lar aluminum with a saturated solution of mercuric chloride acidified with hydrochloric acid. After amalgamation had occurred (about 1 min.), the solvent was decanted and the amalgam was washed by decantation twice with acetone, twice with ether, and then twice with peroxide-free 1,2-dimethoxyethane.

The reduction was carried out by adding to the amalgam prepared above a solution of 1 g. of 1-deoxy-1-diazo-*keto*-D-*galacto*-heptulose pentaacetate[7] in 30 ml. of peroxide-free 1,2-dimethoxyethane. Immediate reaction occurred as evidenced by bubbling and the formation of an orange-gold color on the surface of the amalgam. One very small drop of water was added and the mixture was stirred at room temperature for 24 hr. The mixture was then filtered and the dark colored residue was washed thoroughly with chloroform. Upon removing the solvent from the combined filtrate and washings a dark sirup was obtained. Some of the color was removed by passing a chloroform solution of the sirup through a column (0.9 × 8 cm.) of Magnesol[15]–Celite[16] (5:1 by wt.) followed by 15 ml. of pure chloroform. The yellow effluent was dissolved in 10 ml. of methanol and again concentrated to a sirup. This treatment was repeated. A solution of the sirup in 10 ml. of methanol was then passed through a Darco G60[17] column (0.9 × 8 cm.) followed by 15 ml. of methanol. The colorless effluent was evaporated in a desiccator, over sulfuric acid and under reduced pressure, to a light yellow sirup. The addition of methanol to this sirup and refrigeration gave beautiful bright yellow crystals which were removed by filtration and washed with 50% (by vol.) aqueous methanol; yield 560 mg., m.p. 55–61°. Four recrystallizations from ether–petroleum ether gave crystals of m.p. 65.5–68.5° which on crystallizing from the melt then remelted at 78.5°. Recrystallization from ether–petroleum ether and seeding with the higher melting polymorph of 1-deoxy-*keto*-D-*galacto*-heptulose pentaacetate[13] gave m.p. 78–80°, $[\alpha]^{21}D$ −13.2° (*c* 1.85, U.S.P. $CHCl_3$), recorded[13] 78–79° and −14°. The X-ray powder diffraction pattern[13] of this material was identical with that of an authentic sample of the higher melting polymorph of 1-deoxy-*keto*-D-*galacto*-heptulose pentaacetate.

Silicate column chromatography of the crude reaction mixture from other preparations showed only one zone in addition to a highly colored zone at the column top. Isolation of material from this colorless zone gave 1-deoxy-*keto*-D-*galacto*-heptulose pentaacetate. Although no attempt was made to determine optimum reaction conditions it was found that without the addition of water, less of the dark residue was formed and the deoxy compound was obtained in low yield together with some starting material, the two being separable by virtue of their solubility difference in ether—the starting material being the much less soluble. Larger amounts of water added to the reaction mixture gave correspondingly larger amounts of dark colored residue and lower yields of the 1-deoxy compound.

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(17) Darco Corporation, 60 E. 42nd St., New York, N. Y.

[CONTRIBUTION FROM THE STANFORD RESEARCH INSTITUTE]

Potential Anticancer Agents.[1] I. Model Experiments for Synthesis of 2′-Deoxynucleosides by the 2,3-Episulfide Approach

BY LEON GOODMAN, ALLEN BENITEZ AND B. R. BAKER

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Cyclopentene episulfide has been prepared from cyclopentene oxide in 71% over-all yield by a three-step synthesis which should be compatible with the chemistry of nucleosides. Several other cyclopentane derivatives have been shown to be useful precursors of cyclopentene episulfide. The application of the chemistry of these cyclopentane transformations to the synthesis of 2′-deoxynucleosides is discussed.

The class of nucleosides composed of natural 2-deoxy-D-ribofuranose coupled with fraudulent bases represents a group of potential anticancer agents that should have interesting biological properties. Only one such compound, 6-azathymidine (V, base is 6-azathymine), has been synthesized—by an enzymatic route[2]—and it possessed biological activity. The enzymatic method, however, is tedious, difficult to carry out on a large scale, and has limitations in structural variation.

The first direct chemical synthesis of a nucleoside derived from D-ribofuranose, by condensation of tri-O-acetyl-D-ribofuranosyl bromide with silver theophylline,[3] was reported almost 10 years ago, but efforts to use this standard method[4,5] of coupling 3,5-di-O-acyl-2-deoxy-D-ribofuranosyl halides with heavy metal salts of pyrimidines[6,7] to form V have had no success. These failures can be attributed to the extreme acid lability of 2-deoxy-D-ribofuranose and its derivatives, in particular the 3,5-di-O-acyl-2-deoxy-D-ribofuranosyl halides. The synthesis of 2′-deoxy-D-ribopyranosyltheophylline has been accomplished by the coupling reaction of 3,4-di-O-acetyl-2-deoxy-D-ribopyranosyl chloride with silver theophylline,[8] but a mixture of α- and β-anomers was formed and, although these could be separated, it has not been possible to assign configurations to the two isomers. It can be predicted that, if a method of carrying out the coupling reaction with a 2′-deoxy-D-ribofuranosyl halide derivative could be found, similar objectionable, anomeric mixtures would be encountered.

It is clear from the above that indirect methods will have to be applied to accomplish synthesis of 2′-deoxynucleosides derived from 2-deoxy-furanose sugars. This fact was appreciated quite early by the Cambridge group.[9] These workers attempted to form the 2′-(ethylthio)-D-arabinoside (II, R =

(1) Work carried out under the auspices of the Cancer Chemotherapy National Service Center, National Cancer Institute, in collaboration with Sloan-Kettering Institute for Cancer Research.

(2) A. D. Welch, W. H. Prusoff and L. G. Lajtha, *Trans. Assoc. Am. Physicians*, **68**, 112 (1955).

(3) J. Davoll, B. Lythgoe and A. R. Todd, *J. Chem. Soc.*, 967 (1948).

(4) E. Fischer and B. Helferich, *Ber.*, **47**, 210 (1914).

(5) J. Davoll and B. A. Lowy, THIS JOURNAL, **73**, 1650 (1951).

(6) "Attempts by Lipkin and Sowden to use the Hilbert–Johnson synthesis with 3,5-di-O-benzoyl-2-deoxy-D-ribofuranosyl chloride or bromide and 2,4-diethoxypyrimidine met with no success," private communication from D. Lipkin, Washington University (St. Louis).

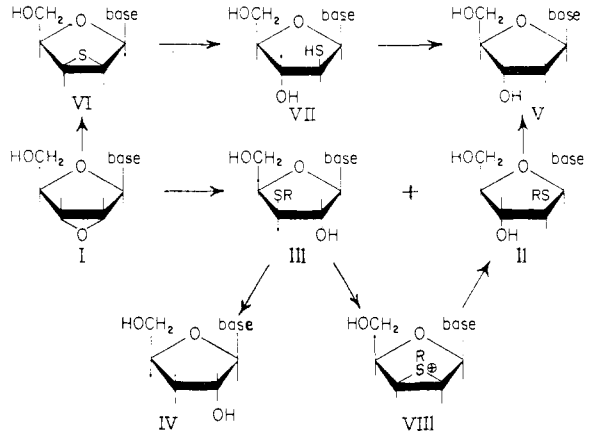
(7) Personal communication from Dr. J. J. Fox, Sloan-Kettering Institute, New York, N. Y.

