**476.** *Interdependence of Molecular Conformation and Conjugation in Aromatic Ethers. Part I.*

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The ultraviolet absorption spectra and rates of bromination of the methyl ethers of o-cresol and 2 : 6-xylenol * and the ethers $o\text{-}C_6H_4O\cdot[CH_2]_{n-3}$ and PhOR, where n is 5, 6, and 7 and R is Me, Et, Pr^i, and Bu^t, and the rates of solvolysis of their chloromethyl derivatives in 90% aqueous ethanol have been determined. The extinction coefficients of methyl 2 : 6-xylyl ether, *tert.*-butoxybenzene, and homochroman, the rates of bromination of these ethers, and the rates of solvolysis of their chloromethyl derivatives are all comparatively small. The data are explained in terms of increase of steric interaction with decrease of θ, the interplanar angle of the ether group and the benzene ring.

In earlier papers [1] the effect of alkyl groups (R) and of the value of n on the rates of unimolecular solvolysis of the chlorides (I) and (II) respectively and on the basic strengths

of the corresponding amines NHPhR and $o\text{-}C_6H_4\cdot NH\cdot[CH_2]_{n-3}$, have been shown to


Scheme A

Scheme B
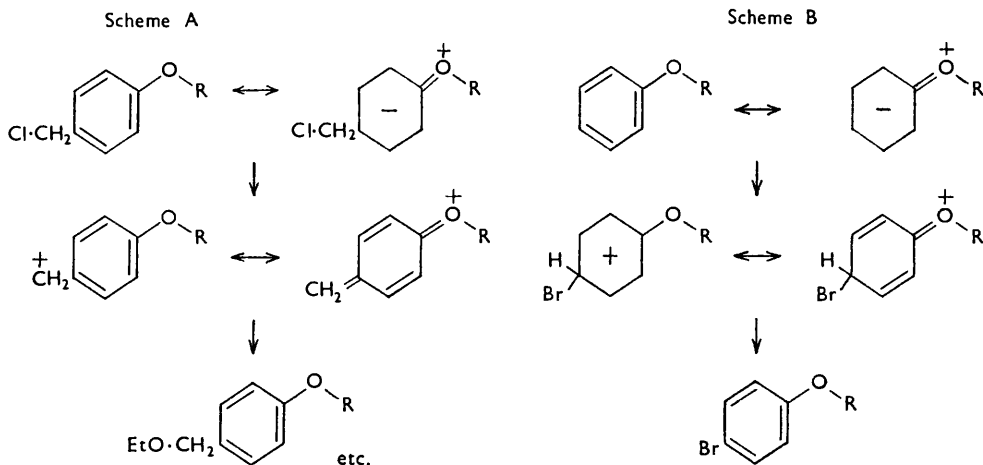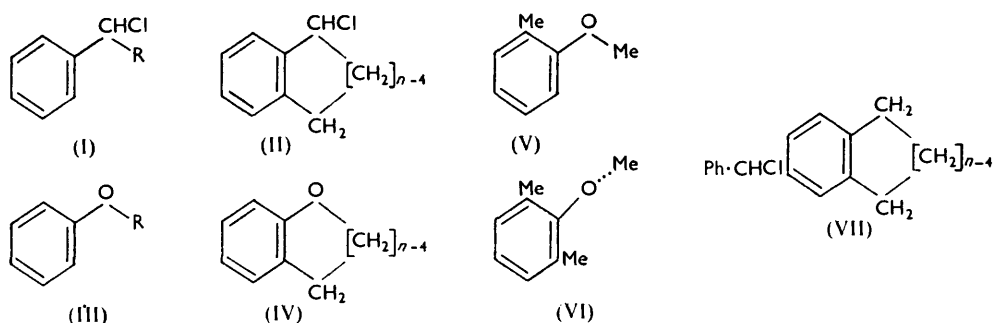
incorporate changes of steric interaction effected by differences in conformation between reactants and transition states or between reactants and products. In all these instances, changes in conformation which may accompany reaction occur in the vicinity of the

* OH = 1 (cf. *J.*, 1952, 5091; 1953, 4202).

[1] Baddeley, Chadwick, and Taylor, *J.*, 1951, 368; 1954, 2405; 1956, 448, 451.

reaction centre and effect changes in steric interaction of the groups attached thereto. We now show that chemical reactivity may be similarly affected by changes in conformation at a distance from the reaction centre. The present work concerns a number of aromatic ethers and their chloromethyl derivatives and serves further to provide evidence for a relation between conformation and conjugation of an ether-oxygen atom and a benzene ring which until now has received very little attention.

