concentration of the extract, produced a sirup (IV) which gave $[\alpha]^{25}D$ −118° (*c* 1.58, methanol).

Anal. Calcd. for $C_6H_{12}O_4S$: S, 17.8; OCH_3, 17.3; mol. wt., 180. Found: S, 17.5; OCH_3, 17.6; mol. wt., 178.

Periodate oxidation[20] showed 2 molar equiv. of periodate consumed, 0.2 molar equiv. of total acids produced, but with no formic acid produced.[7] The excess periodate consumed was probably due to the oxidation of the sulfur to a sulfone or sulfoxide.[21] Compound IV showed no thiolacetate adsorption or free mercapto groups with TTC and SNP. Hydrolysis of IV in 0.5 *N* hydrochloric acid resulted in a change of the specific optical rotation from −118° to +38° in 30 min. at 75°. This is suggestive that the glycoside is predominantly in the β-D-configuration. After hydrolysis was complete, the product was isolated by passing the solution through a column of Amberlite IR-45(OH) resin and concentrating to a sirup. This material, 4-deoxy-4-mercapto-D-ribofuranose, gave a positive test for reducing groups and had R_f 1.36 in irrigant A and 1.5 in irrigant B.

Compound IV gave a crystalline tri-*p*-nitrobenzoate[10]: m.p. 193–194°, $[\alpha]^{25}D$ +85.5° (*c* 0.38, chloroform).

Bis(methyl 4-deoxy-β-D-ribopyranoside) 4,4′-Disulfide (V).—Compound III (1.0 g.) was dissolved in 20 ml. of 2 *N* methanolic sodium methoxide and allowed to stand at 25° for 16 hr. The solution was passed through a column of Amberlite IR-120(H) resin for neutralization and removal of the isopropylidene group. To the effluent was added a few crystals of iodine and the mixture was refluxed for 3 hr. with oxygen bubbling through it. The cooled solution was concentrated to a thick sirup which was dissolved in 10 ml. of water and extracted twice with 25-ml. portions of chloroform to remove the excess iodine. The aqueous solution was concentrated under reduced pressure to dryness and the residue was crystallized from hot ethanol to give m.p. 152°, $[\alpha]^{25}D$ −229° (*c* 0.43 water), yield 0.41 g. (60%). Titration of the product with 0.1 *N* iodine solution[22] showed no thiol activity. Reaction with TTC and SNP gave no color test until after reduction of the disulfide bond with lithium aluminum hydride[23] in diethyl ether. The R_f for V in irrigant A was 1.90, in irrigant B, 2.3.

Anal. Calcd. $C_{12}H_{22}O_8S_2$: S, 17.8. Found: S, 17.5.

Acknowledgment.—The authors gratefully acknowledge Grant No. AM 06782-01 from the Department of Health, Education, and Welfare which helped support this work.

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Sodium–Liquid Ammonia Debenzylations in Nucleoside Synthesis[1]

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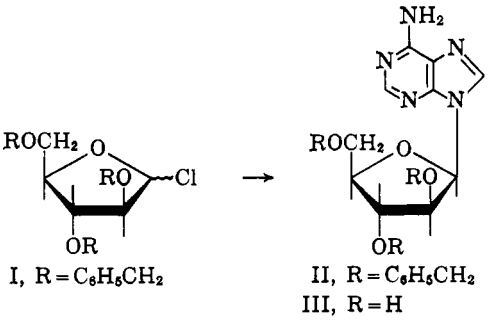
Received July 24, 1964

Recent publications[2] concerning spongoadenosine [(9-β-D-arabinofuranosyl)adenine, III], a nucleoside first synthesized in these laboratories,[3] have disclosed some interesting biological activities for the compound.



I, R = $C_6H_5CH_2$

II, R = $C_6H_5CH_2$

III, R = H

Accordingly the synthesis of III in quantity has become important both for further biological evaluation and for conversion to potentially useful analogs.

The description by Glaudemans and Fletcher[4] of the condensation of 2,3,5-tri-O-benzyl-D-arabinofuranosyl chloride (I) with 6-benzamido purine to give, after deblocking, the desired β-nucleoside (III) offered a practical, direct route to III. However, the final step in the synthesis, the catalytic hydrogenolysis of the intermediate II, was convenient only when small quantities of II were employed.

