoxazole, respectively, by injecting authentic samples under identical conditions. The compound corresponding to the peak with retention time of 160 s (traces) was collected and its IR spectrum was identical with that of authentic *p*-nitrophenoxyamine. The bulk of the chloroform solution was evaporated and the residue was chromatographed on a column of silica gel (2.4 × 20 cm). Elution with light petroleum (bp 30–60 °C)–benzene (1:1, v/v) gave 5-nitro-2-phenylbenzoxazole (0.181 g, 35%): mp 172–173 °C (ethanol); IR and NMR spectra identical with those of an authentic sample.[36] Elution with benzene–chloroform (9:1, v/v) gave *p*-nitrophenyl benzoate (0.92 g, 13%): mp 142 °C; IR and NMR spectra identical with those of an authentic sample. Elution with benzene–chloroform (3:1, v/v) gave benzamide (0.032 g): mp 127–128 °C; IR identical with that of authentic benzamide.

In Situ Formation of *O*-(*p*-Nitrophenyl)benzohydroximoyl Chloride and Its Reaction with *p*-Nitrophenol in the Presence of Antimony Pentachloride. A solution of *p*-nitrophenyl benzohydroxamate (0.51 g, 0.002 mol) in thionyl chloride (2 mL) was heated under reflux for 3 h in a drybox. Excess thionyl chloride was distilled off and to the residue was added *p*-nitrophenol (0.70 g, 0.005 mol), benzonitrile (10 mL), and antimony pentachloride (0.60 g, 0.002 mol). The whole reaction mixture was degassed and heated at 180 °C for 5 h. Excess benzonitrile was removed under vacuum and the residue was digested with boiling chloroform (2 × 20 mL). The chloroform solution was extracted with a saturated solution of sodium bicarbonate (2 × 20 mL) to remove excess *p*-nitrophenol (0.40 g): mp 112 °C. A portion of the dried ($MgSO_4$) chloroform solution was evaporated and the residue was analyzed by GLC (20% SE-30 on Gas-Chrom Q; column temperature, 205 °C (isothermal); He flow rate, 60 mL min^{-1}). Three peaks with retention times of 130, 180, and 1400 s were observed and were tentatively identified as benzamide, *p*-nitrophenoxyamine, and *p*-nitrophenyl benzoate, respectively, by injecting authentic samples under identical conditions. The compound corresponding to the peak with retention time of 180 s was collected and its IR spectrum was found to be identical with that of authentic *p*-nitrophenoxyamine.

The bulk of the chloroform solution was evaporated and the residue was chromatographed on a column of silica gel (2.4 × 20 cm). Elution with benzene–chloroform (9:1, v/v) gave *p*-nitrophenyl benzoate (0.268 g, 60%): mp 141–142 °C; identical in its IR and NMR spectra with authentic *p*-nitrophenyl benzoate. Elution with benzene–chloroform (3:1, v/v) gave benzamide 0.025 g): mp 128 °C; identical IR spectrum with authentic benzamide.

When benzene was used in the above experiment instead of benzonitrile under otherwise identical conditions, *p*-nitrophenoxyamine (73%) and *p*-nitrophenyl benzoate (80%) were obtained. The quantitative analysis was carried out by GLC (6 ft × $^3/_{16}$ in. column; 20% SE-30 on Gas-Chrom Q; 265 °C (isothermal); He flow rate, 65 mL min^{-1}). Triphenylmethane was the internal standard.

