dient. In each case, 13 fractions were collected; 4.8 g of the 1979 extract were used in one experiment, 17.4 g of the 1982 collection in another. A modified Kupchan partition scheme[19] was used to separate the 1984 extracts, yielding hexane (39.99 g), CCl_4 (5.35 g), $CHCl_3$ (5.76 g), EtOAc (0.20 g), and H_2O (0.49 g).

(5*S*,6*S*,9*R*,12*R*)-4,5,6,9-Tetrahydro-6,7,12-trimethyl-6,9-ethanocycloocta[*b*]furan-5-yl Acetate (5-Acetoxynakafuran 8, 1). A portion of fraction 2 (397 mg, eluted with hexane–EtOAc, 24:1) from the Florisil chromatography of the 1979 collection was permeated through Bio Beads S-X8 with CH_2Cl_2–cyclohexane (3:2), affording 1, 232 mg (0.4% dry weight), a colorless oil: $[\alpha]_D$ −31.1° (*c* 3.06, $CHCl_3$); ν_{max} (CCl_4) 3007, 2931, 1735, 1369, 1236, 1161, 851 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (1 H, d, *J* = 7 Hz), 1.02 (3 H, s), 1.20 (1 H, ddd, *J* = 12, 12, 4), 1.54 (1 H, ddq, *J* = 12, 6, 7), 1.69 (1 H, ddd, *J* = 12, 6, 4), 1.79 (3 H, br s), 2.05 (3 H, s), 2.46 (1 H, dd, *J* = 13, 10), 2.56 (1 H, dd, *J* = 13, 6), 3.46 (1 H, dt, *J* = 7.5, 4), 4.96 (1 H, dd, *J* = 10, 6), 6.00 (1 H, br d, *J* = 7.5), 6.09 (1 H, d, *J* = 1.5), 7.12 (1 H, d, *J* = 1.5); ^{13}C NMR ($CDCl_3$) δ 17.5 (q), 18.0 (q), 21.0 (q), 21.5 (q), 29.0 (t), 33.2 (d), 34.5 (d), 37.5 (t), 44.4 (s), 83.5 (d), 113.7 (d), 114.6 (s), 124.9 (d), 138.6 (d), 139.5 (s), 150.0 (s), 170.5 (s); high resolution EIMS, *m/z* 274.1568 (M^+, $C_{17}H_{22}O_3$ requires 274.1568); low resolution EIMS, (relative intensity) *m/z* 274 (40), 232 (16), 215 (16), 214 (59), 199 (100), 187 (11), 185 (10), 178 (9), 158 (21), 123 (23), 121 (45), 107 (26), 107 (15), 105 (11), 96 (22), 95 (37), 91 (16), 77 (14).

(5*S*,6*S*,9*R*,12*R*)-4,5,6,9-Tetrahydro-6,7,12-trimethyl-6,9-ethanocycloocta[*b*]furan-5-ol (5-Hydroxynakafuran 8, 2). A solution of 155 mg of $Ba(OH)_2{\cdot}8H_2O$ (0.49 mmol) in 80% EtOH (15 mL) was added to a 0.5-mL solution of 131 mg of 1 (0.48 mmol) in CH_2Cl_2. The mixture was stirred in a sealed flask at 55 °C for 3 h and then at room temperature overnight. The reaction mixture was neutralized with 4% HCl, the EtOH was removed, in vacuo, and the residual aqueous suspension was extracted with CH_2Cl_2 (5 × 10 mL). The combined CH_2Cl_2 phase was evaporated to give 114 mg of light brown oil; gel permeation through Bio Beads S-X8 with CH_2Cl_2–cyclohexane (3:2) gave 108 mg (97%) of 5-hydroxynakafuran 8 (2) as a colorless oil: $[\alpha]_D$ −65.3° (*c* 2.07, $CHCl_3$); ν_{max} (CCl_4) 3400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (1 H, d, *J* = 7 Hz), 1.19 (3 H, s), 1.26 (1 H, ddd, *J* = 12, 12, 4), 1.65 (2 H, m), 1.81 (3 H, br s), 2.53 (1 H, dd, *J* = 14.5, 5), 2.73 (1 H, dd, *J* = 14.5, 10), 3.45 (1 H, dt, *J* = 7.5, 4), 3.69 (1 H, dd, *J* = 10, 5), 5.99 (1 H, br d, *J* = 7.5), 6.13 (1 H, d, *J* = 1.5), 7.14 (1 H, d, *J* = 1.5); ^{13}C NMR ($CDCl_3$) δ 18.6 (q), 19.9 (q), 22.5 (q), 29.8 (t), 33.5 (d), 34.2 (d), 37.1 (t), 45.9 (s), 82.7 (d), 114.1 (d), 114.3 (s), 124.6 (d), 138.7 (d), 139.9 (s), 152.1 (s); high resolution EIMS, *m/z* 232.1465 (M^+, $C_{15}H_{20}O_2$ requires 232.1464) (M^+, 62) 217 (8), 214 (4), 199 (24), 137 (10), 136 (100), 122 (24), 121 (16), 108 (18), 107 (32), 105 (9), 91 (19), 77 (12), 69 (25), 43 (19).

