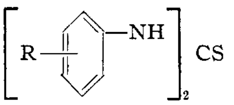
TABLE IV

1,3-BIS-(R-PHENYL)-2-THIOUREAS



R	Yield, %	M.p., °C.	Empirical formula	Analyses, % Found	Analyses, % Calculated
4-CH_3CONH	77.0	241–243	$C_{17}H_{18}N_4O_2S$	[a]	
4-$(C_2H_5)_2CHCH_2O$	76.0	100–102	$C_{25}H_{36}N_2O_2S$	N, 6.49	N, 6.53
4-$C_2H_5CH(CH_3)CH_2CH_2O$	96.0	174–176.5	$C_{25}H_{36}N_2O_2S$	N, 6.53 S, 7.82	N, 6.53 S, 7.48
4-$C_6H_{13}O$	53.6	156–157.5	$C_{25}H_{36}N_2O_2S$	N, 6.38 S, 7.46	N, 6.53 S, 7.48
4-$C_7H_{15}O$	54.3	152–153.5	$C_{27}H_{40}N_2O_2S$	N, 6.17 S, 6.77	N, 6.13 S, 7.02

[a] Converted directly to the thiazoline without analysis.

this was recrystallized from a mixture of isopropyl alcohol and ether giving 25.6 g. of product.

Procedure c. 3-(*p*-Isopentyloxyphenyl)-2-(*p*-isopentyloxyphenylimino)-4,5-dimethyl-4-thiazoline Hydrobromide.—A solution of 20 g. (0.048 mole) of 1,3-bis-(*p*-isopentyloxyphenyl)-2-thiourea and 7.4 g. (0.049 mole) of 3-bromo-2-butanone in 200 ml. of anhydrous ethanol was refluxed for 3 hours. The solution was filtered hot and the filtrate concentrated to a small volume. Addition of ether effected separation of the product, which was then recrystallized four times from ethanol–ether (15 g.).

Procedure d. 3-(*p*-Ethoxyphenyl)-2-(*p*-ethoxyphenylimino)-5-carboxymethyl-4-methyl-4-thiazoline Hydrobromide.—A solution of 18.8 g. (0.059 mole) of 1,3-bis-(*p*-ethoxyphenyl)-2-thiourea and 13.3 g. (0.059 mole) of ethyl *β*-bromolevulinate in 200 ml. of anhydrous ethanol was refluxed for three hours. Distillation of the solvent *in vacuo* left an oily residue, which yielded 6.2 g. of crystalline substance, m.p. 141.5–143°, upon recrystallization from isopropyl alcohol–ether. This proved to be 3-(*p*-ethoxyphenyl)-2-(*p*-ethoxyphenyl)-imino-5-carboxymethyl-4-methyl-4-thiazoline.

Anal. Calcd. for $C_{22}H_{24}N_2O_4S$: N, 6.79; S, 7.77. Found: N, 6.96; S, 8.05.

The filtrate remaining upon separation of the free acid was concentrated. The oil thus obtained was recrystallized from isopropyl alcohol–ether, yielding a crystalline solid of m.p. 159–162°. Three recrystallizations from the same medium gave 7.8 g. of the desired ester, m.p. 158–160°.

3-(*p*-Alkoxyphenyl)-2,4-thiazolidinedione. General Method—A solution of the thiocarbanilide (0.2 mole) and chloroacetic acid (0.21 mole) in 80–100 ml. of acetic acid was refluxed for 5–20 hours and then chilled. The crystalline solid which separated was filtered, partially air-dried, and then washed with *ca.* 1 liter of water. In some cases it was necessary to remove part of the acetic acid by distillation *in vacuo*. The product was recrystallized twice from isopropyl alcohol.