Our choice of aromatic ethers was based on the following considerations : (i) Mesomeric interaction in alkoxybenzenes (III) might be hindered if the alkyl group is sufficiently bulky, as, for example, when it is *tert.*-butyl, to prevent the O–R bond from occupying the plane of the benzene ring, *i.e.*, the position for most effective resonance stabilisation. (ii) When R is methyl, conjugation should be significantly hindered only when both *ortho*-positions are occupied by bulky substituents (cf. V and VI). (iii) When the oxygen atom
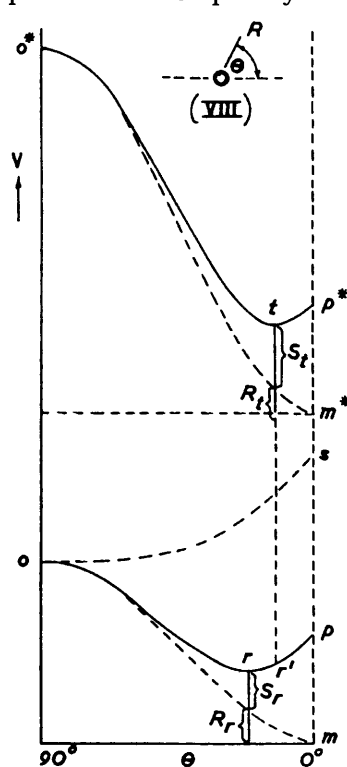
forms part of a ring as in (IV), conjugation should be a maximum when $n = 5$ and should decrease with increase in the value of n insofar as this increase rotates the $O–CH_2$ bond away from the plane of the benzene ring. These considerations are substantiated by the rates of nuclear bromination of the ethers, their ultraviolet absorption spectra, and the rates of unimolecular solvolysis of their chloromethyl derivatives. Ionisation of these derivatives is the rate-determining step in their solvolysis and is represented by scheme A; bromination of the ethers is kinetically of the second order, first order with respect to ether and to bromine, when effected by dilute solutions (*ca.* 0·001M) of bromine in glacial acetic acid,[2] and is conveniently represented by scheme B. In both processes conjugation of the ether-oxygen atom and the benzene ring provides greater resonance stabilisation of the transition state than of the reactant and thereby assists reaction; should conjugation be sterically hindered, the following considerations enable the consequent changes in reactivity to be anticipated.

Let *o* in the Figure be the energy content of the ether PhOR or its chloromethyl derivative when mesomeric and steric interaction of Ph and OR groups are a minimum, *i.e.*, when the interplanar angle θ is 90° (see VIII of the Figure; the plane of the ring is perpendicular to the plane of the paper and is represented by a broken line). Let *om*, given by $-m \cos^2 \theta$ where *m* is the mesomeric energy of stabilisation when θ = 0°, and *os* represent the change of mesomeric and steric interaction respectively with change of θ. Algebraic addition of *om* and *os*, relative to the horizontal through *o*, provides *op*, and the minimum at *r* represents the preferred conformation of the reactant. Again, let *o** be the energy content of the transition state of bromination of the ether or unimolecular solvolysis of its chloromethyl derivative when electromeric and steric interaction of Ph and OR are a minimum, *i.e.*, when θ, as defined above, is 90°; and let *o*m**, given by $-m^* \cos^2 \theta$ where *m** is greater than *m* and is the electromeric energy of stabilisation of the transition state when θ = 0°, represent the change in this energy with change in θ. Algebraic addition of *o*m** and *os*, after the latter has been raised so that *o* coincides with *o**, provides *o*p**, and the minimum at *t* represents the preferred conformation of the transition state.

The energy contents of the reactant (*r*) and the transition state (*t*) are greater by the amounts $(S_r + R_r)$ and $(S_t + R_t)$ respectively than they would have been if steric interaction were independent of θ. S_r and S_t are respectively energies of steric interaction, and R_r and R_t the respective losses of resonance stabilisation. Now *o*p** and *op* converge, as do *o*m** and *om*, with change of θ from 90° to 0° and therefore the perpendicular separation

[2] Robertson. de la Mare, and Johnston, *J.*, 1943, 276.

$(t - r') > (p^* - p) = (m^* - m)$, and the energy difference between t and r, *i.e.*, the activation energy, is greater than $(t - r')$ and is greater by the amount $[(S_t - S_r) + (R_t - R_r)]$ than it would have been, *i.e.*, $(m^* - m)$, if steric interaction were independent of θ. Thus it follows that increase of steric interaction with decrease in the value of θ will hinder chemical reaction by increasing the energy of activation. It is unwise to consider this effect as arising from steric hindrance of resonance stabilisation in the transition state : in fact, as in the Figure, this hindrance may be less in the transition state than in the reactant, *i.e.*, R_t may be less than R_r.

The rate coefficients for solvolysis of the chloromethyl derivatives in 90% aqueous ethanol are listed in Table 1. Comparing results for compounds 1, 2, and 3 shows that the

TABLE 1. *Constants of the Arrhenius equation, $k = Ae^{-E/RT}$, for the formation of hydrogen chloride by the solvolysis of the chlorides in 90% aqueous ethanol.*

No.		$10^5 k_{0\cdot0}$ (min.$^{-1}$)	$10^4 k_{25\cdot0}$ (min.$^{-1}$)	E (kcal./mole)	$10^{-11}A$ (min.$^{-1}$)
1	$4:3:5\text{-MeO·C}_6\text{H}_2\text{Me}_2\text{·CH}_2\text{Cl}$	1·70	3·70	20·0	1·4
2	$4:3\text{-MeO·C}_6\text{H}_3\text{Me·CH}_2\text{Cl}$	250	510	19·6	100
3	$4\text{-MeO·C}_6\text{H}_4\text{·CH}_2\text{Cl}$	55·0	130	20·6	140
4	$4\text{-EtO·C}_6\text{H}_4\text{·CH}_2\text{Cl}$	82·0	185	20·3	120
5	$4\text{-Pr}^i\text{O·C}_6\text{H}_4\text{·CH}_2\text{Cl}$	180	325	18·8	17
6	$4\text{-Bu}^t\text{O·C}_6\text{H}_4\text{·CH}_2\text{Cl}$	33·5	82·0	20·8	120
7	5-Chloromethylcoumaran	2550	3630	17·3	15
8	6-Chloromethylchroman	585	1060	18·8	55
9	7-Chloromethylhomochroman	14·0	18·5	21·0	39