(8) J. Davoll and B. Lythgoe, *J. Chem. Soc.*, 2526 (1949).

(9) J. Davoll, B. Lythgoe and S. Trippett, *ibid.*, 2230 (1951).

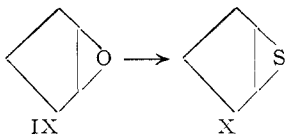
ethyl) by the reaction of sodium ethyl mercaptide with 7-(2′,3′-anhydro-β-D-xylofuranosyl)-theophylline (I). The desulfurization of II would then have led to the desired 2′-deoxynucleoside V. However, only traces of II (less than 1%) were formed, the major product being the 3′-(ethylthio)-D-xyloside (III, R = ethyl), which was desulfurized to the 3′-deoxy-D-riboside (IV).

An approach to the synthesis of 2′-deoxynucleosides which takes advantage of the clean *trans* opening of a 2,3-anhydrofuranose sugar at the 3-position[10] would seem to be possible through the sequence I → VI → VII → V, or by a quite similar path (I → III → VIII → II → V). The necessary



condition for the success of such synthetic schemes is the stereospecific transfer of the sulfur atom from the 3′- to the 2′-position followed by desulfurization; the key intermediates in these sequences are the (2′,3′-thioanhydro-β-D-lyxofuranosyl)-purine (VI) and the corresponding episulfonium salt VIII. Both these intermediates should provide a versatile synthesis of other interesting 2′-deoxynucleosides by use of other nucleophiles (*e.g.*, OR^-, NH_3, NH_2Ar) to open VI or VIII with the introduction of these groups at the 3′-position.

As a guide in understanding the chemistry of these proposed transformations and without the complications of additional functional groups, the cyclopentane ring was chosen as a model to simulate the furanose sugar system. Specifically, methods were found for the conversion of cyclopentene oxide (IX) to cyclopentene sulfide (X)



that proceeded under conditions compatible with the chemistry of nucleosides. The extreme lability of the purine–sugar bond in nucleosides to aqueous acid obviously strongly limits the possible synthetic schemes. Although the transformation IX → X would not give any information concerning the stereochemical changes involved, it seems clear that in going from I to VI a change from an anhydroribose to a thioanhydrolyxose configuration would be required if a *trans* 3-opening of I were assumed, followed by a *trans* ring-closure to form VI.[13]

The most widely used preparative method for episulfides is the direct conversion of epoxides through use of an alkali thiocyanate.[14] Chemically, this appears to be a most attractive route for the preparation of VI; but, as has been made clear by van Tamelen,[15] the method fails in the case of cyclopentene oxide (IX) (and would appear to be unsuitable for the anhydro sugar I) because the mechanism involves the formation of an intermediate XI, which comprises a highly strained system of two *trans* fused five-membered rings when $n = 1$. Another conversion of epoxides to episulfides was reported recently[16] which would be expected to obey the criteria of stereospecificity and avoidance of aqueous acid as demanded for the transformation I → VI but which would be stereochemically possible. Deacetylation, with dilute aqueous alkali, of either the O- or the S-acetyl derivative of 2-mercaptoethanol led to the formation of ethylene sulfide, and the similar treatment of either the O- or the S-acetyl derivative of *trans*-2-mercaptocyclohexanol gave a good yield of cyclohexene sulfide. The cyclic sulfide formation in these cases occurs through the intramolecular elimination of acetic acid and involves the unusual displacement of an acetate ion by the strong nucleophile, mercaptide ion. Harding and Owen[17] opened cyclopentene oxide (IX) with thiolacetic acid and converted the resulting *trans*-2-(acetylthio)-cyclopentanol (XII) to cyclopentene sulfide (X), in low yield, by treatment with hot aqueous sodium bicarbonate solution. The course of these reactions was postulated to be *via* intermediates XIII and XIV. The existence of the intermediate XIII, which possesses two *trans* fused five-membered rings, would be quite improbable and it seems more likely that the course of the formation of X proceeds through intermediate XV. The well-known ability of thiolacetic acid to act as an acetylating agent[18] makes it highly likely that the S-acetate XII could act as such with another molecule of XII. This "disproportionation" of the S-acetate (XII → XVI + XV) would be in agreement with Harding and Owen's[17] kinetic studies on XII. Further, in this work the conversion of the diacetate XV to the cyclic sulfide X was accomplished in 82% yield by the action of dilute aqueous sodium hydroxide, making it clear that XV is an excellent precursor for X. Our efforts to repeat the preparation of X from the S-acetate XII by Harding and Owen's[17] procedure were unsuccessful. The diacetate XV

(10) In addition to the example of 3-opening described above,[9] the ring-opening of methyl 2,3-anhydro-α-D-lyxofuranoside with ammonia gave a 90% yield of methyl 3-amino-3-deoxy-α-D-arabinofuranoside,[11] and 6-dimethylamino-9-(2′,3′-anhydro-β-D-lyxofuranosyl)-purine gave a 79% yield of 3-amino-3′-deoxy-β-D-arabinofuranosylpurine.[12]

(11) B. R. Baker, R. E. Schaub and J. H. Williams, THIS JOURNAL, **77**, 7 (1955).

(12) B. R. Baker and R. E. Schaub, *ibid.*, **77**, 5900 (1955).

(13) C. C. Price and P. F. Kirk, THIS JOURNAL, **75**, 2396 (1953).

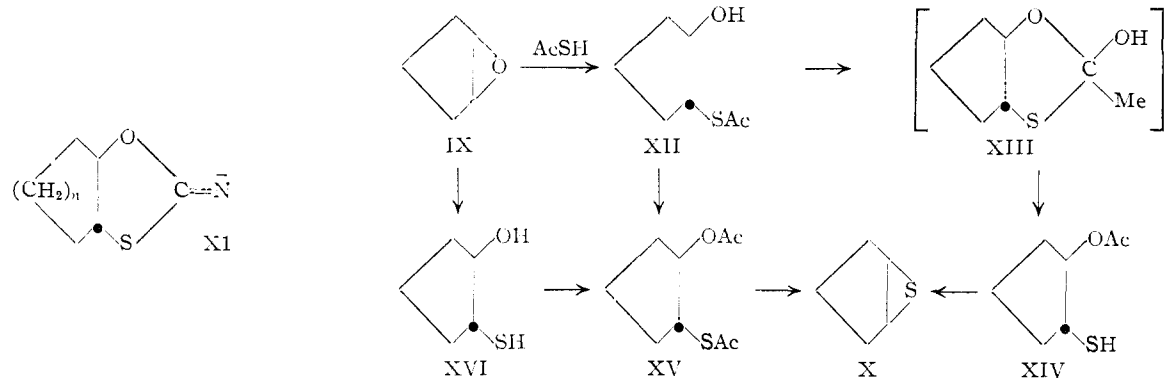
(14) (a) I. G. Farbenind, French Patent 797,621 (1936); (b) H. R. Snyder, J. M. Stewart and J. B. Ziegler, THIS JOURNAL, **69**, 2672 (1947); (c) C. C. J. Culvenor, W. Davies and K. Pausacker, *J. Chem. Soc.*, 1050 (1946).

