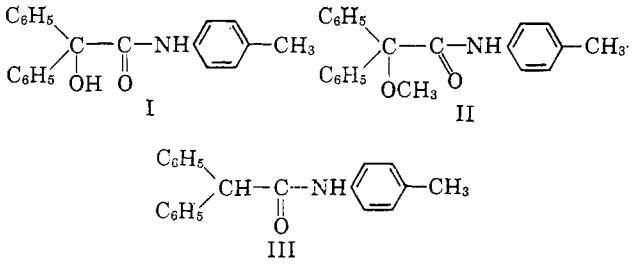
When the reaction with keteneimine was carried out under rigorously anhydrous conditions, *e.g.*, dry hydrogen chloride in ether–dimethyl sulfoxide, the only product isolated was simple N-(*p*-tolyl)diphenylacetamide (III) in 66% yield. Presumably the hydrogen chloride–ketenimine adduct was formed and hydrolyzed to amide during the work-up.

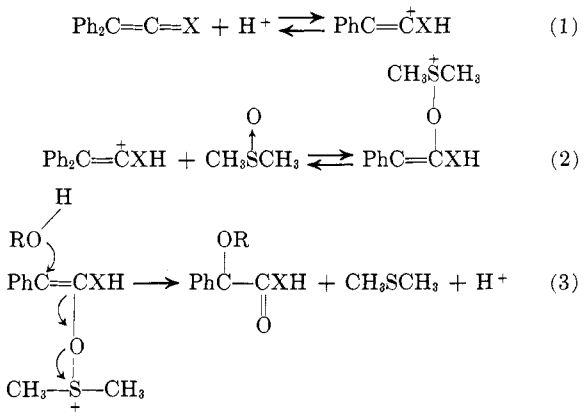


I II

III

The keteneimine was unaffected by prolonged solution in dry or slightly moist dimethyl sulfoxide alone, being recovered on dilution with water.

These results implicate dimethyl sulfoxide participation in a rapid oxidative solvolysis which appears best accomodated by the following mechanism, where =X is either =N–C$_6$H$_4$–CH$_3$ or =O.



Winstein and Smith[7] have discussed the general reactivity of dimethyl sulfoxide as a nucleophile in terms of its ability to form a sulfonium salt intermediate, R–O–$\overset{+}{S}$(CH$_3$)$_2$. The sulfonium intermediate formed in eq. 2 is entirely analogous.

The possibility of *in situ* conversion of α-diazo ketones to α-alkoxy acids as a modification of the Arndt–Eistert synthesis *via* this procedure appears attractive and is being investigated.

Experimental[8]

N-(*p*-Tolyl)-α-hydroxydiphenylacetamide.[9]—To a solution of 0.56 g. (2 mmoles) of diphenylketene-N-*p*-tolylimine[10] in 30 ml. of commercial (undried) dimethyl sulfoxide was added several drops of concentrated hydrochloric acid, and the solution was swirled. The yellow color of the keteneimine disappeared immediately; infrared inspection of petroleum ether (b.p. 30–60°) extracts showed no trace of the characteristic keteneimine band at 5 μ after admixture. After a few moments, the solution was poured into ice–water, and the resulting mixture was extracted with ether which was washed with dilute sodium bicarbonate and water, then dried, and evaporated. The solid residue was recrystallized from ethanol to yield 0.58 g. (1.8 mmoles, 91.5%) of N-(*p*-tolyl)-α-hydroxydiphenylacetamide, m.p. 189–190°, lit.[9] m.p. 189–190°; mixture melting point with authentic material was undepressed.

In one instance, the reaction was run in a flask being swept by nitrogen, and the exit gas was collected in a chilled ether trap containing an excess of methyl iodide. The ether solution was refluxed 4 hr., and the crystalline precipitate was removed. Its infrared spectrum was identical with that of authentic trimethylsulfonium iodide.

Benzilic Acid.—To a solution of several drops of concentrated hydrochloric or perchloric acid in 50 ml. of dimethyl sulfoxide was added dropwise with swirling 1.9 g. (0.01 mole) of diphenylketene. The orange ketene color was immediately discharged on contact. The solution was poured into ice–water, and the resulting precipitate was recrystallized from ethanol to yield 2.1 g. (0.0088 mole, 88%) of benzilic acid, m.p. 149–150°.

