INDUCTIVE EFFECT IN SERIES OF NITRAMINOMONOCARBOXYLIC AND -DICARBOXYLIC ACIDS

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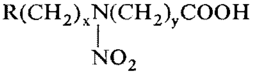
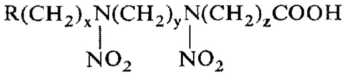
A series of nitraminomonocarboxylic and -dicarboxylic acids have been prepared, and their dissociation constants have been determined in water and 80% methylcellosolve. Electrostatic contribution to the difference in the dissociation constants has been compared according to the MacInnes, Kirkwood–Westheimer, and inductive models. The best agreement was obtained with the Kirkwood–Westheimer model.

In previous papers we described preparation of nitraminodicarboxylic acids either by nitration of structurally suitable aminonitrils[1] or by nitrolytic splitting of 1,3,5-tri(cyanomethyl)hexahydro-*s*-triazine[2]. In connection with studies of influence of structure of these dibasic acids on their dissociation constants, we have now prepared new nitraminomonocarboxylic and -dicarboxylic acids and their derivatives. With respect to that the acid-base properties of nitramino acids have not yet been studied systematically (the only pK_a value published so far was that of 4-nitro-



$$\mathrm{R(CH_2)_x}\underset{\substack{|\\ \mathrm{NO_2}}}{\mathrm{N}}\mathrm{(CH_2)_yCOOH}$$

	R	*x*	*y*		R	*x*	*y*
I	CH_3	0	1	*IV*	COOH	1	2
II	CH_3	0	2	*V*	COOH	2	2
III	COOH	1	1				



$$\mathrm{R(CH_2)_x}\underset{\substack{|\\ \mathrm{NO_2}}}{\mathrm{N}}\mathrm{(CH_2)_y}\underset{\substack{|\\ \mathrm{NO_2}}}{\mathrm{N}}\mathrm{(CH_2)_zCOOH}$$

	R	*x*	*y*	*z*		R	*x*	*y*	*z*
VI	CH_3	0	2	1	*XI*	COOH	2	1	2
VII	CH_3	0	2	2	*XII*	COOH	2	2	2
VIII	COOH	1	1	1	*XIII*	COOH	2	3	2
IX	COOH	1	2	1	*XIV*	COOH	2	6	2
X	COOH	1	3	1	*XV*	COOH	2	10	2

-4-azaheptanedioic acid in aqueous medium[3]) the purpose of the present Paper is the determination of dissociation constants of the prepared series of acids *I*–*V* and *VI*–*XV* and a study of influence of nitramino group and length of the aliphatic chain on pK_a value.

EXPERIMENTAL

The melting points were determined with a Kofler apparatus and are uncorrected. Purity of the compounds was checked by paper chromatography with descendent arrangement using Whatman No 3 paper impregnated with formamide and eluent systems 1,2-dichloroethane (S_1), chloroform (S_2) and tetrachloromethane–chloroform (1 : 1) (S_3). The spots were made visible by the modi-

TABLE I

Dissociation Constants of Aliphatic Nitraminomonocarboxylic and Dicarboxylic Acids at 25°C in Water (pK') and 80% Methylcellosolve (pK'')

Substance	M.p., °C	ν(C=O), cm^{-1}	pK'_1	pK'_2	pK''_1	pK''_2
I	99–100^a	1 722	3·19	—	5·10	—
II	52–53^b	1 702, 1 724	4·16	—	5·72	—
III	153–155^c	1 723	2·31	4·22	4·93	6·84
IV	165–169^d	1 711	3·15	4·63	5·49	7·09
V	162–162·5^e	1 717	3·77^f	5·07^f	5·59^f	6·89
VI	126–129	1 723	3·23	—	5·11	—
VII	118–119	1 703, 1 722	4·21	—	6·08	—
VIII	207–211^g	1 715	3·49	4·73	5·13	5·80
IX	207–209^h	1 723	3·47	4·58	5·21	5·82
X	146–148	1 725	3·49	4·51	5·29	5·88
XI	189–193^i	1 710	3·94	4·90	6·02	6·75
XII	141–143^j	1 715	3·88	4·83	6·04	6·67
XIII	142–143^k	1 697	3·90	4·81	5·84	6·49
XIV	136–138·5^l	1 731	3·99	4·72	5·98	6·65
XV	126–130	1 729	—^{m}	—^{m}	6·11	6·63

