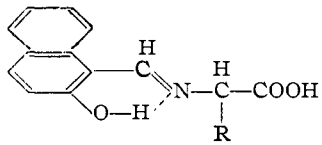
Hydrogenation of the —C=N— linkage was carried out on three of the Schiff bases as indicated in Table I. All three hydrogenated products gave positive ferric chloride tests for phenolic groups. The analyses suggest that with 2-hydroxy-1-naphthylglycylglycine the naphthalene ring may have been hydrogenated to some extent.

For —C=N— linkages of Schiff bases, these hydrogenations required extremely large amounts of catalyst. The glycine Schiff base was not noticeably reduced when 0.1 g. of 20% palladium on charcoal was used per 0.1 g. of Schiff base. The glycylglycine Schiff base was not noticeably reduced when five times its weight of Raney nickel with chloroplatinic acid promoter was employed.

This resistance to hydrogenation, along with the unusual ability of the *o*-hydroxyaldehydes to form Schiff bases with the monoamino acids, can be explained on a basis of intramolecular hydrogen bonding



This explanation is strengthened by analogy with salicylaldehyde anil which, according to Pauling,[9] has a very strong intramolecular hydrogen bond.

(9) Pauling, "Nature of the Chemical Bond," 2nd ed., Cornell University Press, Ithaca, N. Y., 1945, p. 319.

Upon hydrolysis of 2-hydroxy-1-naphthalvaline, -alanine and -methionine, as outlined above, the amino acids were recovered in 92, 80 and 75% yields, respectively.

2-Hydroxy-1-naphthaldehyde has been used as an amino group reagent in the isolation of amino sugars.[10] The stability of the amino acid Schiff bases and their ease of hydrolysis suggest the possibility of extending the use of *o*-hydroxy aromatic aldehydes as amino group reagents in biochemical isolation procedures.

Acknowledgment.—The author is grateful to E. F. Shelberg and associates for micro-elementary analyses, to Morris Freifelder for carrying out the hydrogenations and to J. R. Schenck for his interest and suggestions.

Summary

A number of crystalline Schiff bases of free amino acids, particularly the monoamino acids, were prepared by the reaction of free amino acids with *o*-hydroxy aromatic aldehydes under very mild conditions. Their stability is explained on a basis of intramolecular hydrogen bond formation. This explanation is supported by the fact that they are very difficult to hydrogenate. These Schiff bases can be hydrolyzed under mild conditions to give a good yield of the original amino acids.

(10) Jolles and Morgan, *Biochem. J.*, **34**, 1183 (1940).

NORTH CHICAGO, ILLINOIS RECEIVED FEBRUARY 4, 1947

[CONTRIBUTION FROM THE RESEARCH AND DEVELOPMENT DIVISION, COMMERCIAL SOLVENTS CORPORATION]

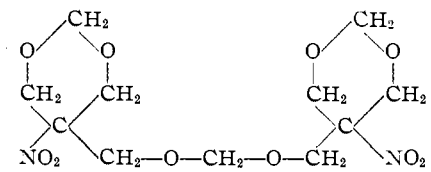
Acetals of Nitro Alcohols and Corresponding Amino Acetals[1]

BY MURRAY SENKUS

The preparation of cyclic acetals from polyhydric nitro alcohols derivable from formaldehyde and primary nitroparaffins has been reported in previous communications from this Laboratory.[2] We now wish to report the preparation of acetals from some monohydric nitro alcohols.

Adkins and Wade Adams had made a study of the catalysis of the formation of acetals from monohydric alcohols and aldehydes.[3] They found that calcium chloride is the most effective catalyst with the lower aldehydes and alcohols while dry hydrogen chloride is best for the higher members of these series. These catalysts were found to be unsuitable for the preparation of acetals from monohydric nitro alcohols owing to the insolubility of calcium chloride in the reaction mixtures used and the volatility of hydrogen chloride during the reactions. Benzenesulfonic acid and *p*-toluenesulfonic acid were found to be most satisfactory for the reactions at hand.

We also wish to report the preparation of 1,5-bis-(1-nitro-3,5-dioxacyclohexyl)-2,4-dioxapentane, from tris-(hydroxymethyl)-nitromethane



and formaldehyde. The structure of this compound is supported by nitrogen analysis and molecular weight determination and by the observation that three moles of formaldehyde reacted with two moles of tris-(hydroxymethyl)-nitromethane to give the calculated amount of product. Analytical data on the diamine obtained by hydrogenation of this compound also support the proposed structure.

(1) Prepared for the 1946 Fall meeting of the Organic Division, A. C. S. The subject matter of this paper is covered by U. S. Patents 2,415,046, 2,363,464, 2,413,249 and 2,413,250.

(2) (a) Senkus, THIS JOURNAL, **63**, 265 (1941); (b) **65**, 1656 (1943).

(3) Adkins and Wade Adams, *ibid.*, **47**, 1358 (1925).

