

**142.** *Interdependence of Molecular Conformation and Conjugation in Aromatic Ethers. Part V.*<sup>1</sup>

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The influence of the inductive interaction of the oxygen atoms on the rates of bromination of the series of diethers (III and IV; X = H) and of the unimolecular solvolysis of their bischloromethyl derivatives (X = CH<sub>2</sub>Cl) has been measured. The interaction through one methylene group ( $n = 1$ ) lowers the reactivity in bromination and solvolysis, as measured by  $\log k$ , by 2 units, and each additional methylene group reduces the interaction by a factor of 0.316.

IN Part I,<sup>2</sup> conformational differences caused by a change in the value of  $n$  were shown to explain the relative rates of bromination of the ethers (I; X = H) and of unimolecular solvolysis of their chloromethyl derivatives (I; X = CH<sub>2</sub>Cl) in the order  $n = 1 \gg 2 \gg 3$ . Similar conformational differences are expected among the diethers (II; X = H) and their chloromethyl derivatives (II; X = CH<sub>2</sub>Cl) but, as shown in Part IV,<sup>1</sup> though the rates of bromination and solvolysis decrease in the order  $n = 1 > 2 > 3$ , a change in the value of  $n$  has much less effect on the chemical reactivity. This diversity was qualitatively interpreted in terms of inductive interaction of the oxygen atoms through the methylene group or groups which bridge them in compounds (II). This interaction, which is greatest when  $n = 1$  and decreases with increase in the value of  $n$ , opposes electromeric release

<sup>1</sup> Part IV, Baddeley and Smith, *J.*, 1961, 2516.

<sup>2</sup> Baddeley, Smith, and Vickers, *J.*, 1956, 2455.

of electrons from the ether-oxygen atom to the benzene ring and thereby hinders bromination of the diethers (II; X = H) and solvolysis of their chloromethyl derivatives. Thus, with respect to these reactions, the inductive interaction of the oxygen atoms partly neutralises the chemical consequences of conformational differences. To obviate this complication, the properties of the diethers (III; X = H) and their chloromethyl derivatives (X = CH<sub>2</sub>Cl), which are expected to be unaffected conformationally by a change

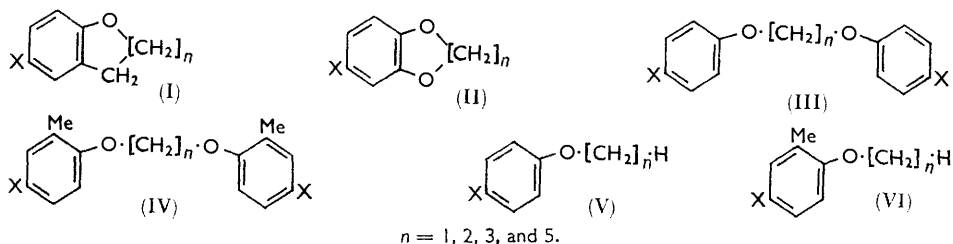


TABLE 1.

Comparison of the ultraviolet absorption spectra of the diethers (III and IV; X = H) and the ethers (V and VI; X = H).

<i>n</i>	Diether (III)		Ether (V)		Diether (IV)		Ether (VI)	
	$\nu_{\max.}$ (cm. <sup>-1</sup> )	$\epsilon/2$	$\nu_{\max.}$ (cm. <sup>-1</sup> )	$\epsilon$	$\nu_{\max.}$ (cm. <sup>-1</sup> )	$\epsilon/2$	$\nu_{\max.}$ (cm. <sup>-1</sup> )	$\epsilon$
1	37,400	1165	36,900	1575	37,200	1392	36,800	1810
2	37,000	1840	36,900	1940	36,800	2050	36,800	1740
3	36,900	2205	36,800	1890	36,800	2060	—	—
5	36,900	2400	—	—	36,800	2320	—	—

in *n*, have been compared amongst themselves and with those of the corresponding monoethers (V; X = H) and their chloromethyl derivatives. The corresponding compounds (IV) and (VI) derived from *o*-cresol are included in the comparison.

The frequencies and extinction coefficients of the major ultraviolet absorption bands of the diethers and ethers are listed in Table 1. They show that the inductive interaction of the oxygen atoms of the diethers increases the frequency of the absorption significantly only when *n* = 1. Further, when *n* = 1, the absorption by an aryloxy-group in the diethers (III) and (IV) is significantly lower than that by an aryloxy-group in the corresponding ethers (V and VI, respectively). The extinction coefficients for the diethers, however, increase continuously with increase in the value of *n*, so that the absorption by the diethers soon exceeds twice that by the corresponding ethers.

