Preparation of 1-D-Glycopyranosylcytosines.—The compounds listed in Table I were prepared by the method of Hilbert and Jansen[11] with a slight change in conditions. It was found that if the reactants were heated in a sealed tube at 90° instead of 80°, crystallization occurred on the walls of the hot tube. When crystals ceased to form the reaction was considered complete. The yields in these reactions were practically quantitative. The free cytosine nucleosides of xylose and arabinose were crystallized from 95% ethanol. Galactopyranosylcytosine was isolated as the hydrochloride in the following manner: The sealed tube was cooled, opened, and the contents poured into a flask and concentrated to a sirup which was taken up in hot 95% ethanol. Concentrated hydrochloric acid was added dropwise until the solution was decidedly acidic whereupon it was cooled slowly and placed in an ice-box overnight. Precipitation occurred in the form of large, colorless crystals. A similar procedure was used for the isolation of the hydrochloride of 1-D-glucopyranosylcytosine. The hydrochloride salts of the other nucleosides listed in Table I were made directly from the free cytosine nucleosides by dissolving them in hot aqueous alcohol, adding concentrated hydrochloric acid dropwise, and cooling. The products crystallized immediately.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Diels–Alder Reactions of α,β-Unsaturated Sulfonyl Compounds

BY H. R. SNYDER, HUGH V. ANDERSON AND DONALD P. HALLADA

Ethylenesulfonic acid, ethylenesulfonyl chloride and methyl vinyl sulfone have been studied as dienophiles in the Diels–Alder reaction. Ethylenesulfonic acid does not react with anthracene; as a strong acid it induces the polymerization of cyclopentadiene and 2,3-dimethyl-1,3-butadiene, rather than reacting with these substances in the Diels–Alder sense. Ethylenesulfonyl chloride is a very active dienophile; it enters into a rapid exothermic reaction with cyclopentadiene, 2,3-dimethyl-1,3-butadiene and isoprene. It reacts with butadiene under somewhat more vigorous conditions. The yields are excellent. The isoprene adduct is shown to be 1,2,5,6-tetrahydro-4-methylbenzenesulfonyl chloride by conversion of the morpholide to 4-toluenesulfomorpholide. Ethylenesulfonyl chloride is somewhat less reactive than maleic anhydride as shown by its failure to combine with anthracene or furan. Methyl vinyl sulfone is a less reactive dienophile than ethylenesulfonyl chloride, but it reacts with 1,3-butadiene, isoprene, 2,3-dimethyl-1,3-butadiene and cyclopentadiene to form the corresponding cyclohexene derivatives in good yields.

Previous reports of Diels–Alder condensations in which α,β-unsaturated sulfonyl compounds serve as dienophiles have concerned only *p*-tolyl vinyl sulfone and 1,1-dioxathia-2-cyclopentene[1,2]; the temperatures employed in reactions with such active dienes as cyclopentadiene and dimethylbutadiene were so high (about 150°) as to suggest that the sulfonyl function does not greatly enhance the dienophilic activity of an adjacent ethylenic group. Since theoretical considerations lead to the prediction of a substantial enhancement, we have examined the behavior of some of the simplest unsaturated sulfonyl compounds in the diene reaction; the present report deals with ethylenesulfonic acid, ethylenesulfonyl chloride and methyl vinyl sulfone.

Cyclopentadiene and 2,3-dimethyl-1,3-butadiene polymerized rapidly when ethylenesulfonic acid was added to their solutions in dioxane or glacial acetic acid. The polymerizations were not inhibited by hydroquinone. It is, of course, not surprising that the strong acid causes the polymerization of the active dienes. There was no evidence of reaction between anthracene and ethylenesulfonic acid, even when mixtures in acetic acid solution were heated for seven days.

In the absence of solvents, ethylenesulfonyl chloride entered into rapid exothermic reaction with cyclopentadiene, 2,3-dimethyl-1,3-butadiene and isoprene. The isoprene adduct was found to be the expected 1,2,5,6-tetrahydro-4-methylbenzenesulfonyl chloride, whose structure was proved by bromination and subsequent dehydrobromination of the morpholide to the known 4-toluenesulfomorpholide. The substituted cyclohexenesulfonyl chlorides which were formed by these reactions could be distilled *in vacuo*, without decomposition, to separate them from the small amount of hydroquinone which was employed to inhibit polymerization of the reactants. The yields, after distillation, were in the neighborhood of 90%. The reaction of ethylenesulfonyl chloride with butadiene proceeded in similar yield but required more strenuous conditions.