Isolation of 5-Hydroxynakafuran 8 (2) from *Dysidea etheria*. Fraction 3 (1.23 g, eluted with hexane–EtOAc, 9:1) from the Florisil chromatography of the 1982 collection was permeated through Bio-Beads S-X4 (column 92 × 4 cm) with hexane–CH_2Cl_2–EtOAc (4:4:1). Six fractions were obtained; fractions 4 (84 mg) and 5 (274 mg) consisted primarily of 2 and dysetherin;[4] these fractions were combined and subjected to low pressure chromatography on silica gel (100 g Whatman LPS-2, 2.5 × 38 cm, $\sim$15 psi N_2). Elution with hexane-Et_2O (3:1) gave 265 mg (0.02% dry weight), a colorless oil. This material was identical in all respects with the product obtained by hydrolysis of 5-acetoxynakafuran 8 (1).

2-Phenylbutanoyl Ester of 5-Hydroxynakafuran 8. Racemic 2-phenylbutyric acid (58 mg, 0.32 mmol) was dissolved in 1 mL of CH_2Cl_2 and 2 mL of $SOCl_2$ and the mixture was refluxed for 3 h. The mixture was then reduced in vacuo, and the residue was dissolved in 2 mL of dry pyridine; a solution of 36 mg of 2 (0.16 mmol) in dry benzene was added, along with 2 mg of (dimethylamino)pyridine. The flask was flushed with N_2, sealed, heated to 55 °C for 4 h, and then left at room temperature overnight. After the solvents were removed, in vacuo, the residue was partitioned between Et_2O and 5% $NaHCO_3$. The Et_2O phase was reduced to 71 mg of a yellow oil which was permeated through Sephadex LH-20 to give the ester 5, 26 mg (43%): $[\alpha]_D$ −33.4° (*c* 2.64, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.3–7.2 (5 H, br s), 7.08 (1 H, d), 6.04 (1 H, d), 6.90 (1 H, br d), 4.90 and 4.80 (each 1 H, dd, ratio $\sim$6:1), 3.38 (1 H, ddd), 2.45 (1 H, dd), 2.30 (1 H, dd), 1.08 (1 H, m), 1.65 (3 H, br s), 1.70–1.40 (3 H, overlapping m), 1.20 (1 H, m), 0.90 (3 H, d), 0.86 (3 H, d), 0.62 (3 H, s); MS, *m/z* (relative intensity) 378 (M^+, 4), 231 (10), 214 (30), 199 (18), 119 (100), 91 (77).

The 5% $NaHCO_3$ phase was acidified with 5% HCl and extracted with CH_2Cl_2 (4 × 10 mL). The CH_2Cl_2 was reduced, in vacuo, to give 24.5 mg of 2-phenylbutyric acid: $[\alpha]_D$ −4.9° (*c* 2.45, $CHCl_3$); optical yield 20%.