The relative rates of bromination of these compounds in glacial acetic acid (Br<sub>2</sub>, M/1000) at 20.0° are listed in Table 2. The diethers were used in only half the concentration of

TABLE 2.

Rates ( $k_{\text{rel.}}$ ) of bromination of the ethers and diethers, relative to that of anisole, in glacial acetic acid at 20.0°.

<i>n</i>	(III; X = H)	(V; X = H)	(IV; X = H)	(VI; X = H)
1	0.0120	1.00	0.064	6.40
2	0.370	3.70	2.03	19.0
3	0.90	3.40	5.00	—
5	1.37	—	7.50	—
∞	(1.44)	—	(7.87)	—

the ethers, and all solutions had the aryloxy-group at the same initial concentration (M/100).

The relative rates are derived from the time intervals for 20% consumption of bromine, and very little diether (<5%) is therefore involved in the measurements; consequently,

the possible effect of bromination at one end of the diether molecule on the rate of bromination at the other does not affect the comparison.

A comparison of the rates for the series of compounds (IV) and (VI) with those for the series of compounds (III) and (V) respectively shows that a methyl group *ortho* to the ether group increases the rate about five times, and that the rates for the diethers are significantly lower than those for the corresponding ethers even when, with  $n = 5$ , the inductive interaction of the oxygen atoms of the diethers is not expected to be appreciable. The way in which the rates for the diethers increase with increase in the value of  $n$  indicates that in the limit, represented by  $n = \infty$ , the rates would be about 5% higher than those for  $n = 5$ ; these estimated rates for  $n = \infty$  are given in Table 3. When the relative reactivities of the diethers in the bromination are represented by  $\log k$ , the lowering of the reactivities by the inductive interaction of the oxygen atoms is given by  $\log k/k_\infty$  (see Table 3). Measured thus, the interaction for a given value of  $n$  is the same for

TABLE 3.

Connection between the rates of bromination ( $k$ ) of the diethers and the number of methylene groups ( $n$ ) separating the ether-oxygen atoms.

$n$	(III; X = H)		(IV; X = H)	
	$\log k/k_\infty$	$[\log (k/k_\infty)]/10^{(5-n)/2}$	$\log k/k_\infty$	$[\log (k/k_\infty)]/10^{(5-n)/2}$
1	-2.08	-0.021	-2.09	-0.021
2	-0.590	-0.019	-0.588	-0.019
3	-0.204	-0.020	-0.197	-0.020
5	-0.021	-0.021	-0.021	-0.021

the diethers (IV) as for the diethers (III). Further, the interaction through one methylene group lowers the reactivity by about 2 (a rate factor of 100), and each additional methylene group reduces the interaction by a factor of  $10^{-1}$ . Thus, as shown in Table 3, the values of  $[\log (k/k_\infty)]/10^{(5-n)/2}$  are almost independent of the value of  $n$ . As shown below, these conclusions apply also to the solvolytic data for the dichlorides (III; X = CH<sub>2</sub>Cl) and (IV; X = CH<sub>2</sub>Cl).

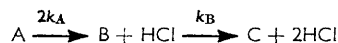
The solvolyses of the dichlorides in 90% aqueous ethanol gave, as illustrated in Table 4, two equivalents of hydrogen chloride and satisfactory rate coefficients ( $k$ ) for overall unimolecular solvolysis; *i.e.*,  $k(t - t_0) = \ln[(T_\infty - T_0)/(T_\infty - T)]$ . These reactions, which must be expected to occur in two steps, can be represented by the following scheme in

TABLE 4.

Rate of formation of hydrogen chloride by solvolysis of the dichloride (IV;  $n = 2$ , X = CH<sub>2</sub>Cl) (0.0005M) in 90% aqueous ethanol (50 ml.) at 0.0°.