(15) E. E. van Tamelen, THIS JOURNAL, **73**, 3444 (1951).

(16) L. W. C. Miles and L. N. Owen, *J. Chem. Soc.*, 817 (1952).

(17) J. S. Harding and L. N. Owen, *ibid.*, 1528 (1954).

(18) F. B. Stewart and P. V. McKinney, THIS JOURNAL, **53**, 1482 (1931).



was prepared in excellent yield from XII by acetylation in pyridine. The sequence IX → XII → XV → X was completed in an over-all yield of 71% and under conditions which would be expected to be compatible with the chemistry of nucleosides. The process represents a considerable improvement over the original synthesis of X by van Tamelen,[15] which proceeded from IX to X by way of *trans*-2-mercaptocyclopentanol (XVI) and *trans*-2-mercaptocyclopentyl chloride in an over-all 15% yield. The use of concentrated hydrochloric acid in van Tamelen's synthesis would preclude its use in the nucleoside area.

An alternate route to X from the oxide IX was investigated *via* the ring-opening of IX with hydrosulfide ion, a reagent which would be expected to be a better nucleophile than thiolacetic acid. The preparation of *trans*-2-mercaptocyclopentanol (XVI) by this reaction had been reported by van Tamelen,[15] who obtained a 32% yield of XVI by using equimolar quantities of the two reagents. A brief study of some of the reaction variables, summarized in Table I, made it clear that high yields of XVI could be obtained from the reaction of IX and hydrosulfide ion. The acetylation of XVI to yield XV, the precursor of X, would complete a synthetic scheme completely compatible with nucleoside chemistry.

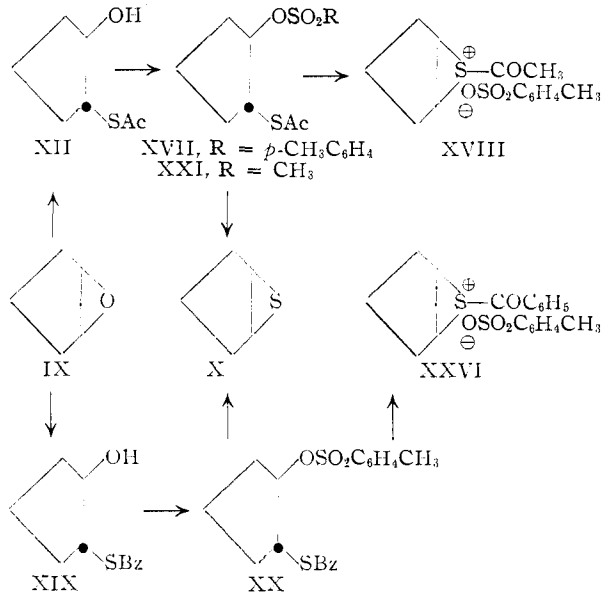
TABLE I[a]

Reagent[b]	Moles of base	Yield of XVI, %	Weight of residue, g.
NaOH	1	38.9	5.92
NaOH	2	63.6	2.15
NaOH[b]	2	55.1	3.79
NaOH	3	75.0	1.81
KOH	2	55.8	2.16
$NaOCH_3$	1	42.1	5.18

[a] Cyclopentene oxide (10.0 g.) was added slowly to the methanol solution of hydrosulfide ion while a slow stream of hydrogen sulfide was maintained and while the temperature was held at −10 to 0°. [b] Basic reagent used to form hydrosulfide ion. [c] The temperature, in this single experiment, was held at 45°.

The competitive reaction of XVI with IX to form bis-(2-hydroxycyclopentyl) sulfide was responsible for the decreased yields when lower molar amounts of hydrosulfide ion were used. The sulfide was isolated as a high-boiling liquid.

It seemed logical to expect that the *p*-toluenesulfonate or methanesulfonate ester of XII would represent a better precursor of X than did XV in view of the ready displacement of sulfonate esters by O-alkyl cleavage. The *p*-toluenesulfonate ester XVII was prepared in good yield by the conventional tosylation in pyridine followed by drowning the reaction mixture in ice-water. The product was a mobile, orange liquid with the correct elemen-



tal analysis; its infrared spectrum was that predicted for the tosylate XVII with an absence of –OH absorption near 3.0 μ, strong S-acetate absorption at 5.91 μ and strong sulfonate ester absorption at 7.33 and 8.51 μ. On standing, even at 0°, the compound became a deep blue liquid whose infrared spectrum was identical with that of the orange liquid. At room temperature the material rapidly changed to a viscous, brown liquid whose infrared spectrum showed a strong band at 5.74 μ[19] which was coupled with a decrease in the S-acetate band at 5.91 μ. New absorption bands at 9.64 and 9.88 μ were characteristic of ionic sulfonate spectra. Since the infrared changes had taken place in a closed system without the intervention of any reagents, it seems most logical to explain the spectral changes by the conversion of XVII to cyclopentene S-acetylepisulfonium tosylate (XVIII).

This postulation receives further support from the spectral changes noted with *trans*-2-(benzoyl-

(19) R. C. Lord and F. A. Miller (*Appl. Spectroscopy*, **10**, 122 (1956)) point out that attachment of an electronegative group to the carbonyl group lowers the wave length of carbonyl absorption.

thio)-cyclopentyl tosylate (XX). The ring-opening of cyclopentene oxide (IX) with thiolbenzoic acid led to an excellent yield of *trans*-2-(benzoylthio)-cyclopentanol (XIX), isolated as a yellow, high-boiling liquid. The tosylate of XIX was prepared as a nicely crystalline, white solid by the conventional technique in pyridine. Compound XX possessed the predicted analysis and infrared spectrum (S-benzoyl at 5.99 and sulfonate ester at 7.41 and 8.48 μ), but on long standing at room temperature in a closed container it became a gum whose infrared spectrum showed a new carbonyl absorption at 5.80 μ and new ionic sulfonate bands at 9.63 and 9.90 μ. These changes are consistent with a conversion of XX to cyclopentene S-benzoylepisulfonium tosylate (XXVI) on standing.

