

483. *Interdependence of Molecular Conformation and Conjugation in Aromatic Ethers. Part IV.**

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The ultraviolet absorption spectra and rates of bromination of veratrole and the diethers $\text{O}\cdot\text{C}_6\text{H}_4\cdot\text{O}\cdot[\text{CH}_2]_n$, *i.e.*, (III) where n is 1, 2, 3, and 5, and the rates of solvolysis of their chloromethyl derivatives in 90% aqueous ethanol have been determined and compared with the corresponding data for methyl *o*-tolyl ether and the ethers $\text{O}\cdot\text{CH}_2\cdot\text{C}_6\text{H}_4\cdot\text{O}\cdot[\text{CH}_2]_n$, *i.e.*, (I; X = H) where $n = 1, 2,$ and 3, and their chloromethyl derivatives. The order of decreasing reactivity for diethers is (IV) > (III; $n = 1$) > (III; $n = 2$) > (III; $n = 3$) whereas that for the monoethers is (I; $n = 1$) \gg (I; $n = 2$) \gg (II) \gg (I; $n = 3$). The differences between these two series are qualitatively interpreted by superimposing inductive effects caused by interaction of the oxygen atoms in the diethers (III) through the methylene chain which joins them and conformational effects provided by the size of the heterocycles.

In Part I,¹ the ultraviolet absorption spectra and rates of bromination of the ethers (I; X = H, $n = 1-3$) and the rates of unimolecular solvolysis of their chloromethyl derivatives (I; X = CH₂Cl) were compared with those of anisole and methyl *o*-tolyl ether (II; X = H) and their corresponding chloromethyl derivatives (see II; X = CH₂Cl). In brief, relative to methyl *o*-tolyl ether, coumaran and chroman were shown to be highly reactive while homochroman has a low reactivity. These differences were explained on the basis that the five- and six-membered heterocycles in (I; $n = 1$ and 2, respectively) enforce a degree of coplanarity and near-coplanarity of the ether group and the benzene ring which is greater than that in methyl *o*-tolyl ether, while the seven-membered heterocycle in (I; $n = 3$) has the opposite effect. Similar conformational effects must be expected to influence the absorption spectra and rates of bromination of the diethers (III; X = H, $n = 1-3$) and the rates of solvolysis of their chloromethyl derivatives (III; X = CH₂Cl). The corresponding data for veratrole and its chloromethyl derivative (IV; X = H and CH₂Cl, respectively) are the appropriate basis for the comparison which is now provided. The data for 3,9-dioxa-1,2-benzocyclonene (III; $n = 5$) are also included.

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

No.	Substituents	$10^4 k_{0,0}$ (min. ⁻¹)	$10^4 k_{25,0}$ (min. ⁻¹)	$10^4 k_{45,0}$ (min. ⁻¹)	E (kcal./mole)	$10^{-11} A$ (min. ⁻¹)
1	3,4-(MeO) ₂	12.6	255		19.6	46.6
2	3,4-O·CH ₂ ·O		42.4	352	20.1	17.3
3	3,4-O·[CH ₂] ₂ ·O		24.3	212	20.5	21.8
4	3,4-O·[CH ₂] ₃ ·O		4.18	37.2	20.7	5.2
5	3,4-O·[CH ₂] ₅ ·O		29.3	243	20.0	8.7

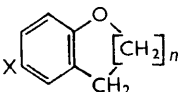
The rate coefficients for the unimolecular solvolysis of the chloromethyl derivatives in 90% aqueous ethanol (see Part I) are listed in Table I, while Table 2 provides a comparison of these solvolyses with those of the chloromethyl derivatives of the monoethers (I; X = CH₂Cl).

* Part III, *J.*, 1958, 4665.

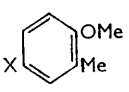
¹ Baddeley, Smith, and Vickars, *J.*, 1956, 2455.

TABLE 2. Comparison of energies of activation and rates of solvolysis at 25° of the chlorides (I, II, III, and IV; X = CH₂Cl).

