1148 cm^{-1} (SO_2); nmr (CCl_4) δ 7.2 (m, 8), 2.4 (s, 3), and 2.3 (s, 3); mass spectrum *m/e* 278, 214, 155, 139, 123, and 91.

Anal. Calcd for $C_{14}H_{14}O_2S_2$: C, 60.43; H, 5.04; S, 23.02. Found: C, 60.43; H, 4.98; S, 23.11.

Exact repetion of the reaction with a 1:2 mol ratio of **1** to **4** gave the same products in the same proportions with recovered **1**. Reaction with a 1:3 mol ratio for 3 hr at 70° gave the same product distribution with unreacted **7**.

Reaction of *p*-Toluenesulfonyl Cyanide (3) with Sodium *p*-Toluenesulfinate (4).—A mixture of **3** (18.1 g, 0.1 mol) and **4** (35.6 g, 0.2 mol) in acetonitrile (600 ml) was stirred under nitrogen at 70° for 3 hr. The reaction mixture was cooled to 25° and filtered. The rsulting solid residue was extracted with two 100-ml portions of methanol and the methanol removed to give 19.7 g (94% based on **3**) of sodium *p*-toluenesulfonate (**5**); properties exactly as described above. The residue from the methanol extraction had an ir spectrum identical with that of sodium cyanate (5.9 g, 91% based on **3**).

The acetonitrile filtrate was cooled to 0° overnight. There were no crystals formed. The acetonitrile was removed by distillation. The resulting solid was recrystallized from hexane to give 24.7 g (89% based on **3**) of *p*-tolyl *p*-toluenethiosulfonate (**7**); properties exactly as described above.

Reaction of a 1:3 mol ratio of **3** to **4** resulted in formation of the same products in the same yields with recovery of unreacted **4**. Reaction of a 1:2 mol ratio for 2 hr at 70° gave the same product distribution with recovered **3**.

Reaction of Sodium Hypochlorite with Sodium *p*-Toluenesulfinate (4) and *β*-Methyl Naphthyl Ketone.—To a mixture of **4** (17.8 g, 0.1 mol) and *β*-methyl naphthyl ketone (Eastman Organic Chemicals, 17.0 g, 0.1 mol) maintained at 70° in acetonitrile (500 ml) was added dropwise over 2 hr Clorox (100 g of solution, 5.25 g NaOCl, 0.07 mol). The white solid residue was collected by filtration and dried to give 18.1 g of solid. Ir and nmr showed this to be a mixture of sodium *p*-toluenesulfinate (**4**) and sodium *p*-toluenesulfonate (**5**). No attempt was made at quantitative analysis.

The acetonitrile was removed from the filtrate. The residue (17.3 g) was dissolved in 100 ml of hot 95% ethanol. Standing overnight at 25° resulted in formation of 1.3 g (11% based on NaOCl) of *β*-naphthoic acid, mp 182–184° (lit.[28] mp 183–184°). The ir and nmr spectra were identical with those of an authentic sample from Eastman.

Reaction of *p*-Toluenesulfonyl Chloride (1) with Sodium *p*-Toluenesulfinate (4) in the Presence of *β*-Methyl Naphthyl Ketone.—The reaction of **1** and **4** (1:3 mol ratio) was carried out exactly as described above except for the presence of *β*-methyl naphthyl ketone (17.0 g, 0.1 mol). The reaction mixture was worked up exactly as described above to give, from the residue, sodium chloride (5.6 g, 96%) and sodium *p*-toluenesulfonate (39.3 g, 195%), and, from the filtrate, *p*-tolyl *p*-toluenethiosulfonate (20.6 g, 74%) and *β*-methyl naphthyl ketone (16.7 g, 98% recovery). There was no evidence for the presence of *β*-naphthoic acid.

Attempted Reaction of Sodium *p*-Toluenesulfinate (4) with 4,4′-Dimethyldiphenyl Disulfone (11).—A mixture of **4** (1.78 g, 0.01 mol) and **11** (1.40 g, 0.0045 mol, isolated from reaction of **1** with **4**) in acetonitrile (100 ml) was heated at 70° for 10 hr. The reaction mixture was cooled and filtered to give 1.68 g (95% recovery) of **4**. The filtrate was concentrated to 50 ml and cooled to 0° overnight. The resulting crystals were collected and dried to give 1.29 g (92% recovery) of **11**.

