The oily filtrate from the crystals was distilled, b.p. 170–171° at 1 mm. (*cis* form) (lit.[5] b.p. 235–242° at 760 mm. for mixture of *cis* and *trans*), yield 18%.

Anal. Calcd. for $C_{14}H_{12}S_2$: C, 68.81; H, 4.95. Found: C, 69.05; H, 4.98.

The higher-melting form has been assigned the *trans* structure by Truce[22] as deduced from its oxidation to the higher-melting sulfone. However, oxidation experiments of either isomer in this Laboratory gave only the *trans*-sulfone.

***trans*-1,2-Dibenzenesulfonylethylene.**—To a cold solution of 3 g. of 1,2-diphenylmercaptoethylene (*cis* or *trans*) in 40 ml. of glacial acetic acid and 10 ml. of acetic anhydride, was added 11 ml. (twice the required amount) of 30% hydrogen peroxide during a period of one hour. After standing overnight, 2.7 ml. more of hydrogen peroxide was added and the reaction mixture was heated at 100° for 2 hours. On cooling, long needles precipitated which were separated by filtration. The yield of product, after purification from glacial acetic acid, m.p. 228–229°, was 72% from the higher-melting sulfide and 35% from the lower-melting sulfide.

Anal. Calcd. for $C_{14}H_{12}O_4S_2$: C, 54.53; H, 3.92. Found: C, 54.41; H, 3.88.

Reaction of 1,2-Dibromoethylene and Cuprous Ethylmercaptide.—The reagents were heated for 8 hours and the product, b.p. 61° at 1 mm., was isolated in the usual way. The analysis indicated that this product was impure ethylmercaptoacetylene.

Anal. Calcd. for C_4H_6S: C, 55.76; H, 7.02. Found: C, 56.60; H, 8.00.

Further distillation did not improve the product. The band characteristic of acetylenic derivatives (3300 cm.$^{-1}$) or the stretching absorption of monosubstituted acetylenes (2100–2140 cm.$^{-1}$) in the infrared spectrum were absent. However, a strong band at 1260 cm.$^{-1}$, which has been assigned to an acetylene bending vibration, was present.

Ethylmercaptocarboxylic Acid.—When the crude ethylmercaptoacetylene was heated in glacial acetic acid with 30% hydrogen peroxide ethylmercaptocarboxylic acid separated. It was purified by crystallization from ethanol, m.p. 145–146°.

Anal. Calcd. for $C_3H_6O_2S$: C, 33.95; H, 5.70; S, 30.20. Found: C, 34.13; H, 5.75; S, 30.29.

Hexaphenylmercaptobenzene.—The preparation was conducted as previously described.[1] After pouring into acid and standing, the precipitate was collected and washed with three 200-ml. portions of acetone. The insoluble residue was dried and extracted with chloroform in a soxhlet for 48 hours. From the chloroform solution, 25 g. (38%) of product resulted which, after crystallization from carbon tetrachloride, melted at 184–185°.

Anal. Calcd. for $C_{42}H_{30}S_6$: C, 69.38; H, 4.15. Found: C, 69.50; H, 4.40.

The acetone washings of the crude hexaphenylmercaptobenzene deposited, after 7 days in a refrigerator, 9.9 g. of crystals. After purification by several crystallizations from glacial acetic acid they melted at 149.5–150°, yield 5 g. (7.6%).

Anal. Calcd. for $C_{42}H_{30}S_6$: C, 69.38; H, 4.15. Found: C, 69.25; H, 4.08.

Hexabenzenesulfonylbenzene.—A solution of 5 g. of hexaphenylmercaptobenzene (m.p. 184–185°) in 400 ml. of glacial acetic acid was treated with 110 ml. (12 times theory) of 30% hydrogen peroxide, added in thirteen portions during 7 days. After addition of each portion, the mixture was slowly heated to 120° and the temperature maintained there for 2 hours before allowing to cool. At the end of the oxidation 0.9 g. of product separated on cooling. After three recrystallizations from glacial acetic acid it melted at 264–266°. The infrared spectrum showed peaks at 1148 and 1333 cm.$^{-1}$.

Anal. Calcd. for $C_{42}H_{30}O_{12}S_6$: C, 54.89; H, 3.29; S, 20.93. Found: C, 55.10; H, 3.57; S, 20.6.

