(4i) for a total yield of 23%. After recrystallization twice from chloroform–hexane, there was obtained pure **5**: mp 91–2 °C; ^{1}H NMR δ 1.58 (s, 3 H), 1.67 (s, 3 H), 1.85 (s, 3 H), 2.39 and 2.61 (AB q, 2 H, J = 14 Hz), 7.23–7.92 (m, 4 H); ^{13}C NMR δ 23.07, 26.52, 27.06 (3 CH_3), 43.70 (C-4), 83.92 (C-5), 103.66 (C-3), 134.41, 133.33, 130.30, 129.55, 128.84, 126.92 (aromatic carbons), 162.11 (C=O); mass spectrum (70 eV) m/e (relative intensity) 300 (M^+), 158 (3-chlorobenzoic acid) (14), 156 (42), 141 (11), 139 (33), 128 (24), 127 (100), 126 (8), 56 (11), 55 (7), 43 (40), 42 (5), 41 (10).

Anal. Calcd for $C_{13}H_{15}N_2O_4Cl$: C, 52.27; H, 5.06; N, 9.38; Cl, 11.87. Found: C, 52.54; H, 4.95; N, 9.48; Cl, 11.85

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Registry No.—**1**, 3975-85-7; **5**, 65442-00-4; 4-chlorobenzoyl peroxide, 94-17-7; benzoyl peroxide, 94-36-0; 2-chlorobenzoyl peroxide, 3033-73-6; 3-chlorobenzoyl peroxide, 845-30-7; 4-bromobenzoyl peroxide, 1712-82-9; 4-fluorobenzoyl peroxide, 582-92-3; 4-methoxybenzoyl peroxide, 849-83-2; 4-nitrobenzoyl peroxide, 1712-84-1; 3,5-dinitrobenzoyl peroxide, 15866-24-7.

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Synthesis of 3-Substituted 2-Isoxazolines and 5,6-Dihydro-1,2,4*H*-oxazines

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3-Nitro-2-isoxazoline (**1a**) can be prepared by nitrosation of 1-chloro-3-nitropropane followed by in situ tautomerization and cyclization. Similarly, 3-nitro-5,6-dihydro-1,2,4*H*-oxazine (**1b**) can be prepared from 1-chloro-4-nitrobutane. The nitro group of compounds **1a** and **1b** is readily substituted by a wide variety of nucleophiles. The resulting 3-substituted 2-isoxazolines and 5,6-dihydro-1,2,4*H*-oxazines are normally obtained in fair to excellent yield.

Studies directed at the application of 2-oxazolines[1] and 5,6-dihydro-1,3,4*H*-oxazines[2] to organic synthesis have been extensive and have certainly reaped substantial reward. On the other hand, 2-isoxazolines have received relatively little attention toward their utilization in synthetic problems.[3] In furthering the study of 2-isoxazolines, we wish to report a convenient synthetic approach which allows for their preparation with a hefty array of 3 substituents.[4] This approach also provides easy access to the corresponding six-membered heterocycles (5,6-dihydro-1,2,4*H*-oxazines) which have hitherto received scant attention.[5]

Key intermediates in our approach are 3-nitro-2-isoxazoline (**1a**) and the corresponding six-membered heterocycle **1b**. These can be prepared in yields of 79 and 48%, respectively, by treating 1-chloro-3-nitropropane and 1-chloro-4-nitrobutane with a combination of *n*-propyl nitrite and sodium nitrite in Me_2SO. A convenient alternative preparation[6,7] of **1a** involves treatment of 1-bromo-3-chloropropane with sodium nitrite in DMF; however, the yield of this reaction is only about 50%.[6]

It is proposed that compounds **1a** and **1b** are formed from the nitro compounds[8] by the mechanism of Scheme I. Support for this mechanism rests in the previously reported ability of the combination of *n*-propyl nitrite and sodium nitrite to nitrosate a primary or secondary nitro compound at the α position.[9] For a primary nitro compound, this nitroso derivative would be expected to tautomerize to a nitrolic acid (α-nitrooxime). Normally the nitrolic acid would then be converted to a carboxylic acid.[9b] Here, however, the nitrolic acid preferentially cyclizes via intramolecular substitution (Scheme I). In the preparation of **1b**, a 15% yield of γ-butyrolactone (**2**) is also obtained. This is consistent with the formation and lactonization of 4-chlorobutyric acid as shown in Scheme I. Apparently conversion of the nitrolic acid to carboxylic acid competes with cyclization in this case.

