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Dimethyl Sulfoxide Oxidation of Primary Alcohols

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DIMETHYL SULFOXIDE OXIDATION OF PRIMARY ALCOHOLS

by

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Carmen Vargas Zenarosa

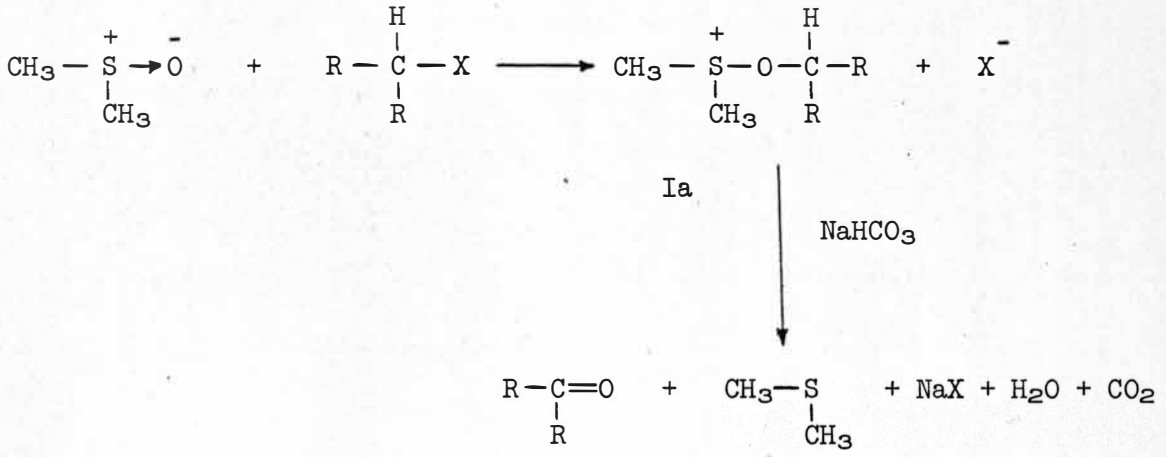
TABLE OF CONTENTS

HISTORICAL

A method of selective oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones has been developed recently, namely the use of dimethyl sulfoxide (DMSO) as the oxidizing agent, either alone or with dicyclohexylcarbodiimide (DCC),[14] acid anhydrides,[1] or alkyl chloroformates[10]. The negatively polarized oxygen atom of the sulfoxide group in DMSO is ideally situated for a transfer to many electron-deficient substrates. The oxygen of the alcohol coordinates with the sulfur atom of DMSO through its oxygen atom; this is followed by β-elemination of dimethyl sulfide, thereby resulting in oxidation of the alcohol to an aldehyde.

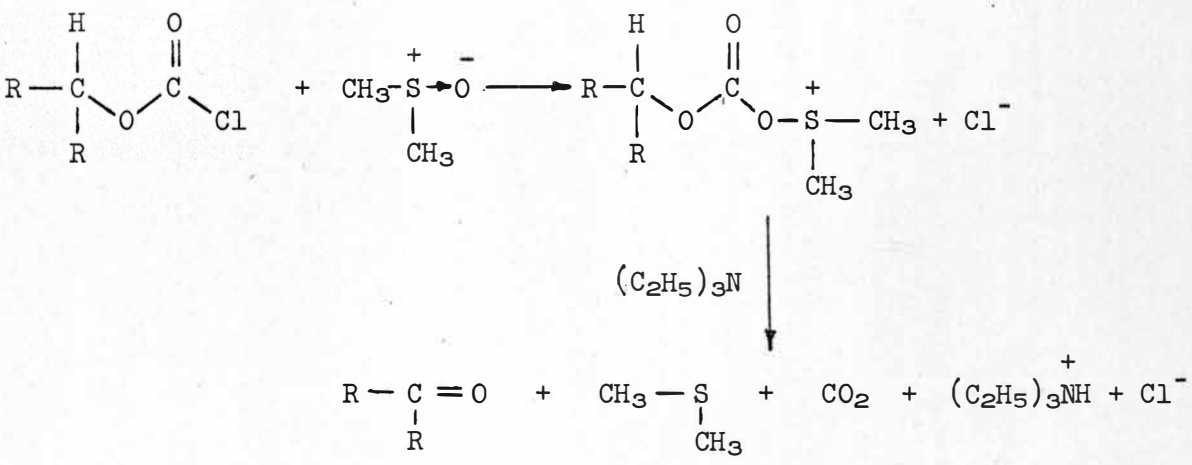
Among the earliest applications of this process have been the oxidation of α-haloketones,[10] α-haloesters,[9] alkylhalides,[11] alkyl tosylates,[11b,20] and epoxides[5]. Upon heating the compounds with DMSO in the presence of an acid acceptor such as sodium bicarbonate, a ketone or an aldehyde is formed. With primary iodides and tosylates, oxidation is often quite efficient; but with less reactive compounds, the formation of olefins and other by-products frequently occurs.

The mechanism usually accepted for this reaction involves nucleophilic displacement of a halide or tosylate by the oxygen atom in DMSO to give the intermediate sulfoxonium compound (Ia), which then decomposes into a carbonyl compound by concerted elimination of a proton and dimethyl sulfide[9,2].



X = halides or
tosylates

Barton and coworkers[4] have reported that alkyl chloroformates (chloroformic acid esters of alcohols) and DMSO react exothermally at room temperature with the formation of a reactive intermediate. The reaction of this intermediate with a base such as triethylamine gave the corresponding aldehydes or ketones, together with dimethyl sulfide. The mechanism proposed was similar to the previous one.

