[CONTRIBUTION NO. 492 FROM THE CENTRAL RESEARCH DEPARTMENT, EXPERIMENTAL STATION, E. I. DU PONT DE NEMOURS & CO.]

The Radiation-induced Isomerization of N-Alkyl-N-vinylsulfonamides[1]

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RECEIVED AUGUST 26, 1958

A new reaction, the isomerization of N-alkyl-N-vinylsulfonamides to N-alkyl-2-sulfonylvinylamines, has been discovered. It occurs on exposure of N-alkyl-N-vinylsulfonamides to ionizing radiation. A radical-chain mechanism is postulated which involves an "addition–elimination" sequence in which both the added and eliminated moieties are $RSO_2\cdot$ radicals. A solid-state effect has been observed in a study of the isomerization of several N-alkyl-N-vinylsulfonamides. N-Methyl-N-vinylbenzenesulfonamide and N-methyl-N-vinyl-*p*-toluenesulfonamide undergo isomerization more readily in the crystalline state than in the liquid state. Conversely, crystalline N-methyl-N-α-styryl-*p*-toluenesulfonamide is apparently unaffected by radiation dosages which are sufficient to cause extensive isomerization of the liquid. The results are interpreted on the basis of the molecular geometry of the crystalline sulfonamides.

A new isomerization was discovered when N-alkyl-N-vinylsulfonamides were exposed to ionizing radiation. The sulfonamides were converted to 2-sulfonylvinylamines.

$$RSO_2N(R')-C(R'')=CH_2 \longrightarrow RSO_2CH=C(R'')NHR'$$

The reaction appears to take place intermolecularly by a radical-chain mechanism and is one of a very few cases noted in which isomerization proceeds by such a path. Recent investigations, by Wiberg and co-workers,[2] have indicated free-radical chain mechanisms for the intermolecular rearrangements of α-methoxystyrene to propiophenone and of 2-methoxypyridine to N-methylpyridone. Apparently the isomerization of 3,3,3-trichloro - 2 - bromopropene to 1,1,2 - trichloro - 3-bromo-1-propene also proceeds in this manner[3a] and similar mechanisms have been suggested for the rearrangement of methyl N-phenylformimidate to N-methylformanilide,[2] and of α-bromoacetoacetic esters to γ-bromoacetoacetic esters.[3b] The novel isomerization of N-bromosuccinimide to β-bromopropionyl isocyanate[4a,b] may possibly proceed intermolecularly by a radical-chain path.[4a]

The present reaction proceeds with both aryl and alkylsulfonamides, though in rather poorer yield with the latter. We have successfully rearranged compounds in which R is phenyl, *p*-tolyl, β-naphthyl, *n*-butyl or methyl; R′ is methyl or *n*-butyl; and R″ is hydrogen or phenyl. Yields varied from 5-10% with some alkylsulfonamides to 95% with N-methyl-N-α-styryl-*p*-toluenesulfonamide. Representative results are shown in Table I. Substitution on the terminal carbon atom of the vinyl group, as in N-methyl-N-β-styryl-*p*-toluenesulfonamide, prevents the rearrangement.

Proof of Structure of Reaction Product.—A sample of N-methyl-N-vinylbenzenesulfonamide exposed to electron irradiation gave a high yield of a crystalline product melting at 130-131°. This product was shown to be N-methyl-2-phenylsulfonylvinylamine (II) on the basis of elemental analysis and infrared, ultraviolet and proton magnetic resonance spectra as well as by identification of the fragments resulting from acid hydrolysis. Confirmation of the structure was obtained through the synthesis of II by an alternative scheme (Fig. 1).

TABLE I

THE ELECTRON-INDUCED ISOMERIZATION OF N-VINYLSULFONAMIDES

$RSO_2N(R')-C(R'')=CH_2$ R	R′	R″	Method[a]	Total dose, joules/g.	Isomerization, %	G-Value[b]
C_6H_5	CH_3	H	1	1460	72	26
p-MeC_6H_4-	CH_3	H	1	500	72	63
p-MeC_6H_4	*n*-C_4H_9	H	3	808	68	32
p-MeC_6H_4	CH_3	C_6H_5	2	88	94	350
β-$C_{10}H_7$	CH_3	H	3	1000	10	4
n-C_4H_9	CH_3	H	3	1345	7	3
CH_3	CH_3	H	3	625	5	6

[a] 1, The crystalline sulfonamide was placed in an ice-cooled dish and allowed to melt spontaneously during irradiation by the combined effects of heating from the electron beam and depression of the melting point by the product formed in the early stages of reaction; 2, the sample was melted and kept in a bath at 40–45° during irradiation; 3, the compound was a liquid; it was cooled in an ice-bath during irradiation. [b] G = molecules of product formed per 100 electron volts of energy absorbed.

The analysis and molecular weight data showed that the product was isomeric with N-methyl-N-vinylbenzenesulfonamide. The infrared spectrum showed bands at 3.0 μ for N–H, 3.25 μ for =C–H, 7.75 and 8.9 μ for sulfone SO_2, and 13.9 and 14.45 μ for a monosubstituted benzene ring. It reacted with phenyl isocyanate to give a substituted area. The ultraviolet spectrum showed strong absorption at 264 mμ (ε 14,900), consistent with the extended conjugation found in structure II.[5] Acid hydrolysis of the reaction product gave methylamine and phenylsulfonylacetaldehyde, isolated as the hydrochloride and the 2,4-dinitrophenylhydrazone (III), respectively. The structure of the dinitrophenylhydrazone was established by an independent synthesis. The conclusions from the degrada-

(1) This paper was presented at the 134th Meeting of the American Chemical Society in Chicago, Ill., September, 1958.