Attempted Reaction of Sodium *p*-Toluenesulfinate (4) with Cyanogen.—A sealed glass ampoule containing **4** (1.78 g, 0.01 mol) and cyanogen (0.52 g, 0.01 mol) in acetronitrile (10 g) was heated at 70° for 8 hr. The cyanogen and acetronitrile were removed to give 1.69 g (95% recovery) of **4**.

Registry No.—**1**, 98-59-9; **2**, 143-33-9; **3**, 19158-51-1; **4**, 824-79-3.

[28] M. Newman and H. Holmes, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 428.

The Reactivity of Some Imide and Sulfonamide Anions with Methyl Iodide in Methanol[1]

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Rate coefficients for reactions of the anions of succinimide phthalimide, benzenesulfonamide, *N*-methylbenzenesulfonamide, and *N*-phenylbenzenesulfonamide and of methoxide ion with CH_3I in CH_3OH have been determined. Reactivity among the nitranion nucleophiles correlates with basicity, except that the benzenesulfonamide anion is about one-third as reactive as expected from its basicity.

Although the conjugate base anions of phthalimide, of succinimide, and of sulfonamides with at least one hydrogen on nitrogen are well known to be alkylated readily, the reactivity of such anions toward saturated carbon appears not previously to have been measured.

We have determined rates of reactions of the anions of succinimide, phthalimide, benzenesulfonamide, *N*-methylbenzenesulfonamide, and *N*-phenylbenzenesulfonamide with methyl iodide in methanol. Rates were determined by potentiometric titration of the iodide ion released. For reasons mentioned below, the rate of reaction of $NaOCH_3$ with CH_3I was also determined. Results are summarized in Table I.

When the amide or imide is quite acidic and the reactivity of its anion toward CH_3I is quite high compared to that of methoxide ion, such a study is straightforward. However, when these conditions are not met there is a complication stemming from incompleteness of conversion of the amide or imide to its conjugate base. The pertinent acid–base equilibrium is that of eq 1, in which "NH" represents the amide or imide and "N^-" its conjugate base.

$$CH_3O^- + NH \overset{K_{eq}}{\rightleftarrows} N^- + CH_3OH \qquad (1)$$

The total rate of displacement of the iodide ion is the sum of components due to CH_3O^- and to the nitranion nucleophile, N^-. When the amide or imide is furnished in excess over $NaOCH_3$, we may write eq 2 and 3, where $[CH_3O^-]_{st} = [CH_3O^-] + [N^-]$.

$$d[I^-]/dt = k_2[CH_3I][CH_3O^-]_{st} \qquad (2)$$

$$= k_N[CH_3I][N^-] + k_0[CH_3I][CH_3O^-] \qquad (3)$$

By equating the right sides of eq 2 and 3 and substituting for $[N^-]$ the product $K_{eq}[NH][CH_3O^-]$ (*cf.* eq 1), one obtains eq 4. Inasmuch as $[CH_3O^-]_{st} = (1 +$

$$k_2[CH_3O^-]_{st} = (k_NK_{eq}[NH] + k_0)[CH_3O^-] \qquad (4)$$

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(1) Based on the Ph.D. Thesis of J. H. Beale, Brown University, 1966. This research was supported in part by a grant from the Petroleum Research Fund administered by the American Chemical Society.

(2) University of California, Santa Cruz, California 95060.

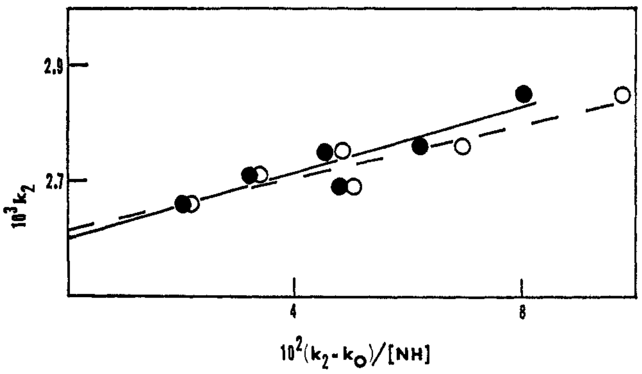

Figure 1.—Plots of data for the reaction of the benzenesulfonamide anion with CH_3I at 52.6°, according to eq 5. Open circles and broken line, first plot; filled circles and solid line, iteration.