The mother liquors on concentration did not yield any more product.

By oxidation in a similar manner of the lower-melting hexaphenylmercaptobenzene, no pure product could be isolated.

Reaction of β-Bromonaphthalene and Cuprous Benzylmercaptide and with Cuprous Ethyl Xanthate.—The reaction of β-bromonaphthalene and cuprous benzylmercaptide, or cuprous ethyl xanthate, was carried out in the usual way. The product in less than 10% yield that could be separated from the unchanged β-bromonaphthalene proved to be β-naphthyl sulfide, m.p. 150–151°. This was identified by analysis and by oxidation with hydrogen peroxide in acetic acid to give β-dinaphthyl sulfone, m.p. 177–178°.

Anal. Calcd. for $C_{20}H_{14}O_2S$: C, 75.45; H, 4.43. Found: C, 75.55; H, 4.66.

Acknowledgment.—The authors thank the A. P. Sloan Foundation for financial help which made this investigation possible. The authors are indebted to Mr. J. Nemeth, Miss C. Higham and Mrs. Ruby Liu for the microanalyses and to Mr. P. E. McMahon and Mr. B. A. Shoulders for the determination of the infrared spectra.

URBANA, ILL.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Stereochemistry of the Base-catalyzed Addition of *p*-Toluenethiol to Propiolic Acid[1,2]

BY WILLIAM E. TRUCE, DAVID L. GOLDHAMER AND ROBERT B. KRUSE

RECEIVED MARCH 27, 1959

An exception to the Rule of *trans*-Nucleophilic Addition has been reported for the base-catalyzed addition of *p*-toluenethiol to sodium propiolate to give *trans-p*-tolylmercaptoacrylic acid. Rates of cyclization of the *cis*- and *trans-p*-tolylmercaptoacrylic acids together with infrared spectral data and dipole moment measurements of the corresponding *cis*- and *trans-p*-tolylsulfonylacrylic acids have elucidated the configurations of *cis*- and *trans-p*-tolylmercaptoacrylic acids.

Montanari and Negrini have reported the formation of "*cis*"- and "*trans*"-*p*-tolylmercaptoacrylic acids (II) and (I), respectively, as shown[3] The melting points of the assigned "*cis*"-(II) and "*trans*"-(I) were 143–144° and 137–138°, respectively. Their "bases"[3] for assignment of configurations were: (a) the rule, formulated by Montanari, that substitution of the halogen of a vinylic-type halide by a nucleophilic agent proceeds with "retention of configuration," (b) isomer II may be converted to isomer I by thermal isomerization: the von Auwers–Skita rule states that the *trans* isomer would be more thermally stable, (c) the

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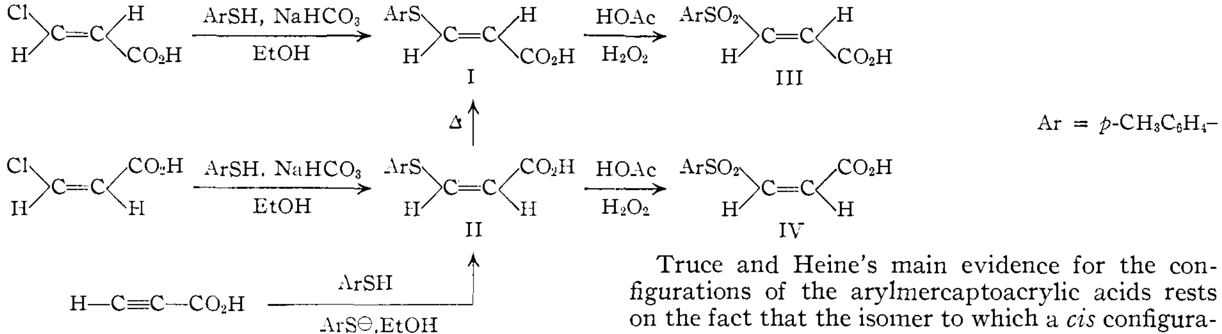
[1] This constitutes Paper X in the series, "Stereospecific Reactions of Nucleophilic Agents with Acetylenes and Vinyl-type Halides"; for preceding paper see THIS JOURNAL, **81**, 592 (1959).