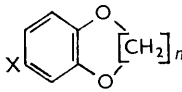
Chlorides (III) and (IV) (X = CH ₂ Cl)	10 ⁴ k _{25.0} ^o (min. ⁻¹)	E (kcal./mole)	E (kcal./mole)	10 ⁴ k _{25.0} ^o (min. ⁻¹)	Chlorides (I) and (II) (X = CH ₂ Cl)
(IV)	255	19.6	19.6	510	(II)
(III; n = 1)	42.4	20.1	17.3	3630	(I; n = 1)
(III; n = 2)	24.3	20.5	18.8	1060	(I; n = 2)
(III; n = 3)	4.18	20.7	21.0	18.5	(I; n = 3)
(III; n = 5)	29.3	20.0	20.6	130	p-MeO·C ₆ H ₄ ·CH ₂ Cl



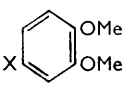
(I)



(II)



(III)



(IV)

The comparison of the solvolyses of the chloromethyl derivatives of the diethers (III; $n = 1-3$) with those of the monoethers (I; $n = 1-3$) shows that while reactivity in both series falls with increase in n , in accordance with the expected influence of change in the value of n on the conformational relation of ether group to benzene ring, the fall (as 10 : 6 : 1) in the former series is much less than that (195 : 57 : 1) in the latter. Further, whereas the chloromethyl derivatives of the monoethers (I; $n = 1$ and 2) are more reactive than the chloromethyl derivative of methyl *o*-tolyl ether (II) by factors of 7 and 2, respectively, those of the diethers (III; $n = 1$ and 2) are less reactive than that of veratrole (IV) by factors of 6 and 10.5, respectively. Similar differences between the two series, shown by the relative rates of bromination which, together with the wavelengths and extinction coefficients for the middle of the three peaks in the region 2500–3000 Å, are listed in Table 3:

TABLE 3. Comparison of the ultraviolet absorption spectra and relative rates of bromination of the ethers (I, II, III, and IV; X = H).

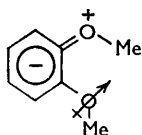
Diethers (III) and (IV) (X = H)	$k_{rel.}$	λ	ϵ	ϵ	λ	$k_{rel.}$	Ethers (I) and (II) (X = H)
(IV)	1.31	2770	2336	1810	2720	1.00	(II)
(III; n = 1)	0.0178	2840	3122	3090	2810	13.7	(I; n = 1)
(III; n = 2)	0.0169	2780	2340	2125	2760	4.9	(I; n = 2)
(III; n = 3)	0.00746	2750	1360	678	2670	0.219	(I; n = 3)
(III; n = 5)	6.8	2750	1322	1575	2710	0.148	C ₆ H ₅ ·OMe

In both series, change of n from 1 to 2 to 3 decreases the rate of bromination, but whereas this change in n in the series of monoethers (I) provides a rate ratio of 62 : 22 : 1, in the diethers (III) it gives only 2.4 : 2.3 : 1. Again, whereas the ethers (I; $n = 1$ and 2) are *more* reactive than methyl *o*-tolyl ether by factors 13.7 and 4.9, respectively, the diethers (III; $n = 1$ and 2) are *less* reactive than veratrole by factors of 74 and 77, respectively. These differences in variation in chemical reactivity in the two series can be qualitatively interpreted in terms of inductive interaction of the oxygen atoms in the diethers through the methylene group or groups which bridge them. This inductive interaction in the compounds (III), which is greatest when n is 1 and decreases rapidly with increase in n to 2 and 3, opposes electromeric release of electrons from ether oxygen atom to benzene ring and thereby hinders bromination of the diethers (III; X = H) and unimolecular solvolysis of their chloromethyl derivatives. Thus, whereas conformational differences alone would provide relative reactivities similar to those observed for the ethers (I and II) and their chloromethyl derivatives, *i.e.*, (III; $n = 1$) \gg (III; $n = 2$) \gg (IV) \gg (III; $n = 3$), the inductive interaction alone would give (IV) > (III; $n = 3$) > (III; $n = 2$) \gg (III; $n = 1$). The observed sequence of reactivities (IV) > (III; $n = 1$) > (III;

$n = 2$) > (III; $n = 3$) can, therefore, be qualitatively interpreted by superimposing these conformational and inductive effects. Part V will be concerned with measuring these inductive effects and will enable the conformational influences in the diethers (III) to be compared with those in the ethers (I).

A decrease in conjugation results in a shorter wavelength and a smaller coefficient of absorption. Thus the spectroscopic data in Table 3 show the conformational influences on conjugation in the diethers to be similar to those in the monoethers. Compounds (I and III; $n = 2$) have very similar absorption bands, $\lambda = 2760$ and 2780 ($\epsilon = 2125$ and 2340 , respectively). In each series of compounds, the change in the value of n from 2 to 1 increases, and by about the same amount in each series, both the wavelength and extinction coefficient of absorption while the change of n from 2 to 3 lowers both the wavelength and coefficient of absorption. This fall in the value of λ and ϵ for the monoethers is, however, greater than that for the diethers.

