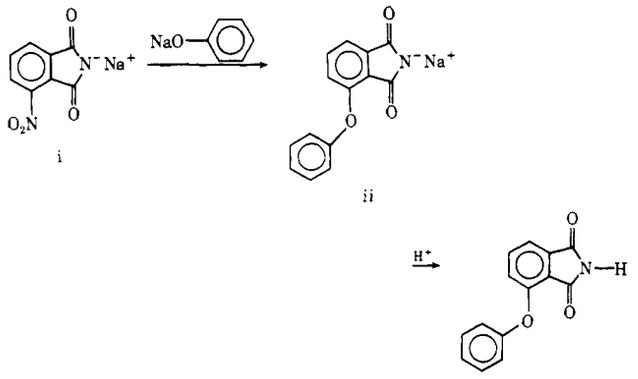
phthalic anhydride, 319-03-9; 4-chlorophthalic anhydride, 118-45-6; aniline, 62-53-3; 4-methoxyaniline, 104-94-9; 4-methylaniline, 106-49-0; 4-chloroaniline, 106-47-8; methylamine, 74-89-5; 8-hydroxyquinoline, 148-24-3; sodium, 1440-23-5; *p*-methylphenol, 106-44-5; *N*-phenylphthalimide, 520-03-6.

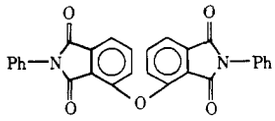
Supplementary Material Available. Tabulated ^{13}C NMR chemical shifts for all phthalimides contained in Tables I, II, and IV (Table VII) as well as **2p**, **2q**, and **5** (7 pages). Ordering information is given on any current masthead page.



i ii

References and Notes

(1) W. Reinders and W. E. Ringer, *Recl. Trav. Chim. Pays-Bas*, **18**, 326 (1899); J. F. Bennett and R. E. Zahler, *Chem. Rev.*, **49**, 273 (1951).
(2) J. H. Gorvin, *Chem. Ind. (London)*, **36**, 1525 (1967).
(3) E. Radlmann, W. Schmidt, and G. E.Nischk, *Makromol. Chem.*, **130**, 45 (1969).
(4) L. Caswell and T. Kao, *J. Heterocycl. Chem.*, **3**, 333 (1966); see also R. Fowler, L. Caswell, and L. Sue, *ibid.*, **10**, 407 (1973), for the reaction of methoxide with *N*-substituted 3-halophthalimides.
(5) For an example, see T. W. M. Spence and G. Tennant, *J. Chem. Soc., Perkin Trans. 1*, 835 (1972).
(6) J. R. Beck, *J. Org. Chem.*, **37**, 3224 (1972); **38**, 4086 (1973); J. R. Beck, R. L. Sobcyak, R. G. Suhr, and J. A. Yahner, *ibid.*, **39**, 1839 (1974); J. R. Beck and J. A. Yahner, *ibid.*, **39**, 3440 (1974).
(7) R. D. Knudsen and H. R. Snyder, *J. Org. Chem.*, **39**, 3343 (1974).
(8) N. Kornblum et al., *J. Org. Chem.*, **41**, 1560 (1976).
(9) See, for example, J. G. Wirth and D. R. Heath, U.S. Patent 3 838 097 (1974).
(10) Yields of >95% can be obtained by pouring the reaction mixture into water and recovering the product by filtration. No attempt was made to maximize the yields of these crude products, which were clean by VPC analysis.
(11) J. Miller, "Aromatic Nucleophilic Substitution", Elsevier, New York, N.Y., 1968, p 137.
(12) J. Miller, ref 11, p 165.
(13) Placement of a negative charge on nitrogen causes the reaction to be very sluggish. Displacement of the nitro group from the phthalimide salt (i) by phenoxide to give ii requires heating at 120 °C for 16 h in DMF. Reaction with the corresponding 4 isomer is incomplete after 48 h at 120 °C.
(14) Support for the contention of steric interaction between the 3 substituent and the ortho carbonyl group is found in the ^{13}C NMR spectrum of 3-nitro-*N*-phenylphthalimide (**1e**) (see Table VII). Both carbonyl B and C-2 of this molecule are shifted upfield relative to the calculated values, which suggests steric compression between the nitro and carbonyl group. For a discussion of steric compression shifts, see G. C. Levy and G. L. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists", Wiley-Interscience, New York, N.Y., 1972, p 24.
(15) Perhaps Me_2SO also levels the rate differences between the different leaving groups. Many examples are known. See, for example, ref 11, Chapter 8.
(16) D. R. Heath and J. G. Wirth, U.S. Patent 3 730 946 (1973).
(17) A detailed study of the reaction of thiophenoxide nucleophiles with these systems will appear in a subsequent publication in this journal.
(18) W. T. Reichle, *J. Org. Chem.*, **37**, 4254 (1972), see also A. B. Newton and J. B. Rose, *Polymer*, **13**, 465 (1972).
(19) One of the more likely products produced is the bisether iii. For a detailed study of this type of reaction, see R. L. Markezich and O. S. Zamek, *J. Org. Chem.*, companion paper, this issue.



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(20) M. S. Newman and P. G. Scheurer, *J. Am. Chem. Soc.*, **78**, 5004 (1956).
(21) R. L. Markezich, unpublished results. See also N. Ishikawa, T. Tanabe, and D. Hayashi, *Bull, Chem. Soc. Jpn.*, **48**, 359 (1975).
(22) D. K. Drew and D. B. Kelly, *J. Chem. Soc.*, 630 (1941).
(23) F. J. Williams, H. M. Relles, J. S. Manello, and P. E. Donahue, *J. Org. Chem.*, companion paper, this issue.
(24) D. R. Heath and J. G. Wirth, U.S. Patent 3 787 475 (1974).
(25) U. Burgerand and R. Huisgen, *Tetrahedron Lett.*, **35**, 3057 (1970).

Reactions of Phenoxides with Nitro-Substituted Phthalate Esters

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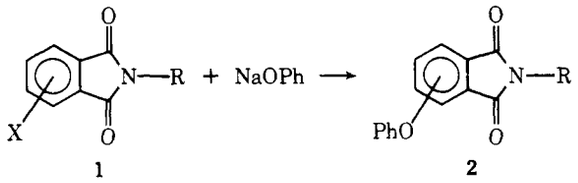
Aromatic nucleophilic nitro displacement by phenoxides on nitro-substituted phthalate esters is discussed. The differences in behavior between the 3-nitro (**5a–d**) and 4-nitro (**4a–d**) isomers were investigated. The 4 isomers gave excellent yields of the phenoxy substituted derivatives **6**. Side reactions were prominent for the 3-nitro isomers in degrees depending on the alkyl groups of the ester function. The majority of the side products can be explained by nucleophilic attack on the alkyl group of the ester, resulting in cleavage of the alkyl–oxygen bond. A rationale for the relative displacement rates of these two isomers is presented.

The reaction of phenoxides with nitro- or halo-substituted phthalimides (**1**) is an excellent synthetic route to ether imide derivatives (**2**).[1] We wish to report the results of studies on the reactions of phenoxides with nitrosubstituted phthalate esters.[2] Examples of aromatic displacement reactions using an ester activating group were reported as early as 1890,[3] but this group was used only in conjunction with other activating groups. The displacement of nitro groups activated by only one ester group was subsequently observed in dipolar aprotic solvents.[4,5] No attack of the nucleophile at either the carbonyl or alkyl group of the ester was observed in any of these systems.

