N-Monoalkylation of Sulfonamides

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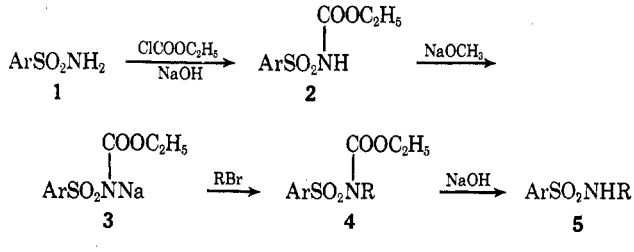
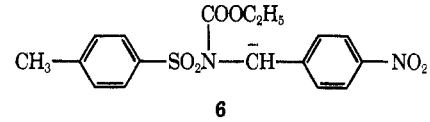
The present paper describes a reliable two-stage process for preparing N-monoalkyl sulfonamides **5** from the corresponding alkyl bromide without going through the alkylamine. The method calls for alkylation of the sodio derivative **3** of sulfonyl carbamate **2**, followed by mild saponification and decarboxylation of the resulting ethyl *N*-(arylsulfonyl)carbamate (**4**) to give **5**.

This work started when a need arose for a practical source of *N*-(3-bromallyl)benzenesulfonamide.[1b] Attempts to prepare 3-bromallylamine failed, so that we could not combine benzenesulfonyl chloride with the amine in the usual way. We then considered the alternate way of alkylating benzenesulfonamide directly with 1,3-dibromopropene. Use of the sodio derivative of benzenesulfonamide, even in excess, gave only the dialkylation product, *N*,*N*-di(3-bromallyl)benzenesulfonamide.[2] The silver salt with 1,3-dibromopropene also gave no sign of the desired monoalkyl compound. With direct alkylation showing little promise, we sought a way of blocking one of the sulfonamide position, and this approach led eventually to sequence **1**–**5** (Scheme I).

SCHEME I



The generality of this method was tested with several bromides. Tables I and II summarize the results, which show that a variety of alkyl bromides can be converted to *N*-monoalkyl sulfonamides in a straightforward way, with the complication of mixtures avoided altogether. Arylsulfonamides combine smoothly with ethyl chloroformate to give the necessary blocked intermediates, the ethyl *N*-(arylsulfonyl)carbamates. Although we did not try the reaction, there seems to be no reason to expect difficulty with alkylsulfonamides. Alkylations **3** to **4** were conducted in various solvents, under various conditions, with yields of alkylation product **4** ranging from 27 to 88%. The only compound that failed to yield a product was trimethylbromoethylammonium bromide. The saponification–decarboxylation step **4** to **5** occurred smoothly to give the monoalkyl product **5** in feasible yield (*cf.* Table II). The exceptions were ethyl *N*-(*p*-nitrobenzyl)-*N*-(*p*-toluenesulfonyl)carbamate, which gave 38% of monoalkyl sulfonamide, and ethyl *N*-(*p*-phenylphenacyl)-*N*-(*p*-toluenesulfonyl)carbamate, which gave only a trace of product. Only with these two carbamates was a deep color observed during the saponification step **4** to **5**. Possibly formation of the corresponding carbanions, *e.g.*, **6**, complicated the procedure.



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Experimental Section

General.—Temperatures are uncorrected. The infrared absorption data were obtained from double-beam instruments, with wavenumbers calibrated against polystyrene. Most curves were obtained with the compounds in chloroform or carbon tetrachloride solutions, some from mineral oil mulls. Nuclear magnetic resonance curves were obtained at 60 MHz, with chemical shifts reported in parts per million downfield from tetramethylsilane. Analyses for elements were performed by Galbraith Laboratories, Knoxville, Tenn., Spang Microanalytical Laboratory, Ann Arbor, Mich., and Scandinavian Microanalytical Laboratory, Herlev, Denmark. Thin layer chromatography made use of silica gel layers from Gelman Instrument Co. (type SG) or from Eastman Kodak Co. (type $K_{301}R$ or Chromogram Sheet 6060), with fluorescence or iodine vapor for bringing out the spots. Volatile solvents were removed routinely in a rotary evaporatory under water pump pressures and at temperatures just above room temperature.

Ethyl *N*-(Arylsulfonyl)carbamate (2).—Ethyl *N*-(benzenesulfonyl)carbamate, precipitated by acidifying the alkaline mixture in which it was formed from ethyl chloroformate and benzenesulfonamide,[3] was obtained in 69% yield. The melting point was 107–109° before and after crystallization from methanol (lit.[3] mp 108–110°).

Anal. Calcd for $C_9H_{11}NO_4S$: C, 47.16; H, 4.80. Found: C, 47.20; H, 4.68.

