Inc.) heated to 200°. The spectrometer was a Bendix Instrument, Type 12-101, which has been modified to include a 1.66-m flight tube, multigate recording, and improved electron-beam focusing. A multichannel Minneapolis–Honeywell Visicorder was used to record the mass spectral data obtained (Table IV).

Nuclear magnetic resonance (nmr) spectra were run on a Varian A-60 spectrometer as *ca.* 50% solutions in CCl_4 with tetramethylsilane as an internal standard unless stated otherwise.

Infrared spectra were recorded on a Beckman Model IR 10 infrared spectrophotometer.

Starting Materials. Unsaturates.—Ethylene (99.9% purity), propylene (99.7% purity), allene (+99% purity), methylacetylene (+98% purity), isobutylene (+99% purity), and 1,3-butadiene (+99% purity) were obtained from the Matheson Co. The pentene-1 used was a Phillips Chemical Co. product of +99% purity. The isoprene was distilled before use and was found to be pure by glpc analysis.

O,O′-Dimethyl Phosphorochloridothioate.—This reagent was obtained from the Monsanto Chemical Co. in +96% purity.

Preparation of Trimethyl Phosphorothionate.—An equimolar quantity of sodium methoxide dissolved in methanol was added slowly to O,O′-dimethyl phosphorochloridothioate with constant stirring. The reaction temperature was kept below 20°. The NaCl precipitate was filtered out of the solution and the methanol was removed on a rotary vacuum evaporator. The remaining liquid was distilled under reduced pressure affording the trimethyl phosphorothionate in *ca.* 70% yield, bp 77–80° (21 mm) [lit.[16] bp 82° (20 mm), 73% yield].

Preparation of O,O′-Dimethylphosphorylsulfenyl Chloride.—Sulfuryl chloride (54.0 g, 0.4 mole) was added dropwise to 62.5 g (0.4 mole) of trimethyl phosphorothionate. The temperature of the reaction was kept below 0° with an ice–salt bath. The reaction was stirred for 30 min after the addition was complete and then the gaseous products and unconsumed sulfuryl chloride were removed using a rotary vacuum evaporator followed by evacuation with an oil pump (1.0 mm). This afforded 64.9 g (92% yield) of the deep yellow $(CH_3O)_2P(O)SCl$, $n^{20}D$ 1.4818 (lit.[7] $n^{20}D$ 1.4820).

General Methods of Addition of O,O′-Dimethylphosphorylsulfenyl Chloride to Unsaturates. A. Liquid Unsaturates.—$(CH_3O)_2P(O)SCl$ was added dropwise to a 5 molar excess of the unsaturate contained in a three-neck flask fitted with a thermometer, a condenser with nitrogen purge, an addition funnel, and a magnetic stirrer. The reaction temperature was kept below 0° with an ice–salt bath. After the addition was complete the reaction mixture was brought slowly to room temperature. The excess olefin was removed under reduced pressure and the remaining oil was taken up in ether. The ethereal solution was washed with 5% $NaHCO_3$ solution until basic and then with water until neutral, and was dried over $MgSO_4$. Then the ether was removed under reduced pressure. The remaining oil (the "crude" product) was then distilled under high vacuum using an apparatus with a heated, packed column and a short-path condenser.

B. Gaseous Unsaturates.—Approximately 12 g of $(CH_3O)_2P(O)SCl$ was placed in a 25-ml, three-neck flask fitted with a thermometer, a condenser with nitrogen purge, and a gas inlet connected through a train of traps and bubblers to the olefin tank. The olefin was blown through the sulfenyl chloride at a moderate rate until the yellow color of the sulfenyl chloride either disappeared or remained constant. The temperature of the reaction was kept below 10° with an ice bath. The product was taken up in 50 ml of ether and was washed until basic with 5% $NaHCO_3$ solution. The ethereal solution was then washed with water until neutral and dried over $MgSO_4$. The ether was removed under reduced pressure and the remaining oil (the "crude" product) was distilled under high vacuum using a heated, packed column and a short-path condenser.

C. Gaseous Unsaturates.—Dried CH_2Cl_2 (100 ml) was placed in a 250-ml, four-neck flask fitted with a thermometer, a condenser with nitrogen purge, a dropping funnel with glass tubing extending below the surface of the methylene chloride. A 5 molar excess of the gaseous unsaturated (*ca.* 0.5 mole) was condensed into a graduated cylinder kept in a Dry Ice–isopropyl alcohol bath. Approximately 0.1 mole of $(CH_3O)_2P(O)SCl$ was added slowly to the unsaturated CH_2Cl_2 solution. The temperature was kept 10–15° below the boiling point of the unsaturated. After the addition was complete the reaction was allowed to come slowly to room temperature. The solution was washed until basic with a 5% solution of $NaHCO_3$, washed with water until neutral, and then dried over $MgSO_4$. The solvent was removed under reduced pressure and the remaining oil (the "crude" product) was distilled under high vacuum using a heated, packed column and a short-path condenser. In all cases the crude product was analyzed by glpc and nmr. Yields were calculated from the above analyses of the crude products (Table I). Decomposition during distillation diminished the yields. All distilled products were also analyzed by nmr and glpc and the nmr parameters of the products are tabulated in Tables II and III.

(16) Reference 4, p 624.

Stereochemistry of Amine Additions to Acetylenic Sulfones and Carboxylic Esters[1]

W. E. TRUCE AND D. G. BRADY

Department of Chemistry, Purdue University, Lafayette, Indiana

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The reactions of amines with ethyl propiolate and several ethynyl sulfones have been studied. Dialkylamines react with these acetylenic compounds to give only *trans*-aminovinyl products. Ethylenimine reacts with both ethyl propiolate and 1-ethylsulfonyl-1-propyne to give mixtures of *cis* and *trans* products, with the relative ratios being solvent dependent, and with *p*-tolylsulfonylacetylene to give only *cis* product. Primary aliphatic amines react with both ethyl propiolate and 1-ethylsulfonyl-1-propyne to give mixtures of *cis* and *trans* products and with *p*-tolylsulfonylacetylene to give only *trans* products. Theories to explain all of these results are presented. In some of these systems the progress of the reactions was successfully followed by nuclear magnetic resonance.

Several years ago, during the course of work involving nucleophilic replacements of halogens from olefinic centers, a pronounced tendency was noted for base-induced additions of thiols to acetylenes to proceed in a *trans* manner.[2] This work, along with the accompanying theory and a few scattered indications in the literature of only one isomer being obtained in such nucleophilic additions, led to the postulation of "the rule of *trans*-nucleophilic addition." It next became of interest to study the applicability of this rule to additions involving nonanionic nucleophiles. The renewed and spreading interest in this area of chemistry[3,4] prompts us to report our observations on the stereochemistry of additions of several amines to acetylenic sulfones and carboxylic esters.

(1) Presented at the 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March 1966.

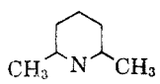
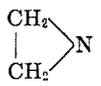
(2) W. E. Truce and J. A. Simms, *J. Am. Chem. Soc.*, **78**, 2756 (1956).

(3) (a) J. E. Dolfini, *J. Org. Chem.*, **30**, 1298 (1965); (b) C. J. M. Stirling, *J. Chem. Soc.*, Suppl I, 5863 (1964).