TABLE I

REACTIONS OF IMIDE AND SULFONAMIDE ANIONS WITH METHYL IODIDE IN METHANOL

Nucleophile	Temp, °C	k_N, M^{-1} sec^{-1}	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, cal deg^{-1} mol^{-1}
$C_6H_5SO_2NCH_3^-$ [a]	25.0	(1.01×10^{-3})[b]		
	30.0	1.68×10^{-3}	17.8	−10.3
	59.9	2.64×10^{-2}		
Succinimide anion	25.0	(3.74×10^{-4})[b]		
	30.0	6.25×10^{-4} [c]	18.0	−11.8
	59.9	9.89×10^{-3} [e]		
Phthalimide anion	25.0	(3.01×10^{-4})[b]		
	30.0	5.11×10^{-4} [d]	18.6	−10.1
	59.9	9.10×10^{-3} [e]		
$C_6H_5SO_2NH^-$ [a]	25.0	(1.70×10^{-4})[b]		
	30.0	2.82×10^{-4}	18.4 ± 0.3	−12.1
	40.6	8.50×10^{-4}		
	52.6	2.61×10^{-3}		
	59.9	4.70×10^{-3}		
$C_6H_5SO_2NC_6H_5^-$	25.0	(1.10×10^{-4})[b]		
	30.0	1.92×10^{-4} [d]	19.7	−8.5
	59.9	3.98×10^{-3} [e]		
$NaOCH_3$	25.0	(2.60×10^{-4}) [b]		
	30.0	4.68×10^{-4}	20.9 ± 0.6	−2.6
	40.6	1.64×10^{-3}		
	52.6	5.23×10^{-3}		
	59.9	1.21×10^{-2}		

[a] See text for method of treating kinetic data. [b] Extrapolated value. [c] Average of two runs. [d] Average of three runs. [e] Average of four runs.

K_{eq}[NH])[CH_3O^-], further substitution and rearrangement afford[3] eq 5.

$$k_2 = k_N + \frac{k_0 - k_2}{K_{eq}[NH]} \qquad (5)$$

According to eq 5, a plot of the observed second-order rate coefficient, k_2, against $(k_0 - k_2)/[NH]$ should be linear with slope $1/K_{eq}$ and intercept k_N. Use of such a plot ot evaluate k_N requires, however, that one know k_0 and [NH]. The former is the rate coefficient for reaction of CH_3O^- with CH_3I and is easily determined separately. The value of [NH] depends on K_{eq} which itself is learned from the slope of the plot. Accordingly, a procedure of iteration was used; it was initially assumed that the only NH present was that in excess of the $NaOCH_3$ added, that is, that reaction 1 had gone to completion. K_{eq} was then estimated from the slope of a plot according to eq 5 and used to reckon a value of [NH] for each reaction mixture. The cycle was repeated until further iteration did not appreciably affect the slope or intercept.

Experiments at several concentrations of excess amide or imide showed that succinimide, phthalimide, and *N*-phenylbenzenesulfonamide are acidic enough so that equilibrium 1 lies essentially fully to the right if excess amide or imide is employed. In these cases k_2 as measured could be equated directly with k_N. With benzenesulfonamide, two cycles of application of eq 5 were sufficient; the first and second cycle plots at 52.6° are presented for purposes of illustration in Figure 1. The k_N values resulting from this treatment of data at four temperatures are listed in Table I; the K_{eq} values varied irregularly with temperature between 164 and 349 M^{-1}. With *N*-methylbenzenesulfonamide, three cycles of application of eq 5 were necessary; the resulting k_N appear in Table I; the K_{eq} from the third cycle were 12 M^{-1} at 30° and 16 M^{-1} at 60°.

Rate coefficients for all runs and details on treatment of them according to eq 5 are given in the thesis of Beale.[1]

In Table I, it is to be noted that the rate coefficients for the nitranion[4] nucleophiles differ at most by a factor of ten and that the reactivity of methoxide ion falls within the range of the nitranion nucleophiles. Entropies of activation are nearly constant among the nitranions, and with one possible exception their rank in reactivity is consistent with their respective enthalpies of activation. The entropy of activation for methoxide ion is distinctly higher than for the nitranions.