(2) K. B. Wiberg, T. M. Shryne and R. R. Kintner, THIS JOURNAL, **79**, 3160 (1957).

(3) (a) A. N. Nesmeynov, R. Kh. Friedlina and V. N. Kost, *Tetrahedron*, **1**, 241 (1957); (b) C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 304.

(4) (a) H. W. Johnson and D. E. Bublitz, THIS JOURNAL, **79**, 753 (1957); **80**, 3150 (1958); (b) J. C. Martin and P. D. Bartlett, *ibid.*, **79**, 2538 (1957).

(5) The strong bathocromic effect of adding an amino group to the terminal carbon of phenyl vinyl sulfone (λ_{max} 225 mμ, ε 13,000)[6] is not unlike that encountered in going from methyl vinyl ketone (λ_{max}^{EtOH} 210 mμ ε 6500) to propyl 2-diethylaminovinyl ketone (λ_{max}^{EtOH} 307 mμ, ε 28,000).

(6) C. C. Price and H. Morita, THIS JOURNAL, **75**, 4747 (1953).

(7) K. Bowden, E. A. Braude, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.*, 45 (1946).

tive work were confirmed by the synthesis of II from phenylsulfonylacetaldehyde and methylamine. Moreover, the melting point of our product (130–131°) is close to that (132–133°) reported by Montanari[8] for N-methyl-2-phenylsulfonylvinylamine (II) prepared by the condensation of methylamine with 2-phenylsulfonylvinyl chloride. Figure 1 summarizes the reactions involved in the structure proof.

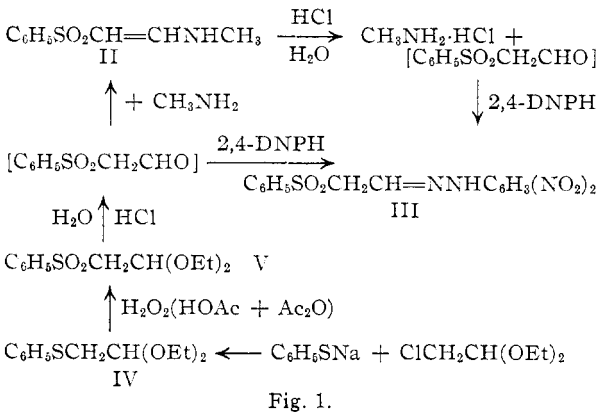
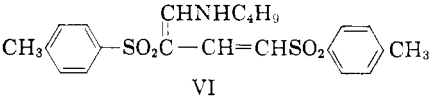


Fig. 1.

That the reaction of phenylsulfonylacetaldehyde with methylamine resulted in the formation of II rather than the isomeric imine, $C_6H_5SO_2CH_2CH{=}NCH_3$, that might be expected, is evident from the spectral data on the compound, in particular, the presence of strong N–H absorption in the infrared and the conjugation evinced by the ultraviolet absorption.

The products of isomerization of N-methyl-N-vinyl-*p*-toluenesulfonamide and N-methyl-N-α-styryl-*p*-toluenesulfonamide, *viz.*, N-methyl-2-*p*-tolylsulfonylvinylamine and N-methyl-2-*p*-tolylsulfonyl-α-styrylamine, were characterized in a manner similar to that just described. In certain other cases, the amines were not isolated, but were identified qualitatively by infrared and ultraviolet spectra of the reaction mixture and quantitatively by alkaline hydrolysis of the mixture and titration of the liberated amine. The N-vinylsulfonamides were stable to boiling 10% sodium hydroxide, while the 2-sulfonylvinylamines were quantitatively hydrolyzed to the corresponding aldehydes and amines.

The case of N-*n*-butyl-N-vinyl-*p*-toluenesulfonamide was unusual. The isomerization product could not be induced to crystallize from a mixture containing at least 70% of this material. However, the crude mixture on standing did slowly crystallize to give a fair yield of a new compound, N-[2,4-bis-(*p*-tolylsulfonyl)-1-butadienyl)]-*n*-butylamine (VI).



VI

Formation of this compound can be envisaged as due to slow hydrolysis of the N-butyl-2-*p*-tolylsulfonylvinylamine with aldol condensation of the resulting *p*-tolylsulfonylacetaldehyde and subsequent condensation of the aldol dehydration product with *n*-butylamine (the other hydrolysis product).

(8) F. Montanari, *Gazz. chim. ital.*, **86**, 415 (1956).

The Mechanism of the Isomerization.—The chain character of the isomerization is indicated by the high *G*-values[9] obtained in the experiments with electrons or X-rays (Tables I & II). G-Values in excess of 10 are seldom, if ever, observed with non-chain reactions. The reaction is inhibited by small amounts of triethylamine, 1,2-ethanedithiol, thiophenol, butyraldehyde or styrene. Pyridine and *p*-toluenesulfonic acid do not catalyze the rearrangement, suggesting that it is not an ionic reaction, which might be catalyzed by base or acid formed during irradiation. The rate of the reaction decreases with increasing dose rate; a plot of log of dose rate *versus* log of percentage rearrangement gives a curve similar to that found for the X-ray-induced polymerization of acrylonitrile,[10] a radical reaction in which bimolecular termination is important. Finally, it has been found that the isomerization can be brought about in the liquid phase or in solution by heating in the presence of azo initiators or peroxides. The chain nature of the reaction obviously rules out any intramolecular mechanism. However, the following mechanism, illustrated for the case of N-methyl-N-vinylbenzenesulfonamide, is in accord with all the experimental facts.