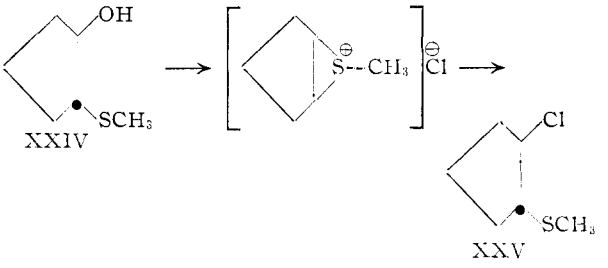
The preparation of *trans*-2-(acetylthio)-cyclopentyl methanesulfonate (XXI) from XII was carried out conventionally in pyridine; the product was an orange oil that was qualitatively more stable than the tosylate XVII.

None of the three sulfonate esters XVII, XX or XXI proved to be as good a precursor of cyclopentene sulfide (X) as the diacetate XV. The methanesulfonate XXI, with dilute aqueous sodium hydroxide, gave a 66% yield of X; under similar conditions XVII gave a 13% yield, while XX gave none of the episulfide. All of these reactions, including that with XV, were heterogeneous, and it is clear that the decreasing solubility of the sulfonate esters was chiefly responsible for the decreasing yields. When the reactions of XVII and XX with sodium hydroxide were conducted in a mixture of triethylene glycol dimethyl ether and water in order to obtain a homogeneous solution, the yields of X were 35 and 25%, respectively.[20] Attempts to convert the sulfonate esters to X with sodium methoxide in methanol were complicated by the difficulty of separating X from methanol by distillation, in spite of the large difference in boiling point of the two (125 and 64°). The difficulty is similar to that encountered in the distillation of mixtures of cyclopentene oxide and diethyl ether. One attempt was made to solvolyze the tosylate XVII in ethanol in the presence of calcium carbonate. It was not possible to identify any pure component of the distilled product; S-acetate, O-acetate, SH, OH and OEt groups were identifiable from the infrared spectrum. Using the same conditions, Harding and Owen[17] converted *trans*-2-(acetylthio)-cyclohexyl tosylate to 2-(acetylthio)-cyclohexyl ethyl ether of presumed *trans* configuration.

The reaction of *trans*-2-(acetylthio)-cyclopentanol (XII) with excess thionyl chloride gave rise to a 33% yield of a distilled liquid whose elemental analysis agreed with that expected for 2-(acetylthio)-cyclopentyl chloride (XXII). The stereochemistry of the functional groups in the distillate is uncertain. It is most probable that at least some of the *trans*-chloride was formed in the reaction, as evidenced by the presence of strong infrared bands at 5.74 and 8.05 μ in the large distillation residue. These are attributed to the presence of cyclopentene S-acetylepisulfonium chloride, which would necessarily only arise from the *trans* compound. A single attempt to convert the distilled chloride XXII to X with dilute aqueous sodium hydroxide gave none of the episulfide and no cleanly identified products, which may indicate that XXII has the *cis* configuration.[21]

At the beginning of this manuscript it was noted that the shift of a sulfur-containing moiety from the 3′- to the 2′-position of a nucleoside by way of an alkylsulfonium intermediate VIII would represent a second approach to the synthesis of a 2′-deoxynucleoside. In order to study the total sequence of steps leading from a 2′,3′-anhydronucleoside to a 2′-(alkylthio)-nucleoside, a brief study of the ring-opening of cyclopentene oxide (IX) with sodium ethyl mercaptide was carried out. It was found that when equimolar quantities of the two reagents were stirred at 0°, a 91% yield of *trans*-2-(ethylthio)-cyclopentanol (XXIII) was formed; when 2 moles of sodium ethyl mercaptide were used the yield of XXIII was 95%. The high nucleophilic character of the mercaptide ion as compared with the hydrosulfide ion is evident from these results.

The attempts to study the transfer of the alkylthio group from the 3′- to the 2′-position (III → II) were carried out using *trans*-2-(methylthio)-cyclopentanol (XXIV), which had been prepared from S-(*trans*-2-hydroxycyclopentyl)-thiuronium sulfate as described by Bordwell and Andersen.[22] The preparation of 2-(methylthio)-cyclopentyl chloride was accomplished in excellent yield either by the use of excess thionyl chloride or with concentrated hydrochloric acid. The latter reagent had been used by van Tamelen[15] to prepare *trans*-2-mercaptocyclopentyl chloride; an intermediate sulfonium ion was postulated to account for the *trans* configuration of the product. It seems most probable that a similar situation is present in the case of *trans*-2-(methylthio)-cyclopentanol (XXIV) and that the product of these chlorinations is *trans*-2-(methylthio)-cyclopentyl chloride (XXV).[21]



Attempts to prepare the *p*-toluenesulfonate ester XXVI of XXIV were made using three different methods, all unsuccessful. Conventional tosylation of XXIV in pyridine led to water-soluble products on drowning the reaction mixture. Compound XXV probably constituted the major reaction product, since it was shown that XXV dis-

(20) Yields in these reactions were estimated from the refractive indices of appropriate distillation fractions since X and the glycol diether could not be cleanly separated with the distillation equipment used.

(21) Neither XXII nor 2-(methylthio)-cyclopentyl chloride (XXV), described below, appeared to be a good model for the study of nucleoside syntheses and an intensive study of their stereochemistry was, therefore, not undertaken.

(22) F. G. Bordwell and H. M. Andersen, THIS JOURNAL, **75**, 4959 (1953).

solved rapidly in a pyridine–water mixture, and the characteristic odor of XXV was evident. The reaction of *p*-toluenesulfonyl chloride with the sodium salt of XXIV prepared in dimethylformamide gave a poor yield of XXV. A major product from this reaction was sodium *p*-toluenesulfinate. Finally, the reaction of XXV with silver *p*-toluenesulfonate in dry acetonitrile gave a large quantity of silver chloride and a viscous brown liquid which showed strong absorption at 9.66 and 9.90 μ, characteristic of ionic sulfonates, and no absorption near 7.3 and 8.5 μ, characteristic of sulfonate esters. The material was probably a polymer containing cyclopentene S-methylepisulfonium tosylate units but was not further investigated. Previous attempts to prepare the *p*-toluenesulfonate of β-hydroxyethyl methyl sulfide with *p*-toluenesulfonyl chloride in pyridine yielded a compound whose analysis indicated it to be β-chloroethyl methyl sulfide,[23] emphasizing the difficulties to be expected with the preparation of the tosylates of 1-hydroxy-2-alkylthio compounds.

The work described above makes it clear that the synthesis of sugar episulfides and nucleoside episulfides (as well as episulfonium intermediates) should be possible from a variety of precursors. Some preliminary work on the application of this model work to the sugar series makes it clear that a generally lower reactivity of SN2 oxide openings and intramolecular SN2 reactions prevails in the sugar series[24] and that the best route to the cyclic sulfides found in the cyclopentane series will possibly not be the best transformation in the sugar and nucleoside area. However, the wide range of activity of attacking sulfur functions and of departing groups demonstrated in these model studies should allow a choice of a more activated combination suitable for transposition of a sulfur on the 3′-position of a nucleoside to the requisite 2′-position for 2′-deoxynucleoside synthesis. The work on these transformations is proceeding and will be reported on at a later date.