N-(*p*-Tolyl)-α-methoxydiphenylacetamide. A.—To a solution of 0.56 g. (2 mmoles) of diphenylketene-N-*p*-tolylimine in a mixture of 15 ml. of dimethyl sulfoxide and 15 ml. of methanol was added several drops of concentrated hydrochloric acid. The solution was, after a few minutes, poured into ice–water, and this was extracted with ether. The ether was washed with dilute sodium bicarbonate and water, then dried, and evaporated. The solid residue was recrystallized from ethanol to give 0.47 g. (1.4 mmoles, 71%) of N-(*p*-tolyl)-α-methoxydiphenylacetamide, m.p. 163–164°; mixture melting point with authentic material (see below) was undepressed.

N-(*p*-Tolyl)-α-methoxydiphenylacetamide. B.—To 50 ml. of dry methanol containing 5 ml. of triethylamine was added 3.3 g. (0.01 mole) of N-(*p*-tolyl)-α-chlorodiphenylacetamide,[11] and the mixture refluxed for 2 hr. The solution was diluted with ice water, and the precipitate was recrystallized from ethanol to yield 2.8 g. (0.0085 mole, 85%) of product, m.p. 163–164°. The infrared spectrum was consistent with the title structure.

Anal. Calcd. for $C_{22}H_{21}NO_2$: C, 79.75; H, 6.50. Found: C, 79.55; H, 6.40.

Reaction of Diphenylketene-N-*p*-tolylimine with Dry Hydrogen Chloride in Dimethyl Sulfoxide–Ether.—In a three-necked flask equipped with a stirrer, gas inlet, and reflux condenser and protected from moisture by a drying tube was dissolved 2.8 g. (0.01 mole) of keteneimine in a mixture of 50 ml. of dry (vacuum distilled from calcium hydride) dimethyl sulfoxide and 100 ml. of dry ether. Dry hydrogen chloride was bubbled in, while the mixture was stirred, until shortly after precipitation of dimethylsulfoxonium chloride was complete. The mixture was stirred under reflux for an additional 15 hr. The ether was decanted, washed with water, dilute sodium bicarbonate, and water, then dried, and evaporated. The residue was recrystallized from ethanol to yield 2.0 g. (0.0066 mole, 66%) of N-*p*-tolyldiphenylacetamide, m.p. 180–181°.

(7) S. G. Smith and S. Winstein, *Tetrahedron*, **3**, 317 (1958).

(8) All melting points are uncorrected.

(9) H. Klinger, *Ann.*, **389**, 261 (1912).

(10) C. L. Stevens and R. J. Gasser, *J. Am. Chem. Soc.*, **79**, 6057 (1957).

(11) C. L. Stevens and J. C. French, *ibid.*, **75**, 657 (1953).

Organic Disulfides and Related Substances. VIII. Preparation and Oxidation of Some Unsymmetrical Dialkyl and Alkyl Pyridinium Disulfides[1]

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Oxidation of 2-aminoethyl disulfide dihydrochloride (1) with hydrogen peroxide afforded an excellent syn-

(1) Reported in part at the 141st National Meeting of the American Chemical Society, Washington, D. C., March, 1962, Abstracts, p. 31N. This investigation was supported by the U. S. Army Medical Research and Development Command, Department of the Army, under Contract No. DA-49-193-MD-2030; we are indebted to Dr. T. R. Sweeney and Dr. D. P. Jacobus of the Walter Reed Army Institute of Research for helpful discussion and for evaluation of several products as antiradiation drugs. Paper VII: L. Field, J. M. Locke, C. B. Hoelzel, and J. E. Lawson, *J. Org. Chem.*, **27**, 3313 (1962).

thesis of the thiolsulfonate **2**,[2] although the product originally was thought to be a disulfoxide.[3] Unsymmetrical disulfides (RSSR′) could give two isomeric thiolsulfonates, as shown by the equations, and their oxidation, therefore, became of considerable interest.

