pound would also give formic acid. The change of the specific optical rotation from $[\alpha]_D$ + 18.9° in D-glucopyranosylamine to +56.0° in compound III may be interpreted as being brought about by inversion of the amino group from the β- to the α-form incidental to the cyclization reaction.

Compound III is most likely the oxazolidone which Bromund and Herbst[2] attempted to prepare unsuccessfully.

EXPERIMENTAL[5]

Reaction of D-*glucopyranosylamine with phosgene.* Into a solution of 12.0 g. (0.067 mole) of D-glucopyranosylamine in 80 ml. of 1*N* sodium carbonate (0.08 mole) was slowly introduced 6.0 g. (0.061 mole) of phosgene at −5° to 0°. The solution was stirred for 2 hr. at 0° and then kept for 18 hr. at 5°. A solid material was recovered by filtration; yield 3.3 g. (24%). It was recrystallized twice from 50 ml. of 70% aqueous methanol and melted at 220–222° (dec.); $[\alpha]^{25}_D$ +56.0° (c, 2.2, H_2O). Infrared absorption at 1738 cm.$^{-1}$ (oxazolidone carbonyl), compared with 1720 cm.$^{-1}$ for authentic 2-oxazolidone. For periodic acid oxidation, the sample was dissolved in 1,2-dimethoxyethane.

Anal. Calcd. for $C_7H_{11}NO_6$: C, 40.99; H, 5.41; N, 6.83. Found: C, 41.16; H, 5.11; N, 6.72.

In other experiments compound III was obtained in yields varying from 6% to 30%.

Acetylation of III. The oxazolidone III (0.85 g., 0.0041 mole), dissolved in 16 ml. of pyridine, was treated with 6.3 g. (0.062 mole) of acetic anhydride added dropwise with stirring at room temperature. The solution was kept for 20 hr. at room temperature, and the product was precipitated by pouring on crushed ice; yield 1.2 g. (88%). Recrystallized twice from methanol-water, it melted at 150–151°; $[\alpha]^{24}_D$ +12.14° (c 0.8, $CHCl_3$).

Anal. Calcd. for $C_{15}H_{19}NO_{10}$: C, 48.26; H, 5.13; N, 3.76. Found: C, 48.62; H, 4.70; N, 3.94.

Acknowledgment. The author thanks Dr. Mack C. Harvey for measuring the infrared absorption spectra of compound III and of 2-oxazolidone and Dr. G. L. Braude and J. A. Cogliano for preparing large batches of D-glucopyranosylamine by pressure reactions of D-glucose with liquid ammonia.

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(5) All melting points are uncorrected. The elemental analyses were done by Clark Microanalytical Laboratory, Urbana, Ill.

Syntheses of 2,5,5-Trimethyl-3-hexanone, 2,5,5-Trimethyl-2-hexanol, 2,3-Epoxyheptane, 2,3-Heptanediol, and 4,4-Dimethyl-1,2-pentanediol

DONALD G. BOTTERON AND GARSON P. SHULMAN[1-3]

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Derivatives of 2,2,5-trimethylhexane with substituents in the 4-position provide the simplest structure for study of elimination reactions in which hydrogen atoms on a highly hindered secondary and an unhindered tertiary carbon atom react competitively with a base. Although syntheses of 2,5,5-trimethyl-3-hexanone and 2,5,5-trimethyl-3-hexanol can be effected by reaction of isopropylmagnesium halides with esters or acid halides[4] of *t*-butylacetic acid, or presumably with 3,3-dimethylbutanal, no convenient method for preparing any of these on a large scale has been reported. The chromic acid oxidation of 3,3-dimethyl-1-butanol (neohexyl alcohol) has been used for the preparation of *t*-butylacetaldehyde and *t*-butylacetic acid.[5]