Initiation

$$\underset{\text{I}}{C_6H_5SO_2N(CH_3)CH{=}CH_2} \xrightarrow{w} R\cdot \qquad (1)$$

$$R\cdot + \text{I} \longrightarrow C_6H_5SO_2N(CH_3)\dot{C}H{-}CH_2R \qquad (2)$$

$$C_6H_5SO_2N(CH_3)\dot{C}HCH_2R \longrightarrow \underset{\text{VII}}{C_6H_5SO_2\cdot} + CH_2N{=}CHCH_2R \qquad (3)$$

Propagation

$$C_6H_5SO_2\cdot + \text{I} \longrightarrow \underset{\text{VIII}}{C_6H_5SO_2N(CH_3)\dot{C}HCH_2SO_2C_6H_5} \qquad (4)$$

$$\text{VIII} \longrightarrow C_6H_5SO_2\cdot + \underset{\text{IX}}{CH_3N{=}CH{-}CH_2SO_2C_6H_5} \qquad (5)$$

$$\text{IX} \xrightarrow{\text{H}^+} CH_3NHCH{=}CHSO_2C_6H_5$$

Termination probably occurs by combination of the radicals VII and VIII with themselves or with one another. The nature of the initiating radical(s) R· formed by irradiation of the vinylsulfonamide (step 1) is not known. It is probable, however, that irradiation causes the molecule to split at its weakest link, the S–N bond, giving rise to a phenylsulfonyl radical and a methylvinylamino radical.

Consideration of steps 4 and 5 shows that the isomerization of the N-vinylsulfonamide to the 2-sulfonylvinylamine (or its aldimine precursor IX) comes about as the result of an "addition–elimination sequence" wherein the added and eliminated moieties are identical. The breakdown of an intermediate radical to give an unsaturated molecule and a new radical (step 5) is a well-known reaction.[11] On the other hand, isomerizations result-

(9) G-Value is defined as the number of molecules of product formed per 100 electron volts of energy absorbed.

(10) I. A. Bernstein, E. C. Farmer, W. G. Rothschild and F. S. Spalding, *J. Chem. Phys.*, **21**, 1303 (1953).

(11) L. Schmerling and J. P. West, THIS JOURNAL, **71**, 2015 (1949); K. E. Wilzbach, F. R. Mayo and R. VanMeter, *ibid.*, **70**, 4069 (1948);

TABLE II

THE EFFECT OF STATE ON THE X-RAY INDUCED REARRANGEMENT OF SOME N-VINYLSULFONAMIDES

Compound	State	Temp., °C.	Dose rate, rads/min.	Total dose, rads × 10^{-5}	Rearrangement,[a] %	G-Value
$C_6H_5SO_2N(CH_3)CH{=}CH_2$	Crystalline	−196	7200	4.3	4	450
	Crystalline	−75	7400	3.7	7	900
	Glass	−75	7200	5.0	0	0
	Crystalline	0	6600	0.66	7	5200
	Crystalline	24	7000	.70	7	4900
	Crystalline	25	6600	.99	10	4900
	Supercooled liquid	23	7900	4.7	9	900
	Supercooled liquid	30	7400	8.9	8	450
	Liquid	38	7400	13	3	110
	Liquid	41	7400	8.1	1	60
	Liquid	40	7900	4.7	0	0
p-$CH_3C_6H_4SO_2N(CH_3)CH{=}CH_2$	Crystalline	−75	7400	6.7	7	500
	Crystalline	25	5900	4.5	13	1300
	Crystalline	25	5800	2.3	9	1800
	Crystalline	25	5400	0.54	2	1700
	Supercooled liquid	52	7900	2.4	4	750
	Liquid	62	7900	2.4	4	750
	Liquid	70	7400	4.4	5	500
p-$CH_3C_6H_4SO_2N(CH_3)C(C_6H_5){=}CH_2$	Crystalline	0–10	7000	5.0	0	0
	Crystalline	50	7000	1.0	0	0
	Crystalline	0–10	10^7 (β)	300	0	0
	Supercooled liquid	40–45	7000	0.90	48	18,000
	Supercooled liquid	40–45	4×10^7 (β)	88	94	350

[a] The extent of rearrangement, determined by –NH intensity in the infrared, is accurate only to about 1%. Zero rearrangement therefore means that –NH absorption was not detectable, indicating less than 0.5% rearrangement. The *G*-values shown are correspondingly approximate.

ing from addition–elimination sequences comparable to 4 and 5 have been noted previously in only a few cases.[1,2]

Isomerization of the aldimine IX to the arylsulfonylvinylamine II appears to take place rapidly, and IX has never been detected in the reaction product. The fact that the reaction of phenylsulfonylacetaldehyde with methylamine gives II rather than IX is strong support for the ready occurrence of this hydrogen shift.