TABLE I

SOME NITRO AND AMINO ACETALS

Product	M. p., °C.	B. p. °C.	Mm.	$n^{20}D$	d^{20}_{20}	Formula	Nitrogen, % Calcd.	Found
bis-(2-Nitroisobutoxy)-methane	62.1					$C_9H_{18}N_2O_6$	11.20	11.18
bis-(2-Nitro-1,3-dimethylpropoxy)-methane	54.5					$C_{11}H_{22}N_2O_6$	10.07	10.12
bis-(2-Nitrobutoxy)-methane		166	4	1.4506	1.1575	$C_9H_{18}N_2O_6$	11.20	10.97
bis-(2-Nitroisobutoxy)-phenylmethane	63.0					$C_{15}H_{22}N_2O_6$	8.58	8.53
bis-(2-Nitroisobutoxy)-*i*-propylmethane	60.0					$C_{12}H_{24}N_2O_6$	9.58	9.74
1,5-bis-(1-Nitro-3,5-dioxacyclohexyl)-2,4-dioxapentane	162.2					$C_{11}H_{18}N_2O_{10}$[a]	8.28	8.03
bis-(2-Aminoisobutoxy)-methane		72–74	2	1.4410	0.9277	$C_9H_{22}N_2O_2$	14.72	14.73
bis-(2-Amino-1,2-dimethylpropoxy)-methane		90–92	2	1.4511	.9342	$C_{11}H_{26}N_2O_2$	12.83	13.07
bis-(2-Aminobutoxy)-methane		126.2–127.7	9.5			$C_9H_{22}N_2O_2$	14.72	14.41
bis-(2-Aminoisobutoxy)-phenylmethane		121–122	2		.9939	$C_{15}H_{26}N_2O_2$	10.51	10.74
bis-(2-Aminoisobutoxy)-*i*-propylmethane		90–92	2	1.4388	.8892	$C_{12}H_{28}N_2O_2$	12.05	12.17
1,5-bis-(1-Amino-3,5-dioxacyclohexyl)-2,4-dioxapentane		215	7	1.4850[b]	1.2413[c]	$C_{11}H_{22}N_2O_6$	10.07	10.07

[a] Mol. wt. Calcd.: 338. Found: 342. [b] $n^{35}D$. [c] d^{33}_{33}.

The nitro acetals which were prepared were hydrogenated to the corresponding amino acetals. The new compounds reported herein are listed in Table I.

Experimental

Preparation of Nitro Acetals.—The following preparation of the **formaldehyde acetal of 2-nitro-2-methyl-1-propanol** is representative of the methods which were used in the preparation of the formals. A mixture of 119 g. (1 mole) of 2-nitro-2-methyl-1-propanol, 17 g. (0.56 mole) of trioxymethylene, 200 ml. of toluene and 0.5 g. of either benzenesulfonic acid or *p*-toluenesulfonic acid was refluxed in a flask connected to a water separator. After the separation of water had ceased, the mixture was washed with an aqueous bicarbonate solution and then with water. Toluene was removed by distillation under diminished pressure. The crude solid product was purified by recrystallization from petroleum ether. The conversions to formals averaged 95%.

The **benzaldehyde acetal of 2-nitro-2-methyl-1-propanol** was prepared by refluxing as above for sixteen hours a mixture of 119 g. (1 mole) of 2-nitro-2-methyl-1-propanol, 70 g. (0.65 mole) of benzaldehyde, 150 ml. of toluene and 1 g. of *p*-toluenesulfonic acid. Unreacted aldehyde and nitro alcohol were then distilled at 5 mm. pressure. The residue together with 5 g. of potassium carbonate and a gram of charcoal was heated at 100° for one hour. After filtration the mixture solidified on standing at room temperature. A recrystallization from petroleum ether yielded 20 g. of a white crystalline product.

The **isobutyraldehyde acetal of 2-nitro-2-methyl-1-propanol** was prepared by refluxing a mixture of 80 g. (0.67 mole) of 2-nitro-2-methyl-1-propanol, 200 g. (2.77 moles) of recently distilled isobutyraldehyde and 0.5 g. of *p*-toluenesulfonic acid in a flask connected to a 4-foot laboratory column which was connected to a water separator. After sixteen hours the mixture was washed with a bicarbonate solution and water. It was treated with decolorizing charcoal and distilled under diminished pressure to remove unreacted aldehyde. The residue was dissolved in 100 ml. of petroleum ether and on cooling to −10°, crystals separated from the solution. The mixture was filtered. Two recrystallizations of the solid from petroleum ether yielded 16 g. of a white crystalline product.

Hydrogenation of Nitro Acetals.—Each of the nitro acetals with the exception of the **formal of 2-nitro-1-butanol** was hydrogenated to the corresponding amino acetal according to a similar procedure. The nitro acetal dissolved in methanol was hydrogenated for two to four hours at 60° and 1000 lb./sq. in. in the presence of Raney nickel catalyst. The mixture was filtered and the product was isolated by rectification of the filtrate. Conversions of nitro acetals to amino acetals averaged 95%. Hydrogenation of **2-nitro-1-butanol formal** under similar conditions yielded a complex mixture. The formal was finally hydrogenated according to the following procedure: A mixture of 75 g. of this formal, 150 ml. of water, 100 g. of carbon dioxide and 10 g. of Raney nickel catalyst was hydrogenated for two hours at 75° and 1900 lb./sq. in. The filtered solution was agitated with 100 ml. of 44% sodium hydroxide solution and the mixture was extracted with three 130-ml. portions of ethyl ether. Fractionation of the ether extract yielded the desired product in 63% conversion.

Summary

The formaldehyde acetals of 2-nitro-2-methyl-1-propanol, 2-nitro-1-butanol and 3-nitro-3-methyl-2-butanol, the benzaldehyde and isobutyraldehyde acetals of 2-nitro-2-methyl-1-propanol and 1,5-bis-(1-nitro-3,5-dioxacyclohexyl)-2,4-dioxapentane have been prepared and some of their physical properties are described. With the exception of 2-nitro-1-butanol formal, each of the nitro acetals was hydrogenated in methanol in presence of Raney nickel to the corresponding amino acetal in excellent yield. 2-Nitro-1-butanol formal was hydrogenated in the presence of carbon dioxide, water and Raney nickel.

TERRE HAUTE, ILLINOIS RECEIVED FEBRUARY 19, 1947