(4) E. Winterfeldt and H. Preuss, *Angew. Chem.*, **77**, 679 (1965).

TABLE I

REACTION OF RR'NH WITH $HC{\equiv}CSO_2C_6H_4CH_3$-*p*

R	R'	Solvent	Reacn time, hr	Temp, °C	Yield, %	Mp, °C	Configuration, % cis	Configuration, % trans
CH_3	CH_3	CH_2Cl_2	2	−75	73	134–135	...	100
C_2H_5	C_2H_5	C_2H_5OH	4	25–30	90	79–81		100
n-C_3H_7	H	C_2H_5OH	4	25–30	85	76–77		100
i-C_3H_7	*i*-C_3H_7	C_2H_5OH	4	25–30	91	140–141		100
		C_2H_5OH	4	25–30	88	114–116		100
C_6H_5	H	C_2H_5OH	20	25–30	80	Wide[a]	15	85
		C_6H_6	4	0	89	88–89	100	...
		C_2H_5OH	4	0, 25–30	64		100	
		CH_2Cl_2	4	0	84		100	

[a] See the Experimental Section.

TABLE II

REACTION OF RR'NH WITH $HC{\equiv}CCO_2C_2H_5$

R	R'	Solvent	Reacn time, hr	Temp, °C	Yield, %	Bp, °C (mm)	Configuration, % cis	Configuration, % trans
CH_3	CH_3	C_2H_5OH	3	0	74	90–91 (2.3), lit.[a] 97–98 (0.5)	..	100
		C_6H_6	3	0	71			100
C_2H_5	C_2H_5	C_2H_5OH	4	25–30	84	97–98 (1.3), lit.[b] 129–130 (18)		100
		C_6H_6	4	25–30	85			100
n-C_3H_7	H	C_2H_5OH	4	25–30	87	53–60 (2)	61	39
		C_6H_6	4	25–30	70	92–95 (5)	64	36[d]
t-C_4H_9	H	C_2H_5OH	4	25–30	84	90–92 (4)	88	12
		C_2H_5OH	4	25–30	81	81–86 (7), lit.[c] 89–95 (12)	54	46
		C_6H_6	4	25–30	80	89–93 (7), lit.[c] 98–103 (12)	10	90

[a] J. Decombe, *Ann. Chem.*, **18**, 108 (1932). [b] F. Straus and W. Voss, *Ber.*, **59B**, 1681 (1926). [c] See ref 3a. [d] Product isolated after distillation is pure *cis* compound.

TABLE III

REACTION OF RR'NH WITH $CH_3C{\equiv}CSO_2C_2H_5$

R	R'	Solvent	Reacn time, hr	Temp, °C	Yield, %	Mp or bp (mm), °C	Configuration, % cis	Configuration, % trans
C_2H_5	C_2H_5	C_2H_5OH	4	25–30	74	143–145 (0.5)	..	100
n-C_3H_7	H	C_2H_5OH	4	25–30	74	119–121 (0.4)	45	55
t-C_4H_9	H	C_2H_5OH	4	25–30	75	96–100	32	68
		C_2H_5OH	4	25–30	73	109–113 (0.4)	70	30
		C_6H_6	4	25–30	80	115–118 (0.3)	18	82

At the outset of this investigation it was of interest to determine what effect, if any, the solvent, the nature of the amine and the nature of the activating group might have on the stereochemistry of the reaction. The most dramatic effect was observed as the nature of the amine was varied. As can be seen from Table I, the reaction of ethylenimine with *p*-tolylsulfonylacetylene results in the formation of only *cis*-1-ethylenimino-2-(*p*-tolylsulfonyl)ethene regardless of the solvent employed. On the other hand, addition of such normal aliphatic amines as dimethylamine, diethylamine, methylamine, and *n*-propylamine to *p*-tolylsulfonylacetylene results in the formation of only the *trans*-aminovinyl *p*-tolyl sulfones. Furthermore, the reaction of this acetylenic sulfone with aniline results in a mixture of *cis* and *trans* products.

With ethyl propiolate and secondary amines (*i.e.*, dimethylamine and diethylamine) only *trans*-oriented adducts are obtained, regardless of the solvent employed. In contrast to these results, the reaction of ethylenimine with ethyl propiolate results in a mixture of ethyl *cis*- and *trans*-β-ethyleniminoacrylate and the relative amounts of the isomers depend upon the solvent employed. When the amine employed in these reactions with ethyl propiolate is a primary amine, a mixture of *cis*- and *trans*-aminovinyl products is formed. These results are summarized in Table II.

With the nonterminal acetylene, 1-ethylsulfonyl-1-propyne, ethylenimine, *n*-propylamine, and *t*-butylamine form mixtures of *cis* and *trans* adducts, but diethylamine results in exclusive *trans* product formation. These results are summarized in Table III.

The configurations and isomer distributions of all adducts are based on their nmr spectra. With those adducts containing both an α- and β-vinyl proton (*i.e.*, where the starting acetylene was a terminal one), the coupling constants for these protons (14 and 9 cps for the *trans* and *cis* configurations, respectively) were used as the basis for configurational assignments. Where the vinyl proton interactions were nonexistent (*i.e.*, starting with nonterminal acetylenes) differences in chemical shifts for various protons were used as the basis for assignment of configuration. For example, in the primary amine adducts from 1-ethylsulfonyl-1-propyne, the amino proton appears as a broad singlet at *ca.* δ 7.38 in the *cis* isomer (*cis*-amino and sulfone

groups). In the *trans* isomer the amino proton again appears as a broad singlet but with a much smaller chemical shift (see Table VI). The chemical shifts of the propenyl methyl protons as well as of the α-vinyl protons can also be used to assign configuration and provide supporting evidence for the configurational assignments based on the amino proton shift. This method also permits configurational assignments in the absence of amino protons. For example, a *cis* relationship between the methyl and sulfone groups is indicated by a corresponding larger chemical shift of the methyl protons (*ca.* δ 0.3 greater than in the *trans* arrangment of methyl and sulfone groups). Also, a *cis* relationship between the amino group and vinyl proton is indicated by a larger chemical shift of the vinyl proton (*ca.* δ 0.25–0.50 greater than with the *trans* arrangement of the amino group and the vinyl proton). It should be pointed out that these correlations are not without precedent since they have been observed either in the same or similar systems.[3b,5] The pertinent nuclear magnetic resonance (nmr) data for all products are summarized in Tables IV, V, and VI.

TABLE IV

NMR DATA FOR $RR'\overset{\beta}{N}CH=\overset{\alpha}{C}HSO_2Ar$

		α[a]		β[a]		J_{HH}[b]	
R	R′	*cis*	*trans*	*cis*	*trans*	*cis*	*trans*
CH_3	CH_3	...	4.9	...	7.3	..	14
C_2H_5	C_2H_5		4.9		7.3		14
n-C_3H_7	H		5.0		7.3		14
C_6H_5	H	5.0	5.7	7.7	7.3	9	14
CH_2(2)–CH_2–N		5.65	...	6.6	...	9	...

[a] Positions given in parts per million (δ) relative to tetramethylsilane (TMS). [b] Coupling constants given in cycles per second.