Effect of State.—The extent of the radiation-induced isomerization of certain vinylsulfonamides has been found to depend markedly on the state of the compound. Thus, N-methyl-N-vinylbenzenesulfonamide and N-methyl-N-vinyl-*p*-toluenesulfonamide are isomerized more efficiently (higher *G*-values, indicating greater chain lengths) in the crystalline state than in the liquid state. On the other hand, crystalline N-methyl-N-α-styryl-*p*-toluenesulfonamide is not detectably altered by a dose of irradiation sufficient to cause extensive isomerization of the compound in the liquid state. Table II shows representative data for the effect of state on the rearrangement of these three compounds. The extent of rearrangement was determined by infrared measurement of the –NH absorption in the irradiated samples, or by basic hydrolysis of the sample and titration of the methylamine produced. Dose rates for X-ray irradiation were estimated by ferrous sulfate dosimetry, but are considered accurate only to within 10–15%. They are, however, self-consistent.

There are few precedents in the literature for this remarkable solid-state effect. Hexamethylcyclotrisiloxane is reported to undergo electron-induced polymerization rapidly and in high *G*-value at temperatures below its melting point; at higher temperatures the polymerization is slow.[12] Willard has recently reported solid-state effects in the γ-ray irradiation of alkyl iodides; at −190°, the *G*-value for iodine production was found to be higher in the glassy state than in the crystalline state for both ethyl iodide and isobutyl iodide.[13] At moderate temperatures, crystalline choline chloride is decomposed to acetaldehyde and trimethylammonium chloride in high *G*-value by ionizing radiation, and certain wide variations in its radiation sensitivity with temperature have been correlated with changes in the crystal structure of

M. S. Kharasch and M. Sage, *J. Org. Chem.*, **14**, 79 (1949); D. M. Oldroyd, G. S. Fisher and L. A. Goldblatt, THIS JOURNAL, **72**, 2407 (1950); J. N. Pitts, R. S. Tolberg and T. W. Martin, *ibid.*, **76**, 2844 (1954); N. Grassie and H. W. Melville, *Proc. Roy. Soc.* (*London*), **199A**, 14 (1949).

(12) E. J. Lawton, W. T. Grubb and J. S. Balwit, *J. Polymer Sci.*, **19**, 455 (1956).

(13) E. O. Hornig and J. E. Willard, THIS JOURNAL, **79**, 2429 (1957); *J. Phys. Chem.*, **62**, 9 (1958).

TABLE III

PHYSICAL PROPERTIES OF N-VINYLSULFONAMIDES

Compound, sulfonamide	M.p., °C.	B.p. °C.	Mm.	Yield, %	$n^{25}D$	λ_{max}^{EtOH} mμ	ε	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
N-Methyl-N-vinylbenzene-	34–35	118	2	67	1.5473	242	6100	54.82	55.00	5.62	5.71	7.10	7.80
N-Methyl-N-vinyl-*p*-toluene-	56–56.5	120–123	3	45	....	240	8300	56.86	57.39	6.20	6.16	6.63	6.92
N-Butyl-N-vinyl-*p*-toluene-	...	120–130	0.1	43	1.5280	242	7340	61.64	61.42	7.56	7.65	5.53	5.91
N-Methyl-N-vinylbutane-	...	100	2	83	1.4691	[a]		47.44	48.13	8.53	8.74	7.91	8.00
N-Methyl-N-vinylmethane-	...	39	0.5	55[b]	1.4705	[a]		35.55	36.66	6.71	6.92	10.37	9.74
N-Methyl-N-α-styryl-*p*-toluene-	82–83			8	....	235	18,300	66.88	66.95	5.96	6.25		
N-Methyl-N-vinyl-β-naphthalene-	...	150–160	0.05	20	....	226	33,500	63.15	63.36	5.30	5.37	5.67	5.95
N-Methyl-N-β-styryl-*p*-toluene-	(a) 106–107			1	....	220	20,400	66.88	66.08	5.96	6.15	4.88	4.92
				5	....	279	18,600						
	(b) 55–57				....	261	15,200	66.88	67.31	5.96	6.04	4.88	4.87

[a] Showed no absorption maximum above 210 mμ. [b] In this case, it was necessary to reduce the period of heating from 10–12 hours to 2–3 hours in order to prevent excessive tar formation and resultant low yield of product.

TABLE IV

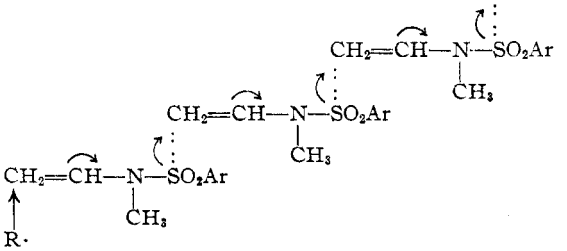
PHYSICAL PROPERTIES OF 2-SULFONYLVINYLAMINES

Compound, amine	M.p., °C.	$\lambda_{max}^{Ethanol}$, mμ (ε)	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
N-Methyl-2-phenylsulfonylvinyl-	130–131	214 (13,200), 264 (14,900)	54.82	54.73	5.62	5.57		
N-Methyl-2-*p*-tolylsulfonylvinyl-	122–123	220 (16,600), 264 (17,500)	56.86	57.03	6.20	6.23	6.63	6.65
N-Butyl-2*p*-tolylsulfonylvinyl-	[a]	222 (19,000),[b] 267 (16,300)[b]						
N-Methyl-β-*p*-tolylsulfonyl-α-styryl-	105–106	221 (18,300), 275 (13,700)	66.88	67.03	5.96	6.33		
N-Methyl-2-β-naphthylsulfonylvinyl-	134–136	223 (75,000), 267 (19,000)	63.15	62.52	5.30	5.38	5.67	5.77