[a] Ref.[9] gives 99–100°C; [b] ref.[10] gives 53–54°C; [c] ref.[11] gives 155°C; [d] ref.[1] gives 165–169°C; [e] ref.[12] gives 163–166°C; [f] ref.[3] gives pK_1 3·78 and pK_2 5·02; [g] ref.[2] gives 207–211°C; [h] ref.[13] gives 207–209°C; [i] ref.[14] gives 189–193°C; [j] ref.[15] gives 141·5–142·5°C; [k] ref.[16] gives 141°C; [l] ref.[13] gives 138·5–140°C; [m] the substance is insoluble in water.

fied Franchimont test described previously[4]. The IR spectra were measured in nujol with a UR-20 spectrophotometer (Zeiss, Jena). Specification of the acids and references concerning their preparation are given in Table I. Samples of the acids for determination of dissociation constants were kept *in vacuo* over phosphorus pentoxide.

3,7-Dinitro-3,7-diazanonanedinitrile

To a suspension of potassium cyanide (6·5 g, 0·10 mol) in water (3·0 ml) 1,3-diaminopropane hydrochloride (7·35 g, 0·05 mol) in water (17·0 ml) was added dropwise with stirring and cooling at 0°C, and, after raising the temperature to 10°C, 37% formaline (8·2 g, 0·10 mol) was added drop by drop. The solution was stirred for another one hour. After extraction with 1,2-dichloroethane (4 × 20 ml), 4·3 g extract was obtained which, during vacuum distillation, underwent decomposition with evolution of hydrogen cyanide. Therefore the liquid was added dropwise to 65% nitric acid (14 ml) and, after addition of ethanol (40 ml) and ether (10 ml) and cooling to 0°C, the dinitrate was filtered off (2·6 g; 29%) having m.p. 130—145°C; after recrystallization (5% nitric acid and ethanol 1 : 4 by vol.) it melted at 148—155°C. For $(NCCH_2NH_2(CH_2)_3.\,.NH_2CH_2CN)^{2+}.2\,NO_3^-$ (278·2) calculated (found): 45·3 (45·2) % HNO_3 (nitrone). The dinitrate prepared (1·2 g, 0·0043 mol) was introduced into a mixture of acetanhydride (1·5 ml, 0·0157 mol), 99% nitric acid (0·1 ml) and 37% hydrochloric acid (0·1 ml). Temperature of the mixture was maintained at 15 to 20°C, and a drop of hydrochloric acid was added every 15 minutes. At the end of the reaction the suspension was poured into water (4·0 ml), and the substance precipitated was filtered off and washed with water. After drying 0·8 g (77·1%) product was obtained melting at 130—138°C; after crystallization from acetonitrile it melted at 139—142°C. For $C_7H_{10}N_6O_4$ (242·2) calculated: 34·71% C, 4·16% H, 34·70% N; found: 34·71% C, 4·32% H, 34·42% N; IR spectrum: $\nu(NO_2)$ 1284, 1520 cm^{-1}, $\nu(C{\equiv}N)$ 2245 cm^{-1}. R_F 0·23 (S_1).

4,11-Dinitro-4,11-diazatetradecanedinitrile

Hexamethylenediamine (23·2 g, 0·2 mol) was added to freshly distilled acrylonitrile (21·2 g, 0·4 mol) at 10°C. The addition of the amine to acrylonitrile was finished by 10 h. heating of the reaction mixture on water bath under reflux. The mixture of substances obtained on cooling was introduced into 65% nitric acid (51 g, 0·809 mol), and the product precipitated on dilution with ethanol (80 ml) and ether (20 ml) was filtered off and washed with ethanol and ether. Yield 64·4 g substance melting at 94—102°C; after recrystallization (ethanol–water 1 : 10) it melted at 115—119°C. For $(NCCH_2CH_2NH_2(CH_2)_6NH_2CH_2CH_2CN)^{2+}.2\,NO_3^-$ (348·3) calculated: (found): 36·18 (35·06) % HNO_3 (nitrone). The nitration procedure of the obtained product was the same as that of preparation of the dinitrile of the compound *X*, the amounts taken in reaction being: 3·26 g of the product obtained, 4·8 ml acetanhydride, 0·18 ml 99% nitric acid and 0·1 ml 37% hydrochloric acid. After 2 hours of reaction at 25°C the substance dissolved, and the dinitrile precipitated on dilution with water (5 ml) was filtered off, and washed with ethanol and ether. Yield 2·1 g (72%) dinitrile m.p. 81—83°C; after recrystallization (ethanol) it melted at 86 to 89·5°C. For $C_{12}H_{20}N_6O_4$ (312·3) calculated: 46·14% C, 6·45% H, 26·90% N; found: 46·30% C, 6·63% H, 27·10% N; IR spectrum: $\nu(NO_2)$ 1279, 1288, 1514 cm^{-1}; $\nu(C{\equiv}N)$ 2242, 2249 cm^{-1}. R_F 0·83 (S_1).