TABLE VII

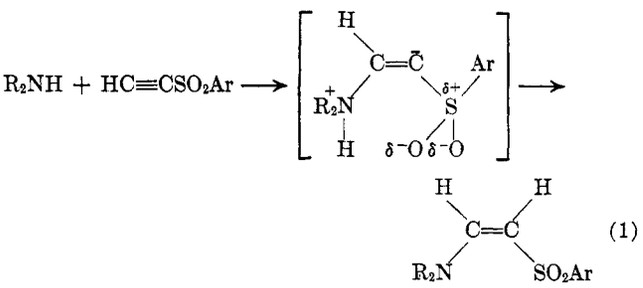
REACTION OF *n*-$C_3H_7NH_2$ WITH $RC{\equiv}CSO_2C_2H_5$[a]

	Yield,		Configuration,[b] %	
R	%	Bp, °C (mm)	*cis*	*trans*
H	40[c]	145–146 (0.3)	..	100
CH_3	74	119–121 (0.4)	45	55
C_2H_5	87	119–121 (0.2)	62	38

[a] All reactions were run in absolute ethanol solvent at room temperature for a period of 4 hr. [b] Based on arrangement of amino and ethylsulfonyl. [c] Adduct partially decomposed during distillation.

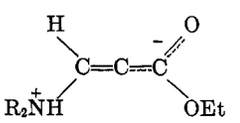
Discussion of Results

Undoubtedly additions of alkylamines and dialkylamines as well as ethylenimine to *p*-tolylsulfonylacetylene follow the same stereochemical path initially to give *trans* addition (*cis* product), whereas a mixture of *cis* and *trans* products (both *cis* and *trans* addition) is involved initially with ethyl propiolate. The stereospecific *trans* character of the addition to the sulfone can be explained on the basis of an electrostatic attraction (and/or attendant hydrogen-bonding forces) between the sulfonyl oxygen atoms and the positively charged nitrogen in the transition state (eq 1). Such



(1)

an attraction would favor a *cis* relationship between the amino and sulfone groupings and thus result in *trans* addition of the amine. Analogous attractions would be less pronounced with the acetylenic carboxylic ester since the unsaturated carbon atoms must remain colinear in order to have resonance stabilization of the incipient carbanion center as shown. On the other



hand, colinearity of the unsaturated carbons with a sulfone grouping need not be a prerequisite for carbanion stabilization.[6]

However, several results remain unexplained, *e.g.*, on the above basis alone all of the resulting aminovinyl

TABLE V

NMR DATA FOR $RR'\overset{\beta}{N}CH=\overset{\alpha}{C}HCO_2C_2H_5$

		α[a]		β[a]		NH[a]		J_{HH}[b]	
R	R′	*cis*	*trans*	*cis*	*trans*	*cis*	*trans*	*cis*	*trans*
CH_3	CH_3	...	4.50	...	7.40	...	...	..	14
C_2H_5	C_2H_5	...	4.55	...	7.40	...	...	..	14
n-C_3H_7	H	4.40	4.70	6.60	7.50	7.70	5.60	9	14
t-C_4H_9	H	4.50	4.80	6.80	7.50	8.0	5.30	9	14
CH_2(2)–CH_2–N		5.15	5.35	6.70	7.55	...	...	9	14

[a] Positions given in parts per million (δ) relative to TMS. [b] Coupling constants given in cycles per second.

TABLE VI

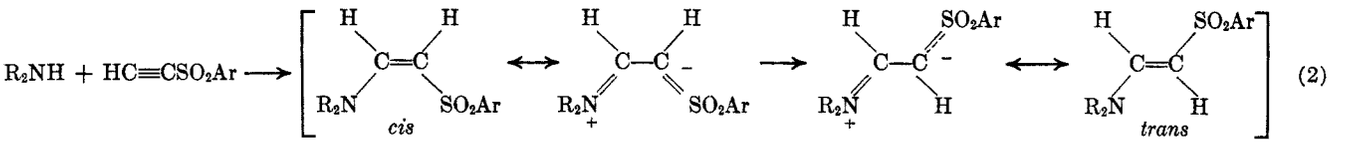
NMR DATA FOR $RR'N\overset{\beta}{C}H_3\diagdown\diagup\overset{\alpha}{C}=CHSO_2C_2H_5$[a]

		α		β		NH	
R	R′	*cis*	*trans*	*cis*	*trans*	*cis*	*trans*
C_2H_5	C_2H_5	...	4.70	...	2.30	...	...
n-C_3H_7	H	4.45	4.70	2.0	2.25	7.30	5.80
t-C_4H_9	H	4.30	4.90	2.05	2.20	7.40	4.55
CH_2(2)–CH_2–N		5.30	5.55	1.90	2.20	...	...

[a] Positions given in parts per million (δ) relative to TMS.

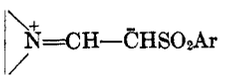
(5) V. M. Potapov, F. A. Trofimov, and A. P. Terent'ev, *Zh. Obshch. Khim.*, **33**, 853 (1963).

(6) D. J. Cram and A. S. Wingrove, *J. Am. Chem. Soc.*, **85**, 1100 (1963).

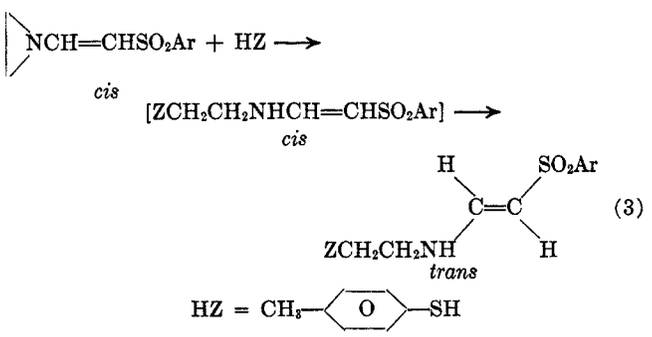


(2)

sulfones should have the *cis* configuration and all of the aminoacrylate esters should be mixtures of *cis* and *trans* isomers. As has been pointed out, only the ethylenimine–*p*-tolylsulfonylacetylene reaction results in exclusive *cis* product formation. Thus postisomerization with other aminovinyl sulfones appears likely. Such isomerization would be facilitated by an appreciable contribution from the immonium resonance form (eq 2). It should be noted here that initial formation of *cis* isomer followed by isomerization was in fact observed when such additions were effected at a low temperature under which conditions the subsequent isomerization could be followed *via* nmr determinations (discussed more fully in a later portion of this paper). It should also be pointed out that spontaneous room temperature *cis* to *trans* isomerization has been suggested, though not theoretically discussed, for aminovinyl ketones.[7-10] Such facilitation of isomerization would not be important in the ethylenimine adducts owing to excessive ring strain for the immonium structure. If ease of immonium struc-



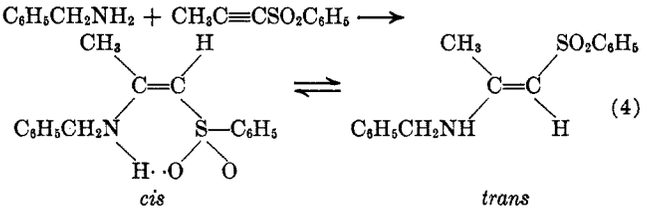
ture participation is indeed the basis for the ease of isomerization, it follows that any *cis*-ethylenimino adduct should readily isomerize once the ring is opened (eq 3). Accordingly, *cis*-1-ethylenimino-2-(*p*-tolylsulfonyl)ethene was treated with *p*-toluenethiol whereupon a high yield of *trans* ring-opened product was obtained. In a control experiment, using excess *cis*-1-ethylenimino-2-(*p*-tolylsulfonyl)ethene, the unconverted ethyleniminovinyl sulfone was shown by nmr to be only *partially* isomerized.