$$\underset{\textbf{5, 9}}{RSSO_2R'} \overset{H_2O_2}{\underset{R'SH}{\rightleftharpoons}} \underset{\textbf{1, 3, 7, 10, 11}}{RSSR'} \overset{H_2O_2}{\underset{RSH}{\rightleftharpoons}} \underset{\textbf{2, 4, 8}}{RSO_2SR'}$$

5, R = $(CH_3)_3C$
9, R = $CH_3(CH_2)_2C(CH_3)_2$

1, R = $Cl^-H_3N^+(CH_2)_2$
3, R = $(CH_3)_3C$
7, R = $CH_3(CH_2)_2C(CH_3)_2$
10, R = $CH_3O_2CCH(NH_3^+Cl^-)C(CH_3)_2$
11, R = $2\text{-}C_5H_4N^+Cl^-$

2, R = $Cl^-H_3N^+(CH_2)_2$
4, R = $(CH_3)_3C$
8, R = $CH_3(CH_2)_2C(CH_3)_2$

R′ = $(CH_2)_2NH_3^+Cl^-$ in all instances

Oxidation of unsymmetrical aryl disulfides (ArSSAr′) usually occurs preferentially on the sulfur atom farthest from electron-withdrawing substituents.[4] Oxidation of unsymmetrical disulfides containing at least one aliphatic group to thiolsulfonates seems to be unreported and offers interesting prospects for examining inductive, field, and steric effects in terms of preferential oxidation. Furthermore, new preparations for unsymmetrical thiolsulfonates open up many synthetic possibilities because thiolsulfonates react with thiols to give disulfides,[2] as shown by the equations.

Introductory studies of disulfides containing at least one aliphatic moiety are reported in this paper, the second moiety being a substituted alkyl or 2-pyridinium group.

Procedures of oxidation resembled those used for preparing **2** and its N,N′-diacetyl derivative.[2] Oxidation of the *t*-butyl aminoethyl disulfide salt (**3**) gave only one isolable unsymmetrical thiolsulfonate (33% yield). The likelihood of electron supply by the *t*-butyl group to the adjoining sulfur atom suggested that the product was more likely to have the oxygen atoms on the sulfur nearer the *t*-butyl group and thus was more likely to be **4** than **5** (the field effect exerted across space by the ammonium ion also might have an important influence, although this influence is unpredictable at present). The product was in fact shown to contain the moiety $-S(CH_2)_2NH_3^+Cl^-$ and, therefore, to be **4** rather than **5**, by the following reactions which produced known disulfides.

$$1 + (CH_3)_3CSO_2H \xleftarrow{Cl^-NH_3^+(CH_2)_2SH} \underset{\textbf{4}}{(CH_3)_3CSO_2S(CH_2)_2NH_3^+Cl^-} \xrightarrow{(CH_3)_3CSH} \textbf{3} + (CH_3)_3CSO_2H$$

Along with the thiolsulfonate **4**, a little taurine (2-aminoethanesulfonic acid) was isolated. Despite careful efforts to separate all products, the other possible thiolsulfonate (**5**) could not be found. The apparent absence of **5** may be a consequence of its instability rather than of selective oxidation of **3** to **4**, however.

Two other products were isolated. One was the symmetrical thiolsulfonate salt (**2**) (28%); the other, **6**, may have been *t*-butyl disulfone. Symmetrical thiolsulfonates also were isolated in the work of Leandri and Tundo.[4] The symmetrical product **2** (and **6**) could have resulted from disproportionation of the *t*-butyl aminoethyl disulfide (**3**) *before* oxidation, or of unsymmetrical thiolsulfonates **4** or **5** *after* oxidation. Formation *during* oxidation is probable however, since in analogous work[5] isolation of symmetrical thiolsulfonates after oxidation of unsymmetrical thiolsulfinates was best attributed to cleavage of the sulfur–sulfur bonds and recombination during oxidation.

2-Methyl-2-pentyl 2′-aminoethyl disulfide hydrochloride (**7**) was oxidized similarly. Isolation of the symmetrical thiolsulfonate **2** as the major product (48% yield) once more pointed to considerable "scrambling" of alkylthio groups during oxidation. Again also, the only unsymmetrical thiolsulfonate isolated (19% yield) resembled **4** in having both oxygens on the sulfur atom nearest the *t*-alkyl group (**8** rather than **9**). Structure **8** was established as with **4**.

