

Retentive Solvolysis. Part X.¹ Retentive Solvolysis of Optically Active *para*-Substituted 1-Phenylethyl *p*-Nitrobenzoates in Phenolic Solvents: Rate, Steric Course, Product Distribution, and Mechanism

By Kunio Okamoto,* Tomomi Kinoshita, Yoichi Takemura, and Haruyuki Yoneda, Department of Hydrocarbon Chemistry, Faculty of Engineering, Kyoto University, Sakyo-ku, Kyoto 606, Japan

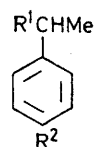
The title compounds (Ia)—(IIIa) were subjected to solvolysis in the presence of sodium phenoxide in pure phenol or in phenol–benzene (1 : 1 w/w) as solvent. Both polarimetric and titrimetric rate constants (k_p and k_t) decrease in the order (Ia) > (IIa) > (IIIa); k_p values for (Ia) and (IIa) exceed those for k_t over the whole range of concentration of added sodium phenoxide, whereas k_p and k_t for (IIIa) coincide with each other. The major products, the phenyl ethers (Ib)—(IIIb), show net retention of configuration; the extent of retention was 16.6% for (Ib) in phenol–benzene at 25°, 34.5% for (IIb), and 90.0% for (IIIb) in phenol at 125°, respectively. The *C*-alkylated products, *o*- and *p*-1-phenylethylphenols, are formed to a small extent only and undergo net inversion with predominant racemization in the phenolysis of (IIa). Variations in the yield and in the extent of retention for (Ib)—(IIIb) have been examined for various concentrations of added sodium phenoxide; variations in the optical rotation of recovered substrate and those in the extent of retention of the phenyl ether have also been determined in the course of each phenolysis. On the basis of this evidence, the mechanisms and steric courses of these reactions are discussed. Maximum rotations of the phenyl ethers (Ib)—(IIIb) and 1-arylethanols (Ic)—(IIIc) have been determined by chemical or n.m.r. shift reagent methods; the absolute configurations of (IIIb) and (IIIc) have also been assigned by the use of a chemical method.

SINCE the earlier investigation of phenolysis of *t*-butyl chloride in phenol–nitrobenzene (1 : 1 mol/mol),^{2a} examples of phenol and its mixtures with some co-solvents playing the role of a typical solvent for S_N1 solvolyses have been accumulated, e.g. ready first-order phenolyses of 1-adamantyl compounds,^{2b} phenolyses with inversion of optically active 1-methylheptyl tosylate and 1-ethyl-1,5-dimethylhexyl *p*-nitrobenzoate,^{2c} exclusive *exo*-product formation in the phenolyses of *exo*- and *endo*-norborn-2-yl tosylates,^{2d} and the existence of a stability-selectivity relationship for phenolyses of alkyl chlorides and *p*-nitrobenzoates.^{2e}

However, one characteristic feature that distinguishes phenol from the usual solvolytic solvents has been found in the phenolysis of 1-phenylethyl chloride.³ In this solvent, solvolysis, which otherwise proceeds with net inversion of configuration,⁴ gives rise to the phenyl ether with net retention of configuration.

Regarding the mechanistic interpretation of retentive phenolysis (or solvolysis) of substrates without a group

imposing configurational restrictions, models such as four-centre species,^{3,5} back-side shielding,^{1,4d} and solvent-separated ion-pairs^{6,7} have been suggested as key



- | | | |
|---------------------------|---|-------------------------------------|
| (I) $R^2 = \text{OMe}$ | a; $R^1 = \text{OCOC}_6\text{H}_4\text{NO}_2-p$ | e; $R^1 = \text{OAc}$ |
| (II) $R^2 = \text{H}$ | b; $R^1 = \text{OPh}$ | f; $R^1 = o\text{-HOC}_6\text{H}_4$ |
| (III) $R^2 = \text{NO}_2$ | c; $R^1 = \text{OH}$ | g; $R^1 = p\text{-HOC}_6\text{H}_4$ |
| | d; $R^1 = \text{OCOCF}_3$ | |

intermediates for the product of retention; some generalized solvolysis schemes which take a retentive product into consideration have also been discussed.^{3a,4d,e,6a}

In view of the diversity of suggested mechanisms,^{1,3,4d,e,5} which is partly ascribed to the dearth of examples † of retentive solvolysis of substrates without a group which limits configurational mobility, we have extended our previous work on the 1-phenylethyl system^{1,3,5} to *para*-substituted 1-phenylethyl *p*-nitrobenzoates with a view to obtaining more information

† Goering and his collaborators have found retentive hydrolyses of *p*-chlorodiphenylmethyl,^{8a,b} *p*-methylidiphenylmethyl,^{7b} 1-phenyl-1-methylpropyl,^{7b,8c} and 1-(*p*-methoxyphenyl)ethyl⁷ *p*-nitrobenzoate in aqueous acetone as solvent.

¹ Part IX, K. Okamoto, T. Kinoshita, and Y. Osada, *J.C.S. Perkin II*, 1975, 253.

² (a) H. Shingu and K. Okamoto, *Nippon Kagaku Zasshi*, 1960, **81**, 111 (*Chem. Abs.*, 1962, **36**, 380b); (b) K. Okamoto, K. Matsubara, and T. Kinoshita, *Bull. Chem. Soc. Japan*, 1972, **45**, 1191; (c) K. Okamoto and T. Kinoshita, *ibid.*, p. 2802; (d) K. Okamoto, T. Kinoshita, and Y. Ito, *ibid.*, 1973, **46**, 2905; (e) K. Okamoto and T. Kinoshita, *Chem. Letters*, 1974, 1037.

³ (a) K. Okamoto, K. Takeuchi, and H. Shingu, *Bull. Chem. Soc. Japan*, 1962, **35**, 525; (b) K. Okamoto, H. Yamada, I. Nitta, and H. Shingu, *ibid.*, 1966, **39**, 299; (c) K. Okamoto, T. Kinoshita, and H. Shingu, *ibid.*, 1970, **43**, 1545; (d) K. Okamoto, T. Kinoshita, and O. Makino, *ibid.*, 1974, **47**, 1770.

⁴ (a) E. D. Hughes, C. K. Ingold, and A. D. Scott, *J. Chem. Soc.*, 1937, 1201; (b) J. Steigman and L. P. Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 2536; (c) K. Okamoto, N. Uchida, S. Saito, and H. Shingu, *Bull. Chem. Soc. Japan*, 1966, **39**, 307; (d) P. B. D. de la Mare, D. M. Hall, and E. Mauger, *Rec. Trav. chim.*, 1968, **87**, 1394; (e) V. J. Shiner, jun., S. R. Hartshorn, and P. C. Vogel, *J. Org. Chem.*, 1973, **38**, 3604.