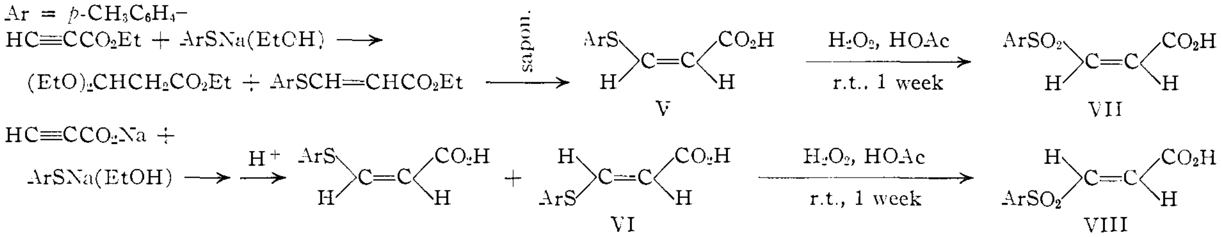
[2] Taken from the Ph.D. theses of Mr. Goldhamer and Mr. Kruse.

[3] F. Montanari and A. Negrini, *Gazz. chim. ital.*, **87**, 1073 (1957).



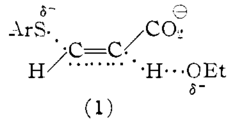
"addition of p-toluenethiol manifests itself in the classical *trans* addition to the triple bond" and (d) the reduction of "*trans*"-β-arylmercapto-α-haloacrylic acids to "*trans*"-β-arylmercaptoacrylic acids.

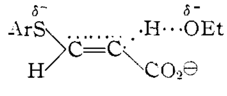
These assignments of geometrical configuration are in conflict with earlier assignments by Truce and Heine, who prepared *cis*- and *trans*-p-tolylmercaptoacrylic acids by the sequence of reactions[4]



The melting points of the assigned *cis*- (V) and *trans*- (VI) are 136–137° and 144–145°, respectively. Their conclusions were: (a) thiolate reagent adds normally to ethyl propiolate by the Rule of *trans*-Nucleophilic Addition[4] to form the *cis*-acid upon saponification and (b) thiolate reagent adds principally in a *cis* fashion to sodium propiolate, with only a small amount of product resulting from *trans* addition being isolated.

This apparent violation of the Rule of *trans*-Nucleophilic Addition by sodium propiolate is presumably a consequence of the fact that the substituent carboxylate anion, bearing a negative charge, impedes normal *trans* addition since this negatively-charged substituent would be forced to swing in toward the field of the entering negatively-charged thiolate ion. Possible transition states for *cis* and *trans* addition are illustrated below by (1) and (2), respectively. The dotted lines represent incipiently formed or broken bonds in the transition state.[1] Intuitively one would expect the coulombic repulsion between a partial


(1)


(2)

negative charge and a full negative charge to be greater than between two partial negative charges. Hence, one would predict on this basis alone that (2) would represent the most energetically favored reaction path.

Truce and Heine's main evidence for the configurations of the arylmercaptoacrylic acids rests on the fact that the isomer to which a *cis* configuration is assigned readily undergoes a Friedel–Crafts cyclization to 6-methylthiochromone under milder conditions than does its geometrical isomer.[4] Montanari and Negrini discounted this evidence for configuration on the basis that they were able to cyclize both acids by converting them to their acid chlorides with thionyl chloride and adding 1.5 equivalents of aluminum chloride to a carbon disulfide solution of the acid chloride at approximately 40°.[5] Their results show, however, that the analogous phenylmercaptoacrylic acid to which they assign the "*cis*" configuration undergoes isomerization during reflux with thionyl chloride. Truce and Heine tested both acids in benzene with phosphorus pentachloride and then aluminum chloride at room temperature. Only at refluxing conditions did the isomer assigned the *trans* structure cyclize.[4] More recently cyclizations have been carried out with carbon disulfide as the solvent to which thionyl chloride and then aluminum chloride were added while maintaining the temperature at 0°. Table I summarizes the fact that cyclization of the isomeric acids results in the more rapid formation of 6-methylthiochromone from the acid assigned the *cis* structure.