Presence of an alkoxycarbonyl function β to the disulfide moiety had an adverse effect. Thus oxidation of the unsymmetrical β-alkoxycarbonyl disulfide (**10**) (obtained in 84% yield by reaction of penicillamine methyl ester hydrochloride with **2**) gave on oxidation only a little taurine, along with amorphous material which did not show a positive thiolsulfonate test.[6] β-Carboxy- and β-alkoxycarbonyl-β-aminothiols and disulfides also failed to give symmetrical thiolsulfonates with aqueous hydrogen peroxide; thus failures resulted with penicillamine methyl ester, pencillamine disulfide (acid and methyl ester), cysteine ethyl ester, and cystine (acid), all as hydrochlorides or in dilute hydrochloric acid.[7]

Oxidation as usual[2] of 2-pyridyl disulfide with hydrogen peroxide in dilute hydrochloric acid gave about 25% of pyridine-2-sulfonic acid.[7] Recovery of most of the disulfide indicated that the positively charged pyridine ring might have reduced the ease of oxidation of the adjoining sulfur atom and, therefore, that oxidation of 2-pyridyl 2′-aminoethyl disulfide dihydrochloride (**11**) might occur selectively on the sulfur atom adjacent to the aminoethyl moiety. Evidently the thiolsulfonate itself did not survive oxidation, because the only material isolated was unchanged **11** (39%).

2-Aminoethyl disulfide dihydrochloride (**1**) reduces lethal effects of ionizing radiation,[8] as does its thiolsulfonate (**2**).[9] Nevertheless, the *t*-butyl aminoethyl disulfide (**3**), the corresponding thiolsulfonate (**4**), and the pyridyl aminoethyl disulfide (**11**) were inactive.[9]

(2) L. Field, T. C. Owen, R. R. Crenshaw, and A. W. Bryan, *J. Am. Chem. Soc.*, **83**, 4414 (1961).

(3) W. G. Christiansen and M. A. Dolliver, U. S. Patent 2,242,236 (1941); *Chem. Abstr.*, **35**, 5647 (1941).

(4) G. Leandri and A. Tundo, *Ann. chim.* (Rome), **44**, 74 (1954); *Chem. Abstr.*, **49**, 4563 (1955).

(5) D. Barnard and E. J. Percy, *Chem. Ind.* (London), 1332 (1960); *cf.* also U. Marangelli, G. Modena, and P. E. Todesco, *Gazz. chim. ital.*, **90**, 681 (1960); *Chem. Abstr.*, **55**, 16510 (1961).

(6) *I.e.*, development of an acidic reaction owing to formation of a sulfinic acid, upon treatment of a thiolsulfonate with a thiol; *cf.* D. Barnard and E. R. Cole, *Anal. Chim. Acta*, **20**, 540 (1959). Increased acidity was obvious with other thiolsulfonates which were amine hydrochlorides, even though these already were slightly acidic in solution.

(7) Unpublished results.

(8) J. F. Thomson, "Radiation Protection in Mammals," Reinhold Publishing Corp., New York, N. Y., 1962, pp. 33, 34, 55, 65.

(9) Private communication from Dr. T. R. Sweeney and Dr. D. P. Jacobus, Walter Reed Army Institute of Research, Washington, D. C.

Experimental[10]

Oxidation of *t*-Butyl 2-Aminoethyl Disulfide Hydrochloride (3). A. Oxidation.—To the disulfide **3** (10.09 g.)[2] in 30 ml. of water, there was added dropwise with stirring and ice cooling during about 15 min. a mixture of 9.4 ml. (100 mmoles) of 30% aqueous hydrogen peroxide and 10 ml. of water. The mixture was allowed to stand at room temperature overnight and then was evaporated below 50° in a rotary evaporator to a sirup containing crystals. After being dried under reduced pressure in a desiccator containing potassium hydroxide, the product was treated with hot chloroform (*ca.* 200 ml.).