(5*S*,6*S*,9*R*,12*R*)-6,9-Dihydro-6,7,12-trimethyl-6,9-ethanocycloocta[*b*]furan-5(4*H*)-one (5-Ketonakafuran 8, 6). A solution of 70.5 mg (0.30 mmol) of 2 in 1 mL of CH_2Cl_2 was added to a stirred suspension of 575.8 mg of pyridinium dichromate in 5 mL of dry pyridine and 2 mL of CH_2Cl_2 at 0 °C. After addition was complete, the temperature was allowed to rise to room temperature over 30 min. The mixture was reduced to a dark brown gum which was suspended in CH_2Cl_2 and filtered through a pad of silica gel and Celite. The filtrate yielded a brown oil upon evaporation. Gel permeation (Bio-Beads S-X8) of this oil gave 43 mg (62%) of 5-ketonakafuran 8 (6) as a colorless oil: $[\alpha]_D$ +35.1° (*c* 1.51, $CHCl_3$); ν_{max} (CCl_4) 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (1 H, d, *J* = 7 Hz), 1.20 (3 H, s), 1.38 (1 H, ddd, *J* = 12, 12, 4), 1.65 (1 H, ddd, *J* = 12, 6, 4), 1.74 (3 H, br s), 2.02 (1 H, ddq, *J* = 12, 6, 7), 3.17 (1 H, d, *J* = 12.9), 3.52 (1 H, d, *J* = 12.9), 3.67 (1 H, dt, *J* = 7.3, 4), 5.82 (1 H, br d, *J* = 7.3), 6.11 (1 H, d, *J* = 1.7), 7.15 (1 H, d, *J* = 1.7); ^{13}C NMR ($CDCl_3$) δ 19.0 (q), 20.2 (qa), 21.7 (q), 33.5 (t), 35.6 (d), 36.3 (d), 40.0 (t), 56.5 (s), 111.5 (d), 113.8 (s), 123.5 (d), 139.0 (d), 140.0 (s), 153.0 (s), 212.0 (s); MS, *m/z* (relative intensity) 230 (M^+, 27), 215 (8), 187 (29), 159 (15), 121, 49 (92), (50), 81 (100).

Isolation of 5-Ketonakafuran 8 (6) from *Dysidea etheria*. During the reisolation of dysetherin,[4] 1 mg (8 × 10^{-5} % dry wt) of 5-ketonakafuran 8 (6) was obtained from the CCl_4-soluble extracts of the 1984 collection by successive gel permeation chromatography through Bio-Beads S-X4 (hexane–CH_2Cl_2–EtOAc, 4:3:1), Sephadex LH-20 (CH_2Cl_2–MeOH, 1:1) and Bio-Beads S-X8 (CH_2Cl_2–cyclohexane, 3:2), followed by low pressure silica gel chromatography (hexane–MeO-*t*-Bu, 17:3). The ketofuran thus obtained was identical with the product of the oxidation of 2.

Acknowledgment. We thank F. Connor, T. Schram, and R. West for assistance in the collection and Dr. Klaus Ruetzler for the identification of *Dysidea etheria*. Professor P. J. Scheuer and Dr. G. Schulte kindly provided a ^1H NMR spectrum of 3. Dr. Guylyn R. Warren provided advice and assistance with the DNA repair assays. The fieldwork was supported by grants from the H. B. Wilkinson and Samuel B. Ryker Foundations and the Continental and Exxon Corporations. Work at Montana State University was supported by grants from the National Cancer Institute (CA 35905), the Office of Sea Grant (Department of Commerce), and the Montana Agricultural Experiment Station.

Registry No. 1, 89837-73-0; 2, 89837-74-1; 5 (isomer 1), 112348-67-1; 5 (isomer 2), 112420-31-2; 6, 112348-68-2; $MeCH_2CH(Ph)CO_2H$, 7782-29-8; $MeCH_2CH(Ph)COCl$, 51260-63-0.

The Relationship between the Brønsted Acidities of Imides and Their Hydrogen-Bonding Acidities toward Oxygen Bases[1]

Jack Hine,* Soonkap Hahn, and Jeongsug Hwang

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

Received July 14, 1987

It is known that for closely related acids and for closely related bases equilibrium constants for hydrogen bonding increase with the Brønsted acidity of the acids and the

---

(1) This investigation was supported in part by Grant No. GM32784 from the National Institutes of Health.

Brønsted basicity of the bases.[2] The slopes of log–log plots of equilibrium constants vs acidity constants for a constant base or of equilibrium constants vs basicity constants for a constant acid are less than 1.0, but the exact value of the slope and the intercept can depend on to what family the acids and bases belong. No study seems to have been made of the effect of changing the acidity of NH acids in a series of closely related acids. In view of the enormous importance of hydrogen bonding by such acid—all the hydrogen bonds between nucleic acid bases are of this type—we have studied the effect of changing the acidity of imides over a wide range on their equilibrium constants for hydrogen bonding as acids. Since the only significantly basic groups in thymine and uracil are unicoordinate oxygen atoms and since cytidine and guanine also contain such basic groups, we have studied bases of this type. This work should form part of the basis for estimating the strength of the individual hydrogen bonds in species that are held together by several hydrogen bonds.

