11.3.2. *anti*-**23**: Ausbeute 165 mg (12%) farbloses Öl. IR. (CCl$_4$): 3550 (O—H). NMR. (100 MHz, CCl$_4$): 5,23 (schmales *m*; H–4), 4,72 (schmales *m*; H$_a$–9'), 4,60 (schmales *m*; H$_b$–9'), 2,95 (br. *s*; H–2), 2,41–2,18 (*m*; H$_b$–10), 1,90 (*d*, $J_{CH_3-5,4}$ = 1,8 Hz; CH$_3$–5), 1,98–1,58 (*m*; 5 aliphatische H), 1,15–0,95 (*m*; 1 H), 1,16 und 0,80 (je ein *s*; CH$_3$–1 und CH$_3$–3). MS. (*m/e*): 204 (*M*$^+$, 56%), 189 (*M* – 15, 34%), 186 (*M* – 18, 13%), 149 (*M* – 55,58%), 137 (*M* – 67, 100%).

C$_{14}$H$_{20}$O (204,30)   Ber. C 82,30   H 9,87%   Gef. C 82,11   H 10,11%

11.4. *Konfigurationszuordnung*: Die Zuordnung der Konfiguration erfolgte durch Aufnahme der 60 MHz-NMR.-Spektren unter Zusatz von Tris-(dipivaloyl-methanato)-europium (Eu(DPM)$_3$). Zu je 60,0 mg *syn*-**23** bzw. *anti*-**23** in 0,3 ml CCl$_4$ wurden genau eingewogene Mengen Eu(DPM)$_3$ gegeben (je 5mal eine Zugabe von ca. 10 mg). Vgl. Fig. 3.

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237. The Effect of Solvent Variation on Nucleophilic Substitution Rates of Methyl Tosylate

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(4. VIII. 72)

Summary. Rates of the reactions between bromide ion and methyl tosylate have been determined in 12 solvents and extrapolated to infinite dilution. The data are correlated with *Parker*'s solvent activity coefficients by means of an empirical equation of the type: $\log k^s - \log k^0 = A \log^0 \gamma_i^s + B$ with the constants A = 0.788 and B = 0,108 and a correlation coefficient of 0.983.

Introduction. – Bimolecular reactions between anionic nucleophiles and neutral substrates are known to be accelerated by several orders of magnitude in certain dipolar aprotic compared with protic solvents [1] [2]. Two factors must be considered

in order to rationalize this rate enhancement; either the transition state is particularly stabilized by solvation, or the nucleophile is destabilized upon transfer from protic to aprotic solvent [3] [4]. Both effects would lead to a lower activation energy. It now appears, as has been suggested some time ago [5], that small anions have in general lower solvation energies in aprotic than in protic solvents, and that the differences in protic-aprotic solvation energies are greater for small than for large anions [1]. Thus, the enthalpies of solvation in dimethylsulfoxide (DMSO) of lithium chloride, bromide and iodide are -214.3, -208.4 and -201.2, while in water they are -212.2, -203.0 and -192.1 kcal mol^{-1} [6]. The trend in DMSO and water is to decrease solvation with increasing size of the anion. The S_N2 transition state may be visualized as some sort of an anion of much larger size than a halide ion in the ground state. Consequently it would be expected to be even less solvated. Enthalpies of solvation of halide ions have been determined in dimethylformamide (DMF)[1]) and methanol [7]. Values are Cl$^-$, 54.5; Br$^-$, 52.5, and I$^-$, 48.5 kcal. mole^{-1} in DMF, and Cl$^-$, 79, Br$^-$, 72, and I$^-$, 63 kcal mole^{-1} in methanol. Solvation enthalpies for the intermediate σ-complexes in S_NAr reactions have been estimated to be 45 kcal mole^{-1} in DMF and 54 kcal mole^{-1} in methanol [7]. Parker's solvent activity coefficients, for transfer of ions from protic solvents [2] [8], suggest that anions undergo loss of energy upon transfer, while cations in general gain solvation energy. They further demonstrate that in bimolecular substitution reactions the rate enhancement and the inversion of the reactivity sequence of the halide ions in aprotic compared to protic media are readily rationalized on the basis of the smaller solvation energy of the anions in the aprotic solvent. Rate studies in molten salt media [9] confirmed the hypothesis that the reactivity order of the unsolvated halide ions is Cl$^-$ > Br$^-$ > I$^-$, which is retained in aprotic, but reversed in protic solvents.