⁵ (a) K. Okamoto, M. Hayashi, and H. Shingu, *Bull. Chem. Soc. Japan*, 1966, **39**, 408; (b) K. Okamoto, K. Komatsu, and H. Shingu, *ibid.*, p. 2785; (c) K. Okamoto, M. Hayashi, K. Komatsu, and H. Shingu, *ibid.*, 1967, **40**, 624; (d) K. Okamoto, K. Komatsu, and H. Shingu, *ibid.*, p. 1677.

⁶ (a) D. J. Raber, J. M. Harris, R. E. Hall, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 1971, **93**, 4821; (b) J. M. Harris, J. F. Fagan, F. A. Walden, and D. C. Clark, *Tetrahedron Letters*, 1972, 3023; (c) J. M. Harris, A. Becker, J. F. Fagan, and F. A. Walden, *J. Amer. Chem. Soc.*, 1974, **96**, 4484.

⁷ (a) H. L. Goering, R. G. Briody, and G. Sandrock, *J. Amer. Chem. Soc.*, 1970, **92**, 7401; (b) H. L. Goering and H. Hopf, *ibid.*, 1971, **93**, 1224.

⁸ (a) H. L. Goering, R. G. Briody, and J. F. Levy, *J. Amer. Chem. Soc.*, 1963, **85**, 3059; (b) H. L. Goering and J. F. Levy, *ibid.*, 1964, **86**, 120; (c) H. L. Goering and S. Chang, *Tetrahedron Letters*, 1965, 3607.

which might shed light on the details of the retentive mechanism.⁹

RESULTS

Rates of Phenolysis of *para*-Substituted 1-Phenylethyl *p*-Nitrobenzoates.—Titrimetric and polarimetric measurements of the phenolysis rate were carried out in phenol–benzene

in kinetic measurements, were isolated by preparative t.l.c. The yields of *para*-substituted styrenes were independently determined by g.l.c. after removing phenol by extraction from the reaction mixture. The yields of the products, *i.e.*, phenyl ether, *ortho*- and *para*-alkylated phenols, and styrene, are given in Table 2 for runs with various concentrations of added sodium phenoxide. The results reveal

TABLE 1
Phenolysis rates of *para*-substituted 1-phenylethyl *p*-nitrobenzoates

| Compound (Ia) | Solvent Phenol–benzene (1 : 1 w/w) | <i>T</i> /°C | [RX]/M | [NaOPh]/N | <i>k_t</i> /s ^{−1} ^a | <i>k_p</i> /s ^{−1} ^a | Relative rate (125°) |
|------------------|--|--------------|--------|-----------|--|--|-------------------------|
| (Ia) | | 25.0 | 0.0998 | 0.0000 | 5.99 × 10 ^{−5} | | |
| | | | 0.0997 | 0.0000 | | 1.14 × 10 ^{−4} | |
| | | | 0.0505 | 0.0510 | 9.58 × 10 ^{−5} | | |
| | | | 0.0501 | 0.0508 | | 1.27 × 10 ^{−4} | |
| | | | 0.0979 | 0.1010 | 1.01 × 10 ^{−4} | | |
| | | | 0.1002 | 0.1001 | | 1.35 × 10 ^{−4} | |
| | | | 0.0969 | 0.1520 | 1.12 × 10 ^{−4} | | |
| | | | 0.1000 | 0.1560 | | 1.45 × 10 ^{−4} | |
| | | | 0.100 | 0.102 | 1.74 × 10 ^{−4} | | |
| | | | 0.0991 | 0.104 | 4.1 × 10 ^{−2} | | 221 |
| | | | 0.0990 | 0.000 | 1.71 × 10 ^{−4} | | |
| | | | 0.0998 | 0.000 | | 2.23 × 10 ^{−4} | |
| (IIa) | Phenol | 125.0 | 0.0989 | 0.103 | 1.85 × 10 ^{−4} | | 1.00 |
| | | | 0.1001 | 0.105 | | 2.45 × 10 ^{−4} | |
| | | | 0.0999 | 0.210 | 2.05 × 10 ^{−4} | | |
| | | | 0.1002 | 0.311 | 2.24 × 10 ^{−4} | | |
| | | | 0.1000 | 0.311 | | 2.90 × 10 ^{−4} | |
| | | | 0.107 | 0.000 | 6.48 × 10 ^{−6} | | |
| | | | 0.0970 | 0.000 | | (6.77 ± 0.67) × 10 ^{−6} | |
| | | | 0.0974 | 0.102 | 7.95 × 10 ^{−6} | | 0.0429 |
| | | | 0.102 | 0.115 | | (8.35 ± 0.37) × 10 ^{−6} | |
| | | | 0.0980 | 0.224 | 9.65 × 10 ^{−6} | | |
| | | | 0.100 | 0.229 | | (1.03 ± 0.07) × 10 ^{−5} | |
| | | | 0.101 | 0.475 | 1.19 × 10 ^{−5} | | |

^a Accurate to within ±1% for *k_t* and within ±3% for *k_p*, unless otherwise noted.

TABLE 2
Product distributions in the phenolysis of *para*-substituted 1-phenylethyl *p*-nitrobenzoates

| Compound (Ia) | Solvent Phenol–benzene (1 : 1 w/w) | <i>T</i> /°C | [RX]/M | [NaOPh]/N | Yield (%) | | | Styrene |
|------------------|--|--------------|--------|-----------|-----------|-------------------------------|-------------------------------|---------|
| | | | | | Ether | <i>o</i> -Phenol ^a | <i>p</i> -Phenol ^a | |
| (Ia) | | 25.0 | 0.0502 | 0.051 | 64.4 | 3.1 | 1.1 | |
| | | | 0.0983 | 0.108 | 59.8 | 4.2 | 1.9 | 31.0 |
| | | | 0.101 | 0.156 | 54.5 | 4.7 | 2.5 | |
| (IIa) | Phenol | 125.0 | 0.0994 | 0.113 | 63.5 | 8.8 | 7.0 | 20.0 |
| | | | 0.0998 | 0.303 | 62.3 | 9.1 | 7.2 | |
| | | | 0.0971 | 0.101 | 8.8 | 0.4 | 3.2 | 55.0 |
| (IIIa) | Phenol | 125.0 | 0.109 | 0.305 | 8.7 | 0.4 | 3.8 | |

^a *C*-Alkylated products.

(1 : 1 w/w) at 25° and in phenol at 125° for the *p*-methoxy-derivative (Ia) and in phenol at 125° for the unsubstituted and *p*-nitro-compounds (IIa) and (IIIa) by the published method.^{2c,3b} Satisfactory first-order kinetic behaviour, as expected for a typical *S_N1* solvolysis, was observed for each of the three *p*-nitrobenzoates over a wide range of initial concentration of added sodium phenoxide. The results are summarized in Table 1.