3-(*p*-Allyloxyphenyl)-5-(2,4-diacetoxybenzylidene)-2,4-thiazolidinedione.—A solution of 5 g. of 3-(*p*-allyloxyphenyl)-2,4-thiazolidinedione, 3 g. of 2,4-dihydroxybenzaldehyde and 4 g. of anhydrous sodium acetate in 20 ml. of acetic anhydride was refluxed for two hours. The mixture was chilled and diluted with isopropyl alcohol. The resulting precipitate was filtered off; it was then suspended in water, filtered, washed thoroughly with water, and air-dried. Recrystallization was effected from isopropyl alcohol.

3-(*p*-Isopentyloxyphenyl)-2-(*p*-isopentyloxyphenylimino)-5-(3-pyridomethylene)-4-thiazolidinone.—A solution of 15 g. (0.034 mole) of 3-(*p*-isopentyloxyphenyl)-2-(*p*-isopentyloxyphenylimino)-4-thiazolidinone, 4.4 g. (0.04 mole) of pyridine-3-aldehyde and 13.6 g. of anhydrous sodium acetate in 35 ml. of acetic acid was refluxed for 3.5 hours. The mixture was chilled overnight, then filtered, air-dried, and washed with a large quantity of water. The product was recrystallized once from isopropyl alcohol, m.p. 172–174° (13.0 g.).

SUMMIT, N. J.

[CONTRIBUTION OF THE FULMER CHEMICAL LABORATORY, THE STATE COLLEGE OF WASHINGTON]

Schiff Bases and Related Substances. III. Acetylation of a Schiff Base–Thiol Adduct[1]

BY GARDNER W. STACY, RICHARD I. DAY[2] AND RICHARD J. MORATH

RECEIVED DECEMBER 16, 1957

The acetylation of a Schiff base–thiol adduct, N-[*α*-(*p*-tolylthio)-benzyl]-aniline (I), proceeds with difficulty. Reaction of I with any of several common acetylating agents gives only small amounts of the desired acetyl derivative, N-[*α*-(*p*-tolylthio)-benzyl]-acetanilide (VI). Evidence that at least one other reaction occurs extensively is found in the isolation of acetanilide, the mercaptal, *α*,*α*-bis-(*p*-tolylthio)-toluene (IV) and *p*-tolyl disulfide. An explanation for the formation of these products is presented. Attempted benzoylation of I results in the formation of *p*-tolyl thiolbenzoate and benzanilide and none of the anticipated benzoyl derivative. The acetyl derivative VI can be synthesized in excellent yield by an indirect method from N-(*α*-acetoxybenzyl)-acetanilide (V). Its structure has been established by Raney nickel desulfurization to N-benzylacetanilide and by hydrolysis to benzaldehyde, aniline and *p*-toluenethiol.

In the hope of gaining further information on the structure and characterization of Schiff base–thiol adducts, we have studied the acetylation of N-[*α*-(*p*-tolylthio)-benzyl]-aniline (I) under a variety of conditions. Acylation of such acyclic substances has not been reported, although cyclic systems containing the S–C–NH grouping undergo acylation without difficulty. Thus Ratner and Clarke[3] were

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(1) Presented in part before the Oregon Section of the American Chemial Society, Salem, Ore., May 21, 1955, and in part at the 1956 and 1957 Northwest Regional Meetings of the American Chemical Society, Seattle, Wash., June 11 and Spokane, Wash., June 13, respectively. Paper II, G. W. Stacy, R. I. Day and R. J. Morath, THIS JOURNAL, **77**, 3869 (1955).

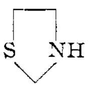
(2) In part abstracted from a thesis submitted by Richard I. Day in partial fulfillment of the requirements for the degree of Doctor of Philosophy, the State College of Washington, June, 1957.

(3) (a) S. Ratner and H. T. Clarke, THIS JOURNAL, **59**, 200 (1937); (b) subsequently, acylation of various substituted thiazolidines has been reported. A. H. Cook and I. M. Heilbron in "The Chemistry of Penicillin," H. T. Clarke, J. R. Johnson and R. Robinson, eds., Princeton University Press, Princeton, N. J., 1949, p. 926.