Reaction rates of bimolecular nucleophilic substitutions may be calculated using a semi-empirical treatment which was developed by Miller for S_NAr reactions [5]. Solvent effects are accounted for in this treatment by using solvation energies of the nucleophiles [7] to calculate the energy levels of the initial and final state of the reaction and to estimate the energy of the transition state. Although the method is in principle applicable to other reactions as well, its application is limited by lack of data, available particularly of solvation energies of anions in aprotic solvents. Parker has rationalized the rates of an impressive number of reactions by using the solvent activity coefficient rate equation [10]. Solvent activity coefficients $^0\gamma^s$ are proportional to the change of chemical potential of a solute ion transfer from a reference solvent to another solvent. Solvent activity coefficients for single ions cannot be determined, but are derived from coefficients of salts, using certain extrathermodynamic assumptions. For reactions of the type (1) the rate

$$Y^- + R\text{--}X \rightleftharpoons YRX^{-\neq} \longrightarrow \text{Products} \tag{1}$$
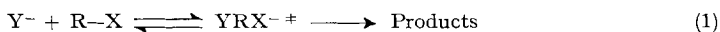
equation is:

$$\log k^S - \log k^0 = \log{}^0\gamma_{Y^-}^S + \log{}^0\gamma_{RX}^S - \log{}^0\gamma_{YRX}^S{}^{\neq}. \tag{2}$$

Assuming $\log \gamma_{RX}^S - \log{}^0\gamma_{YRX-\neq}^S$ to be roughly constant Parker obtained a linear free energy relationship (3) with a limited number of constants, C, varying

$$\log k^S - \log k^0 = \log{}^0\gamma_{Y^-}^S + C \tag{3}$$

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[1])   C. M. Criss, quoted in ref. [7].

only with the type of substrate. In this work we have tried to correlate the substitution rate of methyl tosylate with bromide ion in two protic and 10 aprotic solvents by means of equation (3).
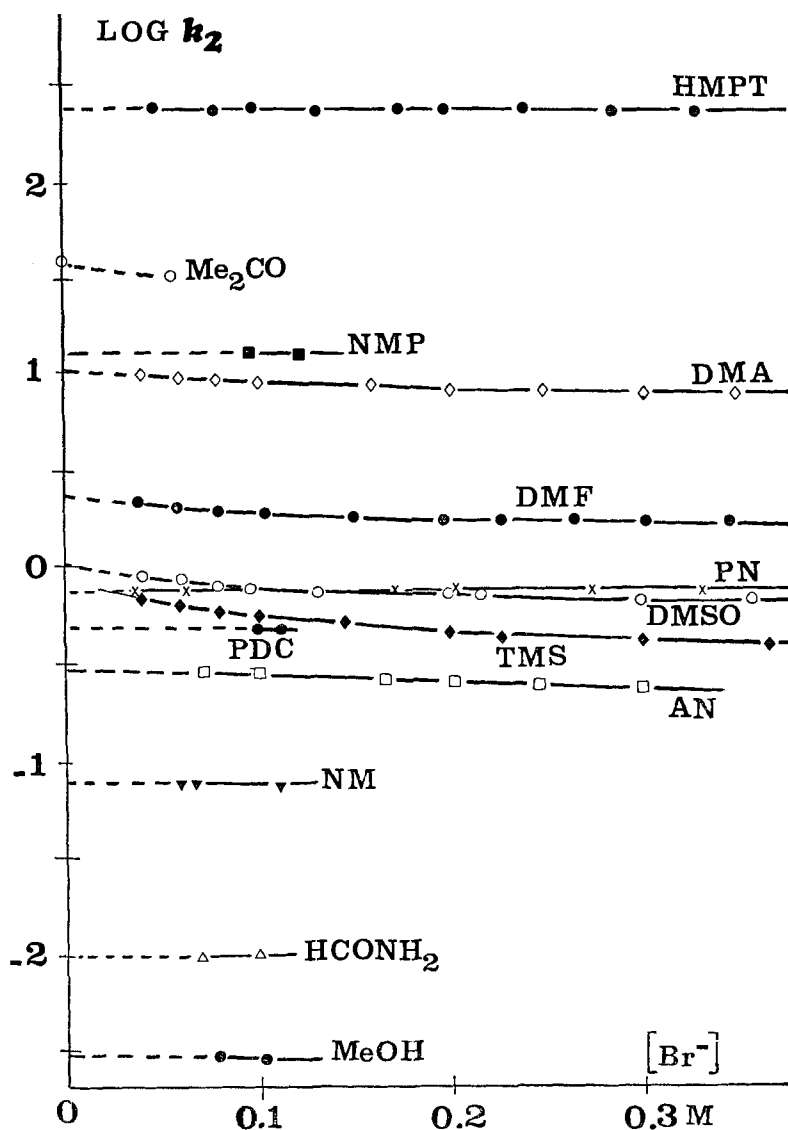