Yields of 0–15% of neohexyl alcohol have been reported for the reaction of ethylene oxide with *t*-butylmagnesium chloride.[6] Repetition and modification using diethylene glycol dimethyl ether as a higher boiling solvent were unsuccessful as was an attempt to oxidize neohexyllithium, formed by addition of *t*-butyllithium to ethylene.[7] After several attempts to synthesize the aldehyde directly were abandoned (see below), a convenient route to the alcohol was discovered. The preparation of neohexyl chloride by addition of *t*-butyl chloride to ethylene[8] was employed; then the halide was converted to the Grignard reagent and oxidized by air. The reaction of neohexylmagnesium chloride with acetone led to the previously unreported 2,5,5-trimethyl-2-hexanol. The synthesis of 2,5,5-trimethyl-3-hexanone was effected through oxidation of neohexyl alcohol to *t*-butylacetic acid by potassium permanganate, preparation of the acid chloride with thionyl chloride, esterification with methanol, and reaction of the ester with isopropylmagnesium bromide. The semicarbazone was prepared and hydrogenated, but no amine was found.

Attempts to prepare *t*-butylacetaldehyde more directly met with limited success. Allyl chloride and *t*-butylmagnesium chloride were used for the preparation of 4,4-dimethyl-1-pentene, which reacted with performic acid to form 4,4-dimethyl-1,2-pentanediol (previously unknown). This was cleaved with lead tetraacetate to give *t*-butylacetaldehyde. However, the yields were low in all three steps (38%, 21%, and 53%, respectively). The

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(1) Du Pont Fellow 1957–1958.

(2) Present address: Archer-Daniels-Midland Co., Minneapolis, Minn.

(3) From a thesis presented by Garson P. Shulman in partial fulfillment of the requirements for the degree of Doctor of Philosophy, Syracuse University, 1959.

(4) F. C. Whitmore and W. S. Forster, *J. Am. Chem. Soc.*, **64**, 2966 (1942).

(5) M. Délacre, *Bull. Acad. roy. Belg.*, **7** (1906). [J. Chem. Soc. Abstracts, 476 (1906)].

(6) R. C. Huston and A. H. Agett, *J. Org. Chem.*, **6**, 123 (1942).

(7) P. D. Bartlett, C. G. Swain, and R. B. Woodward, *J. Am. Chem. Soc.*, **63**, 3229 (1941).

(8) L. Schmerling, *J. Am. Chem. Soc.*, **67**, 1152 (1945).

aldehyde has been prepared by hydrolysis of 1,1-dichloro-3,3-dimethylbutane at high temperature.[9] In a preliminary experiment, no aldehyde was obtained, but our pressure reaction vessel had begun to corrode. Reaction of the halide with sodium methoxide in methanol was unsuccessful, with sodium 1-pentoxide a small amount of the acetal was obtained along with 3,3-dimethyl-1-chloro-1-butene, while with sodium *t*-pentoxide a larger yield of the acetal resulted. It is apparent that interaction of the larger base with the *t*-butyl group minimizes attack on the beta hydrogen to form the vinyl halide (the usual reaction under these conditions), so that displacement occurs preferentially. The reaction was not readily adaptable to large scale runs because of the limited solubility of the sodium *t*-pentoxide in *t*-amyl alcohol.

EXPERIMENTAL

Neohexyl chloride. The reaction of *t*-butyl chloride and ethylene in the presence of aluminum chloride[8] was conducted at atmospheric pressure. A sample of *t*-butyl chloride (A) was mixed with a hydrocarbon solvent (B), then cooled to −20° in a three neck flask fitted with a sealed stirrer, an inlet tube extending below the surface of the liquid, and an outlet tube. Aluminum chloride (20 g.) was added, then ethylene was passed in somewhat more rapidly than it reacted. After 3 hr., addition of ethylene was halted, the mixture was allowed to warm, then the liquid was decanted, washed with water, dried over calcium chloride, and distilled, fractions, b.p. 110–118°, being collected. Run I: A — 200 g.; B — *n*-heptane, 700 ml.; yield 35%. Run II: A — 300 g.; B — hexane, 500 ml.; yield 24%. Run III: A — 400 g.; B — 30–60° ligroin, 1000 ml.; yield 25%. Run IV: A — 400 g.; B — 30–60° ligroin, 500 ml.; yield 36%.