The *k_t* values for *para*-substituted 1-phenylethyl *p*-nitrobenzoates decrease in the order (Ia) > (IIa) > (IIIa) (relative rates 221 : 1.00 : 0.0492 in phenol at 125°) and show a deviation from a linear correlation with σ^+ values.^{10,*}

Products of Phenolyses of *para*-Substituted 1-Phenylethyl *p*-Nitrobenzoates.—The product of the phenolyses, which were carried out with optically active substrates for 10 half-lives under conditions identical with those employed

* The Yukawa–Tsuno treatment¹¹ gives a linear plot. Because of the scarcity of data, a comprehensive examination remains to be published.

that the less reactive (IIIa) gives less phenyl ether, although the run for (IIIa) gave a less satisfactory material balance.

Maximum Rotations and Absolute Configurations for Phenyl *para*-Substituted 1-Phenylethyl Ethers.—Since the rotations for the optically pure samples and the absolute configurations were not known previously for the phenyl ethers (Ib) and (IIIb), they were determined, prior to examination of the steric course of phenolyses, from the unequivocal two-step synthesis (1) of the respective ethers. The



maximum rotation of optically pure (Iib) was also re-examined by the use of the same method.

⁹ For leading references see ref. 4d and P. B. D. de la Mare and B. E. Swedlund in 'Chemistry of Carbon-halogen Compounds,' ed. S. Patai, Interscience, London, 1973, vol. 1, ch. 7.

¹⁰ H. C. Brown and Y. Okamoto, *J. Org. Chem.*, 1957, **22**, 485.

¹¹ Y. Yukawa and Y. Tsuno, *Bull. Chem. Soc. Japan*, 1959, **32**, 971.

As summarized in Table 3, the specific rotation ratios ($B:A$) of ROCOCF_3 and ROH and the ratios ($C:B$) of ROPh and ROCOCF_3 are virtually constant for each of the two-step syntheses, in spite of variations in the concentration of added sodium phenoxide. This indicates that the trifluoroacetates (Id)—(IIId), are formed with complete retention of configuration from the respective 1-phenylethanol (Ic)—(IIc), whereas the phenyl ethers, (Ib)—(IIb), are produced with complete inversion. This method for the demonstration of complete inversion under $\text{S}_{\text{N}}2$ conditions was first employed by Hoffmann and Hughes¹² for preparation of optically active methyl 1-phenylethyl

unknown; reported values of maximum rotation for (Ic)¹⁴ and (IIc)¹⁵ have also been re-examined by the application of this method.

When tris-[3-trifluoroacetyl-(+)-camphorato]europium(III)^{13b} was used as an optically active lanthanide shift reagent, enantiomeric shift differences were found for $\alpha\text{-H}$ of (IIc) and in $o\text{-H}$ (IIc), whereas shift differences were not observed for the protons of (Ic). The results are summarized in Table 4.

From the relative peak areas for each enantiomer and the rotations of partially resolved alcohols, the maximum rotations of (IIc) and (IIc) were determined as 45.7 ± 0.5

TABLE 3
Synthesis of optically active *para*-substituted 1-phenylethyl phenyl ethers (ROPh) from the respective 1-phenylethanol (ROH)

| Optical rotation of ROH ($^\circ$) ^a (A) | Optical rotation of ROCOCF_3 ($^\circ$) ^a (B) | (B):(A) | $[\text{ROCOCF}_3]/\text{M}$ | $[\text{NaOPh}]/\text{N}$ | $T/^\circ\text{C}$ | t/h | Optical rotation of ROPh ($^\circ$) ^b (C) | Yield of ROPh (%) ^b | (C):(B) |
|--|--|-------------------|------------------------------|---------------------------|--------------------|--------------|---|--------------------------------|--------------------|
| (Ic) | (Id) | | | | | | (Ib) | | |
| +15.02 | +34.0 | 2.26 ^d | 0.0990 | 0.400 | 25.0 | 48.0 | +4.71 \pm 0.04 | 9.9 | 0.139 ^d |
| (IIc) | (IIId) | | | | | | (IIb) | | |
| +18.60 | +50.4 | 2.71 ^d | 0.101 | 0.207 | 25.0 | 24.0 | +15.10 \pm 0.07 | 45.4 | 0.300 ^d |
| (IIc) | (IIId) | | | | | | (IIb) | | |
| +9.07 ^b | +10.5 | 1.16 ^d | 0.0810 | 0.124 | 125.0 | 24.0 | -8.99 \pm 0.05 | 9.9 | 0.856 ^d |

^a α_{D} (neat, 1 dm). ^b $[\alpha]_{\text{D}}$ (c 1–30, benzene). ^c Based on ROCOCF_3 . ^d The mean values of duplicate or triplicate measurements of (B):(A) were 2.28 for (I), 2.71 for (II), and 1.16 for (III) and those of (C):(B) were 0.139, 0.304, and 0.889, respectively

sulphide from optically active 1-phenylethyl chloride. Accordingly, on the basis of the (averaged) ratios $B:A$ and $C:B$, the rotations for the optically pure phenyl ethers have been calculated from the maximum rotations of ROH (see next section); the results are tabulated in Table 5 along with their absolute configurations.

TABLE 4

Determination of maximum rotations for 1-phenylethanol (IIc) and 1-(*p*-nitrophenyl)ethanol (IIc) by n.m.r. spectroscopy^a with $\text{Eu}(\text{facam})_3$ ^b

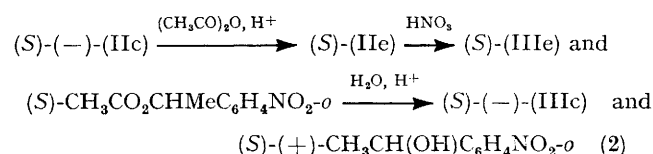
| Compound | Optical rotation ($^\circ$) ^c | Proton | Shifts for enantiomers (p.p.m.) ^d | Peak area ratio | Optical purity (%) | Maximum rotation ($^\circ$) ^e |
|----------|--|-------------------|--|-----------------|--------------------|--|
| (IIc) | -33.8 | $\alpha\text{-H}$ | 1.87; 2.10 | 41.6:6.40 | 73.3 | 46.1 ^{e,f} |
| (IIc) | +9.45 | $o\text{-H}$ | 1.63; 1.57 | 10.4:32.3 | 51.3 | 18.4 ^e |

^a Taken with a 60 MHz n.m.r. instrument. ^b Tris-[3-trifluoroacetyl-(+)-camphorato]europium(III). 0.1–0.2M; shift reagent: ROH molar ratios were in the range 0.5–0.8. ^c For (IIc) α_{L} (neat, 1 dm); for (IIc) $[\alpha]_{\text{L}}$ (c 5–30, benzene). ^d Downfield shift from the original position for *S*- and *R*-enantiomers (see text). ^e The mean values of duplicate measurements were 45.7 for (IIc) and 18.2 for (IIc). ^f Lit.,¹⁵ maximum rotation 44.2°.