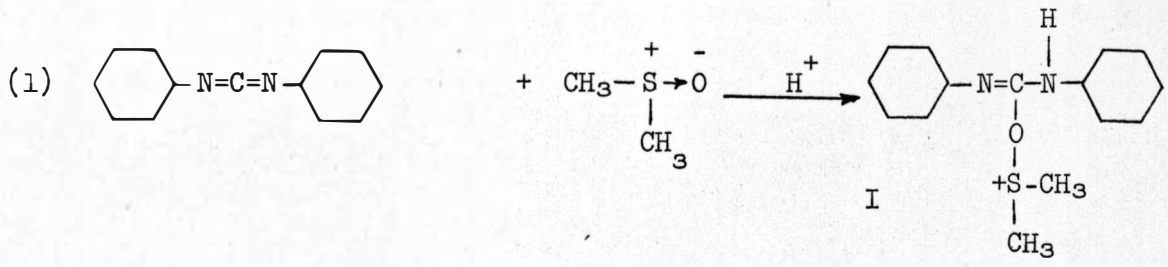


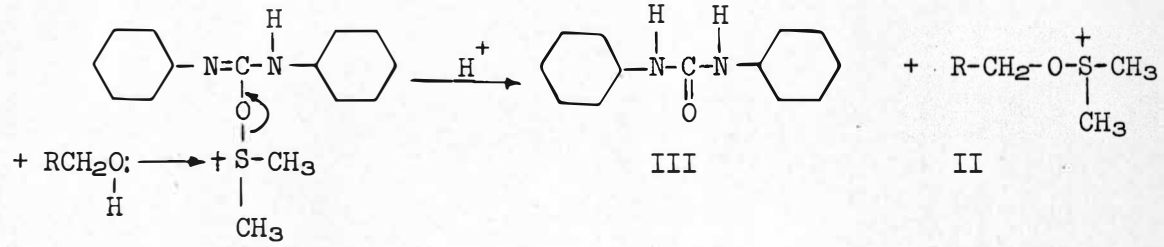
Carbohydrates have been found to be oxidized readily by the system DMSO-P_2O_5.[13] Phosphorous pentoxide has been found to accelerate the

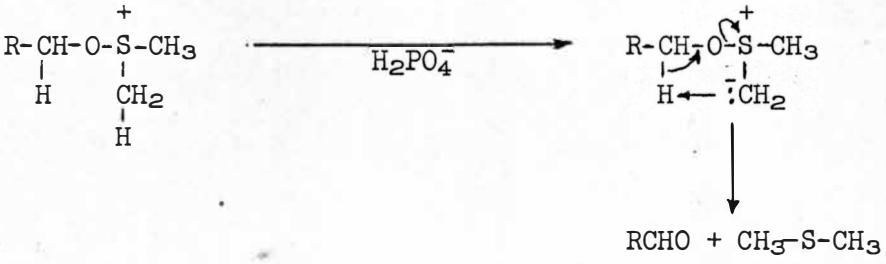
oxidation of hydroxyl groups in carbohydrates to aldehydes and ketones. This method of oxidation is a convenient way to prepare 3-ketoglucose which is a component of some microbial disaccharides.

Pfitzner and Moffatt[15] have done extensive work on this aspect of oxidation using, specifically, dicyclohexylcarbodiimide (DCC), and 100% orthophosphoric acid in dimethylsulfoxide. They have reported that 3—O-acetylthymidine is converted to the 3—O-acetylthymidine-5-aldehyde which was isolated as its 2,4-dinitrophenylhydrazone in 61% yield. No data on the oxidation of purine nucleosides was given.

The mechanism of oxidation resulting from treatment of an alcohol with DMSO and DCC in the presence of a proton source has been elucidated through an isotope experiment[6] and has been postulated to proceed via a nucleophilic attack of DMSO upon the protonated carbodiimide to give the sulfoxonium isourea intermediate (I) which is then attacked by the alcohol to form the alkoxysulfonium compound (II) and the highly insoluble dicyclohexylurea (III). The final step requires the abstraction of a proton from the alpha carbon atom of the alkoxy group and the concerted collapse of the resulting intermediate to the carbonyl compound and dimethyl sulfide.



(2) 

(2) 

Recent work of Lillien[12] has demonstrated that ketenimine undergos acid catalyzed addition of DMSO.

It has also been found that ketenimines undergo similar reactions as the carbodiimides,[18] for example addition of carboxylic acids and peptide bond formation.

INTRODUCTION

The purpose of this work is to investigate the possibility of using diphenylketene-N-p-tolylimine or benzonitrile along with dimethyl sulfoxide as an oxidizing agent. Ketenimine has been chosen because it undergoes reactions similar to carbodiimide,[18] and benzonitrile, because it can act as a Lewis acid to form the sulfoxonium intermediate.

The main purpose of this research is to oxidize the primary alcohol groups of purine nucleosides and carbohydrates. In order to facilitate the study of this reaction, simple primary alcohols were used.

EXPERIMENTAL

All melting points reported were corrected and are expressed in degrees centigrade.

Thin-layer chromatography was performed on silica gel-G and cellulose powder (Darmstadt). Spots were detected by ultraviolet light, iodine vapor, and 2,4-dinitrophenylhydrazine spray.

All ultraviolet measurements were made on a Cary Model-14 spectrophotometer, using 95% ethanol as solvent; and infrared spectra were obtained from samples in Nujol mulls using a Beckmann IR-8 Model instrument. The nuclear magnetic resonance spectra were determined with a Varian A-60 instrument; resonances were measured in cps downfield from tetramethylsilane standard. Elemental analyses were performed by Galbraith Laboratories, Inc. Dry DMSO was prepared by distillation from calcium hydride under reduced pressure and was stored over anhydrous barium oxide.

The stock solution used for the preparation of 2',3'-O-isopropylidenenucleosides was prepared by adding 100 g of pure-fused zinc chloride to a liter of purified acetone. The acetone was purified by distillation from potassium permanganate, dried over anhydrous sodium sulfate and redistilled.

The structure of the products obtained in the following experiments can be found on page 22.