Neohexyl alcohol. In the usual Grignard apparatus were placed 62 g. of magnesium turnings and a few crystals of iodine. A solution of 300 g. of neohexyl chloride in 375 ml. of ether was added slowly, then the mixture was stirred overnight. A 40-ml. portion was removed for the preparation of 2,5,5-tri-methyl-2-hexanol. Oxygen was passed in for 24 hr. at such a rate that none escaped past a 20-mm. head of mercury. The precipitate formed by addition of 100 ml. of water was dissolved by the addition of 500 ml. of 6 *N* hydrochloric acid. The organic phase was washed, dried over magnesium sulfate, then distilled, giving 126 g., boiling range 140–145°, a 50% yield. The reported b.p. is 141°.[6]

2,5,5-Trimethyl-2-hexanol. Reaction of neohexylmagnesium chloride with acetone gave 2,5,5-trimethyl-2-hexanol, boiling range 72–74° at 25 mm., $n^{20}\mathrm{D}$ 1.4260, a 30% yield based on amount of acetone.

Anal.[10] Calcd. for $C_9H_{20}O$: C, 75.0. H, 13.9. Found: C, 75.5. H, 13.8.

t-Butylacetic acid. A solution of 45 g. of sodium carbonate in 450 ml. of water was mixed with 204 g. of neohexyl alcohol in a 22-l. flask equipped with a stirrer and a dropping funnel. A solution of 520 g. of potassium permanganate in 11 l. of water was added over a 5-hr. period. The flask was then cooled in an ice bath and allowed to warm overnight. Excess permanganate was decomposed with sodium sulfite, then the manganese dioxide was removed by filtration. Ten liters of water was removed by distillation, then the remainder was covered with 200 ml. of ether and acidified with hydrochloric acid. The phases were separated, then the aqueous phase was extracted twice with 200 ml. of ether. The extracts were dried over sodium sulfate, then distilled, giving 94 g., boiling range 182–187°, $n^{20}\mathrm{D}$ 1.4115.

Methyl t-butylacetate. *t*-Butylacetic acid was treated with excess thionyl chloride, then methanol was added. A 72% yield of ester, b.p. 124–128°, $n^{20}\mathrm{D}$ 1.4000 was obtained.

2,5,5-Trimethyl-3-hexanone. The ketone, b.p. 74–80° at 27 mm., was prepared in 50% yield from isopropylmagnesium bromide and methyl *t*-butylacetate by the method of Whitmore.[4]

2,5,5-Trimethyl-3-hexanone semicarbazone. The semicarbazone, m.p. 168–169.5°, compared to a reported m.p. of 168–169°,[4] was prepared in 40% yield from 2,5,5-trimethyl-3-hexanone.

4,4-Dimethyl-1-pentene. Reaction of *t*-butylmagnesium chloride with allyl chloride[11] gave 38% of 4,4-dimethyl-1-pentene, b.p. 69–71°.

4,4-Dimethyl-2,3-pentanediol. The procedure used for 2,3-heptanediol (see below) was followed, using 1180 ml. of formic acid, 336 ml. of 30% hydrogen peroxide, and 335 g. of neopentylethylene. The boiling point is 140–141° at 60 mm., $n^{20}\mathrm{D}$ 1.4409.

Anal. Calcd. for $C_5H_{12}O_2$: C, 63.6; H, 12.1. Found: C, 63.3; H, 11.7.

t-Butylacetaldehyde. In a three neck flask fitted with a stirrer and a condenser, 600 ml. of dry benzene, 150 g. of potassium carbonate, and 67.5 g. of 4,4-dimethyl-1,2-pentanediol were mixed, then 228 g. of lead tetraacetate was added in 10-g. portions. When addition was complete, the ice bath was removed, the mixture was stirred for 2 hr., then filtered. The filtrate was distilled, giving 16 g. of *t*-butylacetaldehyde, boiling range 95–105°, reported boiling range 102–103°,[9] and 25 g., boiling point 212° (probably the glycol).

1,1-Dichloro-3,3-dimethylbutane. In a three neck flask fitted with a Dry Ice condenser, sealed stirrer, and inlet tube, 12 g. of anhydrous ferric chloride was cooled in a Dry Ice bath, then 92.5 g. of *t*-butyl chloride (at −40°) was added rapidly. Vinyl chloride was added until it began to reflux, then the Dry Ice bath was removed. The reaction mixture was stirred for 90 min., then the liquid was decanted, washed twice with water, dried over calcium chloride, and distilled, giving an average yield for eight such reactions of 45%, b.p. 45° at 19 mm., compared to a reported b.p. of 57° at 31 mm.[9]

On one occasion, addition of the vinyl chloride so rapidly that it escaped, caused the reaction to proceed violently, and the contents of the flask were lost.

