Retentive Solvolysis. Part 12.[1] Mechanism of the Reaction of Optically Active 1-(*p*-Methoxyphenyl)ethyl Trifluoroacetate with Phenol and Methanol in Benzene and Cyclohexane

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The rate, product distribution, and stereochemical course for the reactions of 0.05—0.1 M-1-(*p*-methoxyphenyl)-ethyl trifluoroacetate (1) with methanol and phenol have been investigated in benzene or cyclohexane as solvent at 25.0 °C. Below 10^{-3}M-methanol or -phenol the total kinetic order is two overall [first order in both the trifluoroacetate(1) and the reactant methanol or phenol]. The rates are virtually independent of the pyridine used to bind the trifluoroacetic acid produced. The major product from the phenol reaction, 1-(*p*-methoxyphenyl)ethyl phenyl ether, shows net retention (6—9%) of configuration along with predominant racemization. In addition, the methyl ether product from the methanol reaction also undergoes net retention (24% with 0.2M-methanol). The formation of the ethers with net retention of configuration can be accounted for by an intermolecular S_Ni mechanism.

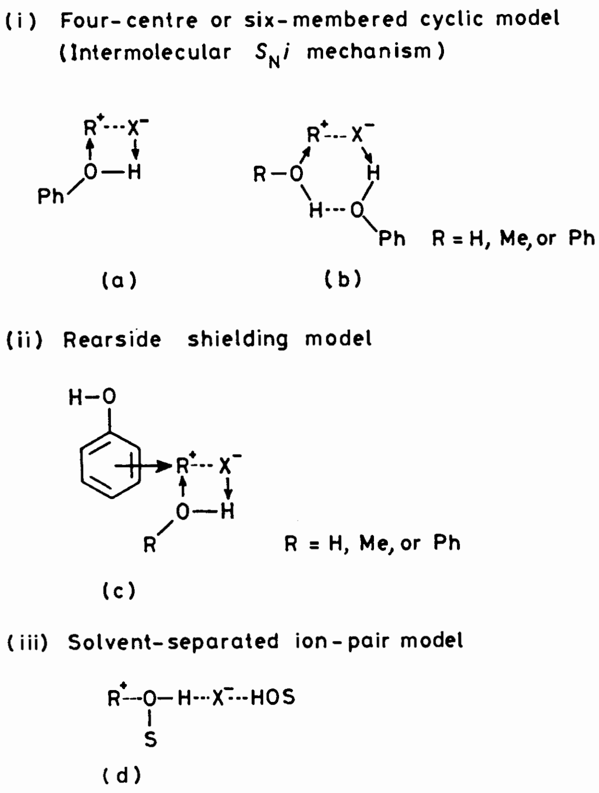
In previous papers we have reported the retentive S_N1 phenolyses of various optically active secondary and tertiary systems without a group which could impose configurational restriction. These systems afford the phenyl ether products with net retention of configuration, and they include 1-phenylethyl,[1-7] 1-phenylpropyl,[1] 2-methyl-1-phenylpropyl,[1] 2,2-dimethyl-1-phenylpropyl; [1] 1-ethyl-1,5-dimethylhexyl chloride[1] and trifluoroacetate[1] and 1-methyl-1-phenylpropyl *p*-nitrobenzoate [1] have also been investigated.

In order to account for the retention of configuration in these phenolyses, we proposed mechanisms involving four-centre and six-membered cyclic models (a) [2,5] and (b) [3,4] (intermolecular S_Ni mechanism),† and a rearside shielding model (c) [6] as key intermediates leading to phenyl ethers of retained configuration. However, it was argued that the intervention of a solvent-separated ion-pair (d) could also explain the formation of the products with retained configuration.[11] This paper describes the significance of the intermolecular S_Ni mechanism, especially the intervention of the four-centre species (a), in retentive solvolysis.

Originally, the four-centre model (a) was proposed to explain the formation of 1-phenylethyl phenyl ether with net retention of configuration in the phenolysis of 1-phenylethyl chloride in the presence of aniline.[2] A six-membered cyclic model (b) was postulated for the competing solvolysis of the same substrate in phenol–water [3] or phenol–methanol [4] mixtures, which yielded 1-phenylethanol or 1-phenylethyl methyl ether with net (6—19%) retention of configuration. In the absence of phenol both hydrolysis and methanolysis proceed with net inversion of configuration.