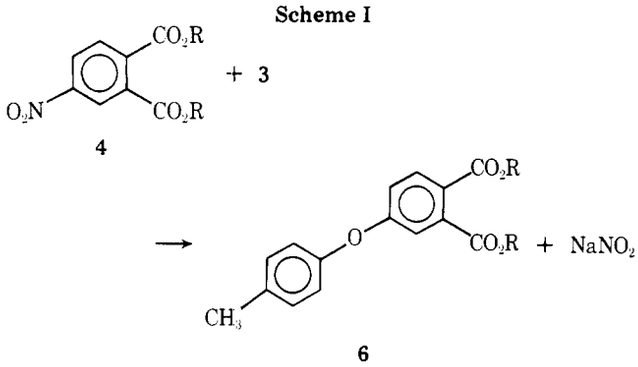


1 2

Results and Discussion

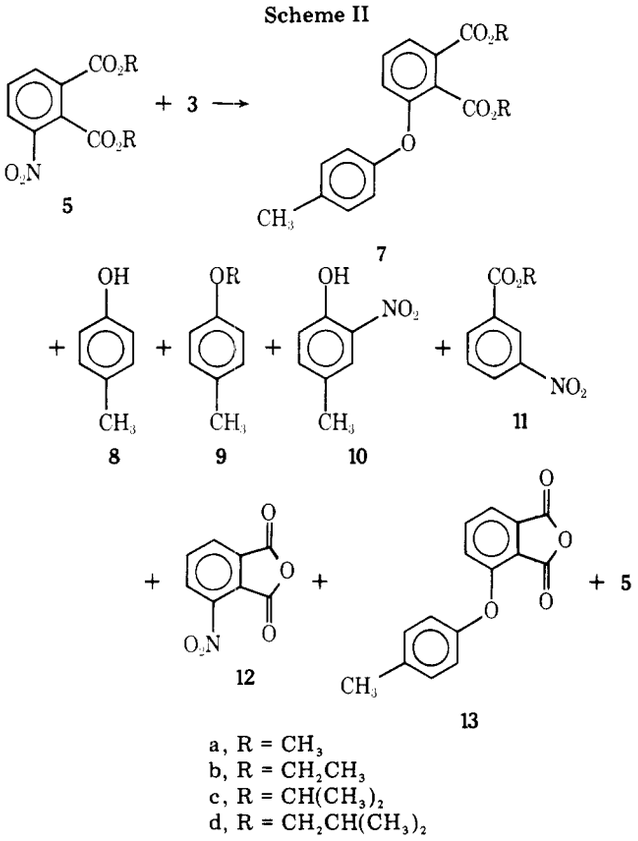
Reactions with Sodium 4-Methylphenoxide. The reaction of sodium 4-methylphenoxide (**3**) with eight dialkyl nitrophthalates (**4a–d** and **5a–d**) was examined to determine

Scheme I



a, R = CH_3
b, R = CH_2CH_3
c, R = $CH(CH_3)_2$
d, R = $CH_2CH(CH_3)_2$

Scheme II

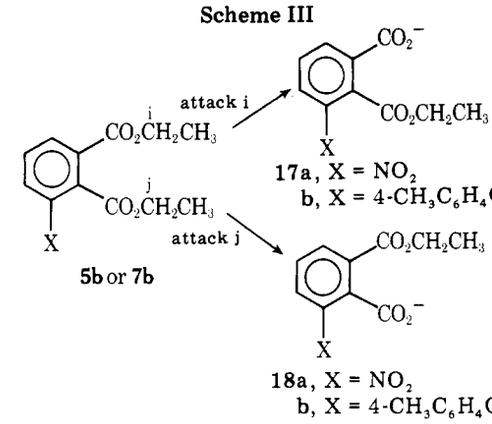


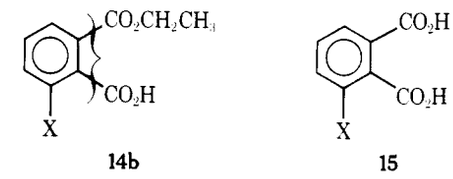
a, R = CH_3
b, R = CH_2CH_3
c, R = $CH(CH_3)_2$
d, R = $CH_2CH(CH_3)_2$

the effect of the alkyl group on the course of the reaction and to judge the importance of the location of the nitro group. The reaction of **3** with the 4-nitro derivatives (**4a–d**) in DMF at 100 °C for 1 h gave excellent yields of the ether derivatives **6a–d** (Scheme I). There was no trace of 4-methylphenyl alkyl ether (**9**) (the product of phenoxide attack at the alkyl group) in any of these systems. The reactions were complete in 1 h; thereafter **6** was slowly destroyed with time by reaction with the sodium nitrite formed as a by-product of the displacement. Attempts to generate the nucleophile in situ by using a carbonate base and 4-methylphenol (**8**) were less successful due to hydrolysis of the ester groups of **4**. These results are summarized in Table I.

The reaction of **3** with the 3-nitro isomers (**5**) proved to be more complex (Scheme II). Several side reactions occurred in addition to nitro displacement. For example, the reaction of **3** with **5b** gave the eight products indicated as well as three unidentified minor products. It is unknown if **12** was formed during the reaction or if compounds such as **14b** or **15** (X = NO_2) were formed and then underwent ring closure during VPC analysis to give **12**. It is likely that **13** originated from **14b**

Scheme III





or **15** (X = 4-$CH_3C_6H_4O$) and was not actually formed during the reaction (see Experimental Section). Subsequent analysis of the reaction mixture by GC/mass spectroscopy indicated the presence of diethyl 3-ethoxyphthalate (**16**) as a minor component.

The majority of these products can be explained as arising from the attack of a nucleophile upon the alkyl group of the esters. Such an attack (Scheme III) in the case of **3** leads to the ether **9** and either **17** or **18**. As has been shown for the corresponding phenyl esters,[6] either **17a** or **18a** can thermally decarboxylate during the reaction to give only the meta derivative corresponding to **11b**. Protonation of either **17a** or **18a** upon workup gives the acid esters **14b** (X = NO_2). The thermal treatment of these materials during VPC analysis can result in the formation of 3-nitrophthalic anhydride (**12**) by loss of ethanol. Attack of **3** at an ester group of **7b** can also generate the ether **9b** as well as the acid ester salts **17b** and **18b**. These salts apparently did not thermally decarboxylate under the reaction conditions but, instead, were protonated on workup and ring closed during VPC analysis to give the observed anhydride **13**. Considering the differences in the carbanionic stabilizing influences of $-NO_2$ vs. 4-$CH_3C_6H_4$, it is not surprising that **17a** and/or **18a** underwent decarboxylation while **17b** and/or **18b** did not.

Formation of **17** and **18** can also result from attack by the nitrite anion generated by nitro displacement at either the alkyl group (which would also produce ethyl nitrite) or at the carbonyl group to give ethoxide. Either of these processes could ultimately give ethoxide and **17** or **18**. Ring closure of **17** or **18** would also generate ethoxide. Formation of **16** results from reaction of this ethoxide with **5b**.

Finally, **10** was probably produced during the workup of the reaction mixture and not during the reaction itself. If the reaction mixture was worked up under neutral rather than acidic conditions, no **10** was found and the amount of **8** recovered was increased. Undoubtedly, nitrous acid produced from the sodium nitrite formed in the nitro displacement reaction reacted with **8** during acidic workup to produce a species (probably the corresponding nitroso compound) which ultimately led to **10**. This hypothesis is supported by appropriate control experiments (see Experimental Section).