The crystals, which did not dissolve, were removed by filtration and proved to be the symmetrical thiolsulfonate (**2**), 1.82 g. (28%), unsharp melting point beginning *ca.* 110°. For purification of **2**, at first unrecognized, it was dissolved in cold methanol; insoluble material was taurine, m.p. and m.m.p. 328–330°, infrared spectrum identical with that of authentic taurine. Addition of ether to the filtered methanol solution precipitated **2**, m.p. and m.m.p. 166–167°, infrared spectrum identical with that of authentic **2**; in a similar experiment, **2** also was characterized by conversion to **3** upon reaction with *t*-butyl mercaptan.

The chloroform filtrate upon slow cooling to room temperature and standing gave crystalline solid. This solid, removed by filtration and dried, was shown (*vide infra*) to be 2-aminoethyl 2′-methyl-2′-propanethiolsulfonate hydrochloride (**4**), 3.06 g. (26%), m.p. 160–165° dec. (foaming). **4** was soluble in water, methanol, and acetic acid. In an earlier experiment, purification seemed best effected by dissolution in cold methanol, filtration, and precipitation with ether. By this means, 2.24 g. of **4** (m.p. 160–162°) and 0.13 g. of taurine eventually were obtained from the crude **4**. Three repetitions of the methanol–ether treatment gave pure **4**, m.p. 161–162°.

Anal. Calcd. for $C_6H_{16}ClNO_2S_2$: C, 30.83; H, 6.90; N, 5.99. Found: C, 31.03; H, 7.01; N, 6.35.

After removal of **4**, the chloroform filtrate was evaporated below 50° to an oil. Partial crystallization occurred in the cold, and filtration separated 0.76 g. of solid. Dissolution in pentane, filtration, and evaporation gave a material (**6**) with m.p. 56–60°, which contained sulfur but not nitrogen. **6** gave an acidic solution when treated with a thiol in water, as expected of a thiolsulfonate,[6] and had strong infrared bands at 1115, 1165, and 1315 cm.$^{-1}$; however, no **3** could be isolated after treatment with 2-mercaptoethylamine hydrochloride, suggesting that **6** was neither the *t*-butyl thiolsulfonate, $(CH_3)_3CSO_2SC(CH_3)_3$, nor **5**. Sublimation gave **6** with m.p. 59–61°. Analysis suggested that **6** may have been *t*-butyl disulfone; insufficient **6** remained for further characterization.

Anal. Calcd. for $C_8H_{18}O_4S_2$: C, 39.65; H, 7.49. Found: C, 39.73; H, 7.95.

The remainder of the oil crystallized when well dried. The crude solid (2.04 g.) pressed on clay plate gave 0.76 g. more of **4**, m.p. 154–157°, making a total yield of crude **4** amounting to 3.82 g. (33%), infrared spectrum identical with that of authentic **4**.

B. Structural Evidence for Thiolsulfonate 4.—For reaction of **4** with *t*-butyl mercaptan, 1.17 g. of **4** in 8 ml. of water was mixed with 0.45 g. of *t*-butyl mercaptan. After 2 days of standing, the unsymmetrical disulfide (**3**) was isolated as described previously.[2] Evaporation of the hydrochloric acid extract gave 0.67 g. (67%) of **3**, which after recrystallization from ethyl acetate had melting and infrared absorption characteristics identical with those of authentic **3**.[2]

A similar reaction with 2-mercaptoethylamine hydrochloride at first failed to give the disulfide **1**. Accordingly, the method of isolation was changed. A mixture of 0.47 g. of **4** and 0.23 g. of 2-mercaptoethylamine hydrochloride in 8 ml. of water was allowed to stand overnight. Water then was removed by evaporation. Recrystallization of the residue from acetic acid gave 0.35 g. (78%) of pure 2-aminoethyl disulfide dihydrochloride (**1**), m.p. and m.m.p. 214–215°, infrared spectrum identical with that of authentic **1**.

Gas formed at the decomposition point (170°) of the **4** proved to be sulfur dioxide, as shown by the characteristic odor, decolorization of dilute aqueous permanganate and bromine vapor, and an acidic reaction with moist litmus paper.

(10) Melting points are corrected. Analyses were by Galbraith Microanalytical Laboratories, Knoxville, Tenn. Evaporation of solvent for isolation of products was effected under reduced pressure.