Perbenzoyl *p*-Nitrophenyl Carbonate. To a solution of peroxybenzoic acid[37] (0.276 g, 0.002 mol) and *p*-nitrophenyl chloroformate[23] (0.403 g, 0.002 mol) in methylene chloride (25 mL) at −15 °C was added dropwise a solution of dry pyridine (0.16 g, 0.002 mol) in methylene chloride (10 mL) with stirring. After 30 min, the solution was washed with 1% sulfuric acid (2 × 20 mL) and water (2 × 20 mL) and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure gave perbenzoyl *p*-nitrophenyl carbonate (0.48 g, 80%): mp 92–93 °C; IR (CCl_4) 3080, 1820, 1780, 1530, 1350, and 1000 cm^{-1} (–O–O–); NMR ($CDCl_3$) δ 8.28 (d, 2 J_o = 8 Hz), 8.00 (d, 2 J_o = 8 Hz), 7.50 (m, 5); mass spectrum, *m/e* 303 ($M^{+\cdot}$), 287 ($M^{+\cdot} - O$), 259 ($M^{+\cdot} - CO_2$), 215 ($M^{+\cdot} - 2CO_2$), 138 ($O_2NC_6H_4O^{+\cdot}$), 105 ($C_6H_5CO^{+\cdot}$), 77 ($C_6H_5^{+\cdot}$). Anal. Calcd for $C_{14}H_9NO_7$: C, 55.45; H, 2.99. Found: C, 55.20; H, 2.96.

The purity of perbenzoyl *p*-nitrophenyl carbonate was also estimated by titrimetric analysis. Thus, perbenzoyl *p*-nitrophenyl carbonate (0.10 g) was added to a saturated solution of potassium iodide in acetone (15 mL) and acetic (2 mL) and the liberated iodine was titrated against a standard solution of sodium thiosulfate (percent peroxide, 99.1).

Thermolysis of Perbenzoyl *p*-Nitrophenyl Carbonate in Anisole. A solution of perbenzoyl *p*-nitrophenyl carbonate (0.758 g, 0.0025 mol) in anisole (10 mL) was degassed and heated at 180 °C for 5 h. Excess anisole was removed under vacuum and the residue was digested with warm chloroform (30 mL). The chloroform solution was treated with a saturated solution of sodium bicarbonate (3 × 30 mL). The aqueous extracts were acidified with hydrochloric aciid (40 mL) and extracted with ether (2 × 50 mL), the dried ($MgSO_4$) ether extracts were evaporated, and the residue was analyzed quantitatively by GLC (11 ft × $^3/_{16}$ in. column; 25% SE-30 on Gas-Chrom Q; 260 °C (isothermal); He flow rate, 60 mL min^{-1}). The components with retention times of 132 and 228 s were collected and their IR spectra were found to be identical with those of authentic benzoic acid and *p*-nitrophenol, respectively. Quantitative analysis (diphenyl ether internal standard) gave the following results: benzoic acid, 20%; *p*-nitrophenol, 60%.

The dried ($MgSO_4$) chloroform solution was added to *n*-hexane (60 mL) and was allowed to settle for 2 h. A brown solid (oligomer?) precipitated and was filtered (0.045 g): mp 165–175 °C; IR (KBr) 3400 (OH), 3030, 2900, 1720 (C=O), 1520, 1335 (NO_2), 1260 cm^{-1} (ArO). The filtrate was evaporated to dryness and the residue was analyzed quantitatively by GLC on the above column but with programmed temperature: 150–225 °C; rate, 4 °C min^{-1}. All the five components were characterized by a comparison of the IR spectra of samples collected by GLC with those of authentic samples. See Table II.

Table II

product	t_R, s	RMRF^{-1}	% yield
diphenyl ether[a]	370	1.00	
2-methoxybiphenyl	1225	1.17	22.5
3-methoxybiphenyl	1388	1.50	3.00
4-methoxybiphenyl	1440	0.98	4.3
2-methoxyphenyl benzoate	2000	0.94	11.5
4-methoxyphenyl benzoate	2370	0.79	3.6

[a] Internal standard.