For the several nitranions, pK_a's in methanol were estimated in several ways: by conductimetric studies in methanol (on solutions made by combining $NaOCH_3$ and the various NH species in various ratios), from the slopes of the aforementioned plots according to eq 5, by adding 3.9 to pK_a's in 50% (w/w) aqueous methanol determined by potentiometric titration with a glass electrode,[5] and by adding 5.0 to pK_a's in water from the literature.[6] Details are given in the Ph.D. thesis of Beale.[1] For any amide or imide, the several estimates were in fair to good agreement with each other. The pK_a's estimated for anhydrous methanol (with average deviations among the estimates) were as follows: *N*-methylbenzenesulfonamide, 15.5 ± 0.3; succinimide, 14.1 ± 0.3; phthalimide, 14.5 ± 0.5; benzenesulfonamide, 14.9 ± 0.1; and *N*-phenylbenzenesulfonamide, 13.3.

The relationship of nucleophilicity to basicity within this series is shown by a plot (Figure 2) of log k_N (at 30°) *vs.* pK_a. The plot is somewhat arbitrary owing to uncertainty in some of the pK_a estimates. The line drawn is based on linear regression analysis of the data plotted except that for benzenesulfonamide ion. The slope, β', is 0.4. With the usual reservation,[7] this β' value suggests that the forming N–C bond is less than half formed at the transition state.

The point in Figure 2 for the benzenesulfonamide ion falls below the line defined by the other nitranions by 0.52 log units, equivalent to a factor of 3.3 in re-

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[3] *Cf.* J. F. Bunnett and L. A. Retallick, *J. Amer. Chem. Soc.*, **89**, 423 (1967).

[4] The term "nitranion" represents an anion with negative charge significantly (but not necessarily exclusively) on nitrogen. It is analogous to the terms "oxyanion" and "carbanion."

[5] M. Paabo, R. A. Robinson, and R. G. Bates, *J. Amer. Chem. Soc.*, **87**, 415 (1965).

[6] A. L. Bacanella, E. Grunwald, H. P. Marshall, and E. L. Purlee, *J. Org. Chem.*, **20**, 747 (1955).

[7] J. F. Bunnett, *Ann. Rev. Phys. Chem.*, **14**, 271 (1963).

activity. The diminished reactivity of benzenesulfonamide anion is reminiscent of discrepancies often observed in similar Brønsted-like plots for hydroxide ion as compared to alkoxide ions or of ammonia as compared to amines.

The autoprotolysis constant for methanol, as pK_s, is 16.9,[8] and pK_a by the usual arbitrary conversion is 18.3. Extrapolation of the line in Figure 2 would lead to a log k_N at pK_a 18.3 some 1.7 log units greater than observed for methoxide ion, equivalent to a 50-fold deficiency in reactivity for this oxyanion nucleophile.

Experimental Section

The several amides and imides were obtained from commercial sources or synthesized by familiar methods and purified by recrystallization to melting points in good agreement with literature values.

In reaction mixtures for kinetic runs, the initial concentration of methyl iodide was typically *ca.* 0.02 *M*, of the sodium derivative of the amide or imide *ca.* 0.06 *M*, and of the free amide or imide variously from *ca.* 0.02 to 0.14 *M*. Details for particular runs are given in the Ph.D. thesis of Beale.[1] Second-order rate coefficients, k_2, were reckoned by linear regression analysis from the expression, $[1/(a - b)] \ln [b(a - x)/a(b - x)] = k_2t$. In general, good second-order kinetics were observed. Enthalpies and entropies of activation were reckoned from standard expressions.[9]

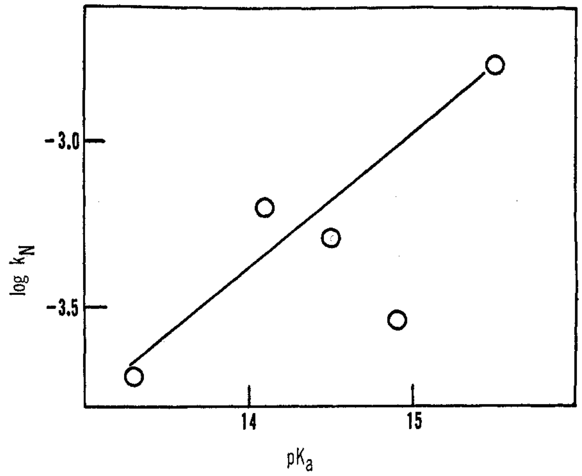

Figure 2.—Relationship of log k_N to pK_a in CH_3OH. From left to right, the points represent the anions of *N*-phenylbenzenesulfonamide, succinimide, phthalimide, benzenesulfonamide, and *N*-methylbenzenesulfonamide, respectively.