Nucleophilic attack of the carbon–nitrogen double bond of compounds **1a** and **1b** could conceivably occur at either carbon (typical of imines) or at nitrogen (β to the nitro group; compare the reactions of nitroolefins). In fact, we have observed only attack at carbon, the nitro group being expelled in the process. Thus, nitro compounds **1a** and **1b** undergo substitution similar to imidoyl chlorides.[10] Tables I and II

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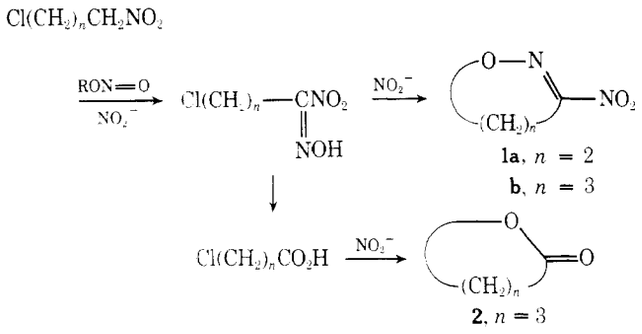
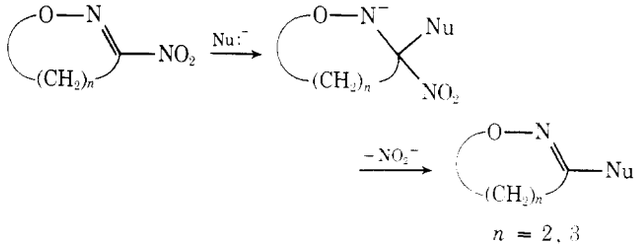
Scheme I



Scheme II



show the results obtained for a number of reactions. Nucleophiles ranging from sodium benzenesulfinate to *n*-butylcadmium can be effectively employed.

Concerning the introduction of an alkyl group, we have examined *n*-butyllithium, lithium *n*-butylcuprate, and *n*-butylcadmium. The first two of these lead to complex mixtures containing only traces, at best, of the substitution product. However, the less reactive organocadmium reagent affords substitution in 51% yield.

A logical mechamism for these reactions involves initial attack by the nucleophile to form a tetrahedral intermediate followed, in a second step, by explusion of nitrite ion (Scheme II). The vastly different rates (less than 1 min at room temperature for *n*-butylcadmium to greater than 1 week for sodium benzenesulfinate) of various nucleophiles are consistent with this stepwise mechanism (as well as other mechanisms[11]) assuming a rate-determining transition to the tetrahedral intermediate.

The best solvents for carrying out substitution are, for the most part, protic ones. Thus, sodium thiophenoxide reacts completely with **1b** in methanol solution within 10 min. In Me_2SO the reaction takes 1 h for completion, despite the higher polarity[12] and the greater nucleophilicity of thiophenoxide in this solvent. Azide ion reacts at least as rapidly with **1a** in aqueous alcohol as in Me_2SO, too. On the other hand, reactions of **1a** and **1b** with cyanide are somewhat faster in Me_2SO than in aqueous solution, although the difference is only a factor of 2 to 3. Clearly the rate-determining transition state for these reactions is more easily attained in protic solvents than in aprotic ones. This suggests hydrogen bonding to the ring nitrogen of compounds **1a** and **1b** facilitating transition to the tetrahedral intermediate. Alternatively, **1a** and **1b** may be fully protonated resulting in enhanced substitution.

Experimental Section

Melting points (uncorrected) were determined on a Mel-Temp capillary apparatus. IR spectra were determined on a Perkin-Elmer 457 spectrophotometer. NMR spectra were measured with a Varian A-60A spectrometer; chemical shifts are expressed in ppm downfield from internal Me_4Si. Mass spectra were recorded on a Hitachi RMU-6 spectrometer. VPC analyses were performed on a Varian 1400 gas chromatograph equipped with a 5 ft × 0.125 in. 1.5% OV-101, Chromosorb G column. Elemental analyses were performed by Chemalytics, Inc., Tempe, Ariz.