4,15-Dinitro-4,15-diazaoctadecanedinitrile

Decamethylenediamine (17·2 g, 0·1 mol) was sprinkled in acrylonitrile (10·6 g, 0·21 mol) and the suspension was refluxed on water bath for 20 hours. On cooling to 20°C and filtration 30·8 g substance was obtained which was, without any further treatment, dissolved in ethanol (70 ml); to the solution obtained 65% nitric acid (15·4 g, 0·244 mol) was added dropwise with stirring at 30—35°C. The suspension obtained was cooled at 25°C, diluted with ether (40 ml), and the substance precipitated was filtered off. Yield 31·3 g (76·6%), m.p. 140—150°C. The product obtained was nitrated with a nitration mixture of acetanhydride (46·2 ml, 0·483 mol), 99% nitric acid (1·8 ml, 0·043 mol) and 37% hydrochloric acid (0·5 ml) at the temperature 35—40°C for one hour. Every 15 minutes further portions (0·1 ml) of hydrochloric acid were added dropwise. Yield of dinitrile was 10·1 g (27·6%), m.p. 59—62°C; after recrystallization (ethanol) it melted at 76—78°C. For $C_{16}H_{28}N_6O_4$ (368·4) calculated: 52·15% C, 7·66% H, 22·81% N; found: 52·14% C, 7·85% H, 22·57% N; IR spectrum: $\nu(NO_2)$ 1 287, 1 502 cm^{-1}; $\nu(C{\equiv}N)$ 2245 cm^{-1}. R_F 0·90 (S_1).

Nitraminomonocarboxylic and -dicarboxylic Acids *VI*, *VII*, *X*, *XIV* and *XV*

Procedure A. Acid nitrile[5] *VI* resp. dinitrile *X* (1·0 g) was heated with 37% hydrochloric acid (5·5 ml resp. 10 ml) under reflux on a water bath for 3 hours. The solution was concentrated *in vacuo*, and the obtained evaporation residue was extracted with acetone, the insoluble portion was filtered off, and the acetone solution was evaporated. The obtained acid *VI* resp. diacid *X* (after washing with ether) was crystallized from water.

Procedure B. Acid nitrile[6] *VII* and dinitriles of acids *XVI* and *XV* (1·0 g) were hydrolyzed in 37% hydrochloric acid (5, 10 and 10 ml, respectively) by refluxing on a water bath for 3, 2 and 5 hours, respectively. In hydrolysis of acid *XV* dinitrile the hydrochloric acid was added in two portions; 5 ml at the beginning of the reaction and 5 ml after one hour of the hydrolysis. After cooling the hydrolysate to 10°C the precipitated acid *VII* resp. diacids *XIV* and *XV* were filtered off, washed with water and recrystallized.