[a] Did not crystallize, compound not isolated. [b] Figure obtained by extrapolation of *k* from a mixture containing 70% amine.

the compound.[14] Finally, it has been observed that some monomers are readily polymerized in the crystalline state on irradiation, while others are quite inert.[15]

It is probable that radical-chain reactions proceed in the crystalline state as a result of an orientation of the molecules which permits propagation of the chain with little or no translational motion of the intermediate radicals. We suggest that the isomerizations of crystalline N-methyl-N-vinylbenzenesulfonamide and N-methyl-N-vinyl-*p*-toluenesulfonamide are associated with just such a favorable orientation of molecules in the crystal. For instance, if the sulfone group of one molecule is adjacent to the terminal carbon of the vinyl group of another, the rearrangement, once initiated, might proceed by way of the chain mechanism proposed above with only a shift of electrons accompanied by little or no displacement of atoms. This can be represented by the scheme



On this basis, the failure of N-methyl-N-α-styryl-*p*-toluenesulfonamide to rearrange in the crystalline state is due to a spatial configuration inappropriate for chain propagation. The difference in the efficiency of rearrangement of glassy and crystalline N-methyl-N-vinylbenzenesulfonamide at −75° may be due to a random orientation of the "frozen-out" molecules in the glassy state. It is more difficult to explain the apparent greater efficiency of rearrangement of the liquid sulfonamide at temperatures just below its melting point (m.p. 34–35°) than at temperatures slightly above it. A possibility is that in the supercooled liquid the molecules are in part lined up as in the crystal.

Experimental

Synthesis of N-Vinylsulfonamides.—Most of the N-alkyl-N-vinylsulfonamides used in the study were prepared by direct vinylation of the parent N-alkylsulfonamides with an acetylene, following the procedure of Cairns and Sauer.[16] The preparation of N-methyl-N-β-styryl-*p*-toluenesulfonamide by this procedure is described below. Attempts to prepare N-methyl-N-vinyl-β-naphthalenesulfonamide by this procedure gave a product which was difficult to purify, so an alternative procedure, described below, was used. Likewise, an indirect method was necessary for the preparation of N-methyl-N-α-styryl-*p*-toluenesulfonamide. Physical constants and analytical data for the vinylsulfonamides are listed in Table III. Table IV gives data for sulfonylvinylamines.

***sis*- and *trans*-N-Methyl-N-β-styryl-*p*-toluenesulfonamide.**—Following the usual procedure for ethynylation of sulfonamides,[16] a mixture of N-methyl-*p*-toluenesulfonamide (122 g., 0.7 mole), phenylacetylene (70 g., 0.7 mole), potassium hydroxide (8 g.) and water (300 ml.) was shaken in a pressure vessel at 180° for 5 hours. The organic material was taken up in benzene, and the extract washed with aqueous potassium hydroxide, dried and distilled through a short column. Two fractions were studied further; I, 21 g., b.p. 168–172° (1 mm.); and II, 4 g., b.p. 172–180° (1 mm.). Both were viscous oils that partially crystallized on standing several days.

Fraction II was recrystallized from 95% ethanol to give 1.7 g. (0.9% yield) of N-methyl-N-β-styryl-*p*-toluenesulfonamide, m.p. 101–103°. Further recrystallization raised its melting point to 106–107°.

Fraction I was recrystallized from methanol to give 9.8 g. (5% yield) of an isomeric N-methyl-N-β-styryl-*p*-toluenesulfonamide, m.p. 55–57°. Two recrystallizations from methanol failed to raise the melting point.

The two compounds had the same composition (Table III). That they are isomers rather than isomorphs was

(14) R. M. Lemmon, M. A. Parsons and D. Chin, THIS JOURNAL, **77**, 4139 (1955); **80**, 2730 (1958); R. L. Collins, *ibid.*, **79**, 6086 (1957).

(15) A. J. Restaino, *et al.*, *ibid.*, **78**, 2939 (1956).

(16) T. L. Cairns and J. C. Sauer, *J. Org. Chem.*, **20**, 627 (1955).

indicated by seeding experiments. Moreover, the infrared spectra, which were consistent with the assigned structure and were very similar at short wave lengths, showed small but significant differences at long wave lengths. That an N-β-styryl group was present in both isomers was shown by refluxing 144 mg. of either one with 99 mg. of 2,4-dinitrophenylhydrazine and 0.25 ml. of 12 *N* hydrochloric acid in 10 ml. of 95% ethanol for 10 minutes. In each case, cooling caused precipitation of an 85–88% yield of phenylacetaldehyde 2,4-dinitrophenylhydrazone, identified by comparison of its melting point (melting point of a mixture showed no depression) and infrared spectrum with those of an authentic sample. The compounds are probably *cis–trans* isomers.