Experimental Section

Tetrafluorosuccinimide was prepared by passing excess ammonia gas into a solution of tetrafluorosuccinic anhydride and heating the product to obtain an ammonium salt, which was acidified to obtain the monoamide. Heating the monoamide with excess phosphorus pentoxide followed by three sublimations of the product gave the imide, mp 66–69 °C (lit.[3,4] mp 49.5 °C and 66.0–66.5 °C).

Light-catalyzed addition of chlorine to citraconimide followed by sublimation gave 2,3-dichloro-2-methylsuccinimide, mp 92–96 °C (lit.[5] mp 93–94.5 °C). Refluxing of some of this imide with 10 times its weight of water followed by recrystallization from chloroform gave 2-chloro-3-methylmaleimide, mp 152–154 °C (lit.[5] mp 147–148.5 °C).

2-Ethyl-2-methylsuccinimide was made from the acid by heating with ammonium hydroxide to 200 °C, vacuum distillation, and recrystallization from hexane to give white crystals, mp 51.5–53 °C (lit.[6] mp 50–51.5 °C).

Alkylation of uracil with 1-bromopentane followed by chromatographic separation and recrystallization from hexane–chloroform gave 1-pentyluracil, mp 72–74 °C (lit.[7] mp 73–74 °C).

Equilibrium constants were determined by infrared measurements with a Pye Unicam PU9516 spectrophotometer with a lithium fluoride prism. The absorbance was expressed as a function of the various relevant equilibrium constants and extinction coefficients. Then, the unknown parameters were determined by the method of nonlinear least squares.[8] The solubility of 2-ethyl-2-methylsuccinimide is high enough (about 1.7 M) that the equilibrium constant for dimerization and the extinction coefficient for the dimer could be obtained fairly reliably, and an equilibrium constant for further polymerization could even be estimated. The extinction coefficient for the dimer was only 8% as large as the one for the monomer. None of the other imides could be transformed as much as 60% to the dimer, and therefore the extinction coefficients of their dimers, at the monomeric N–H stretching peaks where measurements were made, were assumed to be negligible.

Even though the extinction coefficient of monomeric imide was determined when the equilibrium constant for dimerization was determined, it was treated as an unknown in the least-squares determinations of equilibrium constants for complexing with bases: the values obtained were always within 3% of the previous value except in the case of tetrafluorosuccinimide complexing with *N*-methylpyrrolidone, where they averaged 6% smaller. The extinction coefficients initially obtained for the complexes were always small and often slightly negative. The treatments were therefore repeated, to obtain the values listed, with the assumption that absorption by the complex was negligible. The old values were all within 27% of the new ones.

The equilibrium constant for complexing of tetrafluorosuccinimide with hexamethylphosphoramide was so large that it was difficult to measure. The data were treated in the same way used previously for the reaction of 1,8-biphenylenediol with hexamethylphosphoramide.[9] In the three runs that were made, the concentration of tetrafluorosuccinimide, as calculated from the gravimetric method in which the dilute solution had been prepared, had to be multiplied by 0.95, 0.93, and 0.94 to minimize the sum of the squares of the deviations of the calculated from the observed absorbances. This procedure decreased the value of K obtained by about 35%; it decreased the standard deviation of the absorbances to about one-third of their previous value.

The thermodynamic pK_a values for the imides were determined by potentiometric titration at 25 °C in aqueous solution. Activity coefficients were calculated from the Davies equation.[10] Attempts to determine the pK_a of tetrafluorosuccinimide in this way suggested that this imide is too strong an acid to determine its pK_a. However, the ^{19}F NMR spectrum of a titration solution showed two peaks of equal size, as would be expected from the amino acid that would result from hydrolysis of the imide, whose ^{19}F NMR spectrum has only one peak. Further NMR Studies showed that the formation of amido acid took several minutes at acidities in excess of that of 1 M perchloric acid but was too fast to measure in solutions with pHs near the expected pK_a of the tetrafluoro imide; therefore, we make no more attempts to determine the pK_a of this compound. The other pK_a values are estimated to have an uncertainty of about 0.1.