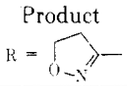
Reagents employed were of the finest commercial grade available. Reagent grade solvents were used as received; other solvents were distilled. Methanol was distilled from magnesium methoxide. Ether and THF were distilled from sodium benzophenone ketyl and were stored under nitrogen.

3-Nitro-5,6-dihydro-1,2,4*H*-oxazine (1b). A 34.4-g (0.25 mol) portion of 1-chloro-4-nitrobutane[13] was added to a solution containing 86.3 g (1.25 mol) of sodium nitrite and 45.2 g (0.51 mol) of *n*-propyl nitrite[14] in 800 mL of Me_2SO. The reaction solution was stirred for 18 h with occasional cooling to keep the temperature below 35 °C. The resulting mixture was poured into ice–water and then extracted with ten portions of CH_2Cl_2. The combined extracts were thoroughly washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. Distillation in vacuo of the crude product gave 15.6 g (48% yield) of **1b** as a greenish-yellow oil: bp 89–91 °C (0.17 Torr); IR (neat) 6.17 (C=N), 6.52, and 7.45 μm (NO_2); NMR ($CDCl_3$) δ 4.22 (t, 2 H, J = 5 Hz), 2.87 (t, 2 H, J = 7 Hz), and 2.17 (m, 2 H); mass spectrum *m/e* 130 (M^+). Anal. Calcd for $C_4H_6N_2O_3$: C, 36.93; H, 4.65; N, 21.53. Found: C, 37.16; H, 4.68; N, 21.78.

An additional 1.0 g (3% yield) of 92% pure (VPC) **1b** was obtained: bp 84–9 °C (0.17 Torr). The distillation forecut contained 3.2 g (15% yield) of 91% pure (VPC) lactone **2**, contaminated by Me_2SO.

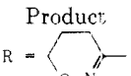
3-Nitro-2-isoxazoline (1a). Procedure A. The preceding procedure was carried out using 1-chloro-3-nitropropane.[15] Pure **1a** was obtained as a greenish-yellow oil in 79% yield: bp 93–4 °C (1.4 Torr) [lit.[6] bp 105–9 °C (5.5 Torr)]. An additional 2% yield of material which was only 80% pure (VPC) was also obtained.

Table I. Substitution Reactions of 3-Nitro-2-isoxazoline (1a)[a]

No.	Product R = 	Registry no.	Nu:	Registry no.	Solvent	% yield[b]
3	R–SC_6H_5	65150-71-2	$NaSC_6H_5$	930-69-8	Methanol	91
4	R–$SO_2C_6H_5$	65150-72-3	$NaO_2SC_6H_5$	873-55-2	Aqueous THF	28[c]
5	R–CN	65150-73-4	NaCN	143-33-9	Me_2SO	85
6	R–C_4H_9	65150-74-5	*n*-Bu_2Cd	3431-67-2	Ether	51
7	R–N_3	65150-75-6	NaN_3	26628-22-8	Aqueous alcohol	69

[a] At room temperature using an excess of the nucleophile. [b] By isolation. [c] After 12 h at 60–65 °C; starting **1a** was recovered in 15% yield.

Table II. Substitution Reactions of 3-Nitro-5,6-dihydro-1,2,4*H*-oxazine (1b)[a]

No.	Product R = 	Registry no.	Nu:	Registry no.	Solvent	% yield[b]
8	R–SC_6H_5	65150-76-7	$NaSC_6H_5$		methanol	82
9	R–CN	65150-77-8	NaCN		Me_2SO	81
10	R–$NHCH_3$	65150-78-9	$MeNH_2$	74-89-5	Aqueous $MeNH_2$	70

[a] At room temperature using an excess of the nucleophile. [b] By isolation.

Procedure B.[16] To a solution of 138 g (2.0 mol) of sodium nitrite and 50.3 g (0.50 mol) of *n*-propyl nitrite[14] in 1 L of Me_2SO was added 157.5 g (1.0 mol) of 1-bromo-3-chloropropane. The reaction solution was stirred for 14 h with occasional cooling to keep the temperature below 40 °C. Work-up was as described for **1b.** Distillation gave 52.1 g (45% yield) of pure **1a.**

Similar treatment of 1-bromo-4-chlorobutane gave **1b** but the crude product had to be chromatographed and only a 10% yield of pure product was obtained.