(3)

There are at least two types of factors by which the above resonance interaction (giving rise to rapid isomerization) can be minimized. One of these involves increased ring strain, as demonstrated by the ethylenimine adduct. The other involves steric inhibition of resonance. In an effort to observe the latter of these two effects, the sterically hindered amines, 2,6-dimethylpiperidine and diisopropylamine, were allowed to react with *p*-tolylsulfonylacetylene. However, both reactions afforded only *trans*-aminovinyl sulfone, indicating the need for further work with even more hindered amines, such as 2,6-di-*t*-butylpiperidine.

Recently it has been reported that the reaction of primary amines with the *nonterminal* acetylenic sulfone, 1-phenylsulfonyl-1-propyne, results in a mixture of *cis*- and *trans*-aminovinyl sulfones (eq 4).[3b] It was tentatively suggested that in this system the *cis* configuration (*cis*-amino and sulfone groups) is stabilized by hydrogen bonding between the amino proton and the sulfonyl oxygen atoms, thus permiting it to exist in equilibrium with the *trans* isomer. Since the adducts arising from the reactions of *n*-propylamine with the *terminal* acetylenic sulfones, *p*-tolylsulfonylacetylene, and ethylsulfonylacetylene, as well as the ring-opened product resulting from the reaction of *p*-toluenethiol with *cis*-1-ethylenimino-2-(*p*-tolylsulfonyl)ethene, have the *trans* configuration, such hydrogen-bonding forces are not of sufficient strength to allow the *cis* configuration to exist in these systems (where the starting acetylenic sulfone is terminal and the amine is a primary aliphatic amine). It was found that as the steric bulk of the substituent on the acetylenic sulfone is increased (see Table VII) a corresponding increase in the *cis* configuration was observed, suggesting that besides hydrogen bonding permitting the existence of *cis* isomer a bulky substituent can help shift the equilibrium. Also, preliminary results from the reactions of aromatic amines with *p*-tolylsulfonylacetylene indicate that mixtures of *cis* and *trans* isomers are formed, possibly owing to stronger hydrogen-bonding forces with the more acidic amino proton.



(4)

At first glance, the results from the reaction of ethylenimine with 1-ethylsulfonyl-1-propyne to form a mixture of *cis* and *trans* adducts seem to be inconsistent with some of the theories previously presented.[11] Since it has been shown that the ethylenimino adducts do not undergo *cis*-to-*trans* isomerization in the absence of thiol catalyst, *trans* compound can be accounted for *via* initial allene formation followed by amine addition (eq 5). Evidence for this isomerization–addition sequence has been presented in a recent publication by Stirling[3b] in which the reactions of N-deuteriodibenzylamine with 1-phenylsulfonyl-1-propyne and 1-phenylsulfonylpropadiene are described (eq 6). The 1-propenyl sulfone is no doubt favored over 2-propenyl sulfone owing to conjugative factors. The incorporation of deuterium in the methyl group suggests an allene intermediate in the 1-phenylsulfonyl-1-propyne reaction.

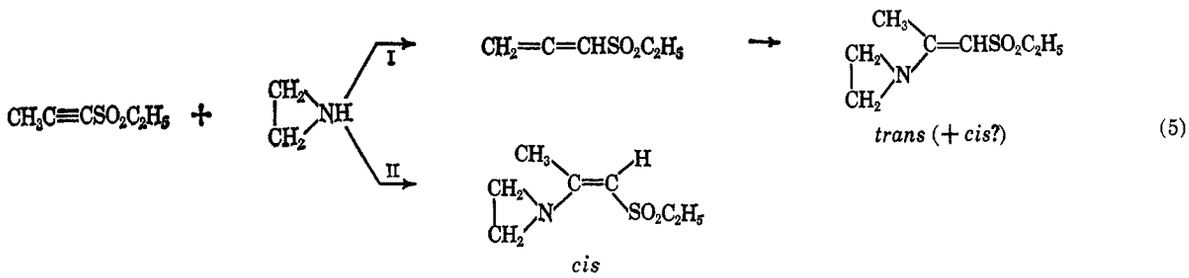
(7) J. Dabrowski, *Spectrochim. Acta*, **19**, 475 (1963).

(8) J. Dabrowski and J. Terpinski, *Bull. Acad. Polon. Sci. Classe* III, **9**, 779 (1961).

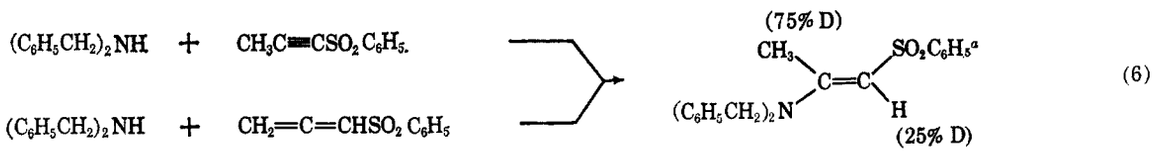
(9) A. N. Nesmeyanov, N. K. Kochetkov, and Ya. V. Dombrovskii, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 179 (1955).

(10) J. Dabrowski and J. Terpinski, *Tetrahedron Letters*, 1363 (1965).

(11) It has been postulated that amines add stereospecifically in a *trans* fashion to acetylenic sulfones owing to transition-state stabilization of the *cis* configuration.



(5)



(6)

[a] = Corrected per cent of incorporated deuterium.

However, it was desirable to prove unequivocally that the amine-catalyzed isomerization from acetylene to allene does indeed occur and furthermore that the isomerization occurs rapidly enough to compete with amine addition to the acetylene. Accordingly, the triethylamine-catalyzed isomerization of 1-ethylsulfonyl-1-propyne to ethylsulfonylpropadiene was followed by nmr. The isomerization was found to occur rapidly in chloroform solution at room temperature (for complete discussion of results see the Experimental Section).

The solvent effect observed in the reaction of ethylenimine with 1-ethylsulfonyl-1-propyne (*i.e.*, 70% *cis*, 30% *trans* in C_2H_5OH *vs.* 18% *cis*, 82% *trans* in C_6H_6) can be explained as follows. As has been observed in this laboratory and elsewhere, change in solvent from benzene to alcohol causes marked acceleration of the reactions of amines with acetylenes. Thus in ethanol solvent a higher yield of *cis* product arises from simple nucleophilic addition across the triple bond (process II) while in benzene solvent this process is sufficiently slow to allow allene formation to predominate and result in an increased yield of *trans* product (process I).