Another role of phenol in the retentive solvolysis, the rearside shielding model (c), was suggested from the fact that for 2,6-dialkylphenols,[6] which are supposed not to take part in the intermolecular S_Ni mechanism for steric reasons, optically active 1-phenylethyl chloride gives rise to the substitution products with retention of configuration. The rearside shielding mechanism has also been proposed for retentive substitutions with water [12] or some carboxylic acids [13] in nitriles as solvent. These phenols and nitriles were presumed to shield the rearside of the substrate by the co-ordination due to π-electrons.‡

In addition to the above mentioned mechanisms, the intervention of the solvent-separated ion-pair model (d) was suggested by Schleyer and his co-workers to explain our previous results.[11] Similarly, Goering and Hopf explained their results for the retentive hydrolyses of



Scheme

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† The intermolecular S_Ni mechanism was first proposed by Ingold and his collaborators [8] for the retentive substitution of 1-phenylethanol by hydrogen bromide.[9,10]

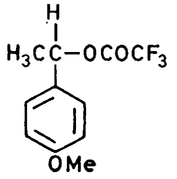
‡ The rearside shielding model appears to have been accepted.[14,15] A similar model, π-complexing of an ion-pair, has recently been proposed by Colter and Dack in interpreting their results for the phenolysis of 1-phenyl-1-methylethyl and fluorenyl chlorides.[16]

various optically active *p*-nitrobenzoates by assuming the existence of a solvent-separated ion-pair species.[17–19]

Thus, although there is supporting evidence for the rearside shielding model (or a double inversion model [15c]), it has been difficult to distinguish between the four-centre model (intermolecular $S_{N}i$ mechanism) and the intervention of a solvent-separated ion-pair because of the subtle energy differences between the two species.[6]

However, it appeared possible to minimize the possibility of the intervention of the solvent-separated ion-pair by utilizing highly non-polar solvents, such as benzene or cyclohexane, thereby depressing further ionization of the tight ion-pair to the solvent-separated ion-pair. In particular, the use of cyclohexane was thought to eliminate the possibility of rearside shielding, thus bringing the significance of the intermolecular $S_{N}i$ mechanism into relief.

For this purpose we required a highly reactive substrate, and we decided to utilize 1-(*p*-methoxyphenyl)ethyl trifluoroacetate (1) since this substrate is known to afford the phenyl ether with retained (15%) configuration in phenolysis in phenol–benzene (1 : 1 w/w) at 25.0 °C.[1] As the substitution reagents we selected phenol and methanol which have often been used in previous work.[1–7]



(1)

With a view to observing only the role of phenol and methanol as substitution reagents and to eliminating their solvent effects, their concentration was kept as low as possible, *i.e.*, two or three mol. equiv. relative to the substrate. Pyridine was used as scavenger of the trifluoroacetic acid liberated in the reaction.

RESULTS AND DISCUSSION

Synthesis of 1-(p-*Methoxyphenyl*)*ethyl Trifluoroacetate.*—The trifluoroacetate was synthesized as previously reported,[1] from optically active 1-(*p*-methoxyphenyl)ethanol and trifluoroacetic anhydride in the presence of pyridine. Because of its instability it was not further purified, but used directly for the reactions described below. The trifluoroacetate was found to be contaminated by small amounts (1—5%) of bis-1-(*p*-methoxyphenyl)ethyl ether which was formed during the work-up. However, it has been proved that the ether does not affect the reaction concerned.

Proof of the Absence of Interaction between 1-(p-*Methoxyphenyl*)*ethyl Trifluoroacetate and Pyridine in Benzene.*—In the reactions of alkyl halides with hydroxylic nucleophiles it is occasionally necessary to add a base to take up the hydrogen halide which often accelerates the reaction or makes it reversible.[20,21] Since it had been demonstrated in a preliminary run at 25.0 °C that the reaction of the trifluoroacetate (1) with methanol or phenol suffers some acceleration by trifluoroacetic acid, and that the reaction with phenol is reversible (Figures 1 and 2), pyridine was selected as scavenger.