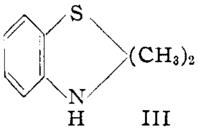
able to acetylate thiazolidine (II) in high yield with acetic anhydride, and Kiprianov and Portnyagina[4] found that III and a number of related benzothiazolines could be benzoylated and acetylated readily.

$\underset{p\text{-}CH_3C_6H_4S}{C_6H_5CHNHC_6H_5}$

I



II



III

In spite of these findings, the acetylation of I did not proceed smoothly under any of a wide variety of conditions. The action of acetic anhydride, acetic anhydride–acetic acid, ketene and acetyl chloride–pyridine gave the acetyl derivative VI in yields of only 14–21% and produced acetanilide, usually in amounts 1.5–3 times greater than VI. The mercaptal IV was also produced in runs using

$$C_6H_5CH(SC_6H_4CH_3\text{-}p)_2$$

IV

acetic anhydride, and p-tolyl disulfide was isolated in acetylations with ketene and with acetyl chloride–pyridine. It was necessary to resort to chromatography to isolate crystalline products. The methods of isolation were shown to be reliable by application to mixtures of known composition.

The unsatisfactory yields in these acetylations cannot be due to instability of VI under the reaction conditions, since it was possible to prepare VI by an independent method and to show that it can be recovered quantitatively after heating with acetic anhydride or acetic anhydride–acetic acid. When N-(α-acetoxybenzyl)-acetanilide (V)[5] is fused with p-toluenethiol, VI is produced in 83% yield.

$$\underset{\text{V}}{C_6H_5CH(OCOCH_3)N(COCH_3)C_6H_5} + p\text{-}CH_3C_6H_4SH \longrightarrow$$

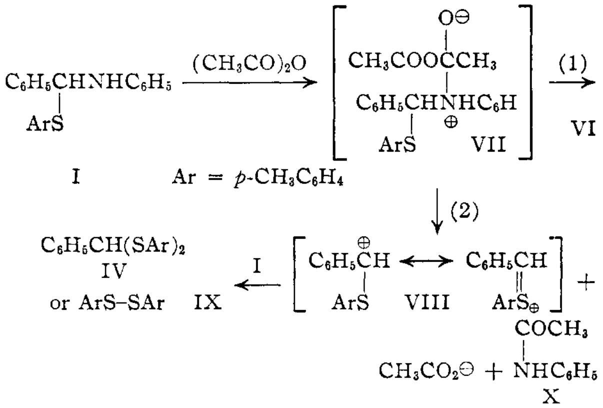
$$\underset{\text{VI}}{C_6H_5CH(SC_6H_4CH_3\text{-}p)N(COCH_3)C_6H_5} \xrightarrow{\text{Raney Ni}}$$

$$C_6H_5CH_2N(COCH_3)C_6H_5 + C_6H_5CH_3$$

This reaction is analogous to the reaction of V with ethanol to yield N-(α-ethoxybenzyl)-acetanilide.[5] The structure of VI was confirmed by desulfurization with Raney nickel[6] to give N-benzylacetanilide and toluene and by hydrolysis to benzaldehyde, aniline and p-toluenethiol. Attempts to oxidize VI to the corresponding sulfone failed, in contrast to the successful oxidation of acetylthiazolidine to a sulfone as reported by Ratner and Clarke.[3]

A possible explanation for the formation of the products observed might be outlined as follows: In the anticipated reaction (1), the intermediate complex VII decomposes to give the acetyl derivative VI. However, it is also possible for VII to decompose by path (2)[7] to form the reactive intermediate VIII, acetate ion and acetanilide. The cation VIII might then react either directly with I or with a molecule of thiol, produced by dissociation[8] of I, to give the mercaptal IV.[9] A similar explanation can be given to account for the reactions of I with acetyl chloride and with ketene.

