coumarins has been prepared. The glucoside acetates of 4-hydroxycoumarin, 4-hydroxy-6-methylcoumarin, 3-phenyl-4-hydroxycoumarin and the monoglucoside acetate of 3,3′-methylenebis-(4-hydroxycoumarin) were prepared by treating the enol silver salts with acetobromoglucose.

2. The diglucoside octaacetate of 3,3′-methylenebis-(4-hydroxycoumarin) and of 3-[6-oxo(1)-benzopyrano(4,3-b)(1)benzopyran-7-yl]-4-hydroxycoumarin glucoside tetraacetate were prepared by coupling the aglucone with acetobromoglucose in the presence of catalytic amounts of quinoline and an excess of silver oxide.

3. The two 4-hydroxycoumarin glucoside tetraacetates unsubstituted on position 3 were successfully deacetylated by the catalytic barium methoxide procedure.

4. The 3-substituted-4-hydroxycoumarin glucoside acetates underwent alcoholysis with the removal of the glucose residue involving a Walden inversion. A course of reaction in which both glucoside residues were removed from 3,3′-methylenebis-(4-hydroxycoumarin) diglucoside octaacetate with the formation of 3,3′-methylene-4,4′-epoxydicoumarin, and 3,3′-methylenebis-(4-hydroxycoumarin) monomethyl ether is proposed

MADISON, WISCONSIN RECEIVED DECEMBER 14, 1943

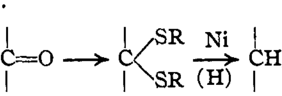
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Carbonyl Reduction by Thioacetal Hydrogenolysis

BY M. L. WOLFROM AND J. V. KARABINOS

In connection with another problem being pursued in this Laboratory, we were interested in convenient methods of synthesis for 1- and 2-desoxy sugar alcohols. The present methods are laborious and are not always of general applicability. The reduction of the 2-desoxyaldoses, synthesized through the glycals, constitutes the only present synthesis for the 2-desoxy sugar alcohols.[1] More numerous are the procedures for the preparation of the 1-desoxy sugar alcohols. These may be prepared through the reduction of a terminal halide in a sugar alcohol and special methods exist for obtaining these halides by utilizing the preferential reactivity of the primary alcohol function.[2] The 1-desoxy sugar alcohols are also preparable by reduction of the ω-desoxy-aldoses, either naturally occurring or synthesized[3] from the aldoses by reduction therein of a terminal halide group. In the acyclic sugar derivatives, a diisopropylidene-*aldehydo*-pentose has reacted with methyl Grignard reagent to produce, after hydrolysis of the isopropylidene groups, a 1-desoxy-hexitol.[4] Reduction of the first carbon of the diazomethyl ketones[5] of the acyclic sugar acetates or the reaction of diazomethane with *aldehydo*-sugar esters,[6] led to the synthesis of 1-desoxy-*keto*-sugar acetates which on reduction with subsequent deacetylation, led to the synthesis of a mixture of two 1-desoxy sugar alcohols.[7]

The remarkable discovery of the simultaneous desulfurizing and reducing action of Raney nickel[8] by Bougault, Cattelain and Chabrier[9] and its subsequent extension by Mozingo and co-workers,[10] offered the promise of establishing a simple and direct route to the 1- and 2-desoxy sugar alcohols. The French workers had demonstrated this reaction with the thiocarbonyl compounds, thiols, disulfides and heterocyclic sulfur (thiophene); the latter group had extended the reaction to sulfides, sulfoxides and sulfones; and Richtmyer, Carr and Hudson[11] had ememployed reductive hydrolysis with Raney nickel in their synthesis of polygalitol (1,5-anhydro-(*levo*)-sorbitol) tetraacetate from the acetates of glucothiopyranose and its disulfide. We have now found that this reaction is applicable to thioacetals, leading to easy reduction to the hydrocarbon stage.



$$\text{C=O} \longrightarrow \text{C}\begin{smallmatrix}\text{SR}\\ \text{SR}\end{smallmatrix} \xrightarrow[\text{(H)}]{\text{Ni}} \text{CH}_2$$

The other products of the reaction are presumably sulfide sulfur (verified in the present work) and the hydrocarbon RH. Following the directions of Mozingo and co-workers, we employed dilute ethanol as the solvent. Under these conditions we have noted that acetaldehyde is formed. This is to be expected from the dehydrogenating action of Raney nickel in the liquid phase,[12] but it may play some part in the reaction by furnishing a source of active hydrogen.