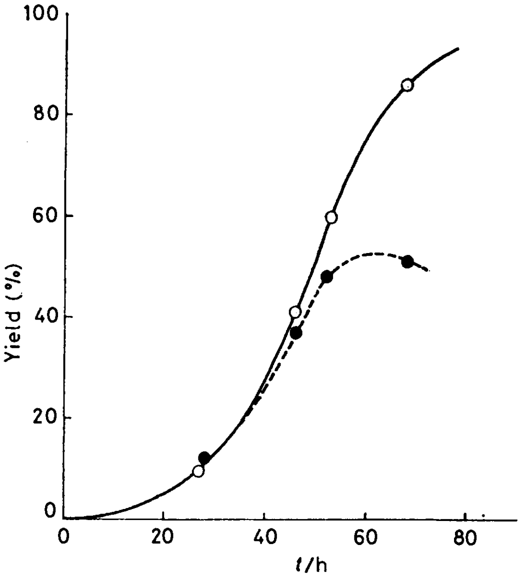


FIGURE 1 Plot of yield (%) against reaction time for the reaction of the trifluoroacetate (1) with methanol in benzene at 25.0 °C. Open circles, 1-(*p*-methoxyphenyl)ethyl methyl ether; closed circles, trifluoroacetic acid

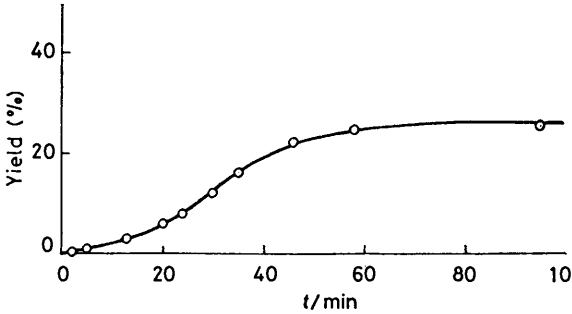


FIGURE 2 Plot of yield (%) of trifluoroacetic acid against reaction time for the reaction of the trifluoroacetate (1) with phenol in benzene at 25.0 °C

Prior to the examination of the substitution reactions in the presence of pyridine, it was necessary to establish whether the trifluoroacetate (1) interacts with pyridine. First, the ^{13}C n.m.r. spectrum of trifluoroacetate (1)–pyridine in $[^{2}H_{6}]$benzene remained virtually unchanged for 10 h at room temperature, indicating that no substantial fraction of the substrate is converted into *N*-1-(*p*-methoxyphenyl)ethylpyridinum trifluoroacetate. Secondly, the optical rotation of the optically active trifluoroacetate (1) in benzene did not show any decrease within experimental error for 300 h at 25.0 °C, when pyridine was added to the benzene solution, indicating that no substantial ionization of the trifluoroacetate (1) occurred in benzene in the presence of pyridine. Clearly pyridine is a safe scavenger of the acid, not perturbing the rate-determining step of the reaction of the trifluoroacetate (1).

Conversely, in the absence of pyridine the optical rotation of the benzene solution of the trifluoroacetate (1) gradually decreased and complete loss of rotation was observed after 50 h at 25.0 °C, indicating that a trace of trifluoroacetic acid, produced by hydrolysis of the substrate (1) in accidentally wet benzene, can assist the ionization.

TABLE 1

First-order rate constants [a] for the reactions of 1-(*p*-methoxyphenyl)ethyl trifluoroacetate with methanol and phenol in benzene in the presence of pyridine at 25.0 °C

Entry	[ROTFA]/M	[MeOH]/M	[PhOH]/M	[Pyridine]/M	$[PhOH]_f$/M [b]	k_1/s^{-1}
1	0.0773	1.40×10^{-3}		0.105		2.26×10^{-9}
2	0.0857	1.01×10^{-2}		0.101		2.59×10^{-8}
3	0.0833	5.06×10^{-2}		0.101		1.94×10^{-7}
4	0.0839	1.01×10^{-1}		0.101		5.85×10^{-7}
5	0.0843	5.03×10^{-1}		0.105		1.14×10^{-5}
6	0.0811	5.10×10^{-1}		0.109		1.16×10^{-5}
7	0.0974	1.13×10^{-1}				1.53×10^{-6}
8	0.0890	2.67×10^{-1}				6.84×10^{-6}
9	0.0919	5.15×10^{-1}				2.49×10^{-5}
10	0.0780		1.02×10^{-3}	0.102	3.21×10^{-4}	6.62×10^{-9}
11	0.0824		1.03×10^{-2}	0.100	3.43×10^{-3}	8.92×10^{-8}
12	0.491		1.03×10^{-2}	0.005 11	9.44×10^{-3}	5.23×10^{-7}
13	0.409		2.06×10^{-2}	0.0102	1.78×10^{-2}	1.11×10^{-6}
14	0.102 [c]		1.01×10^{-1}	0.207	2.63×10^{-2}	2.10×10^{-6}
15	0.196		5.15×10^{-2}	0.0255	3.97×10^{-2}	3.31×10^{-6}
16	0.0817		1.01×10^{-1}	0.103	4.84×10^{-2}	4.59×10^{-6}
17	0.101		1.03×10^{-1}	0.0511	7.20×10^{-2}	1.06×10^{-5}
18	0.103		2.06×10^{-1}	0.102	1.37×10^{-1}	3.44×10^{-5}
19	0.0799		5.09×10^{-1}	0.100	4.19×10^{-1}	4.69×10^{-4}
20	0.0953		1.10×10^{-1}			4.45×10^{-5}
21	0.0758		5.08×10^{-1}			2.17×10^{-3}
22	0.0493 [d]		1.03×10^{-1}	0.0557	5.43×10^{-2}	2.12×10^{-5}