In conclusion it should be remarked that the data now provided (see Tables 2 and 3) show veratrole to be nine times more reactive than anisole in bromination, and its chloromethyl derivative to be twice as reactive as 4-methoxybenzyl chloride in solvolysis. Since a *meta*-methoxyl group withdraws electrons, *e.g.*, 3-methoxy- α -dimethylbenzyl chloride in 90% aqueous acetone at 25° is solvolysed only half as readily as isopropyl chloride,² the present comparison is best explained by the assumption we made in 1951³ that a 3-methoxyl group facilitates electron release from a 4-methoxyl group by a process of electrostatic interaction (see V) which other authors, concerned with other anomalies, have called (V) "built-in solvation." In our instance it requires the methyl group of the 3-methoxyl group to be oriented away from the 4-methoxyl group. This conformational relationship of the two ether groups is possible also in the heterocyclic diether (III; $n = 5$) and may be the cause of the unexpectedly high reactivity of this diether and of its chloromethyl derivative in the bromination and solvolysis, respectively.



(V) "built-in solvation." In our instance it requires the methyl group of the 3-methoxyl group to be oriented away from the 4-methoxyl

EXPERIMENTAL

Diethers.—Veratrole, m. p. $22.0-22.5^\circ$,⁴ 1,3-dioxaindane,⁵ b. p. $172-173^\circ$, 1,4-dioxatetralin,⁶ b. p. $82-83^\circ/6$ mm., 3,7-dioxa-1,2-benzocycloheptene,⁷ b. p. $107-108^\circ/15$ mm. (Found: C, 72.0; H, 6.8. Calc. for $C_9H_{10}O_2$: C, 72.0; H, 6.7%), and 3,9-dioxa-1,2-benzocyclononene,⁷ b. p. $119-120^\circ/9$ mm., were prepared and purified as previously described.

Hydroxymethyl Derivatives from the Diethers.—3,4-Dimethoxybenzyl alcohol,⁸ b. p. $165-168^\circ/9$ mm. (phenylurethane,⁹ m. p. $117-118^\circ$), and 3,4-methylenedioxybenzyl alcohol,¹⁰ m. p. $52.0-52.5^\circ$, were prepared as previously described. 3,4-Dimethylenedioxybenzyl alcohol, b. p. $165-167^\circ/8$ mm. (Found: C, 65.5; H, 6.1. $C_9H_{10}O_3$ requires C, 65.1; H, 6.0%) [*phenylurethane* from ligroin in needles, m. p. $74-74.5^\circ$ (Found: C, 67.4; H, 5.1; N, 5.2. $C_{16}H_{15}NO_4$ requires C, 67.4; H, 5.3; N, 4.9%)], was obtained in 90% yield by the reduction with lithium aluminum hydride of 3,4-dimethylenedioxybenzaldehyde,⁶ m. p. $50-51^\circ$ [*semicarbazone* from ethanol in plates, m. p. $215-215.5^\circ$ (Found: C, 54.0; H, 5.0; N, 18.7. $C_{10}H_{11}N_3O_3$ requires C, 54.3; H, 5.0; N, 19.0%)].

3,4-Trimethylenedioxybenzyl alcohol, b. p. $146-148^\circ/0.11$ mm. (Found: C, 66.9; H, 6.6. $C_{10}H_{12}O_3$ requires C, 66.7; H, 6.7%) [*phenylurethane* from ligroin in needles, m. p. $91-91.5^\circ$ (Found: C, 68.4; H, 5.5; N, 4.7. $C_{17}H_{17}NO_4$ requires C, 68.2; H, 5.7; N, 4.7%)], was similarly obtained from 3,4-trimethylenedioxybenzaldehyde. This compound, b. p. $127-129^\circ/0.25$

² Brown, "Steric effects in conjugated systems," Ed. Gray, Butterworths, London, 1958, p. 100.

³ Baddeley, Holt, Smith, and Whittaker, *Nature*, 1951, **168**, 386.

⁴ Openshaw, "Laboratory Manual of Organic Analysis," Cambridge, 1948, p. 31.

⁵ Perkin, Robinson, and Thomas, *J.*, 1909, **95**, 1979.

⁶ Gattermann, *Annalen*, 1907, **357**, 373.

⁷ Ziegler, Lüttringhaus, and Wohlgemuth, *Annalen*, 1937, **528**, 162.

⁸ Davidson and Bogert, *J. Amer. Chem. Soc.*, 1935, **57**, 905.

⁹ Tiffeneau, *Bull. Soc. Chim. France*, 1911, **9**, 929.