Fig. 1. *Second order rate constants for the reaction of bromide ion with methyl tosylate* at 25.0° as a function of initial salt concentration. For abbreviations see Table. k_2 is expressed in mole$^{-1}\cdot$min^{-1}.

Results[2]. – The reaction between bromide ion and methyl tosylate was measured at 25.0°. Two methods were used for the determination of the rate constants: With

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[2]   The results have been published partially in preliminary form [11].

solvents sufficiently transparent in the UV. at 270 to 280 nm (acetonitrile, sulfolane, dimethylsulfoxide, propionitrile, dimethylformamide, dimethylacetamide and hexamethylphosphoric triamide), the rate was measured spectrophotometrically under pseudo-1st order conditions (method A). Reaction rates for the other solvents (methanol, formamide, propylene carbonate, N-methylpyrrolidone, nitromethane and acetone) were determined under second order conditions, by quenching aliquots of the reaction mixture at suitable time intervals and determining the amount of unreacted halide by potentiometric titration (method B). The rate constants obtained are represented on a logarithmic scale as a function of starting salt concentration in Fig. 1. Tetrabutylammoniumbromide was used as the source of the nucleophile in acetone[3]), nitromethane and propylene carbonate in order to minimize ion pairing. For the other solvents lithium bromide was used. The rate constants in propylene carbonate for lithium and tetrabutyl-ammonium bromide were identical within experimental error. For acetone a correction was applied to the observed rate constant by dividing by the degree of dissociation of the salts [12] [13] [14]. For methanol, formamide, nitromethane N-methylpyrrolidone [15] and propylene carbonate the second order rate constants showed no variation when the initial concentration of nucleophile was altered. Ion pairing is believed to be negligible in these solvents and the observed rate constants are assumed to correspond to those of the free nucleophile.

For the other solvents the rate constant for the free bromide ion was obtained by free-hand extrapolation to infinite dilution of the plots in Fig. 1. This procedure is believed to be more reliable than measurements at only one salt concentration. For a thorough analysis conductivity measurements for all solvents would be needed, in order to account more precisely for the influence of ion pairing. The data obtained in this manner are however sufficiently accurate for our requirements. The Table represents the extrapolated rate constants together with solvent activity coefficients and abbreviations used in this paper.

Table. *Rate constants of the reaction of bromide ion with methyl tosylate extrapolated to infinite dilution*

No.	Solvent	Abbr.	k^s [M^{-1}·min^{-1}]	$\log \dfrac{k^s}{k^0}$	$\log {}^{AN}\gamma_{Br^-}^s$
1	Propylene carbonate	PDC	0.48	0.204	0.5
2	Dimethylsulfoxide	DMSO	1.0	0.522	0.2
3	Sulfolane	TMS	0.82	0.436	0.4
4	Dimethylacetamide	DMA	10.25	1.534	2.0
5	Acetonitrile	AN	0.30	0	0
6	N,N-Dimethylformamide	DMF	2.40	0.903	1.4
7	Nitromethane	NM	0.15	− 0.301	− 0.4
8	N-methylpyrrolidone	NMP	13.20	1.643	1.5
9	Hexamethylphosphoric triamide	HMPT	240.0	2.903	3.4
10	Acetone	Me$_2$CO	47.0	2.190	2.5
11	Methanol	MeOH	0.0027	− 2.045	− 2.3
12	Formamide	HCOHH$_2$	0.0081	− 1.560	− 2.7
13	Propionitrile	PN	0.77	0.410	−

[3]) The previously reported value for acetone [11], based on measurements with lithium bromide, is not corrected for ion pairing.