3-methyl group of 4-methoxy-3-methylbenzyl chloride effects a four-fold increase in the rate coefficient, and an additional methyl group in the 5-position a comparatively large decrease. The contrast, though a consequence of change in value of the non-exponential term (A) of the Arrhenius equation, is evidence for an increase in steric or space interaction of adjacent methoxyl and methyl groups during ionisation of the 3 : 5-dimethyl derivative, an increase which more than neutralises the consequences of electron release by the 3- and the 5-methyl group.

Comparing chlorides 3, 4, 5, and 6 shows that reactivity increases in the order R = $\text{Bu}^t < \text{Me} < \text{Et} < \text{Pr}^i$; this is compatible with the view that these alkyl groups have an inductive effect which increases in the order $\text{Me} < \text{Et} < \text{Pr}^i < \text{Bu}^t$, and that that of the *tert.*-butyl group is more than counterbalanced by increase in steric interaction of this group and the benzene ring during ionisation of 4-*tert.*-butoxybenzyl chloride. The

TABLE 2. *Comparison of energies of activation and relative rates of solvolysis of the chlorides.*

C_{1-5} are arbitrary constants.

R	$\text{C}_6\text{H}_5\text{·CHRCl}$ in 80% aq. EtOH			$4\text{-RO·C}_6\text{H}_4\text{·CH}_2\text{Cl}$ in 90% aq. EtOH	
	E (kcal./mole)	log $C_1 k_{45\cdot0}$		E (kcal./mole)	log $C_2 k_{0\cdot0}$
Me	20·4	3·00		20·6	3·00
Et	20·7	2·37		20·3	3·17
Pr^i	22·9	1·70		18·8	3·52
Bu^t	25·4	0·27		20·8	2·78

	$\text{C}_6\text{H}_4\text{·CHCl·[CH}_2]_{n-3}$ in EtOH		$4\text{-CH}_2\text{Cl·C}_6\text{H}_4\text{·O·[CH}_2]_{n-3}$ in 90% aq. EtOH		$\text{C}_6\text{H}_5\text{CHCl·C}_6\text{H}_4\text{·[CH}_2]_{n-2}$ in EtOH	
	E (kcal./mole)	log $C_3 k_{0\cdot0}$	E (kcal./mole)	log $C_4 k_{0\cdot0}$	E (kcal./mole)	log $C_5 k_{0\cdot0}$
5	20·0	3·00	17·3	3·00	17·3	3·00
6	20·2	2·43	18·8	2·36	17·9	2·88
7	23·9	0·77	21·0	0·74	18·0	2·81

reactivities of these chlorides vary less with change in R than do those of the aralkyl chlorides (I). The differences (see Table 2) may be caused by hyperconjugation; this

provides electron release which decreases in the order Me $>$ Et $>$ Pr^i $>$ Bu^t and operates in the ionisation only of the aralkyl chlorides.

Comparing chlorides 2, 7, 8, and 9 shows that ring closure with formation of the five-membered heterocyclic ring gives, doubtless as a consequence of the imposed coplanarity of the ether group and the benzene ring, a ten-fold increase in rate of ionisation at 0°. Much of this increase is lost when the ring is six-membered, and ionisation is sterically hindered when it is seven-membered. The reactivities of these chlorides and those of the 3-chloro-1 : 2-benzo*cyclo*alkenes (II; $n = 5$, 6, and 7) are listed in Table 2; the remarkable resemblance is not surprising if one assumes that, in both series of chlorides, the changes in steric interaction which accompany ionisation are affected equally by change in the value of n. This change cannot affect conjugation (cf. hyperconjugation[3]) in the diphenyl-methyl chlorides (VII; $n = 5$, 6, and 7) or the corresponding cations, and the reactivities of these chlorides are nearly independent of the value of n (see Table 2).

The ethers were brominated at a convenient rate in glacial acetic acid (m. p. 16·1°) at 20·0°. The time intervals for 20% consumption of bromine and therefrom the calculated relative rates of bromination are listed in Table 3, together with the relative rates of solvolysis of the chloromethyl derivatives related to the ethers. As was expected, there is an overall resemblance between the two lists of rates. When the rates of bromination of anisole and of solvolysis of its chloromethyl derivative are used as standards for comparison, the rates of solvolysis are more affected by decrease in reactivity of the organic reactant (see Nos. 1, 6, and 9) while those of bromination are more affected by increase in reactivity.