Several attempts to obtain an adduct from ethylenesulfonyl chloride and anthracene were made. The conditions tried ranged from refluxing in xylene solution for three hours to standing at room temperature in xylene solution for several weeks, but only anthracene and ethylenesulfonyl chloride were found in the reaction mixtures. No adduct could be isolated by distillation from an equimolar mixture of furan and ethylenesulfonyl chloride which had remained at room temperature for 24 hours. An attempt to dehydrate[3] any adduct which might have formed in such a reaction resulted in the formation of an intractable tar.

(1) K. Alder, H. F. Rickert and E. Windemuth, *Ber.*, **71**, 2451 (1938).

(2) The present work was almost complete when the condensation of methyl ethylenesulfonate with cyclopentadiene was reported by A. Lambert and J. D. Rose [*J. Chem. Soc.*, 46 (1949)]. For examples of condensations in which the dienophile contains both a carbonyl and a sulfonyl group see E. A. Fehnel and M. Carmack, THIS JOURNAL, **70**, 1813 (1948).

(3) M. G. Van Campen and J. R. Johnson, THIS JOURNAL, **55**, 430 (1933).

Although maleic anhydride adds to the diene formed by the rearrangement of 2-ethyl-2-hexenalaniline,[4] ethylenesulfonyl chloride caused decomposition of this material. The decomposition became violent if cooling was inadequate. A sticky tar deposited from the benzene solution in which the reaction was run. Ethylenesulfonyl chloride did not react with either *cis*- or *trans*-1-cyano-1,3-butadiene.

Methyl vinyl sulfone showed less reactivity toward 1,3-butadiene, isoprene, 2,3-dimethyl-1,3-butadiene and cyclopentadiene than did ethylenesulfonyl chloride. In most of the experiments it was necessary to add from 25–75 weight per cent. of benzene to obtain a homogeneous reaction mixture so that an exact comparison between the reactivities of the two dienophiles was not made. Methyl vinyl sulfone and the above dienes gave the corresponding adducts in yields which were in the neighborhood of 80%.

Experimental[5,6]

Preparation of Ethylenesulfonic Acid and Ethylenesulfonyl Chloride.—Ethylenesulfonic acid was prepared by the method of Kohler[7] from ethane-1,2-disulfonyl chloride. The acid was distilled; b.p. 125–130° (0.9 mm.) [lit.[8] b.p. 125° (1 mm.)].

Ethylenesulfonyl chloride was prepared from ammonium ethylenesulfonate by the method of Landau.[9] Ammonium ethylenesulfonate is an unstable material; it undergoes a change to an alcohol-insoluble material when kept in the absence of a solvent at room temperature for two weeks. Ethylenesulfonyl chloride was obtained in 45% yield as a colorless oil; b.p. 30–31° (1 mm.), $n^{20}D$ 1.4680 [lit.[9] 52–56° (10 mm.), $n^{20}D$ 1.4686].

1,2,5,6-Tetrahydrobenzenesulfonyl Chloride.—In a tightly stoppered pressure bottle were placed 5.6 g. (0.044 mole) of ethylenesulfonyl chloride and 3.9 g. (0.073 mole) of 1,3-butadiene. The reaction mixture was kept at room temperature for two days and in a 50°-bath for 20 hours.[10] After the excess butadiene had been allowed to escape, the residue was distilled under reduced pressure to give 1.1 g. (0.0087 mole) of ethylenesulfonyl chloride and 6 g. (93%) of a colorless oil, 1,2,5,6-tetrahydrobenzenesulfonyl chloride; b.p. 75° (0.35 mm.), $n^{20}D$ 1.5132.

Anal. Calcd. for $C_6H_9O_2SCl$: C, 39.88; H, 5.02. Found: C, 40.16; H, 5.10.

1,2,5,6-tetrahydrobenzenesulfonamide was formed from the sulfonyl chloride by treatment with dry ammonia. It was recrystallized from benzene; m.p. 95–95.5°.

Anal. Calcd. for $C_6H_{11}O_2SN$: C, 44.70; H, 6.88. Found: C, 44.97; H, 6.76.

3,4-Dimethyl-1,2,5,6-tetrahydrobenzenesulfonyl Chloride.—To 3.6 g. (0.044 mole) of 2,3-dimethyl-1,3-butadiene in a flask fitted with an efficient condenser was added 4.9 g. (0.04 mole) of ethylenesulfonyl chloride. An exothermic reaction caused the mixture to reflux gently. The reaction mixture was left overnight at room temperature and distilled under diminished pressure to give 6.7 g. (82%) of the sulfonyl chloride, a colorless oil; b.p. 107° (1.3 mm.), $n^{20}D$ 1.5127.