Preparation of Starting Material

Preparation of 2',3'-O-isopropylideneadenosine

The desired isopropylidene derivative was prepared according to the method of Baddiley[3]. The purine nucleoside, 0.003 mole, which had been previously dried over phosphorous pentoxide under reduced pressure for at least 5 hr was dissolved in 250 ml of $ZnCl_2$-acetone stock solution. The slightly cloudy mixture was kept at room temperature for at least 20 hr, and evaporated under reduced pressure to about one third of its original volume. The concentrated solution was poured into 1 l of warm barium hydroxide solution which had been prepared by adding 150 g of barium hydroxide octahydrate to 1 l of water. The resulting solution was cooled to room temperature and CO_2 gas passed through until it was no longer alkaline to litmus. The resulting mixture was filtered, and the precipitate was washed first with boiling water, then with methanol (about 350 ml). The filtrate was evaporated at a temperature below 40° to about one third of the original volume. During the evaporation, the 2',3'-O-isopropylidene derivative crystallized. The mixture was allowed to stand overnight, and the crystals were collected by filtration and dried at 100°. A small amount of the product was isolated from the mother liquor after evaporation to dryness at 40° or below. The amount of material recovered from the mother liquor was relatively small compared to the first crop of crystals isolated, so this step was later omitted from the process. The combined solids were recrystallized from boiling

95% methanol. Pure white needle-like crystals were obtained in 59% yield, m.p. 219-221°, lit.[3] 220°.

Preparation of 1,2:3,4-di-O-isopropylidene-α-D-galactose

The method of Van Grunenberg and coworkers[21] was used for the preparation of the isopropylidene derivative of α-D-galactose. The finely-powdered galactose, 0.55 mole, gave 90 g of a syrupy product. Thin-layer chromatography showed a single spot. Infrared spectra gave an absorption ν max 3580 cm^{-1} and 1115 cm^{-1}, for O-H and C-O stretching vibrations, respectively. Nuclear magnetic resonance spectrum of a perdeuterated dimethylsulfoxide solution of isopropylidene derivative gave two sets of triplets centered at δ=1.3 and δ=3.5 ppm, a complex multiplet centered at δ=4.4 ppm, and a doublet centered at δ=5.45 ppm. The ratio of the relative areas were 12:5:2:1, respectively.

Preparation of N-(p-tolyl)-diphenylacetamide

The method of Stevens and French[17] was followed for the preparation of N-(p-tolyl)-diphenylacetamide. Diphenylacetic acid, 72 g, 0.168 mole, treated with 45 ml, 0.3 mole, of thionylchloride, and subsequently with 39 g, 0.182 mole, of p-toluidine, gave 141.7 g, 75% yield of crude product, m.p. 178-182°. After one recrystallization from methanol, the m.p. was 179-180°, lit.[17] 180-181°.

Preparation of diphenylketene-N-p-tolylimine

The method of Stevens and Singhal[19] was followed in the preparation of diphenylketene-N-p-tolylimine. Dried N-(p-tolyl)-diphenylacetamide,

0.022 mole, when reacted with 50 g of alumina and 25 g of phosphorous pentoxide, gave 8.2 g of diphenylketene-N-p-tolylimine (87% yield based on the acetamide). Recrystallization from acetone gave a crystalline yellow product, m.p. 82-84°.

Oxidation of Primary Alcohols to Aldehydes

General procedure for oxidation

Five millimoles of the alcohol was dissolved in 15 ml of DMSO containing 30 millimoles of diphenylketene-N-p-tolylimine. Polyphosphoric acid or 100% anhydrous polyphosphoric acid, 30 millimoles, dissolved in dry DMSO was then gradually added to the above solution. The reaction mixture was stirred for 20 hr at room temperature, poured into a beaker of ice-water, and extracted with three 250 ml portions of ether. The resulting aqueous solution was then treated with excess 2,4-dinitrophenylhydrazine (DNP). In cases where the compounds were soluble in ether, the aldehydes were separated from the rest of the ether soluble materials by evaporating the solvent and dissolving the residue in a small amount of ethanol. This solution was then poured into 300 ml of ice-water. The insoluble α-hydroxy and the unsubstituted diphenyl-N-p-tolylacetamide was separated by filtration leaving the aldehydes in solution. After chilling the solution, the yellow 2,4-dinitrophenylhydrazone of the corresponding aldehyde was removed by filtration. Thin-layer chromatography, using toluene-ethylacetate (1:1) as solvent showed the presence of dinitrophenylhydrazine as an impurity. After recrystallization of

the crude product from ethanol, yellow needles were obtained which gave one diffuse spot on a thin-layer chromatogram.

The ether extract was washed with sodium bicarbonate solution, then water, and dried over anhydrous sodium sulfate. Fractional crystallization of the crude white crystalline product from ethanol gave as the first fraction a material which melted at 190-193° [N-(p-tolyl)-α-hydroxyphenylacetamide, m.p. lit.[10] 189-190°, ν_{max} 3410 cm^{-1}(O-H), 3370 cm^{-1}(N-H), 1675 cm^{-1}(C=O)], and a second fraction melting at 180-181° [diphenyl-N-p-tolylacetamide, m.p. lit.[14] 180-181°, ν_{max}3370 cm^{-1} (N-H), 1675 cm^{-1}(C=O)]. Thin-layer chromatographic examination of the mother liquor left after fractional recrystallization of the α-hydroxy and the unsubstituted diphenyl-N-p-tolylacetamide showed a large and a small spot. The R_f value for the small, slow-moving component did not correspond to the value for either amide.