An alternative technique for removal of the benzyl blocking group of II was sought and the use of sodium in liquid ammonia was investigated. The numerous examples of debenzylation of S- and N-benzyl groups with sodium in ammonia made this a logical choice; surprisingly, however, there is virtually no mention in the literature of the use of this method for cleaving O-benzyl groups.[5] Recent work in this laboratory[6] described the smooth removal of both the O- and S-benzyl group of 6-amino-3-O-benzyl-5-S-benzyl-6-deoxy-1,2-O-isopropylidene-5-thio-L-idofuranose through the action of sodium in liquid ammonia. We wish to draw attention to this method of O-debenzylation because of its convenience and its applicability in situations where previously described methods of O-debenzylation are inappropriate.[7] It was possible to effect the conversion of II to III in high yield using sodium in liquid ammonia; this modification of the Glaudemans–Fletcher procedure[4] is especially convenient for large-scale synthesis of III. The stability of the adenine ring to the action of sodium in ammonia is noteworthy; there are numerous references to the reduction of nitrogen-containing heterocycles by this reducing agent.[9]

Experimental

To a stirred suspension of 3.75 g. (6.98 mmoles) of 9-(2′,3′,5′-tri-O-benzyl-β-D-arabinofuranosyl)adenine (II)[4] in 160 ml. of liquid ammonia was added a total of 600 mg. (26 mg.-atoms) of sodium in portions over 10–12 min. by which time the characteristic deep blue color persisted. At this point, the blue color

(1) This work was carried out under the auspices of the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, U. S. Public Health Service, Contract No. PH43-64-500. The opinions expressed are those of the authors and are not necessarily those of the Cancer Chemotherapy National Service Center.

(2) (a) M. Hubert-Habart and S. S. Cohen, *Biochim. Biophys. Acta*, **59**, 468 (1962); (b) G. A. LePage and I. G. Junga, *Cancer Res.*, **23**, 739 (1963); (c) J. J. Brink and G. A. LePage, *ibid.*, **24**, 312 (1964).

(3) (a) W. W. Lee, A. Benitez, L. Goodman, and B. R. Baker, *J. Am. Chem. Soc.*, **82**, 2648 (1960); (b) E. J. Reist, A. Benitez, L. Goodman, B. R. Baker, and W. W. Lee, *J. Org. Chem.*, **27**, 3274 (1962).

(4) C. P. J. Glaudemans and H. G. Fletcher, Jr., *ibid.*, **28**, 3004 (1963).

(5) H. Smith, "The Chemistry of Nonaqueous Ionizing Solvents," Vol. I, Part 2, "Organic Reactions in Liquid Ammonia," G. Jander, H. Spandau, and C. C. Addison, Ed., Interscience Publishers, Inc., New York, N. Y., 1963. Reductive fission with metal ammonia reagents is reviewed (p. 156). The author mentions unpublished work by W. Grassman, E. Wunsch, and G. Fries which is quoted by W. Grassman and E. Wunsch [*Fortschr. Chem. Org. Naturstoffe*, **13**, 487 (1956)], in which they report the regeneration of L-tyrosine and serine from their respective O-benzyl ethers using sodium and ammonia.

(6) L. Goodman and J. E. Christensen, *J. Org. Chem.*, **29**, 1787 (1964).

(7) In addition to the method of catalytic debenzylation already mentioned, it has been demonstrated[8] that carbohydrate benzyl ethers are readily acetolyzed. Acetolysis conditions are totally incompatible with nucleoside stability, however.

(8) R. Allerton and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **76**, 1757 (1954).

(9) Ref. 5, p. 276.

was discharged by the careful addition of ammonium chloride and the reaction was evaporated to dryness under a stream of nitrogen. The solid residue was triturated with 50 ml. of benzene (to remove bibenzyl), then was dissolved in 40 ml. of water. The aqueous solution was treated with Norit, then acidified with acetic acid to cause the precipitation of product (III). Filtration gave 1.53 g. (82%) of colorless product, m.p. 255–256° dec. (uncor.), which was identical in all respects with authentic spongoadenosine (III).[3]

In a larger run, 13 g. of II gave 6.1 g. (94%) of product III, m.p. 254–256° dec.[10]

(10) Private communication from Dr. R. R. Engle, of Riker Laboratories, Inc., Northridge, Calif.

Pinacol and Pinacolone Derivatives of Some Acylferrocenes

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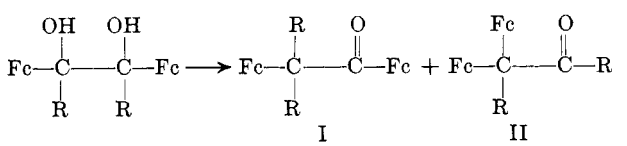
Received June 11, 1964

Several examples of the bimolecular reduction of ferrocenyl ketones have been reported in the literature.[1] Weliky and Gould, using methylmagnesium bromide and cobaltous chloride, obtained the pinacol derivative of benzoylferrocene and effected its conversion to the pinacolone. From the Clemmensen reduction of acetylferrocene, Pauson and Watts isolated an 87% yield of ethylferrocene and a 3% yield of the pinacolone derivative.