Results

To correct for effects of polymerization (via hydrogen bonding) of the imides on their hydrogen bonding with the bases, we measured the apparent extinction coefficients of the imides over a range of concentrations that covered all the concentrations used in studying their hydrogen bonding to bases. In all cases, the apparent extinction coefficient decreased at some of the higher concentrations. With 2-ethyl-2-methylsuccinimide, the solubility was high enough that this decrease was as much as 89%. When we assumed that only dimerization was occurring, a least-squares treatment of the absorbance values gave an equilibrium constant for dimerization of 69 M^{-1} but an extinction coefficient of -23 M^{-1} cm^{-1} for the dimer at 3420 cm^{-1}. The agreement of the observed with the calculated absorbances is improved by allowing for additional polymerization, and, in addition, physically possible values were obtained for all the parameters. The equilibrium constant for adding an additional monomer unit to an existing polymer was assumed to be the same for any polymer (but not for the monomer). The dimer and higher polymers were assumed to have extinction coefficients proportional to the number of monomer units they contain. This is similar to the procedure used in studying the hydrogen bonding of *N*-alkylamides.[11,12] The dimerization equilibrium constant (standard deviation), 59 (3) M^{-1}, additional polymerization equilibrium constant, 26 (5) M^{-1}, monomer extinction coefficient, 240 (2) M^{-1} cm^{-1}, and the extinction coefficient increment, 9.5 (3) M^{-1} cm^{-1}, for another monomer unit in the polymer lowered the standard deviation of the observed from the calculated apparent

---

[2] Hine, J. *Structural Effects on Equilibria in Organic Chemistry*; Wiley: New York, 1975; Sections 6-8.

[3] Sankina, L. V.; Kostikin, L. I.; Ginsburg, V. A. *J. Org. Chem. USSR (Engl. Transl.)* **1972**, *8*, 1345–1346.

[4] Henne, A. L.; Zimmer, W. E. *j. Am. Chem. Soc.* **1951**, *73*, 1103–1105.

[5] Earl, R. A.; Clough, F. W.; Townsend, L. B. *J. Heterocycl. Chem.* **1978**, *15*, 1479–1483.

[6] Overberger, C. G.; Wang, D. W. *J. Org. Chem.* **1981**, *46*, 2757–2764.

[7] Baker, B. R.; Kawazu, M. *J. Med. Chem.* **1967**, *10*, 302–304.

[8] Hamilton, W. C. *Statistics in Physical Sciences*; Ronald: New York, 1964; Sections 4.1 and 5.3.

[9] Hine, J.; Hahn, S.; Miles, D. E. *J. Org. Chem.* **1986**, *51*, 577–584.

[10] Davies, C. W. *J. Chem. Soc.* **1938**, 2093–2100.

[11] LaPlanche, L. A.; Thompson, H. B.; Rogers, M. T. *J. Phys. Chem.* **1965** *69*, 1482–1488.

[12] Graham, L. L.; Chang, C. Y. *J. Phys. Chem.* **1971**, *75*, 776–783 and 784–788.

Table I. pK_a Values, Extinction Coefficients, and Equilibrium Constants for Dimerization of Imides[a]

imide	pK_a	ϵ_{imide}, M^{-1} cm^{-1}	wavelength, cm^{-1}	K, M^{-1}	max % dimer	highest concn, M
2-ethyl-2-methylsuccinimide	9.34	240	3420	59	41	0.30
1-pentyluracil		202	3410	61	56	0.024
2-chloro-3-methylmaleimide	7.54	254	3400	10.4	16	0.011
2,3-dichloro-2-methylsuccinimide	5.84	197	3380	29	48	0.031
tetrafluorosuccinimide	2.1[b]	178	3340	4.4	12	0.019

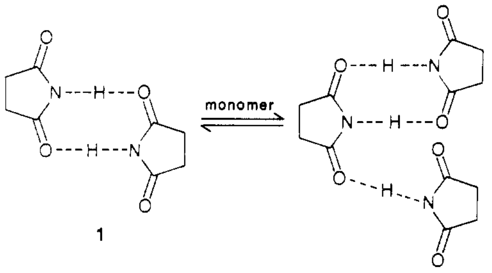
[a] K values and ϵ values in carbon tetrachloride and pK_a values in water, all at 25 ± 1 °C. [b] Estimated as described in text.