Time ( $t$ ) (hr.)	0	2	4	7	10.5	24	29
Titre ( $T$ ) (ml. of 0.01N-NaOH)	0.16( $T_0$ )	0.47	0.77	1.16	1.56	2.78	3.13
$10^4 k$ (min. <sup>-1</sup> )	—	5.56	5.65	5.55	5.46	5.47	5.53
Time (hr.)	34	47	54	60	74	$\infty$	
Titre (ml. of 0.01N-NaOH)	3.38	3.95	4.15	4.29	4.54	4.96( $T_\infty$ )	
$10^4 k$ (min. <sup>-1</sup> )	5.44	5.52	5.48	5.46	5.48	—	

which the dichloride (A) gives chloride (B) by solvolysis of one of its two equivalent chloromethyl groups, and then (B) gives (C) by solvolysis of the other chloromethyl group:



If the rates of these two steps are denoted by  $-d[A]/dt = 2k_A[A]$  and  $d[C]/dt = k_B[B]$ , respectively, the amount of hydrogen chloride at time  $t$  after the commencement of the reaction is given by the following equation in which  $A_0$  represents the initial amount of the dichloride:

$$[\text{HCl}]/A_0 = T/0.5T_\infty = 2(1 - e^{-2k_A t}) + (e^{-2k_A t} - e^{-k_B t})2k_A/(2k_A - k_B)$$

This equation gives  $\frac{1}{T} \ln [T_\infty / (T_\infty - T)] = \text{Constant}$  for the three cases tabulated below:

Case	$T/0.5T_\infty$	$\frac{1}{T} \ln [T_\infty / (T_\infty - T)]$
(a) $k_B \gg k_A$ .....	$2(1 - e^{-2k_A t})$	$2k_A$
(b) $k_B \sim k_A$ .....	$2(1 - e^{-k_A t})$	$k_A$
(c) $k_B = 0$ .....	$1 - e^{-2k_A t}$	$2k_A$

Case (c) is excluded since the solvolyses of the dichlorides provide two equivalents of hydrogen chloride. The data do not differentiate between cases (a) and (b) but, since the reacting ends of the molecules are separated from one another by two phenyl groups, two ether-oxygen atoms, and 2—5 methylene groups, change from  $\text{CH}_2\text{Cl}$  to  $\text{CH}_2\cdot\text{OH}$  or  $\text{CH}_2\cdot\text{OEt}$  at one end of the molecule is unlikely greatly to facilitate solvolysis at the other. We conclude, therefore, that  $k_B \approx k_A$  and that the difference between them cannot be calculated from our results.

The rate coefficients are listed in Table 5. The instability of the diethers (III and IV;

TABLE 5.  
Constants of the Arrhenius equation,  $k = A \exp(-E/RT)$ , for the formation of hydrogen chloride by the solvolysis of the chlorides in 90% aqueous ethanol.

No.	$10^4 k_0$ (min. <sup>-1</sup> )	$10^4 k_{25}$ (min. <sup>-1</sup> )	$E$ (kcal./mole)	$10^{-11} A$ (min. <sup>-1</sup> )
1	—	(0.56)	—	—
2	0.417	15.9	23.7	2951
3	1.33	42.8	22.5	1547
4	2.32	67.3	21.8	533
5	—	(5.4)	—	—
6	5.48	172	22.5	4470
7	14.8	386	21.3	1330
8	26.5	644	20.7	814
9	5.28	125	20.6	124
10	8.21	187	20.3	122
11	7.10	164	20.4	125
12	25.0	511	19.7	107
13	47.5	915	19.3	110

$n = 1$ ) towards acidic reagents precluded the preparation of their chloromethyl derivatives. A comparison of the rates for the dichlorides Nos. 2—4 and 6—8 shows that a methyl group *ortho* to the ether group increases the rate about ten-fold; in the chlorides Nos. 12 and 13 (cf. Nos. 9—11) the *o*-methyl group causes only a five-fold increase in the rate. The way in which the rates for the dichlorides increase with increase in the value of  $n$  indicates that in the limit,  $n = \infty$ , the rates at 25° would be about 5% higher than those for  $n = 5$ . If the reactivities of the dichlorides are denoted by  $\log k_n$ , the lowering of the reactivities by the inductive interaction of the oxygen atoms is given by  $\log (k_n/k_\infty)$  (see Table 6). The data, thus assembled, show the rates of bromination of the diethers and

TABLE 6.  
Connection between the rates of solvolysis ( $k_{25}$ ) of the dichlorides Nos. 1—8 and the number of methylene groups ( $n$ ) separating the ether-oxygen atoms.