N-Methyl-N-α-styryl-*p*-toluenesulfonamide.—β-Phenyl-β-N-methylaminoethanol (m.p. 42°) was synthesized in 29% over-all yield by an adaptation of the procedure of Steiger[17] for the synthesis of ethyl 1-amino-1-phenylacetate, followed by lithium aluminum hydride reduction of the ester. To a solution of the β-phenyl-β-N-methylaminoethanol (15 g., 0.1 mole) in 125 ml. of anhydrous pyridine was added slowly a solution of *p*-toluenesulfonyl chloride (57 g., 0.3 mole) in 150 ml. of pyridine, while maintaining the temperature of the mixture at 40–45°. Addition required about one hour, and the mixture was then allowed to stand overnight at room temperature. It was poured into a mixture of hydrochloric acid and ice and extracted with benzene. Evaporation of the dried benzene extracts gave 22 g. (32% yield) of the ditosylate, which melted at 103–104° after recrystallization from absolute ethanol.

Anal. Calcd. for $C_{23}H_{25}S_2O_5N$: C, 60.12; H, 5.48; N, 3.05. Found: C, 59.85; H, 5.34; N, 3.16.

The ditosylate (17.5 g.) was refluxed for 2.5 hours with 75 ml. of alcoholic potassium hydroxide. After cooling, the solid mass was slurried with 125 ml. of water and the N-methyl-N-α-styryl-*p*-toluenesulfonamide filtered off. Recrystallization from ethyl alcohol gave 8.3 g. (75% yield) of product melting at 82–83° (Table III). The structure of the product was confirmed by its ultraviolet and infrared spectra, and by its acidic hydrolysis to acetophenone, the dinitrophenylhydrazone of which was isolated. After recrystallization from ethanol–benzene, it melted at 239–240°. A mixture with an authentic sample (m.p. 239–240°) melted at 239–240°.

N-Methyl-N-vinyl-β-naphthalenesulfonamide.[18]—A solution of N-methyl-β-naphthalenesulfonamide (67.5 g., 0.3 mole) in 100 ml. of pyridine was cooled in an ice-bath while ethylene oxide (26 g., 0.6 mole) was added. The mixture was extracted with chloroform. The crude product obtained on evaporation of the dried chloroform solution was recrystallized from chloroform–petroleum ether to give 40 g. (49% yield), of N-methyl-N-2-hydroxyethyl-β-naphthalenesulfonamide (m.p. 58.5–62°). Treatment with *p*-toluenesulfonyl chloride as described above gave the tosyl ester in 66% yield, m.p. 87.5–88.5°.

Anal. Calcd. for $C_{20}H_{21}NO_5S_2$: C, 57.26; H, 5.04. Found: C, 57.92; H, 5.13.

A solution of the tosylate (10 g.) in 50 ml. of 10% alcoholic potassium hydroxide was refluxed for 2 hours, diluted with 50 ml. of water, and extracted with ether. Evaporation of the dried ether extracts gave a viscous pale-yellow oil (5.5 g.) that was distilled through a short column. The fraction (3.3 g., 58% yield) boiling at 150–160° (0.05 mm.) was collected and found to be essentially pure N-methyl-N-vinyl-β-naphthalenesulfonamide (Table III).

Hydrolysis of N-Methyl-2-phenylsulfonylvinylamine.—The sulfonylvinylamines were susceptible to acid hydrolysis even at room temperature. A 0.50-g. sample of N-methyl-2-phenylsulfonylvinylamine was shaken with 130 ml. of a saturated solution of 2,4-dinitrophenylhydrazine in 2 *N* HCl at room temperature for 3 hours. The copious yellow precipitate that formed was filtered off and washed with water. After drying in vacuum, it weighed 0.80 g. and melted at 172–175° (m.p. varied with rate of heating). Its infrared spectrum was identical with that of authentic sample of phenylsulfonylacetaldehyde 2,4-dinitrophenylhydrazone.

Anal. Calcd. for $C_{14}H_{12}O_6N_4S$: C, 46.15; H, 3.30; S, 8.79; N, 15.38. Found: C, 45.91; H, 3.41; S, 8.60; N, 15.34.

Another sample of N-methyl-2-phenylsulfonylvinylamine was warmed in 2 *N* hydrochloric acid for 3 hours. Insoluble organic material was removed by ether extraction, and the aqueous layer was evaporated to dryness to give a quantitative yield of methylamine hydrochloride, m.p. 227–228°. It was identified by its infrared spectrum.

Synthesis of N-Methyl-2-phenylsulfonylvinylamine.—Phenylmercaptoacetaldehyde diethyl acetal (IV) was prepared in 60% yield by refluxing equimolar amounts of chloroacetal and sodium phenylmercaptide in absolute ethanol.[19] The product boiled at 93° (2 mm.), $n^{25}D$ 1.5198. Oxidation of IV to phenylsulfonylacetaldehyde diethyl acetal (V) was carried out according to the procedure of Pomerantz and Conner.[20] To a stirred solution of IV (30 g.) in a mixture of acetic acid (67 ml.) and acetic anhydride (67 ml.) cooled to 0–5° was added dropwise 36 ml. of 30% hydrogen peroxide over a period of 30 minutes. The mixture was allowed to come slowly to room temperature and stand for 3 days. It was heated to 40–50° for 2 hours, and the solvent was then removed by vacuum distillation at a flask temperature not in excess of 50°. The product, a pale yellow, viscous oil (26.5 g., $n^{25}D$ 1.5512) could not be distilled without decomposition. Infrared analysis showed a strong sulfone band at 7.9 mμ and indicated that the product was principally the desired acetal. A portion (258 mg.) of the product was refluxed for 12 hours with 198 mg. of 2,4-dinitrophenylhydrazine and 2.5 ml. of hydrochloric acid in 30 ml. of 95% ethanol. Phenylsulfonylacetaldehyde 2,4-dinitrophenylhydrazone precipitated on cooling (335 mg., 92% yield). After recrystallization from 25 ml. of benzene, it melted at 172–175°.

