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Free-Radical Chain Isomerization of *N*-Vinylsulfonamides

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Several new *N*-vinylsulfonamides were synthesized and photochemically or thermally caused to isomerize to β-sulfonylvinylamines. The chain length for the isomerization of *N*-methyl-*N*-(α-styryl)-*p*-toluenesulfonamide photoinitiated by benzoin methyl ether is estimated to be 1430.

The irradiation of certain *N*-vinylsulfonamides with high energy electrons was reported to induce a free-radical chain reaction leading to the formation of β-sulfonylvinylamines.[1] The same transformation was found to occur upon photolysis or thermolysis of an azonitrile initiator in the presence of an *N*-vinylsulfonamide.[2] This paper details our study of the generality of the photo- and thermal rearrangement of *N*-vinylsulfonamides and describes the synthesis of several new *N*-vinylsulfonamides.

Stacey, Sauer, and McKusick[1] proposed the mechanism shown in Scheme I for the radiation-induced rearrangement of *N*-methyl-*N*-vinylbenzenesulfonamide to *N*-methyl-2-benzenesulfonylvinylamine. Certain *N*-vinylsulfonamides were found to undergo electron-induced topotactic rearrangement in the crystalline state.

Scheme I

Initiation

$$C_6H_5SO_2N(CH_3)CH{=}CH_2 \longrightarrow R\cdot$$
(1)

$$R\cdot + 1 \longrightarrow C_6H_5SO_2N(CH_3)\dot{C}HCH_2R \downarrow$$

$$C_6H_5SO_2\cdot + CH_3N{=}CHCH_2R$$

Propagation

$$C_6H_5SO_2\cdot + 1 \longrightarrow C_6H_5SO_2N(CH_3)\dot{C}HCH_2SO_2C_6H_5 \downarrow$$

$$C_6H_5SO_2\cdot + CH_3N{=}CHCH_2SO_2C_6H_5 \downarrow$$

$$CH_3NHCH{=}CHSO_2C_6H_5$$

More recently, Graftieaux and Gardent[3] reported the light-induced rearrangement of 3-*p*-toluenesulfonyl-7,8-dimethoxy-4,5-dihydro-3*H*-benzazepine-3 (**2**) to the sulfone, **3**. A mechanism involving homolytic S–N scission with recombination of the radicals in a solvent cage was suggested; however, no evidence was presented to rule out a Stacey–Sauer–McKusick chain mechanism.

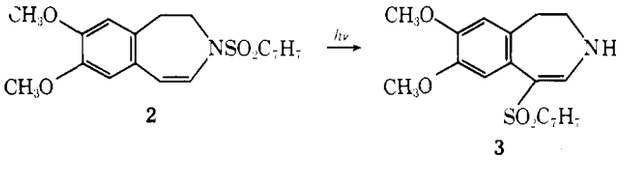

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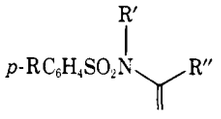
Table I
***N*-Vinylsulfonamides, *p*-$RC_6H_4SO_2NR'C(R'')=CH_2$**

Compd	R	R′	R″
5[1]	CH_3	CH_3	H
6	CH_3O	CH_3	H
7[4]	CH_3	CH_3	C_6H_5
8	CH_3	*p*-$CH_3OC_6H_4$	C_6H_5
9	CH_3	CH_3	*p*-$CH_3OC_6H_4$
10	Br	CH_3	C_6H_5
11	CH_3	CH_3	*p*-BrC_6H_4
12	CH_3O	CH_3	C_6H_5
13	CH_3	*p*-$(CH_3)_2NC_6H_4$	C_6H_5
14	CH_3	C_2H_5	CH_3
15	H	C_2H_5	CH_3

Results

Synthesis. Three general methods were used for the preparation of the *N*-vinylsulfonamides of general formula **4**. The literature[4] reaction of acetylene with an *N*-alkylar-