Experimental[25]

Cyclopentene Oxide (IX).—The preparation of IX is given in detail since the following represents a reproducible, good-yield synthesis in contrast to the methods listed in the literature.

To a mixture containing 52.8 g. (0.297 mole, 1% excess) of N-bromosuccinimide (Arapahoe Chemicals) and 100 ml. of distilled water was added dropwise, with vigorous stirring, 20.0 g. (0.294 mole) of cyclopentene over a period of 10 minutes. The temperature of the mixture was maintained at 18–25° by ice cooling. The reaction mixture was then stirred at room temperature for 2.5 hours. The organic phase was separated, and the aqueous layer was extracted with three 20-ml. portions of ether. The combined organic phase and ether extract was dried over anhydrous sodium sulfate and was filtered. The ether was removed from the filtrate with the water-aspirator vacuum and a bath temperature of 25–36°. The yellow residue weighed 52.0 g. (theoretical yield of the bromohydrin is 48.5 g.; succinimide is present in the residue).

The residue was added slowly (10 minutes) to 69 g. of 30.2% (0.520 mole) aqueous sodium hydroxide while the temperature of the reaction was kept at 12–15° by the use of ice cooling. The mixture was stirred for a further 2 hours at 2–10°. The organic phase (22.2 g.) was separated from the aqueous phase and was dried over anhydrous sodium sulfate. The dried organic phase was vacuum distilled (17 mm.) with a maximum bath temperature of 80°. The distillate (17.2 g.) was collected in a Dry Ice–acetone-bath and was redistilled, at atmospheric pressure, to yield 12.75 g. (52.6%) of cyclopentene oxide, b.p. 99–101° (lit.[26] gives b.p. 100–101° and 31.7% over-all yield from cyclopentene[27] or 80–85% yield from *trans*-2-chlorocyclopentanol[28]). When the synthesis was carried out with 100 g. of cyclopentene the yield was 62–70%. With 200 g. of cyclopentene (and eliminating the ether extraction of the bromohydrin by direct addition of the excess base to the aqueous mixture) the yield was 54–57%. It was not found possible to effect an efficient separation of the oxide IX and diethyl ether by distillation, a situation separately noted by Owen and Smith,[27] which precluded the use of ether as an extracting solvent.

***trans*-2-(Acetylthio)-cyclopentanol (XII).**—The directions of Harding and Owen[18] were followed. An 87.4% yield of product was obtained by allowing a mixture of 10.3 g. (0.123 mole) of the oxide IX and 9.8 g. (0.129 mole) of thiolacetic acid (Practical) to stand at room temperature for 18 days. The product had b.p. 68° (0.2 mm.), n^{17}D 1.5162 (lit.[17] b.p. 69° (0.001 mm.), n^{17}D 1.5133). A 62.8% yield was obtained after a reaction time of 6 days.

***trans*-2-(Acetylthio)-cyclopentyl Acetate (XV).**—To a cold solution of 19.11 g. (0.183 mole) of acetic anhydride containing 0.25 g. of *p*-toluenesulfonic acid monohydrate was added 10.0 g. (0.0624 mole) of *trans*-2-(acetylthio)-cyclopentanol (XII). The solution was stored in a stoppered flask at room temperature for 24 hours and then was neutralized with a small excess of sodium bicarbonate contained in 100 ml. of distilled water. The aqueous mixture was extracted with three 15-ml. portions of methylene chloride. The extracts were combined, washed twice with 20-ml. portions of distilled water, dried over anhydrous magnesium sulfate, and filtered. The filtrate was first distilled from a Claisen flask at atmospheric pressure to remove the solvent and then 11.79 g. (93.4%) of *trans*-2-(acetylthio)-cyclopentyl acetate, b.p. 76.5° (0.5 mm.), n^{22}D 1.4897 (Harding and Owen[17] gave the constants as 90° (0.5 mm.), n^{22}D 1.4888), was collected.

Reaction of *trans*-2-(Acetylthio)-cyclopentyl Acetate (XV) with Aqueous Sodium Hydroxide.—A mixture of 7.0 g. (0.0346 mole) of *trans*-2-(acetylthio)-cyclopentyl acetate (XV) and 175 ml. of aqueous 0.40 *N* (0.070 mole) sodium hydroxide was stirred under nitrogen at room temperature for 23 hours. The reaction mixture was then brought to *p*H 7–8 with 1 *N* hydrochloric acid. The aqueous mixture was extracted with one 20-ml. and three 12-ml. portions of methylene chloride. The extracts were combined, washed once with 20 ml. of distilled water, dried over anhydrous magnesium sulfate, and filtered. The filtrate was first distilled at atmospheric pressure, using a short Vigreux column to remove the solvent, and then 2.53 g., n^{25}D 1.5218, of cyclopentene sulfide (X) was collected at 69–70° (65 mm.). An additional 0.30 g., n^{55}D 1.5218, of the material was collected by raising the temperature of the stillpot to 135° and reducing the pressure to 1 mm. The total yield of the product was 82%. A residue of 0.16 g. of material remained in the stillpot. Harding and Owen[17] reported cyclopentene sulfide (X) to boil at 45° (15 mm.), n^{17}D 1.5222.

When XV was allowed to react with an equimolar quantity of methanolic sodium methoxide at 0–25° for 2.25 hours, a 54% yield of X was collected.

Reaction of Cyclopentene Oxide (IX) with Sodium Hydrosulfide.—A well-stirred solution of 9.60 g. (0.238 mole) of sodium hydroxide in 85 ml. of reagent methanol was saturated with hydrogen sulfide by passing in the gas at −10 to 0° during 1.25 hours. While a slow stream of gas was maintained, 10.0 g. (0.119 mole) of cyclopentene oxide (IX) was added dropwise to the cold solution over a period of 30 minutes and stirring was continued for 1 hour longer at ice-bath temperature. The solution was allowed to stand at room temperature for 17 hours and was diluted with 200 ml.

(23) Dr. H. P. Marshall, unpublished results from University of California at Los Angeles.

(24) The reactions of thiolacetic acid and hydrosulfide ion with methyl 2,3-anhydro-β-D-ribofuranoside are markedly slower than with cyclopentene oxide (IX). The conditions used to open a nucleoside epoxide with sodium ethyl mercaptide[9] are much more severe than those required for the reaction with IX.

(25) Melting points were taken on the Fisher–Johns apparatus and are uncorrected. Boiling points are uncorrected.

(26) R. B. Rothstein and M. Rothstein, *Compt. rend.*, **209**, 761 (1939).