Facile *cis–trans* isomerization, as discussed previously, also accounts for exclusive *trans* product formation in the reaction of secondary aliphatic amines (excluding ethylenimine) with both ethyl propiolate and 1-ethylsulfonyl-1-propyne. However, in contrast to what was found with the *terminal* acetylenic sulfones, hydrogen bonding between the amino proton and the carbonyl oxygen (in the primary amine adducts from ethyl propiolate) is of sufficient strength to allow mixtures of *cis* and *trans* isomers to exist. In fact, preliminary isomerization results indicate that the *cis* configuration is the thermodynamically favored one.

The solvent effect in the reaction of ethylenimine with ethyl propiolate has been satisfactorily explained elsewhere[3a] and needs be reviewed only briefly. In nonprotic solvents, where the amine itself is the sole proton source, internal *cis* proton transfer predominates, resulting primarily in *trans* product formation (*cis* addition). In protic solvents proton transfer from solvent competes with the *cis* proton transfer process resulting in increased net *trans* addition of the amine.

In an effort to determine the kinetic product ratio in some of these systems, the following nmr studies were made. Equimolar amounts of amine and acetylenic compound, dissolved in a small amount of solvent, were placed in an nmr tube (see the Experimental Section) and the region for either the α- or β-vinyl proton (depending upon choice of solvent and acetylenic compound) was scanned at short time intervals. In the reaction of *t*-butylamine with ethyl propiolate in ethanol solvent the ratio of *cis*-to-*trans* product remained essentially constant indicating only slight *trans*-to-*cis* isomerization (time 4.00 min, 35% *trans*–65% *cis;* time 120 min, 32% *trans*–68% *cis*). When this same reaction was carried out in benzene solvent a higher per cent of *trans* isomer was observed initially with once again *trans*-to-*cis* isomerization occurring (time 26 min, 74% *trans*–26% *cis;* time 260 min, 33% *trans*–67% *cis*). The ratio of *cis*-to-*trans* isomers remained constant in the reaction of ethylenimine with ethyl propiolate in both benzene and ethanol solvent (benzene solvent, 92% *trans*–8% *cis;* ethanol solvent, 52% *trans*–48% *cis*). In the reaction of diethylamine with ethyl propiolate in ethanol solvent only *trans* proton signal (J_{HH} = 14 cps at δ 7.1) was observed initially. However, as the reaction progressed a weak *cis* proton signal was observed (J_{HH} = 9 cps at δ 5.9; maximum 14% at time 60 min) and then rapidly disappeared leaving only *trans* proton signal. The reaction of diethylamine with *p*-tolylsulfonylacetylene in benzene solvent at room temperature showed only *trans* proton signal even when the reaction solution was mixed thoroughly and immediately scanned. However, when the reaction of both diethylamine and *n*-propylamine with *p*-tolylsulfonylacetylene was carried out at −25° a strong *cis* proton signal (J_{HH} = 9 cps at δ 4.7 and 4.6 for the diethylamine and *n*-propylamine reactions, respectively) was observed initially. The appearance of this strong *cis* signal, in both cases, was accompanied by a weak *trans* signal (J_{HH} = 14 cps at δ 4.9 and 5.0 for the diethylamine and *n*-propylamine reactions, respectively) which gradually increased in intensity at the expense of the *cis* signal. As the reactions neared completion (as evidenced by the disappearance of the acetylenic proton signal at δ 3.7) the reaction tubes were rapidly warmed to room temperature and recooled to −25°. During this time the *cis*-to-*trans* isomerization was accelerated greatly. Finally, when the reaction tube was allowed to warm slowly to room temperature and allowed stand for 10 min the *cis* signal had completely disappeared and *did not* reappear upon cooling to −25°.

The diethylamine–ethyl propiolate as well as the *n*-propylamine– and diethylamine–*p*-tolylsulfonylacetylene reactions are of particular significance since they demonstrate that (a) with the ester and secondary amines *cis* and *trans* mixtures are formed (as postulated) and the *cis* compound rapidly isomerizes to the *trans* compound, and (b) with the sulfone, *cis* isomer is formed initially (as postulated) followed by rapid isomerization to the *trans* isomer at room temperature. It should also be pointed out that a solvent effect, as discussed for the ethylenimine–ethyl propiolate reaction, was observed in the *t*-butylamine–ethyl propiolate reaction.

In summary, it can be concluded that (a) amine additions to terminal acetylenic sulfones, owing to transition-state stabilization of the *cis* configuration, proceed stereospecifically in a *trans* manner to give *cis* adduct (in adducts where immonium-type resonance is likely, this stereospecific addition is followed by an extremely rapid isomerization to the more stable *trans* configuration); (b) amine additions to ethyl propiolate, owing to transition-state linearity of the unsaturated carbon π system, are nonstereospecific processes (with secondary amine adducts, where immonium-type resonance is likely, any *cis* isomer formed rapidly isomerizes to the more stable *trans* configuration; in the absence of this type of resonance, solvent-dependent mixtures of *cis* and *trans* isomers are formed; with primary amine adducts the *cis* configuration is preferred owing to hydrogen bonding); (c) amine additions to nonterminal acetylenic sulfones possessing a γ proton are complicated by allene formation.

Work is continuing in this laboratory on further elucidating the factors which control the stereochemistry of amine additions to acetylenes. Furthermore, adducts have been obtained from tertiary amines and acetylenes (*e.g.*, $Me_3N{\cdot}HCl + HC{\equiv}CCO_2Et \xrightarrow[CH_2Cl_2]{R_3N}$ *trans*-$Me_3\overset{+}{N}CH{=}CHCO_2Et\ Cl^-$), and will be reported on later. The possibility that such vinylammonium structures may be involved as intermediates in certain amine-catalyzed additions to acetylenes is also of interest.

Experimental Section[12]

Starting Materials.—Ethyl propiolate of high purity was obtained from the Aldrich Chemical Co. and was used without further purification. Ethylenimine was generously supplied by the Dow Chemical Co. and was stored over caustic soda pellets. Other amines used were either taken from freshly opened bottles of analytical reagent grade chemicals or distilled prior to use.

***p*-Tolylmercaptoacetylene.**—This compound was prepared according to the procedure of Parham and Stright[13] by treating *cis*-1,2-bis(*p*-tolylmercapto)ethene with *n*-butyllithium in ether solvent. It was found that a higher yield could be obtained by filtering off the lithium thiolate prior to hydrolysis of the reaction mixture. The product distilled at 80–82° (6 mm) [lit.[14] bp 77–79° (3 mm)] as a clear liquid but rapidly turned dark red. The product was isolated in 50% yield.

Ethylmercaptoacetylene.—This compound was prepared according to known procedures[15] by treating *cis*-1,2-bis(ethylmercapto)ethene with 2 equiv of sodium amide in liquid ammonia followed by addition of 1 equiv of methyl iodide. The clear liquid product was isolated in 31% yield and had bp 90–92° (lit.[15] bp 91.5–92°).

1-Ethylmercapto-1-propyne.—This compound was prepared by treating *cis*-1,2-bis(ethylmercapto)ethene with 2 equiv of sodium amide in liquid ammonia followed by addition of 2 equiv of methyl iodide according to known procedures.[16] The colorless product had bp 132–134° (lit.[16] bp 134–144°) and was isolated in 50% yield.