The product distributions for the reaction of **3** with **5a–d** are contained in Table II. These results indicate that the alkyl

Table I. Displacement Yields for 4-Nitro Isomers (4)

Registry no.	Compd	Alkyl group	Nucleophile	Conditions	% Yield of 6 (VPC)
610-22-0	4a	CH_3–	3	1 h (100 °C), DMF	98
				2 h (100 °C), DMF	90
				5 h (100 °C), DMF	86
2050-19-3	4b	C_2H_5–	3	1 h (100 °C), DMF	93
				2 h (100 °C), DMF	93
				3 h (100 °C), DMF	87
	4b	C_2H_5–	4-$CH_3C_6H_4OH/K_2CO_3$	1.5 h (100 °C), DMF	15
				16 h (100 °C) + 6.5 h (135 °C), DMF	48
				16 h (100 °C) + 24 h (135 °C), DMF	41
	4b	C_2H_5–	4-$CH_3C_6H_4OH/Na_2CO_3$	5.5 h (150 °C), DMF	37
				16 h (150 °C), DMF	46
13325-36-5	4c	–$CH(CH_3)_2$	3	1 h (100 °C), DMF	95–99
53577-26-7	4d	–$CH_2CH(CH_3)_2$	3	1 h (125 °C), DMF	95–99

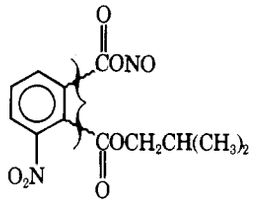
Table II. Reactions of Dialkyl 3-Nitrophthalates (5) with 3 in DMF at 150 °C for 3 h. VPC % Yields

R	Registry no.	8	10	9	11	12	5	13	7
CH_3	13365-26-9	5	1	61	11	17	4	7	12
CH_3CH_2	62351-79-5	4	15	24	9	7	10	5	39
$(CH_3)_2CH$	63181-75-9	6	14	5	2		10	1	53
$(CH_3)_2CHCH_2$	63181-76-0		22	≤1			8		74

group greatly influenced the course of the reaction. Changing the alkyl group from methyl to ethyl to isopropyl to isobutyl changed the yield of the ethers (**9a–d**) formed by attack at the alkyl group from 61 to 24 to 5 to ≤ 1. Concurrently, the amount of the other side products resulting from this alkyl (or carbonyl) group attack also decreased in this series. For example, the nitro ester (11) formed by decarboxylation decreased steadily from R = methyl (11%) to R = isobutyl (0%). Simultaneously, as the percent of alkyl (or carbonyl) attack decreased, the yield of the nitro displacement product (**7a–d**) increased steadily from 12 to 74%. The yield of **7d** in the isobutyl system could not be increased further. Apparently the sodium nitrite produced attacked the remaining **5d** and deactivated it for further displacement. This suggestion is supported (Table II) by the fact that approximately 22% of unreacted 4-methylphenol is isolated (in the form of 2-nitro-4-methylphenol) following workup at the end of the reaction.

The ease of the apparent attack of the phenoxide nucleophile at the alkyl group of the ester is surprising in the light of what has been reported in the literature. Until Bunnett's[7] disclosure of the formation of dimethyl ether from the reaction of sodium methoxide with methyl benzoate, the bimolecular cleavage of the alkyl oxygen bond in the hydrolysis of carboxylic esters was almost unknown.[8] Recently, there have been other reports[9] of this type of reaction, although few examples have been reported in which alkyl ethers of phenols were formed. It appears, however, that in these 3-nitro-substituted phthalate esters, S_N2 attack of the phenoxide nucleophile at the alkyl group is prominent and takes place not only with the methyl esters, but also with the ethyl esters and even to a small degree with the isopropyl systems.[10]

It is noteworthy that no other products were detected by VPC analysis in the diisobutyl 3-nitrophthalate system. It is likely that, at least in the very hindered isobutyl system, nitrite attacks a carbonyl group, rather than the alkyl group, to give **19**. Thereafter, the conversion of **19** to the sodium salt of **14d** by reaction with another nucleophile (nitrite, isobutoxide, or phenoxide) should be facile. Once these conversions have occurred, decomposition of this salt by intramolecular E2 elimination to give isobutylene and monosodium 3-nitrophthalate is feasible. If this occurred, the product would not be observed by VPC analysis.



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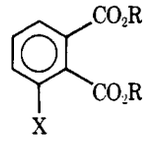
Relative Rates of Nitro Displacement in 4 and 5. A competition reaction containing equivalent amounts of **4d, 5d,** and **3** produced **6d** as the only product. It can be estimated that the 4 isomer **4d** reacted at least two orders of magnitude *faster* than the 3-nitro isomer **5d.** This is in marked contrast to the relative rates of displacement in the phthalimide series where the 4-nitro isomers displaced several times *slower* than the corresponding 3-nitro isomers.[1]

In the case of **4d** vs. **5d,** the reason for the large rate difference is probably steric in origin. In the Meisenheimer intermediate from **6d** (**20**), little steric inhibition of resonace should be encountered (especially in the conformer drawn) and stabilization of the negative charge by the para ester carbonyl should be substantial. On the other hand, there is no Meisenheimer complex conformer derived from **5d** capable of resonance stabilization of the negative charge, which would be as free of steric interactions as **20.** In **21** or **22** resonance stabilization of the negative charge by the ortho ester carbonyl would simultaneously require severe steric compressive interactions to be generated, thus making **21** or **22** much higher in energy than **20.** Assuming similar ground-state energies for **4d** and **5d,** this energy difference for the intermediates would account for the rate difference.

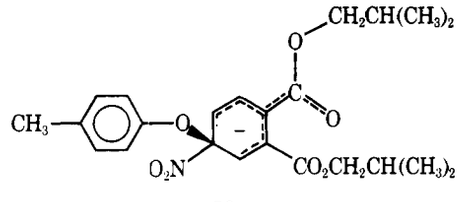
Spectral data are in agreement in this argument. The 2-carbobutoxy group in **5d** resides mainly in its least sterically hindered conformation, in which the carbonyl carbon and both oxygens are in a plane perpendicular to the plane of the ring. The carbonyl stretching region in the infrared spectrum of **5b** shows two strong bands at 1735 and 1745 cm^{-1}. The former is in agreement with an aryl-conjugated ester carbonyl (1-carboalkoxy),[11] while the latter is what would be expected for an unconjugated, saturated ester carbonyl.[11] This is consistent with a 2-carboalkoxy group having no appreciable overlap with the aromatic ring. On the other hand, **4b** showed only a single

Table III. Reaction of Sodium Nitrite with I at 150 °C in DMF



I

Registry no.	R	X	Equiv of $NaNO_2$	% starting material remaining				
				0.5 h	1.0 h	3.0 h	5.0 h	10.0 h
131-11-3	CH_3–	H	2	83	55	13	5	
84-66-2	CH_3CH_2–	H	2	100	96	88	79	59
84-69-5	$(CH_3)_2CHCH_2$–	H	2	91	86	86	84	82
	CH_3–	NO_2	2	13	4	0		
	CH_3CH_2–	NO_2	2	88	68	23	9	
	CH_3–	H	1	73	60	55	55	