Table II. Equilibrium Constants for Hydrogen Bonding of Imides to Various Bases[a]

	K, M^{-1}					
imide	N-methyl-2-pyrrolidone	Me_2SO	$(CH_2)_4SO$	$(Me_2N)_3PO$	THF[b]	EtOAc
2-ethyl-2-methylsuccinimide	30	64	72	270		
	(1)	(3)	(2)	(20)		
2-chloro-3-methylmaleimide	90	136	143	758		
	(2)	(7)	(3)	(15)		
2,3-dichloro-2-methylsuccinimide	330	480	560	6700		
	(10)	(30)	(20)	(500)		
tetrafluorosuccinimide	7700	7300	10000	450000	240	87
	(400)	(300)	(500)	(80000)	(10)	(3)
p-fluorophenol[c]	234	310[d]	430[d]	3630	18	12

[a] In carbon tetrachloride at 25 ± 1 °C. Values in parentheses are estimated standard deviations. [b] Tetrahydrofuran. [c] From ref 16 unless noted otherwise. [d] Calculated from the equilibrium constant for complexing with m-nitrophenol in ref 9 by assuming that a log–log plot of K values for this phenol vs the values for p-fluorophenol is a straight line.

extinction coefficients from 2.34 to 2.14 M^{-1} cm^{-1}. These values may be rationalized in terms of the following structural equation for transformation of dimer 1 to trimer 2. Formation of the dimer gives two hydrogen bonds; every additional monomer unit that is added thereafter adds only one new hydrogen bond. It is thus not surprising that the equilibrium constant for dimerization is larger than the equilibrium constant for adding a new monomer unit to an already existing polymer. With N-alkylamides, the equilibrium constants for further polymerization is considerably larger than the equilibrium constant for dimerization.[11,12] This is because ordinary N-alkylamides can form a doubly hydrogen bonded dimer only from their cis conformations, but they exist predominantly at trans conformers. The linear dimer of an amide (or imide) has a more basic oxygen atom and a more acidic NH group than the monomeric species does. This tends to make the equilibrium constants for further polymerization larger. This factor must affect the equilibrium constants for polymerization of our imides, but it is outweighed by the extra hydrogen bond formed in dimerization. The same relative weights of the factors involved explains why hydrogen-bonding polymerization of imides beyond the dimer stage has been reported to be too minor to detect.[13-15]



1

2

The other imides were not soluble enough for reliable equilibrium constants to be obtained by least-squares treatment without additional assumptions. We assumed that the extinction coefficients of the dimers were neglible. The resulting equilibrium constants are listed in Table I along with the pK_a values and the maximum extents of conversion to the dimer obtained in the concentration range (also listed) studied. If we had assumed that the extinction coefficients of the other dimers were the same as that we found for the dimer of 1-ethyl-1-methylsuccinimide, the K values for these imides in Table I would be 10–17% larger. If the equilibrium constants for further polymerization of these imides and the extinction coefficients of their polymers are similar to the value obtained for 2-ethyl-2-methylsuccinimide, the calculated K values for 1-pentyluracil and 2,3-dichloro-2-methylsuccinimide would be about 5% smaller, but the values for the other two imides would not be significantly affected.

Equilibrium for hydrogen bonding to bases was also studied by infrared measurements. By use of excesses of the bases, whose extinction coefficients at the N–H stretching frequencies where the measurements were made are quite small (and were allowed for), the fraction of the imide transformed to the complex ranged from zero to at least 91% for 2-ethyl-2-methylsuccinimide, 81% for 2-chloro-3-methylmaleimide, 86% for 2,3-dichloro-2-methylsuccinimide, and 96% for the four stronger bases used with tetrafluorosuccinimide. Hydrogen bonding to dimeric imide was neglected. The dimer was usually present in considerably lower concentrations than the monomer, and its most plausible structure contains no free acidic hydrogen atom. The values obtained for the imides and for the reference acid p-fluorophenol[16] are listed in Table II.

Figure 1 is a log–log plot of the equilibrium constants obtained for the various imides vs the values for p-fluorophenol hydrogen bonding to the same bases, also in carbon tetrachloride. The relatively good straight lines obtained show that relative basicities toward imides are the same as toward the reference OH acid. The slopes (standard deviations) of the lines for 2-ethyl-2-methylsuccinimide, 0.70 (0.14); 2-chloro-3-methylmaleimide, 0.75 (0.05); 2,3-dichloro-2-methylsuccinimide, 1.10 (0.05); and tetrafluorosuccinimide, 1.42 (0.08), increase monotonically with increasing acidities of the imides. This sort of trend

---

(13) Tsuboi, M. *Bull. Chem. Soc. Jpn.* **1951**, *24*, 75–77.

(14) Lord, R. C.; Porro, T. J. *Z. Elektrochem.* **1960**, *64*, 672–676.