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(1) M. Bergmann, H. Schotte and W. Leschinsky, *Ber.*, **56**, 1052 (1923); E. Fischer, *ibid.*, **47**, 196 (1914).

(2) *Cf.* R. M. Hann, A. T. Ness and C. S. Hudson, THIS JOURNAL, **66**, 73 (1944).

(3) *Cf.* E. Fischer and K. Zach, *Ber.*, **45**, 3761 (1912).

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(5) M. L. Wolfrom and R. L. Brown, THIS JOURNAL, **65**, 1516 (1943).

(6) P. Brigl, H. Mühlschlegel and R. Schinle, *Ber.*, **64**, 2921 (1931); M. L. Wolfrom, D. I. Weisblat, W. H. Zophy and S. W. Waisbrot, THIS JOURNAL, **63**, 201 (1941).

(7) Unpublished work of Dr. B. W. Lew of this Laboratory.

(8) M. Raney, U. S. Patent 1,628,190 (1927).

(9) J. Bougault, E. Cattelain and P. Chabrier, *Bull. soc. chim.*, [5] **5**, 1699 (1938); *ibid.*, [5] **7**, 780, 781 (1940).

(10) R. Mozingo, D. E. Wolf, S. A. Harris and K. Folkers, THIS JOURNAL, **65**, 1013 (1943); V. du Vigneaud, D. B. Melville, K. Folkers, D. E. Wolf, R. Mozingo, J. C. Keresztesy and S. A. Harris, *J. Biol. Chem.*, **146**, 475 (1942).

(11) N. K. Richtmyer, C. J. Carr and C. S. Hudson, THIS JOURNAL, **65**, 1477 (1943).

(12) W. Reeves and H. Adkins, *ibid.*, **62**, 2874 (1940).

D-Galactose diethyl thioacetal (mercaptal) was reduced to L-fucitol but a higher yield (66%) was obtained when the pentaacetate was employed. In view of the ready availability of the aldose thioacetals and their acetates, this procedure gives easy access to the 1-desoxy sugar alcohols. Extension to D-glucose diethyl thioacetal pentaacetate yielded L-gulomethylitol pentaacetate.

The high acidity required for aldose thioacetal formation destroys the acid-sensitive ketoses[13] and thus the thioacetals of the ketoses cannot be obtained directly from the sugars. They are obtainable from the *keto*-acetates[14] and recently a general method for the synthesis of *keto*-acetates has been devised.[15] D-Fructose diethyl thioacetal (mercaptole) pentaacetate was subjected to hydrogenolysis and yielded 2-desoxy-(*levo*)-sorbitol pentaacetate, albeit in rather low yield. Even with this low yield, the present method is preferable to the former procedure[1] and it is possible that future work may lead to better reaction conditions and higher yields. Deacetylation to the parent alcohol, while not carried out in the present work, is a well-known and relatively simple process.

The above-described reduction of a carbonyl to a methylene group by means of neutral Raney nickel in dilute alcohol, offers promise in general organic preparative work. A previous reduction of a mercaptal with zinc dust and alkali is recorded[16] and recently the desulfurizing action of Raney nickel alloy and alkali in the hydrogenolysis of aromatic sulfonic acids has been described.[17] The present general methods for the reduction of a carbonyl group to the methylene stage are the Clemmensen reduction, the Wolff–Kishner method, high-pressure catalytic methods and electrolytic reduction. The thioacetal hydrogenolysis procedure adds an alternative method and descriptions are made of applications to benzaldehyde, benzophenone, acetophenone, heptanal and heptanone-2, producing in turn, toluene, diphenylmethane, ethylbenzene and heptane. The intermediate thioacetals are readily obtained and were used without purification.