TABLE I

CYCLIZATION OF *cis* vs. *trans*-p-TOLYLMERCAPTOACRYLIC ACIDS

Period, min.	Configuration (m.p., °C.)	Conversion, %	Yield, %	Acid recovd., %
10	*cis* (136–137)	71	89	20
	trans (144–145)	>2.3	25	91
60	*cis* (136–137)	85	87	1.3
	trans (144–145)	39	83	53

Both acids were oxidized to the corresponding *cis*- and *trans*-p-tolylsulfonylacrylic acids (VII) and (VIII) using mild conditions to avoid isomerization during the course of reaction. The melting points of the *cis*- and *trans*-sulfones were 125–125.5° and 123–124°, respectively [M. and N. 123–125° (IV) and 125° (III)].

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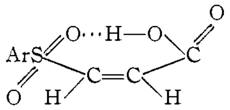
(4) W. E. Truce and R. F. Heine, THIS JOURNAL, **79**, 5311 (1957).

(5) F. Montanari and A. Negrini, *Ricerca Sci.*, **27**, 3058 (1957).

The following infrared spectral data support these assignments of configurations for the sulfonylacrylic acids: (a) appearance of an OH stretching absorption band at 3118 cm.$^{-1}$ is observed for the *trans* isomer whereas this band is absent in the *cis* isomer. Internal hydrogen bonding is prevalent in the *cis* isomer and therefore the OH stretching vibrations appear in the bonded state similar to the dimeric form of acids. Furthermore the *trans* compound does not give rise to a broad absorption region with many submaxima between 3000 and 2500 cm.$^{-1}$ as does the *cis* isomer[6]; (b) internal hydrogen bonding lowers the carbonyl (C=O) stretching frequency as displayed by the *cis*- (VII) band at 1685 cm.$^{-1}$ and the *trans*-(VIII) band at 1730 cm.$^{-1}$, a shift of 45 cm.$^{-1}$ [7]; and (c) a mixture of both acids displays two separate and distinct carbonyl stretching frequency bands. Unfortunately the ethylenic C–H bending vibrations are not useful for stereochemical correlation of these acids since the strong sulfone bands interfere.



Dipole moment measurements have been determined for the isomeric *p*-tolylsulfonylacrylic acids for the purpose of determining the relative geometries of these unsymmetrically substituted olefins. A solution method as described by DeVries and Brown[8] using a heterodyne beat apparatus was employed and the molar polarization at infinite dilution was calculated by the Hedestrand equation.[9] 1,4-Dioxane was utilized as the solvent even though absolute dipole moments of the solute molecules cannot be determined due to interaction between solvent and solute molecules. However, in stereochemical investigations,[10] absolute values are of little interest. Since the solute used was a carboxylic acid, it was necessary that the acid be in the free monomeric state to the greatest extent possible. Accordingly measurements were made at mole fractions as low as 5.98×10^{-4} to 6.45×10^{-4} in dioxane.[11] Dioxane seemed particularly suitable, as it is a good solvent for carboxylic acids, and freezing-point measurements indicate that benzoic acid is monomeric in it.[12] This was confirmed by spectroscopic measurement, a single C=O stretching band being observed, whereas two are shown in carbon tetrachloride, corresponding to monomer and dimer.[6] The results of the dipole moment measurements are given in Table II.

From Table II it is observed that in dioxane isomer VII has a dipole moment of 5.10 D. whereas isomer VIII has a lower dipole moment of 4.39 D.

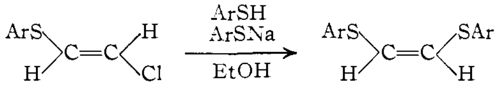
TABLE II

DIPOLE MOMENTS OF *cis*- AND *trans*-*p*-TOLYLSULFONYLACRYLIC ACIDS IN DIOXANE

Compound	$P_{2\infty}$	P_e	μ, D.
VII	531.96	45.24	5.10
VIII	431.92	36.34	4.39

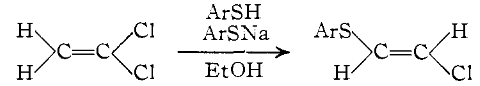
A precision of 1% or better readily can be attained in moments of 1.5 D. and higher.[13] Based upon these experimental results VII is assigned the *cis* configuration and VIII the opposite *trans* configuration.