4

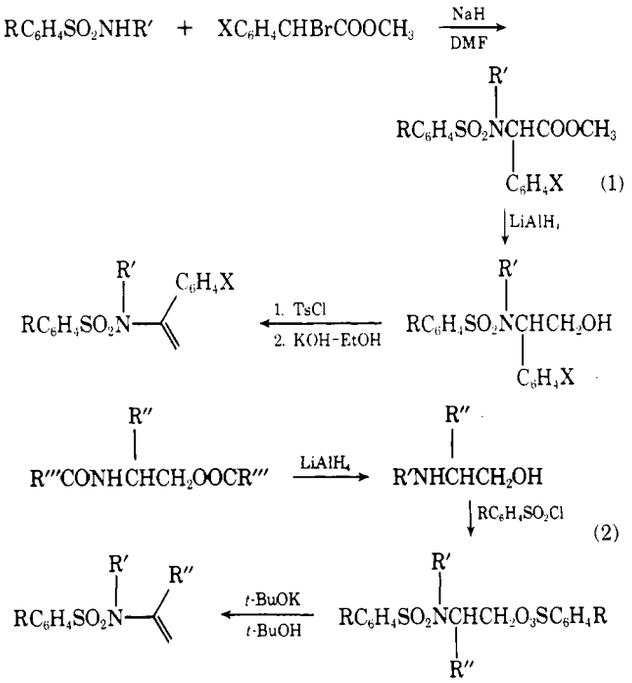
enesulfonamide was used for the preparation of **4** where R″ = H. For the preparation of *N*-(α-styryl)sulfonamides (**4**, R″ = aryl), the procedure[1] outlined in eq 1 was used, and the procedure of eq 2 was used to prepare *N*-2-(alkenyl)sulfonamides (**4**, R″ = alky). The *N*-vinylsulfonamides prepared by these procedures are listed in Table I. The properties of the new *N*-vinylsulfonamides are summarized in Table II, and the properties of some of the intermediates are summarized in Table III.

The reaction sequence of eq 1 does not appear to be entirely general for the preparation of *N*-(α-styryl)sulfonamides as evidenced by an interesting anomalous reaction which was found to occur in attempting to carry out the first step (eq 1) when R = CH_3, R′ = isopropyl, and R″ =

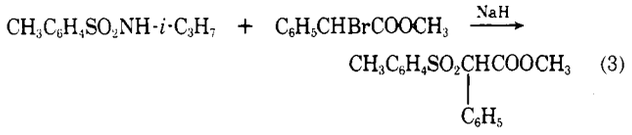
Table II
Properties of *N*-Vinylsulfonamides

Compd[a]	Mp, °C (recrystn solvent)	Method of synthesis[b]	Nmr, δ (60 MHz, CDCl3), (H_3) H_1 / N H_2
6	liq, bp ~112 (0.005 mm)	A	4.08–4.45 (m, H_1, H_2), 6.81–7.80 (m, H_3)
8	78–81 (ethanol)	B	5.19 (H_1), 5.42 (H_2)
9	79–82 (ether–hexane)	B	4.79 (H_1), 5.33 (H_2)
10	76.5–78 (methanol)	B	4.91 (H_1), 5.40 (H_2)
11	108–109 (methanol)	B	4.85 (d, H_1, J_{12} = 1 Hz), 5.43 (d, H_2, J_{12} = 1 Hz)
12	86.5–88.5 (methanol)	B	4.85 (H_1), 5.39 (H_2)
13	131.5–133.5 (ethanol)	B	5.19 (H_1), 5.44 (H_2)
14	64.5–68 (heptane)	C	4.75 (H_1), 5.05 (H_2)
15	liq, bp 97–103° (0.05 mm)	C	4.69 (H_1), 5.03 (q, H_2, J_{2CH_3} = 1 Hz)

[a] Satisfactory analytical data (±0.4% for C, H, N) were reported for all new compounds listed in the table with the exception of 14 and 15 (N): Ed. [b] Method A is described in ref 4. Method B is described in eq 1. Method C is described in eq 2.