3,6-*Dinitro*-3,6-*diazaheptanoic acid* (VI) was prepared by the procedure *A*, yield 78%, m.p. 122—128°C; after recrystallization (water) it melted at 126—129°C. For $C_5H_{10}N_4O_6$ (222·2) calculated: 27·03% C, 4·53% H, 25·10% N; found: 27·16% C, 4·53% H, 25·30% N; IR spectrum: $\nu(C{=}O)$ 1723 cm^{-1}. Methyl ester: Dry hydrogen chloride gas was introduced into suspension of the nitrile (4·2 g) in methanol (55 ml) at 20—30°C until saturation. The solution obtained was concentrated to 1/5 of the original volume, diluted with water and extracted with dichloromethane (3 . 10 ml). By evaporation of the solvent the ester of the compound *VI* was obtained in a yield of 3·7 g (77·1%), m.p. 50·5—53·0°C; after recrystallization (methanol) it melted at 52—54°C. For $C_6H_{12}N_4O_6$ (236·2) calculated: 30·51% C, 5·12% H, 23·73% N; found: 30·78% C, 5·26% H, 23·47% N; IR spectrum: $\nu(NO_2)$ 1273, 1528 cm^{-1}. $\nu(C{=}O)$ 1748 cm^{-1}. R_F 0·56 (S_2), 0·14 (S_3).

4,7-*Dinitro*-4,7-*diazaoctanoic acid* (VII) was prepared by the procedure *B* in the yield 97·4%, m.p. 117—118°C; after recrystallization (H_2O) it melted at 118—119°C. For $C_6H_{12}N_4O_6$ (236·2) calculated: 30·51% C, 5·12% H, 23·71% N; found: 30·22% C, 5·17% H, 23·69% N; IR spectrum: $\nu(NO_2)$ 1277, 1291, 1528 cm^{-1}, $\nu(C{=}O)$ 1703, 1722 cm^{-1}.

3,7-*Dinitro*-3,7-*diazanonanedioic acid* (X) was prepared by the procedure *A* in the yield 44·8%, m.p. 141—147°C; after recrystallization (H_2O) it melted at 146—148°C. For $C_7H_{12}N_4O_8$ (280·2) calculated: 30·00% C, 4·32% H, 20·00% N; found: 29·91% C, 4·45% H, 19·80% N; IR spectrum $\nu(NO_2)$ 1291, 1512 cm^{-1}, $\nu(C{=}O)$ 1710 cm^{-1}.

4,11-*Dinitro*-4,11-*diazatetradecanedioic acid* (XIV) was prepared by the procedure *B* in the yield 86%, m.p. 135—138°C; after recrystallization (ethanol) it melted at 136·5—138·5°C. For $C_{12}H_{22}N_4O_8$ (350·3) calculated: 41·14% C, 6·33% H, 15·99% N; found: 41·01% C, 6·37% H, 16·02% N; IR spectrum: $\nu(NO_2)$ 1281, 1505 cm^{-1}, $\nu(C{=}O)$ 1733 cm^{-1}. Dimethyl ester. The compound *XIV* (5·0 g) was heated in thionyl chloride (12 ml) with addition of dimethylformamide (0·1 ml) at 40°C for one hour. Thereafter the excess thionyl chloride was distilled and the residue was stirred with methanol (50 ml) at 25°C for one hour. After distilling methanol the residue was mixed with water, the insoluble residue was filtered off and washed with water, methanol and ether. Yield 3·9 g (72·2%), m.p. 41—43°C; after recrystallization (methanol) the substance melted at 41·5—43·5°C. For $C_{14}H_{26}N_4O_8$ (378·4) calculated: 44·43% C, 6·92% H, 14·80% N; found: 44·35% C, 7·15% H, 14·87% N; IR spectrum: $\nu(NO_2)$ 1288, 1508 cm^{-1}; $\nu(C{=}O)$ 1735 cm^{-1}.

4,15-*Dinitro*-4,15-*diazaoctadecanedioic acid* (XV) was prepared by the procedure *B* in the yield 74·2%, m.p. 127—130°C; after recrystallization (H_2O) the product melted at 127—130°C. For $C_{16}H_{30}N_4O_8$ (406·4) calculated: 47·28% C, 7·44% H, 13·78% N; found: 47·02% C, 7·24% H, 13·93% N; IR spectrum: $\nu(NO_2)$ 1282, 1295, 1508 cm^{-1}. $\nu(C{=}O)$ 1728 cm^{-1}. Dimethyl ester. The compound *XV* was esterified by the procedure described in preparation of the ester of acid *XIV*. Yield 65·0%, m.p. 29—31°C; after recrystallization (methanol) the product melted at 31 to 31·5°C. For $C_{18}H_{34}N_4O_8$ (434·5) calculated: 49·76% C, 7·88% H, 12·89% N; found: 49·99% C, 8·14% H, 12·98% N; IR spectrum: $\nu(NO_2)$ 1288, 1510 cm^{-1}, $\nu(C{=}O)$ 1730 cm^{-1}.