The ultraviolet absorption spectra of the ethers in solvent hexane have three peaks in the region 2500—3000 Å; the values of $\lambda_{max.}$ and ε are given in the Experimental section. Wave numbers and extinction coefficients for the middle peaks are included in Table 3 and,

TABLE 3. *Comparison of the ultraviolet absorption spectra and relative rates of bromination of the ethers and the rates of solvolysis of their chloromethyl derivatives.*

No.		Absorption spectra		Bromination in acetic acid		Solvolysis
		$\nu_{max.}$ (cm.$^{-1}$)	ε	$t_{20\%}$ (min.)	$k_{rel.}$	$10^2 k_{25\cdot0}$ (min.$^{-1}$)
1	1 : 3 : 2-C$_6$H$_3$Me$_2$·OMe	37,300	334	29	0·39	0·037
2	1 : 2-C$_6$H$_4$Me·OMe	36,800	1812	1·7	6·3	5·11
3	PhOMe	36,900	1579	10·7	1·0	1·29
4	PhOEt	36,900	1938	1·44	7·4	2·07
5	PhOPr^i	36,600	1920	2·38	4·5	3·60
6	PhOBu^t	37,000	454	6·5 *	1·3	0·90
7	Coumaran	35,300	3095	0·14	76	36·3
8	Chroman	36,200	2125	0·38	28	10·6
9	Homochroman	37,500	678	7·75	1·4	0·186

* See Experimental Section

like the rates of bromination and solvolysis, afford evidence for steric hindrance of mesomerism in methyl 2 : 6-xylyl ether, *tert.*-butoxybenzene, and homochroman (1, 6, and 9 respectively). Care has to be exercised in comparing relative ultraviolet absorption spectra with relative rate and equilibria data. In the latter, a re-orientation of atomic nuclei, in both the reacting molecules and the surrounding solvent, takes place from ground state to transition state or product.

EXPERIMENTAL

Materials.—Ethers. Anisole, b. p. 154°/758 mm., its 2-methyl derivative, b. p. 168°/776 mm., n_D^{18} 1·5220, and its 2 : 6-dimethyl derivative, b. p. 178°/766 mm., n_D^{17} 1·5068, were obtained by reaction of phenol, o-cresol, and 2 : 6-xylenol respectively with alkali and dimethyl sulphate.[4] Phenetole, b. p. 49·5°/8 mm., was obtained from phenol and diethyl sulphate, and *iso*propoxy-benzene, b. p. 177—178°/760 mm., n_D^{20} 1·4989, from phenol and *iso*propyl iodide in the manner

[3] Baddeley and Gordon, *J.*, 1952, 2190.
[4] Barger and Silberschmidt, *J.*, 1928, 2924.
[5] Smith, *J. Amer. Chem. Soc.*, 1934, **56**, 718.

described by R. A. Smith.[5] *tert.*-Butoxybenzene was afforded [6] by acid-catalysed interaction of phenol and *iso*butene. A stream of *iso*butene, generated by heating a mixture of *tert.*-butyl alcohol (2 parts by weight) and sulphuric acid (1 part of 30%) under reflux condenser, was passed into a mixture of phenol (47 g.), carbon tetrachloride (250 c.c.), and 96% sulphuric acid (25 mg.) at 8°. Subsequently, the mixture was washed with 15% sodium hydroxide solution (5 × 75 c.c.) and water, and dried (Na_2SO_4). It gave *tert.*-butoxybenzene (25 g., 33%), b. p. 60°/8 mm., 184°/760 mm., n_D^{20} 1·4895 (Found : C, 80·4; H, 9·6. Calc. for $C_{10}H_{14}O$: C, 80·0; H, 9·3%). Coumaran, b. p. 77—80°/8 mm., $n_D^{15·5}$ 1·5528 (picrate,[7] m. p. 75·5—76°), was given by the action of aqueous sodium carbonate solution on the product of interaction of hydrobromic acid and 2-*o*-methoxyphenylethanol [8] (phenylurethane, m. p. 80—81°). Catalytic hydrogenation of coumarin over Raney nickel gave 3 : 4-dihydrocoumarin, b. p. 136—139°/10 mm., m. p. 24—24·5°, which afforded 3-*o*-hydroxyphenylpropan-1-ol, b. p. 168—169°/6 mm. (benzoate,[9] m. p. 98—98·5°), on reduction by lithium aluminium hydride in ether; after ½ hr. at 150°, a mixture of the propanol and syrupy phosphoric acid gave chroman (94% of theory), b. p. 81°/6 mm., $n_D^{17·5}$ 1·5513. Homochroman was prepared from 4-*o*-hydroxyphenylbutan-1-ol : A homogeneous mixture of this butanol (19·4 g.), 48% hydrobromic acid (170 c.c.), and acetic acid was boiled under reflux for 3 hr. When cold, the mixture was diluted with water and extracted with ether; the extracts were washed with water, and the ether was removed by distillation. The residue, in ethyl methyl ketone (250 c.c.), was transferred to the Hershberg dropping funnel of a modified form of the high-dilution apparatus described by Ziegler and Lüttringhaus [10] (addition was made with a Hershberg dropping funnel rather than by slow displacement with mercury) and gradually added to a vigorously stirred suspension of potassium carbonate (40 g.) in boiling ethyl methyl ketone (600 c.c.). After the mixture had boiled under reflux for 20 hr., the solvent was separated by fractional distillation, and the residue was filtered. Fractional distillation of the filtrate gave homochroman (11·1 g., 64%), b. p. 86—88°/7 mm., m. p. 28—29° (Found : C, 80·9; H, 7·8. Calc. for $C_{10}H_{12}O$: C, 81·1; H, 8·1%). An alternative preparation involved 4-*o*-*methoxyphenylbutan-1-ol*, b. p. 150—151°/7 mm. (Found : C, 73·0; H, 8·7. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·9%), which was obtained by reduction of ethyl 4-*o*-methoxyphenylbutanoate [8] with lithium aluminium hydride; the butanol was converted into homochroman in the same way as was 4-*o*-hydroxyphenylbutan-1-ol. This butanol was prepared from 1-tetralone (cf. Friess [11]) : A moist chloroform solution of perbenzoic acid (1·2 mol.) [12] was mixed with 1-tetralone (14·6 g.) in the dark at 25°; after 7 days, the mixture was washed with aqueous 2N-sodium carbonate (1·2 mol.), then with water, and dried (Na_2SO_4); distillation gave the lactone (12·6 g.), b. p. 134—144°/11 mm. (Found : acid equiv., 153. Calc. for $C_{10}H_{10}O_2$: acid equiv., 162), of 4-*o*-hydroxyphenylbutanoic acid. The lactone (12 g.) was reduced by lithium aluminium hydride and 4-*o*-*hydroxyphenylbutan-1-ol* (6·9 g.), b. p. 147—149°/0·34 mm., m. p. 48—49° (Found : C, 72·7; H, 8·5. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·4%), was that part of the product which was soluble in sodium hydroxide solution but insoluble in a saturated solution of sodium hydrogen carbonate.