In summary, the fact that addition of *p*-toluenethiolate reagent to sodium propiolate gives an acrylic acid derivative which is isomeric with that obtained when *p*-toluenethiolate reagent is added to ethyl propiolate and the product is hydrolyzed has led to the conclusion that one of these additions proceeds in violation of the Rule of *trans*-Nucleophilic Addition. That such violation occurs with sodium propiolate is supported by infrared spectral evidence, relative rates of cyclization and dipole moment measurements all of which show that compound VIII is of the *trans* configuration. One of the arguments[3] used against our assignments of configuration is that nucleophilic substitution of a vinylic halide "proceeds with retention of configuration": however, this is not valid, since exceptions are well established. For example, *trans*-1-chloro-2-(*p*-tolylmercapto)-ethene (IX) reacts with *p*-toluenethiol to produce *cis*-bis-(*p*-tolylmercapto)-ethene (X)[14]



IX X

Furthermore, such "substitution" may even take place with the nucleophile becoming attached to an ethylenic carbon atom not originally bearing the halogen, as with vinylidene chloride (XI)[14]



XI IX

Possibly the formation of the *trans* product I from *cis*-chloroacrylic acid[3] could be accounted for by an initial dehydrohalogenation to form the intermediate propiolic acid, followed by *cis* addition of the elements of *p*-toluenethiol; the *cis* compound II could arise from *trans*-chloroacrylic acid *via* an addition–elimination or an "incipient" carbanion mechanism.[15] At least according to the Rule of *trans* Elimination, the *cis*-chloroacrylic acid would be expected to undergo base-catalyzed elimination of HCl more readily than the *trans* isomer. Nor does the thermal interconversion of isomers V and VI, presumably from the less to the more stable form,[3] establish the configurations of these compounds, since many cases are known where the *trans* isomer is not the more thermodynamically

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[6] M. M. Davies and G. B. B. M. Sutherland, *J. Chem. Phys.*, **6**, 755 (1938).

[7] L. J. Bellamy, "The Infrared-red Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, p. 161.

[8] T. DeVries and P. Brown, THIS JOURNAL, **73**, 1811 (1951).

[9] G. Hedestrand, *Z. physik. Chem.*, **32**, 428 (1929).

[10] L. E. Sutton and G. C. Hampson, *Trans. Faraday Soc.*, **31**, 950 (1935).

[11] C. P. Smyth, "Dielectric Behavior and Structure," McGraw-Hill Book Co., Inc., New York, N. Y., 1955, p. 303.

[12] E. N. Lassettre, *Chem. Revs.*, **20**, 277 (1937).

[13] L. E. Sutton in E. A. Braude and F. C. Nachod, "Determination of Organic Structures by Physical Methods," Chapter 9, Academic Press, Inc., New York, N. Y., 1955, p. 381.

[14] W. E. Truce and M. M. Boudakian, THIS JOURNAL, **78**, 2748 (1956).

[15] W. E. Truce and R. Kassinger, *ibid.*, **80**, 1916 (1958).

stable form. Also, the tendency for *trans* addition to the triple bond may be offset by a number of factors, such as coulombic or steric forces, or the nature of the nucleophile. For example, Jones and Whiting[16] have evidence of over-all *cis* addition of amines to acetylenic hydroxy-acids. Finally, the "reduction" of "*trans*"-*β*-*p*-tolylmercapto-*α*-chloroacrylic acid to "*trans*"-*p*-tolylmercaptoacrylic acid, used as configurational evidence by Montanari and Negrini,[3] may result from either an incorrect configurational assignment to the chloro-acid or isomerization during the replacement of the chlorine with hydrogen.

Experimental[17]

Rates of Cyclization of *cis*-*vs*. *trans*-*p*-Tolylmercaptoacrylic Acids.—*cis*- and *trans*-*p*-tolylmercaptoacrylic acids were prepared by the method of Truce and Heine.[4]