Oxidation of ethyl alcohol

In a manner similar to that described above, ethyl alcohol was oxidized to acetaldehyde which was isolated as its 2,4-dinitrophenylhydrazone derivative, m.p. 162-165°, in 21% yield. After a second recrystallization, it gave yellow needle crystals which melted at 163-164.5°, lit.[7] 167°. The infrared spectrum of the material showed absorption at ν_{max}3310 (N-H), 1620 (C=N), 1328 (NO_2), and 1590 (NO_2) cm^{-1}. The ultraviolet spectrum of the solution of the same compound gave an absorption λ_{max}348 and 235 mμ with ϵ_{max} of 11,700 and 5,300,

respectively. The nmr spectrum of a perdeuterated dimethyl sulfoxide solution gave a doublet centered at δ=2.05 ppm, a complex multiplet centered between δ=7.8 to 8.4 ppm, a doublet centered at δ=8.87 ppm, and a singlet at δ=11.4 ppm. The ratio of the relative areas were 3:3:1:1, respectively. All the shifts were relative to an internal standard of tetramethylsilane. The spectral data of an authentic sample prepared by treating the corresponding aldehyde with acidic 2,4-dinitrophenylhydrazine were found to be identical with the 2,4-dinitrophenylhydrazone prepared above. The melting points and the thin-layer chromatograms of these two compounds were in agreement.

Oxidation of β-phenylethyl alcohol

The general method of oxidation, as described above, was used to oxidize β-phenylethyl alcohol. The modification for ether-soluble materials was followed. Two and one half grams of the 2,4-dinitrophenylhydrazone derivative of β-phenylacetaldehyde were obtained when 3.66 g of the alcohol were used, corresponding to a 28.4% yield based on the alcohol, m.p. 123-126°. A second recrystallization in ethanol gave yellow crystals, m.p. 124-125°; ν_{max} 3310 (N-H), 1620 (C=N), 1585 (NO_2), 1330 (NO_2) cm^{-1}; and λ_{max}^{EtOH} 348, 230 mμ; ϵ_{max} 12,400, 6,000, respectively. An authentic sample of the dinitrophenylhydrazone prepared from phenylacetaldehyde and 2,4-dinitrophenylhydrazine and the above compound were found to have identical physical properties, m.p. 123-125°. Thin-layer chromatography of these products using toluene-ethyl acetate (1:1) as solvent indicated similar R_f values. Nuclear magnetic resonance spectra

were compared with the authentic material and were found to be identical. Both showed a doublet centered at δ=3.68 ppm, a singlet at δ=7.3 ppm, a complex multiplet centered at δ=8.1 ppm, a doublet centered at δ=8.8 ppm, and a singlet at δ=11.35 ppm using perdeuterated dimethyl sulfoxide as solvent. The ratio of the relative areas was 2:5:3:1:1, respectively.

Oxidation of 2',3'-O-isopropylideneadenosine

In a manner similar to the one described above, 2',3'-O-isopropylideneadenosine was oxidized to 2',3'-O-isopropylideneadenosine-5-aldehyde. The reaction mixture, after standing for 20 hr, was poured into ice-water. The ultraviolet spectrum of this aqueous solution gave a strong absorption band at 240 mμ. When an excess of 2,4-dinitrophenylhydrazone was added to the aqueous solution, a yellow precipitate was obtained. Recrystallization of this crude product from ethanol gave yellow needle-like crystals in a 7% yield based on the isopropylidene derivative, m.p. 128-131°; λ_{max}^{EtOH} 355, 260 mμ, with ϵ_{max} 26,750 and 19,000, respectively. The filtrate gave no absorption at 240 mμ, but two new bands at 355 and 275 mμ. Nuclear magnetic resonance spectrum of a perdeuterated dimethyl sulfoxide solution of the 2,4-dinitrophenylhydrazone derivative gave a doublet centered at δ=1.4 ppm, a triplet centered at δ=3.6 ppm, three sets of multiplets centered at δ=4.2, 5.2, and 8.0 ppm, and a singlet at δ=10.8 ppm. The relative areas were 6:2:1:3:6:1, respectively. Microanalysis values agreed with the calculated percentage for $C_{19}H_{20}N_9O_7 \cdot H_2O$.

Anal. Calc. for $C_{19}H_{20}N_9O_7 \cdot H_2O$: C, 45.48; H, 3.97; N, 23.1.

Found: C, 45.4; H, 4.28; N, 23.38.

In spite of many attempts, the remaining 2,4-dinitrophenylhydrazones of 2',3'-O-isopropylideneadenosine were not separated from the water-dimethylsulfoxide solution, as shown by the ultraviolet absorption at 355 and 275 mμ. These absorption bands were consistent with the assigned superimposition of the chromophores of adenosine and an aldehyde dinitrophenyl hydrazone.

Oxidation of 1,2:3,4-di-O-isopropylidene-α-D-galactose

1,2:3,4-di-O-isopropylidene-α-D-galactose was oxidized using the general method previously described. After oxidation, the ultraviolet spectra of the aqueous solutions were taken before and after the reaction with 2,4-dinitrophenylhydrazine. The absorption band at 240 mμ had disappeared after the reaction and was replaced by the absorption bands at 355 and 257 mμ. The aqueous suspension of the 2,4-dinitrophenylhydrazone derivative was then filtered, and the precipitate was recrystallized from EtOH to give light yellow crystals, m.p. 205-208° (decomp.); λ_{max}^{EtOH} 355 mμ (ϵ_{max} 8,700); and, ν_{max} 3340 (N-H), 1675 (C=N), 1575 (NO_2), 1326 (NO_2) cm^{-1}. Thin-layer chromatographic examination of this derivative showed it to be different from the original starting material. A nuclear magnetic resonance spectrum gave two sets of triplets centered at δ=1.3 and 3.5 ppm, a multiplet centered at δ=4.4 ppm, a multiplet centered at δ=8.2 ppm, and a singlet at δ=11.4 ppm. The ratio of the relative areas were 13:3:2:3:1, respectively.

