Experimental

The Cyanoethylation of Diols.—To a 1-l., round-bottom, three-neck flask equipped with a condenser, stirrer, and thermometer there was added 2 moles of a diol (HOROH) and 30 g. of Dowex-1 resin, X-8 (8% cross-linked), in its hydroxide form (approx. 90 meq.). The ion exchange resin was observed to swell 250–300% of its dry volume in diols. To this mixture, 4 moles of acrylonitrile was added dropwise, with stirring, keeping the reaction temperature between 28–38° by external cooling. The addition required approximately 2 hr. The reaction mixture was stirred overnight at room temperature. The ionexchange resin was filtered off and the filtrate was washed several times with saturated sodium chloride solution. The washed filtrate, which was now essentially the crude product, was a yellowish oil. It was purified by distillation in vacuum. The following compounds were prepared:

Bis(β-cyanoethoxy)ethane-1,2 was prepared from ethylene glycol, yield: 93.5%. It was a faintly yellow oil, b.p.: lit., 158°/2 mm.[12]; Found: 155–161°/0.2–0.3 mm.; infrared peaks: 1125 cm.$^{-1}$, 2250 cm.$^{-1}$.

Anal. Calcd. for $C_8H_{12}N_2O_2$: N, 16.67. Found: N, 16.97.

Bis(β-cyanoethoxy)butane-1,4 was prepared from butanediol-1,4,yield: 81.1%. It was a faintly yellow oil, b.p. 172–174°/0.05–0.1 mm.; infrared peaks: 1125 cm.$^{-1}$, 2250 cm.$^{-1}$.

Anal. Calcd. for $C_{10}H_{16}N_2O_2$: N, 14.28. Found: N, 14.49.

The Carbamylethylation of Diols.—In carbamylethylation, a solvent was used to dissolve the solid alkylating agent acrylamide. In order for the reaction to occur, the solvent must be a swelling agent for the ion exchange resin. *t*-Butyl alcohol was found to be suitable for this purpose since it was both inert to acrylamide and a swelling agent for Dowex-1 resin. Because of the initial diol content, the solution of the reactants in *t*-butyl alcohol was observed to swell the ion-exchange resin to a greater extent than that of the products.

To a 1-l., three-neck, round-bottom flask, fitted with condenser, thermometer, and stirrer there was charged 1 mole of a diol, 2 moles of acrylamide, and 100–200 g. of *t*-butyl alcohol. The mixture was warmed to 50° with stirring whereupon a solution was formed. To this solution there was added 30 g. of Dowex-1 resin, X-8, in its hydroxide form. After about 20 min. of stirring, the exothermic initial reaction raised the reaction temperature to 60–65°. The reaction mixture was held at 50–60° with stirring for an additional 20 hr. The solution was filtered with suction; the filtrate was concentrated *in vacuo;* and the residue, a yellow oil, was poured into excess acetone and chilled in a refrigerator overnight whereupon the product precipitated as white crystals. The crystals were collected, washed with acetone, recrystallized from dioxane or *t*-butyl alcohol, and dried. The following are the compounds prepared:

Bis(β-carbamylethoxy)diethyl ether was prepared from diethylene glycol. Yield: 60%; m.p.: lit., 103–104°[12]; Found: 94.5–96°.

Anal. Calcd. for $C_{10}H_{20}N_2O_5$: C, 48.39; H, 8.06; N, 11.28. Found: C, 48.55; H, 8.20; N, 11.4.

Bis(β-carbamylethoxy)pentane-1,5 was prepared from 1,5-pentanediol. Yield: 61%; m.p. 119.5–120°.

Anal. Calcd. for $C_{11}H_{22}N_2O_4$: C, 53.66; H, 9.00; N, 11.37. Found: C, 53.94; H, 9.13; N, 11.59.

Bis(β-carbamylethoxy)triethyl ether was prepared from triethylene glycol. Yield: 52%; m.p. 93.5–94.5°.

Anal. Calcd. for $C_{12}H_{24}N_2O_6$: C, 49.32; H, 8.22; N, 9.59. Found: C, 49.30; H, 8.38; N, 9.59.

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[12] H. A. Bruson and T. W. Riener, *J. Am. Chem. Soc.*, **65**, 23 (1943).

Pyrolysis of Dibenzyl Sulfones

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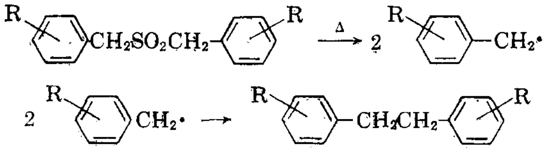
Sulfones are among the most stable organic compounds. Most sulfones can be distilled at atmospheric pressure with no decomposition. Since the sulfur atom is already fully oxidized, oxidations can be carried out at other sites on the molecule without affecting the sulfone group. The sulfone linkage is also not affected by acids and bases at moderate temperatures.