(27) L. N. Owen and P. N. Smith, *J. Chem. Soc.*, 4026 (1952).

of water. The solution was cooled to 0° and, with stirring, 5 *N* sulfuric acid was added slowly until the *p*H was 2. Four portions of methylene chloride (40, 25, 20 and 20 ml.) were used to extract the solution and the combined extracts were washed with 50 ml. of saturated sodium bicarbonate solution and 35 ml. of water. After drying over magnesium sulfate and filtration, the extracts were distilled from a short Vigreux column, first at atmospheric pressure and finally at reduced pressure, with the following fractions collected: (1) 1.2 g., b.p. 97–97.5° (15 mm.), $n^{20}D$ 1.5219; (2) 4.8 g., b.p. 97.5–98° (15 mm.), $n^{20}D$ 1.5218; (3) 2.1 g., b.p. 98° (15 mm.), $n^{20}D$ 1.5220; (4) 0.8 g., flashed over at 1 mm., $n^{20}D$ 1.5219; (5) residue, 2.15 g. Fractions 1–4 represent a 63.6% yield of *trans*-2-mercaptocyclopentanol (XVI) (van Tamelen[15] recorded the constants as b.p. 92–94° (15 mm.), $n^{25}D$ 1.5190, and Harding and Owen[17] gave b.p. 97° (15 mm.), $n^{17}D$ 1.5180). The results of other ring-openings of IX by hydrosulfide ion are given in Table I.

From the high-boiling residues collected from several experiments there was separated, by distillation, the bis-(2-hydroxycyclopentyl) sulfide, b.p. 134–155° (0.013 mm.), $n^{20}D$ 1.5411.

Anal. Calcd. for $C_{10}H_{18}O_2S$: C, 59.4; H, 8.97. Found: C, 58.8; H, 9.06.

trans-2-(Acethylthio)-cyclopentyl *p*-Toluenesulfonate (XVII).—A solution of 4.0 g. (0.025 mole) of *trans*-2-(acetylthio)-cyclopentanol (XII), 20 ml. of reagent pyridine and 8.0 g. (0.042 mole) of *p*-toluenesulfonyl chloride was prepared and allowed to stand in a stoppered flask at 0° for 48 hours. At the end of this time the solution was a dark orange and contained a heavy crystalline precipitate. The mixture was poured onto 250 g. of ice and the orange oil was separated. The aqueous layer was extracted with 50 ml. of benzene and the extract was added to the orange oil. The benzene solution was extracted with five 250-ml. portions of ice-water and was dried over magnesium sulfate. The solution was filtered and the filtrate was evaporated *in vacuo*, finally at 0.5 mm., maintaining the temperature at 20–25°. The residue was a mobile, orange liquid. In the infrared it had $\lambda_{max(\mu)}^{film}$ 5.75 (either O-acetate carbonyl or acetylsulfonium carbonyl, very weak band), 5.90 (S-acetate carbonyl, strong band), 7.35 and 8.51 (sulfonate ester), 12.23 (*p*-di-substituted benzene).

Anal. Calcd. for $C_{14}H_{18}O_4S_2$: C, 53.5; H, 5.77. Found: C, 53.7; H, 6.00.

On standing in the refrigerator, or on short warming to 40°, the mobile, orange liquid changed to a mobile, deep blue liquid whose infrared spectrum was virtually identical with that of the orange liquid. On standing at room temperature for approximately 1 day, the blue liquid changed to a viscous, brown tar whose infrared spectrum indicated deep-seated changes. In the infrared it had $\lambda_{max(\mu)}^{film}$ 5.75 (probably acetylsulfonium carbonyl, strong band); 5.92 (S-acetate carbonyl, medium band); 7.33 and 8.50 (sulfonate ester); 8.05, 9.65, 9.89, 14.12 and 14.65 (sulfonate ion); 12.22 (*p*-di-substituted benzene).

Attempts were made to prepare compound XVII by using equimolar quantities of *trans*-2-(acetylthio)-cyclopentanol (XII), *p*-toluenesulfonyl chloride and pyridine in benzene solution. The reaction was extremely slow and an appreciable quantity of *p*-toluenesulfonyl chloride was recovered.

trans-2-(Benzoylthio)-cyclopentanol (XIX).—A mixture of 5.0 g. (0.0595 mole) of cyclopentene oxide (IX) and 8.63 g. (0.0625 mole) of thiolbenzoic acid[28] was stored in a stoppered flask at room temperature for 9 days. Heat was evolved when the reagents were mixed. When the mixture was heated under vacuum to remove excess thiolbenzoic acid, a quantitative yield of XIX remained as a viscous, yellow liquid. Its infrared spectrum showed a strong S-benzoate carbonyl band at 6.05 μ. A small amount of the residue was evaporatively distilled at 80–90° (0.001–0.005 mm.) to give a bright yellow distillate, $n^{20}D$ 1.5930.

Anal. Calcd. for $C_{12}H_{14}O_2S$: C, 64.8; H, 6.35. Found: C, 65.0, 64.7; H, 6.39, 6.44.

trans-2-(Benzoylthio)-cyclopentyl *p*-Toluenesulfonate (XX).—A mixture of 1.00 g. (0.0045 mole) of *trans*-2-(benzoylthio)-cyclopentanol (XIX), 1.02 g. (0.0053 mole) of *p*-toluenesulfonyl chloride and 4 ml. of reagent pyridine was stored in a stoppered flask at 0° for 1 hour and at room temperature for 1 hour. The solution remained clear so an additional 0.40 g. (0.0021 mole) of tosyl chloride was added, whereupon rapid precipitation occurred. The mixture was stored in the refrigerator for 48 hours, allowed to warm to room temperature for 3 hours, and poured onto 150 g. of ice. A yellow oil separated which soon solidified and was taken up in 35 ml. of methylene chloride. The organic solution was washed with three 80-ml. portions of water, dried over magnesium sulfate, and filtered; the filtrate was evaporated at room temperature *in vacuo* (finally at 1 mm.), to leave 1.55 g. (91%) of solid residue. The residue was recrystallized from hot Skellysolve B (100 ml./g.) and gave white needles, m.p. 81.5–84°. A second, similar recrystallization lowered the melting point to 79.5–80.5°.

Anal. Calcd. for $C_{19}H_{20}O_4S_2$: C, 60.6; H, 5.36; S, 17.04. Found: C, 60.4; H, 5.54; S, 16.79.