Reaction of dimethyl sulfoxide with the acidic solution of benzonitrile and n-helptyl alcohol

Anhydrous orthophosphoric acid, 24.5 g, 0.25 mole, in 20 ml of dry DMSO was added to a solution of n-heptyl alcohol, 325 g, 0.25 mole, benzonitrile, 147 g, 2.5 moles, and 60 ml of dry DMSO. The solution was stirred vigorously for an hour and was allowed to stand for a period of 20 hr, poured into 200 ml of ice-water, and extracted with ether. The ether was evaporated and the resulting residue distilled. A first fraction, 10.62 g, b.p. 150-157°; lit.[10] 155°, was obtained. The infrared spectrum of the residue left after distillation gave absorption maxima at ν_{max} 1650 (C=O), 3348 and 3175 (N-H_2), 3030 (C-H, aromatic), and 750 (C-H, aromatic bending vibration) cm^{-1}. Yellow needle-like crystals were isolated when the aldehyde obtained previously, was reacted with 2,4-dinitrophenylhydrazine. After the second recrystallization from ethanol, material was obtained with the following properties: m.p. 106-107°, ν_{max} 3310, 1620, 1590 cm^{-1}. The nmr spectrum was identical with that of the authentic sample prepared by the treatment of enanthaldehyde with acidic 2,4-dinitrophenylhydrazine. Both materials gave a doublet centered at δ=0.9 ppm, a broad singlet at δ=1.35 ppm, a complex multiplet centered at δ=8.0 ppm, a doublet centered at δ=8.8 ppm, and a singlet at δ=11.25 ppm. The ratio of the relative areas were 3:10:3:1:1, respectively.

Determination of the optimum amount of diphenylketene-N-p-tolylimine

The optimum amount of diphenylketene-N-p-tolylimine was determined

by reacting a 0.4 mole and two portions of 0.01 mole of β-phenylethyl alcohol, separately, with 2.99 g (0.01 mole), 8.87 g (0.03 mole), and 2.99 g (0.01 mole) of the ketenimine, respectively. The conditions used were the same as in the previous reactions. The same amount of polyphosphoric acid (5 ml) and dimethylsulfoxide (40 ml) were used in each trial. The crystalline 2,4-dinitrophenylhydrazone derivatives, after one crystallization from ethanol, gave yields of 7%, 27%, and 2.5%, respectively, based on the alcohol used. Melting points (123-125°), ultraviolet, infrared, and nmr spectra all agreed with those of the β-phenylethyl alcohol 2,4-dinitrophenylhydrazone prepared previously.