Reaction of 1,1-dichloro-3,3-dimethylbutane with bases. A mixture of one mole of 3,3-dimethyl-1,1-dichlorobutane, two moles of sodium acetate, and 300 ml. of water was placed in the sealed reaction vessel of the Aminco hydrogenation apparatus and heated to 300°. After the bomb had cooled, the halide was recovered. A mixture of 11.2 g. of sodium methoxide, 15.5 g. of 3,3-dimethyl-1,1-dichlorobutane, and 50 ml. of methanol was refluxed for 18 hr. The mixture was filtered, dried, and distilled, 10 g. of the halide being recovered.

A solution of 9.2 g. of sodium in 200 ml. of *n*-amyl alcohol was mixed with 32 g. of 3,3-dimethyl-1,1-dichlorobutane, then refluxed for 8 hr., cooled, washed twice with water, and dried over magnesium sulfate. Distillation gave 11.0 g., boiling range 110–112°, probably 3,3-dimethyl-1-chloro-1-butene (negative 2,4-dinitrophenylhydrazine test, positive halogen test after sodium fusion), and 10.5 g. of pot residue after the *n*-amyl alcohol was removed at 135–138°. The pot residue was hydrolyzed by hydrochloric acid to a compound which gave a test with 2,4-dinitrophenylhydrazine, indicating that it contains *t*-butylacetaldehyde diamyl acetal.

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(9) L. Schmerling, *J. Am. Chem. Soc.*, **68**, 1650 (1946).

(10) Microanalysis by Drs. Weiler and Strauss, Oxford, England.

(11) Following the procedure used with allyl bromide, F. C. Whitmore and A. H. Homeyer, *J. Am. Chem. Soc.*, **55**, 4555 (1933).

A solution of 10 g. of sodium in 200 ml. of *t*-amyl alcohol (prepared by 18 hr. refluxing) was mixed with 31 g. of 3,3-dimethyl-1,1-dichlorobutane, then refluxed for 8 hr. The material was washed with water, dried, and distilled, giving 27 g. of pot residue, after products boiling below 120° had been removed.

This residue was washed three times with 50 ml. of water, leaving 20 g. The material was refluxed with 50 ml. of 12 *N* hydrochloric acid, washed with water, dried, and distilled, giving 20 g. of *t*-amyl chloride, b.p. 86–89°, and 2 g. of *t*-butylacetaldehyde, b.p. 108–110°. The 3 g. of pot residue was acid to litmus and smelled like an organic acid.

2,3-Epoxyheptane. A mixture of 9.8 g. of 2-heptene and 325 ml. of ether containing 0.1 mole of perphthalic acid was left in a refrigerator for 5 days. The solution was decanted, washed with sodium bicarbonate solution, ferrous sulfate solution, then twice with water, dried over magnesium sulfate, and distilled, giving 4.0 g. of material, boiling range 125–130°, n^{20}_D 1.4080, and 3.0 g., b.p. 135° n^{20}_D 1.4119. The yield is 61%.

Anal. of high boiling fraction: Calcd. for $C_7H_{14}O$: C, 73.6; H, 12.3. Found: C, 73.8. H, 12.6.

2,3-Heptanediol. A mixture of 100 ml. of 88% formic acid and 30 ml. of 30% hydrogen peroxide was placed in a three neck flask fitted with a thermometer, a stirrer, and a dropping funnel. After the mixture had been warmed to 40°, 19.6 g. of 2-heptene was added dropwise over a 25-min. period, then the mixture was left overnight. Water and formic acid were removed by distillation at reduced pressure, then the residue was mixed with an ice-cold solution of 16 g. of sodium hydroxide in 30 ml. of water, warmed to room temperature, and left for 2 hr. The mixture was extracted with five 50-ml. portions of ethyl acetate, the extracts were dried over magnesium sulfate and distilled, giving 13 g., b.p. 81° at 3 mm., n^{20}_D 1.4420 and 6.5 g., boiling range 91–94° at 3 mm., n^{20}_D 1.4445.