Chloromethyl derivatives from the ethers. These were prepared from the hydroxymethyl compounds : solutions of these alcohols (*ca.* 3 g.) in light petroleum (b. p. 60—80°; 500 c.c.) at 0° were saturated with dry hydrogen chloride; the solutions were dried ($CaCl_2$), solvent was volatilised at 40° under reduced pressure, and the residues were extracted with light petroleum (b. p. <40°). Removal of solvent afforded the required chloromethyl derivatives which were either recrystallised or flash-distilled in nitrogen at reduced pressure. This general procedure minimised formation of resins and afforded the following chlorides : 4-methoxybenzyl chloride, b. p. 80°/0·2 mm. (Found : Cl, 22·2. Calc. for C_8H_9OCl : Cl, 22·7%); 4-methoxy-3-methyl-benzyl chloride, b. p. 88—90°/0·15 mm. (Found : Cl, 20·7. Calc. for $C_9H_{11}OCl$: Cl, 20·8%); 4-*methoxy-3* : 5-*dimethylbenzyl chloride*, b. p. 98—99°/0·32 mm. (Found : Cl, 19·0. $C_{10}H_{13}OCl$ requires Cl, 19·2%); 4-ethoxybenzyl chloride, b. p. 91°/0·95 mm. (Found : Cl, 20·0. Calc. for $C_9H_{11}OCl$: Cl, 20·8%); 4-*iso*propoxybenzyl chloride, b. p. 88—90°/0·7 mm. (Found : Cl, 18·4. $C_{10}H_{13}OCl$ requires Cl, 19·2%); 5-*chloromethylcoumaran*, needles, m. p. 41—42°, from light petroleum (Found : Cl, 20·3. C_9H_9OCl requires Cl, 21·0%); 6-*chloromethylchroman*, b. p.

[6] Stevens and Bowman, U.S.P. 2,655,546/1953.
[7] Chatelus, *Ann. Chim. (France)*, 1949, **4**, 530.
[8] Hardegger, Redlich, and Gal, *Helv. Chim. Acta*, 1945, **28**, 631.
[9] Semmler, *Ber.*, 1906, **39**, 2851.
[10] Ziegler and Lüttringhaus, *Annalen*, 1937, **528**, 155.
[11] Friess, *J. Amer. Chem. Soc.*, 1949, **71**, 14.
[12] Braun, *Org. Synth.*, Coll. Vol. I, 1941, p. 434.

124°/0·15 mm. (Found : Cl, 19·4. $C_{10}H_{11}OCl$ requires Cl, 19·5%) ; and 7-*chloromethylhomo-chroman*, b. p. 113°/0·2 mm. (Found : Cl, 17·7. $C_{11}H_{13}OCl$ requires Cl, 18·0%). 4-*tert.*-Butoxybenzyl chloride, b. p. 75—77°/0·3 mm., was obtained from the corresponding alcohol by the action of thionyl chloride in the presence of pyridine ; it tended to decompose on distillation and its chlorine content was low.

Hydroxymethyl derivatives from the ethers. 4-Methoxybenzyl alcohol,[13] b. p. 131—132°/9 mm., m. p. 22—23° (phenylurethane,[14] m. p. 90·5—91·5°), was afforded by reduction of *p*-anisaldehyde with lithium aluminium hydride ; the experimental procedure was that described by Nystrom and Brown.[15] Similar reduction of 4-methoxy-3-methylbenzaldehyde,[16] b. p. 126—127°/10 mm. (oxime, m. p. 70—71°), gave 4-methoxy-3-methylbenzyl alcohol, b. p. 134—135°/8 mm. (phenylurethane,[17] m. p. 89—89·5°).