A solution of the phenylsulfonylacetaldehyde diethyl acetal (25 g.) in 300 ml. of 65% ethanol with 35 ml. of 12 *N* hydrochloric acid was refluxed for 24 hours. The solvent was evaporated in vacuum and the residue taken up in ether. At this point, washing the ether with water to remove traces of acid resulted in loss of a large amount of the aldehyde due to an unfavorable solubility coefficient between water and ether. As a result, evaporation of the dried ether layer gave only 13 g. of oil, assaying 23% aldehyde. The remainder was unhydrolyzed acetal.

Methylamine was bubbled through a solution of this mixture in 50 ml. of 95% EtOH, at 15–20° for one hour, and the solution then allowed to stand at room temperature for 4 days. Vacuum evaporation left a viscous yellow oil which partly crystallized on standing. Ethyl acetate was added, and the white crystalline N-methyl-2-phenylsulfonylvinylamine (0.9 g., 27% yield) was filtered off. The product melted at 131.5–132.5° and was identical in every respect with the product of isomerization of N-methyl-N-vinylbenzenesulfonamide.

1-Phenyl-3-methyl-3-(2-phenylsulfonylvinyl)-urea.—A mixture of N-methyl-2-phenylsulfonylvinylamine (3.5 g.) and phenyl isocyanate (2.2 g.) in 45 ml. of benzene was refluxed for 1.5 hours. On cooling, crystals separated (3.8 g.) which were virtually insoluble in benzene, ethyl acetate or ethyl alcohol, m.p. 145–148°. Infrared and analytical data indicated that the product was 1-phenyl-3-methyl-3-β-phenylsulfonylvinylurea.

Anal. Calcd. for $C_{15}H_{16}O_3SN_2$: C, 60.75; H, 5.10; N, 8.86. Found: C, 61.30; H, 5.51; N, 8.92.

Electron Irradiations.—The source of electrons was a 2-Mev. Van de Graaff accelerator, operating at a beam current of 250 microamperes. Samples were placed in glass or aluminum dishes covered by Mylar polyester film. The dishes were swept with nitrogen prior to irradiation. The samples were passed back and forth through the electron beam at such a rate that the incident radiation corresponded to 11 watt-sec. per cm.^{2} per pass. With one-minute intervals between passes, overheating of the samples was not serious, even in the absence of external cooling.

X-Ray Irradiations.—X-Ray irradiations were carried out by placing 1-g. samples of the sulfonamide in a Mylar covered glass vessel 9.5 cm. high and 2.2 cm. in diameter at the bottom. The vessel was half-immersed in a bath of the desired temperature, and centered beneath the X-ray target of the Van de Graaff accelerator. The distance from the target to the sample was 10 cm. The dose rate was estimated by ferrous sulfate dosimetry in a like vessel. The degree of isomerization of the samples was determined by

(17) R. E. Steiger, *Org. Syntheses*, **22**, 23 (1942).

(18) Dr. K. L. Howe synthesized several of the intermediates.

(19) W. Autenrieth, *Ber.*, **24**, 161 (1891).

(20) A. Pomerantz and R. Connor, THIS JOURNAL, **61**, 3386 (1939).

infrared analysis, based on the intensity of the N–H band at 2.9 μ.

Irradiation of N-Methyl-N-vinylbenzenesulfonamide.—Crystalline N-methyl-N-vinylbenzenesulfonamide (40 g.) was placed in a crystallizing dish 117 cm.^{2} in cross section. The dish was covered with 0.25 mil. Mylar polyester film and set in an ice-bath. It was passed through a beam of 2-Mev. electrons 60 times, the incident irradiation amounting to about 11 watt-sec./cm.^{2}/pass. The total absorbed dose amounted to 7.7×10^4 watt-sec. The product, a mixture of gum and crystals, was crystallized from 40 ml. of ethyl acetate to give 15.8 g. (40% conversion, $G = 24$) of N-methyl-2-phenylsulfonylvinylamine (m.p. 130–131°).

Irradiation of *cis*- and *trans*-N-Methyl-N-β-styryl-*p*-toluenesulfonamide.—Thin samples of each isomer were exposed to 440 watt-sec./cm.^{2} of 2-Mev. electrons. There was no evidence of isomerization to a sulfonylvinylamine in either case, the infrared spectra of the irradiated samples showing no absorption band in the N–H region. However, the irradiation isomerized about 20% of the low-melting isomer to the high-melting isomer, which was isolated by fractional crystallization.