Anal. Calcd. for $C_8H_{13}O_2SCl$: C, 46.03; H, 6.28. Found: C, 46.20; H, 6.41.

The sulfonanilide was prepared by the Hinsberg method. 3,4-Dimethyl-1,2,5,6-tetrahydrobenzenesulfonanilide was recrystallized from 33% alcohol; m.p. 102–103°.

Anal. Calcd. for $C_{14}H_{19}O_2SN$: C, 63.36; H, 7.22. Found: C, 63.44; H, 7.34.

2,5-Methylene-1,2,5,6-tetrahydrobenzenesulfonyl Chloride.—In a small flask cooled by an ice–salt-bath was placed 12.6 g. (0.1 mole) of ethylenesulfonyl chloride. To this was added dropwise 6.3 g. (0.095 mole) of cold, freshly prepared cyclopentadiene.[11] A vigorous reaction as each drop was added caused some of the cyclopentadiene to be lost as vapor. After standing overnight, the reaction mixture was distilled under reduced pressure to give 10.4 g. (57%) of a colorless oil; b.p. 85.5° (0.4 mm.), $n^{20}D$ 1.5202. There remained in the distilling flask *ca.* 6 ml. of a dark viscous material which hardened to a rubbery solid. The distillate was analyzed.

Anal. Calcd. for $C_7H_9O_2SCl$: C, 43.64; H, 4.71. Found: C, 43.87; H, 4.66.

The sulfonyl chloride was converted to 2,5-methylene-1,2,5,6-tetrahydrobenzenesulfonamide with dry ammonia. The amide was recrystallized from benzene; m.p. 114–115°.

Anal. Calcd. for $C_7H_{11}O_2SN$: C, 48.53; H, 6.40. Found: C, 48.72; H, 6.42.

1,2,5,6-Tetrahydro-4-methylbenzenesulfonyl Chloride.—A solution of a few milligrams of hydroquinone in 6.8 g. (0.1 mole) of isoprene was placed in a 30-ml. flask fitted with a reflux condenser. To this solution was added 10 g. (0.079 mole) of ethylenesulfonyl chloride. An exothermic reaction caused the mixture to reflux gently for 40 minutes. The reaction mixture was allowed to stand at room temperature for 24 hours and then distilled through a five-inch Fenske column. There was obtained 14.6 g. (95%) of a colorless oil; b.p. 87° (0.8 mm.), $n^{20}D$ 1.5089.

Anal. Calcd. for $C_7H_{11}O_2SCl$: C, 43.18; H, 5.70. Found: C, 43.19; H, 5.73.

The sulfonamide was prepared by the dropwise addition of the sulfonyl chloride to a large excess of liquid ammonia. The residue left by the evaporation of ammonia was extracted with dry ether, and the sulfonamide was recrystallized from ether–petroleum ether (b.p. 40–41°); m.p. 104–105°.

Anal. Calcd. for $C_7H_{13}O_2SN$: C, 47.97; H, 7.48. Found: C, 47.92; H, 7.56.

1,2,5,6-Tetrahydro-4-methylbenzenesulfomorpholide.—To 14.0 g. (0.16 mole) of dry morpholine contained in a 50-ml. flask cooled in an ice-bath was added dropwise 4.0 g. (0.026 mole) of the sulfonyl chloride. The reaction mixture was allowed to warm to room temperature. After standing at room temperature for 24 hours, the mixture was treated with 100 ml. of concentrated hydrochloric acid. The insoluble product was collected on a filter and recrystallized from petroleum ether (b.p. 40–42°). The yield of white crystalline solid was 2.5 g. (50%); m.p. 79–81°.

Anal. Calcd. for $C_{11}H_{19}O_3SN$: C, 54.01; H, 7.74. Found: C, 54.14; H, 7.90.

Bromination of 1,2,5,6-Tetrahydro-4-methylbenzenesulfomorpholide.—A solution containing 2.0 g. (0.0082 mole) of the morpholide and 2.92 g. (0.0164 mole) of N-bromosuccinimide dissolved in 80 ml. of benzene was refluxed for 24 hours. The reaction mixture was cooled to 5° and the precipitated succinimide was removed by filtration. The solvent was removed under reduced pressure, leaving a brown residue which partially crystallized on standing.