[a] Initial rate constant (see text). [b] K_{25}° (in benzene) 2.15; K_{25}° (in cyclohexane) 127.9; calculated from the data in ref. 23. [c] Optically active trifluoroacetate (1). [d] In cyclohexane as solvent.

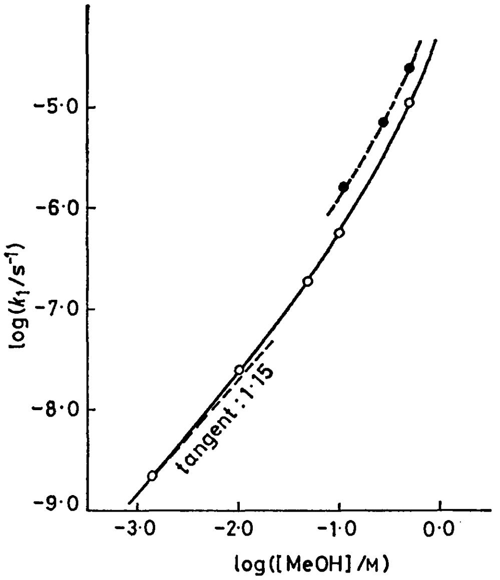


FIGURE 3 Plot of log k_1 against log [MeOH] for the reaction of the trifluoroacetate (1) with methanol in benzene at 25.0 °C. Open circles, reactions in the presence of pyridine (0.10M); closed circles, reactions in the absence of pyridine

Kinetic Order in Methanol in the Presence or Absence of Pyridine.—The rates were followed by g.l.c. for runs with 10^{-3}M-methanol, whereas titration was used for the runs at concentrations $>10^{-2}$M. The initial rate constants k_1 measured in the presence of pyridine, were calculated from graphic plots of trifluoroacetic acid or the methyl ether concentration against reaction time, using equation (1) where $[\Delta x/\Delta t]_0$ stands for the tangent of the curve at time zero and $[ROTFA]_0$ the initial concentration of the trifluoroacetate (1).* The rate constants are given in Table 1.

Then the kinetic order at various methanol concentrations was calculated from the tangents of the curved plot of logarithms of k_1 against the logarithms of methanol concentrations (Figure 3). As illustrated in Figure 3, the kinetic order in methanol was determined to be very close to unity at lower concentrations of methanol (1.15 at [MeOH] 1.40×10^{-3}M). Similar kinetic observation with respect to methanol was reported on the reaction of triphenylmethyl chloride with methanol in benzene.[22]

$$k_1 = [\Delta x/\Delta t]_0/[ROTFA]_0 \qquad (1)$$

The rates were also followed without added pyridine in benzene. A plot of the product concentration against the reaction time is illustrated in Figure 1. As mentioned before there is a definite trend towards higher rates as the reaction progresses. In addition, the trifluoroacetic acid concentration decreased after *ca.* 50% completion, whereas the methyl ether formation continued to increase. This anomalous decrease in trifluoroacetic acid concentration most probably comes from the consumption of the acid by excess of methanol to afford methyl trifluoroacetate, as was proved by a control run with methanol and trifluoroacetic acid. The

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* It was found that in the presence of 0.1M-pyridine the trifluoroacetate (1) gives the methyl ether (a nucleophilic substitution product) and the carbinol (a transesterification product) in the ratio 2 : 1. However, this does not affect the rate of the S_N type reaction in the early stages of the reaction.

initial rate constants were calculated by equation (1), as for the case for the presence of pyridine, at various methanol concentrations (0.1M), and are summarized in Table 1. As illustrated in Figure 3, the plot of log k_1 *versus* log $[MeOH]_0$ showed a tendency similar to the case for the presence of pyridine but drifted slightly upwards. The minor rate depressions observed in the presence of pyridine is probably due to complexing of methanol with pyridine by hydrogen bonding, which slightly reduces the concentration of free methanol in benzene.[22]

As mentioned above, the reaction is exactly first order in methanol (second order overall) at lower concentrations of methanol. Since the spontaneous ionization of substrate (1) has been ruled out, it is conceivable that one molecule of methanol can assist the ionization process electrophilically in the rate-determing step, or else the reaction proceeds by the S_N2 mechanism. The possibility of the incursion of the latter mechanism, however, can be ruled out from the stereochemical results described in a later section.