In spite of this stability, there are recorded examples of the decomposition of sulfones. Dibenzyl sulfone has been reported[1] to pyrolyze at 290° to yield stilbene and toluene as sole products. Ingold[2] has described the decomposition of dibenzyl sulfone. Once again the products isolated included stilbene and toluene. The cyclic sulfone formed by the reaction of two moles of a diazo compound with sulfur dioxide decomposes to form an olefin.[3] Cava[4] has reported that 1,3-dihydroisothianaphthene (I) on pyrolysis forms *o*-xylene, benzocyclobutene (II), and 1,2,5,6-dibenzo-1,5-cyclooctadiene (III).

Recently, LaCombe[5] at Union Carbide Chemicals Co. has pyrolyzed benzyl isopropyl sulfone and obtained a mixture of isobutylbenzene, sulfur dioxide, toluene, bibenzyl, and propylene.

In this laboratory, pyrolyses of dibenzyl sulfones at low pressures and temperatures of 600–700° have given high yields of the corresponding bibenzyls. The following sulfones have been prepared and pyrolyzed: dibenzyl sulfone, di-*p*-xylyl sulfone, bis(4-methylnaphthyl-1-methyl) sulfone, bis(4-isopropylbenzyl) sulfone, and bis(4-benzylbenzyl) sulfone. The mechanism of the reaction is believed to be cleavage of the sulfone to benzyl radicals with elimination of sulfur dioxide and subsequent coupling of the radicals:



This sulfone pyrolysis is a new method of synthesis of symmetrical diarylethanes. It is useful, also, for producing benzyl and substituted benzyl free radicals cleanly and in high yields.

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[1] E. Fromm and O. Achert, *Ber.*, **36**, 534 (1903).

[2] C. K. Ingold and J. A. Jessop, *J. Chem. Soc.*, 708–713 (1930).

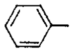
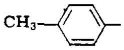
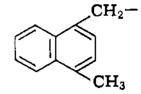
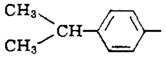
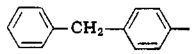
[3] L. V. Vargha and E. Kovacs, *Ber.*, **75**, 794 (1942).

[4] M. P. Cava and A. A. Deana, *J. Am. Chem. Soc.*, **81**, 4266 (1959).

[5] E. M. LaCombe and B. Stewart, *J. Am. Chem. Soc.*, **83**, 3457 (1961).

TABLE I

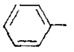
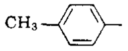
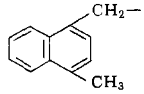
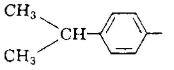
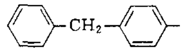
PREPARATION OF SULFONES (RCH$_2$SO$_2$CH$_2$R)[a]

R	Yield,[b] %	M.P.[c]	C, %[f]		H, %[f]		S, %[f]	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
	78	148–149[d]						
	35	201–202[e]						
	60	242–246	77.01	77.08	5.88	6.05	8.56	8.43
	90	143–144	72.72	72.76	7.88	8.12	8.69	10.01
	90	212–214	78.83	78.84	6.10	6.21	7.51	7.27

[a] The sulfones were all prepared by the peracetic acid oxidation of sulfides derived from the reaction of the appropriate chloromethyl compound with sodium sulfide. [b] Based on R—CH$_2$Cl. [c] Uncorrected. [d] Reported: 151–151.5°[6]; 151.0°[7]; 149.5°.[8] [e] Reported: 197°.[9a,b] [f] Analyses by Schwarzkopf Microanalytical Laboratory.

TABLE II

PYROLYSIS OF SULFONES (RCH$_2$SO$_2$CH$_2$R) TO DIARYLETHANES (RCH$_2$CH$_2$R)

R	Pyrolysis Temp.	Pressure, Mm.	Yield, %	M.P.[a]	C, %[e]		H, %[e]	
					Calcd.	Found	Calcd.	Found
	650	0.1	91	52.5[b]				
	600–700	0.1	86	81–82[c]				
	600	0.3	52	154–155	92.90	93.02	7.09	7.28
	660	0.3	66	57.5–58.0[d]	90.22	90.10	9.77	9.90
	650	0.1	80	96–97	92.82	93.01	7.19	7.21

[a] Uncorrected. [b] Reported: 52°.[10] [c] Reported: 82.3°, 85°.[11] [d] Reported: 58.[12] [e] Analyses by Schwarzkopf Microanalytical Laboratory.