H. Instead of obtaining the sulfonamido ester, a sulfone was obtained in low yield along with isopropylamine (eq 3).

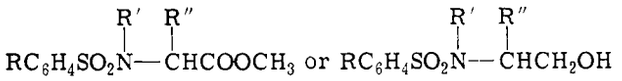


Apparently, the steric hindrance at the nitrogen atom of the sulfonamide caused the reaction to follow the anomalous course. The same sulfone was formed when *N*-methyl-*p*-toluenesulfonamide was allowed to react with methyl-α-chlorophenyl acetate and sodium hydride. The amount of sulfone found to accompany the desired sulfonamide ester in various other preparations seemed to increase when the substitution on the α-halo ester would be expected to increase the acidity of the tertiary hydrogen atom.

Photoinitiated Isomerization of *N*-Vinylsulfonamides. Several photoinitiators commonly used for photopolymerizations were found to be useful in photoinitiation of the isomerization of *N*-vinylsulfonamides to β-sulfonylvinylamines. The initiators examined were benzoin methyl ether, Michler's ketone–benzophenone, benzophenone–isopropyl alcohol, and a hexaarylbiimidazole-2-mercaptobenzoxazole. The irradiation experiments are summarized in Table IV. From the relatively small doses required to produce substantial rearrangement, it is apparent that rearrangement proceeds by a mechanism involving a chain reaction. The benzoin methyl ether initiated isomerization of **7** in benzene solution was determined to have a chain length of 1430 assuming a quantum efficiency of 0.2 for dissociation of benzoin methyl ether, which is the value measured (at 366 mμ) by Pappas and Chattopadhyay[5] for formation of α,α′-diisopropoxybibenzyl from benzoin isopropyl ether. The photorearrangement of the *N*-vinylsulfonamides is strongly inhibited by oxygen consistent with a free-radical chain mechanism. The introduction of an alkyl substituent to the vinyl group of the *N*-vinylsulfonamide greatly facilitates the photoinitiated rearrangement as can be seen by comparing (Table IV) the rearrangement of **14** with **5** and **6**.

Thermal Rearrangement of *N*-Vinylsulfonamides. When *N*-vinylsulfonamides are heated above the melting point in the presence of air, they undergo rearrangement to β-sulfonylvinylamines. The thermal rearrangement is less facile in an inert atmosphere such as nitrogen. Perhaps oxidation produces an unstable intermediate which serves to

Table III
Properties of Intermediates (A and B) in Synthesis of *N*-Vinylsulfonamides[a]



Type of intermediate	R, R′, R″ same as in compound	Mp, °C (recrystn solvent)
A	7	87.5–88.5 (ether)
A	9	104.5–105.5 (ether)
A	10	98–100 (ether–hexane)
A	11	112.5–113.5 (methanol)
A	12	104–107 (methanol)
A	13	114–119 (methanol)
B	12	97–99 (ether–hexane)
B	13	192–195 dec (methanol)

[a] Satisfactory analytical data (±0.4% for C, H, N) were reported for all new compounds listed in the table: Ed.