Discussion. – In *Parker*'s linear free energy relationship [10] a value of -2 ± 0.8 has to be used as the characteristic constant for tosylate substrates in order to correlate reaction rates with solvent activity coefficients. The uncertainty in C is considerable. This has been accomodated by the observation, that the position of the transition state (on the reaction coordinate) for substitution and elimination of tosylates, depends to a certain degree on the reaction conditions [16]. In the preliminary communication we reported reasonable agreement between experimental and theoritical values calculated with equation (3). *However*, we also found disturbing deviations which could not be accounted for. In addition, the solvent activity coefficients available at that time [2] are now considered to be unreliable [8]. The original set of coefficients was obtained by splitting the solvent activity coefficients of salts into their components by means of several extrathermodynamic assumptions. The new set of values is based on only one assumption, namely that a negligible liquid junction potential exists between cells of aprotic solvents with a salt bridge consisting of tetraethylammonium picrate. The choice of this assumption is justified in ref. [8].

There is much better agreement if the rate constants are not correlated with *Parker*'s equation, but rather with an empirical equation of the form:

$$\log k^S - \log k^0 = A \log^0 \gamma_{Y^-}^S + B. \tag{4}$$

The subscript 0 refers to the reference solvent (acetonitrile). Least square analysis of the data in the Table (Fig. 2) gives a straight line with slope $A = 0.788$ and an intercept $B = 0.108$. The correlation coefficient is 0.983. The same method with the old set of activity coefficients, yields a correlation coefficient, which is only 0.900.
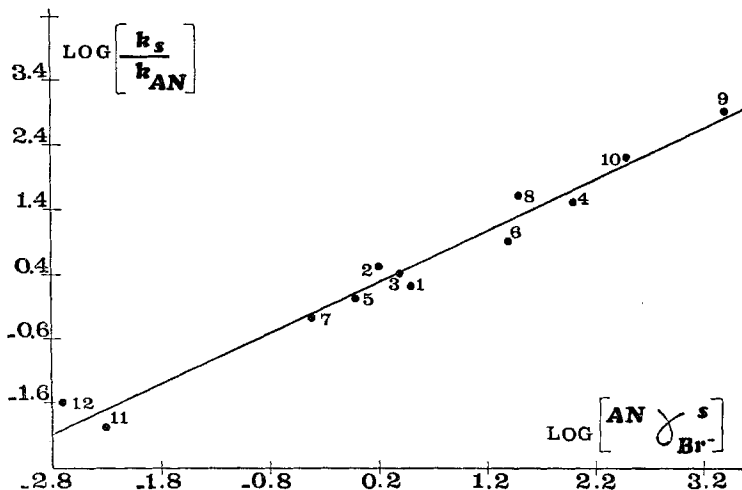

Fig. 2. *Correlation between substitution rates and solvent activity coefficients* of bromide ion using eq. (4). Data are taken from the Table. The constants are $A = 0.788$, $B = 0.108$.

Contrary to the results obtained from eq. (3), Fig. 2. clearly suggests that all the data for aprotic as well as protic solvents can be correlated with *Parker*'s activity coefficients. In particular, propylene carbonate, which was considered to be an

exception because of the deviation by 1.7 logarithmic units from the calculated value (using eq. (3)) now lies well within the expected range. The theoretical significance of the constants A and B is not yet clear. However it seems reasonable to assume that in all solvents studied, the solvent activity coefficient of the transition state is a constant fraction of the solvent activity coefficient of the anion. This would require the transition state species not to change the position on the reaction coordinate upon change in solvent in going from the ground state to the transition state. The intercept B might be interpreted as being due to the change in solvation of the substrate. It would be expected to be small with tosylate substrates, as only atoms close to the reactive center should be affected in going to the transition state.