The sulfones were prepared by the general method of Overberger,[6] *i.e.*, the reaction of the appropriate benzyl halide with sodium sulfide, and peracetic acid oxidation of the resulting dibenzyl sulfide to the sulfone. The preparation and pyrolysis of the sulfones are described in the Experimental and in Tables I and II.

Experimental

Sulfone Preparation.—The five sulfones reported in this work were prepared by the general method of Overberger, Ligthelm, and Swire[6] from the corresponding benzyl chloride. This procedure consisted of treating the chloride with sodium sulfide nonahydrate in refluxing ethanol for several days, isolating the sulfide and then oxidizing the sulfide to the sulfone with peracetic acid at 60–90°. Yields are given in Table I as well as analyses for compounds not previously reported. Two halides which were not available commercially, *p*-isopropylbenzyl chloride and *p*-benzylbenzyl chloride were prepared according to the method of Baker and Nathan[13] and Maquin and Gault,[14] respectively.

Sulfone Pyrolysis.—The general procedure for the pyrolysis of the benzyl sulfones to the diarylethane is shown by the description of the decomposition of the simplest in the series, dibenzyl sulfone. Further details are given in Table II.

The equipment used to pyrolyze the sulfones consisted of a Vycor tube 30 in. long and 1 in. in diameter closed at one end. The open end was attached to a cold finger which was in turn connected to two traps cooled with a Dry Ice–acetone bath. The second trap was connected to a vacuum pump. The Vycor tube was enclosed within three electric furnaces; a 4-in. furnace which was used to distill the sulfone (at a temperature 50° above the melting point) and two additional furnaces which were actually the pyrolyzing units. The weighed sample which was to undergo pyrolysis was placed in a ceramic boat at the closed end of the tube, the pump turned on, and the heating units brought up to temperature. Thirty minutes were usually sufficient to distill a 1-g. sample through the furnaces.

Dibenzyl sulfone (1.55 g., 6.4 mmoles) was pyrolyzed at a pressure of 0.1 mm. and a temperature of 650°. The re-

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(6) C. G. Overberger, S. P. Ligthelm, and E. A. Swire, *J. Am. Chem. Soc.*, **72**, 2856 (1950).

(7) H. Rheinbolt and E. Giesbrecht, *J. Am. Chem. Soc.*, **68**, 973 (1946).

(8) G. Vogt and A. Henniger, *Ann.*, **165**, 362 (1873).

(9) (a) Z. Martynowicz, *Chem. Abstr.*, **5**, 1600 (1911); (b) Z. Martynowicz, *Chem. Zentr.*, **II**, 1048 (1910).

(10) "Dictionary of Organic Compounds," Vol. II, Heilbron, Oxford Press, New York, 1953, p. 61.

(11) Ref. 10, p. 449.

(12) Beilstein's "Handbuch der Organischen Chemie," Vol. 5, Verlag Julius Springer, Berlin, 2nd ed., p. 528.

(13) J. W. Baker and W. S. Nathan, *J. Chem. Soc.*, 1840 (1935).

(14) C. Maquin and H. Gault, *Compt. rend.*, **234**, 629–631 (1957).

covered material amounted to 1.04 g. (91% yield of bibenzyl). Recrystallization from ethanol gave a product, m.p. 52.5° (reported[10] 52°). A mixed melting point with an authentic sample of bibenzyl showed no depression. The infrared spectra were identical.

Alkaline Degradation of Dihydrostreptomycin

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Wolfrom and Polglase[1] have reported the preparation of a compound, designated decaacetyldideguanyldihydrostreptomycin, from dihydrostreptomycin, by alkaline degradation followed by acetylation. The intermediate compound, herein designated dideguanyldihydrostreptomycin was not isolated.[1] This latter compound was required for studies on the mechanism of action of streptomycin,[2] and the present note is concerned with its preparation and characterization.

Experimental

Dideguanyldihydrostreptomycin Bicarbonate.—Dihydrostreptomycin sesquisulfate (5.0 g.) was dissolved in 20 ml. of water and 250 ml. of a saturated solution of barium hydroxide was added. The barium sulfate precipitate was filtered off and the filtrate was refluxed for 28 hr. (until evolution of ammonia had ceased). The straw-colored reaction mixture was cooled and the excess of barium hydroxide was neutralized with carbon dioxide gas. The solution was filtered and concentrated to a sirup. The sirup was dissolved in warm methanol and filtered. Crystalline material (2.48 g., 68%) was obtained following cooling overnight. A portion of the product was recrystallized from hot methanol and dried at room temperature for analysis. M.p., 156°; $[\alpha]^{24}\text{D}$ −121° (*c* 1, water).