Maximum Rotations and the Absolute Configurations of *para*-Substituted 1-Phenylethanol.—In view of recent successes of the n.m.r. shift reagent method for the determination of the maximum rotations of some asymmetric compounds,¹³ this method was applied for 1-(*p*-nitrophenyl)ethanol (IIc) whose maximum rotation was heretofore

and $18.2 \pm 0.2^\circ$, respectively. The former value is slightly greater than that reported, 44.2° ,¹⁵ which was determined by the resolution method.

For the determination of the absolute configuration of (IIc), a three-step synthesis (2) of optically active (IIc)



was carried out according to Ford-Moore and Rydon.¹⁶ Maximum rotations and absolute configurations of the compounds relevant to phenolyses of (Ia)—(IIa) are tabulated in Table 5.

Steric Course for Phenolyses of *para*-Substituted 1-Phenylethyl *p*-Nitrobenzoates.—The net steric course was deduced for the formation of products in phenolysis by comparing the optical purity and absolute configuration for the purified products with those of the substrate; the values for maximum rotations of optically pure compounds in Table 5 were employed. The results are summarized in Table 6.

Phenyl ether formation in the phenolyses of (Ia)—(IIa) proceeds with net retention of configuration. Since the racemization of the phenyl ether (Ib) may increase in phenolysis at higher temperatures, it is shown in Table 6 that the extent of retention increases in the order (Ib) < (IIb) < (IIIb), whereas the phenolysis rates decrease in the sequence (Ia) > (IIa) > (IIIa).

The percentage retention for (IIb) (90.0%) is one of the

¹² H. M. R. Hoffmann and E. D. Hughes, *J. Chem. Soc.*, 1964, 1244.

¹³ (a) M. Kainosho, K. Ajisaka, W. H. Pirkle, and S. D. Beare, *J. Amer. Chem. Soc.*, 1972, **94**, 5924; (b) M. D. McCreary, D. N. Lewis, D. L. Wernick, and G. M. Whitesides, *ibid.*, 1974, **96**, 1038; (c) H. L. Goering, J. N. Eikenberry, G. S. Koerner, and C. J. Lattimer, *ibid.*, p. 1493.

¹⁴ M. P. Balfe, A. Evans, J. Kenyon, and K. Nandi, *J. Chem. Soc.*, 1946, 803.

¹⁵ E. Downer and J. Kenyon, *J. Chem. Soc.*, 1939, 1156.

¹⁶ A. H. Ford-Moore and H. N. Rydon, *J. Chem. Soc.*, 1946, 679.

highest known in phenolysis of a substrate without a group restricting configurational mobility.*

The changes in the extent of retention for phenyl ethers and those in the optical purity of recovered *p*-nitrobenzoates were also examined at 25–75% conversion in the course of phenolysis. As illustrated in Figure 1 and Table 7, they decrease with progress of the phenolysis in

DISCUSSION

Phenolysis of 1-(p-Methoxyphenyl)ethyl p-Nitrobenzoate.—Addition of sodium phenoxide in phenol–benzene (1 : 1 w/w) gives rise to a decrease in the yield and in the extent of retention of 1-(*p*-methoxyphenyl)ethyl phenyl ether (Ib); it also brings about a two-stage rise in k_t

TABLE 5
Maximum rotation ($^\circ$) ^a of *para*-substituted (*R*)-1-phenylethyl (*R*) derivatives

| <i>para</i> -Substituent | ROH | Hydrogen phthalate | ROCOCH ₂ H ₄ NO ₂ ^{<i>p</i>} | ROCOCF ₃ | ROPh | <i>o</i> -RC ₆ H ₄ OH | <i>p</i> -RC ₆ H ₄ OH |
|--------------------------|----------------------|--------------------|--|-------------------------|-------|---|---|
| MeO | +45.2 ^{b,c} | +32.3 ^d | −18.0 | +104 | −14.4 | | |
| H | +45.7 ^b | +15.8 ^d | −39.8 | +123, +128 ^e | −37.4 | +27.85 ^f | −10.26 ^f |
| NO ₂ | +18.2 | +36.4 | −54.4 | +20.5 | +17.7 | | |

^a $[\alpha]_D$ (*c* 1–30, benzene). ^b α_D (neat, 1 dm). ^c For maximum rotation see ref. 14; for absolute configuration see O. Cervinka, *Coll. Czech. Chem. Comm.*, 1965, **30**, 1684. ^d Ref. 15. ^e In CCl₄, *c* 1.49 at 19°; recalculated from the literature ²⁷ value (114.3°). ^f Ref. 3b.

TABLE 6

Net steric course for solvolysis products in the phenolysis of *para*-substituted 1-phenylethyl *p*-nitrobenzoates (RX)

| Compound (Ia) | Solvent Phenol–benzene (1 : 1 w/w) | <i>T</i> /°C 25.0 | [RX]/ <i>M</i> { $[\alpha]_D$ ($^\circ$)} | [NaOPh]/ <i>N</i> | Net steric course, $[\alpha]_D$ ($^\circ$) ^a | | |
|------------------|--|----------------------|--|-------------------|---|-------------------------------|-------------------------------|
| | | | | | Ether | <i>o</i> -Phenol ^b | <i>p</i> -Phenol ^b |
| | | | 0.0502 | 0.0513 | 21.4% ret. (−0.390) | | |
| | | | {−2.28} | | 16.6% ret. (+1.64) | | |
| | | | 0.0983 | 0.1075 | 15.0% ret. (−0.292) | | |
| | | | {+12.31} | | 34.5% ret. (+16.7) | 9.35% inv. (+2.33) | 11.58% inv. (−1.06) |
| | | | 0.101 | 0.156 | 34.3% ret. (+15.9) | 9.78% inv. (+2.48) | 12.1% inv. (−1.12) |
| (IIa) | Phenol | 125.0 | {−2.28} | 0.113 | 90.0% ret. (+9.90) | | |
| | | | 0.0994 | 0.303 | 87.5% ret. (+9.75) | | |
| | | | {+34.5} | | | | |
| | | | 0.0998 | | | | |
| | | | {+34.5} | | | | |
| (IIIa) | Phenol | 125.0 | 0.0971 | 0.101 | | | |
| | | | {−33.8} | | | | |
| | | | 0.305 | 0.305 | | | |
| | | | {−34.2} | | | | |

^a In benzene, *c* 1–30 at 21–33°. ^b C-Alkylated products.

