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The general reaction of intramolecular nucleophilic substitution of unactivated aryl groups by thioamide anion in dipolar aprotic amide solvent is extended by the syntheses of 6-chloro-5-methoxy-2-methylbenzothiazole from 2',4'-dichloro-5'-methoxythioacetanilide and 6-methoxy-2-methylbenzothiazole from 4'-methoxy-2'-nitrothioacetanilide. The six-membered fused ring heterocycles, 2-methyl-4*H*-1,3-benzothiazine and 6,8-dichloro-3-methyl-1*H*-4,1,2-benzothiadiazine are also prepared.

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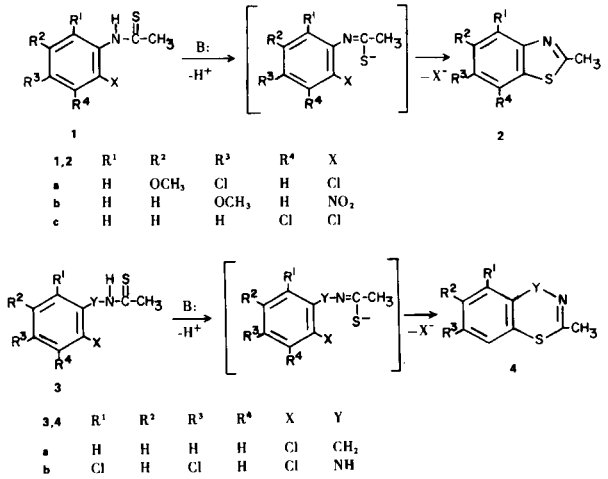
The marked increase in nucleophilicity of many anions toward a variety of substrates in dipolar aprotic solvents has been reviewed (1), and accounts, at least in part, for the reaction of unactivated aryl halides with thiolate ion in aprotic amide solvents to produce aryl thioethers (2).

Use of this phenomenon to produce benzo-fused heterocycles by intramolecular substitution of unactivated aryl groups has been largely unexplored. A series of 1*H*-4,1,2-benzothiadiazines have been prepared by Gibson and co-workers by intramolecular nucleophilic substitution of halide (exclusive of chloride) in acetonitrile (3a-d). Reactivity was attributed to "transiently activated halogen," but is more likely the result of increased nucleophilicity of transiently anionic sulfur, also offered as a possible explanation by the authors. Wikel and Paget have synthesized *s*-triazolo[3,4-*b*]benzothiazoles by displacement of chloride by the anion of variously substituted 4-(2-chlorophenyl)-1,2,4-triazole-3-thiols in DMF (4). In 1966, we prepared 2-methylnaphtho[2,3-*d*]-thiazole by intramolecular substitution of bromide by the anion of 3-bromo-2-thioacetonaphthalide in DMF (5). Recently, this reaction has been expanded to include synthesis of several 2-methylbenzothiazoles (6).

Noteworthy are the syntheses of two additional 2-methylbenzothiazoles. 6-Chloro-5-methoxy-2-methylbenzothiazole (**2a**) has been prepared from the anion of 2',4'-dichloro-5'-methoxythioacetanilide in 1-methyl-2-pyrrolidinone, representing displacement of chloride from an aryl substrate containing a deactivating or electron donating group *para* to the leaving group. Also, 6-methoxy-2-methylbenzothiazole (**2b**) has been synthesized from 4'-methoxy-2'-nitrothioacetanilide. This synthesis makes use of the comparatively facile displacement of nitro groups in S_NAr reactions (7,8), and extends the utility of this general method. Support for an S_NAr mechanism as opposed to aryne intermediacy is given by the synthesis of 7-chloro-2-methylbenzothiazole (**2c**) from 2',3'-dichlorothioacetanilide, employing 1,1,3,3-tetramethylguanidine as the base. All previous examples were unsubstituted at a position *ortho* to the leaving group, providing an opportunity for aryne formation.

The six-membered fused ring heterocycles 2-methyl-



4*H*-1,3-benzothiazine (**4a**) and 6,8-dichloro-3-methyl-1*H*-4,1,2-benzothiadiazine (**4b**) have also been prepared as shown.