This carbamate (as in **2**) shows ir absorptions ($CHCl_3$) at 1155 and 1350 (SO_2N), 1750 (C=O), and 3390 cm^{-1} (NH); nmr ($CDCl_3$) δ 1.15 (t, 3, J = 8.0 Hz, CH_2CH_3), 4.15 (q, 2, J = 8.0 Hz, OCH_2CH_3), and 7.8 ppm (m, 6, NH plus aromatic H's).

Ethyl *N*-(*p*-toluenesulfonyl)carbamate, prepared from *p*-toluenesulfonamide essentially according to the directions given for the phenyl compound, was obtained as white crystals; mp 80–82° (lit.[4] 75–77°; 82–84°); ir ($CHCl_3$) 1160, 1350, 1750, and 3390 cm^{-1}.

Sodio Derivative of Ethyl *N*-(Arylsulfonyl)carbamate (3).[5]—The sodium salt was obtained as a white solid, mp 220–222°, in 59–75% yield by neutralizing the corresponding carbamate (30

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(2) *A priori*, mixtures of unchanged sulfonamide, monoalkylated sulfonamide, and dialkylated sulfonamide would always have to be contended with, the ratio of products being dependent on the relative rates of the first and the second alkylation [*cf.* D. Klamann, G. Hofbauer, and F. Drahowzal, *Monatsh. Chem.*, **83**, 870 (1952); Z. Földi, *Chem. Ber.*, **55**, 1535 (1922); M. de Montmollin and P. Matile, *Helv. Chim. Acta*, **12**, 870 (1929); D. H. Peacock and U. C. Dutta, *J. Chem. Soc.*, 1303 (1934)]. Preparation of monoalkyl compounds in this way may also be further complicated by the insolubility of certain monoalkylated sulfonamides in alkali, in which case separating the monoalkyl from the dialkyl sulfonamide becomes troublesome [see references in W. J. Gensler and J. C. Rockett, *J. Amer. Chem. Soc.*, **77**, 3262 (1955)].

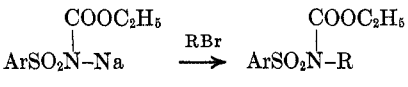
(3) F. J. Marshall and M. V. Sigal, Jr., *J. Org. Chem.*, **23**, 927 (1958).

(4) E. S. Levchenko, E. S. Kozlov, and A. V. Kirsanov, *Chem. Abstr.*, **56**, 4654*a* (1962) [*Zh. Obshch. Khim.*, **31**, 2381 (1961)]; K. Lanyi and Zs. Szabo, *Chem. Abstr.*, **56**, 7194 (1962) [*Acta Chim. Acad. Sci. Hung.*, **29**, 85 (1961)].

(5) O. C. Billeter, *Chem. Ber.*, **37**, 690 (1904).

TABLE I

ETHYL N-(ALKYL)-N-(ARYLSULFONYL)CARBAMATE (4) BY ALKYLATING THE SODIO DERIVATIVE OF ETHYL N-(ARYLSULFONYL)CARBAMATE (3)



Alkyl bromide, g (mmol)	Sodio deriv, g (mmol)	Solvent (ml)	Time, hr; temp[n]	Yield[b] of product, %
$BrCH{=}CHCH_2Br$, 10 (50)	12.6 (50)[a]	CH_3OH plus H_2O	[c]	27[a]
p-$NO_2C_6H_4CH_2Br$, 0.18 (0.83)	0.25 (1.0)[a]	DMSO (3)	2¼; *ca.* RT[d]	85[a]
p-$C_6H_5C_6H_4\overset{O}{\overset{\|}{C}}CH_2Br$, 1.9 (6.9)	2.0 (8.0)[a]	DMSO	2⅓; RT[e]	62[a]
$C_2H_5OOCCH_2Br$, 0.52 (3.1)	1.0 (4.1)[a]	DMSO (8)	50; RT[f]	87[a]
$C_6H_5CH_2Cl$, 2.3 (18)	5.3 (20)[g]	DMSO (27)	20; RT[h]	58[g]
p-$BrC_6H_4CH_2Br$, 5.2 (21)	6.0 (23)[g]	DMSO (40)	6¼; RT[i]	80[g]
$C_6H_5CH{=}CHCH_2Br$, 2.0 (10)	2.9 (11)[g]	Acetone–water 9:1 (25)	16; RT[j]	~80[g]
$CH_3CH_2CH_2CH_2Br$, 0.68 (5)	1.5 (5.5)[g]	DMF (20)	16; RT[k]	~60[g]
$C_6H_5CH_2CH_2Br$, 1.9 (10)	2.9 (12)[g]	DMF (40)	18; RT[l]	88[g]
$(CH_3)_3\overset{+}{N}CH_2CH_2Br\ \bar{B}r$, 2.46 (10)	2.92 (11)[g]	DMSO (30)	24; RT	0[m]