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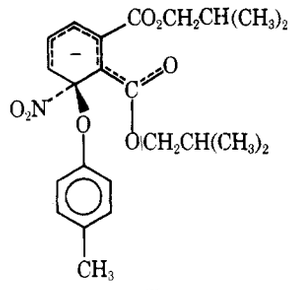

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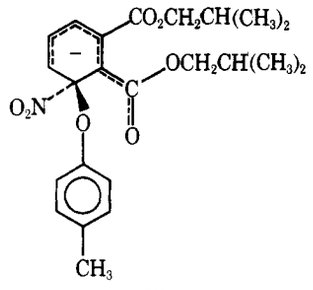

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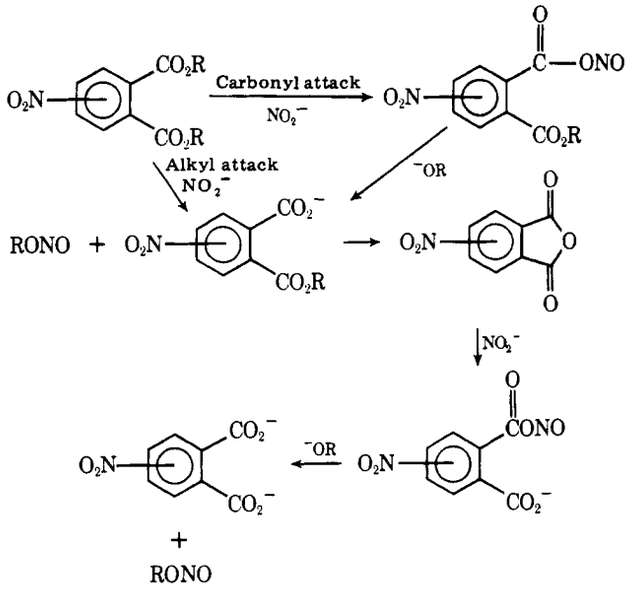
carbonyl band at 1735 cm^{-1} typical of normal aryl-conjugated ester carbonyls.

The Reaction of Sodium Nitrite with Phthalate Esters. Reactions were carried out in DMF at 150 °C using 1 or 2 equiv of anhydrous sodium nitrite and the following esters: dimethyl phthlate, diethyl phthalate, diisobutyl phthalate, dimethyl 3-nitrophthalate, and diethyl 3-nitrophthalate. The amount of unreacted ester was monitored as a function of time (Table III).

Several interesting results were obtained: (1) the more hindered the ester group, the slower the rate of destruction (isobutyl < ethyl < methyl); (2) substitution of a nitro group on the phthalate ring increased the rate of destruction; (3) 2 equiv of sodium nitrite were necessary for complete destruction of the esters. In all of these reactions a precipitate was formed at a rate corresponding to the rate of ester destruction.

At the present time, it is not possible to distinguish nitrite attack at the carbonyl from nitrite attack at the alkyl group, although in either case 2 equiv of nitrite are necessary. A change in alkyl groups from methyl to isobutyl should hinder attack at both the carbonyl group and the alkyl group. Substitution of a nitro group on the phthalate ring should facilitate nucleophilic attack on the carbonyl group, but it should also increase the efficiency of the phthalate salt as a leaving group if attack does take place at the alkyl group. Since 2 equiv of sodium nitrite are necessary for total ester destruction and the resulting product has no alkyl groups present, the two mechanisms for phthalate ester destruction by sodium nitrite given in Scheme IV are plausible.

Scheme IV



In summary, the reaction of phenoxides with nitrophthalate esters was found to be greatly dependent upon the structure of the ester derivative. Side reactions were prominent for the 3-nitro isomers in degrees depending on the alkyl groups of the ester function (Me > Et > isopropyl > isobutyl). The majority of the side products can be explained by nucleophilic attack on the alkyl group of the ester, resulting in cleavage of the alkyl oxygen bond. The corresponding 4-nitro esters gave essentially quantitative yields of the phenoxy-substituted products and were at least two orders of magnitude more reactive than the 3-nitro derivatives.

Further studies of the displacement of nitro and halo groups in derivatives of phthalic acid will be presented in subsequent papers.

Experimental Section

Infrared spectra were taken on a Perkin-Elmer 457 grating infrared spectrophotometer in chloroform solution or as a KBr pellet. Mass spectra were determined on a CEC 21-104 analytical mass spectrometer at 70 eV. Vapor-phase chromatography (VPC) was carried out on a Hewlett Packard 5750 research chromatograph using a 6 ft 10% UCW-98 on 80/100 Chromosorb W column with temperature programming and a thermal conductivity detector. Melting points were determined on a Thomas-Hoover instrument and are uncorrected. C, H, N analyses were determined on a Perkin-Elmer 240 C, H, N analyzer.

Anhydrous DMF and Me_2SO were purchased from Burdick and Jackson Laboratories. 4-Methyl-2-nitrophenol (**10**) and methyl 4-methylphenyl ether (**9a**) were obtained from the Aldrich Chemical

Co. The sodium salt of 4-methylphenol was prepared by reaction with anhydrous sodium methoxide as has been described previously.[1] For displacement reactions, temperatures listed are oil bath temperatures. In general, the actual solution temperatures were 2–5 °C cooler.

VPC yields were determined by using an internal standard (*m*-terphenyl, biphenyl, or *o*-terphenyl) in the reaction mixture. Aliquots were removed at timed intervals and added to a 1.2 N hydrochloric acid solution. This mixture was extracted with ether and the ether extracts were dried over anhydrous magnesium sulfate and then subjected to VPC analysis. Peak areas were calculated by weighing photocopies of each peak and were corrected for detector response differences.

Preparation of Nitro Esters 4 and 5. These esters were prepared by refluxing a mixture of 3- or 4-nitrophthalic anhydride, a catalytic amount of *p*-toluensulfonic acid, and equal volumes of the appropriate alcohol and xylene (ca. 25% concentration). The reaction mixtures were worked up with an ether extraction (bicarbonate wash) to give the crude nitro ester. ^{1}H NMR spectra and elemental analyses follow (^{13}C NMR assignments are contained in the Supplementary Material, Table VI). The aromatic multiplets in the ^{1}H NMR of **4a–d** were superimposable on one another and distinctly different from those of **5a–d.**

4a: mp 66–67 °C (lit. 65 °C);[12] ^{1}H NMR ($CDCl_3$) δ 1.40 (methyl, s, 6), 7.7–8.6 (aromatic, m, 3).

4b: mp 33–35 °C (lit. 33–34 °C);[13] ^{1}H NMR ($CDCl_3$) δ 1.40 (methyl, t, J = 7 Hz, 6), 4.44 (methylene, q, J = 7 Hz, 4) 7.7–8.6 (aromatic, m, 3).

4c: mp 41–42 °C [lit. bp 172 °C (3 Torr)];[14] ^{1}H NMR ($CDCl_3$) δ 1.40 (methyl, d, J = 6 Hz, 12), 5.32 (methine, septet, J = 6 Hz, 2), 7.7–8.6 (aromatic, m, 3).

4d: ^{1}H NMR ($CDCl_3$) δ 1.04 (methyl, d, $J \simeq$ 7 Hz, 12), 1.6–2.4 (methine, m, 2), 4.14 (methylene, d, $J \simeq$ 6 Hz, 4), 7.7–8.6 (aromatic, m, 3). Anal. Calcd for $C_{16}H_{21}NO_6$: C, 59.43; H, 6.55; N, 4.33; mol wt 323. Found: C, 59.7; H, 6.6; N, 4.3; mol wt 323 (mass spectrum).