EXPERIMENTAL

Melting points were determined using a Thomas-Hoover capillary melting point apparatus; all melting points are uncorrected. Ir spectra were taken on an Infracord Spectrophometer, Model 137. The nmr spectra were obtained with a Varian Model A-60. Mass spectra were obtained with an AEI-MS902 spectrometer. The elemental analyses were performed by the analytical division of Kodak's Research Laboratories.

Sodium hydride was used as a mineral oil dispersion, and assumed to be a 50% concentration.

2',4'-Dichloro-5'-methoxythioacetanilide (**1a**).

2',4'-Dichloro-5'-methoxythioacetanilide (**1a**) was prepared from 2',4'-dichloro-5'-methoxyacetanilide (15 g.) and phosphorus pentasulfide (15 g.) in toluene (150 ml.). The reaction was stirred at reflux for four hours. After cooling to 30° and decanting from the tarry insolubles, the toluene solution was twice extracted with 10% sodium hydroxide (100 ml.). The alkali extract was chilled to 10° and acidified with hydrochloric acid. The precipitated product was collected and recrystallized from ether/hexane, (11 g., 73%), m.p. 118-120°.

Anal. Calcd. for $C_9H_9Cl_2NOS$: C, 43.2; H, 3.6; N, 5.6. Found: C, 42.8; H, 4.1; N, 5.6.

4'-Methoxy-2'-nitrothioacetanilide (**1b**).

4'-Methoxy-2'-nitrothioacetanilide (**1b**) was prepared as above from 4'-methoxy-2'-nitroacetanilide (10 g.) and phosphorus penta-

sulfide (10 g.) in refluxing benzene (125 ml.) for six hours, (5 g., 46%), m.p. 100-101°.

Anal. Calcd. for $C_9H_{10}N_2O_3S$: C, 47.8; H, 4.5; N, 12.4. Found: C, 47.5; H, 4.9; N, 12.4.

2′,3′-Dichlorothioacetanilide (**1c**).

2′,3′-Dichlorothioacetanilide (**1c**) was prepared as above from 2′,3′-dichloroacetanilide (30 g.) and phosphorus pentasulfide (20 g.) in toluene at 90° for two hours, (25 g., 77%) m.p. 85-87°.

Anal. Calcd. for $C_8H_7Cl_2NS$: C, 43.7; H, 3.2; N, 6.4. Found: C, 43.6; H, 3.5; N, 6.3.

N-(2-Chlorobenzyl)thioacetamide (**3a**).

N-(2-Chlorobenzyl)thioacetamide (**3a**) was prepared from *N*-(2-chlorobenzyl)acetamide (15 g.) and phosphorus pentasulfide (15 g.) in refluxing benzene (100 ml.) for six hours. The benzene solution was decanted from the tarry insolubles and cooled to 30°. The solution was then washed with 10% alkali (100 ml.), followed by a wash with 5% aqueous acetic acid (100 ml.). The benzene layer was dried and concentrated to a brown oil which was used without further purification, (10 g., 61%). The infrared spectrum (neat) showed complete absence of starting material (CO, 1612 cm^{-1}) and exhibited absorption typical of thioamides at 3105, 1533, 1497, and 1183 cm^{-1}.

Thioacetic Acid 2,4,6-Trichlorophenylhydrazide (**3b**).

Thioacetic acid 2,4,6-trichlorophenylhydrazide (**3b**) was prepared from acetic acid 2,4,6-trichlorophenylhydrazide (15 g.) and phosphorus pentasulfide (20 g.) in refluxing toluene (200 ml.) for twenty hours. The toluene solution was decanted hot from the tarry insolubles and stripped to one-half volume. The precipitated crystals were collected and recrystallized from xylene, (10 g., 60%), mp. 176-178°; mass spectrum: m/e = 267.94 (M^+); nmr (DMSO-d_6): δ = 2.38 (s, 3H, CH_3), δ = 7.50 (s, 2H, arom.).