Table IV
Photoinitiated Isomerization of N-Vinylsulfonamides

Compd (wt in mg)	Initiator[a] (wt in mg)	Conditions and dose[b]	% rearrangement[c]
5 (400)	BME (20)	N_2, 94°, <1.5 J/cm^2 (C arc)	10
6 (200)	BME (10)	N_2, rt, ~1.5 J/cm^2 (C arc)	20–33
7 (300)	BME (30), 0.5 ml of CH_3CN	N_2, 180 mJ/cm^2 (366 mμ)	18
7 (300)	BME (30), 0.5 ml of C_6H_6	N_2, 180 mJ/cm^2 (366 mμ)	26[d]
7 (150)	Ph_2CO (0.1 *M*), 0.963 ml of *i*-PrOH, 0.188 ml of C_6H_6	N_2, 720 mJ/cm^2 (366 mμ)	27
7 (150)	CDM HABI (1), 0.25 ml of C_6H_6	N_2, 720 mJ/cm^2 (366 mμ)	11
7 (150)	CDM HABI (0.25), 2MBO (0.025), 0.25 ml of C_6H_6	N_2, 720 mJ/cm^2 (366 mμ)	60
7 (75)	BME (7.5), 0.13 ml of $CDCl_3$	N_2, 540 mJ/cm^2 (366 mμ)	50
7 (75)	BME (7.5), 0.13 ml of $CDCl_3$	Air, 540 mJ/cm^2 (366 mμ)	0
10 (150)	BME (15), 0.25 ml of C_6H_6	Air, 180 mJ/cm^2 (366 mμ)	0
10 (150)	BME (15), 0.25 ml of C_6H_6	N_2, 180 mJ/cm^2 (366 mμ)	19
12 (150)	BME (15), 0.25 ml of C_6H_6	N_2, 180 mJ/cm^2 (366 mμ)	38
12 (150)	BME (15), 0.25 ml of C_6H_6	Air, 180 mJ/cm^2 (366 mμ)	11
13 (150)	BME (15), 0.15 ml of C_6H_6, 0.15 ml of MeCN	N_2, 720 mJ/cm^2 (366 mμ)	0
14 (150)	BME (16), 0.25 ml of C_6H_6	N_2, 720 mJ/cm^2 (366 mμ)	41
14 (150)	BME (15), 0.25 ml of C_6H_6	Air, 720 mJ/cm^2 (366 mμ)	8–14

[a] BME, benzoin methyl ether; CDM HABI, 2-*o*-chlorophenyl-4,5-di-*m*-methoxyphenylimidazole dimer; 2MBO, 2-mercaptobenzoxazole. [b] The 366-mμ exposures were carried out in rectangular 1-cm. Pyrex cells using a filtered high pressure Hg lamp at a dose rate of about 100 μW/cm^2. The carbon arc exposures were carried out with a Bausch and Lomb 4.5-A carbon arc. At the photoinitiator concentrations used, much more than 99% of the incident light at 366 mμ was absorbed. [c] Degree of rearrangement is determined by nmr. [d] Assuming a quantum efficiency of 0.2 for BME initiation (see ref 5), this corresponds to 1430 isomerizations per initiating radical.

Table V
Thermal Rearrangement of N-Vinylsulfonamides[a]

Compd	Conditions (hr, temp in °C, atm)	% rearrangement
7	1, 95, air	35
7	1, 95, N_2	0
8	1.5, 95, air	0
9	1, 95–99, air	19
10	1, 95, air	17
11	1, 114, air	44
11	1, 116, N_2	34
12	1, 95–100, air	29
12	1, 95–99, N_2	16.5
13	4, 133, air	100
14	1, 95–99, air	0

[a] The extent of rearrangement was estimated by nmr using the spectra of the starting material and the product as standards.

initiate the rearrangement. The thermal rearrangement of *N*-vinylsulfonamides is summarized in Table V. The products of rearrangement were obtained on a preparative scale by heating the *N*-vinylsulfonamides above the melting point with azobisisobutyronitrile initiator either in air or nitrogen. The properties of the resulting β-sulfonylvinylamines are summarized in Table VI.

Experimental Section

***N*-Methyl-*N*-vinyl-*p*-methoxybenzenesulfonamide (6). Method A.** A mixture of 15 g of *N*-methyl-*p*-methoxybenzenesulfonamide, 40 ml of benzene, and 0.595 g of powdered potassium hydroxide was heated at 160° in a 240-cc Hastalloy shaker bomb under 220–305 psi of acetylene for 16 hr. The resulting mixture was filtered, and the filtrate was washed twice with 10% aqueous sodium hydroxide and once with water. After the mixture dried, the solvent was removed *in vacuo*, and the residue was distilled in a short-path column at ~112° (0.005 mm) to give 8.4 g of *N*-methyl-*N*-vinyl-*p*-methoxybenzenesulfonamide as a viscous liquid (see Table II).