5a: mp 69–70 °C (lit. 67–69 °C);[12] ^{1}H NMR ($CDCl_3$) δ 4.00 (methyl, s, 3), 4.07 (methyl, s, 3), 7.7–8.6 (aromatic, m, 3).

5b: mp 44–45 °C (lit. 46 °C);[13] ^{1}H NMR ($CDCl_3$) δ 1.40 (methyls, triplet, $J \simeq$ 7 Hz, 6), 4.40 and 4.50 (methylenes, quartets, $J \simeq$ 7 Hz, 4), 7.5–8.5 (aromatic, m, 3).

5c: mp 41–42 °C; ^{1}H NMR ($CDCl_3$) δ 1.39 and 1.43 (methyls, doublets, J = 6 Hz, 12), 5.25 and 5.35 (methines, septets, J = 6 Hz, 2), 7.5–8.5 (aromatic, m, 3). Anal. Calcd for $C_{14}H_{17}NO_6$: C, 56.94; H, 5.80; N, 4.74; mol wt 295. Found: C, 57.0; H, 6.0; N, 4.7; mol wt 295 (mass spectrum).

5d: bp 165–166 °C (0.25 Torr); ^{1}H NMR ($CDCl_3$) δ 1.00 (methyl, d, $J \simeq$ 7 Hz, 12), 1.6–2.4 (methine, m, 2), 4.08 and 4.15 (methylenes, each d, $J \simeq$ 7 Hz, 4), 7.40–8.35 (aromatic, m, 3). Anal. Calcd for $C_{16}H_{21}NO_6$: C, 59.43; H, 6.55; N, 4.33; mol wt 323. Found: C, 59.8; H, 6.6; N, 4.0; mol wt 323 (mass spectrum).

Reaction of 3 with 4-Nitro Esters 4a–d to give 6a–d. An equimolar mixture of **3** and the desired nitro ester was stirred with DMF (10% solution) under nitrogen for 1 h at 150 °C. The cooled reaction mixture was added to 1.2 N hydrochloric acid and extracted with ether. The ether extracts were washed with 1.2 N HCl, water, 5% sodium carbonate, water, and a saturated salt solution. The ether solution was dried and concentrated to give the crude product, **6,** in 90–95% yield. This material was purified by distillation for **6b–d.** ^{1}H and ^{13}C NMR data for these compounds are in the supplementary material (Tables IV and V).

6a: oil. Anal. Calcd for $C_{17}H_{16}O_5$: C, 68.0; H, 5.4; Found: C, 67.8; H, 5.5.

6b: bp 163–165 °C (0.05 Torr); n^{24}_D 1.5482. Anal. Calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14; mol wt 328. Found: C, 69.7; H, 5.9; mol wt 328 (mass spectrum).

6c: bp 175–177 °C (0.05 Torr); n^{24}_D 1.5330. Anal. Calcd for $C_{21}H_{24}O_5$: C, 70.77; H, 6.79; mol wt 356. Found: C, 71.7; H, 7.0; mol wt 356 (mass spectrum).

6d: bp 194–199 °C (0.20 Torr); n^{24}_D 1.5292. Anal. Calcd for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34; mol wt 384. Found: C, 71.5; H, 7.5; mol wt 384 (mass spectrum).

Reaction of 4b with 4-Methylphenol and Potassium Carbonate. A mixture of 2.67 g (0.01 mol) of **4b,** 1.08 g (0.01 mol) of **8,** 1.38 g (0.01 mol) of anhydrous potassium carbonate, 1.41 g of *m*-terphenyl, and 26 mL of anhydrous DMF was stirred at 100 °C under nitrogen for 16 h and then at 135 °C for additional 24 h. Aliquots were removed at timed intervals and worked up as described above. Analysis indicated the presence of **4b, 6b,** and a peak with the same retention time as 4-nitrophthalic anhydride. There was no peak present with the retention time of the ether **9b** (see Table I).

Reaction of Diethyl 3-Nitrophthalate (5b) with 3. Identification of Products. A mixture of 4.84 g (0.037 mol) of **3,** 9.94 g (0.037 mol) of **5b,** and 100 mL of anhydrous DMF was stirred at 150 °C for 3 h under nitrogen. The mixture was cooled to room temperature and poured into a large excess of 1.2 N HCl. This solution was thoroughly extracted with ether; the ether extracts were washed with water and a saturated sodium chloride solution, and were dried over anhydrous magnesium sulfate. The dried ether extracts were concentrated to give a brown oil. Analysis of this oil by VPC showed the presence of 11 peaks. Coinjection of authentic samples allowed for the tentative assignment of structure to compounds **8, 9b, 10, 11b, 12, 5b, 13,** and **7b** (in order of retention time). The crude reaction mixture was dissolved in ether and washed with a 5% sodium bicarbonate solution, which removed compounds **12** and **13** (thought to have arisen from carboxylic acid derivatives). The ether solution was reconcentrated and the residue was fractionally distilled through a short-path distillation head. The following fractions were collected: (1) 48–60 °C (0.01 mm); (2) 50–126 °C (0.01 mm); (3) 126–163 °C (0.05 mm); (4) 164–165 °C (0.05 mm); (5) 165 °C (0.05 mm).

Fraction 1 contained compounds **8** and **9b.** Washing an ethereal solution of this mixture with a 10% sodium hydroxide solution removed compound **8.** A ^{1}H NMR of this mixture showed two singlets of almost equal height at 1.6 and 1.65 ppm for the methyl groups of **8** and **9b.** Fraction 2 contained mostly compound **11b** as well as some **8.** Infrared and ^{1}H NMR analysis of this fraction were very similar to the spectra of an authentic sample of **11b** (see below). Fraction 3 was very minor. Fraction 4 contained a trace of compound **5b** ($-NO_2$ band at 1530 cm^{-1} in infrared) and compound **7b.** Fraction 5 contained only compound **7b** as evidenced by its ^{13}C and ^{1}H NMR. The infrared showed a strong carbonyl band at 1720 cm^{-1} and the complete absence of a band at 1530 cm^{-1} for the $-NO_2$ group.

A sample of the original brown oil was analyzed by GC/mass spectroscopy on a Varian MAT-111 equipped with a 10 ft by 2 mm column packed with 3% OV-17 on 100/120 Gas Chrom Q. The compounds were identified in order of elution. The *m/e* values for the parent and base ions as well as for other key ions are as follows: compound, *m/e* (% of base): **9b,** 136 (58), 108 (100), 107 (88); **8,** 108 (85), 107 (100); **11b,** 167 (30), 150 (100); **16,** 266 (4), 221 (40), 193 (29), 44 (100); **5b,** 222 (12), 194 (100); **13,** 254 (100), 181 (63); **7b,** 328 (43), 237 (100), 165 (55).

Reaction of Dimethyl 3-Nitrophthalate (5a) with 3. The reaction of **5a** with **3** was run as described for **5b** to given an oil. Analysis by VPC showed the presence of seven peaks (**7a** and **13** were one peak) and by co-enrichment with authentic samples the structures for the compounds **8, 10, 9a, 11a, 12, 5a, 13,** and **7a** were assigned. The following compounds were identified in order of elution by GC/mass spectroscopy. The *m/e* values for the parent and base ions as well as for other key ions are as follows: compound, *m/e* (% of base): **8,** 108 (42), 107 (65), 28 (100); **9,** 122 (100), 121 (53), 107 (36), 77 (39); **11a,** 181 (17), 150 (100), 104 (3); dimethyl 3-methoxyphthalate (**16a**), 224 (7), 193 (100); **5a,** 208 (100); 104 (35); one peak **13,** 254 (20), 237 (100), 209 (31); **7a,** 300 (51).