4-Methoxy-3 : 5-dimethylbenzyl alcohol was obtained as follows : (i) 4-Bromo-2 : 6-xylenol[18] in the presence of alkali was methylated with dimethyl sulphate by use of the procedure described by Barger and Silberschmidt.[4] Under anhydrous conditions the *methyl ether*, b. p. 117—120°/13 mm. (Found : Br, 37·0. $C_9H_{11}OBr$ requires Br, 37·2%), afforded a Grignard derivative which with carbon dioxide gave 4-*methoxy*-3 : 5-*dimethylbenzoic acid*, needles (from aqueous ethanol), m. p. 188—189° (Found : C, 66·6 ; H, 6·7% ; equiv., 183. $C_{10}H_{12}O_3$ requires C, 66·7 ; H, 6·7% ; equiv., 180). The ethyl ester was prepared by the Fischer–Speier method and gave 4-*methoxy*-3 : 5-*dimethylbenzyl alcohol*, b. p. 142—144°/9 mm. (Found : C, 72·0 ; H, 8·5. $C_{10}H_{14}O_2$ requires C, 72·3 ; H, 8·4%) by reduction. The *phenylurethane* separated from ligroin in needles, m. p. 107—107·5° (Found : N, 5·0. $C_{17}H_{19}O_3N$ requires N, 4·9%).

4-Ethoxybenzyl alcohol,[19] b. p. 135—137°/10 mm., was afforded by reduction of *p*-ethoxy-benzaldehyde,[20] b. p. 249°/760 mm. (semicarbazone, m. p. 196—198°), with lithium aluminium hydride.

4-*iso*Propoxybenzyl alcohol, b. p. 144—146°/12 mm., n_D^{20} 1·5190 (Found : C, 72·2 ; H, 8·5. $C_{10}H_{14}O_2$ requires C, 72·3 ; H, 8·4%) [α-*naphthylurethane*, m. p. 98—99° (Found : N, 4·3. $C_{21}H_{21}O_3N$ requires N, 4·2%)], was obtained in 90% yield by reduction of ethyl 4-*iso*propoxy-benzoate with lithium aluminium hydride. *p*-*iso*Propoxybenzoic acid,[21] m. p. 160—161° (Found : C, 66·7 ; H, 6·6% ; equiv., 184. Calc. for $C_{10}H_{12}O_3$: C, 66·7 ; H, 6·7% ; equiv., 184), was prepared from *p*-bromophenyl *iso*propyl ether,[21] b. p. 230—234°/760 mm.

4-tert.-*Butoxybenzyl alcohol*, b. p. 154—155°/16 mm., n_D^{20} 1·5112 (Found : C, 72·6 ; H, 8·7. $C_{11}H_{16}O_2$ requires C, 73·3 ; H, 8·9%), was afforded by reduction as above of *p-tert.*-butoxy-benzoic acid. Preparation of this acid from *p*-nitroaniline involved *p*-fluoronitrobenzene, *p-tert.*-butoxynitrobenzene, *p-tert.*-butoxyaniline, *p-tert.*-butoxybenzonitrile, and *p-tert.*-butoxy-benzamide. *p*-Fluoronitrobenzene was prepared by an adaptation of the Schiemann reaction described by Flood :[22] *p*-nitroaniline (552 g.) was stirred into concentrated hydrochloric acid (383 c.c.), and the hydrochloride was separated, washed with ether, and dried ; a third of the hydrochloride (557 g.) was added to a stirred mixture of concentrated hydrochloric acid (330 c.c.) and water (270 c.c.) at <5°, and a solution of sodium nitrite (240 g.) in water (300 c.c.) was gradually added ; the temperature of the mixture was not allowed to exceed 7°, and the rest of the hydrochloride was then gradually added. When diazotisation was complete (starch–iodide) the mixture was cooled to 0° and ice-cold fluoroboric acid, prepared by gradual addition of boric acid (200 g.) to cold hydrofluoric acid (60% ; 430 g.) in a Polythene beaker, was added. The temperature of the mixture was kept below 10° by vigorous cooling and stirring. After 0·5 hr. the precipitate of *p*-nitrobenzenediazonium borofluoride was separated, washed successively with ice-cold water (160 c.c.), methanol (160 c.c.), and ether (180 c.c.), dried in a current of air, and decomposed by heat. The volatile products were thoroughly washed with 10% sodium hydroxide solution and afterwards with water, dried ($CaCl_2$), and fractionally distilled ; they gave *p*-fluoronitrobenzene[23] (120 g., 21·5%), b. p. 93—95°/20 mm., m. p. 26—27°. Subsequent

[13] Mastagli, *Ann. Chim. (France)*, 1938, **10**, 281.
[14] Kindler, *Arch. Pharm.*, 1927, **265**, 401.
[15] Nystrom and Brown, *J. Amer. Chem. Soc.*, 1947, **69**, 1197.
[16] Gattermann, *Ber.*, 1898, **31**, 1150 ; *Annalen*, 1907, **357**, 355.
[17] Quelet and Allard, *Compt. rend.*, 1937, **204**, 130 ; Quelet, Allard, Ducasse, and Germain, *Bull. Soc. chim. France*, 1937, **4**, 1092.
[18] Auwers and Markovits, *Ber.*, 1908, **41**, 2336.
[19] Von Braun, Michaelis, Fischer, and Murjahn, *Annalen*, 1933, **507**, 5.
[20] Gattermann, *Annalen*, 1907, **357**, 347.
[21] Bradley and Robinson, *J.*, 1926, 2361.
[22] Flood, *Org. Synth.*, Coll. Vol. II, p. 295.
[23] Schiemann and Pillarsky, *Ber.*, 1929, **62**, 3040.