The expected *N*-methyl derivatives were isolated from reactions of succinimide, benzenesulfonamide, and *N*-methylbenzenesulfonamide under the conditions of rate measurement and were identified by melting point and/or infrared spectrum.

Registry No.—Methyl iodide, 74-88-4; $C_6H_5SO_2NCH_3^-$, 28627-66-9; succinimide anion, 28627-67-0; phthalimide anion, 28627-68-1; $C_6H_5SO_2NH^-$, 28627-69-2; $C_6H_5SO_2NC_6H_5^-$, 28627-70-5; $NaOCH_3$, 124-41-4.

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[8] R. G. Bates, "Solute–Solvent Interactions," J. F. Coetzee and C. D. Ritchie, Ed., Marcel Dekker, New York, N. Y., 1969, p 52.

[9] J. F. Bunnett, "Investigation of Rates and Mechanisms of Reactions," S. L. Friess, E. S. Lewis, and A. Weissberger, Ed., 2nd ed, Part I, Interscience, New York, N. Y., 1961, p 199.

Mercaptoethanol Catalysis for Hydrolysis of *N*-Benzyl-3-cyanopyridinium Bromide. A Model for the Nitrilase Reaction[1]

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Contribution No. 1928 from the Department of Chemistry, Indiana University, Bloomington, Indiana 47401

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The hydrolysis of *N*-benzyl-3-cyanopyridinium bromide is subject to marked catalysis by dilute aqueous solutions of mercaptoethanol. Under neutral or slightly acidic conditions, the predominant reaction product is the corresponding amide. Under conditions more acidic than pH 3, appreciable amounts of the corresponding acid are formed as well. First-order rate constants for the disappearance of nitrile at fixed concentrations of mercaptoethanol exhibit a bell-shaped dependence upon pH with a maximum near pH 7. First-order rate constants for the disappearance of nitrile at constant values of pH exhibit saturation with respect to mercaptoethanol concentration; under sufficiently basic conditions, excess mercaptoethanol actually causes inhibition of nitrile hydrolysis. These observations are interpreted in terms of (1) addition of mercaptoethanol to the nitrile function to form a thioimidate followed by hydrolysis of the thioimidate to yield the corresponding amide or acid, (2) addition of mercaptoethanol to both the nitrile and thioimidate to form 1,4 adducts which are kinetically inert, and (3) rate-determining formation of the thioimidate on the acidic side of the pH–rate maximum and rate-determining hydrolysis of this intermediate on the basic side.

Among functional groups at the acyl level of oxidation, nitriles are perhaps the most resistant to hydrolysis. The nitrile group is quite stable to both nucleophilic and electrophilic attack and, in consequence, strenuous conditions must usually be employed to effect hydrolysis under either basic or acidic conditions.[3-8] Nevertheless, enzymes have been identified in several sources which are capable of effecting rapid hydrolysis of nitriles at ambient temperatures in neutral aqueous solutions (see below). Our concern with these reactions centers on the elucidation of catalytic pathways through which these enzymes may function.

The basic hydrolysis of nitriles, including benzonitrile,[5,6] propionitrile,[7] and phenylacetonitriles,[9] is kinetically first order in both substrate and hydroxide

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[2] Career Development Awardee of the National Institutes of Health, Grant K3 GM 10248-03; Research Fellow of the Alfred P. Sloan Foundation.

[3] J. D. McLean, B. S. Rabinovitch, and C. A. Winkler, *Can. J. Res., Sect. B*, **20**, 168 (1942).

[4] B. S. Rabinovitch, C. A. Winkler, and A. R. P. Stewart, *ibid.*, **20**, 121 (1942).

[5] K. B. Wiberg, *J. Amer. Chem. Soc.*, **77**, 2519 (1955).

[6] K. B. Wiberg, *ibid.*, **75**, 3961 (1953).

[7] B. S. Rabinovitch and C. A. Winkler, *Can. J. Res. Sect. B*, **20**, 185 (1942).

[8] R. Breslow, R. Fairweather, and J. Keana, *J. Amer. Chem. Soc.*, **89**, 2135 (1967).

[9] E. Angelescu, G. Vasiliu, and D. Zavoianu, *Rev. Chim., Acad. Repub. Pop. Roum.*, **7** (2), 655 (1962); *Chem. Abstr.*, **61**, 4168*d* (1962).