2-Methyl-2-pentyl 2′-Aminoethyl Disulfide Hydrochloride (7).—2-Methyl-2-pentanethiol (11.8 g.)[11] was added to the thiolsulfonate **2** (25.7 g.)[2] in water (50 ml.). Addition of ethanol (150 ml.) gave a homogeneous solution from which crystals quickly separated. After 16 hr., the crystals were removed by filtration (taurine, 4.0 g.). Removal of ethanol (35°, 25 mm.) left a clear aqueous solution, which was shaken with chloroform while potassium hydroxide (22 g.) in water was added. The solution was extracted six times more with chloroform, and the combined chloroform extracts then were filtered into 12 ml. of concentrated hydrochloric acid in 50 ml. of methanol. Evaporation of the chloroform–methanol solution below 35° gave a crystalline mass. This mass was dissolved in 2-propanol and separated from 0.5 g. of insoluble **1**. The solution was evaporated and the residue was crystallized from acetone to give 15.7 g. (68%) of the disulfide **7** as plates having m.p. 103.5–104°.

Anal. Calcd. for $C_8H_{20}ClNS_2$: C, 41.80; H, 8.77; Cl, 15.43; N, 6.10; S, 27.90. Found: C, 41.76; H, 8.60; Cl, 15.51; N, 6.17; S, 27.87.

Oxidation of the Disulfide 7. A. Oxidation.—Hydrogen peroxide (2.6 ml., 25.3 mmoles, of 30% aqueous solution) and water (2.5 ml.) were added to a solution of 3.00 g. of **7** and a trace of iodine in 10 ml. of ice-cold water. The solution was kept at 0° for 2 hr. and then at 30° for 20 hr. The solution was separated by filtration from a little gummy precipitate and was evaporated below 30° to an oil. The oil after being scratched and kept under vacuum (1 mm.) for 20 hr. gave a partly crystalline mass, which was taken up in cold chloroform. Filtration separated crystals which were washed with chloroform and found to be nearly pure **2**, 0.8 g. (48%), m.p. 168–170° (unchanged by recrystallization and undepressed by authentic **2**),[2] infrared spectrum identical with that of **2**.

The filtrate was again evaporated to an oil. The oil was suspended in ether, and the mixture was made homogeneous with a minimum of chloroform and then clouded slightly by addition of ether. After 3 days at 5°, soft crystals of the thiolsulfonate **8** separated (0.33 g., 10%, m.p. 112–117°). Two further crops were obtained by evaporating the mother liquors and repeating the process. The combined crops of **8** were dissolved in a little ethanol and considerable ether was added. Refrigeration and filtration separated a little precipitate. The filtrate was evaporated and the residue taken up in acetone–ether. Upon refrigeration, 2-aminoethyl 2′-methyl-2′-pentanethiolsulfonate hydrochloride (**8**) slowly separated (0.66 g., 19%), m.p. 120–123°, soluble in water, positive thiolsulfonate test,[6] infrared spectrum with strong absorption at 1110 and 1320 cm.$^{-1}$ but otherwise similar to that of **7**.

Anal. Calcd. for $C_8H_{20}ClNO_2S_2$: C, 36.69; H, 7.70; Cl, 13.54; N, 5.35; S, 24.49. Found: C, 36.64; H, 7.60; Cl, 13.85; N, 5.52; S, 24.49.

B. Structural Evidence for Thiolsulfonate 8.—Solutions of **8** (52 mg.) and of 2-aminoethanethiol hydrochloride (24.5 mg.) in water (1-ml. each) were mixed; the acidity increased. After 40 min., the solution was washed twice with ether and the aqueous layer was evaporated below 30°. The residue was recrystallized from ethanol to give **1**, 35 mg. (78%), identical with authentic **1** (as shown by m.p. 214–216°, the mixture melting point, and the infrared spectrum).