On standing at room temperature, the white crystalline product slowly changed to a yellow gum. The resulting product was subjected to infrared examination after 1 month and proved to be a mixture of *trans*-2-(benzoylthio)-cyclopentanol *p*-toluenesulfonate (XX) and cyclopentene S-benzoylepisulfonium *p*-toluenesulfonate (XXVI). Infrared spectrum: $\lambda_{max(\mu)}^{film}$ 5.80 (benzoylepisulfonium C=O); 6.02 (S-benzoyl C=O, much reduced in intensity); 7.85, 8.95, 9.63, 9.90 and 14.05 (ionic sulfonate); 12.23 (*p*-di-substituted benzene); 14.50 (mono-substituted benzene).

trans-2-(Acetylthio)-cyclopentyl Methanesulfonate (XXI).—To a solution of 2.89 g. (0.018 mole) of *trans*-2-(acetylthio)-cyclopentanol (XII) in 15 ml. of reagent pyridine was added, in 1 portion, 4.01 g. (0.035 mole) of methanesulfonyl chloride. The mixture became warm immediately, darkened rapidly, and deposited a crystalline precipitate. The mixture was left in the refrigerator in a stoppered flask for 24 hours and was then poured onto 200 g. of ice, an orange oil separating. The oil was separated and dissolved in 50 ml. of methylene chloride. The methylene chloride solution was washed with four 100-ml. portions of ice-water and dried over magnesium sulfate. After this solution was filtered, the methylene chloride was removed *in vacuo* (finally at 1 mm.) at room temperature. The residue was an oil that weighed 3.05 g. (71%) and had the expected infrared spectrum for XXI. Infrared spectrum: $\lambda_{max(\mu)}^{film}$ 5.75 (trace, C=O of acetylepisulfonium isomer), 5.90 (strong, C=O of S-acetate), 7.35 and 8.50 (sulfonate ester). Hydroxyl absorption at 2.90 μ was very weak.

Reaction of *trans*-2-(Acetylthio)-cyclopentyl *p*-Toluenesulfonate (XVII) with Base.—A solution of 7.85 g. (0.025 mole) of *trans*-2-(acetylthio)-cyclopentyl *p*-toluenesulfonate (XVII), 2.02 g. (0.050 mole) of sodium hydroxide, 71 ml. of triethylene glycol dimethyl ether (Ansul Ether 161), and 54 ml. of water was stirred at room temperature for 2.5 hours and was then stored at 0° for 15.5 hours. The neutral solution contained a small amount of an orange oil. The reaction mixture was extracted with one 25-ml. and two 20-ml. portions of methylene chloride and the combined extracts were washed with two 100-ml. portions of water, dried over magnesium sulfate, and filtered. The filtrate was distilled from a short Vigreux column, initially at atmospheric pressure to remove methylene chloride and finally at reduced pressure, with the following fractions collected at 100 mm. pressure: (1) 0.89 g., b.p. 45–125°, $n^{25}D$ 1.4860; (2) 16.19 g., b.p. 125–157°, $n^{20}D$ 1.4269; (3) 2.03 g., b.p. 157°, $n^{25}D$ 1.4224. Based on the refractive indices of cyclopentene sulfide and trimethylene glycol dimethyl ether of 1.5218 and 1.4218, respectively, the yield of episulfide X was 35.2%. Only 13% of X could be isolated when the reaction of XVII and base was carried out in water.

When the tosylate XVII was refluxed with moist ethanol in the presence of calcium carbonate, a low yield of distillate, b.p. 49–50° (0.5 mm.), was collected in two fractions, $n^{20}D$ 1.4867 and 1.4865. These fractions had identical infrared spectra, which showed them to be a mixture containing S-acetate, O-acetate, SH, OH and OEt groups.

Reaction of *trans*-2-(Benzoylthio)-cyclopentyl *p*-Toluenesulfonate (XX) with Base.—A mixture of 10.0 g. (0.0266 mole) of *trans*-2-(benzoylthio)-cyclopentyl *p*-toluenesulfonate (XX), 2.15 g. (0.0532 mole) of sodium hydroxide, 65 ml. of triethylene glycol dimethyl ether and 68 ml. of water was stirred at room temperature for 26 hours, during which time all the solid material went into solution. The final solution had *p*H 8. The reaction work-up was exactly as described above for the similar reaction of *trans*-2-(acetylthio)-cyclopentyl *p*-toluenesulfonate (XVII). Distillation,

(28) P. Noble, Jr., and D. S. Tarbell, *Org. Syntheses*, **32**, 101 (1952).

as above, gave the following fractions at 100 mm. pressure: (1) 2.09 g., b.p. 82–145°, $n^{25}D$ 1.4523; (2) 4.21 g., b.p. 145–152°, $n^{25}D$ 1.4311; (3) 12.39 g., b.p. 152–155°, $n^{25}D$ 1.4226. The yield of cyclopentene episulfide (X), calculated from the refractive indices of these fractions, was 24.8%. No episulfide could be isolated when the reaction was attempted in water.

Reaction of *trans*-2-(Acetylthio)-cyclopentyl Methanesulfonate (XXI) with Base.—A mixture of 7.0 g. (0.029 mole) of *trans*-2-(acetylthio)-cyclopentyl methanesulfonate (XXI) and 147 ml. of aqueous 0.4 *N* (0.059 mole) sodium hydroxide was stirred, under nitrogen, for 23.5 hours at room temperature. The mixture was neutralized to *p*H 6 with 2.15 ml. (0.00215 mole) of 1 *N* hydrochloric acid and the reaction was worked up as described for the similar reaction of XV. The episulfide was collected in 3 fractions, 1.93 g. (65.7%), whose collective properties had b.p. 68.5–70° (65 mm.), $n^{25}D$ 1.5148–1.5220.

Opening of Cyclopentene Oxide (IX) with Sodium Ethyl Mercaptide.—A solution of 6.43 g. (0.119 mole) of sodium methoxide and 50 ml. of reagent methanol was added slowly, during 30 minutes, with stirring, to 7.39 g. (0.119 mole) of cold (−5 to 0°) ethanethiol and stirring was continued for an additional 30 minutes. Cyclopentene oxide (10.0 g., 0.119 mole) was added dropwise, with stirring, to the chilled solution during a 30-minute period and the resulting solution was stirred 1 hour longer. The reaction mixture was allowed to stand at room temperature for 16 hours and was then diluted with 140 ml. of water. The cold, well-stirred solution was acidified to *p*H 2 with 3 *N* sulfuric acid and extracted with 5 portions of chloroform (40, 25, 20, 20 and 20 ml.). The combined extracts were washed with one 40-ml. portion of saturated sodium bicarbonate solution and one 30-ml. portion of water, dried over magnesium sulfate, filtered, and distilled from a short Vigreux column, first at atmospheric pressure and finally at reduced pressure, with the following fractions collected at 0.5 mm.: (1) 0.53 g., b.p. 65°, $n^{20}D$ 1.5060; (2) 10.03 g., b.p. 65–70°, $n^{20}D$ 1.5079–1.5085; (3) 4.43 g., b.p. 70–71°, $n^{20}D$ 1.5085; (4) 0.85 g., b.p. 71°, $n^{20}D$ 1.5079. The combined fractions represent a 91.1% yield of *trans*-2-(ethylthio)-cyclopentanol (XXIII). When 2 moles of sodium ethyl mercaptide was used the yield of XXIII was 94.7%. Fraction 3 was submitted for analysis.

Anal. Calcd. for $C_7H_{14}OS$: C, 57.5; H, 9.65; S, 21.9. Found: C, 56.8; H, 9.82; S, 21.6.