(15) Susi, H.; Timasheff, S. N.; Ard, J. S. *J. Biol. Chem.* **1964**, *239*, 3052–3054.

(16) Taft, R. W.; Gurka, D.; Joris, L.; Schleyer, P. v. R.; Rakshys, J. W. *J. Am. Chem. Soc.* **1969**, *91*, 4801–4808.

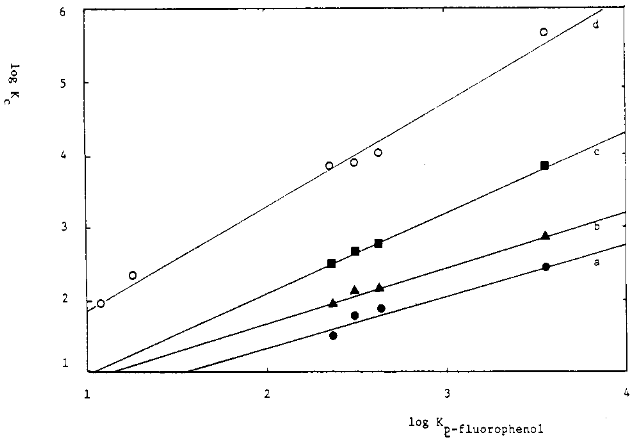


Figure 1. Log–log plot of equilibrium constants for hydrogen bonding of four imides to various bases vs values for *p*-fluorophenol hydrogen bonding to the same bases. (a) 2-ethyl-2-methylsuccinimide (●), (b) 2-chloro-3-methylmaleimide (▲), (c) 2,3-dichloro-2-methylsuccinimide (■), (d) tetrafluorosuccinimide (○).

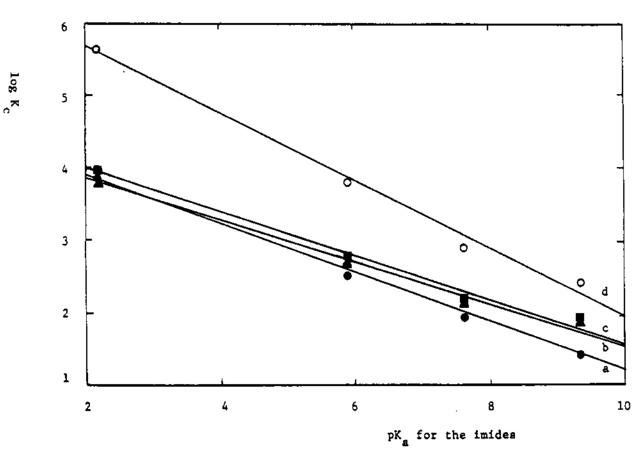


Figure 2. Plot of logarithms of equilibrium constants for hydrogen bonding of various imides to four bases vs pK_a values for the imides. (a) *N*-methyl-2-pyrrolidone (●), (b) dimethyl sulfoxide (▲), (c) tetramethylene sulfoxide (■), (d) hexaphosphoramide (○).

has been observed previously with OH acids.[2]

Figure 2 is a log–log plot of the equilibrium constants in carbon tetrachloride for the four stronger bases vs the pK_a values of the imides in water, both at 25 °C. Since we were not able to determine the pK_a of tetrafluorosuccinimide, we estimated it by assuming that the tetrafluoro substituents would have the same effect on the pK_a of succinimide (9.35 at an unstated temperature[17]) that they do on the pK_a of pyrrolidinium ions (11.305[18]). The pK_a of 3,3,4,4-tetrafluoropyrrolidinium ions is 4.05;[19] hence the pK_a of tetrafluorosuccinimide should be about 2.1. The relatively good straight lines are analogous to those reported previously for phenols.[2]

Such straight lines as those in Figures 1 and 2 are presumably just approximations to parts of long gradual curves; extrapolation of the straight line leads to the improbable conclusions that 2-ethyl-2-methylsuccinimide would be a stronger hydrogen bonder than tetrafluorosuccinimide toward a very weak base and that *N*-methyl-2-pyrolidone would be stronger than hexamethylphosphoramide toward a very weak acid. The absolute values of the slopes of the lines for *N*-methyl-2-pyrolidone (0.34), dimethyl sulfoxide (0.29), tetramethylene sulfoxide (0.31), and hexamethylphosphoramide (0.46) show an imperfect tendancy to increase with increasing hydrogen-bonding basicity.