Dehydrobromination of the Bromination Product from 1,2,5,6-Tetrahydro-4-methylbenzenesulfomorpholide to *p*-Toluenesulfomorpholide.—The crude, brown, partially crystallized bromination product was dissolved in 50 ml. of anhydrous pyridine, and the mixture was refluxed for 24 hours. The pyridine was removed under reduced pressure, and the brown residue was treated with 50 ml. of cold 15% hydrochloric acid. The crude product was collected on a filter. Successive recrystallizations from ethanol (charcoal) and petroleum ether (b.p. 40–42°) resulted in a white, crystalline product; m.p. 143–145° (lit.[12] m.p. 147°). The melting point of the compound showed no depression when admixed with an authentic sample of *p*-toluenesulfomorpholide. The infrared absorption spectrum of the product

(4) H. R. Snyder, R. B. Hasbrouck and J. F. Richardson, *ibid.*, **61**, 3558 (1940).

(5) Microanalyses by Mrs. Jane Wood, Miss Emily Davis and Miss Rachel Kopel. Infrared analysis by Miss Elizabeth Petersen.

(6) All melting points are corrected.

(7) E. P. Kohler, *Am. Chem. J.*, **19**, 733 (1897); **20**, 680 (1898).

(8) V. V. Alderman and W. E. Hanford, U. S. Patent 2,348,705, *C. A.*, **39**, 711 (1945).

(9) E. F. Landau, THIS JOURNAL, **69**, 1219 (1947).

(10) The reaction times allowed were convenient and were not minimum or optimum times.

(11) G. A. Perkins and A. O. Cruz, THIS JOURNAL, **49**, 518 (1927).

(12) J. Sand, *Ber.*, **34**, 2908 (1901).

derived from the isoprene adduct was identical with that of an authentic sample.

Preparation of Methyl Vinyl Sulfone.—The method of Buckley, Charlish and Rose[13] was used to prepare methyl vinyl sulfone from β-chloroethyl methyl sulfide.[14] The sulfone was distilled; b.p. 115–120° (19 mm.).

1,2,5,6-Tetrahydrophenyl Methyl Sulfone.—A solution of 3.5 g. (0.033 mole) of methyl vinyl sulfone and 3.7 g. (0.074 mole) of 1,3-butadiene in 5 ml. of benzene was placed in a pressure bottle and kept in a 50°-bath for 11 days. After the solvent had been removed, the reaction mixture was distilled under diminished pressure to give 1.5 g. of methyl vinyl sulfone. The residue was dissolved in benzene–petroleum ether (89–92°) from which it crystallized upon cooling. After three recrystallizations from this solvent, 1,2,5,6-tetrahydrophenyl methyl sulfone was obtained; m.p. 43–44°.

Anal. Calcd. for $C_7H_{12}O_2S$: C, 52.47; H, 7.55. Found: C, 52.57; H, 7.57.

3,4-Dimethyl-1,2,5,6-tetrahydrophenyl Methyl Sulfone.—A solution of 5 g. (0.047 mole) of methyl vinyl sulfone and 3.87 g. (0.047 mole) of 2,3-dimethyl-1,3-butadiene in 4 ml. of benzene was left at room temperature for 12 hours and on the steam-cone for four days. The solvent was removed under reduced pressure, and the residue was distilled. There was obtained 7.2 g. (81%) of 3,4-dimethyl-1,2,5,6-tetrahydrophenyl methyl sulfone; b.p. 129° (0.6 mm.). Cubic crystals formed slowly in the distillate until it had completely solidified. It was recrystallized from benzene–petroleum ether (89–92°); m.p. 73–73.5°.

Anal. Calcd. for $C_9H_{16}O_2S$: C, 57.41; H, 8.57. Found: C, 57.41; H, 8.63.

2,5-Methylene-1,2,5,6-tetrahydrophenyl Methyl Sulfone.—A mixture of 7.4 g. (0.07 mole) of methyl vinyl sulfone and 5.0 g. (0.075 mole) of cyclopentadiene began to reflux slowly after a brief induction period. The mixture was left at room temperature for four days and then heated on a steam-cone for 15 minutes. Distillation of the reaction mixture gave 10 g. (83%) of a pale yellow viscous liquid; b.p. 132–134° (1.3 mm.). This liquid crystallized in an ice-bath. The 2,5-methylene-1,2,5,6-tetrahydrophenyl methyl sulfone was recrystallized from benzene–petroleum ether (89–92°); m.p. 55–56°.

Anal. Calcd. for $C_8H_{12}O_2S$: C, 55.78; H, 7.02. Found: C, 55.96; H, 7.26.