When acetic acid is present in the acid anhydride, there is the alternate possibility that the nitrogen atom of the adduct would accept a proton from the acetic acid instead of complexing with the carbonyl of the acetic anhydride; decomposition of this intermediate by breaking of the C–N bond would lead to the cation VIII and aniline, and these in turn would lead to the same observed products. The addition of acetic acid to the reaction mixture facilitates the formation of the mercaptal IV, as under these circumstances the average yield of IV is increased to 74%.[10]



An attempt to benzoylate the adduct I using benzoyl chloride–pyridine gave an unanticipated result. Unlike the reaction of I with acetyl chloride–pyridine, none of the N-acyl derivative of I was found. The only products obtained were p-tolyl thiolbenzoate and benzanilide. The isolation of p-tolyl thiolbenzoate in this instance suggests that the corresponding thiolacetate may have formed in the acetylation experiments. It is possible, therefore, that some of the oily fractions isolated in these experiments may have contained this thiolacetate, which is reported to be a liquid.[11] A result paralleling the one just described has been reported by Grillot, *et al.*,[12] who have prepared compounds similar to I, but containing tertiary rather than secondary amino groups. When some of these compounds were treated with p-nitrobenzoyl chloride, thiol-p-nitrobenzoates were obtained.

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[4] A. I. Kiprianov and V. A. Portnyagina, *J. Gen. Chem. (U.S.S.R.)*, English translation, **25**, 2223 (1955).

[5] (a) H. R. Snyder, D. B. Bright and J. C. Lorenz, THIS JOURNAL, **73**, 1836 (1951); (b) A. W. Burgstahler, *ibid.*, **73**, 3021 (1951); (c) H. S. Angel and A. R. Day, *ibid.*, **72**, 3874 (1950).

[6] It is interesting to note that debenzylation of the nitrogen did not occur. This is in agreement with the recent work of Y. Liwschitz, A. Zilkha and Y. Amiel, THIS JOURNAL, **78**, 3067 (1956), in which the preservation of a benzyl-to-nitrogen linkage under conditions of catalytic hydrogenation was attributed to the presence of an acyl group.

[7] Cleavage of a C–N bond, as indicated in path 2, has been observed previously in respect to the reaction of N,N-dialkylanilines with acid halides; *cf.* (a) V. Auger, *Compt. rend.*, **139**, 299 (1904); (b) W. Staedel, *Ber.*, **19**, 1947 (1886); (c) O. Hess, *ibid.*, **18**, 685 (1885).

[8] M. P. Schubert, *J. Biol. Chem.*, **121**, 539 (1937).

[9] The possibility of the alternate reaction of the thiol (or I) with the sulfur atom of VIII as the reactive site (rather than the carbon atom) may explain the presence of p-tolyl disulfide in the reaction mixtures, C and D.

[10] This interpretation and the fact that increased acid concentration results in greater yields of mercaptal are consistent with the mechanism which has been proposed for the formation and hydrolysis of acetals, J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, p. 244. These results should also be compared with the cleavage reaction of N-benzylideneaminobenzoic acids with p-toluenethiol to form the corresponding amino acid and the mercaptal IV (ref. 1).

[11] C. Rabaut, *Bull. soc. chim. France*, [3] **27**, 690 (1902).

[12] G. F. Grillot, *et al.*, THIS JOURNAL, **76**, 3969 (1954).

Experimental[13]

Studies Involving the Acetylation of I.[14]—The acetylation procedures used in these studies are given below. In each instance, the same general procedure of chromatographic isolation of products was employed. The residue from each reaction mixture, obtained upon removal of the solvent under reduced pressure, was dissolved in 10 ml. of benzene; 5 ml. of this solution was placed on a 25-g. alumina column, which had been prepared using petroleum ether (b.p. 30–75°).[15] Most of the eluates gave residues which contained some yellow or brown oil in addition to crystals. Acetanilide was removed from the appropriate eluates by extraction with water. Each of the residues in question was treated successively with the same 5-ml. portion of boiling water. This extraction procedure was repeated twice more with two additional 1-ml. portions of water. A second crop of crystals (acetanilide) was obtained in the same manner from the filtrate after it had been concentrated to *ca.* 0.5 ml.