[a] Benzenesulfonyl derivative. [b] No special effort was made to determine optimal conditions. [c] After the reaction mixture in 250 ml of methanol had been stirred for 19 hr at room temperature, water (150 ml) was added and the temperature was held at the boiling point for 12 hr. Volatiles were removed *in vacuo* at 50°, and the residue was extracted with benzene. The carefully dried extract was freed of solvent, and the residue was chromatographed through neutral alumina with benzene as eluent. Solvent-free ethyl N-(3-bromoallyl)-N-(benzenesulfonyl)carbamate was obtained as a viscous water-white oil (4.7 g), homogeneous according to thin layer chromotography; $n^{24}D$ 1.5436; ir (CCl_4) 3075, 3050 (BrCH=CHR), 1737 (C=O), 1375, and 1175 cm^{-1}; nmr (CCl_4) δ 1.15 (t, 3, J = 6.0 Hz, CH_2CH_3), 4.10 (q, 2, J = 6.0 Hz, CH_2CH_3), 4.40 (q, 2, J = 6.0 Hz, CH_2N), 6.30 (m, 2, olefinic H's), and 7.70 ppm (m, 5, aromatic H's). *Anal.* Calcd for $C_{12}H_{14}BrNO_4S$: C, 41.38; H, 4.02. Found: C, 41.59; H, 4.02. [d] Adding 15 ml of water to the reaction mixture precipitated essentially pure ethyl N-(*p*-nitrobenzyl)-N-(benzenesulfonyl)carbamate, which melted at 110–112° before crystallization from aqueous methanol and at 111.5–112.5° after crystallization; ir ($CHCl_3$) 1730, 1520, 1375, 1350, and 1170 cm^{-1}; nmr ($CDCl_3$) δ 1.10 (t, 3, J = 7.0 Hz, CH_2CH_3), 4.10 (q, 2, J = 7.0 Hz, CH_2CH_3), 5.10 (s, 2, NCH_2), 7.4–8.2 (m, 9, aromatic H's). *Anal.* Calcd for $C_{16}H_{16}N_2O_6S$: C, 52.74; H, 4.43. Found: C, 52.54; H, 4.32. The same product was obtained in 66% yield when the reaction solvent was boiling aqueous ethanol. [e] Dilution of the reaction mixture (protected from air) with 125 ml of water gave a sticky solid, which after crystallization from 95% ethanol appeared as yellow crystals of ethyl N-(*p*-phenylphenacyl)-N-(benzenesulfonyl)carbamate (1.8 g), mp 145–147°. The same product was obtained in 45% yield when the alkylation was performed with hot aqueous ethanol. Crystallization from aqueous acetone furnished analytically pure material; mp 150.5–152°; ir ($CHCl_3$) 1735, 1700, 1360, 1170 cm^{-1}. *Anal.* Calcd for $C_{23}H_{21}NO_5S$: C, 65.23; H, 5.00. Found: C, 65.41; H, 4.80. [f] Benzene extraction of the reaction mixture that had been diluted with water, followed by removal of solvent from the extract, left residual white ethyl N-(carbethoxymethyl)-N-(benzenesulfonyl)carbamate (0.86 g), which melted at 52.5–54.5° before and at 56.5–58° after crystallization from chloroform–petroleum ether (bp 30–60°); ir ($CHCl_3$) 1735, 1360, 1170 cm^{-1}; nmr ($CDCl_3$) δ 0.97–1.35 (m, 6, $2CH_3$), 3.9–4.5 (m, 4, $2OCH_2$), 4.55 (s, 2, NCH_2), 7.55–8.1 ppm (m, 5, aromatic H's). *Anal.* Calcd for $C_{13}H_{17}NO_6S$: C, 49.52; H, 5.43. Found: C, 49.70; H, 5.55. [g] *p*-Toluenesulfonyl derivative. [h] The reaction mixture (nitrogen atmosphere) was diluted with water and extracted with ether. The extract was rinsed with bicarbonate and with water, then dried and stripped of solvent. Refrigeration of the residue for several days gave an oil–solid mixture that was pressed on filter paper and washed with cold petroleum ether. The resulting ethyl N-benzyl-N-(*p*-toluenesulfonyl)carbamate (3.5 g, mp 52–55°) was recrystallized from petroleum ether to furnish white, crystalline product; mp 56–58°; ir ($CHCl_3$) 1725, 1355, 1168 cm^{-1}. *Anal.