***N*-Methyl-*N*-(α-styryl)-*p*-bromobenzenesulfonamide (10). Method B.** To a slurry of 345 ml of anhydrous dimethylformamide and 11.5 g of a 50% dispersion of sodium hydride in mineral oil was added 55.4 g of *N*-methyl-*p*-bromobenzenesulfonamide. The mixture was stirred for 2 hr at which time the hydrogen evolution had ceased. The mixture was then cooled in an ice bath at 10° and treated with 50.8 g of methyl α-bromophenylacetate. The mixture was stirred at room temperature for 1 hr. The resulting solution was poured into ice water and extracted twice with benzene. The benzene extracts were combined and washed twice with water, once with 1% aqueous sodium hydroxide, and twice with water. The benzene solution was dried over Drierite and evaporated *in vacuo* to give 72.3 g of oil. Cooling while scratching with hexane caused crystallization to occur. Filtration gave 55.9 g of solid. Recrystallization from ether–hexane gave 33.8 g of crystals of *N*-methyl-*N*-(α-carbomethoxybenzyl)-*p*-bromobenzenesulfonamide, mp 94.5–97.5°. An additional recrystallization raised the melting point to 98–100°.

Anal. Calcd for $C_{16}H_{16}NBrO_4S$: C, 48.1; H, 4.05; N, 3.52. Found: C, 47.6, 47.8; H, 3.96, 4.09; N, 3.39, 3.30.

To a stirred slurry of 1.85 g of lithium aluminum hydride and 125 ml of tetrahydrofuran cooled in an ice bath was added a solution of 33 g of *N*-methyl-*N*-(α-carbomethoxybenzyl)-*p*-bromobenzenesulfonamide in 83 ml of tetrahydrofuran at a rate such that the temperature remained near 28°. The mixture was stirred at room temperature for 1.25 hr, treated with an additional 0.2 g of lithium aluminum hydride, and stirred for 0.75 hr. The mixture was cooled, treated with 15 ml of water and stirred for 30 min. The mixture was filtered, and the filtrate was evaporated *in vacuo* to 27.2 g of oil. This residue was treated with 50 ml of 10% sodium hydroxide and sufficient ethanol to give a homogeneous solution at the reflux. After refluxing for 1 hr, the mixture was concentrated *in vacuo* to remove ethanol and was then treated with water and ether. The ether extract was washed twice with water, dried, and evaporated to 16.5 g of *N*-methyl-*N*-[α-(hydroxymethyl)benzyl]-*p*-bromobenzenesulfonamide as a viscous oil which could not readily be crystallized.

To a stirred solution of 18 g of *p*-toluenesulfonyl chloride in 80 ml of pyridine was added dropwise with warming a solution of 16.5

Table VI
Rearrangement Products of *N*-Vinylsulfonamides[a]

Conditions[b]	Mp, °C (recrystn solvent)	Comments
6 (1 g) AIBN (50 mg) 2.5 hr, 90°, N_2	132.5–135.5 (ethyl acetate)	Nmr δ 2.71 (d, J = 5 Hz, NCH_3)
8 (1 g) AIBN (40 mg) 2 hr, 95°, air	Glass	$\epsilon_{3200\,\text{Å}}^{\text{benzene}}$ 7500, no **8** remained
10 (1 g) AIBN (15 mg) 2 hr, 95°, air	155–156.5 (ethyl acetate–heptane)	Nmr δ 2.71 (d, J = 5 Hz, NCH_3), 4.70 (vinyl H)
11 (750 mg) AIBN (15 mg) 3.5 hr, 100°, air	117–119 (benzene–heptane)	Nmr δ 2.65 (d, J = 5 Hz, NCH_3), 4.66 (vinyl H)
12 (1 g) AIBN (10 mg) 3 hr, 95–100°, air	94.5–97.5 (ether–heptane)	Nmr δ 2.70 (d, J = 5 Hz, NCH_3), 4.70 (vinyl H)
13 (750 mg) AIBN (15 mg) 1.5 hr, 135°, N_2	103–107	$\epsilon_{3550\,\text{Å}}^{\text{ether}}$ 10,100 (sh, tail to 4700 Å) Nmr suggests isomeric mixture
14 (700 mg) AIBN (15 mg) 3 hr, 95–104°, air	88–91 (cyclohexane)	Nmr [two isomers (2:1)] δ 4.53 and 4.98 (vinyl H trans and cis to N)