$n$	(III; X = $\text{CH}_2\text{Cl}$ )		(IV; X = $\text{CH}_2\text{Cl}$ )	
	$\log (k_n/k_\infty)$	$[\log (k_n/k_\infty)]/10^{(5-n)/2}$	$\log (k_n/k_\infty)$	$[\log (k_n/k_\infty)]/10^{(5-n)/2}$
1	(-2.10)	(-0.021)	(-2.097)	(-0.021)
2	-0.648	-0.021	-0.573	-0.018
3	-0.218	-0.022	-0.243	-0.024
5	-0.021	-0.021	-0.020	-0.020

the rates of unimolecular solvolysis of the dichlorides to be remarkably similar in their dependence on the value of  $n$ ; had the dichlorides Nos. 1 and 5 of Table 5 been available

they would have been expected to provide the rate constants shown in parentheses in this Table.

## EXPERIMENTAL

*Materials.*—The following diethers were prepared and purified by processes described previously: methylene glycol diphenyl ether,<sup>3</sup> m. p. 14.5° [*dibromo-derivative* (from light petroleum), needles, m. p. 74—76° (Found: C, 44.0; H, 2.8; Br, 44.4. C<sub>13</sub>H<sub>10</sub>Br<sub>2</sub>O<sub>2</sub> requires C, 43.6; H, 2.8; Br, 44.8%); ethylene glycol diphenyl ether,<sup>4</sup> m. p. 96—97°; trimethylene glycol diphenyl ether,<sup>5</sup> m. p. 60—61.5°; and pentamethylene glycol diphenyl ethers<sup>6</sup> m. p. 46—47°; and methylene glycol di-*o*-tolyl ether,<sup>7</sup> m. p. 30—31°; ethylene glycol di-*o*-tolyl ether,<sup>8</sup> m. p. 83—84°; and trimethylene glycol di-*o*-tolyl ether,<sup>9</sup> m. p. 30° (Found: C, 79.3; H, 7.6. Calc. for C<sub>17</sub>H<sub>20</sub>O<sub>2</sub>: C, 79.7; H, 7.8%); *pentamethylene glycol di-*o*-tolyl ether*, b. p. 152—154°/0.08 mm. (Found: C, 80.0; H, 8.2. C<sub>19</sub>H<sub>24</sub>O<sub>2</sub> requires C, 80.3; H, 8.4%) [*dibromo-derivative* (from light petroleum) needles, m. p. 69—71 (Found: C, 51.9; H, 5.2; Br, 35.9. C<sub>19</sub>H<sub>22</sub>Br<sub>2</sub>O<sub>2</sub> requires C, 51.6; H, 5.0; Br, 36.2%)].

All but two of the above diethers reacted in benzene with hydrogen cyanide in the presence of aluminium chloride as described by Gattermann.<sup>9</sup> They gave the 4,4'-ethylene-<sup>9</sup> m. p. 119—120° [dianil<sup>9</sup> (from benzene), plates, m. p. 185—186°], 4,4'-trimethylene-<sup>9</sup> m. p. 135—136° (dioxime,<sup>9</sup> m. p. 152—153°), and 4,4'-pentamethylene-dioxydibenzaldehyde, needles (from light petroleum), m. p. 94—95° (Found: C, 73.4; H, 6.2. C<sub>19</sub>H<sub>20</sub>O<sub>4</sub> requires C, 73.1; H, 6.4%) [*dioxime* (from ethanol), needles m. p. 156—158° (Found: N, 7.9. C<sub>19</sub>H<sub>22</sub>N<sub>2</sub>O<sub>4</sub> requires N, 8.2%)], and corresponding 2,2'-dimethyl derivatives, m. p. 191—192° (ref. 9), m. p. 114—115° (ref. 9) [*dioxime* (from ethanol), needles, m. p. 183—184° (Found: N, 8.0. C<sub>19</sub>H<sub>22</sub>O<sub>4</sub>N<sub>2</sub> requires N, 8.2%)], and 76—78° (rosettes from ligroin) (Found: C, 74.3; H, 7.0. C<sub>21</sub>H<sub>24</sub>O<sub>4</sub> requires C, 74.1; H, 7.1%) [*dioxime* (from ethanol), needles, m. p. 168—170° (Found: C, 68.1; H, 7.0; N, 7.1. C<sub>21</sub>H<sub>26</sub>O<sub>4</sub>N<sub>2</sub> requires C, 68.1; H, 7.0; N, 7.6%)], respectively. 4,4'-Methylene-dioxydibenzaldehyde, needles m. p. 85—86° (Found: C, 70.7; H, 4.7. C<sub>15</sub>H<sub>12</sub>O<sub>4</sub> requires C, 70.3; H, 4.7%) [*dioxime* (from ethanol), needles m. p. 176—178° (Found: N, 9.6. C<sub>15</sub>H<sub>14</sub>O<sub>4</sub>N<sub>2</sub> requires N, 9.8%)], and its 2,2'-dimethyl derivative, needles, m. p. 148—155° (from ligroin) (Found: C, 71.8; H, 5.6. C<sub>17</sub>H<sub>16</sub>O<sub>4</sub> requires C, 71.8; H, 5.6%) [*dioxime* (from ethanol), needles, m. p. 195—197° (Found: C, 64.5; H, 5.7; N, 8.3. C<sub>17</sub>H<sub>18</sub>O<sub>4</sub>N<sub>2</sub> requires C, 65.0; H, 5.7; N, 8.9%)], were obtained by the Williamson synthesis.