In the reaction with *t*-butyl mercaptan, the thiol (30 mg.) was added to a suspension of 50.4 mg. of **8** in 1 ml. of ethanol, followed by water (2 ml.). After 25 hr., excess thiol was removed by extraction with pentane, and chloroform (2 ml.) and aqueous potassium hydroxide (5 ml., 0.1 *N*) were added. Three extractions with chloroform, immediate extraction of the chloroform layers with dilute hydrochloric acid, and evaporation of the acid extract gave gummy crystals. Dissolution in 2-propanol, filtration from a little residue, dilution with cyclohexane, and storage at 5° overnight gave the disulfide **3**, 25 mg. (64%), identical in melting behavior[2] and infrared spectrum with authentic **3**.[2]

2-Methyl-1-amino-1-methoxycarbonyl-2-propyl 2′-Aminoethyl Disulfide Dihydrochloride (10).—The thiolsulfonate **2** (3.90 g.) was added to a stirred solution of DL-penicillamine methyl ester hydrochloride (3.00 g.)[12] in water (30 ml.). The solution, which rapidly became strongly acidic, was let stand for 30 min. Chloro-

(11) Containing 1% or less of a higher boiling isomer. Kindly furnished by J. C. Morris, Laramie Petroleum Research Center, U. S. Department of the Interior, Bureau of Mines, Laramie, Wyo.

(12) Prepared from DL-penicillamine as reported by H. M. Crooks, Jr., "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949, p. 470; 73% yield, m.p. 174–176° (reported 173–175°).

form then was added, the aqueous layer was saturated with salt, and the mixture was shaken during addition of potassium hydroxide (4.5 g.) in water. The aqueous layer was extracted six times with chloroform, the extracts being filtered directly into concentrated hydrochloric acid (4.5 ml.) in methanol (55 ml.). Evaporation of the chloroform–methanol–acid mixture below 30° gave an oil, which was dissolved in 2-propanol; the solution was diluted with cyclohexane and scratched. The disulfide **10** separated as hard crystals, 3.9 g. (84%), m.p. 171–172°.

Anal. Calcd. for $C_8H_{20}Cl_2N_2O_2S_2$: C, 30.86; H, 6.48; Cl, 22.78; N, 9.00; S, 20.60; neut. equiv., 311. Found: C, 31.01; H, 6.66; Cl, 22.54; N, 8.82; S, 20.63; neut. equiv., 313 (potentiometric titration of the **10** with alkali showed two distinct end points corresponding to consumption of 1 and then 2 moles of alkali per mole of **10**).

2-Pyridyl 2′-Aminoethyl Disulfide Dihydrochloride (11).—2-Pyridinethiol (11.1 g.)[13] in 40 ml. of alcohol was added to 25.7 g. of the thiolsulfonate **2** in water (30 ml.) and concentrated hydrochloric acid (*ca.* 0.12 mole) with stirring. A small amount of precipitate which separated was dissolved by adding a little more water. After 20 hr. of stirring, the solvent was evaporated, and the residue was dissolved in water. Extraction with chloroform removed 4.4 g. of 2-pyridyl disulfide (infrared spectrum identical with that of authentic 2-pyridyl disulfide). The aqueous solution then was shaken with chloroform while an iced aqueous solution of potassium hydroxide (28 g.) was added. The water layer was extracted twice more with chloroform. Each chloroform layer was immediately extracted with hydrochloric acid (the total amount was 60 ml. of 12 *N*, of which half was used for the first extraction). The combined acid extracts were evaporated to a thick oil, which crystallized completely upon addition of anhydrous ethanol and scratching. After an overnight period at 5°, 15.5 g. of crude **11** was collected. Repeated recrystallizations from absolute alcohol, with use of decolorizing carbon, gave 2-pyridyl 2′-aminoethyl disulfide dihydrochloride (**11**) as colorless prisms, 12.8 g. (82%; conversion, 49%), m.p. 144–145° (sealed capillary); **11** was deliquescent at high relative humidity.

Anal. Calcd. for $C_7H_{12}Cl_2N_2S_2$: C, 32.42; H, 4.66; N, 10.81; S, 24.74. Found: C, 32.27; H, 4.46; N, 10.90; S, 24.74.

(13) M. A. Phillips and H. Shapiro, *J. Chem. Soc.*, 584 (1942).