Reaction of Diisopropyl 3-Nitrophthalate (5c) with 3. The reaction of **5c** with **3** was run as described for **5b** to give an oil. The structures of the products in this oil were identified by co-enrichment with authentic samples. In addition, the structures of **9c** [*m/e* 150, 108 (– propylene)], **5c,** and **7c** were verified by GC/mass spectroscopic analysis of the reaction mixture.

Reaction of Diisobutyl 3-Nitrophthalate (5d) with 3. A mixture of 3.17 g (0.0244 mol, *0.0043 mol excess*) of **3,** 6.50 g (0.0201 mol) of **5d,** and 40 mL of DMF was stirred under nitrogen at 150 °C for 3 h. The reaction mixture was worked up as described for **5b** to give 7.86 g of oily residue. A 0.50-g sample of this residue was analyzed by ^{13}C NMR spectroscopy (Me_2SO-d_6) and found to contain **7d** (approximately 70 mol %), 2-nitro-4-methylphenol (**10**) (approximately 25 mol %), and **5d** and/or acid esters corresponding to **5d** (**14d,** approximately 5 mol%).

The remainder (7.36 g) of the crude product was redissolved in 650 mL of ether and extracted with 5% NaOH (which removed most of the color from the organic layer), water, and saturated NaCl, and then dried ($MgSO_4$). Solvent evaporation now gave 5.41 g of an orange oil which by VPC and ^{13}C NMR (Me_2SO-d_6) was virtually pure **7d.**

The remaining 4.91 g of crude product was distilled under vacuum. Fraction 1: bp 182–186 °C (0.20 mm); 0.77 g; VPC and ^{13}C NMR (Me_2SO-d_6) analysis indicated this was approximately 90% **7d** and approximately 10% **5d.** Fraction 2: bp 187–190 °C (0.20 mm); 3.72 g; VPC indicated this was >99% **7d;** the mass spectrum showed a molecular ion at 384 (calcd 384). The overall yield of **7d** (fraction 2 + 90% of fraction 1 + 2 × 0.50 g ^{13}C NMR samples) was approximately 70%. This latter fraction also gave correct elemental analyses.

Anal. Calcd for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 71.5; H, 7.4.

Identification of Isobutyl 4-Methylphenyl Ether (9d). A mixture of 0.47 g of **3**, 1.17 g of **5d**, and 12.0 mL of anhydrous DMF was stirred at 150 °C for 3.5 h under a nitrogen atmosphere. The mixture was cooled to room temperature and added to neutral water in an attempt to prevent the formation of **10**. The mixture was extracted thoroughly with methylene chloride and the methylene chloride extracts were washed extremely thoroughly with a 5% sodium hydroxide solution. The methylene chloride phase was dried and subjected to GC/mass spectroscopic analysis, which showed the presence of the ether **9d** [*m/e* 164, 108 (− isobutylene)]. This spectrum was identical with the spectrum of a sample of **9d** which was prepared from the reaction of **3** with isobutyl bromide. The structure of the sample from bromo displacement was also verified by its ^{1}H NMR ($CHCl_3$): δ 1.0 (ether aliphatic methyls, doublet, $J \simeq 6$ Hz, 6); 1.6–2.3 (ether methine, m, 1); 2.25 (aromatic methyl, s, 3); 3.63 (ether methylene, d, $J \simeq 6$ Hz, 2); 6.90 (aromatic, center of A_2B_2, 4).

Determination of the Extractability by Sodium Bicarbonate of 12 and 13 from Diethyl Ether. A mixture of 0.0953 g of **12**, 0.1255 g of **13**, 0.0380 g of biphenyl, and 15 mL of anhydrous diethyl ether was subjected to VPC analysis. The ethereal solution was washed with 2 × 15 mL of 5% aqueous sodium bicarbonate solution and dried over anhydrous magnesium sulfate. The ethereal solution was again subjected to VPC analysis, which showed none of **12**, but did show the presence of ca. 65% of the initial amount of **13**. This extractive procedure was repeated using the corresponding phthalic acid derivatives. After washing with 5% sodium bicarbonate, there was no trace of either of the diacids in the ether. Since extraction of the crude reaction product from **5b** + **3** with bicarbonate removed all traces of **13**, it is likely that **13** is arising from ring closure during VPC analysis of **14b** or **15** (X = 4-$CH_3C_6H_4O$).

Determination of the Importance of pH on the Formation of 2-Nitro-4-methylphenol (10) During Work-up of Mixtures Containing 4-Methylphenol (8) and Sodium Nitrite. A mixture of 2.30 g of **3**, 2.44 g of sodium nitrite, 4.92 g of diisobutyl phthalate, and 49 mL of anhydrous DMF was stirred under nitrogen at 140 °C. After 5 h, the mixture was cooled to room temperature and divided into three equal portions, which were worked up as follows: (1) The mixture was added to 150 mL of neutral water and the aqueous mixture was extracted thoroughly with ether. The ether extracts were washed with 1.2 N HCl and a saturated NaCl solution. After being dried over anhydrous $MgSO_4$, the ethereal solution was concentrated and the residue was analyzed by ^{13}C NMR, which showed only **8** and the starting diester. (2) The mixture was added to 150 mL of a 1% acetic acid solution. This solution was worked up as described above. Analysis by ^{13}C NMR showed 83% of **8** and 17% of **10**. (3) The mixture was added initially to 1.2 N HCl and worked up as described above. Analysis by ^{13}C NMR showed 3% of **8** and 97% of **10**.

Reactions of Dialkyl Esters with Sodium Nitrite. Dimethyl Phthalate and Sodium Nitrite. A mixture of 2.5210 g of dimethyl phthalate, 1.7916 g of sodium nitrite (2 equiv), and 2.0019 g of biphenyl (internal standard) was stirred in 25 mL of DMF in a 150 °C oil bath under nitrogen. Aliquots were removed at timed intervals and worked up by adding them to a 1.2 N HCl solution and extracting the mixture with methylene chloride. The resulting organic solution was subjected to VPC analysis. The results are tabulated in Table III.

The reaction was repeated except that no internal standard was used. The reaction mixture was heated for 5 h at 150 °C, cooled to room temperature, and filtered. The precipitate was washed with fresh DMF and thoroughly dried to give >80% (some DMF present) of disodium phthalate; no methyl ester protons were detected by ^{1}H NMR.

Competition Reaction between Diisobutyl 3- and 4-Nitrophthalate. A mixture of 1.8423 g of **4d** (0.0057 mol), 1.8423 g of **5d** (0.0057 mol), and 0.6555 g of *o*-terphenyl was stirred at room temperature with 24 mL of anhydrous DMF under nitrogen. A small aliquot was removed at zero time and added to 1.2 N HCl and extracted with methylene chloride. VPC analysis of this material showed that the two starting esters did not separate. To this mixture was added 0.7407 g (0.0057 mol) of sodium *p*-methylphenoxide (**3**) and the stirred homogeneous mixture was placed in a 100 °C oil bath. Aliquots were removed at 1 and 2 h and worked up as described above. VPC analysis of each point showed that only **6d** was formed. The mixtures were subsequently enriched with **7d** and reexamined by VPC to ensure that none of it was present.