The dialdehydes with lithium aluminium hydride in tetrahydrofuran gave the *di*-(*p*-hydroxymethylphenyl ether) of (a) methylene glycol, needles (from ethanol), m. p. 121—122° (Found: C, 68.9; H, 6.2. C<sub>15</sub>H<sub>16</sub>O<sub>4</sub> requires C, 69.2; H, 6.2%) [*bisphenylurethane* (from ethylene chloride), needles, m. p. 193—194° (Found: N, 5.7. C<sub>29</sub>H<sub>26</sub>O<sub>6</sub>N<sub>2</sub> requires N, 5.6%)], (b) ethylene glycol, needles (from ethanol), m. p. 170—171° (Found: C, 70.1; H, 6.7. C<sub>16</sub>H<sub>18</sub>O<sub>4</sub> requires C, 70.1; H, 6.6%) [*bisphenylurethane* (from ethylene chloride), needles, m. p. 201—203° (Found: N, 5.5. C<sub>30</sub>H<sub>28</sub>O<sub>6</sub>N<sub>2</sub> requires N, 5.5%)], (c) trimethylene glycol, needles (from ligroin), m. p. 145—146° (Found: C, 70.6; H, 6.8. C<sub>17</sub>H<sub>20</sub>O<sub>4</sub> requires C, 70.8; H, 6.9%) [*bisphenylurethane*, m. p. 197—198° (Found: N, 5.2. C<sub>31</sub>H<sub>30</sub>O<sub>6</sub>N<sub>2</sub> requires N, 5.3%)], and (d) pentamethylene glycol, needles (from ligroin), m. p. 122—123° (Found: C, 72.0; H, 7.4. C<sub>19</sub>H<sub>24</sub>O<sub>4</sub> requires C, 72.1; H, 7.6%) [*bisphenylurethane*, m. p. 166—167° (Found: N, 5.2. C<sub>33</sub>H<sub>34</sub>O<sub>6</sub>N<sub>2</sub> requires N, 5.1%)], and the corresponding *di*-(4-hydroxymethyl-2-methylphenyl) ethers, (a) m. p. 121—122° (Found: C, 70.7; H, 7.0. C<sub>17</sub>H<sub>20</sub>O<sub>4</sub> requires C, 70.8; H, 6.9%) [*bisphenylurethane*, m. p. 195—196° (Found: N, 5.1. C<sub>31</sub>H<sub>30</sub>O<sub>6</sub>N<sub>2</sub> requires N, 5.3%)], (b) m. p. 129—130° (Found: C, 71.0; H, 7.0. C<sub>18</sub>H<sub>22</sub>O<sub>4</sub> requires C, 71.5; H, 7.3%) [*bisphenylurethane*, m. p. 199—201° (Found: N, 5.1. C<sub>32</sub>H<sub>32</sub>O<sub>6</sub>N<sub>2</sub> requires N, 5.2%)], (c) m. p. 130—132° (Found: C, 71.9; H, 7.7. C<sub>19</sub>H<sub>24</sub>O<sub>4</sub> requires C, 72.1; H, 7.6%) [*bisphenylurethane*, m. p. 189—190° (Found: N, 5.2. C<sub>33</sub>H<sub>34</sub>O<sub>6</sub>N<sub>2</sub> requires N, 5.1%)], and (d) m. p. 112—113° (Found: C, 73.3; H, 8.1. C<sub>21</sub>H<sub>28</sub>O<sub>4</sub> requires C, 73.3; H, 8.1%) [*bisphenylurethane*, m. p. 172—173° (Found: N, 5.0. C<sub>35</sub>H<sub>38</sub>O<sub>6</sub>N<sub>2</sub> requires N, 4.8%)].