Anal. Calcd. for $(C_{19}H_{37}O_{12}N_3)_2 \cdot H_2CO_3$: C, 44.2; H, 7.2; N, 7.9. Found: C, 44.4; H, 7.4; N, 7.9.

Acetylation with acetic anhydride and pyridine gave the decaacetate (m.p. 259–260°) described previously.[1]

Dideguanyldihydrostreptomycin.—This was obtained from the bicarbonate derivative described above following heating for 2 hr. at 110° *in vacuo*.

Anal. Calcd. for $C_{19}H_{37}O_{12}N_3$: C, 45.6; H, 7.5; N, 8.3; N—CH_3, 5.8; C—CH_3, 5.4. Found: C, 45.3; H, 7.7; N, 8.1; N—CH_3, 5.0; C—CH_3, 5.6.

Dideguanyldihydrostreptomycin Trihydrochloride.—Dideguanyldihydrostreptomycin bicarbonate (2.0 g.) was suspended in 25 ml. of cold methanol and concd. hydrochloric acid was added dropwise until the mixture was acidic to Congo Red paper. The solution was filtered and seven volumes of acetone were added. The amorphous precipitate was collected by centrifuging, washed with acetone, and dried; yield 2.1 g. (91%).

Anal. Calcd. for $C_{19}H_{37}O_{12}N_3 \cdot 3HCl$: N, 6.9. Found: N, 6.9.

In a potentiometric titration of dideguanyldihydrostreptomycin trihydrochloride, 3 equivalents of sodium hydroxide were consumed. The two primary amino groups are weakly basic (*pK* about 6.3). The secondary amino group had a *pK* of 7.9, corresponding to the *pK* of this group in streptomycin.[3]

Acknowledgment.—This work was supported by a grant (M.T. 750) from the National Research Council of Canada.

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(1) M. L. Wolfrom and W. J. Polglase, *J. Am. Chem. Soc.*, **70**, 2835 (1949).

(2) W. J. Polglase, to be published.

(3) J. Fried and O. Wintersteiner, *J. Am. Chem. Soc.*, **69**, 79 (1947).

The Nitration of 2′,5′-Dialkoxyacetophenones[1]

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The compositions of the products obtained from nitration of 2′, 5′-diethoxy- and 2′, 5′-di-*n*-butoxyacetophenone have been determined and compared with those previously reported for 2′,5′-dimethoxyacetophenone.[2]

For nitrations carried out at −20° in concentrated nitric acid, all three 2′,5′-dialkoxyacetophenones yielded mixtures of the 4′- and 6′-nitro derivatives, with the latter accounting for approximately three fourths of the product (see Table I). A small increase in the proportion of 4′-substitution with increasing alkoxy group size was observed. The results are consistent with a direct attack on the ring by the electrophilic reagent[3] and with preferential stabilization of the transition state involved in 6′-substitution through conjugation of the 2′-alkoxy group with the carbonyl side chain.[2]

Table I

Nitration[a] of 2′,5′-Dialkoxyacetophenones in Concentrated Nitric Acid

Run	Alkoxy Groups	%, 4′Nitro[b]	%, 6′-Nitro[b]
A[c]	Dimethoxy	21	79
B[c,d]	Dimethoxy	23	77
1	Diethoxy	28 (26)	72 (74)
2[e]	Diethoxy	27	73
3	Di-*n*-butoxy	26	74
4	Di-*n*-butoxy	31 (31)	69 (69)

[a] At −20°; addition and aging periods 4 and 2.5 hr., respectively, unless otherwise noted. [b] Data in parentheses based on infrared analyses; all others based on alumina chromatography. [c] Ref. 2. [d] Addition and aging periods 90 and 15 min., respectively. [e] Addition and aging periods 1 and 2.5 hr., respectively.

Product compositions for nitrations carried out at −20° in a mixture of nitric and sulfuric acids

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(1) Research supported in part by National Science Foundation Grant G7358.

(2) C. A. Howe, C. R. Hamel, E. D. Stedman, and F. Hyman, *J. Org. Chem.*, **25**, 1245 (1960).

(3) An increase in the proportion of 6′ substitution with increasing alkoxy group size would have provided evidence for attack *via* the carbonyl side chain [see K. L. Nelson, *J. Org. Chem.*, **21**, 153 (1956)].