Based on the result, it can be estimated that under these reaction conditions, the difference in rate between these two isomers toward reaction with **3** is *at least* two orders of magnitude. The calculation employed follows (where A = **4d** and B = **5d**):

$$\frac{k_A}{k_B} = \frac{\log A_0 - \log (A_0 - x)}{\log B_0 - \log (B_0 - x)}$$

where A_0 = initial concentration of A (4 isomer) = 1, B_0 = initial concentration of B (3 isomer) = 1, $(A_0 - x)$ = amount of A (4 isomer) unreacted = 1% = 0.01, and $(B_0 - x)$ = amount of B (3 isomer) unreacted = 99% = 0.99.

$$\frac{k_A}{k_B} = \frac{0 - \log(0.01)}{0 - \log(0.99)} = \frac{-(-2.00)}{-(-0.004)} \simeq \frac{2.00}{0.004} = 500$$

Preparation of Authentic Samples. 3-(4-Methylphenoxy)phthalic Anhydride (13). A sample of 3-(4-methylphenoxy)-*N*-phenylphthalimide was prepared from 3-nitro-*N*-phenylphthalimide and **3**.[1] A mixture of 200 mL of ethylene glycol, 40 mL of 25% aqueous NaOH, and 19.74 g of 3-(4-methylphenoxy)*N*-phenylphthalimide was heated at reflux (135 °C in solution) for 18 h and then added to 2000 mL of 1 N HCl with stirring and cooling. The precipitated solid was filtered, washed with 0.1 N HCl, then with water, and dried in vacuo at 60 °C. The yield of 3-(4-methylphenoxy)phthalic acid was 15.61 g (96%): ^{1}H NMR (Me_2SO-d_6) δ 2.30 (methyl, s, 3), 6.7–7.7 (aryl, m, 7), 9.2 (–COOH, br s, 2); IR (KBr) C=O 1688, (s) 1708 (s), OH 2900 cm^- (br); ^{13}C NMR will appear in a subsequent publication.[6] A mixture of 54.4 g of this diacid, 300 mL of acetic acid, and 40.8 g of acetic anhydride was heated at reflux for 2 h and then all solvent was removed in vacuo. The residue, after being recrystallized from cyclohexane, gave 39.6 g (78%) of **13**: mp 117–118 °C; ^{1}H NMR ($CDCl_3$) δ 2.33 (methyl, s, 3), 6.7–7.7 (aryl, m, 7); IR (KBr) C=O 1782 (vs), 1840 cm^{-1} (s); ^{13}C NMR was in accord with the assigned structure;[6] UV (Et_2O) λ_{max} 229 (ε 20 800), 333 mμ (ε 5200), $\lambda_{shoulder}$ 324 mμ (ε 4900).

Anal. Calcd for $C_{15}H_{10}O_4$: C, 70.9; H, 3.9; mol wt 254. Found: C, 70.8; H, 4.1; mol wt 254 (mass spectrum).

Dimethyl 3-(4-Methylphenoxy)phthalate (7a). A mixture of 1.00 g of 3-(4-methylphenoxy)phthalic acid, 1.02 g of potassium carbonate, 0.93 g of dimethyl sulfate, 1 mL of 10% methanolic potassium hydroxide, and 20 mL of acetone was heated at reflux under a nitrogen atmosphere for 6 h. The mixture was cooled to 25 °C and the salts were removed by filtration. These salts were washed thoroughly with acetone and the combined acetone filtrates were added to water and extracted well with chloroform. The chloroform extracts were washed with 5% sodium bicarbonate and water and dried over anhydrous magnesium carbonate. The solution was concentrated to give 0.75 g (68% yield) of **7a** as an oil. The structure of the compound was established by its ^{1}H and ^{13}C NMR spectra: ^{1}H NMR ($CDCl_3$) δ 2.15 (s, 3), 3.83 (s, 6), 7.25 (m, 7); see supplementary material (Table V) for ^{13}C NMR data.

Anal. Calcd for $C_{17}H_{16}O_5$: C, 68.0; H, 5.4; mol wt 300. Found: C, 68.3; H, 5.5; mol wt 300 (mass spectrum).

Diethyl 3-(4-Methylphenoxy)phthalate (7b). A solution containing 11.0 g (0.043 mol) of 3-(4-methylphenoxy)phthalic anhydride (**13**), 20 mL (15.8 g, 0.34 mole) of ethanol, and 1.0 g of *p*-toluenesulfonic acid hydrate in 180 mL of xylene was treated as has been described for the esterification of the nitro anhydrides. In this manner, the product **7b** was obtained as an oil, 13.98 g (99%); ^{1}H NMR ($CDCl_3$) δ 1.26 and 1.33 (ester methyls, both triplets, $J \simeq 7$ Hz, 6), 2.30 (aromatic methyl, s, 3), 4.33 (ester methylenes, q, $J \simeq 7$ Hz, 4), 6.70–7.80 (aromatic, m, 7); see supplementary material (Table V) for ^{13}C NMR data.

Anal. Calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14; mol wt 328. Found: C, 69.5; H, 6.4; mol wt 328 (mass spectrum).

The following ester was prepared by a method analogous to the preparation of **7b** above.

Diisopropyl 3-(4-Methylphenoxy)phthalate (7c). ^{1}H NMR ($CDCl_3$) δ 1.31 and 1.37 (ester methyls, doublets $J \simeq 6$ Hz, 12), 2.30 (aromatic methyl, s, 3), 5.23 and 5.28 (ester methines, septets, $J \simeq$ Hz, 2), 6.74–7.80 (aromatic, m, 7); ^{13}C NMR, see supplementary material (Table V).

Anal. Calcd for $C_{21}H_{24}O_5$: C, 70.77; H, 6.79; mol wt 356. Found: C, 70.5; H, 7.0; mol wt 356 (mass spectrum).

Preparation of Alkyl m-Nitrobenzoates (11). A mixture of *m*-nitrobenzoyl chloride, the anhydrous alcohol of choice, and dried pyridine was stirred under nitrogen for 16 h. The cooled mixture was added to 1.2 N hydrochloric acid and the solid was collected and dried. The ^{13}C NMR data for the compound are in the supplementary material.

11a: 86% yield; mp 78–80 °C (lit. 78 °C);[13] ^{1}H NMR ($CDCl_3$) δ 4.05 (methyl, s, 3); by using *o*-nitrobenzoyl chloride, a sample of methyl *o*-nitrobenzoate was prepared and shown to separate from the meta isomer by VPC analysis.

11b: 66% yield, mp 40–41 °C (lit. 41 °C);[13] IR ($CHCl_3$) carbonyl at 1715, nitro bands 1525 and 1350 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.43 (methyl, t, 3), 4.22 (methylene, q, 2).

11c: 60% yield, oil; ^{1}H NMR ($CDCl_3$) δ 1.40 (methyl, d, 6), 5.25

(methine, septet, 1), 7.60 (aromatics, t, 1), 8.33 (aromatic, m, 2), 8.75 (aromatic, m, 1).

Preparation of Alkyl 4-Methylphenyl Ethers (9). A mixture of the appropriate alkyl iodide, **3**, and THF was refluxed under nitrogen fro 16 h. The mixture was then cooled, filtered, and added to water. The aqueous solution was extracted with ether and the ether extracts were washed and dried to give the crude product. ^{13}C NMR data for the compounds are in the Supplementary Material.