Determination of Dissociation Constants

The dissociation constants were determined by potentiometric titration[7] of monoacid and diacid solutions having concentrations 5 . 10^{-3}M and 2·5 . 10^{-3}M, respectively, in water and 80% aqueous methylcellosolve. In the both cases 0·1M aqueous tetramethylamonium hydroxide was used as the titration reagent. pH values of the solutions were determined with the use of a PHM 4 apparatus (Radiometer, Copenhagen). Dissociation constants of the diacids were obtained by the method of Noyes described by Albert and Serjeant[8] using the equations $K_1 = (y_1z_2 - y_2z_1) : (x_1y_2 - x_2y_1)$ and $K_2 = (x_1z_2 - x_2z_1)/(y_1z_2 - y_2z_1)$, where $x = [H^+]\ (B - C + [H^+])$, $y = 2C - (B + [H^+])$, and $z = [H]^{+2}\ (B + [H^+])$. *B* stands for concentration of the base added and *C* is total concentration of the acid. Calculation was carried out according to a programme in Autocode MOST with a digital computer Odra 1013. The programme involved the corrections for dilution and influence of $[H^+]$.

RESULTS AND DISCUSSION

Dissociation constants of nitraminomonocarboxylic and dicarboxylic acids in water and 80% (by wt.) methylcellosolve are given in Table I. Substitution of a methylene group in the chain of aliphatic acid by a nitramino group results in an acidity increase. Comparison of pK_a of butyric acid (4·85) with that of 3-nitro-3-azabutanoic acid (*I*) (3·19), or pK_a of enanthic acid (4·89) with that of 3,6-dinitro-3,6-diazaheptanoic acid (*VI*) (3·23) shows that the pK_a difference is 1·66 in the both cases. This identical pK_a difference suggests that the substitution of a methylene group in position 3 by a nitramino group affects the acidity substantially, whereas the same substitution in the position 6 has no further effect on acidity. The strong effect in β position to carboxylic group is due to electron-withdrawing NO_2 group and substitution of a chain carbon atom by nitrogen.

Separation of nitramino group from carboxylic group by two methylene groups is manifested by an acidity increase, however, the second methylene group diminishes the pK_a difference to mere 0·67. Thus pK_a of valeric acid (4·81) and 4-nitro-4-azapentanoic acid (*II*) (4·16), caprylic acid (4·90) and 4.7-dinitro-4,7-diazaoctanoic acid (*VII*) (4·21) show the mentioned decrease of inductive effect. When comparing the influence of a second nitramino group in the chain separated from the first one by again two methylene groups it must be stated that no acidity increase is observed with acids *VII* compared to *II* as it was the case with the pair *I* and *VI*.

The carboxylic acids studied can be hold for substituted acetic acids. For correlation according to the Hammett equation the Taft's aliphatic σ_I constants[17] were used. By the least squares method linear regressions were calculated from the known σ_I and pK_a values in water[18] (*1*) and 80% (by wt.) methylcellosolve[15] (Eq. (*2*)). With the use of these equations and the measured pK_a values it was possible to calculate σ_I constants for the following substituents: $CH_3N(NO_2)$— (*A*), $CH_3N(NO_2)CH_2$— (*B*), $CH_3N(NO_2)(CH_2)_2N(NO_2)$— (*C*) and $CH_3N(NO_2)(CH_2)_2N(NO_2)CH_2$—(*D*).

$$\mathrm{p}K'_a = 4{\cdot}899 - 4{\cdot}349\sigma_I\ ; \quad s = \pm 0{\cdot}070\ ; \quad r = 0{\cdot}998\ (\text{water}) \qquad (1)$$

$$\mathrm{p}K''_a = 6{\cdot}838 - 3{\cdot}770\sigma_I\ ; \quad s = \pm 0{\cdot}035\ ; \quad r = 0{\cdot}999\ (80\%\ \text{methylcellosolve}) \qquad (2)$$

Substituent	*A*	*B*	*C*	*D*
σ_I	0·428	0·233	0·432	0·180

From the results it follows that insertion of a methylene group between the substituent *A* or *C* and carboxylic group results in decrese of σ_I.