[a] Satisfactory analytical data (±0.4% for C, H, N) were reported for all new compounds listed in this table with the exception of the entry for 14: Ed. [b] AIBN, azobisisobutyronitrile.

g of *N*-methyl-*N*-[α-(hydroxymethyl)benzyl]-*p*-bromobenzenesulfonamide in 60 ml of pyridine over a period of 15 min. The temperature was maintained at ~40° during the addition. The resulting solution was stirred overnight at room temperature, cooled to 10°, and treated with a few pieces of ice. After 15 min, the solution was poured into a mixture of ice and hydrochloric acid. The resulting gummy precipitate was collected by filtration, dissolved in benzene, washed twice with water, dried over Drierite, and evaporated *in vacuo* to give 25.6 g of *N*-methyl-*N*-(α-phenyl-β-*p*-toluenesulfonoxyethyl)-*p*-bromobenzenesulfonamide as a viscous oil.

A mixture of 25.6 g of *N*-methyl-*N*-(α-phenyl-β-*p*-toluenesulfonoxyethyl)-*p*-bromobenzenesulfonamide, 115 ml of ethanol, and 13 g of potassium hydroxide was stirred for 2 hr at reflux under nitrogen. The resulting gummy precipitate was extracted with ether–hexane. The extract was washed twice with water, dried, and evaporated to 14 g of oil. Recrystallization from methanol gave 8.66 g of crystals of *N*-methyl-*N*-(α-styryl)-*p*-bromobenzenesulfonamide: mp 73.5–76° (a second recrystallization from methanol raised the melting point to 76.5–78°); nmr ($CDCl_3$) δ 3.09 (NCH_3), 4.91 (vinyl H cis to phenyl), 5.40 (vinyl H cis to N), 7.23–7.75 (aromatic).

Anal. Calcd for $C_{15}H_{14}NSO_2Br$: C, 51.1; H, 4.00; N, 4.00; Br, 22.7. Found: C, 50.7; H, 3.96; N, 3.78; Br, 22.0.

***N*-Ethyl-*N*-2-propenyl-*p*-toluenesulfonamide (14). Method C.** To a stirred slurry of 40 g of lithium aluminum hydride in 750 ml of tetrahydrofuran was added a solution of 110 g of 2-acetamidopropyl acetate (prepared by the reaction of acetic anhydride with 2-amino-1-propanol) in 250 ml of tetrahydrofuran at a rate such that gentle reflux was maintained. Stirring at reflux was continued for 9 hr. The mixture was cooled in ice, treated with 100 ml of water, stirred for 1.5 hr, and filtered. The filtrate was dried with Drierite and evaporated *in vacuo* to 54.2 g of liquid. Distillation gave 34.2 g of *N*-ethyl-*N*-β-hydroxyisopropylamine, bp 60–67° (7–38 mm).

Anal. Calcd for $C_5H_{13}NO$: C, 58.2; H, 12.7; N, 13.6. Found: C, 58.6; H, 12.7; N, 13.5.

To a stirred solution of 15.2 g of *N*-ethyl-*N*-β-hydroxyisopropylamine in 300 ml of pyridine was added a solution of 89 g of *p*-toluenesulfonyl chloride in 250 ml of pyridine at a rate such that the temperature remained at 40–45°. After stirring overnight at room temperature, the solution was cooled to 10°, treated with a few pieces of ice, and after 20 min poured into excess ice and hydrochloric acid. The resulting gum was collected by decantation, dissolved in ether, washed with dilute hydrochloric acid and water, dried, and evaporated to 28.6 g of amber oil. Recrystallization from ether-hexane gave 18.2 g of crystals of *N*-ethyl-*N*-(3-*p*-toluenesulfonoxy-2-propyl)-*p*-toluenesulfonamide.