Each of the residues (including those which had been extracted with water) was dissolved in 1 ml. of warm ethanol, and the solutions were allowed to stand overnight at −10° after they had been seeded to induce crystallization. The crystals were separated with the aid of filter stick; like crystalline fractions were combined and recrystallized from ethanol. Products were obtained in the following order from the eluates removed from the column: α,α-bis-(*p*-tolylthio)-toluene (IV) or *p*-tolyl disulfide (IX), N-[α-(*p*-tolylthio)-benzyl]-acetanilide (VI) and acetanilide (X).

A. **Acetic Anhydride.**—To 1.527 g. (5.0 mmoles) of I was added 1.02 g. (10 mmoles) of acetic anhydride. The mixture was stirred under nitrogen for 18 hr. while being heated on a steam-bath. The recovery from the alumina column was 87%, from which the following products were obtained after recrystallization: IV, 56 mg. (13% yield), m.p. 78–80°, lit.[1] m.p. 79.5–80.5° (mixed m.p. 78–80°); VI, 142 mg. (16% yield), m.p. 111.5–112° (mixed m.p. 111.5–112°, see indirect synthesis in the sequel); X, 171 mg. (51% yield), m.p. 113–113.5° (mixed m.p. 113–113.5°).[16]

B. **Acetic Anhydride–Acetic Acid.**—To 1.527 g. (5.0 mmoles) of adduct was added 1.60 g. (27 mmoles) of glacial acetic acid and 0.56 g. (5.5 mmoles) of acetic anhydride. The reaction mixture was refluxed under nitrogen for 0.5 hr. The recovery from chromatography was 97%, and after recrystallization the following products were obtained: IV, 286 mg. (68% yield); VI, 124 mg. (14% yield); X, 150 mg. (44% yield).

C. **Ketene.**—A solution of 1.527 g. (5.0 mmoles) of I in 20 ml. of benzene was partially distilled to remove any traces of moisture, cooled and treated with ketene (36–38 mmoles).[17] The mixture was stirred throughout this period and allowed to stand for 3 hr. The recovery from chromatography was 75%, and after recrystallization the following products were obtained: IX, 25 mg. (8% yield), m.p. 44.5–45°, lit.[18] m.p. 48° (mixed m.p. 44.5–45°); VI, 125 mg. (14% yield); X, 66 mg. (20% yield).

D. **Acetyl Chloride–Pyridine.**[19]—A suspension of 1.527 g. (5.0 mmoles) of I in 0.5 ml. (491 mg., 6.2 mmoles) of anhydrous pyridine was allowed to cool in an ice-bath, and 0.5 ml. (553 mg., 7.0 mmoles) of acetyl chloride was added dropwise with stirring. The mixture was stirred for 10 min. and then was heated on a steam-bath for the same length of time. The mixture again was cooled in an ice-bath while 5 g. of ice was added with stirring. After the aqueous phase had been separated, the remaining oil was washed twice by stirring with 5-ml. portions of water. The oil was taken up in benzene and dried by azeotropic distillation. The recovery from chromatography was 71%, and after recrystallization the following products were obtained; IX, 45 mg. (15% yield); VI, 177 mg. (20% yield); X, 151 mg. (45% yield).

Chromatographic Isolation of IV, VI and X from Mixtures of Known Composition.—A mixture, composed of 150 mg. of IV, 230 mg. of VI and 220 mg. of X dissolved in 5 ml. of warm benzene, was chromatographed by the procedure used in separating the products from the acetylation reaction mixtures. This mixture was composed of approximately the same relative amounts of these compounds as were obtained above in A. The total weight of the various fractions from the chromatogram was 597 mg. (99.5% recovery). The following recoveries of pure compounds were obtained after recrystallizations: IV, 139 mg. (93%); VI, 202 mg. (88%); X, 168 mg. (76%).