9b: 81% yield; bp 140 °C (15 Torr); ^1H NMR ($CDCl_3$) δ 1.35 (t, 3), 2.13 (s, 3), 3.95 (q, 2), and an A_2B_2 aryl region centered at 6.90 (m, 4).

9c: 76% yield; ^1H NMR ($CDCl_3$) δ 1.30 (d, 6), 2.25 (s, 3), 4.45 (septet, 1), 6.90 (center of A_2B_2 aromatic, 4).

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Registry No.—**3**, 1121-70-6; **6a**, 63181-68-0; **6b**, 63181-69-1; **6c**, 63181-70-4; **6d**, 63181-71-5; **7a**, 63181-72-6; **7b**, 63215-75-8; **7c**, 63181-73-7; **7d**, 63181-74-8; **8**, 106-44-5; **9b**, 622-60-6; **9c**, 22921-10-4; **9d**, 33426-69-6; **10**, 119-33-5; **11a**, 618-95-1; **11b**, 618-98-4; **11c**, 6268-23-1; **13**, 63181-77-1; **14d**, 63181-78-2; **16a**, 32136-52-0; sodium nitrite, 7632-00-0; 3-nitrophthalic anhydride, 641-70-3; 4-nitrophthalic anhydride, 5466-84-2; 3-(4-methylphenoxy)-*N*-phenylphthalimide, 63181-79-3; 3-(4-methylphenoxy)phthalic acid, 63181-80-6.

Supplementary Material Available: A discussion of the ^1H and ^{13}C NMR data as well as the ^{13}C NMR assignments for 4–11 and **14d** (Tables IV–VI) (9 pages). Ordering information is given on any current masthead page.

References and Notes

(1) F. J. Williams and P. E. Donahue, *J. Org. Chem.*, this issue, companion paper.
(2) Related preliminary work was carried out in our laboratories: see D. R. Heath and J. G. Wirth, U.S. Patent 3 787 475 (1974).
(3) See J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, **49**, 273, 312 (1951), and references cited therein.
(4) D. R. Heath and J. G. Wirth, U.S. Patent 3 763 210 (1973).
(5) J. R. Beck, *J. Org. Chem.*, **38**, 4086 (1973); N. Kornblum et al., *ibid.*, **41**, 1560 (1976).
(6) F. J. Williams, H. M. Relles, P. E. Donahue, and J. S. Manello; *J. Org. Chem.*, this issue, companion paper.
(7) J. F. Bunnett, M. M. Robinson, and F. C. Pennington, *J. Am. Chem. Soc.*, **72**, 2378 (1950).
(8) For a discussion of the $B_{AL}2$ mechanism for ester hydrolysis, see E. S. Gould, "Mechanism and Structure in Organic Chemistry", Holt, Rinehart, and Winston, New York, N.Y., 1959, p 342.
(9) See, for example, R. A. Sneen and A. M. Rosenberg, *J. Org. Chem.*, **26**, 2099 (1961); E. W. Wadsworth and T. I. Crowell, *Tetrahedron Lett.*, **13**, 1085 (1970); E. W. Thomas and T. I. Crowell, *J. Org. Chem.*, **37**, 744 (1972); E. E. Smissman, M. D. Corbeth, S. El-Antably, and K. C. Kroboth, *ibid.*, **37**, 3944 (1972), and references contained therein. For a discussion of the reaction of sodium phenoxide with methyl trichloroacetate to give anisole, see A. C. Pierce and M. M. Joullie, *ibid.*, **27**, 3968 (1962).
(10) We have found that ether formation also takes place in the reaction of sodium phenoxide with diethyl phthalate and ethyl *m*-nitrobenzoate. These and other studies of this type of reaction will be presented in a separate communication.
(11) L. J. Bellamy, "The Infrared Spectra of Complex Molecules", Wiley, London, 1962, p 179.
(12) D. Twiss and R. V. Heinzelmann, *J. Org. Chem.*, **15**, 496 (1950).
(13) "Dictionary of Organic Compounds", 4th ed, Oxford University Press, New York, N.Y., 1965.
(14) E. V. Kuynetsov and A. P. Bogdanov, *T. Kazan. Khim-Tekhnol. Inst.*, **No. 26**, 78 (1959).
(15) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", Pergamon Press, New York, N.Y., 1959, p 85.
(16) (a) G. L. Nelson, G. C. Levy, and J. D. Cargioli, *J. Am. Chem. Soc.*, **94**, 3089 (1972); (b) K. N. Scott, *ibid.*, **94**, 8564 (1972).

A Direct Synthesis of Phenoxy-Substituted Phthalic Anhydrides by Aromatic Nucleophilic Displacement

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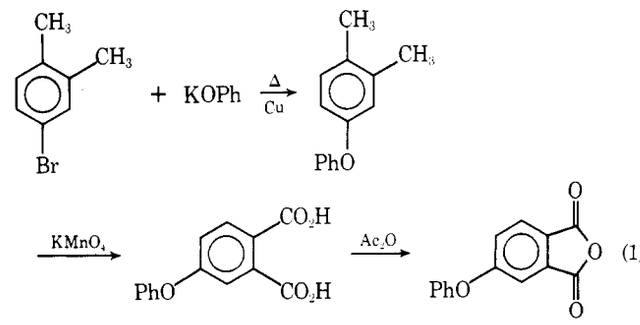
Phenoxides react with nitro-, fluoro-, or chloro-substituted phthalic anhydrides to give phenoxy-substituted phthalic anhydrides. The success of the reaction was dependent upon the reaction conditions employed and the identity of the leaving group (F > Cl > NO_2). All three systems suffered from the reaction of the anhydride linkage with solvent (DMF) at higher temperature, and the nitro system was further complicated by reaction of the anhydride linkage with the sodium nitrite by-product. Using the fluoro system, yields of >85% were obtained for the phenoxyphthalic anhydrides.

As part of our continuing effort to understand the reaction of phenoxides with derivatives of nitro-substituted phthalic acids, we investigated the activating effect of the anhydride linkage in phthalic anhydrides. Previous results have shown that phenoxides react with nitro- and halo-substituted phthalimides,[1] nitro-substituted phthalonitriles,[2] and nitro-substituted phthalate esters.[3] The successful reaction of phenoxides with anhydride derivatives would give phenoxy-substituted phthalic anhydrides and would constitute a considerable improvement over existing syntheses (see eq 1 for an example[4]).



(1)

Results and Discussion

Reaction of Nitrophthalic Anhydrides. Reaction of 3-nitrophthalic anhydride (**1a**) with sodium phenoxide (Scheme I; X = NO_2, Y = H) in DMF at 25 °C produced a mixture of ring-opened acid ester salts **4** and **5** and *no* product (**2**) from nitro displacement. If, after 0.5 h at 25 °C, an equivalent amount of methyl iodide was added to the reaction mixture, the only products formed were the diesters **6** (21%) and **7** (79%) in excellent yield.[5] There was no trace of starting anhydride **1a** or displacement product **2a**. Therefore, in DMF at 25 °C, sodium phenoxide exclusively attacked the carbonyl carbons and, preferentially, the carbonyl α to the nitro group. In addition, because of the total absence of starting material, one can conclude that *if* there was an equilibrium between **1a/3** and **4/5** at room temperature, it was far to the right in favor of **4** and **5**.