1-Ethylmercapto-1-butyne.—This compound was prepared by treating *cis*-1,2-bis(ethylmercapto)ethene with 2 equiv of sodium amide in liquid ammonia followed by addition of 2 equiv of ethyl bromide according to known procedures. The colorless product had bp 60–61° (25 mm), $n^{21}D$ 1.4885 [lit.[16] bp 52° (17 mm), $n^{20}D$ 1.4890] and was isolated in 68% yield.

Oxidation of Sulfides.—Oxidation of all acetylenic sulfides to the corresponding sulfones was effected by slowly adding a chloroform solution of *m*-chloroperbenzoic acid (twice as many moles as of sulfide) to a cold, stirred chloroform solution of the sulfide (90 ml of chloroform per 9 g of acid). After addition was complete the solution was allowed to stand at 0° for 1 day and then at room temperature for 1 day. The precipitated *m*-chlorobenzoic acid was removed by filtration and the filtrate was washed thoroughly with a saturated sodium bicarbonate solution containing a small amount of sodium sulfite. The chloroform layer was then dried over anhydrous magnesium sulfate. The excess solvent was removed *in vacuo* to leave the crude sulfone. Purification was effected either by recrystallization from chloroform–hexane or by vacuum distillation.

***p*-Tolylsulfonylacetylene.**—*p*-Tolylmercaptoacetylene (6.6 g, 0.0054 mole) was treated with 85% *m*-chloroperbenzoic acid (22.5 g, 0.110 mole of peracid) to give, after recrystallization, 6.8 g (70%) of sulfone isolated as white platelets, mp 73–74° (lit.[17] mp 74–75°).

Ethylsulfonylacetylene.—Ethylmercaptoacetylene (6.6 g, 0.077 mole) was treated with 85% *m*-chloroperbenzoic acid (32.5 g, 0.160 mole of peracid) to give, after distillation, 3.6 g (40%) of sulfone isolated as a colorless liquid, bp 46–48° (0.2 mm). The low yield is no doubt due to partial solubility of the sulfone in water.

1-Ethylsulfonyl-1-propyne.—1-Ethylmercapto-1-propyne (5.0 g, 0.05 mole) was treated with 85% *m*-chloroperbenzoic acid (26.5 g, 0.13 mole of peracid) to give, after distillation, 4.7 g (71%) of sulfone isolated as a clear liquid, bp 82–83° (0.4 mm), $n^{20}D$ 1.4765.

Anal. Calcd for $C_5H_8O_2S$: C, 45.43; H, 6.10; S, 24.26. Found: C, 45.42; H, 6.04; S, 24.00.

1-Ethylsulfonyl-1-butyne.—1-Ethylmercapto-1-butyne (5.0 g, 0.044 mole) was treated with 85% *m*-chloroperbenzoic acid (18.3 g, 0.090 mole of peracid) to give, after distillation, 5.7 g (89%) of sulfone isolated as a clear liquid, bp 87–88° (0.4 mm), $n^{20}D$ 1.4725.

Anal. Calcd for $C_6H_{10}O_2S$: C, 49.31; H, 6.90; S, 21.90. Found: C, 49.38; H, 6.83; S, 21.96.

***trans*-1-Dimethylamino-2-(*p*-tolylsulfonyl)ethene.**—A solution of 1.0 g (0.0055 mole) of *p*-tolylsulfonylacetylene in 100 ml of methylene chloride was placed in a 300-ml, three-necked flask equipped with a stirrer, Dry Ice condenser, and a piece of glass tubing extending to the bottom of the flask. The solution was cooled in a Dry Ice–acetone bath and 15 ml of dimethylamine was allowed to distil slowly into the stirred solution. After addition was complete the reaction solution was allowed to warm to room temperature over a period of 2 hr. The solvent was then removed *in vacuo* leaving a light yellow, solid residue. Purification was effected by recrystallization from an ethanol–pentane mixture to yield 0.90 g (73%) of pure *trans*-1-dimethylamino-2-(*p*-tolylsulfonyl)ethene, mp 134–135°.

Anal. Calcd for $C_{11}H_{15}NO_2S$: C, 58.63; H, 6.71; N, 6.22; S, 14.26. Found: C, 58.29; H, 6.47; N, 6.19; S, 14.07.

(12) All microanalytical analyses were carried out by C. S. Yeh and staff of the Purdue Chemistry Microanalytical Laboratory. Elemental analyses were obtained only in representative cases. The nmr spectra of other adducts leave no doubt that the structural assignments are correct. All nmr spectra were run on a Varian A-60 spectrometer operating at 60 Mc/sec using TMS as an internal standard. All melting points and boiling points are uncorrected. All infrared spectra were run on a Perkin-Elmer Model 137 B Infracord spectrophotometer. In all reactions the equipment was flamed out and all reactions were run in a nitrogen atmosphere. The nmr spectra of the adducts were taken on crude as well as on the purified products to preclude isomerization during purification steps.

(13) W. E. Parham and P. L. Stright, *J. Am. Chem. Soc.*, **78**, 4783 (1956).

(14) W. E. Truce, H. E. Hill, and M. M. Boudakian, *ibid.*, **78**, 2760 (1956).

(15) J. F. Arens and T. Doornbos, *Rec. Trav. Chim.*, **75**, 481 (1956).

(16) H. J. Boonstra and J. F. Arens, *ibid.*, **79**, 866 (1960).

(17) L. Maioli and G. Modena, *Ric. Sci.*, **29**, 1931 (1959).

cis-**1-Ethylenimino-2-(*p*-tolylsulfonyl)ethene.**—This compound was prepared by adding the amine slowly to a stirred solution of *p*-tolylsulfonylacetylene. The amount of amine used was varied from an equimolar amount to 5 moles of amine per 1 of the acetylene. The reaction temperatures were varied from 0° to room temperature. The solvents used were ethanol, methylene chloride, benzene, and dimethyl sulfoxide. Yields varied from 64 to 89%. The product was recrystallized from a benzene–hexane mixture, mp 88–89°. In all cases the nmr spectra were taken on the crude product to preclude possible isomerization during purification. In all cases only *cis* product was formed.

Anal. Calcd for $C_{11}H_{13}NO_2S$: C, 59.19; H, 5.87; N, 6.28; S, 14.34. Found: C, 59.50; H, 5.98; N, 6.48; S, 14.36.

Other Amine Additions to *p*-Tolylsulfonylacetylene.—All other amines were allowed to react with *p*-tolylsulfonylacetylene by slowly adding a solution of 1 equiv of the amine to a stirred solution of the sulfone under conditions given in Table I. Shorter reaction times (less than 20 hr) with aniline resulted in decreased yields. In the case where the amine was aniline two crops of crystals were isolated, one with mp 78–84° was shown by nmr to be a mixture of *cis* and *trans* isomers (65% *trans*, 35% *cis*) and the other with mp 145–150° was shown to be primarily *trans* isomer.

Anal. Calcd for $(C_2H_5)_2NCH{=}CHSO_2C_7H_7$ ($C_{13}H_{19}NO_2S$): C, 61.64; H, 7.56; N, 5.53; S, 12.63. Found: C, 61.72; H, 7.38; N, 5.69; S, 12.85.

trans-**1-(*n*-Propylamino)-2-ethylsulfonylethene.**—*n*-Propylamine (0.50 g, 0.0085 mole) was allowed to react with ethylsulfonylacetylene (1.0 g, 0.0085 mole) in ethanol solvent according to the general procedure given above. After 4 hr, evaporation of solvent at room temperature and distillation of the viscous residue gave 1.0 g (67%) of a clear, viscous liquid which was shown by nmr to be *trans* product, bp 144–145° (0.3 mm).