Some Anomalous Results in the Bimolecular Displacement Reaction

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Recently[1] a new factor affecting reactivity in the bimolecular nucleophilic displacement reactions was observed by Bunnett.[2,3] Bunnett tentatively identifies this new factor as London interactions between nucleophile and polarizable substituent at or near the reaction site. He concludes that due to London forces there is a lowering of the transition state energy when the transition state structure is such as to bring highly polarizable atoms close to one another with a resultant increase in reaction rate. After allowances for steric and electrical effects, a change to a substituent of higher polarizability will cause more acceleration, or less deceleration, the greater the effective polarizability of the nucleophile.

(1) The work herein was taken in part from the Ph.D. thesis of S. Lowell, Adelphi University, 1963.

(2) J. F. Bunnett, *J. Am. Chem. Soc.*, **79**, 5969 (1957).

(3) J. F. Bunnett and J. D. Reinheimer, *ibid.*, **84**, 3284 (1962).

The *ortho*- and *para*-methyl- and *ortho*- and *para*-bromo-substituted benzyl halides afford an excellent opportunity to observe indications of London forces in rate ratios with minimum considerations for electrical effects. The total polar effects will be nearly identical for the corresponding *para* and *ortho* substituents and will cancel in the ratios, $o\text{-CH}_3/p\text{-CH}_3$ and $o\text{-Br}/p\text{-Br}$, if the susceptibility constants ρ and ρ^* are nearly identical.[4] This has been observed to be generally true.[5] Similar reasoning for minimization of the total polar effects in the benzyl system has been offered by Bunnett.[3] Table II, composed from the kinetic data given in Table I, presents the values for the ratio $k_{o\text{-R}}/k_{p\text{-R}}$ (R = Me and Br) for each of the three nucleophiles. It is apparent that the aforementioned ratio nearly cancels the total polar effects of the substituents (ref. 4).

Table II also presents values for the adjusted rate ratios given by the expression

$$\frac{\left(\frac{k_{o\text{-R}}}{k_{p\text{-R}}}\right)_{y}}{\left(\frac{k_{o\text{-R}}}{k_{p\text{-R}}}\right)_{MeO^-}} \equiv \frac{\left(\frac{k_y}{k_{MeO^-}}\right)_{o\text{-R}}}{\left(\frac{k_y}{k_{MeO^-}}\right)_{p\text{-R}}} \qquad (1)$$

y = MeO^-, $C_6H_5S^-$, and I^-
R = H, Me, and Br

in which differences in nucleophilicities are cancelled. This expression also cancels conformational differences, since the conformational changes accompanying a change of site, $p \rightarrow o$, for a given substituent should be constant and independent of the attacking reagent. Solvent effects would obviously cancel in the adjusted rate ratios if all the data were available in the same solvent. Since this is not the case, one must consider what change would occur in the value of the ratio

$$\left[\frac{\frac{k_{o\text{-R}}}{k_H}}{\frac{k_{p\text{-R}}}{k_H}}\right]_{I^-}$$

with a change of solvent (acetone to methanol). The changes in a given absolute reaction rate which accompany a change in the dipole moment of the solvent are known to be small for this charge type (charged nucleophile with neutral substrate).[6] Since the resultant small changes in absolute reaction rates are incorporated in numerator and denominator of the preceeding ratio, the value of the ratio should remain unchanged. The adjusted rate ratios only should indicate interactions arising between the nucleophile and the *ortho* substituent (London, steric, or other may be significant).

The polarizabilities for the three nucleophiles employed are suggested by the ions OH^-, 1.89; SH^-, 5.28; and I^-, 7.10 (all units $cm.^3 \times 10^{-24}$); the polarizabilities of the *ortho* substituents are H, 0.42; CH_3, 2.19; and Br, 3.34 (units the same as above).[7]

(4) A plot of log (k/k_0) *vs.* σ for *p*-substituted benzyl chlorides and a plot of log (k/k_0) *vs.* σ^* for *o*-substituted benzyl chlorides for I^- in acetone at 20° produces parallel lines for substituents -F, -Cl, -Br, -I, $-NO_2$, and $-CH_3$. The ρ- and ρ^*-values are, therefore, nearly identical. It is interesting to note only the *o*-methyl falls well off the line.

(5) R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 649.

(6) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 347–9.

(7) Values taken from, Landolt-Bornstein and J. A. A. Ketelaar, "Chemical Constitution," 2nd Ed., Elsevier Publishing Co., New York, N. Y., 1958, p. 91.