3-Thiophenoxy-5,6-dihydro-1,2,4*H*-oxazine (8). A 0.97-g (0.042 g-atom) portion of cleaned Na^0 was added to 20 mL of anhydrous methanol. After the initial reaction subsided, the mixture was refluxed until complete reaction was attained. To the cooled (10 °C) solution was added 4.98 g (45 mmol) of distilled thiophenol followed, after 10 min, by 2.59 g (20 mmol) of **1b.** The resulting solution was burgundy colored; within 10 min the color faded. After 15 min 100 mL of aqueous 1% NaOH was added and the product was extracted into CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and concentrated at reduced pressure. The crude product was chromatographed on silica gel. Elution with cyclohexane/ethyl acetate (90:10) afforded 0.69 g of diphenyl disulfide: mp 57–8.5 °C; mmp (with an authentic sample, mp 58.5–9.5 °C) 57.5–9 °C.

Further elution afforded 3.15 g (82% yield) of **8** as an oil: bp 119–20 °C (0.12 Torr); IR (neat) 3.28, 6.42 (shoulder), 6.78, 13.37, 14.49 (Ph), and 6.32 μm (Ph and C=N); NMR ($CDCl_3$) δ 7.83 (m, 5 H), 3.95 (t, 2 H, J = 5 Hz), and 1.80–2.35 (m, 4 H). Anal. Calcd for $C_{10}H_{11}NOS$: C, 62.13; H, 5.74; N, 7.25; S, 16.60. Found: C, 62.19; H, 5.96; N, 7.32; S, 16.90.

3-Thiophenoxy-2-isoxazoline (3). The preceding procedure was duplicated using **1a.** Chromatography as before gave diphenyl disulfide followed by a 91% yield of **3** as an oil: bp 104–5 °C (0.14 Torr); IR (neat) 3.28, 6.45, 6.78, 13.44, 14.53 (Ph), and 6.37 μm (Ph and C=N); NMR ($CDCl_3$) δ 7.42 (m, 5 H), 4.32 (t with fine structure, 2 H, J = 10 Hz), and 2.92 (t with fine structure, 2 H, J = 10 Hz). Anal. Calcd for C_9H_9NOS: C, 60.31; H, 5.06; N, 7.81; S, 17.89. Found: C, 60.47; H, 5.18; N, 7.98; S, 17.81.

3-Phenylsulfonyl-2-isoxazoline (4). To a solution of 49.20 g (300 mmol) of sodium benzenesulfinate in 90 mL of water and 30 mL of THF was added 3.39 g (29 mmol) of **1a.** The resulting solution was heated under nitrogen at 60–65 °C for 13 h, poured into water, and extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and concentrated at reduced pressure to a solid, mp 75–84 °C. This crude product was twice recrystallized from ethanol to give 1.25 g (20% yield) of sulfone **4:** mp 98.5–9.5 °C; IR (KBr) 3.28, 6.77, 13.22, 14.70 (Ph), 6.33, 6.29 (Ph and C=N), 7.56, and 8.62 μm (sulfone); NMR ($CDCl_3$) δ 7.5–8.2 (m, 5 H), 4.55 (t with fine structure, 2 H, J = 11 Hz), and 3.30 (t with fine structure, 2 H, J = 11 Hz). Anal. Calcd for $C_9H_9NO_3S$: C, 51.17; H, 4.29; N, 6.63; S, 15.18. Found: C, 50.96; H, 4.39; N, 6.59; S, 14.90.

The combined mother liquors from the recrystallizations were chromatographed on silica gel. Elution with CH_2Cl_2 afforded 0.49 g (15% yield) of starting **1a** followed by 0.48 g (8% yield) of **4,** mp 95–8 °C.

Treatment of sulfide **3** with two equivalents of *m*-CPBA in CH_2Cl_2/ether for 40 h provided an independent synthesis of sulfone **4.** This product was identical to **4** obtained by the substitution reaction: mp 98.5–9.5 °C; mmp 98–9 °C.