Anal. Calcd. for $C_7H_{16}O$ (b.p. 81°): C, 63.6; H, 12.1. Found: C, 65.0; H, 11.7.

Anal. (b.p. 91–94°): Found: C, 63.7; H, 12.0.

DEPARTMENT OF CHEMISTRY
SYRACUSE UNIVERSITY
SYRACUSE, N. Y.

Isolation and Partial Characterization of a Glucoside from *Rivea corymbosa* (L.) Hallier Filius

W. B. COOK AND W. EUGENE KEELAND[1a,b,c]

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During an investigation of the seed of *R. corymbosa*,[2] in an attempt to isolate the physiologically active constituents, a new glucoside was isolated in 1956. Primary interest was in the alkaloidal constituents of the seed and study of the glucoside was delayed until 1958. The glucoside was isolated from the ethanolic extract of the defatted pulverized seed. The white, crystalline glucoside had a melting point of 241–241.6° and has been assigned the molecular formula of $C_{28}H_{46}O_{12}$.[3] The infrared spectrum of the glucoside indicated the presence of only hydroxyl and ether functional groups. The acetate of the glucoside was prepared and recrystallized to a constant melting point of 247–248°. A determination of the acetyl groups present in the glucoside acetate indicated the presence of seven hydroxyl groups. (The infrared spectrum of the acetate indicated complete acetylation.) The glucoside heptaacetate has been assigned molecular formula $C_{42}H_{60}O_{19}$.

The glucoside gave negative alkoxyl tests, indicating ethers of the cyclic or bridged type. It has been shown that the aglucone is sensitive to low *p*H (*i.e.* a carbonyl is generated as a result of acid hydrolysis of the glucoside). Therefore, it is possible that the aglucone may contain a hemiacetal functional group.

The glucoside was hydrolyzed by suspending it in methanol-water solution with emulsin. The sugar moiety was identified as glucose by paper chromatography and confirmed by the preparation of its phenylosazone and pentaacetate. The aglucone melts at 166–168° and has been assigned the formula $C_{22}H_{36}O_7$. It formed a tetraacetate melting at 206–208°. Analysis indicated the presence of a terminal methyl group.

The absence of unsaturation was confirmed by negative tests with bromine water, ozone,[4] and tetranitromethane.

Dehydrogenation of the glucoside, using 5% palladium on charcoal at 350°, resulted in the isolation and identification of the following compounds: (a) phenanthrene, (b) 2-methylnaphthalene, and (c) 10 methyl-2-ethylphenanthrene.

It is postulated that the carbon skeleton of the aglucone is a hydrogenated pyranonaphthalene which contains four hydroxyls and three bridged ether groups.

When administered to rabbits, the glucoside exhibited about five times the potency as a central nervous system stimulant as did the initial ethanolic extract of *R. corymbosa*. Doses above the level of 31.6 mg./kg. proved fatal to test animals in 5–10 min.

EXPERIMENTAL[5a,b]

Isolation of glucoside. The ethanol soluble extract of *R. corymbosa* was dissolved in warm, distilled water. Concentration of the solution precipitated the glycoside as a white

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(1) (a) Abstracted from the Ph.D. thesis of W. Eugene Keeland, Montana State College, 1960. (b) This research was supported by the Medical Research Foundation, Stanford University, Palo Alto, Calif. (c) Present address: Tift College, Forsyth, Georgia.

(2) The seeds were identified as the seed of *R. corymbosa* by Dr. R. E. Schultes of Harvard University, Cambridge, Mass.

(3) M. C. Perezamador and J. Herran, *Tetrahedron Letters*, No. 7, 30, 1960, reported a compound with similar melting point. The molecular formula, optical rotation, and acetyl analysis differ significantly from that reported here.

(4) Ozonolyses were run by Dr. John Belew, Baylor University, Waco, Tex.

(5) (a) Microanalyses were run by Berkeley Analytical Laboratory, University of California, Berkeley, Calif. (b) Optical rotations were run by Schwarzkopf Microanalytical Laboratory, Woodside 77, N. Y.