Thermolysis of Perbenzoyl *p*-Nitrophenyl Carbonate in Benzonitrile. A solution of perbenzoyl *p*-nitrophenyl carbonate (0.758 g, 0.0025 mol) in benzonitrile (10 mL) was degassed and heated at 180 °C for 7 h. Excess benzonitrile was removed under vacuum and the residue was extracted with warm chloroform (25 mL). The chloroform solution was extracted with a saturated solution of sodium bicarbonate (3 × 25 mL). The aqueous extracts were acidified with hydrochloric acid (40 mL) and extracted with ether (2 × 40 mL). The dried ($CaCl_2$) ether extracts were evaporated, and the residue was analyzed quantitatively by GLC (11 ft × $^3/_{16}$ in. column; 25% SE-30 on Gas-Chrom Q; 260 °C (isothermal); He flow rate, 62 mL min^{-1}). The components with retention times of 126 and 222 s were collected and shown to be benzoic acid (IR spectra) (25.3%) and *p*-nitrophenol (62%), respectively, identical with authentic samples.

The dried ($MgSO_4$) chloroform solution was added to *n*-hexane (60 mL) and allowed to settle for 2 h. A brown precipitate was filtered (0.050 g): mp 164–170 °C; IR (KBr) 3400 (OH), 3030, 2900, 1720 (C=O), 1520, 1335 (NO_2), 1260 cm^{-1} (ArO). The filtrate was evaporated to dryness and the residue was analyzed quantitatively by GLC on the above column but with programmed temperature: 150–225 °C; rate, 4 °C min^{-1}. 2- (11.3%), 3- (1.8%), and 4-cyanobiphenyl (5.4%) were collected (diphenyl ether internal standard) and identified by comparison of their IR spectra with those of authentic samples.

Acid-Catalyzed Thermolysis of Perbenzoyl *p*-Nitrophenyl Carbonate in Anisole. A solution of perbenzoyl *p*-nitrophenyl carbonate (0.303 g, 1 mmol) in anisole (4.9 g, 50 mmol) and trifluoroacetic acid (5 mL) was placed in a three-necked flask fitted with a reflux condenser and a thermometer, and the mixture was heated to 70 °C and kept at that temperature for 60 h under dry nitrogen. The reaction mixture was diluted with ether (50 mL) to give a clear, fluorescent solution. This was washed with water (2 × 50 mL) and then extracted with 5% aqueous

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$NaHCO_3$ solution (2 × 60 mL). The $NaHCO_3$ extracts were neutralized with dilute HCl and extracted with ether (2 × 200 mL). The ethereal extracts were dried (Na_2SO_4) and evaporated to give a colorless residue (68 mg). Gas chromatography (column temperature, 190 °C; 15% SE-30 on Gas-Chrom Q; He flow rate, 55 mL min^{-1}) showed a major peak (t_R, 80 s) and a very small peak (t_R, 340 s). These were identified as benzoic acid and *p*-nitrophenol, respectively (see above). Subsequently, the residue was chromatographed on a column of silica gel (2.4 × 10 cm). Elution with benzene gave benzoic acid (0.049 g, 40%): mp 121–122 °C, identical with an authentic sample.

The original solution was evaporated on a steam bath and anisole removed under reduced pressure [53–55 °C (2 mm). GLC (conditions as above) of the residue showed five peaks with retention times of 90, 140, 340, 1200, and 1600 s, respectively. The components were collected and identified as *o*- and *p*-methoxyphenols, *p*-nitrophenol, *o*- and *p*-methoxyphenyl benzoates, respectively, by a comparison of their IR spectra with those of authentic samples.

Extraction with saturated $NaHCO_3$ solution removed *p*-nitrophenol (0.108 g, 78%): mp 113–114 °C. Extraction with 10% NaOH solution removed *o*- and *p*-methoxyphenols (0.052 g, 42%). The neutral residue (0.108 g, 48%) exhibited two peaks corresponding to *o*- and *p*-methoxyphenyl benzoates, the ratio of which was estimated quantitatively as ortho (16.3%) and para (31.7%) (diphenyl ether internal standard).