* Calcd for $C_{17}H_{19}NO_4S$: C, 61.24; H, 5.74. Found: C, 61.52; H, 5.86. [i] The product, isolated by diluting the reaction mixture with water and extracting with ether, was crystallized from aqueous methanol to give ethyl N-(*p*-bromobenzyl)-N-(*p*-toluenesulfonyl)carbamate (80%); mp 84–85°; ir ($CHCl_3$) 1720, 1350, 1170 cm^{-1}; nmr ($CDCl_3$) δ 1.11 (t, 3, J = 7.0 Hz, CH_2CH_3), 2.38 (s, 3, $ArCH_3$), 4.09 (q, 2, J = 7.0 Hz, CH_2CH_3), 4.94 (s, 2, NCH_2), 7.1–7.7 ppm (m, 8, aromatic H's). *Anal.* Calcd for $C_{17}H_{18}BrNO_4S$: C, 49.53; H, 4.40. Found: C, 49.37; H, 4.24. [j] The crude, solvent-free product (2.9 g, 81%), obtained by ether extraction of the reaction mixture that had been diluted with water, consisted according to thin layer chromatography (R_f 0.43 with benzene solvent) essentially of a single product; actually, hydrolysis of this material gave N-cinnamyl-*p*-toluenesulfonamide in the same yield and quality as hydrolysis of the purified product. Column chromatography over Fisher alumina using first ligroin and then benzene afforded 0.9 g of colorless oily ethyl N-(cinnamyl)-N-toluenesulfonyl)carbamate showing a single thin layer chromatographic spot (R_f 0.43); $n^{25}D$ 1.5920; ir ($CHCl_3$) 1720, 1340, 1160 cm^{-1}; nmr ($CDCl_3$) δ 1.16 (t, 3, J = 7.0 Hz, CH_2CH_3), 2.37 (s, 3, $ArCH_3$), 4.12 (q, 2, J = 7.0 Hz, CH_2CH_3), 4.60 (d, 2, J = 6.0 Hz, NCH_2), 6.50 (m, 2, olefinic H's), 7.1–7.9 ppm (m, 9, aromatic H's). *Anal.* Calcd for $C_{19}H_{21}NO_4S$: C, 63.49; H, 5.89. Found: C, 63.49; H, 6.06. [k] The solvent-free product isolated from its ether extract appeared as a near-colorless oil (1.0 g, 71%), $n^{25}D$ 1.5075, estimated by thin layer chromatography to be more than 80% pure. Column chromatography as in footnote *j* gave 0.38 g (26%) of colorless oily ethyl N-butyl-N-(*p*-toluenesulfonyl)carbamate, homogeneous according to thin layer chromatography (R_f 0.35); $n^{25}D$ 1.5082; ir ($CHCl_3$) 1720, 1345, 1170 cm^{-1}; nmr ($CDCl_3$) δ 0.97 (d, J = 6 Hz, $CH_2CH_2CH_3$), 1.20 (d, J = 7 Hz, OCH_2CH_3), 1.6 (m, $CH_2CH_2CH_3$), 2.40 (s, 3, $ArCH_3$), 3.7–4.3 (m, 4, NCH_2 plus OCH_2), 7.25 and 7.77 ppm (two d's, J = 9 Hz, aromatic H's). The δ 0.97–1.6 ppm signals integrate to a total of 10 protons. *Anal.* Calcd for $C_{14}H_{21}NO_4S$: C, 56.16; H, 7.07. Found: C, 56.14; H, 7.17. [l] The crude product obtained as described in footnote *j* emerged as an oil, which after standing for a day afforded pure, white crystals of ethyl N-(phenethyl)-N-(*p*-toluenesulfonyl)carbamate (3.8 g); mp 77–78°; ir ($CHCl_3$) 1720, 1345, 1160 cm^{-1}; nmr ($CDCl_3$) δ 1.15 (t, 3, J = 7.0 Hz, CH_2CH_3), 2.40 (s, 3, $ArCH_3$), 3.00 (deformed t, 2, J = 8.0 Hz, (NCH_2)), 4.05 (m, 4, $ArCH_2$ plus OCH_2), 7.3 (m, C_6H_5), 7.73 ppm (d, J = 8 Hz, $CH_3C_6H_4$). The last two signals correspond to a total of 9 protons. *Anal.* Calcd for $C_{18}H_{21}NO_4S$: C, 62.23; H, 6.09. Found: C, 62.35; H, 6.31. [m] The starting trimethyl(bromoethyl)ammonium bromide was recovered to an extent of 88%. The same process using aqueous ethanol as solvent and a 16-hr reflux period led to a 79% recovery of starting material. [n] RT = room temperature.