cis-*p*-Tolylmercaptoacrylic acid (0.71 g., 0.0031 mole) was dissolved in 20 ml. of carbon disulfide. The mixture was stirred in a 50-ml., three-neck, round-bottom flask equipped with a condenser, drying tube and thermometer. The flask containing the solution was immersed in a Dewar filled with water and ice. Thionyl chloride (0.50 g., 0.0042 mole) then was added slowly without altering the temperature. Aluminum chloride (0.84 g., 0.0063 mole) was added to the solution at a slow rate, through an addition tube to exclude moisture, while stirring rapidly. The temperature did not rise above 2° during the addition. The mixture was stirred for an hour, and then poured over crushed ice. Three ml. of concentrated hydrochloric acid was added and the mixture extracted with three 25-ml. portions of ether. The combined ether layers were washed with two 35-ml. portions of 5% sodium bicarbonate solution and the bicarbonate washings were acidified with hydrochloric acid. The resulting aqueous solution was extracted with two 15-ml. portions of ether and the ether layers were evaporated to obtain 0.01 g. of starting material, *cis*-*p*-tolylmercaptoacrylic acid, m.p. 136°, mixture m.p. with an authentic sample, 136°. A small amount of tarry material also was present.

The ethereal solution of 6-methylthiochromone was evaporated and the residue recrystallized from 30–60° petroleum ether to yield 0.55 g. (87% conversion) of crude 6-methylthiochromone, m.p. 63–65°. Further recrystallization from ligroin with charcoal filtration resulted in prisms, m.p. 69°, which did not depress the melting point of an authentic sample (lit.[18] m.p. 69–70°). The *trans* compound was treated similarly and both experiments were repeated, decreasing the reaction time to 10 min. Quantitative results for these rates are recorded below.

	10 min.		60 min.	
	trans	*cis*	*trans*	*cis*
Init. amt., g.	0.43	0.66	0.53	0.71
Recovd. acid, g.	0.39	0.13	0.28 + tars	0.01 + tars
Cyclic prod., g.	>0.01 crude	0.47	0.19	0.55
Conversion, %	>2.3	71	39	85
Yield, %	25	89	83	87
Recovd. acid, %	91	20	53	1.3

Preparation of *cis*-*p*-Tolylsulfonylacrylic acid.—*cis*-*p*-Tolylmercaptoacrylic acid was prepared by treating ethyl propiolate with a mixture of sodium *p*-toluenethiolate and *p*-toluenethiol in absolute ethanol to form ethyl *p*-tolylmercaptoacrylate, which then was hydrolyzed and neutralized to the free acid (m.p. 136–137°).[4] A prolonged room temperature oxidation (1 week) of 3.00 g. (0.0155 mole) of *cis*-*p*-tolylmercaptoacrylic acid in a solution of 3.5 ml. of 30% hydrogen peroxide and 30 ml. of glacial acetic acid resulted in the formation of 3.03 g. (0.0141 mole) of *cis*-sulfone, recrystallized from an ethanol–water mixture, yield 90.8%, m.p. 125–125.5°.

Anal. Calcd. for $C_{10}H_{10}O_4S$: C, 53.1; H, 4.43; neut. equiv., 226. Found: C, 53.07; H, 4.35; neut. equiv., 225.6.

An infrared spectrum of the *cis*-sulfone displayed the following principal bands: 3.52(m-b), 5.94(s), 6.29(s), 6.90(m), 7.10(m), 7.29(s), 7.67(b), 8.10(s), 8.45(m), 8.75(s), 9.25(s), 9.84(m), 10.39(m), 12.04(m), 12.39(m), 14.24(m-b) and 14.83(m-b) μ: phases, Nujol mull.

Preparation of *trans*-*p*-Tolylsulfonylacrylic Acid.—*trans*-*p*-Tolylmercaptoacrylic acid was prepared by treating sodium propiolate with a mixture of sodium *p*-toluenethiolate and *p*-toluenethiol in absolute ethanol, then hydrolyzing to the free acid and finally fractionally crystallizing from absolute ethanol to obtain the pure *trans*-acid (m.p. 144–145°).[4] This product, 1.94 g. (0.01 mole), was dissolved in a solution of 50 ml. of glacial acetic acid and 5.0 ml. of 30% hydrogen peroxide slightly warmed and then allowed to stand at room temperature for one week. The mixture was poured over cracked ice and then evaporated by means of an air jet to a solid residue. The solid was recrystallized from an ethanol–water mixture with the formation of 1.87 g. (0.00865 mole) of sulfone, m.p. 123–124°, yield 86.5%. A mixture of *cis*- and *trans*-*p*-tolylsulfonylacrylic acids gave a depressed melting point, m.p. 108–118°.