<sup>3</sup> Bentley, Haworth, and Perkin, *J.*, 1896, **69**, 166.

<sup>4</sup> Simons, U.S.P. 2,396,893/1946.

<sup>5</sup> Lohmann, *Ber.*, 1891, **24**, 2632.

<sup>6</sup> von Braun and Steindorff, *Ber.*, 1905, **38**, 959.

<sup>7</sup> Arnold, *Annalen*, 1887, **240**, 202.

<sup>8</sup> Cope, *J. Amer. Chem. Soc.*, 1935, **57**, 572.

<sup>9</sup> Gattermann, *Annalen*, 1907, **357**, 378.

Solutions of the above diols (~3 g.) in ethylene dichloride (500 ml.) at 0° were saturated with dry hydrogen chloride and dried (CaCl<sub>2</sub>). The solvent was volatilised at 40° under reduced pressure, and the residual dichloro-compounds were extracted with light petroleum and purified by recrystallisation. They are the *di*-(*p*-chloromethylphenyl ether) of (b) m. p. 170—171° (Found: Cl, 22.4. C<sub>16</sub>H<sub>16</sub>Cl<sub>2</sub>O<sub>2</sub> requires Cl, 22.8%), (c) m. p. 108—109° (Found: Cl, 21.3. C<sub>17</sub>H<sub>18</sub>Cl<sub>2</sub>O<sub>2</sub> requires Cl, 21.8%), and (d) m. p. 90—92° (Found: Cl, 19.7. C<sub>19</sub>H<sub>22</sub>Cl<sub>2</sub>O<sub>2</sub> requires Cl, 20.1%); and the *di*-(4-chloromethyl-2-methylphenyl ether) of (b) m. p. 131—133° (Found: Cl, 20.4. C<sub>18</sub>H<sub>20</sub>Cl<sub>2</sub>O<sub>2</sub> requires Cl, 20.9%), (c) m. p. 91—92° (Found: Cl, 19.6. C<sub>18</sub>H<sub>22</sub>Cl<sub>2</sub>O<sub>2</sub> requires Cl, 20.1%), and (d) m. p. 43—44° (Found: Cl, 18.4. C<sub>21</sub>H<sub>26</sub>Cl<sub>2</sub>O<sub>2</sub> requires Cl, 18.6%).

*p*-*n*-Propoxybenzyl alcohol, b. p. 144—146°/13 mm., m. p. 26—27° (Found: C, 71.8; H, 8.4. C<sub>10</sub>H<sub>14</sub>O<sub>2</sub> requires C, 72.3; H, 8.4%) [*phenylurethane* (from light petroleum), needles, m. p. 83—84° (Found: C, 71.7; H, 6.6; N, 5.1. C<sub>17</sub>H<sub>19</sub>NO<sub>3</sub> requires C, 71.6; H, 6.7; N, 4.9%)], was obtained by the reduction of *p*-*n*-propoxybenzoic acid with lithium aluminium hydride. With hydrogen chloride in light petroleum over calcium chloride it gave 4-*n*-propoxybenzyl chloride, b. p. 95°/0.8 mm. (Found: Cl, 18.6. C<sub>10</sub>H<sub>13</sub>ClO requires Cl, 19.2%).

*Kinetic Results*.—The results in Tables 2 and 5, apart from those for the solvolyses of the dichlorides [(III) and (IV); X = CH<sub>2</sub>Cl], were obtained by the techniques previously described.<sup>2</sup> Values given in parentheses in Tables 2, 5, and 6 were obtained by extrapolation.

*Solvolysis of the Dichlorides (III and IV; X = CH<sub>2</sub>Cl) in 90% Aqueous Ethanol*.—The limited solubility of these compounds in 90% aqueous ethanol prevented the use of 0.005M-solutions suitable for the previously described technique, and 0.0005M-solutions were used. These solutions, to which lacmoid had been added, were titrated in the thermostat-bath at selected intervals of time with a 0.0100N-solution of sodium hydroxide in 90% aqueous ethanol at the temperature of the thermostat. Table 4 provides a sample run. Each solvolysis was repeated several times. The rate coefficients are listed in Table 5.