Experimental

Preparation of Raney Nickel Catalyst.—The nickel catalyst was prepared from nickel–aluminum alloy (Raney) according to the procedure of Mozingo and co-workers,[18] employing their later-described[10] modifications. The nickel should be washed well to remove all traces of alkali.

A. Preparation of Desoxyhexitols

1-Desoxy-D-galactitol (L-Fucitol) Pentaacetate (Procedure A).—To 1.00 g. of D-galactose diethyl thioacetal (mercaptal) pentaacetate[19] was added 100 cc. of 70% ethanol and 15 g. of Raney nickel catalyst and the mixture was refluxed for five hours. At the end of this period a filtered test portion of the solution no longer evolved ethyl mercaptan on acidification with hydrochloric acid and heating. The nickel was removed by centrifugation and was washed several times with hot ethanol by centrifugation followed by decantation, and the centrifugates were combined. (It was noted that the nickel residue evolved hydrogen sulfide (tested with lead acetate paper) on treatment with dilute hydrochloric acid.) These were concentrated under reduced pressure at 40° to a volume of 10–20 cc., whereupon the product crystallized and was collected by filtration after cooling in an ice-bath; yield 0.55 g. (66%), m. p. 118–121°. Pure material was obtained on one recrystallization from ethanol; m. p. 126–127° unchanged on admixture with authentic L-fucitol pentaacetate of m. p. 126–127°, spec. rot. +20.9° (17°, *c* 2.8, $CHCl_3$, D line). The constants recorded[20] for L-fucitol pentaacetate are: m. p. 127°, spec. rot. +20.5° (25°, *c* 3.0, $CHCl_3$, D line).

1-Desoxy-D-glucitol (1-Desoxy-(*levo*)-sorbitol, L-Gulomethylitol) Pentaacetate.—D-Glucose diethyl thioacetal pentaacetate[21] (0.50 g.) was subjected to hydrogenolysis as in the preceding experiment (procedure A) and the reaction product was isolated in the same manner; yield 0.25 g. (60%), m. p. 98–101°. Pure material was obtained on further crystallization from ethanol; m. p. 102–103°, m. p. 102–104° on admixture with authentic L-gulomethylitol pentaacetate of m. p. 103–104°, spec. rot. +22° (17°, *c* 0.7, $CHCl_3$, D line), +20° (20°, *c* 0.5, MeOH, D line). The recorded[4] constants for L-gulomethylitol pentaacetate are: m. p. 105–106°, spec. rot. +21° (21°, *c* 2, MeOH, D line).

2-Desoxy-D-mannitol (2-Desoxy-(*levo*)-sorbitol, 2-Desoxy-D-glucitol) Pentaacetate.—D-Fructose diethyl thioacetal pentaacetate[14] (500 mg.) was subjected to hydrogenolysis as in procedure A except that the time of reaction was decreased to three hours. On concentration of the centrifugate under reduced pressure there was obtained a sirup (300 mg.) which crystallized with some difficulty; yield 82 mg. (20%), m. p. 68–70°, spec. rot. +31° (24°, *c* 2.8, $CHCl_3$, D line). Pure material was obtained on further crystallization from ether–petroleum ether; m. p. 85–87° unchanged on admixture with an authentic specimen of 2-desoxy-(*levo*)-sorbitol of m. p. 86–87°. The constants for this substance are: m. p. 86–87°, spec. rot. +35° (25°, *c* 3, $CHCl_3$, D line).[22]

1-Desoxy-D-galactitol (L-Fucitol) from D-Galactose Diethyl Mercaptal.—D-Galactose diethyl thioacetal[19] (1.00 g.) was subjected to hydrogenolysis as described in procedure A except that the reaction time was decreased to one hour and the nickel residues were washed thoroughly with water. The centrifugate was concentrated under reduced pressure to a thin sirup which was brought to crystallization by the addition of absolute ethanol; yield 140 mg. (24%) in 2 crops, m. p. 149–151°. Pure material was obtained on recrystallization from absolute ethanol; m. p. 152–153° unchanged on admixture with authentic L-fucitol of like m. p., spec. rot. +4.4° (25°, *c* 3, saturated aqueous borax solution, D line). The recorded[23] constants for L-fucitol are: m. p. 153–154°, spec. rot. +4.7° (20°, *c* 3, aqueous borax (1 part borax: 10 parts water) solution).