A phenylurethan was prepared from XXIII conventionally. After two recrystallizations from petroleum ether it had m.p. 75.6–76.0°. The compound had strong infrared absorption (in KBr) at 3.03 and 6.47 μ (NH), 5.91 μ (urethan carbonyl) and 8.06 μ (C–O–C).

Anal. Calcd. for $C_{14}H_{19}NO_2S$: C, 63.4; H, 7.22. Found: C, 63.6; H, 7.19.

Reaction of *trans*-2-(Acetylthio)-cyclopentanol (XII) with Thionyl Chloride.—To a solution of 10.0 g. (0.0624 mole) of *trans*-2-(acetylthio)-cyclopentanol (XII) and 10 ml. of methylene chloride, which was cooled in a Dry Ice–acetone-bath, was added dropwise over a period of 10 minutes 22.3 g. (0.187 mole) of thionyl chloride. The solution was stored at −80° for 2 hours and then was kept at −5° in a stoppered flask for 65 hours. At the end of the storage period, the reaction mixture had changed from light yellow to very dark brown in color. The solution was reduced to a high-boiling residue by evaporation at water-pump vacuum, first at room temperature and then at 40° for an additional hour. The residue was distilled from a short Vigreux column and 3.76 g. (32.7%) of 2-(acetylthio)-cyclopentyl chloride (XXII) was collected at 55° (0.5 mm.), $n^{20}D$ 1.5140. An analytical sample, $n^{20}D$ 1.5150, was collected as a central fraction during the distillation.

Anal. Calcd. for $C_7H_{11}OSCl$: C, 47.1; H, 6.21. Found: C, 47.1; H, 6.42.

A dark residue (5.64 g.), which did not distil at 0.5 mm. with a pot temperature of 190°, remained. Its infrared spectrum showed a strong band at 5.75 μ, suggestive of the presence of cyclopentene S-acetylepisulfonium chloride, as well as absorption at 5.90 μ (S-acetate carbonyl).

When the distillate XXII was stirred with aqueous sodium hydroxide at room temperature, no cyclopentene sulfide (X) could be isolated in the reaction work-up.

***trans*-2-(Methylthio)-cyclopentanol (XXIV).**—To a solution of 28.7 g. (0.717 mole) of sodium hydroxide in 350 ml. of distilled water was added 50.0 g. (0.120 mole) of S-(*trans*-2-hydroxycyclopentyl)-thiuronium sulfate[22] over a period of 20 minutes while the temperature was maintained at 15–20°. The mixture was stirred for a further 40 minutes at 20°, after which time the solution was clear. To the well-stirred solution was added 15.1 g. (0.120 mole) of dimethyl sulfate over a period of 5 minutes and the temperature rose from 20 to 30°. The turbid solution was stirred at room temperature for a further 2.5 hours.

The *p*H of the solution was adjusted to 5 with 30% sulfuric acid and the solution was extracted with ten 30-ml. portions of ether. The ether extracts were dried over magnesium sulfate, filtered, and the filtrate distilled through a short Vigreux column at atmospheric pressure to remove ether. The residue was distilled *in vacuo* to yield 15.95 g. (50.5%), b.p. 67–68° (1.5 mm.), $n^{20}D$ 1.5162. The analytical sample had b.p. 68° (1.5 mm.), $n^{20}D$ 1.5160.

Anal. Calcd. for $C_6H_{12}OS$: C, 54.5; H, 9.15; S, 24.25. Found: C, 54.3; H, 9.02; S, 24.04.

A phenylurethan was prepared from XXIV. After two recrystallizations from Skellysolve B it had m.p. 76.3–77°. The compound (in KBr) showed strong infrared absorption at 3.05 and 6.48 μ (NH), 5.91 μ (urethan carbonyl) and 8.10 μ (C–O–C).

Anal. Calcd. for $C_{13}H_{17}NO_2S$: C, 62.1; H, 6.82. Found: C, 62.5; H, 6.94.

trans-2-(Methylthio)-cyclopentanol (XXIV) was allowed to react with excess benzoyl chloride in pyridine. After 1 hour at 0° the reaction mixture was poured onto ice and the yellow oil separated. It was washed thoroughly with ice-water and stirred with a solution of sodium bicarbonate in water at 70–75° for several hours in order to destroy contaminating benzoic anhydride. The dried oil was evaporatively distilled at a bath temperature of 65–70° (0.020 mm.), giving a colorless distillate, $n^{20}D$ 1.5492–1.5499, of *trans*-2-(methylthio)-cyclopentyl benzoate.

Anal. Calcd. for $C_{13}H_{16}O_2S$: C, 66.1; H, 6.83. Found: C, 66.2; H, 6.83.

***trans*(?)-2-(Methylthio)-cyclopentyl Chloride (XXV).**

(a) **Thionyl Chloride Method.**—To a solution of 10.0 g. (0.0756 mole) of *trans*-2-(methylthio)-cyclopentanol (XXIV) and 10 ml. of methylene chloride, which was cooled to −80°, was added dropwise over a period of 10 minutes 27.0 g. (0.227 mole) of thionyl chloride. The solution became light yellow in color. It was stored at −80° for 2 hours and then at −5° for 69 hours. At the end of the storage period the reaction mixture had changed from a light yellow to a very dark brown color. The solution was evaporated *in vacuo* (water-pump vacuum), first at room temperature and then at 40° for an additional 2 hours. The residue was distilled, using a short Vigreux column, and several fractions totaling 10.6 g., b.p. 67–68° (8 mm.), $n^{20}D$ 1.5125–1.5130, were collected. These were combined and redistilled, giving the following fractions at 15.5 mm.: (1) 2.33 g., b.p. 80°, $n^{20}D$ 1.5124; (2) 3.63 g., b.p. 80°, $n^{20}D$ 1.5124; (3) 3.22 g., b.p. 80°, $n^{20}D$ 1.5125; (4) 0.48 g., $n^{20}D$ 1.5127. The yield of XXV was 84.7%. Fraction 2 was submitted for analysis.

Anal. Calcd. for $C_6H_{11}SCl$: C, 47.8; H, 7.36. Found: C, 47.7; H, 7.41.

(b) **Hydrochloric Acid Method.**—To 25 ml. (0.30 mole) of concentrated hydrochloric acid was added dropwise, with vigorous stirring, 2.85 g. (0.022 mole) of XXIV. The addition required 12 minutes and the mixture was stirred at room temperature for 6.5 hours, then stored at 0° for 39 hours. The mixture was extracted with five 10-ml. portions of methylene chloride and the combined extracts were washed with 20 ml. of saturated sodium bicarbonate and 20 ml. of water. After being dried over magnesium sulfate, the extracts were distilled from a short Vigreux column, first at atmospheric pressure to remove methylene chloride, then at reduced pressure to yield 2.88 g. (89%) of material, b.p. 78–78.5° (14 mm.), $n^{20}D$ 1.5112–1.5122, possessing an infrared spectrum identical with that from the thionyl chloride reaction.

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