We wish to report bimolecular reduction of several alkylferrocenyl ketones to the corresponding vicinal diols and subsequent conversion of the diols to the rearranged diferrocenyl ketones. Yields of the diferrocenyl pinacols were 31 to 60% and of the diferrocenyl pinacolones 42 to 60%.

Acetylferrocene failed to undergo the two-step reaction described herein to the pinacolone derivative. However, *n*-propionyl-, *n*-butyryl-, and *n*-valerylferrocene all underwent bimolecular reduction in the presence of amalgamated magnesium to give the corresponding pinacol. With the exception of the bimolecular reduction product of *n*-propionylferrocene, which formed as a monohydrate, the diols were unstable and tended to undergo air oxidation with regeneration of the original ketones.

Rearrangement of the diols could lead to two possible structures for the pinacolones. All of the pinacolones



Fc = ferrocenyl
R = C_2H_5–, *n*-C_3H_7–, *n*-C_4H_9–

were shown to have structure II by virtue of strong carbonyl absorption at 1710 cm.$^{-1}$. All alkylferrocenyl ketones used in this study in which the aromatic moiety is directly attached to the carbon atom of the carbonyl group showed carbonyl absorption at 1675 cm.$^{-1}$ (carbon tetrachloride). No absorption bands at 1675 cm.$^{-1}$ were observed in any spectra of the pinacolones.

The formation of II would be expected with the anticipated migration of the aromatic group rather than the alkyl group during the pinacol–pinacolone rearrangement.[2]

No indications were found of the presence of substances having structure I in any instance. Column chromatography of the pinacolones on Alcoa F-20 activated alumina using 20% benzene in petroleum ether (60–90°) as the eluting agent always gave rise to only one band. The infrared data plus the facts that only one component could be isolated from the pinacolones through column chromatography and that all the pinacolones melted over a narrow temperature range, even before chromatography, tend to indicate that the rearranged ketones are of structure II and are not contaminated with significant amounts of products of structure I.

The pinacolones failed to form either 2,4-dinitrophenylhydrazones or oximes and could not be reduced by either the Clemmensen or Wolff–Kishner reactions. However, confirmatory evidence for the presence of a carbonyl group, in addition to the infrared data, was obtained through the ultraviolet spectra of the pinacolones which showed maximal absorption at 270 mμ.

Experimental[3]

Acylferrocenes.—The liquid ketones were synthesized by the procedure of Vogel[4]; most refractive indices have not been reported hitherto. *n*-Propionylferrocene was obtained as a red oil, b.p. 95–97° (0.1 mm.), $n^{25}D$ 1.6195 (lit.[5] m.p. 38–39°).

Anal. Calcd. for $C_{13}H_{14}FeO$: C, 64.49; H, 5.83. Found: 64.29; H, 6.11.

n-Butyrylferrocene upon distillation had b.p. 120–122° (0.25 mm.), $n^{25}D$ 1.6079 [lit.[6] b.p. 144–146° (1.5 mm.), $n^{20}D$ 1.6073]. *n*-Valerylferrocene upon distillation had b.p. 119–121° (0.08 mm.), $n^{25}D$ 1.5943 [lit.[7] b.p. 110–120° (air-bath temperature) (0.01 mm.), m.p. 36–38°].

Anal. Calcd. for $C_{15}H_{18}FeO$: C, 66.68; H, 6.71. Found: C, 66.82; H, 7.01.

Preparation of Diferrocenyldiols.—The diferrocenyldiols prepared through bimolecular reduction of the acylferrocenes are listed in Table I. Preparation of 4,5-diferrocenyl-4,5-octanediol (R = *n*-C_3H_7, Table I) exemplifies the general procedure. A solution of *n*-butyrylferrocene (41.8 g., 0.16 mole) and 2.5 g. of mercuric chloride in 75 ml. of dry tetrahydrofuran was added in a slow but steady stream to a boiling mixture of magnesium (2.2 g., 0.09 g.-atom) in 30 ml. of dry benzene. The reaction mixture was heated under reflux with stirring for 36 hr., with protection from atmospheric moisture. The cooled mixture was treated with 15 ml. of water and heated at reflux for 1 hr. Solid was removed by filtration and was extracted with several portions of boiling benzene. The combined filtrates were concentrated *in vacuo*, and the solid residue was washed with petroleum ether (60–90°) until the washings were only faintly yellow. The analytical sample was obtained as brown plates from benzene–

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(2) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 477.

(3) All melting points are uncorrected. Infrared spectra were determined with a Perkin-Elmer Model 21 spectrophotometer. The author wishes to thank Messrs. J. E. Sharpe and R. L. Hill for the microanalyses and Mr. R. A. Jewell for the infrared spectra.

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(5) K. L. Rinehart, Jr., R. J. Curby, Jr., and P. E. Sokol, *J. Am. Chem. Soc.*, **79**, 3420 (1957).

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