A mixture of 14 g of potassium *tert*-butoxide, 100 ml of *tert*-butyl alcohol, and 17 g of *N*-ethyl-*N*-(3-*p*-toluenesulfonoxy-2-propyl)-*p*-toluenesulfonamide was stirred at reflux under nitrogen for 1 hr, cooled, diluted with ice water, and extracted with ether. The ether extract was washed twice with water, dried, and evaporated to a crystalline residue. Recrystallization from heptane gave 6.8 g of crystals of *N*-ethyl-*N*-2-propenyl-*p*-toluenesulfonamide: mp 64.5–68°; nmr ($CDCl_3$) δ 1.16 (triplet, J = 7 Hz, CH_3 of C_2H_5), 1.89 (vinyl CH_3), 2.44 (aromatic CH_3), 3.42 (quartet, J = 7 Hz, CH_2N), 4.75 (vinyl H cis to CH_3), 5.05 (vinyl H cis to N), 7.24–7.80 (aromatic).

Anal. Calcd for $C_{12}H_{17}NO_2S$: C, 60.4; H, 7.15; N, 5.86. Found: C, 60.0; H, 7.28; N, 5.40.

Methyl 2-*p*-Toluenesulfonyl-2-phenylacetate. A mixture of 300 ml of dimethylformamide, 9.6 g of 50% sodium hydride dispersed in mineral oil, 42.5 g of *N*-isopropyl-*p*-toluenesulfonamide, and 45.8 g of methyl-α-bromophenyl acetate was stirred for 3 hr at 45°. The mixture was poured into ice water and extracted with ether. The ether extract was washed with water three times, dried, and evaporated *in vacuo* to 61 g of oil. Crystallization from heptane and then from methanol gave 14.7 g of methyl-2-(*p*-toluenesulfonyl)-2-phenyl acetate: mp 114–117° (an additional recrystallization from methanol raised the melting point to 124–126°); nmr ($CDCl_3$) δ 2.41 (aromatic CH_3), 3.75 ($COOCH_3$), 5.08 (tertiary CH), 7.13–7.58 (aromatic).

Anal. Calcd for $C_{16}H_{16}O_4S$: C, 63.1; H, 5.30; N, 0.00; S, 10.5; mol wt, 304. Found: C, 63.2; H, 5.30; N, <0.03; S, 10.7; mol wt, 304 (mass spectrum)

The mass spectrum of the product showed, in addition to the parent peak (*m/e* 304), a large peak at *m/e* 149 corresponding to loss of $C_6H_5CHCOOCH_3$.

The same product was obtained from the reaction of *N*-methyl-*p*-toluenesulfonamide with methyl α-chlorophenylacetate and sodium hydride in dimethylformamide. Methylamine was evolved from the reaction mixture.

Registry No.—**6**, 52260-06-7; **8**, 52260-07-8; **9**, 52260-08-9; **10**, 52260-09-0; **11**, 52260-10-3; **12**, 52260-11-4; **13**, 52260-12-5; **14**, 52260-13-6; **15**, 52260-14-7; *N*-methyl-*p*-methoxybenzenesulfon-

amide, 7010-86-8; *N*-methyl-*p*-bromobenzenesulfonamide, 703-12-8; methyl α-bromophenylacetate, 3042-81-7; *N*-methyl-*N*-(α-carbomethoxybenzyl)-*p*-bromobenzenesulfonamide, 52260-15-8; 2-acetamidopropyl acetate, 52260-16-9; *N*-ethyl-*N*-β-hydroxyisopropylamine, 24417-04-7; *p*-toluenesulfonyl chloride, 98-59-9; methyl 2-*p*-toluenesulfonyl-2-phenylacetate, 33829-52-6; *N*-isopropyl-*p*-toluenesulfonamide, 21230-07-9.

References and Notes

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Steric and Electrostatic Interactions in Reactions of Carbohydrates. III.[1] Direct Displacement of the C-2 Sulfonate of Methyl 4,6-*O*-Benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-β-D-gluco- and -mannopyranosides[2]

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Heating of an *N,N*-dimethylformamide solution of methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-β-D-glucopyranoside (**2**) and methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methysulfonyl-β-D-mannopyranoside (**4**) with potassium benzoate resulted in direct displacement of the C-2 sulfonyloxy group giving the corresponding D-manno- (**14**, 62%) and D-gluco (**13**, 70%) derivatives. Methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-α-D-glucopyranoside (**1**) gave, under the same experimental conditions, only very small amount (~3%) of a product which could be the product of direct displacement (**15**), whereas methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-α-D-mannopyranoside (**3**) did not undergo direct displacement at all. The greater reactivity of **4** *vs.* **2** and the unreactivity of **1** and **3** toward the direct nucleophilic displacement was rationalized in terms of torsional strain and electrostatic and steric nonbonding interactions in the corresponding transition states.