To approximate the environment of an actual reaction mixture, the same weights of IV, VI and X as above were combined with 194 mg. of the oily residues from the various fractions of a run from A. The recovery from the column was 97%, and the recoveries of the recrystallized products were: IV, 113 mg. (75%); VI, 235 mg. (102%); X, 167 mg. (76%).

Indirect Synthesis of N-[α-(*p*-Tolyethio)-benzyl]-acetanilide (VI).—A mixture of 14.2 g. (0.05 mole) of N-(α-acetoxybenzyl)-acetanilide[20] and 24.8 g. (0.20 mole) of *p*-toluenethiol was melted on a steam-bath and heated for 1 hr. After it had been cooled, the mixture was dissolved in 450 ml. of ether, and this solution was extracted with two 200-ml. portions of 5% sodium hydroxide solution, washed three times with 50-ml. portions of water and dried over anhydrous sodium sulfate. Removal of the ether left a brown residue which weighed 17.0 g. (98% yield), m.p. 99.5–110.5°. The crude product was recrystallized from 30 ml. of 95% ethanol to give 14.4 g. (83%), m.p. 111.5–112°.

Anal. Calcd. for $C_{22}H_{21}NOS$: C, 76.04; H, 6.09; N, 4.03; S, 9.23. Found: C, 76.20; H, 6.00; N, 3.95; S, 9.05.

Stability of VI under Acetylating Conditions.—A mixture of 869 mg. (2.5 mmoles) of VI and 510 mg. (5.0 mmoles) of acetic anhydride was heated on a steam-bath for 18 hr., after which volatile material was removed by distillation under reduced pressure. A residue of 870 mg. (quantitative recovery) of a colorless, crystalline solid was obtained, m.p. 111.5–112°. To this residue was added a mixture of 5 mmoles each of acetic anhydride (510 mg.) and acetic acid (304 mg.), and the mixture was treated in the same manner as above. The colorless, crystalline residue again represented a quantitative recovery of VI, 869 mg., m.p. 108.5–111°.

Desulfurization of VI with Raney Nickel.—The procedure used was similar to that employed by Mozingo, *et al.*,[21] for certain sulfides. A solution of 3.475 g. (0.01 mole) of VI in 140 ml. of 75% ethanol was heated with 30 ml. of a 75% ethanol suspension of freshly prepared Raney nickel.[22] After the mixture had been stirred for 15 min., the solution was filtered, diluted with water to 500 ml. and distilled until 18 ml. of distillate had been collected. A small organic phase consisting of toluene was separated (539 mg., 59%) and identified by physical constants and nitration to 2,4-dinitrotoluene.

The residue was concentrated to a volume of 375 ml. and extracted twice with 50-ml. portions of ether; the extracts were dried over anhydrous sodium sulfate and then over Drierite. The ether was removed by distillation under reduced pressure. The residue crystallized upon seeding; the yield of N-benzylacetanilide was 2.01 g. (90%), m.p. 56–57°, lit.[7a] m.p. 58° (mixed m.p. 56–57°).

Acid Hydrolysis of VI.—A mixture of 20 ml. of 10% hydrochloric acid and 1.00 g. (2.9 mmoles) of VI was distilled over a 3-hr. period while the initial liquid level of the

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[13] All melting points are corrected. The microanalytical work was performed by Galbraith Laboratories, Knoxville, Tenn.

[14] In preliminary experiments which demonstrated the resistance of I to acetylation, treatment of I in benzene with acetic anhydride resulted in recoveries of 71–77%. Direct treatment of I with boiling anhydride also led to recovery of starting material (45%).

[15] Aluminum oxide (Woelm), non-alkaline, activity grade 1 was employed, Alupharm Chemicals, Elmont, N. Y. The elution solvents were petroleum ether (b.p. 30–75°), benzene, ether, methanol and the customary combinations of these solvents.