TABLE 7

Changes in extent of retention for phenyl ether (ROPh) and in optical purity of recovered *p*-nitrobenzoate (RX) in the course of the phenolysis

| Compound (Ia) | Solvent Phenol–benzene (1 : 1 w/w) | <i>T</i> /°C 25.0 | <i>t</i> /h 0.4 | [RX]/ <i>M</i> { $[\alpha]_D$ ($^\circ$)} | [NaOPh]/ <i>N</i> | Con- version (%) | RX recovered | | ROPh formed | |
|------------------|--|----------------------|--------------------|--|-------------------|------------------------|------------------------------|-----------------------|------------------------------|-----------------------------|
| | | | | | | | Re- covery (%) | Racemiz- ation (%) | Yield (%) | Net steric course (%) |
| | | | | 0.0996 | 0.102 | 26.0 | { $[\alpha]_D$ ($^\circ$)} | | { $[\alpha]_D$ ($^\circ$)} | |
| | | | 1.4 | {−17.40} | 0.102 | 51.0 | {−10.17} | 34.6 | {−2.78} | 19.9 ret. |
| | | | 24.0 | 0.0996 | 0.108 | 100.0 | 47.3 | 51.8 | 29.1 | 18.5 ret. |
| | | | | {−17.40} | | | {−7.49} | | {−2.58} | |
| | | | | 0.0983 | | | 0.0 | | 59.8 | 16.6 ret. |
| | | | | {+12.31} | | | | | {+1.64} | |
| (IIa) | Phenol | 125.0 | 1.0 | 0.103 | 0.104 | 48.8 | 46.9 | 33.5 | 30.0 | 38.0 ret. |
| | | | 16.0 | {−28.1} | 0.113 | 100.0 | {−18.69} | | {−15.0} | |
| | | | | 0.0994 | | | 0.0 | | 63.5 | 34.5 ret. |
| | | | | {+34.5} | | | | | {+16.7} | |
| (IIIa) | Phenol | 125.0 | 21.0 | 0.0993 | 0.129 | 51.0 | 35.0 | 0.00 | 4.2 | |
| | | | | {−32.4} | | | {−32.8} | | | |
| | | | 42.0 | 0.0993 | 0.129 | 75.0 | 23.2 | 0.00 | 6.5 | 88.2 ret. |
| | | | | {−33.2} | | | {−33.8} | | {+9.53} | |
| | | | 240.0 | 0.0971 | 0.101 | 100.0 | 0.0 | | 8.8 | 90.0 ret. |
| | | | | {−33.8} | | | | | {+9.90} | |

^a In benzene, *c* 1–30 at 25–32°.

the cases of (Ia) and (IIa), whereas they do not vary during phenolysis of (IIIa).

* Solvolyses of 2,2-dimethyl-1-phenylpropyl and 2,2-dimethyl-1-(*p*-nitrophenyl)propyl *p*-nitrobenzoates in phenol as solvent give phenyl ethers with net 91 and 97% retention, respectively, in the presence of triethylamine at 125°.

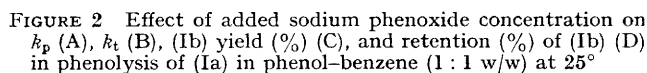
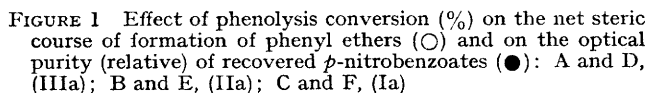
from the value in the absence of added phenoxide (Figure 2). The two-stage process consists of an initial rather steep increase and a subsequent small rise; similar rises in k_t have also been observed in acetolyses of cholesteryl and 2-(2,4-dimethoxyphenyl)ethyl

that the added phenoxide ion attacks, competitively with a phenol molecule, a phenolysis intermediate to give less phenyl ether, and secondly, that a phenol molecule gives the phenyl ether (Ib) with *retention* of configuration, whereas phenoxide ion produces (Ib) with *inversion* of configuration by back-side attack on a chiral intermediate.

In addition, as shown in Figure 1 and Table 7, it was found that the optical purity of recovered *p*-nitrobenzoate (Ia) and the extent of retention of (Ib), decrease with progress of the phenolysis.

Furthermore, the intimate ion-pair can return to the chiral (Ia), and also react with a phenol molecule in the solvation shell to give a second chiral ion-pair intermediate (Int.) with retention of configuration.*

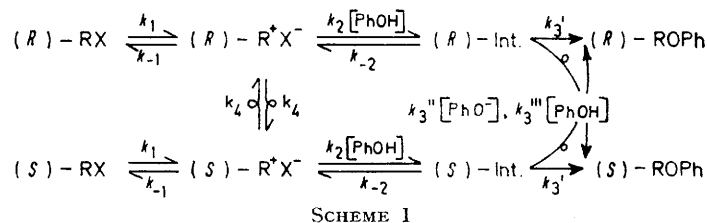
As regards the second ion-pair intermediate (Int.), it is conceivable that it gives rise to a retained phenyl



* This does not mean that there is no chance for the first intermediate to react with phenoxide ion or a phenol molecule to give an inverted phenyl ether. In fact, such a possibility has been proved in the case of phenolysis of the 1-methylheptyl system.^{2c}

$$\begin{aligned} \dagger \quad k_p &= \frac{k_1}{1 + \frac{k_{-1}}{2k_4 + k_2k_3/(k_3 + k_{-2})}} \\ k_t &= \frac{k_1}{1 + \frac{k_{-1}}{k_2k_3/(k_3 + k_{-2})}} \\ k_3 &= k_3' + k_3''[\text{PhO}^-] + k_3'''[\text{PhOH}] \end{aligned}$$

For a more complex scheme for retentive solvolysis see ref. 4d.



ether (Ib), but it can also react with phenoxide ion or a phenol molecule to give an inverted product although this inversion cannot become predominant over the retentive formation of (Ib).

Thus, from these considerations, Scheme 1, similar to those previously proposed,^{3a,4c} can be postulated for phenolysis of (1a). This is, needless to say, the simplest among those which can explain the retentive phenolysis of (1a), but there is no evidence for the existence of dissociation of the second ion-pair intermediate (Int.) into a free carbonium ion.[†] In Scheme 1 [PhOH]

¹⁷ S. Winstein and E. Clippinger, *J. Amer. Chem. Soc.*, 1956, **78**, 2784.