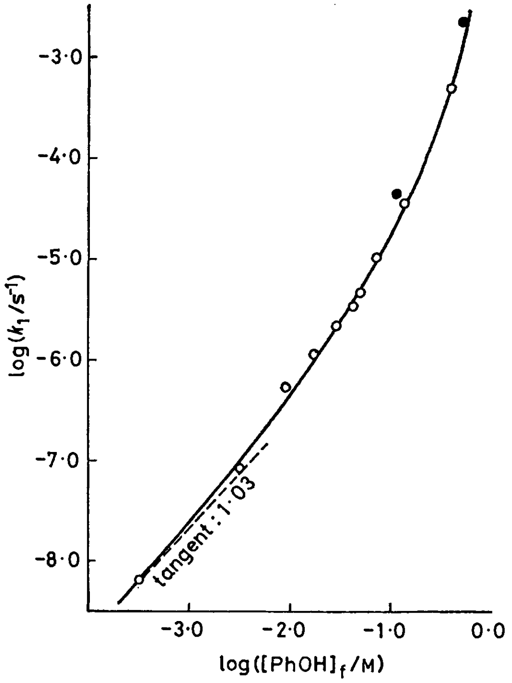

FIGURE 4 Plot of log k_1 against log $[PhOH]_f$ for the reaction of the trifluoroacetate (1) with phenol in benzene at 25.0 °C. Open circles, reaction in the presence of pyridine; closed circles, reaction in the absence of pyridine

Kinetic Order in Phenol in the Presence or Absence of Pyridine.—In a manner similar to the methanol reaction, the rates were first examined in the presence of pyridine. It has been reported that phenol forms a complex with pyridine by hydrogen bonding, and thermodynamic data for the complexation have been reported for the benzene solution.[23] In the present reaction the increase in the pyridine concentration decelerated the reaction as is evident from a comparison of entries 11 and 12, and also 14, 16, 17, and 20 in Table 1. Therefore, it was assumed that only free phenol molecules can effect ionization of the trifluoroacetate, and the logarithms of the initial rate constant k_1, calculated from equation (1), were plotted against the logarithms of the concentrations of free phenol, calculated from the thermodynamic data (Figure 4). The kinetic order decreases from 3 to 1.03 in the concentration range 10^{-1}—10^{-4}M free phenol, indicating an order of unity at lower concentrations.

The dependence of the reaction order on the phenol concentration, combined with the absence of ionization of the trifluoroacetate (1) in benzene and the stereochemical results, suggests that phenol most probably assists the ionization as an electrophile as is known for several solvolytic reactions.[24] It is notable that under the same conditions, in benzene at 25.0 °C, the kinetic order is unity for both phenol and methanol, but the rate with phenol is higher than that with methanol. This means that both phenol and methanol do not play a role as a nucleophile, but as an electrophile, and that the transition state $R^+ \cdots {}^-O_2CCF_3 \cdots H{-}OR$ is more prefered by phenol than by methanol. It has been reported for the S_N1 reaction of t-butyl bromide in nitromethane that the rate increases linearly with concentration of added hydroxylic reactant in the order PhOH > H_2O > EtOH.[24a]

When the rates were followed without pyridine, the reaction was not only accelerated as it progressed, but also stopped at about one-fourth conversion of substrate (1) (Figure 2). The reverse process which apparently stops the reaction must be the cleavage of the phenyl ether by the trifluoroacetic acid produced. In this context it is known that hydrogen chloride can cleave 1-phenylethyl phenyl ether readily at room temperature.[25]

The initial rate constants, calculated by the use of equation (1), fall virtually on the curve obtained in the presence of pyridine, as illustrated in Figure 4. This is reasonable provided the reaction proceeds *via* an ionization process electrophilically assisted by one molecule (or more at high concentrations) of phenol, irrespective of the presence or absence of pyridine.

Maximum Rotations and Absolute Configurations of 1-(p-*Methoxyphenyl)ethyl Methyl Ether and* 1-(p-*Methoxyphenyl)ethyl Trifluoroacetate* (1).—Optically active 1-(*p*-methoxyphenyl)ethyl methyl ether was prepared by the reaction of optically active lithium 1-(*p*-methoxyphenyl)-ethoxide and dimethyl sulphate in dimethyl sulphoxide. The methyl ether prepared in this manner exhibited the same sign of optical rotation as the starting 1-(*p*-methoxyphenyl)ethanol.