3-Cyano-2-isoxazoline (5). To a solution of 2.94 g (60 mmol) of sodium cyanide in 100 mL of Me_2SO was added 5.60 g (48 mmol) of **1a.** After 15 min the reaction was worked up as described for compound **1b.** The crude product was distilled at reduced pressure to give 3.94 g (85% yield) of **5:** bp 117–8 °C (35 Torr); IR (neat) 4.46 (C≡N) and 6.41 μm (C=N); NMR ($CDCl_3$) δ 4.63 (td, 2 H, J = 10 Hz) and 3.23 (td, 2 H, J = 10 Hz). Anal. Calcd for $C_4H_4N_2O$: C, 50.00; H, 4.20; N, 29.15. Found: C, 49.72; H, 4.19; N, 29.10.

3-Cyano-5,6-dihydro-1,2,4*H*-oxazine (9). To a mixture of 4.67 g (95 mmol) of powdered sodium cyanide and 90 mL of Me_2SO was added 3.84 g (29.5 mmol) of **1b.** After 2.5 h the reaction was worked up as described for **1b.** Distillation in vacuo of the crude product gave 2.63 g (81% yield) of 99% (VPC) pure **9:** bp 65–7 °C (0.18 Torr). The analytical sample was prepared by chromatographing this material on silica gel (CH_2Cl_2 elution) and redistilling: IR (neat) 4.70 (C≡N) and 6.41 μm (C=N); NMR ($CDCl_3$) δ 4.18 (t, 2 H, J = 5 Hz), 2.43 (t, 2 H, J = 6 Hz), and 2.03 (m, 2 H). Anal. Calcd for $C_5H_6N_2O$: C, 54.53; H, 5.49; N, 25.44. Found: C, 54.26; H, 5.51; N, 25.63.

3-Butyl-2-isoxazoline (6). Cadmium chloride (79.97 g, 0.44 mol, predried in vacuo over P_2O_5) was flame dried under nitrogen and suspended in 500 mL of anhydrous ether. To the suspension was cautiously added 150 mL of a 2.4 M *n*-butyllithium in hexane solution. The resulting mixture was refluxed with stirring under nitrogen for 15 h[17] and then allowed to stand at room temperature for 3 h. The clear, colorless solution which separated from a black precipitate was transferred under a positive nitrogen pressure to an addition funnel. A 160-mL (ca. 60 mmol as *n*-butylcadmium) portion of this solution was added[18] dropwise over 30 min to a cooled (15 °C) solution of 6.85 g (59 mmol) of **1a** in 50 mL of anhydrous ether. Insoluble cadmium salts were then filtered off and washed with ether. The combined filtrate and washings were washed with saturated aqueous KCl, dried (Na_2SO_4), and concentrated at reduced pressure to an oil. Distillation in vacuo gave 4.55 g of 95% pure (VPC) **6,** contaminated by small amounts of several materials. Pure **6** was obtained by chromatography on silica gel. After elution of 19 mg of unidentified impurities with cyclohexane/ethyl acetate (80:20), 3.84 g (51% yield) of **6** was isolated: bp 46–7 °C (0.25 Torr); IR (neat) 6.20 μm (C=N); NMR ($CDCl_3$) δ 4.27 (t, 2 H, J = 10 Hz), 2.91 (t, 2 H, J = 10 Hz), 2.38 (t, 2 H, J = 7 Hz), 1.2–1.7 (m, 4 H), and 0.92 (distorted t, 3 H). Anal. Calcd for $C_7H_{13}NO$: C, 66.11; H, 10.30; N, 11.01. Found: C, 66.33; H, 10.03; N, 11.29.

3-Azido-2-isoxazoline (7). To a solution containing 8.58 g (132 mmol) of sodium azide in 35 mL of water and 50 mL of ethanol was added 5.75 g (50 mmol) of **1a.** The resulting solution was stirred at room temperature for 40 h and was then poured into water. Extraction with CH_2Cl_2, drying (Na_2SO_4), and concentration at 180 Torr gave an oil. This was cautiously distilled behind a safety shield[19] in vacuo to give 3.86 g (69% yield) of pale yellow **7:** bp 58–60 °C (1.2 Torr); IR (neat) 4.68 (N_3) and 6.26 μm (C=N); NMR ($CDCl_3$) δ 4.50 (t, 2 H, J = 10 Hz) and 2.95 (t, 2 H, J = 10 Hz). Anal. Calcd for $C_3H_4N_4O$: C, 32.15; H, 3.60; N, 49.98. Found: C, 32.50; H, 3.59; N, 49.91.