Substitution of a methylene group by nitramino group in dicarboxylic acids results in an acidity increase, too, the difference being observed with the both pK_a values. The largest acidity increase in water is encountered in the case of pentanedioic acid (pK'_1 4·32; pK'_2 5·46) and 3-nitro-3-azapentanedioic acid (*III*) (pK'_1 2·31; pK'_2 4·22), *i.e.* ΔpK'_1 and ΔpK'_2 are 2·01 and 1·24, respectively. With increasing chain length the difference in pK_a is gradually decreased. In the case of heptanedioic and 4-nitro-4-azaheptanedioic acids the respective differences are ΔpK'_1 0·69, ΔpK'_2 0·41. Introduction of a further nitramino group increases ΔpK_a. For 3,5-dinitro-3,5-diazaheptanedioic acid the values ΔpK'_1 and ΔpK'_2 are 0·97 and 0·75, respectively. 3-Azapentanedioic acid[3] is about equally acidic as 3-nitropentanedioic acid[3], and 3-nitro-3-azapentanedioic acid (*III*) measured by us corresponds in its acidity to 3,3-dinitropentanedioic acid[3].

The difference between the both pK_a values of a dicarboxylic acid is characteristical. It decreases with increasing chain length between the both carboxylic groups, which reflects the effect of the charge of carboxylate group on dissociation of the other carboxylic group. This change can be predicted on the basis of an electrostatic calculation. Mac Innes[19] proposed a simple relation (*3*), where C and S are constants, and n stands for the number of atoms of the aliphatic chain between the both carboxylic groups. The constant C should express the difference $pK_2 - pK_1$ of a dicarboxylic acid with infinite aliphatic chain. Theoretically the constant C should be equal to statistical factor (log 4).

$$pKr = pK_2 - pK_1 = C + S/n \tag{3}$$

From the results of measurements of Bonhomme[20] who determined the pK_a values of dicarboxylic acids of the type $HOOC(CH_2)_nCOOH$ for $n = 3$ to 8 in aqueous and aqueous–ethanolic solutions (20, 40, 60, 80% C_2H_5OH) and from the values of C constants determined by her (which are within 0·68 and 1·02 for 40% and 80% C_2H_5OH, respectively) a discrepancy can be seen with respect to the abovementioned theory. The result of measurements in 40% C_2H_5OH is closest to the theoretical value. Also the results of our measurements of pK_a of nitraminodicarboxylic acids and the C values determined differ considerably from the value of statistical factor.

The results of linear regressions according to Eq. (*3*) are given in Table II and Fig. 1. The constant C is the same for all the measurements in water and in methylcellosolve, its average value being 0·372. Whereas the pKr values calculated for the results of measurements in water lie on one straight line, those determined in methylcellosolve divided into three groups with different slopes S: acids *III*–*V* (having only one

TABLE II

Linear Regression for Dicarbocylic Acids according to Eq. (*3*)

Acids	Solvent	C	S	r^a	n^a
Alkanoic[b]	H_2O	0·774	1·110	0·945	6
	40% C_2H_5OH	0·681	1·511	0·912	8
	80% C_2H_5OH	1·018	1·611	0·947	8
	80% MCS[c]	0·831	1·207	0·980	6
III–*XIV*	H_2O	0·346	4·572	0·990	8
III–*V*	80% MCS[c]	0·412	4·572	0·993	3
VIII–*X*	80% MCS[c]	0·378	1·440	0·990	3
XI–*XV*	80% MCS[c]	0·356	2·576	0·972	5

[a] r Correlation coefficient; n number of members for correlation; [b] see ref.[20]; [c] MCS = methylcellosolve.

nitramino group in their chain), *VIII*–*X* (where nitramino groups are separated from carboxylic groups by one methylene group) and *XI*–*XV* (with two methylene groups between nitramino and carboxylic groups). There is almost no difference between the values of slopes calculated for dicarboxylic acids of the type HOOC.$.(CH_2)_nCOOH$ ($n = 1$ to 8) in water ($S = 1{\cdot}11$) and in 80% methylcellosolve ($S = 1{\cdot}20$), the both values being close to unity. With nitraminodicarboxylic acids the values of the slope S are considerably differing and are higher than those of aliphatic acids with carbon chains.