TABLE II

N-ALKYLARYLSULFONAMIDE (*cf.* **5**) BY HYDROLYSIS AND DECARBOXYLATION OF ETHYL *N*-(ALKYL)ARYLCARBAMATE (*cf.* **4**)

$$ArSO_2N(COOC_2H_5)R \longrightarrow ArSO_2NHR$$

Carbamate (R), g (mmol)	NaOH [and solvent (ml)]	Time, hr; temp[k]	Yield of product, %[a]
$BrCH{=}CHCH_2-$,[b] 3.5 (10)	2.9 g [C_2H_5OH (400) + H_2O (200)]	21; RT[c]	93[b]
p-$BrC_6H_4CH_2-$,[d] 0.40 (1.0)	3% aq NaOH (10) [C_2H_5OH (15) + THF (5)]	15½; RT[e]	85
$C_6H_5CH_2-$,[d] 1.7 (5.2)	1% aq NaOH (100) [C_2H_5OH (200)]	17½; stir[f] RT	83
p-$NO_2C_6H_4CH_2-$,[b] 1.5 (4.1)	5% aq NaOH (40) [THF (15)]	20½; stir[g] RT	38[b]
$C_6H_5CH{=}CHCH_2-$,[d] 0.24 (0.69)	1% alc NaOH (15)	4; reflux[h]	78
$CH_3CH_2CH_2CH_2-$[d]	1% alc NaOH	4; reflux[i]	74
$C_6H_5CH_2CH_2-$[d]	1% alc NaOH	4; reflux[j]	76
p-$C_6H_5C_6H_4COCH_2-$[d]	1% alc NaOH	4; reflux	<1

[a] No special effort was made to find optimal conditions. [b] Refers to the benzenesulfonyl derivative. [c] Most of the alcohol solvent was removed under reduced pressure, and the aqueous residue was acidified with 5% hydrobromic acid. The ether extract from this acid mixture was washed with water and with bicarbonate solution, dried, and stripped of all volatiles. The residual water-white, viscous *N*-bromoallylbenzenesulfonamide (2.6 g) was homogeneous by thin layer chromatography (R_f 0.26 with benzene); $n^{26}D$ 1.5712; ir (neat) 3300, 3075, 1625, 1325, 1165 cm^{-1}; nmr (CCl_4) δ 3.55 (q, 2, $J \cong 5$ Hz, CH_2N), 6.00 (m, 3, olefinic H's plus NH), 7.60 ppm (m, 5, aromatic H's). *Anal.* Calcd for $C_9H_{10}BrNO_2S$: C, 39.13; H, 3.62; N, 5.07. Found: C, 39.24; H, 3.54; N, 5.11. [d] Refers to the *p*-toluenesulfonyl derivative. [e] The reaction mixture, after acidification with 5% hydrochloric acid, was concentrated *in vacuo* at room temperature. Filtration afforded white crystals of analytically pure *N*-(*p*-bromobenzyl)-*p*-toluenesulfonamide; mp 115–117°; ir ($CHCl_3$) *ca.* 3500, 1330, 1160 cm^{-1}. *Anal.* Calcd for $C_{14}H_{14}BrNO_2S$: C, 49.42; H, 4.15. Found: C, 49.59; H, 4.36. [f] When alcohol was removed from the hydrolysis reaction mixture, the glistening white crystals of product were collected on the funnel (0.7 g, mp 109–111°). Acidification of the filtrate gave more of the same white material (0.4 g, mp 112–113°); ir ($CHCl_3$) 3360, 1332, 1160 cm^{-1}. *N*-Benzyl-*p*-toluenesulfonamide prepared from *p*-toluenesulfonyl chloride and benzylamine melted at 111–112°; the mixture melting point was 111–113°. [g] *N*-(*p*-Nitrobenzyl)-benzenesulfonamide, isolated as described in footnote *e*, showed mp 121.5–122.5°. In another preparation, crystallization of the product from aqueous methanol brought the melting point to 122–123.5°; ir ($CHCl_3$) 3390, 1520, 1348, and 1160 cm^{-1}. *Anal.* Calcd for $C_{13}H_{12}N_2O_4S$: C, 53.42; H, 4.14. Found: C, 53.28; H, 4.20. [h] The hydrolysis reaction mixture, diluted with 25 ml of water, was extracted thoroughly with benzene. The benzene solution was shaken with 5% aqueous sodium bicarbonate, 5% hydrochloric acid, and water, dried, and finally stripped of solvent. The residual white crystalline *N*-cinnamyl-*p*-toluenesulfonamide showed mp 110–111° [P. A. Briscoe, F. Challenger, and P. S. Duckworth, *J. Chem. Soc.*, 1755 (1956), and E. E. Schweizer, L. D. Smucker, and R. J. Votral, *J. Org. Chem.*, **31**, 467 (1966) report mp 108–109 and 110°]; ir ($CHCl_3$) 3500, 1330, 1160 cm^{-1}. [i] The isolation procedure followed footnote *h* except that ether was used for extraction instead of benzene. White *N*-butyl-*p*-toluenesulfonamide was obtained with mp 40–41°. A sample of the same material prepared from *p*-toluenesulfonyl chloride and butylamine and crystallized from aqueous methanol melted at 40–42° both before and after mixing with the hydrolysis product. [j] By following essentially the same procedure as given in footnote *i*, *N*-phenethyl-*p*-toluenesulfonamide was obtained as white needles, mp 65–66° [G. R. Proctor and R. H. Thomson, *J. Chem. Soc.*, 2302 (1957), and M. S. Kharasch and H. M. Priestley, *J. Amer. Chem. Soc.*, **61**, 3425 (1939), report mp 66 and 67°]; ir ($CHCl_3$) *ca.* 3400, 1330, 1160 cm^{-1}. [k] RT = room temperature.

g, 0.13 mol) with sodium (3.0 g, 0.13 g-atom) dissolved in methanol (750 ml); ir 1175 and 1375 (SO_2N) and 1660 cm^{-1} (C=O).