3-Methylamino-5,6-dihydro-1,2,4*H*-oxazine (10). To 60 mL of aqueous 40% methylamine was added 3.85 g (29.6 mmol) of **1a.** The resulting solution was stirred at 20–25 °C (occasional cooling) for 17 h and then poured into 100 mL of saturated aqueous KCl containing 1% w/v NaOH. Extraction with CH_2Cl_2 followed by washing of the extracts with water, drying (Na_2SO_4), and concentration at reduced pressure gave an oil. This was chromatographed on silica gel. Elution with ethyl acetate afforded 2.36 g (70% yield) of pure **10.** The analytical sample was kugelrohr distilled at 90 °C (0.1 Torr)[20] and dried in vacuo over KOH pellets: IR (neat) 2.85–3.15 (N–H) and 6.23 μm (C=N); NMR ($CDCl_3$) δ 5.05 (broad s, 1 H, shifts with concentration, exchanges with D_2O), 3.78 (t, 2 H, J = 6 Hz), 2.69 (d, 3 H, J = 5 Hz, collapses to an s on D_2O exchange), and 1.8–2.4 (m, 4 H). Anal. Calcd for $C_5H_{10}N_2O$: C, 52.61; H, 8.82; N, 24.54. Found: C, 52.76; H, 8.74; N, 24.58.

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Registry No.—**1a,** 1121-14-8; **1b,** 65150-79-0; 1-chloro-4-nitrobutane, 41168-66-5; propyl nitrite, 543-67-9; 1-chloro-3-nitropropane, 16694-52-3; 1-bromo-3-chloropropane, 109-70-6.

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(7) For another approach, see: V. A. Tartakovskii et al., *Dokl. Akad. Nauk SSSR,* **167,** 844 (1966).
(8) The conversion of 1-bromo-3-chloropropane to **1a** presumably goes by the same route after prior conversion to 1-chloro-3-nitropropane and the corresponding nitrite ester.
(9) (a) N. Kornblum and P. A. Wade, *J. Org. Chem.*, **38,** 1418 (1973); (b) N. Kornblum, R. K. Blackwood, and D. D. Mooberry, *J. Am. Chem. Soc.*, **78,** 1501 (1956).
(10) R. Bonnett, "The Chemistry of the Carbon-Nitrogen Double Bond", Wiley-Interscience, New York, N.Y., 1970, p 597.
(11) Alternatives include S_N2 and S_N1 mechanisms. The wide range in rates as a function of the nucleophile is inconsistent with an S_N1 process.
(12) The dielectric constant of Me_2SO is 47; that of methanol is 33; J. A. Riddick and W. B. Bunger, "Techniques of Chemistry", Vol. 2, Wiley-Interscience, New York, N.Y., 1970.
(13) Prepared in 78% yield by treating 1-chloro-4-iodobutane with one equivalent of silver nitrite.

(14) Prepared analagously to *n*-butyl nitrite: W. A. Noyes, "Organic Syntheses", Collect. Vol. II, Wiley, New York, N.Y., 1943, p 108.
(15) Prepared in 64% yield from 1-chloro-3-iodopropane.
(16) A convenient modification of the procedure of ref 6.
(17) The reagent obtained employing a shorter reaction time affords a lower yield of **6**. Presumably this is due to *n*-butylcadmium chloride.
(18) Addition of **1a** to an excess of the cadmium reagent gave **6**, too.
(19) A sample of impure **7** detonated during VPC analysis (injector temperature 180 °C) destroying a syringe.
(20) Impure **10** rapidly decomposed at 100 °C on contact with air.

Basic Methanolysis of Benzoylmethylaminopyridines and Their *N*-Oxide and Methyl Quaternary Derivatives