There are two further models much more important for correlation of transmission of polar effects of substituents: inductive model[21] and Kirkwood–Westheimer model. The former presumes polarisation of bonds between the substituent and the reaction centre. The influence of a substituent depends on number and nature of inserted atoms. This model can be expressed by Eq. (*4*), where ε is transmission coefficient of atoms inserted between the substituent and reaction centre. Value of

$$\log\left(K_1/4K_2\right) = \varrho\sigma\varepsilon^n \qquad (4)$$

TABLE III

Comparison of the ΔpK^{H_2O} Found and Calculated according to Method of Kirkwood and Westheimer

Acid	Found	Calculated			
		R_M^a	R^b	R_F^c	D_E^d
III	1·31	1·05	1·18	1·35	12·5
IV	0·87	0·72	0·86	1·06	15·0
V	0·71	0·54	0·64	0·81	18·6
VIII	0·63	0·48	0·57	0·72	20·1
IX	0·50	0·41	0·50	0·69	20·2
X	0·42	0·30	0·40	0·52	25·5
XI	0·36	0·30	0·40	0·52	25·5
XII	0·34	0·27	0·34	0·49	25·5
XIV	0·12	0·10	0·14	0·22	50·0

[a] R_M distance of the protons of carboxylic groups in the maximum extended molecule; [b] R arithmetic mean of the proton distances; [c] R_F distance of the protons in a molecule having free rotation; [d] D_E effective dielectric constant.

this coefficient depends on both the atoms and bonds between them[22]; π bonds have higher transmission coefficients than the saturated bonds *e.g.* sp^3 and sp^2 carbon atoms have 0·48 and 0·67, respectively.

When correlating the acids measured by us (*III*–*XIV*) in water we obtained $\varepsilon = 1{\cdot}29$. This calculated value of ε is much too high, even though there are also nitrogen atoms with free electron pair in the chain. However, the number of sp^3 carbon atoms in the chain of the molecules is higher, and the ε values should be substantially lower. Therefrom it can be deduced that the inductive model does not fit our case.

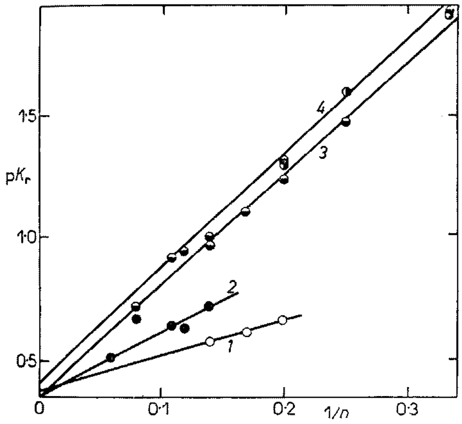


FIG. 1

Dependence of Difference in Dissociation Constants (p*Kr*) on Distance of Carboxylic Groups (1/*n*)

80% methylcellosolve: *1* acids *VIII*–*X* (○), *2* *XI*–*XV* (●), *4* *III*–*V* (◑); water: *3* acids *III*–*V*, *VIII*–*X* and *XII*–*XV* (◒).

The latter model considers the electrostatic influence of the field. Kirkwood and Westheimer[23] presumed the molecule located in a cavity with low dielectric constant surrounded by solvent. For dipolar substituents they derived Eq. (5), where

$$\log (K_1/\sigma K_2) = e^2/2{\cdot}303kRTD_E \qquad (5)$$

the important factors are the dielectric constant (D_E, which is a function of the shape and size of the molecule) and the distance of the protons (R). For determination of D_E of the molecule it was necessary, first of all, to calculate its volume. The van der Waals volume was calculated from atomic increments[24], and D_E was calculated according to Edward[25]. The results are given in Table III. Comparison of the found and the calculated ΔpK values shows that the model of a molecule with free rotation fits well the acids *III* to *V*. For longer chains better agreement was attained with average R values calculated as an arithmetic mean between freely rotating and maximum expanded chain ($R = (R_F + R_M)/2$).

On the basis of the results obtained and comparisons carried out it can be stated that out of the three considered models for correlation of dissociation constants and molecular structure of dicarboxylic acids the electrostatic model fits best, the transmission of polar effects of substituents being not dependent on nature and number of the atoms located between the two carboxylic groups.

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