Anal. Calcd for $C_9H_{10}NNaO_4S$: C, 43.03; H, 3.98. Found: C, 43.30; H, 4.09.

Crystallization raised the melting point to 221–223°. Adding hydrochloric acid to an aqueous solution of the sodium derivative regenerated ethyl *N*-(benzenesulfonyl)carbamate, mp 108.5–109.5°.

The sodio derivative of ethyl *N*-(*p*-toluenesulfonyl)carbamate was prepared in 95% yield in a manner analogous to that used with the phenyl compound.

Alkylation of Sodio Derivatives 3.—Generally the sodio derivative was stirred with the alkyl bromide (in slight molar deficiency) in solvents such as methanol, aqueous ethanol, and dimethyl sulfoxide for periods ranging from 2 hr to 2 days. In most of the preparations, water was added after the reaction period, and the product was collected by filtration or by extraction. Table I gives details.

***N*-Alkylarylsulfonamides (5).**—The carbamates **4** were hydrolyzed and decarboxylated by exposure to sodium hydroxide, generally with stirring. Acidification precipitated the monoalkyl sulfonamide **5**. Table II presents details.

1,3-Dibromopropene. A. By Allylic Bromination of 1-Bromopropene.—According to its gas–liquid chromatographic assay, the 1-bromopropene used here consisted of one part cis material and eight parts trans. A mixture of 1-bromopropene (100 g, 0.83 mol), *N*-bromosuccinimide (147 g, 0.83 mol) and benzoyl peroxide (0.61 g) in carbon tetrachloride (750 ml) was boiled and stirred for for 2 hr under a blanket of nitrogen. The cooled mixture was filtered, and the filtrate was fractionated through a short vacuum-jacketed Vigreux column. The product, 1,3-dibromopropene, weighed 105 g (64%), boiled at 62–69° (30 mm) [lit.[6] bp 60–66° (25 mm)], and showed two peaks in gas–liquid chromatography with retention times the same as those from the dehydration procedure.

B. From 1,3-Dibromo-2-hydroxypropane.—Phosphorus pentoxide (9.8 g, 0.069 mol) was added in small portions over a 3-hr period to 1,3-dibromo-2-hydroxypropane (10.0 g, 0.040 mol) in a moisture-protected flask. The mixture was stirred during the addition until, when most of the reagent was in, the increased viscosity made stirring impossible. After standing for 0.5 hr at room temperature, the mixture was warmed on the steam bath for 1 hr and then allowed to cool. Ice (250 g) was added followed by 5% aqueous sodium hydroxide until the mixture was basic. Extraction with ether gave a solution of the crude product, which was rinsed three times with water, twice with 2 *N* hydrochloric acid, several times with saturated aqueous bicarbonate, finally with water, and was then dried with sodium sulfate. Fractionation through a 6-in. Vigreux column gave 1.9 g (21%) of the desired 1,3-dibromopropene, $n^{26}D$ 1.5600 (lit.[6] $n^{25}D$ 1.552–1.557), bp 150–156° (lit.[7] bp 156°).

Anal. Calcd for $C_3H_4Br_2$ (cis and trans): C, 18.00; H, 2.00; Br, 80.00. Found: C, 18.02; H, 2.02; Br, 80.03.

The 1,3-dibromopropene, as a cis–trans mixture, showed two peaks of roughly equal area in gas–liquid chromatography; ir (CCl_4) 3070 and 3080 (RCH=CHR), 1620 cm^{-1} (RCH=CHBr); nmr (CCl_4) δ 3.95 (m, 2, CH_2Br), 6.40 ppm (m, 2, olefinic H's).

Dehydration of 1,3-dibromo-2-hydroxypropane with phosphorus oxybromide[7] instead of phosphorus pentoxide offered no advantage.

A higher fraction (2.1 g, 17%) proved to be 1,2,3-tribromopropane, $n^{26}D$ 1.5800 (lit.[8] $n^{18}D$ 1.584), bp 220° (lit[7] bp 220°), nmr (CCl_4) δ 3.85 (d, 4, J = 3 Hz, $2CH_2Br$), 4.30 ppm (quintet, 1, J = 3.0 Hz, CHBr), and was homogeneous according to gas–liquid chromatography.