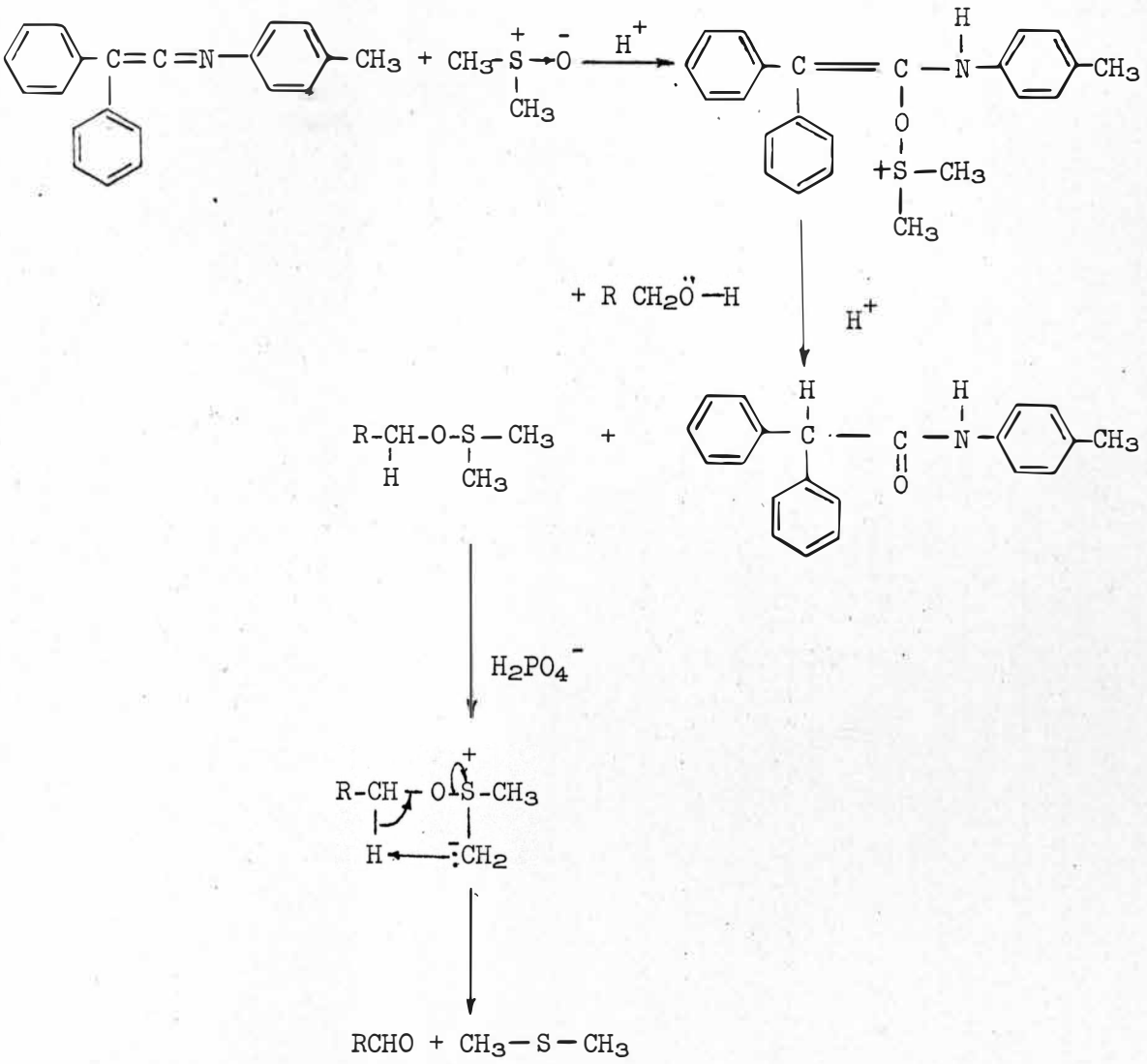
DISCUSSION

Oxidation reactions using diphenylketene-N-p-tolylimine, were studied using model compounds. The optimum proportion of the ketenimine was determined by performing three reactions, each of which contained the same amount of PPA and DMSO, but varying amounts of diphenylketene-N-p-tolylimine. The yield was best when three or six equivalents of ketenimine were used per equivalent of the alcohol. However, when excess alcohol, relative to ketenimine, was used, a considerable decrease in yield was observed. This may be attributed to the fact that other side reactions may predominate. One of these side reactions involves the addition of the aldoxy group of the alcohol to the alpha carbon atom of the ketenimine rather than to the positively polarized sulfur atom of the DMSO[12]. This was not anticipated since the carbon atom was more sterically hindered to the nucleophilic attack by the alkoxy group than the positive sulfur atom. Also the use of orthophosphate anion generated in the reaction was expected to drive the reaction forward by the abstraction of a proton on the carbon atom alpha to the sulfoxide group.

Two alcohols were oxidized to aldehydes as described in the previous section; ethyl alcohol and β-phenylethyl alcohol, in 21% and 28% yields, respectively, based on the amount of alcohol used. In each case two white crystalline products were isolated from the ether extract. These two products were compared with the authentic N-(p-tolyl)-diphenylacetamide and N-(p-tolyl)-α-hydroxyacetamide and found to be identical.

Thin-layer chromatography of the mother liquor gave a slow moving component which travels at the same rate as the product obtained when the alcohol was treated with diphenylketene-N-p-tolylimine and hydrochloric acid. In view of the above result and of the work done by Moffatt and Pfitzner[15] and by Lillien[11], we believe that the reaction goes by the following paths:

Path A:



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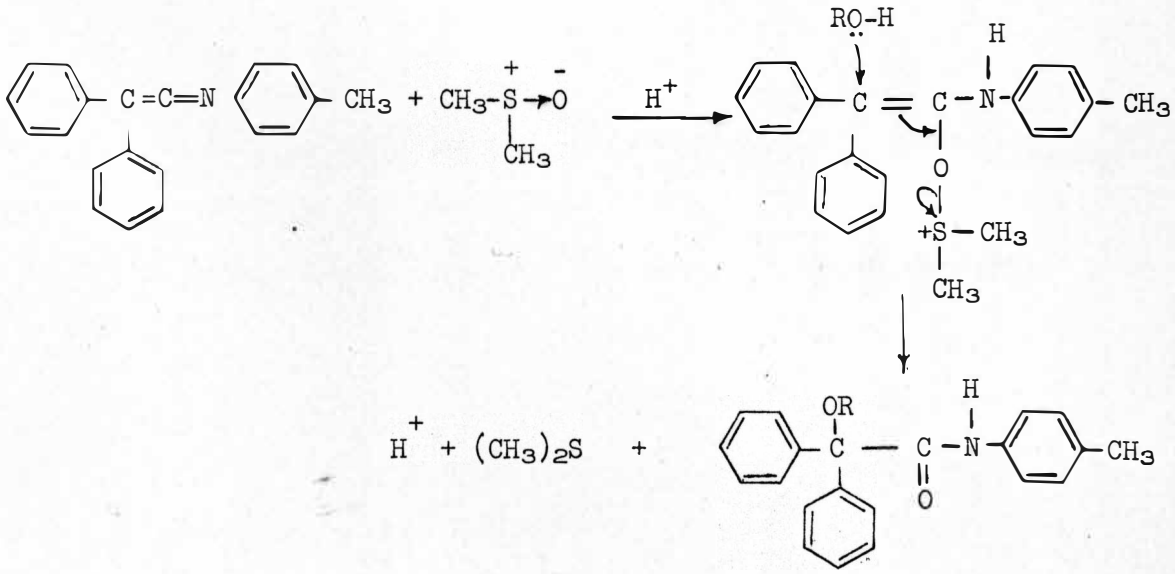


Since the purpose of this investigation was to develop a method of oxidation of carbohydrates and nucleosides on a preparative scale, the micro-technique of thin-layer chromatography was not used for isolation.

Oxidation of methyl glucoside resulted in the formation of various products, as shown by thin-layer chromatographic examination of the reaction mixture. Moffatt et al.[14] proposed that elimination of thymidine from thymidine-5′-phosphate or from thymidine derivatives possessing a free 3′-hydroxy group was a consequence of oxidation of this group to a ketone, followed by spontaneous β-elimination of the heterocyclic base or the 5′-phosphate. In view of these observations, the secondary