Irradiation of N-Butyl-N-vinyl-*p*-toluenesulfonamide.—A sample of N-butyl-N-vinyl-*p*-toluenesulfonamide (1.0 g.) was placed in a Beckman cup 3.14 cm.^{2} in cross section. The cup was set in an aluminum dish that was covered with 0.25 mil Mylar film and swept out with nitrogen. The dish was placed in an ice-bath and exposed to 660 watt-sec./cm.^{2} of 2-Mev. electrons. The product, a brown viscous oil, was taken up in ethyl acetate. It did not crystallize on standing in the cold for several days. Attempts to isolate the product by vacuum distillation or sublimation were unsuccessful due to its instability at high temperatures. Infrared and ultraviolet spectra of the crude product indicated the presence of N-butyl-2-*p*-tolylsulfonylvinylamine. Alkaline hydrolysis showed that the product contained about 70% of the vinylamine. A sample of the crude reaction mixture (0.2 g.) was dissolved in 10 ml. of ethyl alcohol with 2,4-dinitrophenylhydrazine (0.16 g.). The solution was heated to reflux, 0.2 ml. of hydrochloric acid was added and refluxing continued for 3–4 minutes. The orange-red dinitrophenylhydrazine, which separated on cooling, was filtered off, dried and recrystallized from 20 ml. of benzene. The product (0.16 g., 55% yield) melted at 182–184°. A mixture with an authentic sample of *p*-tolylsulfonylacetaldehyde 2,4-dinitrophenylhydrazone (m.p. 183–185°) melted at 182–184°.

Anal. Calcd. for $C_{15}H_{14}N_4O_6S$: C, 47.62; H, 3.73; N, 14.81. Found: C, 47.80; H, 3.70; N, 14.34.

On standing in air, the crude reaction mixture slowly crystallized. Recrystallization from ethyl acetate gave a white crystalline product (m.p. 190.5°–191°) which was found to be N-[2,4-bis-(*p*-tolylsulfonyl)-1-butadienyl]-*n*-butylamine (VI), λ_{max}^{EtOH} 226 (ϵ 22,500), 325 mμ (ϵ 27,000).

Anal. Calcd. for $C_{22}H_{27}NO_4S_2$: C, 60.96; H, 6.28; N, 3.23; S, 14.77. Found: C, 61.01; H, 6.40; N, 3.42; S, 15.30.

Azo-initiated Isomerization of N-Methyl-N-vinyl-*p*-toluenesulfonamide.—A solution of 50 mg. of α,α'-azodiisobutyronitrile in 1.00 g. of N-methyl-N-vinyl-*p*-toluenesulfonamide was heated for 3 hours in an oil-bath at 90°. Crystallization of the reaction mixture from 1.5 ml. of ethyl acetate gave 0.50 g. (50% yield) of N-methyl-2-*p*-tolylsulfonylvinylamine (m.p. 122–123°). In like manner the other sulfonamides studied (Table III) all underwent azo-catalyzed isomerization. Yields were in the range 30–70%.

WILMINGTON 98, DEL.

[CONTRIBUTION FROM THE BIOCHEMISTRY DEPARTMENT, UNIVERSITY OF PITTSBURGH, SCHOOL OF MEDICINE]

A Synthesis of Cyclopropane-*cis*-1,2-diacetic Acid[1–3]

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RECEIVED JULY 28, 1958

A synthesis of cyclopropane-*cis*-1,2-diacetic acid of unequivocal stereostructure is described. Cyclohexa-1,4-diene was treated with dibromocarbene to give 7,7-dibromonorcar-3-ene which was oxidized to 3,3-dibromocyclopropane-*cis*-1,2-diacetic acid. The replacement of the bromine atoms by hydrogens was effected by hydrogenolysis over Raney nickel in methanolic potassium hydroxide. The reaction between cyclohexa-1,4-diene and methyl diazoacetate was shown to afford a mixture composed of at least three compounds, namely, a methyl norcarene-7-carboxylate, a methyl cycloheptadienecarboxylate and a doubly unsaturated derivative of methyl cyclohexaneacetate. Single crystal data for 7,7-dibromonorcar-3-ene for cyclopropane-*cis*-1,2-diacetic acid and some related cyclopropane derivatives are presented.

The results of chemical, physical and microbiological studies[3–5] left little doubt regarding the *cis* configuration of the cyclopropane fatty acids, lactobacillic and dihydrosterculic acids, but final proof for the assigned structures will depend on a comparison of these natural materials with synthetic specimens of unequivocal constitution. Procedures for the preparation of cyclopropane fatty acids of established *trans* configuration have been recorded,[4] but routes to the corresponding *cis* isomers remained to be developed. The present investigation was undertaken with the aim of devising such procedures.

Our studies of long-chain cyclopropane fatty acids have shown that *cis–trans* isomers in this series differ little in the very physical properties which are useful for purification purposes. Thus, in order to have assurance regarding stereochemical homogeneity of the final products, methods of synthesis had to be devised which precluded the presence of mixtures of stereoisomers in the final products. Taking into account this reasoning, it seemed desirable to prepare an intermediate of unquestionable *cis* configuration which could be converted into long-chain *cis*-cyclopropane fatty acids without the risk of *cis–trans* inversion during the process. Cyclopropane-*cis*-1,2-diacetic acid (I) seemed ideally suited for this purpose since methods are available for its conversion into acids of the general structure II, and since the separation of the carboxyl groups from the centers of asymmetry could be expected to eliminate the possibility of *cis–trans* inversions during these transformations.

(1) This study is dedicated to the memory of my former collaborator, Salvador F. Orochena, who died unexpectedly on January 23, 1958. K. H.

(2) Supported by Grants from the American Cancer Society, upon recommendation of the Committee on Growth of the National Research Council, and by the U. S. Public Health Service.

(3) A preliminary communication describing some of the results of this investigation has appeared in THIS JOURNAL, **79**, 3608 (1957).

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