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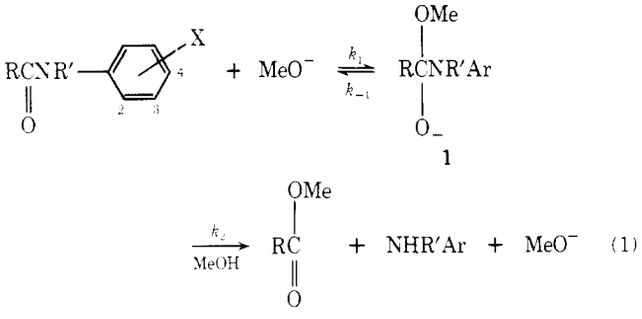
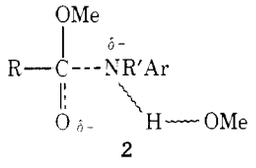
Rate data for the basic methanolysis of PhCON(Me) derivatives of pyridine, pyridine *N*-oxide, and 1-methylpyridinium iodide are reported. Positional reactivities are 4 ≫ 2 > 3 (pyridine), 4 > 3 > 2 (*N*-oxide), and 4 ≫ 3 (methylpyridinium). The heterocycles are also considered as substituted *N*-aryl-*N*-methylbenzamides; when combined with published data, these results yield a linear Hammett plot (ρ = 3.2). Mechanistic implications of this finding are discussed.

The effect of substituents on the rate of basic hydrolysis and methanolysis of anilides (eq 1) is most interesting since



(1)

all types of Hammett plots are possible, depending on the particular structure and reaction conditions. Thus linear,[1] curved,[2] and intersecting straight line[3] plots have been obtained, depending on the mechanisms or mechanism change. Of particular interest is the possibility of change from rate-determining breakdown of **1** (mechanism A, solvent assisted C–N cleavage via transition state **2** with Hammett $\rho \approx 3$[1,2]) to

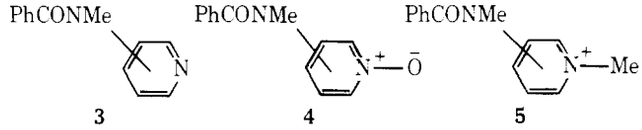


2

rate-determining formation of 1 (mechanism B, $\rho \approx 1.3$[4]) for strongly electron-withdrawing aryl substituents. This mechanism change should be accompanied by a decrease in slope of a Hammett plot.

In the case of *N*-aryl-*N*-methylbenzamides (R = Ph; R′ = Me) the current knowledge seems best fitted by invoking mechanism A for all substituents studied, except 4-nitro where reaction is by mechanism B.[5] The necessity for a strong resonance withdrawing effect for mechanism B is suggested by the observation that the 3,5-dinitro-substituted compound probably reacts by mechanism A, though the total withdrawing effect (σ = 1.42) is greater than that of the 4-nitro (σ^- = 1.26). To probe further into this possible change we decided to extend the range of electron-withdrawing substituents by considering pyridine derivatives with the aza function being regarded as an aromatic substituent.

We have previously noted[6] the similarity in effects of the 4-nitro and 4-aza groups in the methanolysis of *N*-arylacetamides. In this paper we report on the reactivities of the heterocyclic entities **3, 4,** and **5**.[7] Though the Hammett equation



3 **4** **5**

is not generally applicable to ortho substituents, we have included 2-substituted compounds so as to compare reactivity of a complete series with their behavior in basic ester hydrolysis (BEh) and nucleophilic displacement of ring halogen (S_NAr) reactions. This latter reaction, also powerfully aided by electron-withdrawing substituents, provides the substituent effect data for aza functions[8] with which the correlation of the methanolysis results can be attempted. It is apparent from $\sigma^-_{4N^+Me}$ = 2.32 that we are indeed dealing with strong electron-withdrawing substituents.

Results and Discussion

Reactions were followed spectrophotometrically by either standard UV or stopped flow procedures. The species monitored are indicated in the tables. Pseudo-first-order rate constants were obtained at a series of methoxide concentrations and second-order rate constants, k_e, were obtained from k_ψ/[MeO⁻] or from a plot of k_ψ vs. [MeO⁻].

Rate constants at 100 °C were required for comparison with other arylbenzamide results. These were generally obtained by substantial extrapolation from Arrhenius plots.

The 2-methylazonium compound alone showed anomalous behavior in that addition of base produced an immediate UV spectral change, followed by a much slower change. This latter change gave a first-order plot but with nonreproducible results. An NMR investigation showed that more than one organic species was formed in the initial reaction and subsequent spectral changes were complex. The reaction was not investigated further.

Salt effects, generally unimportant in these reactions,[2] were noted in reactions of the other methylazonium isomers. It appeared that both ionic strength and specific salt effects were occurring since a certain minimum concentration of lithium perchlorate was needed before a linear k_ψ vs. [MeO⁻] plot

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