B. Thioacetal Formation and Hydrogenolysis of Several Simple Aldehydes and Ketones

Thioacetal Formation.—The aldehyde or ketone (0.1 mole) was added slowly with cooling (ice-bath), to a mixture of 20 cc. (*ca.* 2.7 moles) of ethyl mercaptan, 2.5 g. of freshly fused zinc chloride and 2 g. of anhydrous sodium

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[13] E. Fischer, *Ber.*, **27**, 673 (1894).

[14] M. L. Wolfrom and A. Thompson, This Journal, **56**, 880 (1934); *cf.* P. Brigl and R. Schinle, *Ber.*, **66**, 325 (1933).

[15] M. L. Wolfrom, S. W. Waisbrot and R. L. Brown, This Journal, **64**, 2329 (1942).

[16] C. Kelber and A. Schwarz, *Ber.*, **44**, 1693 (1911); **45**, 2484 (1912).

[17] E. Schwenk, D. Papa, B. Whitman and Helen Ginsberg, *J. Org. Chem.*, **9**, 1 (1944).

[18] R. Mozingo, H. Adkins and L. Richards, "Organic Syntheses," **21**, 15 (1941).

[19] M. L. Wolfrom, This Journal, **52**, 2467 (1930).

[20] M. L. Wolfrom, W. J. Burke and S. W. Waisbrot, *ibid.*, **61**, 1828 (1939).

[21] (a) W. Schneider and Johanna Sepp, *Ber.*, **51**, 226 (1918); (b) M. L. Wolfrom, This Journal, **51**, 2190 (1929).

[22] Unpublished work of Dr. M. Konigsberg of this Laboratory.

[23] E. Votoček and B. Potměšil, *Ber.*, **46**, 3653 (1913).

sulfate, contained in a glass-stoppered bottle. The aldehydes reacted more vigorously than the ketones. The mixture was maintained at 5° for twenty hours and then at room temperature for four hours, whereupon it was poured into 50 cc. of ice and water in a separatory funnel. The water-insoluble layer was washed consecutively with 10% aqueous sodium hydroxide and water, and dried with sodium sulfate. This crude product was used directly for the hydrogenolysis. The yields were nearly quantitative.

Hydrogenolysis of Benzaldehyde Diethyl Thioacetal.—The hydrogenolysis was carried out on 0.01 mole of the thioacetal as described in procedure A. After a reaction period of two hours, the mixture was diluted with 300 cc. of water and distilled until the cessation of ethanol distillation. The process was repeated on the distillate and to the azeotrope distilling over was added sufficient water to separate the toluene which was collected, dried and distilled; yield 0.60 g. (65%), b. p. 110° at 750 mm., $n^{25}\mathrm{D}$ 1.498. The generally accepted constants for toluene are: b. p. 111° at 760 mm., $n^{16}\mathrm{D}$ 1.4978.

Hydrogenolysis of Acetophenone Diethyl Thioacetal.—The thioacetal (0.01 mole) was treated in the manner described above for the hydrogenolysis of benzaldehyde diethyl thioacetal; yield of ethylbenzene 0.70 g. (66%), b. p. 134° at 750 mm., $n^{25}\mathrm{D}$ 1.498. The accepted constants for ethylbenzene are: b. p. 136° at 760 mm., $n^{14.6}\mathrm{D}$ 1.4983.

Hydrogenolysis of Heptanone-2 Diethyl Thioacetal.—The hydrogenolysis was carried out on 0.01 mole of the thioacetal as described in procedure A. The reaction product was distilled out of the reaction mixture, the distillate was diluted with a large volume of water and extracted twice with ether. The ether extract was washed with 50% calcium chloride aqueous solution, then with water, dried over sodium sulfate and distilled; yield 0.50 g. (50%), b. p. 96–100° at 750 mm., $n^{25}\mathrm{D}$ 1.390. The accepted constants for heptane are: b. p. 98.4° at 760 mm., $n^{23}\mathrm{D}$ 1.3867.