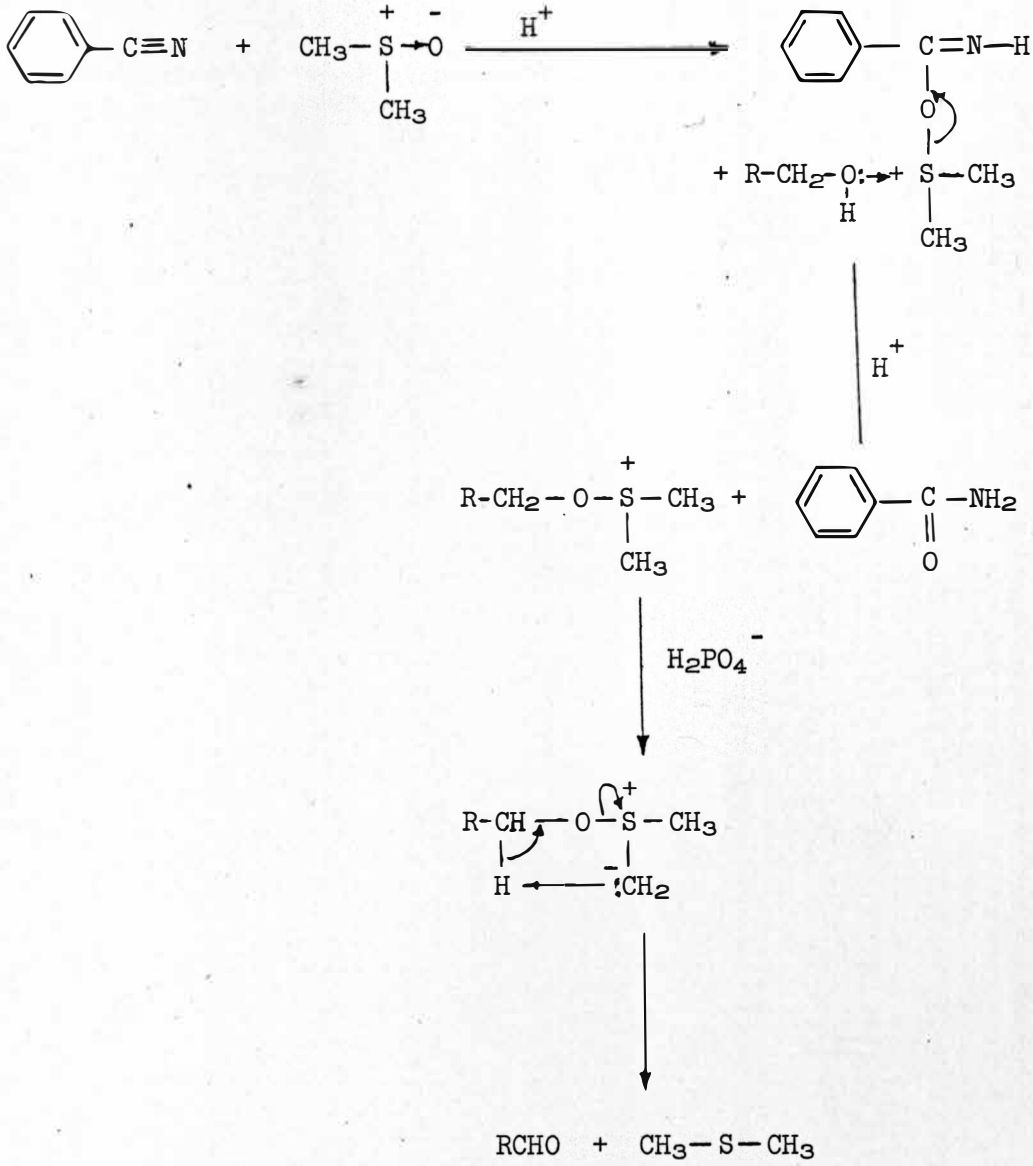
hydroxyl groups on the compounds studied were protected as isopropylidene derivatives.

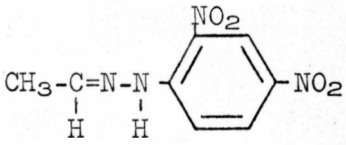
When the above-mentioned method was used to oxidize 2',3'-O-isopropylideneadenosine and 1,2:3,4-di-O-isopropylidene-α-D-galactose, problems in isolation were encountered. Both the derivative and the DMSO were soluble in water; and since it could not be extracted with water-immisible solvents, the only available method of removing the DMSO from the solution was by evaporation. This process, however, required prolonged heating of the compound at very low pressures, which resulted in side reactions. The 2,4-dinitrophenylhydrazone derivative of 2',3'-O-isopropylideneadenosine and 1,2:3,4-di-O-isopropylidene-α-D-galactose were isolated in 7% yield based on the isopropylidene derivative. Ultraviolet, infrared, and nmr spectra were consistent with the assigned structures, shown in figure I. Thin-layer chromatographic examination of the derivatives using toluene-ethyl acetate (1:1) and saturated butanol gave a single spot for each product which was different from the starting material.

The structure of 2',3'-O-isopropylideneadenosine was proven by spectral and elemental analyses. This compound showed ultraviolet maxima at 355 mμ (ϵ_{max} 26,750) and at 260 mμ (ϵ_{max} 19,000) which is consistent with the assigned superimposition of the chromophores of adenosine (λ_{max} 350 mμ, ϵ_{max} 9,000) and an aldehyde dinitrophenylhydrazone (λ_{max} 350 mμ, ϵ_{max} 20,000); λ_{max} 260 mμ (ϵ_{max} 10,000)[21]. The nmr spectrum is consistent with the assigned structure. The elemental analysis confirmed

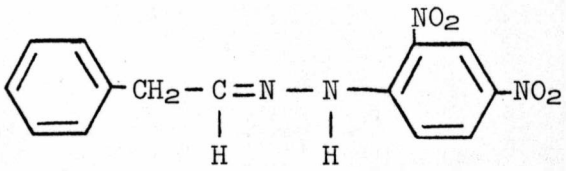
that this compound is the 2,4-dinitrophenylhydrazone derivative of 2',3'-O-isopropylideneadenosine-5'-aldehyde. The structure of 1,2:3,4-di-O-isopropylidene-α-D-galactose, 2,4-dinitrophenylhydrazone was proven by spectral analyses. The infrared spectrum, obtained from a sample nujol mull, showed absorption maxima at 3340 cm^{-1} corresponding to N-H stretching vibration and at 1655 cm^{-1} and 1326 cm^{-1} corresponding to $-NO_2$ vibrations. This compound showed ultraviolet absorption maxima at 355 mμ (ϵ_{max} 12,950) and 257 mμ (ϵ_{max} 8,700) which are consistent with the absorptions of an aldehyde dinitrophenylhydrazone[16]. NMR spectrum of this derivative is consistent with the assigned structure.