[16] In subsequent sections melting point and mixed melting point data which are identical or very similar to those reported here will not be reiterated. All acetylation experiments were run in duplicate, and the results were found to be in good agreement.

[17] J. W. Williams and C. D. Hurd, *J. Org. Chem.*, **5**, 122 (1940).

[18] R. Otto and A. Rössing, *Ber.*, **20**, 2091 (1887).

[19] An experiment employing acetic anhydride–pyridine was also carried out; however, since none of the acetyl derivative VI was isolated (a 19% yield of acetanilide was obtained), further studies with this reagent were discontinued.

[20] H. R. Snyder, R. H. Levin and P. F. Wiley, THIS JOURNAL, **60**, 2025 (1938).

[21] R. Mozingo, *et al.*, *ibid.*, **65**, 1013 (1943).

[22] This was prepared from 30 g. of alloy, which was kept at 45–55° for 1 hr. after addition to the sodium hydroxide solution

reaction mixture was maintained by addition of water. The turbid distillate was collected in a cold solution of 2,4-dinitrophenylhydrazine in 2 *N* hydrochloric acid. This mixture was allowed to stand overnight at 0°, after which the solid was collected by filtration and washed with 2 *N* hydrochloric acid followed by water. The *p*-toluenethiol was separated by allowing the resulting solid to stand in a vacuum desiccator over moist sodium hydroxide pellets for 2.5 days. The sodium hydroxide was then dissolved in water, the solution filtered, the ice-cold filtrate acidified with hydrochloric acid and the resulting *p*-toluenethiol removed by filtration; yield 118 mg. (33%), m.p. 41–43°, lit.[23] m.p. 44°. The solid which remained after standing in the desiccator was benzaldehyde 2,4-dinitrophenylhydrazone; yield 768 mg. (93%), m.p. 227–236°, lit.[24] m.p. 235°.

The contents of the distilling flask were filtered, and the filtrate was neutralized with 10% sodium hydroxide solution to liberate aniline. Bromine water was added in slight excess, and the resulting precipitate was removed by filtration, washed with water and dried; 2,4,6-tribromoaniline was obtained as a gray solid; yield 685 mg. (72%), m.p. 118–120°, lit.[25] m.p. 119–120°.

Oxidative Decomposition of VI.—This reaction was carried out under conditions similar to those used by Caldwell and Sayin for oxidation of sulfides.[26] To an ice-cold solution of 869 mg. (2.5 mmoles) of VI in a mixture of 5 ml. each of acetic acid and acetic anhydride was added dropwise with stirring 1 ml. of 30% hydrogen peroxide. The reaction mixture was allowed to stand in an ice-bath overnight and then at 20° for 3 hr. Removal of excess acetic acid–acetic anhydride gave 930 mg. of a viscous yellow residue containing some suspended solid. This material was dissolved in 10 ml. of benzene, and one-half of this solution was chromatographed resulting in the isolation of 151 mg. (89% yield) of acetanilide, m.p. 113–113.5°.[27]

Reaction of I with Benzoyl Chloride–Pyridine.—To a solution of 611 mg. (2.0 mmoles) of I in 5 ml. of anhydrous pyridine and 10 ml. of anhydrous benzene was added dropwise 0.50 ml. (606 mg., 4.3 mmoles) of benzoyl chloride. The resulting mixture was heated in a water-bath at 60–70° for 0.5 hr. and then poured into 100 ml. of water. The benzene phase was separated, and the aqueous phase was extracted with 10 ml. of benzene. The combined benzene solutions were washed successively with several 25-ml. portions of water, 5% sodium carbonate solution and again with water. The benzene solution was diluted to 5 ml. and was chromatographed. The first three fractions gave, after two recrystallizations from ethanol, 154 mg. (34% yield) of colorless *p*-tolyl thiolbenzoate, m.p. 76–76.5°, lit.[11] m.p. 75° (mixed m.p. 76–76.5°).