The optically active trifluoroacetate (1) was prepared with retention of configuration from the corresponding optically active alcohol by a literature method,[7] and the previously reported value for the maximum rotation[7] was revised. The maximum rotations of the relevant compounds are listed in Table 2.

Stereochemical Course of the Reactions with Phenol or Methanol.—Optically active 1-(*p*-methoxyphenyl)ethyl trifluoroacetate (1) afforded the phenyl ether with partially (7—9%) retained configuration, when it was subjected to the reaction with phenol in the presence of pyridine. In addition, a similar reaction with methanol also gave rise to the methyl ether with partially (24%) retained configuration. In the absence of pyridine the methyl ether formed suffers much racemization due to the concurrent proton-assisted ionization of the trifluoroacetate (1), but it still has a retained configuration albeit to a small extent.* The reaction conditions and results are in Table 3.

When the reaction with phenol was carried out in cyclohexane, the phenyl ether with retained configuration was also isolated (Table 3). Consequently, this rules out the possibility of rearside shielding by benzene to bring about the retentive steric course since for cyclohexane rearside shielding is difficult.

TABLE 2

Maximum rotations (°) [a] of (R)-1-(p-methoxyphenyl)ethyl derivatives

ROH [b]	ROCOCF$_3$ [c]	ROPh [c]	ROMe
+50.3	+160	−22.2	+123

[a] $[\alpha]_D$ (in benzene). [b] The previously cited value [7] for the neat sample has been revised and estimated from the literature values, α_{5461} and α_{5780}, for the neat alcohol at 15.0 and 28.25 °C.[25] [c] The previously reported value [7] has been revised.

Considering the first-order kinetics in both phenol and methanol at low concentrations and the absence of ionization of the substrate (1) without phenol or methanol, one should expect the intervention of an intermolecular S_Ni transition state (or intermediate), at least partly if not wholly, to account for the formation of partially retained ethers, although one cannot rule out the possible coexistence of rearside attack of phenol or methanol on the ion-pair intermediate to explain part of the racemization of the ether products.

TABLE 3

Net steric course for the ether product in the reactions of 1-(p-methoxyphenyl)ethyl trifluoroacetate with methanol and phenol at 25.0 °C

Solvent	t/h	[ROTFA]/M {ROTFA $[\alpha]_D$ (°)} [a]	[MeOH]/M or [PhOH]/M	[Pyridine]/M	Conversion [b] (%)	Yield (%) {$[\alpha]_D$ (°)}	Net steric course (%)
Benzene	349	0.110 {−58.7}	0.190 [c]	0.124	44.2	39.7 {−10.7}	23.7 ret.
	69	0.0516 {+86.7}	0.105 [c]		85.7 [d]	70.1 {+3.0}	4.5 ret.
	136	0.0497 {+80.0}	0.106 [e]	0.0592	82.7	71.6 {−0.72}	6.5 ret.
	264	0.102 {+88.6}	0.101 [e]	0.207	62.2	53.7 {−1.19}	9.7 ret.
Cyclohexane	117	0.0493 {+88.6}	0.103 [e]	0.0557	60.9 [d]	56.9 {−0.59}	4.8 ret.

[a] In benzene, c 3—6 at 25.0 °C. [b] Measured by titration. [c] Methanol. [d] Measured by g.l.c. [e] Phenol.

In conclusion, our data strongly suggest the existence of the intermolecular S_Ni mechanism for the reaction of substrate (1) with phenol or methanol in benzene or cyclohexane as solvent. Consequently, in the phenolyses,[1-7] including those of substrate (1),[1] the solvent phenol also plays a role as a component of the intermolecular S_Ni reaction. In other words, it is most probable that in retentive phenolyses [1-7] the four-centre model (a) can play a role as a key intermediate, although the rearside shielding model (c) has already been shown to be another probable model.[6]

EXPERIMENTAL

M.p.s and b.p.s are uncorrected. I.r. spectra were measured with a Hitachi 215 spectrophotometer. ^{1}H N.m.r. spectra were taken with a Hitachi R-24 (60 MHz) spectrometer. ^{13}C N.m.r. spectra were recorded on a JEOL FX 100 (25.00 MHz) spectrometer operating in the Fourier transform mode. The optical rotations were determined with a JASCO DIP-SL polarimeter using a cell with path-length 0.5 dm except when otherwise noted. G.l.c. was performed with a Hitachi 163 gas chromatograph with a flame ionization detector using a 3 mm stainless steel column. Elemental analyses were performed at the Microanalytical Centre, Kyoto University, Kyoto.