1-Ethylsulfonyl-2-(*n*-propylamino)-1-butene.—*n*-Propylamine (0.41 g, 0.0069 mole) was allowed to react with 1-ethylsulfonyl-1-butyne (1.0 g, 0.0069 mole) in ethanol solvent in the general manner. After 4 hr, evaporation of solvent at room temperature and distillation of the residue gave 1.23 g (87%) of pure, colorless product, bp 119–121° (0.2 mm). The nmr spectra both before and after distillation indicated that the product was a mixture of 64% *cis* (*cis* amino and sulfone groupings) and 36% *trans* isomers. In the *cis* isomer, the amino proton appears as a broad singlet at δ 7.05 and the α-vinyl proton as a sharp singlet at 4.3. In the *trans* isomer, the amino proton appears as a broad singlet at δ 5.3 and the α-vinyl proton as a sharp singlet at 4.55.

Anal. Calcd for $C_9H_{19}NO_2S$: C, 52.67; H, 9.33; N, 6.82; S, 15.58. Found: C, 52.56; H, 9.22; N, 6.80; S, 15.60.

Amine Additions to 1-Ethylsulfonyl-1-propyne.—All amine additions to 1-ethylsulfonyl-1-propyne were carried out by slowly adding a solution of 1 equiv of amine in 20 ml of solvent to a stirred solution of sulfone (1.50 g, 0.0114 mole in 25 ml of solvent) at room temperature. All reactions were run for a period of 4 hr. The solvent was removed *in vacuo* at room temperature and nmr spectra were taken on crude as well as on purified product. In all cases, except the *t*-butylamino adduct, the products were vacuum distilled. The *t*-butylamino adduct was recrystallized from an ethanol–hexane mixture.

Anal. Calcd for t-$C_4H_9NH(CH_3)C{=}CHSO_2C_2H_5$ ($C_9H_{19}NO_2S$): C, 52.66; H, 9.33; N, 6.82; S, 15.61. Found: C, 52.72; H, 9.26; N, 6.57; S, 15.37.

trans-**Ethyl β-Dimethylaminoacrylate.**—To a 100-ml, three-necked flask equipped with a stirrer, condenser, and an addition funnel was added a solution of 2.0 g (0.020 mole) of ethyl propiolate in 25 ml of absolute ethanol (benzene). To this cold (0°), stirred solution was added 3.0 g (0.067 mole) of dimethylamine. After addition was complete the solution was allowed to stir for 2.5 hr at 0° and the solvent was removed *in vacuo* to leave a clear, liquid residue. Distillation of this liquid gave 2.1 g (74%) of pure *trans*-ethyl β-dimethylaminoacrylate, bp 90–91° (2.3 mm).

Other Amine Additions to Ethyl Propiolate.—All other amine additions to ethyl propiolate were carried out by slowly adding a solution of 1 equiv of amine in 20 ml of solvent to a stirred solution of ethyl propiolate (2.0 g, 0.020 mole in 25 ml of solvent). All reactions were run at room temperature for 4 hr. The solvent was removed *in vacuo* at room temperature and nmr spectra were taken on crude product before distillation as well as on the pure products. All products were vacuum distilled and the *n*-propylamine and *t*-butylamine adducts underwent *trans*-to-*cis* isomerization during distillation.

Anal. Calcd for n-$C_3H_7NHCH{=}CHCO_2C_2H_5$ ($C_8H_{15}O_2N$): C, 61.12; H, 9.62; N, 8.91. Found: C, 60.86; H, 9.52; N, 9.23.

Anal. Calcd for t-$C_4H_9NHCH{=}CHCO_2C_2H_5$ ($C_9H_{17}O_2N$): C, 63.12; H, 10.01; N, 8.18. Found: C, 63.32; H, 10.00; N, 8.00.

Ring Opening of 1-Ethylenimino-2-(*p*-tolylsulfonyl)ethene with *p*-Toluenethiol.—To a 100-ml, round-bottom flask equipped with a magnetic stirrer was added a solution of 0.75 g (0.0034 mole) of 1-ethylenimino-2-(*p*-tolylsulfonyl)ethene in 50 ml of absolute ethanol. To this solution was added 0.40 g (0.0034 mole) of *p*-toluenethiol. The solution was allowed to stir at room temperature for 24 hr. At the end of this time the solvent was removed *in vacuo* to leave 1.10 g (96%) of a light yellow solid, mp 110–116°. After several recrystallizations from a benzene–hexane mixture 0.80 g (70%) of pure *trans*-1-[2-(*p*-tolylmercapto)]ethylamino-2-(*p*-tolylsulfonyl)ethene was obtained, mp 121–122°. The infrared spectrum of this compound exhibited an N–H band at 3300, olefinic band at 1610, and sulfone bands at 1260 and 1125 cm^{-1}. The nmr spectrum exhibits strong singlets at δ 2.3 and 2.4 (total relative area 6) for the six methyl protons, a multiplet at 3.0 (relative area 4) for the four methylene protons, a doublet at 5.0 (relative area 1.1, J_{HH} = 14 cps) for the α-vinyl proton, and a multiplet centered at 7.4 (relative area 9.4) for the eight aromatic protons and the β-vinyl proton.

Control Run on Ring Opening of *cis*-1-Ethylenimino-2-(*p*-tolylsulfonyl)ethene.—The same experimental procedure given above was followed using 0.30 g (0.0013 mole) of 1-ethylenimino-2-(*p*-tolylsulfonyl)ethene and 0.07 g (0.0006 mole) of *p*-toluenethiol. After 40 hr the solvent was removed *in vacuo* leaving a light yellow oil. The nmr spectrum of this oil exhibited three sets of α-vinyl proton signals, two *trans* (δ 5.0 and 5.85, J_{HH} = 14 cps), and one *cis* (δ 5.65, J_{HH} = 9 cps). The *trans* proton signal at δ 5.0 corresponds exactly with the signal for *trans*-ring-opened product. The α-proton signal at δ 5.65 and the β-proton signal at δ 6.6 correspond exactly to *cis*-1-ethylenimino-2-(*p*-tolylsulfonyl)ethene. This leaves only the signal at δ 5.85 unaccounted for and this has been assigned to *trans*-1-ethylenimino-2-(*p*-tolylsulfonyl)ethene. The amino proton signal appears at δ 6.2. From these data the starting material was shown to be 30% isomerized to *trans* compound.

Isomerization of 1-Ethylsulfonyl-1-propyne.—To an nmr tube was added a solution of 100 mg of 1-ethylsulfonyl-1-propyne in 0.5 ml of deuteriochloroform. To this solution was added a few drops of triethylamine. The solution was mixed thoroughly and the region from δ 5.0 to 7.0 was scanned at short time intervals. This region was chosen because it has been reported[18] that the allene proton signals in phenylsulfonylpropadiene appear at δ 5.46 (doublet) and 6.30 (triplet). After 1 min the doublet at δ 5.46 and triplet at 6.2 were clearly visible. These two signals gradually increased with time at the expense of the methyl proton (δ 2.1) signal of the acetylene. After 10 min the solution contained 38% allene and after 30 min the solution contained 65% allene.