After two recrystallizations from ethanol, residues from fractions 7–13 gave 36 mg. (9% yield) of colorless benzanilide, m.p. 163–163.5°, lit.[28] m.p. 161–162° (mixed m.p. 163–163.5°).

Acknowledgments.—This investigation was supported in part by a grant (G1100) from the National Science Foundation. Also R.J.M. wishes to express appreciation for a predoctoral fellowship (N-4077) from the National Institutes of Health, Public Health Service, during the tenure of which a part of this work was carried out.

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(23) E. Fischer, *Ber.*, **48**, 93 (1915).

(24) T. Curtius and G. M. Dedichen, *J. prakt. Chem.*, [2] **50**, 241, 264 (1894).

(25) R. Fittig and E. Büchner, *Ann.*, **188**, 14, 26 (1877).

(26) W. T. Caldwell and A. N. Sayin, This Journal, **73**, 5125 (1951).

(27) Oxidation of VI with potassium permanganate solution gave similar result but a lower yield of acetanilide (49%).

(28) J. B. Cohen, *J. Chem. Soc.*, **59**, 67 (1891).

PULLMAN, WASHINGTON

COMMUNICATIONS TO THE EDITOR

KINETICS OF DISPLACEMENT REACTIONS AT THE SULFUR ATOM. II. STEREOCHEMISTRY

Sir:

In bimolecular nucleophilic substitutions at atoms of the second row of the Periodic Table, the problem arises of the structure of the transition state. Recently Sommer and Bennett[1] have examined the reactivity of a bridgehead organosilicon chloride and have tentatively suggested that in direct displacements at silicon the entering group does not necessarily make an angle near 180° with the leaving group and the central atom, but there might be other directions of attack. While awaiting further, more detailed information on this extremely interesting subject we wish to communicate some results which indicate to what extent in direct substitutions at sulfur (and conceivably at other second-row atoms), attack from the back side is favored over attack from other directions.

The reaction under investigation was the isotopic exchange between organic thiosulfates and (S^{35}) sulfite ion

$$\mathrm{R{-}S{-}SO_3{}^- + SO_3{}^{*=} \rightleftharpoons R{-}S{-}SO_3{}^{*-} + SO_3{}^{=}}$$

for which a mechanism of direct displacement at sulfur previously had been established.[2] The present results concern the α-branched alkyl series, that is, for R = Me, Et, *i*-Pr and *t*-Bu. In water at 25°, *p*H 7.9 and ionic strength of 0.5 these relative rates have been measured[3]:

R =	Me	Et	*i*-Pr	*t*-Bu[4]
$100k/k_{\mathrm{Me}}$	100	50	0.7	0.0006

It appears very reasonable to attribute the observed reactivity differences to steric hindrance at the transition state. This is borne out by the following considerations: (i) the electronic effect of a methyl group β- to the seat of substitution is quite negligible, as might be inferred from the almost equal rates of exchange of sulfite ion with benzyl- and *p*-methylbenzyl thiosulfates,[5] (ii) although the rate consistently decreases along the series, by far the greatest drop occurs between two members of the series (*i*-Pr and *t*-Bu), a behavior characteristic of steric effects, (iii) the reaction under consideration being a direct displacement at sulfur, it is easily seen that the above series of reactions is the sulfur

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(1) L. H. Sommer and O. F. Bennett, This Journal, **79**, 1008 (1957).

(2) Part I: A. Fava and G. Pajaro, *ibid.*, **78**, 5203 (1956).

(3) Under the conditions specified the bimolecular rate constant for the methyl derivative is $k = 2.2 \times 10^{-1}$ (mole/l.)$^{-1}$ sec.$^{-1}$.

(4) Extrapolated from data between 60° and 90°.

(5) A. Fava and A. Iliceto, unpublished results.