Anal. Calcd for $C_3H_5Br_3$: C, 12.81; H, 1.78; Br, 85.41. Found: C, 12.84; H, 1.80; Br, 85.45.

1,3-Dibromopropene with the Sodio Derivative of Benzenesulfonamide.—A mixture of 1,3-dibromopropene (10 g, 0.050 mol), benzenesulfonamide (12 g, 0.075 mol), sodium hydroxide

(6) Compare A. T. Bottini, B. J. King, and J. M. Lucas, *J. Org. Chem.*, **27**, 3688 (1962), who utilize the procedure of F. L. Greenwood, M. D. Kellert, and J. Sedlak, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 108, for the allylic bromination of 2-heptene.

(7) J. v. Braun and M. Kuhn, *Chem. Ber.*, **58**, 2168 (1925). Stanley M. Klainer and Joseph Casella contributed to developing this preparation of 1,3-dibromopropene, which develops less tar and shows better reproducibility than the preferred phosphorus oxybromide method of Braun and Kuhn.

(8) I. M. Heilbron, Ed., "Dictionary of Organic Compounds," Vol. 3, Oxford University Press, New York, N. Y., 1934, p 809.

(2.0 g, 0.050 mol), water (400 ml), and 95% alcohol (700 ml) was stirred for 18 hr. After several separation steps, the only alkali-soluble material that could be identified was unchanged benzenesulfonamide (0.8 g). Other products included a trace of solid (40 mg) whose melting point (123–125°) and infrared absorption spectrum agreed with those of diphenyl sulfone; a trace of oil whose R_f value suggested its identity as unchanged 1,3-dibromopropene; 3.7 g (19%) of *N*,*N*-di(3-bromallyl)benzenesulfonamide with R_f (benzene) 0.58 and with $n^{25}D$ 1.5801; and 3.1 g (15%) of *N*,*N*-di(3-bromallyl)benzenesulfonamide with R_f (benzene) 0.28 and with $n^{22}D$ 1.5704. The absorption curves for the last two materials were essentially the same, both showing ir (neat) 3075, 1613, 1350, 1170 cm^{-1}; nmr (CCl_4) δ 3.82 (q, 4, J = 4 Hz, $2CH_2N$), 6.15 (m, 4, olefinic H's), and 7.60 ppm (m, 5, aromatic H's). A roughly 1:1 mixture of the last two materials was analyzed.

Anal. Calcd for $C_{12}H_{13}Br_2NO_2S$: C, 36.46; H, 3.29; Br, 40.51. Found: C, 36.42; H, 3.33; Br, 40.70.

1,3-Dibromopropene with the Silver Derivative of Benzenesulfonamide.—The silver salt was prepared[9,10] by adding silver nitrate (0.25 g, 1.5 mmol) in 2 ml of water to a stirred solution of benzenesulfonamide (0.2 g, 1.5 mmol) and sodium hydroxide (0.6 g) in 2 ml of water. The resulting brown-yellow silver derivative of benzenesulfonamide was collected, washed with 95% alcohol and ether, and dried in a desiccator. The derivative weighed 0.33 g and showed mp 220–230° dec.

A heterogeneous mixture of 1,3-dibromopropene (0.2 g, 1 mmol), the silver derivative (0.32 g, 1.2 mmol), and ether (45 ml) was stirred at room temperature for 16 hr. Processing the reaction mixture afforded no sign of *N*-(3-bromallyl)benzenesulfonamide. According to thin layer chromatographic evidence, the viscous oily product contained *N*,*N*-di(3-bromallyl)benzenesulfonamide. This was substantiated by recovery of the same material from column chromatography (neutral alumina) and comparing its nmr curve with the corresponding material obtained from the sodio derivative. The neat crude oil before separation showed an ir peak at 3200 cm^{-1}, an indication that a propargyl group might be present.

(9) A. Hantzsch and E. Voegelen, *Chem. Ber.*, **34**, 3142 (1901).
(10) J. Casella, unpublished work at Boston University.