In connection with some other work we became interested in direct displacement of the C-2 sulfonyloxy group of pyranosides. Our previous findings that the stereochemical course of the addition of CH_3Li, CH_3MgX, and $NaBH_4$ to the C-2 and C-4 carbonyl carbon atom strongly depended upon the anomeric configuration of the corresponding hexopyranosiduloses[1,3] suggesting that the torsional strain and nonbonding steric and electrostatic interactions in the corresponding transition states are the decisive factors in determining the stereochemical course of these reactions, prompted us to investigate the possible relationship between the anomeric configuration and the reactivity of a C-2 sulfonyloxy group of hexopyranosides toward direct displacement.

Except for displacement of the *p*-tolylsulfonyl group of methyl 4,6-*O*-benzylidene-3-deoxy-2-*O*-*p*-tolylsulfonyl-α-D-*ribo*-hexopyranoside with azide,[4] direct displacement of a C-2 sulfonyloxy group of a furanoside or a pyranoside ring with a charged nucleophile has not been yet reported. The use of an uncharged nucleophile, *e.g.*, hydrazine, did result in displacement of the C-2 sulfonate in both furanoside[5-7] and pyranoside[8] rings. The unreactivity of the C-2 sulfonyloxy group toward displacement with charged nucleophiles was attributed to the electron-withdrawing effect of the anomeric carbon atom and to the unfavorable dipolar interaction in the transition state.[9-13] The greater reactivity of uncharged nucleophiles is displacement of the sulfonyloxy group at the C-2 carbon atom was ascribed to the reversal of polarity of one of the polar bonds in the transition state resulting in a dipolar attractive force.[11] Although some speculations on the reactivity of a C-2 sulfonyloxy group of β-D-glycopyranosides having the C-1 aglycon group equatorially oriented have been entertained,[11] direct displacement of the C-2 sulfonate of a β-D-glycopyranoside was not thus far attempted.

The following substrates were chosen for our study: methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-α-D-glucopyranoside (**1**),[3] methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-β-D-glucopyranoside (**2**), methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-α-D-mannopyranoside (**3**), and methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-β-D-mannopyranoside (**4**).

It is known[14,15] that the reactivity of a sulfonyloxy group directly attached to a six-membered ring (cyclohexane or glycopyranoside) toward direct displacement with a nucleophile will generally depend upon (a) gound-state energy (conformational free-energy) of the substrate and (b) energy of the corresponding transition state.

Whereas the ground state energy of α- and β-D-glucopyranosides **1** and **2** and α-D-mannopyranoside **3** should not be significantly different, the conformational free-energy of β-D-mannopyranoside **4**, should be considerably higher due to the unfavorable dipolar interaction between the axially oriented C-2 methylsulfonyloxy group and the C_1–O_1 and the C_1–O_5 dipoles. Consequently, the activation energy for direct displacement of the C-2 sulfonyloxy group of β-D-mannopyranoside **4** should be lower than for displacement of the C-2 sulfonyloxy group of α- and β-D-glucopyranosides **1** and **2**, and α-D-mannopyranoside **3**.

However, as has been already stated, the reactivity of a sulfonyloxy group toward direct displacement does not depend solely upon the ground state energy of a substrate, but also upon the transition state energy level, *i.e.*, torsional strain, nonbonded steric and electrostatic interactions between the approaching nucleophile and/or leaving sulfonate and other substituents of a six-membered pyranoside ring.

Thus, the "axial" attack of a charged nucleophile to the C-2 atom of **1** (α-D-glucopyranoside) resulting in transition