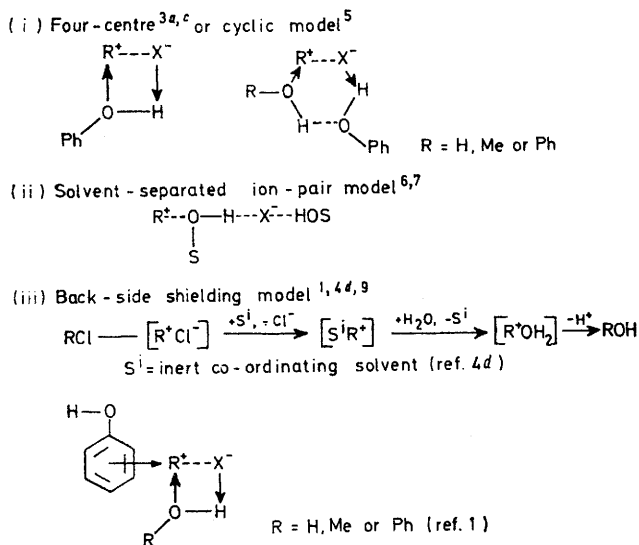
¹⁸ A. H. Fainberg and S. Winstein, *J. Amer. Chem. Soc.*, 1956, **78**, 2780.

¹⁹ S. Winstein and G. C. Robinson, *J. Amer. Chem. Soc.*, 1958, **80**, 169.

²⁰ S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck, and G. C. Robinson, *J. Amer. Chem. Soc.*, 1956, **78**, 328.

signifies a phenol molecule in the solvation shell of R^+X^- .

As for the structure of the second ion-pair intermediate (Int.) which can give rise to a retained phenyl ether, a variety of models (Scheme 2) have been proposed. The results of this study give no novel facts which can discriminate between the four-centre and solvent-separated ion-pairs. However, in view of the characteristic effect of phenol on the steric course,^{1,3c} the four-centre model³ and/or the back-side shielding model¹ seems probable in retentive phenolysis.



Phenolyses of 1-Phenylethyl and 1-(p-Nitrophenyl)ethyl p-Nitrobenzoates.—In phenolyses of the unsubstituted and *p*-nitro-derivatives (IIa) and (IIIa), addition of sodium phenoxide gives rise to no variation in the yield and in the extent of retention for the respective phenyl ethers (IIb) and (IIIb); it brings about only linear rise

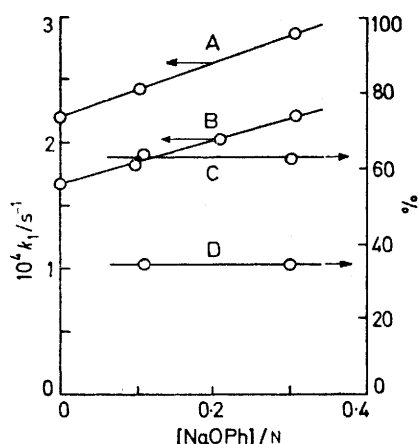


FIGURE 3 Effect of added sodium phenoxide concentration on k_p (A), k_t (B), (IIb) yield (%) (C), and retention (%) (D) in phenolysis of (IIa) in phenol as solvent at 125°

in k_t , probably caused by normal salt effects.¹⁸ These are illustrated in Figures 3 and 4, respectively. These

results clearly indicate that no phenoxide ion, but only a phenol molecule, contributes to the formation of the phenyl ether in these phenolyses.

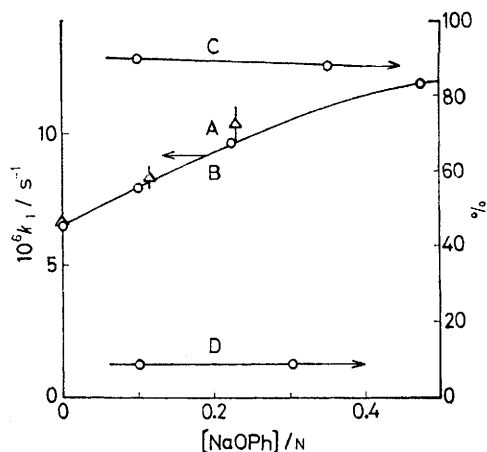
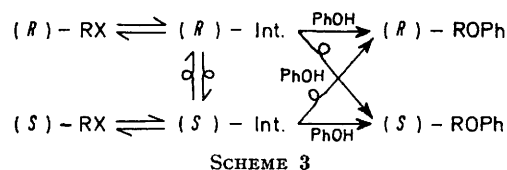
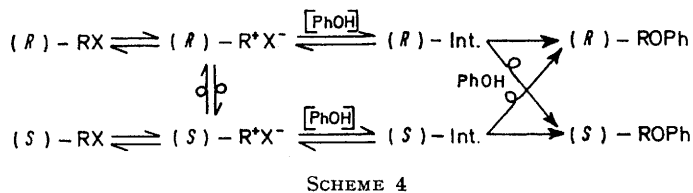


FIGURE 4 Effect of added sodium phenoxide concentration on k_p (A), k_t (B), (IIIb) yield (%) (C), and retention (%) (D) in phenolysis of (IIIa) in phenol as solvent at 125°

In the phenolysis of (IIa), k_p exceeds and increases in parallel with k_t over the whole range of added phenoxide ion concentration (Figure 4); the optical purity of recovered (IIa) and the extent of retention of (IIb) decrease during the course of phenolysis (Figure 1 and Table 7). The results can be explained by a solvolysis scheme involving a single intermediate (Int.) which can racemize and also give rise to a retained phenyl ether (Scheme 3). However, considering that there are two

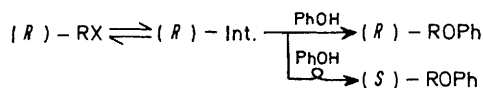


discrete intermediates in the case of (Ia), and that only the second (Int.) can give rise to the retained phenyl ether (Ib), it is conceivable that phenolysis of (IIa) also proceeds along the paths suggested for (Ia). Scheme 4 explains all the results observed in the phenolysis of (IIa).



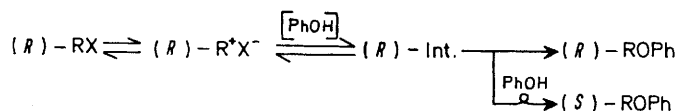
In the phenolysis of (IIIa), k_p coincides with k_t over the whole range of phenoxide ion concentrations (Figure 4); the optical purity of recovered (IIIa) and the extent of retention of (IIIb) show no appreciable change during the course of phenolysis (Figure 1 and Table 7). The results can be interpreted, as in the case of (IIa), by Scheme 5 which involves a single intermediate (Int.), which *cannot* racemize but can give rise

to a retained phenyl ether. However, for the same reason for (IIa), Scheme 6 which involves two intermediates seems more probable, though no firm conclusions are possible.