preparations of this compound were simplified by using sodium fluoroborate (see Vogel [24]) in place of hydrofluoroboric acid. Our method of preparing *p-tert.*-butoxynitrobenzene was somewhat different from that of Bowden and Green [25] and gives slightly better yields. Potassium (33·6 g.) was dissolved in *dry tert.*-butyl alcohol (480 c.c.) at 80—90°, then cooled to 23°, and *p*-fluoronitrobenzene (120 g.) was quickly added. The mixture was vigorously shaken and set aside for 24 hr. at room temperature, then heated for 10 min. on the steam-bath; *tert.*-butyl alcohol was volatilised under reduced pressure and the residue was extracted with ether (4 × 150 c.c.). The extracts were washed with sodium hydroxide solution and with water, and dried (Na_2SO_4); they afforded *p-tert.*-butoxynitrobenzene as a pale-yellow liquid (116 g., 66%), b. p. 150—151°/11 mm. The product (110 g.) in 95% aqueous ethanol (440 c.c.) was stirred and boiled under reflux with iron powder (180 g.) and concentrated hydrochloric acid (44 c.c.) for 3 hr. Aqueous ethanol (1 : 19; 200 c.c.) was added, the mixture was cooled, made slightly alkaline by ammonia (*d* 0·88), and distilled with steam; the distillate was saturated with common salt and extracted with ether; concentration of the extracts gave *p-tert.*-butoxy-aniline [25] which recrystallised from light petroleum (b. p. 60—80°) in needles (73 g., 78%), m. p. 72—74° (Found : C, 72·6; H, 8·7; N, 8·7. Calc. for $C_{10}H_{15}ON$: C, 72·7; H, 9·1; N, 8·5%). This amine (72 g.) was converted into *p-tert.*-butoxybenzonitrile (28 g., 37%), b. p. 94—95°/0·8 mm., by the method described by Clark and Read.[26] A mixture of the nitrile (27 g.), 3% hydrogen peroxide solution (810 g.), and a 25% solution of potassium hydroxide (45 g.) was stirred and its temperature was slowly raised to 45°. Heating was discontinued and the mixture was stirred for 2 hr. and then kept at *ca.* 5° for 2 hr. The colourless precipitate of p-tert.-*butoxybenzamide* was separated and washed with water; it crystallised from hot water in needles (21 g., 70%), m. p. 134—135·5° (Found : C, 69·1; H, 7·7; N, 7·3. $C_{11}H_{15}O_2N$ requires C, 68·4; H, 7·8; N, 7·2%). A mixture of the amide (20 g.) and sodium hydroxide solution (200 c.c. of 4%) was boiled under reflux for 18 hr., cooled, extracted with ether, and carefully acidified with 2N-sulphuric acid. The precipitate of p-tert.-*butoxybenzoic acid* was separated and washed with water; it crystallised from aqueous ethanol in needles (19 g., 95%), m. p. 138—140° (Found : C, 68·0; H, 7·1%; equiv., 195. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·2%; equiv., 194).

5-Hydroxymethylcoumaran, b. p. 152—155°/8 mm. (Found : C, 71·8; H, 6·8. $C_9H_{10}O_2$ requires C, 72·0; H, 6·7%), was obtained in 51% yield by reduction of 5-formylcoumaran with lithium aluminium hydride; its *phenylurethane* separated from ligroin in needles, m. p. 88·5—89° (Found : C, 71·5; H, 5·9; N, 5·2. $C_{16}H_{15}O_3N$ requires C, 71·4; H, 5·6; N, 5·2%). Gattermann's reaction [16] was used in the preparation of *5-formylcoumaran*; this compound (9·9 g., 62%), b. p. 140—142°/8 mm. (Found : C, 72·9; H, 5·4. $C_9H_8O_2$ requires C, 73·0; H, 5·4%), was given by interaction of coumaran (13 g.), aluminium chloride (15 g.), anhydrous hydrogen cyanide (11·9 g.), and dry hydrogen chloride in sodium-dried benzene (15 c.c.); its *semicarbazone* separated from ethanol in needles, m. p. 211·5—212° (Found : C, 58·4; H, 5·1; N, 20·3. $C_{10}H_{11}O_2N_3$ requires C, 58·5; H, 5·4; N, 20·5%).

6-Hydroxymethylchroman, b. p. 159—160°/7 mm. (Found : C, 73·3; H, 7·2. $C_{10}H_{12}O_2$ requires C, 73·2; H, 7·3%), gave a *phenylurethane* as needles, m. p. 91·5—92° (Found : C, 72·2; H, 5·9; N, 5·2. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·0; N, 5·0%), from ligroin, and was obtained (68% of theory) by reduction of *6-formylchroman* as above; this aldehyde (60%), b. p. 152—155°/9 mm. (Found : C, 73·8; H, 6·1. $C_{10}H_{10}O_2$ requires C, 74·1; H, 6·2%), was prepared from chroman by the Gattermann reaction and gave a *semicarbazone* which separated from methanol in needles, m. p. 218—218·5° (decomp.) (Found : C, 60·0; H, 5·8; N, 19·0. $C_{11}H_{13}O_2N_3$ requires C, 60·3; H, 5·9; N, 19·2%).