Anal. Calcd. for $C_{10}H_{10}O_4S$: C, 53.1; H, 4.43; neut. equiv., 226. Found: C, 53.1; H, 4.46; neut. equiv., 225.9.

Its infrared absorption spectrum showed the following bands and intensities: 3.15(s), 3.51(m), 5.78(s), 6.17(s), 6.30(s), 6.73(s), 6.91(m), 7.28(s), 7.72(s), 7.78(s), 8.39(s), 8.48(s), 8.78(s), 9.25(s), 9.86(s), 11.00(m), 12.34(m), 12.50(m), 13.28(b), 13.70(b) and 15.35(m-b) μ: phases, Nujol mull. An infrared spectrum of a mixture of *cis* and *trans*-*p*-tolylsulfonylacrylic acids showed the following bands and intensities: 3.04(s), 3.42(m), 5.72(s), 5.87(s), 6.10(s), 6.24(s), 6.84(m), 7.24(s), 7.66(s), 7.74(s), 8.02(m), 8.34(s-m), 8.43(s), 8.73(s-m), 9.22(s), 9.83(s), 10.38(b), 10.97(m), 12.44(vb), 13.27(b), 13.73(b) and 15.33(b) μ: phases, Nujol mull.

Materials and Method for Dipole Moment Determinations. Purification of Dioxane for Dipole Moment Studies.[19]—A mixture of two liters of commercial dioxane, 27 ml. of concentrated hydrochloric acid and 200 ml. of water was refluxed for 12 hours, during which time a slow stream of nitrogen was bubbled through the solution to entrain acetaldehyde. The solution was cooled, and potassium hydroxide pellets were added slowly with shaking until they no longer dissolved and a second layer separated. The dioxane was decanted, treated with fresh potassium hydroxide pellets to remove adhering aqueous liquor, decanted into a clean flask, and refluxed with sodium for 10–12 hours. The sodium metal remained bright throughout this operation. The solvent was then refluxed and distilled from fresh sodium and stored out of contact with air; reflux ratio 1:20, b.p. 101°, $n^{20}D$ 1.4221.

The heterodyne beat method[20] was employed to measure the dielectric constants of the dioxane solutions. All measurements were made at 25 ± 0.01°. Since the mole fraction never exceeded 0.02, the relationship between density and concentration is assumed to be linear. The molar refractivity, *MR*, for the solvent was evaluated by means of the Lorentz–Lorenz equation using refractive indices measured with a Bausch and Lomb refractometer. A solution method was used to evaluate the molar refractivities of the solutions.[20]

The value of the change in dielectric with mole fraction was evaluated from five different concentrations by means of the method of least squares. The molar polarization at infinite dilution was calculated by the Hedestrand equation,[9] using known values for dioxane solvent.

The dipole moment itself was calculated from the values of the molar polarization at infinite dilution and from the electronic polarization by the expression[21]

$$\mu = 0.0128[(P_{2\infty} - P_e)T]^{1/2} \times 10^{-18} \text{ e.s.u.}$$

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[16] E. R. H. Jones and M. C. Whiting, *J. Chem. Soc.*, 1423 (1949).

[17] All microanalyses were carried out by Mrs. C. S. Yeh and Mrs. B. Groten of the Purdue Chemistry Microanalytical Laboratory. All infrared spectra were run by Mrs. W. Dilling of the Purdue Chemistry Infrared Laboratory using a Perkin-Elmer infrared spectrophotometer, model 21. All boiling and melting points are uncorrected.

[18] F. Krollpfeiffer, *et al.*, *Ber.*, **58**, 1654 (1925).

[19] K. Hess and H. Frahm, *Ber.*, **71**, 2627 (1938).

[20] C. P. Smyth, "Physical Methods of Organic Chemistry," A. Weissberger, Editor, Vol. I, Part II, Interscience Publishers, Inc., New York, N. Y., 1949, Chapter XXIV.

[21] P. Debye, "Polar Molecules," Dover Publications, New York 1945.

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LAFAYETTE, IND.