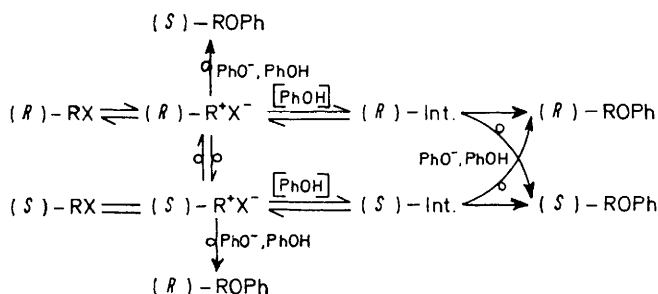
SCHEME 5

Generalized Scheme for Phenolysis.—Since complex generalized schemes, which take the retentive product into consideration, have been proposed by several investigators,^{4d,e,6a,21} it seems pertinent to postulate a generalized scheme for the phenolysis.



SCHEME 6

In the phenolyses of 1-phenylethyl chloride^{3a} and of (Ia), the first ion-pair intermediate does not react with phenoxide ion, whereas 1-methylheptyl and 1-ethyl-1,5-dimethylhexyl systems^{2c} give rise to phenyl ethers with inversion of configuration during phenolysis and the inverted phenyl ethers are directly produced from the first intermediate (the intimate ion-pair). Considering these two cases of reactivity of intimate ion-pair, one can propose the generalized Scheme 7 as one of the



SCHEME 7

simplest among those which explain all the results observed in the phenolyses of 1-phenylethyl, 1-methylheptyl, and 1-ethyl-1,5-dimethylhexyl systems. In Scheme 7, the inversion course for product formation from the first intimate ion-pair is added to Scheme 3 proposed for the phenolysis of (Ia); the second intermediate (Int.) is the key intermediate for the retentive phenolysis. In other words, it is characteristic of Scheme 7 that the retained phenyl ether derives only

from the second intermediate (Int.), and that it has a structure preferably depicted by a four-centre or back-side shielding model.^{1,3a,c}

EXPERIMENTAL

I.r. spectra were taken with a Hitachi model 215 spectrophotometer, n.m.r. spectra with a Hitachi model R24 60 MHz instrument, and g.l.c. was performed with a Hitachi model 023—6003 instrument with an ionization detector. Optical rotations were measured with a JASCO DIP-SL polarimeter. Microanalyses were performed by the Elemental Analysis Centre, Kyoto University.

Materials.—Resolution of 1-phenylethanol (IIc) and 1-(*p*-methoxyphenyl)ethanol (Ic) were performed by the Pope-Peachey method²² and by a modified Kenyon method,¹⁴ respectively. The resolution of 1-(*p*-nitrophenyl)ethanol (IIc) was performed by the use of the brucine salt of the hydrogen phthalate in acetone-chloroform (3:1 v/v) as solvent. The *p*-nitrobenzoates of (Ic),^{7a} (IIc),²³ and (IIc)²⁴ were prepared by reactions of corresponding alcohols with *p*-nitrobenzoyl chloride in pyridine. *p*-Methoxy-²⁵ and *p*-nitro-styrene²⁶ were prepared by known methods. Sodium phenoxide was prepared by refluxing a toluene solution of phenol with sodium metal. Karl Fischer titration indicated the water content of phenol to be <10⁻³M.

Synthesis of para-Substituted 1-Phenylethyl Trifluoroacetates.—According to the method of Bourne *et al.*,²⁷ 1-phenylethyl trifluoroacetate (IIId) was prepared from (IIc) and trifluoroacetic anhydride in pyridine at 0°. The trifluoroacetates (Id) and (IIId) were synthesized just prior to use, owing to their thermal instability to heat,* in a manner similar to (IIId). From (+)-(Ic) {[α]_D^{18.0} +15.02 ± 0.01° (neat, 1 dm)} (+)-(Id) (60.4%), [α]_D^{21.5} +34.5° (c 28.7, benzene), ν_{max.} (CCl₄) 2 980, 1 780, 1 600, 1 510, 1 250, and 1 150 cm⁻¹, δ (CCl₄) 1.45 (d, CH₃), 3.60 (s, CH₃O), 5.83 (q, methine H), and 6.6—7.2 (m, 4 ArH), was obtained. From (+)-(IIc) {[α]_D^{29.8} +11.1° (c 3.85, benzene)} (+)-(IIId) (85.5%), [α]_D^{29.5} +12.5° (c 5.65, benzene), ν_{max.} (CCl₄) 2 980, 1 790, 1 530, 1 350, 1 230, 1 170, and 1 150 cm⁻¹, δ (CCl₄) 1.72 (d, CH₃), 6.05 (q, methine H), and 7.5—8.2 (m, 4 ArH) (Found: C, 45.0; H, 3.98. C₁₀H₁₀F₃NO₄ requires C, 45.3; H, 3.8%), was obtained. From (+)-(Ic) {[α]_D^{26.5} +18.6° (neat 1 dm)} (+)-(Id), b.p. 49—50° at 4.0 mmHg (lit.,²⁷ 74° at 15 mmHg), [α]_D^{28.5} +50.2° (c 7.29, benzene), [α]_D^{29.4} +53.0° (c 2.13, CCl₄), was obtained.

Synthesis of Optically Active 1-(*p*-Methoxyphenyl)ethyl Phenyl Ether.—A solution of (R)-(+)-(Id) (1.70 g), [α]_D^{21.5} +34.0° (c 28.7, benzene), synthesized just prior to use, in anhydrous DMF (68.0 ml) containing sodium phenoxide (0.400M) was prepared under dry nitrogen, and was maintained at 25° for 48 h. After work-up t.l.c. (silica gel) of the residual oil gave (S)-(+)-1-(*p*-methoxyphenyl)ethyl phenyl ether, (S)-(+)-(Ib) (0.124 g, 9.9%), [α]_D^{22.5} +4.71° (c 8.90, benzene); the structure was assigned on the basis of spectral data and elemental composition (Table 8). From the reaction mixture 1-(*p*-methoxyphenyl)ethanol (0.250 g, 20.0%), [α]_D^{24.0} +14.9° (neat, 1 dm), was obtained.

* The trifluoroacetate (Id) was stable for several hours at 0°.

²¹ V. J. Shiner, jun. and R. D. Fisher, *J. Amer. Chem. Soc.*, 1971, **93**, 2553.

²² S. H. Wilen, R. Davidson, R. Spector, and H. Steffanou, *Chem. Comm.*, 1969, 603.

²³ H. L. Goering and J. P. Blanchard, *J. Amer. Chem. Soc.*, 1954, **76**, 5405.

²⁴ R. Fuchs and C. A. Van der Werf, *J. Amer. Chem. Soc.*, 1954, **76**, 1631.

²⁵ M. R. Quelet, *Comp. rend.*, 1936, **202**, 956.

²⁶ A. M. Shuv and N. A. Barba, *Zhur. obskhei Khim.*, 1963, **33**, 1504.