Registry No.—2 (Ar = Ph), 32111-09-4; **2** (Ar = $C_6H_4CH_3$-*p*), 5577-13-9; **3** (Ar = Ph), 32111-11-8; **4** (Ar = Ph, R = CH_2CH=$CHBr$), 32111-12-9; **4** (Ar = Ph, R = $CH_2C_6H_4NO_2$-*p*), 32207-42-4; **4** (Ar = Ph, R = CH_2COC_6HPh-*p*), 32111-13-0; **4** Ar = Ph, R = CH_2COOEt), 32120-94-8; **4** (Ar = $C_6H_4CH_3$-*p*, R = CH_2Ph), 32120-95-9; **4** (Ar = $C_6H_4CH_3$-*p*, R = $CH_2C_6H_4Br$-*p*), 32120-96-0; **4** (Ar = $C_6H_4CH_3$-*p*, R = CH_2CH=$CHPh$), 32120-97-1; **4** (Ar = $C_6H_4CH_3$-*p*, R = Bu), 32120-98-2; **4** (Ar = $C_6H_4CH_3$-*p*, R = CH_2CH_2Ph), 32120-99-3; **5** (Ar = Ph, R = CH_2CH=$CHBr$), 32121-00-9; **5** (Ar = $C_6H_4CH_3$-*p*, R = $CH_2C_6H_4Br$-*p*), 10504-96-8; **5** (Ar = $C_6H_4CH_3$-*p*, R = CH_2Ph), 1576-37-0; **5** (Ar = Ph, R = $CH_2C_6H_4NO_2$-*p*), 32121-03-2; **5** (Ar = $C_6H_4CH_3$-*p*, R = C_2CH=$CHPh$), 32121-04-3; **5** (Ar = $C_6H_4CH_3$-*p*, R = CH_2CH_2Ph), 5450-75-9; *cis*-1,3-dibromopropene, 32121-06-5; *trans*-1,3-dibromopropene, 32121-07-6; 1,2,3-tribromopropane, 96-21-9; *N*,*N*-di(3-bromoallyl)benzenesulfonamide, 32111-14-1.

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Nucleosides. LXXI. 3′-Amino-3′-deoxyhexopyranosyl Nucleosides. VI. Reactions of Some Mesyloxy Nucleosides[1]

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The reactions of variously mesylated 1-(3-acetamido-3-deoxy-β-D-glucopyranosyl)uracils were studied in order to examine the behavior of their neighboring groups. Alkaline treatment of the 2′,4′,6′-trimesylate (**5**) afforded the 4′,6′-dimesylate of the 2,2′-anhydromanno nucleoside **6** which by further alkaline treatment gave 1-(3-acetamido-2,6-anhydro-3-deoxy-4-*O*-mesyl-β-D-mannosyl)uracil (**7**) and 1-(3-acetamido-2,6-anhydro-3-deoxy-β-D-talosyl)uracil (**8**). The nmr spectra of **7** and **8** were consistent with the bicyclo[2.2.2]octane system for their carbohydrate moieties. Treatment of 1-(3-acetamido-3-deoxy-2,4-di-*O*-mesyl-6-*O*-trityl-β-D-glucosyl)-uracil (**12**) with alkoxide gave the 2,2′-anhydro derivative **13** which was detritylated and then hydrolyzed in alkali to the 4′-mesylate of 3′-acetamidomannosyluracil (**16**). When nucleoside **12** is detritylated first and then treated with alkali, 1-(3-acetamido-3-deoxy-β-D-talopyranosyl)uracil (**19**) was formed which was converted to its crystalline triacetate **20** and hydrogenated to the 5,6-dihydro derivative **21**. The unexpected chemical shift for the 2′-acetoxy signal in the nmr spectrum of **21** relative to **20** was observed and assigned unequivocally by the syntheses and spectral comparison with the analogous 4′,6′-di-*O*-deuterioacetylated derivatives **25** and **26**. Attempts to prepare a 2,6′-anhydro nucleoside **31** from 1-(3-acetamido-2-*O*-acetyl-3-deoxy-β-D-glucopyranosyl)uracil (**29**) *via* its 4′,6′-dimesylate **30** was not successful. The 6′-mesylate **32** of **29** was displaced by nucleophiles (iodide or benzoate) to afford compounds **33**. Treatment of the 6′-iodo analog **33b** with silver fluoride in pyridine afforded 1-(3-acetamido-2-*O*-acetyl-3,6-dideoxy-β-D-*xylo*-hex-5-enopyranosyl)uracil (**34**).

Previous reports[2] from this laboratory dealt with the syntheses of 3′-deoxy-3′-aminohexopyranosyl nucleosides from uridine as part of a program designed toward the synthesis of analogs of certain nucleoside antibiotics[2e] containing amino sugar moieties. It was found[2d] that treatment of 1-(3-acetamido-3-deoxy-2-*O*-mesyl-4,6-*O*-benzylidene-β-D-glucosyl)uracil (**1**) with sodium methoxide gave the crystalline 2,2′-anhydromannosyl nucleoside **2** in high yield as the sole product rather than the oxazoline derivative **3**

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(2) (a) K. A. Watanabe and J. J. Fox, *Chem. Pharm. Bull.*, **12**, 975 (1964); (b) *J. Org. Chem.*, **31**, 211 (1966); (c) K. A. Watanabe, J. Beranek, H. A. Friedman, and J. J. Fox, *ibid.*, **30**, 2735 (1965); (d) ref 2b; (e) J. J. Fox, K. A. Watanabe, and A. Bloch, *Progr. Nucleic Acid Res. Mol. Biol.*, **5**, 251 (1966).