Acknowledgment. We thank the National Science Foundation (GP-3361X and CHE 78-04805) for support of this work and the Graduate Council, University of Alabama, for a Fellowship (to M.N.I.).

Biosynthesis of the Boron-Containing Macrolide Antibiotic Aplasmomycin by *Streptomyces griseus*

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Received December 18, 1980

Abstract: The biosynthesis of aplasmomycin in *Streptomyces griseus* strain SS-20 was studied by feeding experiments with ^{13}C-labeled precursors. ^{13}C NMR analysis of the antibiotic samples biosynthesized from [1-^{13}C]-, [2-^{13}C]-, and [1,2-$^{13}C_2$]acetate and from [$^{13}CH_3$]methionine showed that each half of the molecule is made up from seven intact acetate units providing carbons 1–14 and three methyl groups originating from methionine, which are located in positions 18, 19, and 20. Feeding experiments with [1,3-$^{13}C_2$]glycerol have shown unequivocally that glycerol is an intact precursor of the three-carbon starter unit of the polyketide chain. A possible mechanism for the conversion of glycerol into a suitable starter unit is proposed. Treatment of deboroaplasmomycin with boric acid led to reinsertion of the boron, demonstrating the chemical feasibility of a biosynthetic pathway involving first formation of the macrocyclic ring system followed by insertion of boron as the terminal step.

The boron-containing antibiotic aplasmomycin was isolated from a strain of *Streptomyces griseus*[1] obtained from shallow sea and mud as part of a screening program for new metabolites from marine microorganisms. Structure determination[2] by an X-ray analysis of the silver salt showed that it is a macrodiolide containing 40 carbon atoms and one boron. The compound is a symmetrical dimer which closely resembles boromycin,[3] the only other boron-containing natural product known. Its 16 chiral centers have identical configurations in the two halves of the molecule and its stereochemistry corresponds to that of boromycin at all centers except C-9 in one half of the boromycin molecule. In contrast to boromycin, aplasmomycin does not contain an amino acid moiety. Recently, two cometabolites of aplasmomycin, aplasmomycins B and C,[4] were isolated and identified as the monoacetate (at C-9) and the diacetate (at C-9 and C-9′) of aplasmomycin, respectively.

Aplasmomycin inhibits the growth of gram-positive bacteria, including mycobacteria, in vitro and is active against *Plasmodium berghei* in vivo.[1] Aplasmomycin and aplasmomycin B, but not aplasmomycin C and desboroaplasmomycin, show ionophoric properties, mediating net K^+ transport across a bulk phase.[4] The ion carrier activity correlates with antibiotic activity of these four compounds, aplasmomycin B having about equal antibiotic activity as aplasmomycin, whereas the other two are inactive. The metal ion specificity is rather pronounced for monovalent cations, with a preference for K^+, Rb^+, and Cs^+.

In the present communications we report results which establish the overall biosynthetic origin of aplasmomycin.

Results

The biosynthesis of aplasmomycin was studied in *Streptomyces griseus* strain SS-20 which was grown in a medium containing glucose and Kobu-cha (processed sea weed) and salt. On the basis of time-course studies, the labeled precursors were added to the cultures at 48 h after inoculation, and the cultivation was continued for an additional 48 h. Aplasmomycin could be isolated in yields of about 10 mg/L by chloroform extraction of the broth followed by preparative layer chromatography.

Because of the symmetry of the molecule, the ^{13}C NMR spectrum of aplasmomycin shows only 20 signals. An unequivocal assignment of every signal in the spectrum rests on the characteristic chemical shifts, multiplicities, single-frequency decoupling, comparison with several derivatives and model compounds, specific deuteration experiments, and analysis of one-bond carbon–carbon couplings of pairs of carbon atoms.[5]

The structure of aplasmomycin strongly suggests its formation by the polyketide (acetogenin) pathway. In analogy to the formation of most other macrolide antibiotics[6] one might expect aplasmomycin to be of a mixed acetate/propionate origin, i.e.,

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