Isoprene–Methyl Vinyl Sulfone Adduct.—A solution of 10 g. (0.094 mole) of methyl vinyl sulfone, 6.8 g. (0.1 mole) of isoprene, and a few milligrams of hydroquinone in 5 ml. of benzene was heated under reflux for ten days. The benzene was removed under reduced pressure, and the residue was distilled. There was recovered 5.5 g. of methyl vinyl sulfone. The adduct (5.9 g., 80.5% based on unrecovered methyl vinyl sulfone) was a colorless liquid; b.p. 125–126° (1.2 mm.), $n^{20}D$ 1.5066. Crystals formed in this liquid on cooling. They were separated from an oil and recrystallized from ether–petroleum ether (40–42°); m.p. 55–56°.

Anal. Calcd. for $C_8H_{14}O_2S$: C, 55.14; H, 8.10. Found: C, 54.97; H, 8.10. The oil was distilled to give a colorless liquid; $n^{20}D$ 1.5070. This material could not be induced to crystallize and is probably a mixture of isomers. It represented *ca.* 25% of the product.

Anal. Calcd. for $C_8H_{14}O_2S$: C, 55.14; H, 8.10. Found: C, 55.33; H, 8.39.

URBANA, ILL. RECEIVED JANUARY 22, 1951

(13) G. D. Buckley, J. L. Charlish and J. D. Rose, *J. Chem. Soc.*, 1514 (1947).

(14) "Organic Syntheses," Col. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 136.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Conversion of Cholestanone to Cholesterol[1,2]

BY WILLIAM G. DAUBEN AND JEROME F. EASTHAM

When the enol acetate of cholestenone was reduced with excess lithium aluminum hydride, four stenols were formed in the following yields: cholesterol (32%), epicholesterol (16%), Δ^4-cholestene-3β-ol (4%) and Δ^4-cholestene-3α-ol (4%). In addition to these cholestenols, cholestenone was obtained in 34% yield. Inverse addition, temperature variation (−15 to 100°) and quantity of hydride had little effect on the course of this reaction. The stereochemical results exhibited no similarity to those reported for the reduction of either Δ^4- or Δ^5-cholestenone.

Cholesterol specifically labeled with isotopic carbon could serve as a useful tool for the study of the metabolic fate of this sterol in the animal body. Recently, methods for the preparation of cholesterol labeled at carbon atom twenty-six[3] and for the preparation of cholestenone labeled at carbon atom three[4] were described. The desirability of employing a ring-labeled sterol in other studies has led to a search for a convenient method for the transformation of cholestenone (I) to cholesterol (II). A procedure for such a conversion has been reported by Reich and Lardon[5] but the method is rather long and the over-all yield quite low.

The conversion of (I) to (II) posed two distinct problems, namely, effecting the migration of the carbon–carbon double bond and the reduction of the carbonyl group. McKennis and Gaffney[6] demonstrated that lithium aluminum hydride reduces this carbonyl group to an approximately equimolar mixture of the α(IV) and β(V) isomers of Δ^4-cholestenol. Furthermore, Shoppee[7] recently showed that a similar reduction of the isomeric Δ^5-cholestenone proceeds in high yield but, in contra-distinction to the foregoing, mainly the β-isomer (cholesterol) is formed. With respect to the migration of the double bond (Δ^4 to Δ^5), it has been found that such a rearrangement does occur in the preparation of the enol acetate (VI) of cholestenone.[8] These considerations made reduction of (VI) appear as an interesting possible approach to the preparation of cholesterol from cholestenone.

Catalytic hydrogenation of enol esters is known to lead to hydrogenolysis of the acyloxy group[9] and, indeed, Inhoffen[10] has reported that catalytic hydrogenation of (VI) itself yielded only cholestane. Since the conclusion of the present investigation,

(1) This work was supported by a grant from the University of California Cancer Fund.

(2) A preliminary announcement of this work was reported in a Communication to the Editor, THIS JOURNAL, **72**, 2305 (1950).

(3) A. I. Ryer, W. H. Gebert and N. M. Murrill, *ibid.*, **72**, 4247 (1950); W. G. Dauben and H. L. Bradlow, *ibid.*, **72**, 4248 (1950).

(4) R. B. Turner, *ibid.*, **72**, 579 (1950).

(5) H. Reich and A. Lardon, *Helv. Chim. Acta*, **29**, 671 (1946).

(6) H. McKennis and G. W. Gaffney, *J. Biol. Chem.*, **175**, 217 (1948).

(7) C. W. Shoppee and G. H. R. Summers, *J. Chem. Soc.*, 687 (1950).

(8) V. Westphal, *Ber.*, **70**, 2128 (1937).

(9) E. J. Roll and R. Adams, THIS JOURNAL, **53**, 3469 (1931).

(10) V. H. Inhoffen, G. Stoeck, G. Kolling and U. Stoeck, *Ann.*, **568**, 52 (1950).