The eight lines in Figures 1 and 2 were described by 16 parameters, eight slopes and eight intercepts. We can also use the method of Miller[20] and apply eq 1, which contains

$$\log K_{\text{b-im}} = a\text{p}K_{\text{HB}} + b\text{p}K_a + c\text{p}K_{\text{HB}}\text{p}K_a + d \qquad (1)$$

only four parameters. In this equation $K_{\text{b-im}}$ is the equilibrium constant for complexing of an imide with an oxygen base, pK_{HB} is the logarithm of the equilibrium constant for hydrogen bonding of *p*-fluorophenol with the same base, and pK_a is the value for the imide. Least-squares treatment of the 18 *K* values in Table II gave values of *a*, 1.61 (0.10); *b*, –0.10 (0.02); *c*, –0.08 (0.05); and *d*, 0.62 (0.25). The standard deviation of the calculated from the observed values of log $K_{\text{b-im}}$ was 0.15, which is near 0.14, the average standard deviation of the points from the lines in Figure 2.

Registry No. $(Me)_2S{=}O$, 67-68-5; $HO_2C(CF_2)_2CO_2H{\cdot}NH_3$, 112296-54-5; $HO_2C(CF_2)_2CONH_2$, 425-08-1; $HO_2CCH_2C(Me)(Et)CO_2H$, 631-31-2; $Br(CH_2)_4Me$, 110-53-2; *p*-FC_6H_4OH, 371-41-5; tetrafluorosuccinimide, 377-33-3; 2,3-dichloro-2-methylsuccinimide, 69636-49-3; 2-chloro-3-methylmaleimide, 69636-50-6; 2-ethyl-2-methylsuccinimide, 77-67-8; *N*-methylpyrrolidone, 872-50-4; tetramethylene sulfoxide, 1600-44-8; hexamethylphosphoramide, 680-31-9; 1-pentyluracil, 13350-87-3; tetrafluorosuccinic anhydride, 699-30-9; citraconimide, 1072-87-3; uracil, 66-22-8.

Supplementary Material Available: Sample data on a specific run are listed in Table III and plotted in Figure 3 (2 pages). Ordering information is given on any current masthead page.

---

[17] Kornfeld, E. C.; Jones, R. G.; Parke, T. V. *J. Am. Chem. Soc.* **1949**, *71*, 150–159.

[18] Perrin, D. D. *Dissociation Constants of Organic Bases in Aqueous Solution*; Butterworths: London, 1972; compound 5370.

[19] Roberts, R. D.; Spencer, T. A. *Tetrahedron Lett.* **1978**, 2557–2558.

[20] Miller, S. I. *J. Am. Soc.* **1959**, *81*, 101–106.

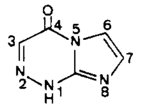
Characterization of New Mesomeric Betaines Arising from Methylation of Imidazo[2,1-*c*][1,2,4]triazin-4(1*H*)-one, Pyrazolo[5,1-*c*][1,2,4]triazin-4(1*H*)-one, and 1,2,4-Triazolo[5,1-*c*][1,2,4]triazin-4(1*H*)-one[1]

Jaume Farràs, Empar Fos, Regina Ramos, and
Jaume Vilarrasa*

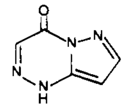
Department of Organic Chemistry, University of Barcelona(III), 08028 Barcelona, Catalonia, Spain

Received June 22, 1987

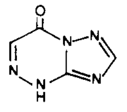
We report here the structure elucidation of the methylation products of imidazo[2,1-*c*][1,2,4]triazin-4(1*H*)-one (**1**) pyrazolo[5,1-*c*][1,2,4]triazin-4(1*H*)-one (**2**), and 1,2,4-triazolo[5,1-*c*][1,2,4]triazin-4(1*H*)-one (**3**), which forces us to correct a tentative proposal[2] regarding one of the methyl derivatives of **3**. The ylide-like or betaine-like structure of some of them is independently confirmed by NOE experiments and by ^{1}H, ^{13}C, and ^{15}N NMR spectra of selectively ^{15}N-labeled products.



1



2



3

---

[1] Presented in part at the XIX Reunión Bienal de la Real Sociedad Española de Química (Santander, September 1982). For a precedent paper, within our Diazo-, Azo-, and Azidoazoles series, see ref 5b.

[2] Tennant, G.; Vevers, R. J. S. *J. Chem. Soc. Perkin Trans. 1* **1976**, 421.

0022-3263/88/1953-0887$01.50/0