7-Hydroxymethylhomochroman. A solution of aluminium chloride (13·0 g., 0·093 mole) and acetyl chloride (7·5 g., 0·096 mole) in ethylene chloride (20 c.c.) was gradually added to a stirred solution of homochroman (11·0 g., 0·074 mole) in ethylene chloride (50 c.c.) at <5°. After 30 min., the mixture was poured on ice and hydrochloric acid and afforded 7-acetylhomo-chroman [27] (12·9 g., 92%), b. p. 155—157°/5 mm., n_D^{15} 1·5642 (Found : C, 75·8; H, 7·8. Calc. for $C_{12}H_{14}O_2$: C, 75·8; H, 7·4%); the semicarbazone separated from ethanol in plates, m. p. 205—205·5° unchanged by further crystallisation (Cagniant [27] gives m. p. 215·5°). Hypochlorite oxidation of this ketone gave *homochroman-7-carboxylic acid* (92%) as needles, m. p. 165—165·5° (Found : C, 68·5; H, 6·6%; equiv., 193. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·3%;

[24] Vogel, " Practical Organic Chemistry," Longmans, Green & Co., London, 1948, p. 584.
[25] Bowden and Green, *J.*, 1954, 1795.
[26] Clarke and Read, *Org. Synth.*, Coll. Vol. I, 1941, p. 514.
[27] Cagniant, *Compt. rend.*, 1949, **229**, 889.

equiv., 192) after recrystallisation from aqueous ethanol; reduction of the ethyl ester by lithium aluminium hydride gave *7-hydroxymethylhomochroman* (78%), b. p. 128—129°/0·19 mm. (Found : C, 74·0; H, 7·7. $C_{11}H_{14}O_2$ requires C, 74·2; H, 7·9%) ; its *phenylurethane* crystallised from ligroin in needles, m. p. 83—83·5° (Found : N, 4·8. $C_{18}H_{19}O_3N$ requires N, 4·7%).

Rates of Bromination of the Ethers in Acetic Acid.—These rates were measured by the technique used by Robertson, de la Mare, and Johnston;[2] the times for 20% reaction with the ether (0·01M) and bromine (0·001M) in acetic acid at 20° and the relative rates are listed in Table 3. The solvent was purified by the procedure of Orton and Bradfield[28] and had m. p. 16·1°. After each measurement the product was examined for phenolic material; bromination only of *tert.*-butoxybenzene afforded such material and this difficulty was overcome by addition of an amount of anhydrous sodium acetate sufficient to react with hydrogen bromide produced by bromination. This addition increased (by *ca.* 30%) the rate of bromination of all the ethers except of *tert.*-butoxybenzene (here the addition effected a decrease of *ca.* 30% in the rate), and correction is made appropriately in the list of relative values. Each reaction was repeated several times.

Rates of Solvolysis of the Chloromethyl Derivatives.—A flask was charged with aqueous ethanol (1 : 10 v/v), fitted with a ground-in stopper, and brought to the temperature of the thermostat. Chloromethyl derivative, sufficient to provide an approx. 0·01M-solution of hydrogen chloride when reaction was complete, was added, and the mixture was shaken. At selected times, samples (10 c.c.) were pipetted into ice-cold acetone (120 c.c.) and titrated (to ethanolic lacmoid) with 0·01N-sodium hydroxide. Each reaction was repeated several times and at more than one temperature. The rate coefficients and other parameters of the Arrhenius equations are listed in Table 1. Ethanol used as solvent was purified as described by Lund and Bjerrum,[29] and acetone by boiling it for 6 hr. with potassium permanganate and potassium hydroxide and collecting the fraction of b. p. 57—58° under anhydrous conditions.

Ultraviolet Absorption Spectra of the Ethers in Hexane.—These were measured by means of a Hilger " Uvispek " photoelectric spectrophotometer. The solvent was purified as described by Graff *et al.*,[30] then shaken for 8 hr. with concentrated sulphuric acid (the acid was renewed after the first 4 hr.), washed with alkali and then with water, dried (K_2CO_3), and distilled (b. p. 66—67°) through a packed column in an all-glass apparatus. The values of $\lambda_{max.}$ and ε are listed in Table 4.

TABLE 4. *Ultraviolet absorption spectra of the ethers in hexane.*

	$\lambda_{max.}$			ε		
2 : 6-$C_6H_3Me_2$·OMe	2725	2680	2650	300	334	310
o-C_6H_4Me·OMe	2780	2720	2650 *	1768	1812	1245
PhOMe	2775	2710	2650	1475	1579	1125
PhOEt	2780	2710	2650	1815	1938	1340
PhOPr^i	2800	2730	2670	1700	1920	1360
PhOBu^t	2800	2700	2640	125	454	460
Coumaran	2890	2830	2740 *	3055	3095	2250
Chroman	2840	2760	2700 *	2520	2125	1500
Homochroman	2720	2670	2600 *	694	678	450

* Shoulder.

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[28] Orton and Bradfield, *J.*, 1927, 983.
[29] Lund and Bjerrum, *Ber.*, 1931, **64**, 210.
[30] Graff, O'Connor, and Skau, *Ind. Eng. Chem. Anal.*, 1944, **16**, 556.