Hydrogenolysis of Heptanal Diethyl Thioacetal.—The thioacetal (0.01 mole) was treated in the manner described above for the hydrogenolysis of heptanone-2 diethyl thioacetal; yield of heptane 0.40 g. (40%), b. p. 98–100° at 750 mm., $n^{25}\mathrm{D}$ 1.395.

Hydrogenolysis of Benzophenone Diethyl Thioacetal.—The thioacetal (0.01 mole) was subjected to hydrogenolysis as described in procedure A. The sirup obtained on solvent removal from the centrifugate was dissolved in ether, dried with sodium sulfate, and the solvent removed; yield 1.3 g. (77%), b. p. 255° at 740 mm. A boiling point of 261–262° at 760 mm. is recorded for diphenylmethane. Further identification was afforded by the preparation[24] of the 2,4,2′,4′-tetranitro derivative which after two recrystallizations from glacial acetic acid melted at 170–173° (accepted value 172°).

Identification of Acetaldehyde Formed During the Hydrogenolysis.—In one of the experiments (the hydrogenolysis of heptanal diethyl thioacetal) the gases escaping from the top of the condenser during the refluxing were bubbled through 5 cc. of a solution of 2,4-dinitrophenylhydrazine (1 g. of the hydrazine dissolved in 7 cc. of concentrated sulfuric acid, then diluted with 100 cc. of methanol followed by 25 cc. of water). After one hour, crystalline needles separated which after two recrystallizations from ethyl acetate–ethanol were identified as acetaldehyde 2,4-dinitrophenylhydrazone by melting point (161–163°) and mixed melting point (unchanged) with an authentic sample (m. p. 162–164°).

Summary

1. It is shown that the carbonyl group of aldehydes and ketones may be reduced to the hydrocarbon stage by the hydrogenolysis of their thioacetals with Raney nickel in dilute ethanol solution.

2. Examples are cited for the diethyl thioacetals of *aldehydo*-D-galactose (and its pentaacetate), *aldehydo*-D-glucose pentaacetate, *keto*-D-fructose pentaacetate, benzaldehyde, heptanal, heptanone-2, acetophenone and benzophenone.

[24] Shriner and Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 2nd ed., 1940, p. 163.

COLUMBUS, OHIO RECEIVED MARCH 8, 1944

[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY[1a]]

Pyrolysis of Nicotine to Myosmine

BY C. F. WOODWARD, ABNER EISNER AND PAUL G. HAINES

Two new processes have been developed in this Laboratory for the preparation of nicotinic acid from nicotine. One involves the catalytic, vapor-phase, air oxidation of nicotine to nicotinonitrile,[1b] which is hydrolyzable to either nicotinic acid[2] or nicotinamide,[3] whereas the second employs the catalytic, liquid-phase, sulfuric acid oxidation of nicotine directly to nicotinic acid.[4]

It appeared that an alternative method could be employed for a stepwise conversion of nicotine to nicotinic acid which would utilize a preliminary pyrolysis of the alkaloid to β-alkyl and β-alkenyl pyridines prior to oxidation of these products.

This paper discloses the results obtained in a study of the pyrolytic reaction. Preliminary experiments indicated that the yields of such products as β-picoline, β-ethylpyridine, and β-vinylpyridine were too low to justify the utilization of this reaction in the preparation of nicotinic acid from nicotine. This investigation revealed, however, that myosmine (III) can be produced in fair yields, and most of the data herein reported were obtained in an attempt to determine the optimum pyrolytic conditions for the production of this rare alkaloid.

Brief references to the pyrolysis of nicotine have been made previously by Cahours and Étard,[5] but the two experiments reported were

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[1] (a) This is one of four Regional Research Laboratories operated by the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture. Article not copyrighted.

[1] (b) Woodward, Badgett and Willaman, accepted for publication in *Ind. Eng. Chem.*

[2] McElvain and Goese, THIS JOURNAL, **63**, 2283 (1941).

[3] Krewson and Couch, *ibid.*, **65**, 2256 (1943).

[4] Woodward, Badgett and Kaufman, accepted for publication in *Ind. Eng. Chem.*

[5] Cahours and Étard, *Compt. rend.*, **90**, 275 (1880); **92**, 1079 (1881).