Reactions of Amines with Ethyl Propiolate and *p*-Tolylsulfonylacetylene in Nmr Tubes.—In all ethyl propiolate reactions, 0.242 g (0.0025 mole) of ester was dissolved in 0.5 ml of solvent. To this solution was added an equimolar amount of amine. In ethanol solvent the region from δ 6.0 to 8.3 was scanned at short time intervals. In benzene solvent the region from δ 4.0 to 6.0 was scanned owing to the strong benzene proton signal in the β-vinyl proton region. The reactions were observed to be much more rapid in alcohol solvent.

In all *p*-tolylsulfonylacetylene reactions, 0.20 g (0.0011 mole) of sulfone and an equimolar amount of amine were used. The region from δ 4.0 to 6.5 was scanned.

The results of all of these reactions are discussed in detail in the Discussion Section of this paper.

Infrared Data.[19]—All terminal acetylenic sulfides and sulfones exhibit the characteristic strong acetylenic carbon–hydrogen stretch at 3300 cm^{-1} as well as a strong carbon–carbon triple bond stretch in the 2050- to 2200-cm^{-1} region. The nonterminal acetylenic sulfides exhibit a very weak carbon–carbon triple bond stretch at 2180 cm^{-1}. The corresponding sulfones, however, show a very strong band at *ca.* 2200 cm^{-1}. All the acetylenic sulfones display the characteristic strong sulfone absorption

(18) C. J. M. Stirling, *J. Chem. Soc.*, Supp I, 5856 (1964).

(19) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1962.

in the 1300- to 1350-cm^{-1} and 1140- to 1160-cm^{-1} regions. All aminovinyl sulfones exhibit, in addition to the characteristic sulfone bands which are shifted to slightly longer wavelengths, rather strong olefinic absorption in the 1570- to 1640-cm^{-1} region. All the aminoacrylate esters display a strong carbonyl absorption at *ca.* 1670 cm^{-1} in addition to strong olefinic absorption in the 1580- to 1590-cm^{-1} region.

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Organic Disulfides and Related Substances. XVIII. Synthesis and Disproportionation of 2-(Aryldithio)ethylamine Hydrochlorides[1a,b]

LAMAR FIELD, TIMOTHY F. PARSONS,[1c] AND D. E. PEARSON

Department of Chemistry of Vanderbilt University, Nashville, Tennessee 37203

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Synthesis was achieved of unsymmetrical disulfides of the structure p-$XC_6H_4SS(CH_2)_2NH_3^+Cl^-$, both to permit evaluation for protection against ionizing radiation and clarification of factors which influence disproportionation of this model class of unsymmetrical disulfides. Thermally induced disproportionation in water, where X = H in the unsymmetrical disulfide, was accelerated by strong acid, alkali, or a thiol, and was inhibited by dilute acid. Kinetics of the series showed first-order dependence on the unsymmetrical disulfide, with an activation energy of 22.6 kcal/mole. There was good correlation of rates with Hammett σ constants (ρ = 1.9). Steric effects were negligible in an *ortho*-substituted analog, and the order of increasing resistance to thermally induced disproportionation was $NO_2 \ll Cl < H < CH_3 \lesssim CH_3O \lesssim 2,4,6\text{-}(i\text{-}C_3H_7)_3$. Acrylamide was not polymerized during the disproportionation. Photochemically induced disproportionation resulted essentially in inversion of the order of resistance, and acrylamide then was polymerized. Evidently the thermal process is largely heterolytic and the photochemical one largely homolytic. The thermally less stable disulfides often were easier to purify than the thermally more stable ones, because of their greater resistance to the destructive effects of even diffuse light.

The chemistry of unsymmetrical disulfides is of interest and significance synthetically and mechanistically, as well as in areas such as biochemistry (*e.g.*, protein cross linking, denaturation), industrial chemistry (*e.g.*, vulcanization), and polymer chemistry (*e.g.*, initiation, chain transfer, polysulfide polymers).[2] Another basis of interest, that of antiradiation drugs, was outlined earlier for 2-(aryldithio)ethylamine derivatives of type **1**.[3]

$$p\text{-}XC_6H_4SS(CH_2)_2NH_3^+Cl^- \xrightarrow{\Delta \text{ or } h\nu} 0.5(XC_6H_4S)_2 + 0.5[Cl^-H_3N^+(CH_2)_2S]_2 \quad (1)$$

(**1**; $-Cl^-H_3N^+(CH_2)_2SO_2H$)

$$p\text{-}XC_6H_4SH + Cl^-H_3N^+(CH_2)_2SO_2S(CH_2)_2NH_3^+Cl^-$$

(**2**)

Unsymmetrical disulfides of structure **1** afford a valuable tool for studying disproportionation to the symmetrical disulfides (eq 1). When the reaction is performed in water, the symmetrical aryl disulfide is the only sparingly soluble component of the mixture, and the reaction can be followed by its isolation. Disproportionation ordinarily is reversible and leads to an equilibrium mixture. However, with disulfides like **1** (at least where X = H[1b]), sparing solubility of the aryl disulfide forces the reaction to completion with no indication of reversibility. Capitalizing on the easy isolation of the aryl disulfide, we previously qualitatively correlated resistance to disproportionation with various structural features.[1b,3-5] This paper clarifies in more detail the nature of the disproportionation and factors which can influence it, with disulfides of type **1** as models.

Synthesis of disulfides **3–7**, shown in Table I, was done much as described earlier (eq 1),[6] except that after reaction of the thiol with thiosulfonate **2** unreacted thiol was extracted, after which **1** was converted to its free base. Since some products could not be recrystallized (facile disproportionation) this method minimized presence of a symmetrical disulfide which might be formed by attack of excess thiol. After formation of the free base by neutralization, it was extracted and then reconverted to its hydrochloride. Except for analogous *ortho*-substituted compounds, where disproportionation also was a problem,[1b] unreacted thiol usually has not been removed before neutralization; its further reaction during work-up of reaction mixtures undoubtedly resulted previously in conversions generally higher than those of Table I.[7] 2-(2,4,6-Triisopropylphenyldithio)ethylamine hydrochloride (**8**) was prepared using mercaptoethylamine and the aromatic thiolsulfonate.[7]

Purity of products **3–8** resulted from retention of by-product sulfinic acid as its salt in the aqueous layer after neutralization and from retention of disproportionation products either in the organic layer (XArS-SArX), when it was treated with acid, or in the acid layer (cystamine dihydrochloride) from which the desired product precipitated. Evidence of purity was that **3–8** showed no haziness when dissolved in water, a method proved with **4** to reveal as little as 0.5%

(1) (a) This investigation was supported by the U. S. Army Medical Research and Development Command, Department of the Army, under Research Contract No. DA-49-193-MD-2030. Abstracted from part of the Ph.D. dissertation of T. F. P., Vanderbilt University, May 1964; (b) paper XVII: L. Field and H. K. Kim, *J. Med. Chem.*, **9**, 397 (1966); (c) DuPont Postgraduate Teaching Assistant, 1962–1963.

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