Materials.—Reagents were of reagent grade quality except when otherwise noted. Benzene and cyclohexane were refluxed over sodium and distilled. Methanol was refluxed over magnesium methoxide and distilled. Pyridine, 2,6-lutidine, and triethylamine were dried over potassium hydroxide and distilled. Phenol was distilled just prior to use. The resolution of 1-(p-methoxyphenyl)ethanol was performed by a modified Kenyon method.[26]

Optically Active 1-(p-*Methoxyphenyl)ethyl Trifluoroacetate* (1).—This was prepared according to the method of Bourne *et al.*[27] The physical properties and spectral data were reported in the previous article.[7] The purity of the trifluoroacetate was determined by dissolving an accurately weighed portion of the sample in 60% acetone and titrating the liberated trifluoroacetic acid with a standardized ethanolic potassium hydroxide solution. The purity was generally 95—99%. The temperature-programmed (150—220 °C) g.l.c. analysis of the trifluoroacetate on a 1 m PEG 20M column revealed contamination with 1—5% of bis-1-(p-methoxyphenyl)ethyl ether. The maximum specific rotation was determined as 160 ± 1° (25 °C, benzene) from three preparative runs.

Optically Active 1-(p-*Methoxyphenyl)ethyl Methyl Ether*.—To optically active 1-(p-methoxyphenyl)ethanol {0.555 g, 3.65 mmol; $[\alpha]_D^{25}$ +13.5° (c 2.53, benzene)} in tetrahydrofuran (10 ml) was added a 1.07M-n-butyl-lithium in hexane (3.41 ml, 3.65 mmol) over 2 min at 5—10 °C. After 15 min

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* In view of the fact that methanol gives rise to the predominantly inverted methyl ether when it is subjected to ordinary nucleophilic substitutions of optically active 1-phenylethyl chloride (refs. 4 and 6; K. Okamoto, N. Uchida, S. Saito, and H. Shingu, *Bull. Chem. Soc. Japan*, 1966, **39**, 307), the formation of the methyl ether with retained configuration is a remarkable stereochemical result; a search for other similar examples with methanol and other hydroxylic nucleophiles is in progress.

at 5 °C the solvent was evaporated off at 0 °C and 2 mmHg. The residue was allowed to warm to 25 °C and then dimethyl sulphoxide (DMSO) (10 ml) was added and the resulting solution stirred at 25 °C for 15 min. From 2 ml of the DMSO solution was recovered optically active starting alcohol {0.075 g; $[\alpha]_D^{25}$ +13.8° (*c* 3.16, benzene)}, whose optical purity was identical with that of the alcohol before n-butyl-lithium treatment. To the rest of the DMSO solution was added dimethyl sulphate (0.74 g, 5.8 mmol) over 2 min and the resulting solution stirred for 30 min at 25—28 °C. The solution was poured into chilled 25% ammonia, diluted to 100 ml with water, and extracted with pentane. The pentane solution was washed with 10% NaCl, dried ($MgSO_4$), and subjected to distillation to afford optically active 1-(*p*-methoxyphenyl)ethyl methyl ether {0.182 g; b.p. 80—84 °C at 2 mmHg; $[\alpha]_D^{25}$ +32.9° (*c* 5.91, benzene)}. The maximum specific rotation of completely retained methyl ether was calculated to be +123° taking into account the value of +50.3° for that of the alcohol. I.r. and n.m.r. spectra were in complete agreement with those of an authentic sample.