The same result was observed when benzonitrile was used instead of diphenylketene-N-p-tolylimine. The aldehyde, isolated by distillation and its 2,4-dinitrophenylhydrazone derivative, were identical to the authentic samples. The residue left after distillation was found to be the primary aromatic amide, benzamide. The reaction is believed to proceed as follows:

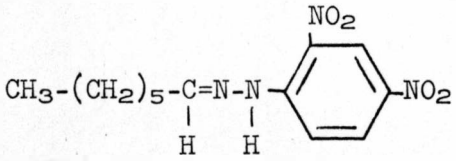

C≡N
+
CH3—S→O
CH3
H+
C=N—H
O
+ R-CH2—O:→+ S—CH3
H
CH3
H+
R-CH2—O—S—CH3 +
CH3
C—NH2
O
H2PO4-
R-CH—O—S—CH3
H
:CH2
RCHO + CH3—S—CH3



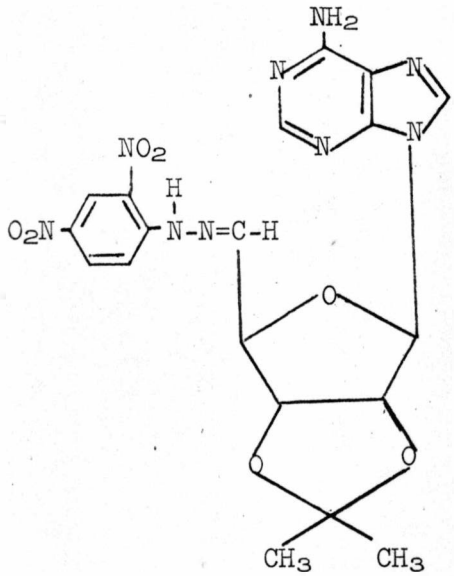
acetaldehyde, 2,4-dinitrophenylhydrazone



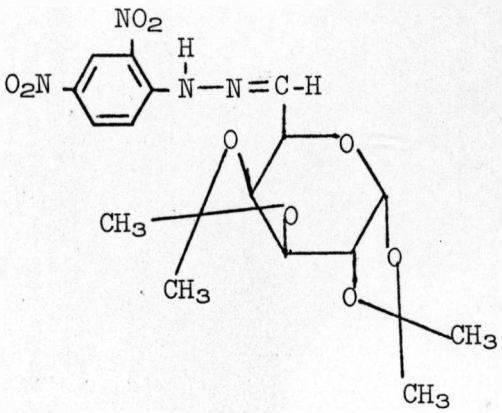
β-phenylacetaldehyde, 2,4-dinitrophenylhydrazone



heptaldehyde, 2,4-dinitrophenylhydrazone



2',3'-O-isopropylideneadenosine-5'-aldehyde 2,4-dinitrophenylhydrazone



1,2:3,4-di-O-isopropylidene-β-D-galactose- -aldehyde 2,4-dinitrophenylhydrazone

SUMMARY

The oxidation of primary alcohols to the corresponding aldehydes was studied. In this reaction, DMSO is believed to coordinate with the alcohol through its oxygen atom, similar to the mechanism proposed by Pfitzner and Moffatt[14]. This was followed by elimination of dimethyl sulfoxide. Model compounds were used to facilitate identification and isolation. Two different Lewis acids were used instead of the dicyclohexylcarbodiimide in the Pfitzner-Moffatt reagent; namely, diphenylketene-N-p-tolylimine and benzonitrile. The results were not as good as expected, probably due to competing side reactions and problems in isolation.

All of the model compounds were identified by comparing the spectral data, melting point, and thin-layer chromatograms with authentic samples. Spectral data of the 2,4-dinitrophenylhydrazone derivative of the nucleoside and the carbohydrate were consistent with the assigned structure.

BIBLIOGRAPHY

1. Albright, J. D. and Goldman, L., J. Am. Chem. Soc., 87, 4214 (1965).

2. a.) Baizer, M. M., ibid., 25, 670 (1960).
   b.) Jones, D. N. and Saud, M. A., J. Chem. Soc., 4657 (1963).
   c.) Nace, H. R. and Monagle, J. J., J. Org. Chem., 24, 1792 (1959).

3. Baddiley, J., J. Chem. Soc., 1348 (1951).

4. Barton, D. H. R., Garner, B. J., and Wightman, R. H., ibid., 1855 (1964).

5. Cohen, T. and Tsuji, T., J. Org. Chem., 26, 1681 (1961).

6. Fenselau, A. H. and Moffatt, J. C., J. Am. Chem. Soc., 88, 1762 (1966).

7. Hodgman, C. D., ed., "Handbook of Chemistry and Physics", Chemical Rubber Publishing Co., 41st ed., 1960, p. 764.

8. Hodgman, C. D., ed., ibid., 1960, p. 966.

9. Hunsberger, I. M. and Tien, J. M., Chem. Ind., (London), 88 (1959).

10. a.) Iacona, R. N., Rowland, A. T., and Nace, H. R., J. Org. Chem., 29, 3495 (1964).
    b.) Kornblum, N. et al., J. Am. Chem. Soc., 79, 6562 (1957).

11. a.) Johnson, A. P. and Pelter, A., J. Chem. Soc., 520 (1964).
    b.) Kornblum, N. et al., J. Am. Chem. Soc., 81, 4113 (1957).

12. Lillien, I., J. Org. Chem., 29, 1631 (1964).

13. Onodera, K., Hiraso, S., and Kashimura, N., J. Am. Chem. Soc., 87, 4651 (1965).

14. Pfitzner, K. E. and Moffatt, J. G., ibid., 87, 5661 (1965).

15. Pfitzner, K. E. and Moffatt, J. G., ibid., 87, 5671 (1965).

16. Selignan, R. B. et al., Anal. Chem., 28, 191 (1956).

17. Stevens, C. L. and French, J. C., J. Am. Chem. Soc., 75, 657 (1953).

18. Stevens, C. L. and Singhal, G. H., J. Org. Chem., 29, 34 (1964).

19. Stevens, C. L. and Munk, M. E., J. Am. Chem. Soc., 80, 4065 (1958).

20. Traynelis, V. and Heigenrother, W. N., J. Am. Chem. Soc., 86, 298 (1964).

21. Van Grunenberg, H., Bredt, C., and Freudenberg, W., ibid., 60, 1507 (1938).

VITA

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