¹⁰ Barger, *J.*, 1908, **93**, 567.

mm. [*semicarbazone* from methanol in needles, m. p. 183—184° (Found: C, 56.4; H, 5.5; N, 17.8. $C_{11}H_{13}N_3O_3$ requires C, 56.2; H, 5.5; N, 17.9%)], was prepared from 3,7-dioxa-1,2-benzocycloheptene by Gattermann's method.¹¹

3,4-Pentamethylenedioxybenzyl alcohol. 3,9-Dioxa-1,2-benzocyclononene (11 g.) in ethylene chloride (80 ml.) was gradually added to a cold (−7°) solution of acetyl chloride (9.8 g.) and aluminium chloride (8.5 g.) in ethylene chloride (20 ml.). The mixture was poured on ice and hydrochloric acid; the organic layer was separated, washed with water, 2*N*-sodium hydroxide solution, and again with water, and dried (K_2CO_3). Distillation gave 11-*acetyl-3,9-dioxa-1,2-benzocyclononene* (10 g.), b. p. 139—140°/0.13 mm. (Found: C, 70.7; H, 7.2. $C_{13}H_{16}O_3$ requires C, 70.9; H, 7.3%) [*semicarbazone* from ethanol in needles, m. p. 198—198.5° (Found: C, 60.2; H, 6.5; N, 15.5. $C_{14}H_{19}N_3O_3$ requires C, 60.6; H, 6.9; N, 15.2%)]. The oxidation of this ketone (16 g.) with alkaline hypochlorite gave 3,9-*dioxa-1,2-benzocyclononene-11-carboxylic acid* (15.5 g.) which separated from aqueous ethanol in needles, m. p. 138—138.5° (Found: C, 64.6; H, 6.4%; equiv., 223. $C_{12}H_{14}O_4$ requires C, 64.9; H, 6.3%; equiv., 222). The ethyl ester, obtained from the acid (15 g.) by the action of ethanolic hydrogen chloride, was reduced by lithium aluminium hydride (3 g.) and gave the required *benzyl alcohol* (12.2 g.), b. p. 154—156°/0.26 mm. (Found: C, 68.8; H, 7.7. $C_{12}H_{16}O_3$ requires C, 69.2; H, 7.7%) [α -*naphthylurethane* from ligroin in slender needles, m. p. 86.5—87° (Found: N, 3.7. $C_{23}H_{23}NO_4$ requires N, 3.7%)].

Chloromethyl Derivatives from the Diethers.—The following chlorides were prepared from the hydroxymethyl compounds as previously described;¹ 3,4-dimethoxybenzyl chloride,¹² m. p. 50—50.5° (Found: Cl, 18.8. Calc. for $C_9H_{11}O_2Cl$: Cl, 19.0%); 3,4-methylenedioxybenzyl chloride,¹³ m. p. 23—23.5° (Found: Cl, 20.1. Calc. for $C_8H_7ClO_2$: Cl, 20.8%); 3,4-dimethylenedioxybenzyl chloride, b. p. 124—125°/0.07 mm. (Found: C, 58.3; H, 4.8; Cl, 19.2. $C_9H_9ClO_2$ requires C, 58.5; H, 4.9; Cl, 19.2%); 3,4-trimethylenedioxybenzyl chloride, b. p. 128°/0.11 mm. (Found: C, 60.8; H, 5.7; Cl, 17.7. $C_{10}H_{11}ClO_2$ requires C, 60.5; H, 5.5; Cl, 17.9%); and 3,4-pentamethylenedioxybenzyl chloride, b. p. 143°/0.35 mm. (Found: C, 63.6; H, 6.8; Cl, 15.3. $C_{12}H_{13}ClO_2$ requires C, 63.6; H, 6.6; Cl, 15.7%).

The rates of bromination of the diethers in acetic acid, the rates of solvolysis of the chloromethyl derivatives in 90% aqueous ethanol, and the ultraviolet absorption spectra of the ethers in hexane were measured by the techniques previously described.¹

The kinetic data are listed in Tables 1, 2, and 3, and the values of λ_{max} and ϵ in Table 4.

TABLE 4. Ultraviolet absorption spectra of the diethers in hexane.

	λ_{max}		ϵ			
Veratrole.....	2830	2770	2730	1780	2336	2264
1,3-Dioxaindane.....	2900	2840	2800	2328	3122	2992
1,4-Dioxatetralin.....	2840	2780	2750 *	2384	2340	
3,7-Dioxa-1,2-benzocycloheptene.....	2810 *	2750	2690 *		1360	
3,9-Dioxa-1,2-benzocyclononene.....	2810 *	2750	2700		1322	1318

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¹¹ Gattermann, *Ber.*, 1898, **31**, 1150.

¹² Decker and Pschorr, *Ber.*, 1904, **37**, 3404.

¹³ Decker and Koch, *Ber.*, 1905, **38**, 1741.