[CONTRIBUTION FROM THE ORGANIC CHEMICAL RESEARCH LABORATORIES, LEPETIT S.P.A., MILAN]

Synthesis of Derivatives of a New Heterocyclic Ring. 1,3-Dihydro-2,3,5-benzothiadiazepine 2,2-Dioxide

BY UBERTO M. TEOTINO AND GIORGIO CIGNARELLA

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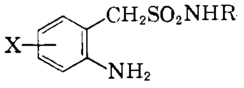
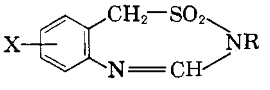
The Ladenburg reaction, when extended to 2-aminobenzylsulfonamide (Ia), leads to 1,3-dihydro-2,3,5-benzothiadiazepine 2,2-dioxide (IIa), a new heterocyclic ring. 2-Amino-5-bromobenzylsulfonamide (Ib) gives the cyclic 8-bromo derivative IIb, thus showing that the reaction may run also with ring substituted 2-aminobenzylsulfonamides. On the contrary, 2-aminobenzylsulfonylmethylamine (Ic) and 2-amino-benzylsulfonanilide (Id) give N,N'-bis-(2-methylaminosulfonylmethylphenyl)-formamidine (IVa) and N,N'-bis-(2-anilinosulfonylmethylphenyl)-formamidine (IVb), thus showing that no ring closure occurs when the sulfonamide nitrogen is substituted by alkyl or phenyl.

The Ladenburg reaction, originally used for the preparation of benzimidazoles,[1–3] has been applied to various α-diamino compounds for synthesizing pyrimidine[4,5] and quinazoline derivatives[6] and to 2-aminosulfonamides for synthesizing 1,4-dihydro-1,2,4-benzothiadiazines,[7–9] even substituted at C-3 when ethyl orthoformate was used as the condensing agent.[10]

It seemed of interest to ascertain whether the Ladenburg reaction could be extended also to 2-aminobenzylsulfonamides of formula I where





Ia, R = X = H
Ib, R = H, X = Br
Ic, R = CH_3, X = H
Id, R = C_6H_5, X = H

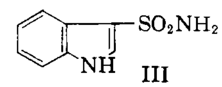
IIa, R = X = H
IIb, R = H, X = Br

the two amino groups are the extremes of a 6-member chain. In this way it would be possible to obtain seven-membered heterocyclic rings, such as the hitherto unknown 1,3-dihydro-2,3,5-benzothiadiazepine 2,2-dioxides (II).

The 4,1,2-, 1,3,4- and 3,1,5-benzothiadiazepines are recorded in the literature.[11] Recently Katz and co-workers[12] described a product, $C_8H_8N_2O_3S$, obtained by treating *o*-mercaptobenzhydrazide with formaldehyde which, in the authors' opinion, could be a 5,3,2-benzothiadiazepinone. The starting 2-aminobenzylsulfonamides, also unknown, were prepared by treating a 2-nitrobenzyl chloride with thiourea according to Johnson and Sprague,[13,14] converting the 2-nitrobenzyl sulfonylchloride so obtained by ammonia or monosubstituted amines into the corresponding 2-nitrobenzylsulfonamides and finally reducing the nitro group with hydrogen over a palladium catalyst.

For the subsequent Ladenburg reaction we selected ethyl orthoformate as the condensing agent because of its smooth reactivity both with unsubstituted and monosubstituted sulfonamides.[10] The reaction was carried out in propylene glycol at 120–130° for 4 to 7 hours with an excess of ethyl orthoformate (4:1).

When unsubstituted 2-aminobenzylsulfonamide (Ia) is treated with ethyl orthoformate a compound, $C_8H_8N_2O_2S$, melting at 234° is obtained. Two different structures can be suggested for this product: the benzothiadiazepine structure IIa resulting from the reaction of ethyl orthoformate with both amino groups of 2-aminobenzylsulfonamide and the 3-indolesulfonamide structure III resulting from the reaction of ethyl orthoformate with the amino and the methylene groups, this latter activated by the sulfonamide group and the benzene ring.



III

The substance of m.p. 234° is acidic in nature. The *pK* value, determined spectrophotometrically, is 10.0.

When an alkaline solution of the product is allowed to stand for many hours or is heated for a few minutes no precipitate is formed in acid solution, whereas the diazo reaction both in this solution and in the shortly heated acid suspension is positive.

The instability of the substance in acids and alkalies disagrees with the indolesulfonamide structure in view of the stability of the indole nucleus under the experimental conditions employed. On the other hand, this instability agrees with the behavior of the analog benzothiadiazine 1,1-

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