Reaction of 1-(p-*Methoxyphenyl*)*ethyl Trifluoroacetate* (1) *with Methanol in Benzene*.—The trifluoroacetate {1.013 g, 3.953 mmol; $[\alpha]_D^{25}$ −58.7 ± 0.2° (*c* 5.08, benzene)} was mixed with a benzene solution (35 ml) containing pyridine (0.353 g, 4.46 mmol) and methanol (0.220 g, 6.85 mmol). After the mixture had been kept at 25.0 °C for 15 days in a thermostat a portion was withdrawn and titrated with standardized ethanolic potassium hydroxide to show the liberation of 44.2% trifluoroacetic acid. The benzene solution was vigorously stirred with 10% NaOH for 2 h at room temperature, washed with water, and dried ($MgSO_4$). Evaporation of the benzene afforded a yellow oil, which on separation with t.l.c. (SiO_2, benzene) afforded 1-(p-*methoxyphenyl*)*ethyl methyl ether* {R_F 0.35; 0.261 g, 39.7%; $[\alpha]_D^{25}$ −10.7 ± 0.4° (*c* 2.81, benzene)}; $\nu_{max.}$ (neat) 2 940, 2 840, 1 610, 1 515, 1 450, 1 375, 1 290, 1 250, 1 180, 1 105, 1 040, and 840 cm^{-1}; $\delta(CCl_4)$ 1.30 (3 H, d, *J* 6.0 Hz), 3.05 (3 H, s), 3.70 (3 H, s), 4.05 (1 H, q *J* 6.0 Hz), 6.50 (2 H, d, *J* 8.0 Hz), and 6.90 (2 H, d, *J* 8.0 Hz) (Found: C, 72.2; H, 8.6. $C_{10}H_{14}O_2$ requires C, 72.25; H, 8.5%). In addition, there were obtained *p*-methoxystyrene (R_F 0.75; 0.050 g, 9.4%) and 1-(*p*-methoxyphenyl)ethanol (R_F 0.20; 0.208 g, 34.6%).

Reaction of 1-(p-*Methoxyphenyl*)*ethyl Trifluoroacetate* (1) *with Phenol in Benzene*.—(A) *Isolation of products*. The trifluoroacetate {3.085 g, 12.43 mmol; $[\alpha]_D^{25}$ +80.0 ± 0.3° (*c* 3.66, benzene)} was dissolved in a benzene solution (250 ml) containing pyridine (1.172 g, 14.81 mmol) and phenol (2.498 g, 26.54 mmol). After the solution had been kept at 25.0 °C for 6 days in a thermostat, titration exhibited the liberation of 82.7% trifluoroacetic acid. A part of the solution (120 ml) was vigorously stirred with 10% NaOH for 2 h at room temperature, washed with water, dried ($MgSO_4$), and the benzene evaporated. Separation of the residual oil by means of preparative t.l.c. (SiO_2, benzene) afforded 1-(*p*-methoxyphenyl)ethyl phenyl ether {R_F 0.7; 1.017 g, 74.6%; $[\alpha]_D^{25}$ −0.72 ± 0.06° (*c* 10.0, benzene)}. I.r. and n.m.r. spectra were superimposable on those previously reported.[7] In addition, there were obtained *p*-methoxystyrene (R_F 0.88; 0.0136 g, 1.7%), bis-1-(*p*-methoxyphenyl)ethyl ether (R_F 0.3; 0.014 g, 1.7%), and 1-(*p*-methoxyphenyl) ethanol (R_F 0.15; 0.082 g, 9.1%).

(B) *Optical stability of* 1-(p-*methoxyphenyl*)*ethyl phenyl ether*. The rest of the above mixture was kept at 25.0 °C for further 8 days and then worked up as described above. 1-(*p*-Methoxyphenyl)ethyl phenyl ether obtained by means of t.l.c. (SiO_2, benzene) showed $[\alpha]_D^{25}$ −0.86 ± 0.26° (*c* 7.02, benzene). The phenyl ether, after standing overnight at room temperature in a liquid state, exhibited $[\alpha]_D^{25}$ −0.67 ± 0.29° (*c* 4.80, benzene), which was essentially unchanged.

Kinetic Measurements.—(A) *Measurements by titration*. The usual pipetting out technique was employed. A 20 ml measuring flask containing a benzene solution of 1-(*p*-methoxyphenyl)ethyl trifluoroacetate, pyridine, and methanol (or phenol) was immersed in a thermostat controlled at 25.0 ± 0.05 °C. Portions (1.000 ml) were withdrawn at intervals and quenched with chilled acetone (20 ml). The trifluoroacetic acid liberated was titrated with 0.01N-KOH in ethanol using lacmoid as indicator. The trifluoroacetic acid concentration was plotted against time, and the first-order rate constant calculated from equation (1) (see text). Measurements in the presence of 2,6-lutidine or triethylamine were carried out in a similar manner.

(B) *Measurements by g.l.c.* The rates at phenol or methanol concentrations as low as 0.001M were determined by following the amount of the product, 1-(*p*-methoxyphenyl)ethyl methyl or phenyl ether, by temperature programmed (150—220 °C) g.l.c. on a 1 m PEG 20M column. Biphenyl and hexamethylbenzene were used as internal standards for methanolysis and phenolysis, respectively.

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