²⁷ E. J. Bourne, M. Stacey, J. C. Tatlow, and R. Worrall, *J. Chem. Soc.*, 1958, 3268.

The results of duplicate runs with variable phenoxide concentrations are summarized in Table 3.

Synthesis of Optically Active 1-(*p*-Nitrophenyl)ethyl Phenyl Ether.—In a manner similar to (Ib), (IIIb) was prepared from (IIId); the results are summarized in Table 3. Spectral data and elemental composition, from which the structure was assigned, are tabulated in Table 8.

Nitration of (S)-(-)-1-Phenylethanol.—Optically active 1-(*p*-nitrophenyl)ethanol (IIIc) was prepared according to the method of Ford-Moore and Rydon.¹⁶ From (IIc) (2.54 g) $[\alpha]_D^{27.0} -39.65^\circ$ (neat, 1 dm)] (IIIc) (1.24 g, 35.7%) (lit.,¹⁶ 23%), b.p. 160–165° at 4 mmHg (lit.,¹⁶ 145–155° at

products were assigned on the basis of spectral data and elemental compositions (Table 8).

Titrimetric Rate Measurements.—The usual aliquot technique^{3a,b} was employed. The diminution of base concentration was followed by titration with standard hydrochloric acid (0.05N), using Bromophenol Blue as indicator. In each case the reaction was followed to at least 70% conversion; smooth first-order linear relationships were obtained.

Polarimetric Rate Measurements.—The previously reported procedure^{2c} was followed. Each reaction mixture (5 ml) was cooled after a specified time, and mixed with

TABLE 8

B.p.s, m.p.s, spectral data, and elemental compositions for the products in phenolyses of (Ia) and (IIIa)

| B.p. (°C) [m.p. (°C)] | (Ib) 150—160 at 3 mmHg | (If) 160—165 at 3 mmHg | (Ig) 170—175 at 4 mmHg | (IIIb) 215—220 at 0.05 mmHg | (IIIf) [108.5—109.2] ^a | (IIIg) [110.1—110.9] ^a |
|---------------------------|--|------------------------------|------------------------------|-----------------------------------|--------------------------------------|--------------------------------------|
| | $\nu_{\max}/\text{cm}^{-1}$ ^b | | | | | |
| $\nu_{\text{C-H}}$ | 2 950 2 900 1 450 | 2 940 2 890 1 450 | 2 940 2 890 1 450 | 2 950 2 880 1 450 | 2 950 2 880 1 450 | 2 960 2 880 1 450 |
| $\nu_{\text{arom. ring}}$ | 1 600 1 500 | 1 600 1 500 | 1 600 1 500 | 1 600 1 500 | 1 600 1 500 | 1 600 1 500 |
| $\nu_{\text{O-H}}$ | | 3 430 | 3 610 3 350 | | 3 620 | 3 600 3 500 |
| $\nu_{\text{C-O-C}}$ | 1 230 1 210 | 1 230 | 1 230 | 1 220 | | |
| $\nu_{\text{C-NO}}$ | | | | 1 520 1 350 | 1 520 1 350 | 1 520 1 350 |
| | τ ^b | | | | | |
| Ring H | 2.71—3.15 (m, 9 H) | 2.70—3.15 (m, 8 H) | 2.65—3.07 (m, 8 H) | 1.80—2.60 (m, 9 H) | 1.85—2.66 (m, 8 H) | 1.80—2.60 (m, 8 H) |
| Methine H | 4.83 (q) | 5.30 (q) | 5.30 (q) | 5.30 (q) | 5.38 (q) | 5.40 (q) |
| CCH_3 | 8.42 (d) | 8.53 (d) | 8.53 (d) | 8.40 (d) | 8.35 (d) | 8.33 (d) |
| OCH_3 | 6.30 (s) | 6.30 (s) | 6.30 (s) | | | |
| OH | | 4.95 (s) | 4.90 (s) | | 5.05 (s) | 5.00 (s) |
| Elemental composition | | | | | | |
| Calc. C (%) | 78.9 | 78.9 | 78.9 | 69.1 | 69.1 | 69.1 |
| Found C (%) | 79.25 | 78.75 | 78.9 | 69.4 | 69.35 | 69.35 |
| Calc. H (%) | 7.05 | 7.05 | 7.05 | 5.4 | 5.4 | 5.4 |
| Found H (%) | 7.2 | 7.2 | 7.25 | 5.55 | 5.6 | 5.45 |

^a Uncorrected; recrystallized from n-hexane. ^b In CCl_4 .

2 mmHg), $[\alpha]_D^{28.2} -6.40 \pm 0.06^\circ$ (*c* 3.42, benzene), and 1-(*o*-nitrophenyl)ethanol (1.469 g, 42.2%) (lit.,¹⁶ 32%), b.p. 140–150° at 4 mmHg (lit.,¹⁶ 125–140° at 2 mmHg), $[\alpha]_D^{26.1} +18.77 \pm 0.02^\circ$ (*c* 8.370, benzene), were obtained.

Isolation of the Phenolysis Products.—As a representative run, isolation of the products in phenolysis of (Ia) is described in the following. A solution (95.0 ml) of (S)-(+)-(Ia) (2.89 g), $[\alpha]_D^{26.2} +12.31^\circ$ (benzene), in phenol-benzene (1 : 1 w/w) containing sodium phenoxide (0.1075N) was kept at $25.0 \pm 0.1^\circ$ for 24 h. After work-up, (S)-(+)-(Ib) (1.495 g, 59.8%), b.p. 150–160° at 3 mmHg, $[\alpha]_D^{28.5} +2.52^\circ$ (*c* 30.0, benzene), *o*-1-(*p*-methoxyphenyl)ethylphenol (0.1085 g, 4.15%), b.p. 160–170° at 4 mmHg, *p*-1-(*p*-methoxyphenyl)ethylphenol (0.0529 g, 1.85%), b.p. 170–180° at 4 mmHg, and *p*-methoxystyrene (0.456 g, 31.0%), b.p. 85–90° at 13 mmHg (lit.,²⁷ 91–94° at 16 mmHg), were obtained. The structures of the C-alkylated

benzene (5 ml). The optical rotation of the mixture was measured immediately at room temperature. The optical rotations at four or more specified reaction times were treated graphically, and a smooth first-order linear relationship was obtained. The rate data are summarized in Table 1, along with the titrimetric data.

N.m.r. Measurements.—The shift reagent, tris-[3-trifluoroacetyl-(+)-camphorato]europium(III), was weighed into a n.m.r. tube and dissolved in CCl_4 (0.3 ml). The substrate was measured into the tube with a syringe, and the tube was capped, and then the solution was mixed by tipping the tube back and forth. After recording a spectrum, more shift reagent was added and the process was repeated. The results of the shift reagent method are summarized in Table 4.

[5/392 Received, 25th February, 1975]