Analysis of the data available in the literature, in terms of equation (4), reveals a slope of A = 0.612 and an intercept B = −0.80 for the reaction of *n*-butylbromide with azide ions (9 solvents, correlation coefficient 0.93) [17]. For methyl iodide with chloride ion the constants are A = 0.813 and B = 0.33 (8 solvents, correlation coefficient 0.96) [18], for methyl iodide with thiocyanate ion A = 0.538 and B = 0.16 (9 solvents, correlation coefficient 0.66) [18]. Eq. (4) correlates the data quite well and systematic variations of the different parameters could allow further conclusions to be made concerning the general applicability of the treatment.

Experimental Part

Materials. Lithium bromide (*Merck*, suprapur.) was dried for 3 days at 180°/12 Torr. Tetra-*n*-butylammonium bromide (*Fluka*) was recristallized two times from petroleum ether and stored in a desiccator at ca. 0°; m.p. 29°. The solvents were purified by standard methods and were free of impurities and water [19] [20].

Kinetic measurements. Stock solutions of lithium bromide or tetra-*n*-butylammonium bromide were made up in the appropriate solvent, and the salt concentration verified by argentometric titration using a silver electrode connected to a *Metrohm* E 510 pH-meter.

Method A. 3.0 ml of halide solution was thermostated for 10 to 15 min. in a UV.-cell in the cell compartment of a *Perkin-Elmer* 402 spectrophotometer. A stock solution of methyl tosylate was made up ca. 1.2 M in benzene. The substrate was added to the cell by means of a micro pipette, so that the initial concentration was 2.0×10^{-3} M. After stirring the concent of the cell the decrease of absorbance was recorded at 273 nm. First order rate constants were obtained from plots of $(A_t - A)$ *vs.* time, and the second order rate constant by dividing by the salt concentration. Each point in Fig. 1 represents an average value from 3 to 4 runs a maximum error of 5% of the mean.

Method B. Stock solutions of bromide (0.1–0.3 M) and of methyl tosylate (1.2–2 M) were made up in the appropriate solvent. 10.0 ml of the bromide solution was thermostated at 25.0° in a constant temperature bath. To this solution was added, with vigorous stirring, also thermostated at 25.0°, 2.0 ml of tosylate solution and the timer was started simultaneously. At appropriate time intervals the reaction was quenched with 40 ml of 10% sulfuric acid. The amount of unreacted bromide ion was determined by potentiometric titration.

Rate constants were obtained from the equation

$$ k_2 = \frac{1}{t} \frac{2.303}{(a-b)} \log \frac{b}{a} \frac{(b-x)}{(a-x)} \tag{5} $$

with a and b representing the initial concentrations of tosylate and bromide, respectively, and x the concentration of bromide ion at time t. The points in Fig. 1 represent averages of 15 determinations with a standard deviation of max. 5% for the mean value.

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238. Germa-2-dioxa-1,3-cycloalcanes

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Summary. The action of the α-, β- and γ-diols on the dialkyl(aryl)-bis(dialkylamino) germanes $R_2Ge(NR'_2)_2$ leads, in high yields, to the dialkyl(aryl)-2,2-germa-2-dioxa-1,3-cycloalkanes.

The IR. and NMR. spectral study in the presence of $Eu(Dpm)_3$ allowed to demonstrate a dimerisation by coordination in some of these heterocycles. In this complex, the germanium is hexacoordinated by association with the two oxygens of the second associate molecule. Its hybridation state is sp_3d_2 or spd_4 (D_{3h} symmetry, prismatic structure).

These low energy association are ruptured in solution at moderate temperatures; these heterocycles are monomers by ebulliometry in benzene.

This association is disfavoured by the presence of substituents on the cycle and by hindering substituents with donor effect on the germanium.

The diminution of nucleophilicity of the oxygens by mesomeric effect with neighbouring π systems also prevents any association.

Introduction. – La synthèse de germadioxacycloalcanes peut être réalisée suivant différentes méthodes qui font intervenir de façon générale l'action d'un diol avec une molécule germaniée renfermant deux groupements susceptibles de réagir avec les groupements hydroxyles: par exemple, les dihalogéno-[1], dialcoxy-[2]–[4] et dihydro-