Anal. Calcd. for $C_8H_7Cl_3N_2S$: C, 35.6; H, 2.6; N, 10.4. Found: C, 35.2; H, 2.7; N. 10.4.

6-Chloro-5-methoxy-2-methylbenzothioazole (**2a**).

6-Chloro-5-methoxy-2-methylbenzothiazole (**2a**) was prepared from **1a** (5.0 g.) and sodium hydride (0.75 g.) in 1-methyl-2-pyrrolidinone (35 ml.) at 160° for four hours. The reaction was drowned into water (150 ml.), the product collected and recrystal-from ether/hexane, (2.0 g., 47%), m.p. 107-109°.

Anal. Calcd. for C_9H_8ClNOS: C, 50.6; H, 3.8; N, 6.6. Found: C, 50.5; H, 3.8; N, 6.5.

6-Methoxy-2-methylbenzothiazole (**2b**).

6-Methoxy-2-methylbenzothiazole (**2b**) was prepared from **1b** (4.0 g.) and sodium hydride (0.75 g.) in 1-methyl-2-pyrrolidinone (25 ml.) at 150° for one hour. The reaction mixture was drowned into water (150 ml.) and twice extracted with 25-ml. portions of ether. The combined extracts were dried, and decolorized with carbon.

To a few mls. of the extract was added an ether solution of picric acid, and the resulting picrate salt was collected, m.p. 172-175°. The remaining ether extract was concentrated to an oil, (2.2 g., 65%). The infrared spectrum was identical to an authentic sample.

Anal. (Picrate) Calcd. for $C_{15}H_{12}N_4O_8S$: C, 44.1; H, 3.0; N, 13.7. Found: C, 44.1; H, 3.1; N, 13.6.

7-Chloro-2-methylbenzothiazole (**2c**).

7-Chloro-2-methylbenzothiazole (**2c**) was prepared from **1c** (5 g.) and 1,1,3,3-tetramethylguanidine (8 g.) in 1-methyl-2-pyrrolidinone (20 ml.) at 150° for two hours. The reaction was worked up as above; picrate, m.p. 119-121°. The remaining ether extract was concentrated to a solid, which was recrystallized from hexane, (3.5 g., 83%), m.p. 38-39°.

Anal. (Picrate) Calcd. for $C_{14}H_9ClN_4O_7S$: C, 40.7; H, 2.2; N, 13.6. Found: C, 40.3; H, 2.3; N, 13.8.

2-Methyl-4*H*-1,3-benzothiazine (Picrate) (**4a**).

2-Methyl-4*H*-1,3-benzothiazine (Picrate) (**4a**) was prepared from **3a** (4.5 g.) and sodium hydride (0.5 g.) in 1-methyl-2-pyrrolidinone (25 ml.) at 150° for three hours. The reaction was drowned into water (150 ml.) and twice extracted with 25-ml. portions of ether. The combined extracts were dried, decolorized and then mixed with an ether solution (50 ml.) containing picric acid (5 g.). The precipitated picrate salt was collected and recrystallized from methanol, (2.3 g., 26%), m.p. 144° dec.

Anal. Calcd. for $C_{15}H_{12}N_4O_7S$: C, 45.9; H, 3.1; N, 14.3. Found: C. 45.9; H, 3.2; N, 14.1.

6,8-Dichloro-3-methyl-1*H*-4,1,2-benzothiadiazine (**4a**).

6,8-Dichloro-3-methyl-1*H*-4,1,2-benzothiadiazine (**4b**) was prepared from **3b** (2 g.) and sodium hydride 90.5 g.) in 1-methyl-2-pyrrolidinone (25 ml.) at 150° for two hours. The reaction was drowned into water, the product collected and recrystallized from ether/hexane, (1.3 g., 76%), m.p. 137-141°; mass spectrum: m/e = 231.96 (M^+); nmr (acetone-d_6): δ = 2.14 (s, 3H, CH_3), δ = 7.00 (d, 1H, arom.), 7.28 (d, 1H, arom.).

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