third ampoule provided with a break-seal and cooled with liquid nitrogen. The ampoule was sealed off, allowed to warm to −78° and then placed in an ice-bath. These precautions were taken to prevent too rapid warming of the mixture. At 0°, a white slush, presumably zinc chloride and germanium tetramethyl, was observed in the ampoule. The ampoule was removed from the ice-bath, attached to a vacuum manifold and opened. A nearly quantitative yield of germanium tetramethyl was evaporated into a receiver cooled with liquid nitrogen. Total non-condensable gases, principally methane, were measured, analyzed with the mass spectrometer, and discarded. A mass spectrometric analysis of the condensable fraction showed only a trace of germanium tetrachloride. The impurities of the combined condensable and non-condensable fractions totaled less than one mole per cent. No zinc compounds volatile at room temperature were observed.

In the second preparation a calculated 100% excess of germanium tetrachloride was used. After sealing off the reaction ampoule, it was immediately removed from the liquid nitrogen and allowed to warm directly to room temperature. Crystals of zinc chloride appeared only after 30 minutes, presumably because of the solubility in the excess germanium tetrachloride. After standing overnight at room temperature the ampoule was attached to the vacuum manifold and was opened. The excess germanium tetrachloride was almost completely removed by a single bulb-to-bulb vacuum distillation through a short column of potassium hydroxide pellets in series with the receiving bulb and attached to the manifold. This proved to be a very convenient way to remove the chloride compounds as the pellets retained sufficient water even under vacuum to hydrolyze the germanium tetrachloride. Mass spectrometric analysis of the product after removal of the chlorides indicated a purity comparable with that of the first preparation.

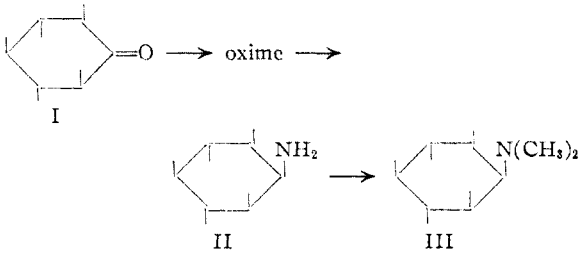
NATIONAL BUREAU OF STANDARDS
WASHINGTON, D. C.

Cyclitol Derivatives. IV. 2-Keto-*myo*-inositol Thiosemicarbazone and 2-Dimethylamino-2-desoxy-*myo*-inositol[1]

BY H. GEORGE LATHAM, JR., EVERETTE L. MAY AND ERICH MOSETTIG

RECEIVED DECEMBER 6, 1951

The first communication[2] of this series included among other N-containing cyclitols, the thiosemicarbazone of D,L-2-keto-*epi*-inositol (*rac-epi*-inosose) and an N,N-dimethylinosamine (either D,L-2-dimethylamino-2-desoxy-*epi*-inositol or D,L-4-dimethylamino-4-desoxy-*myo*-inositol) derived from this cyclose. We now wish to report two corresponding isomeric compounds which have been prepared from 2-keto-*myo*-inositol (*scyllo*-inosose) (I).



Carter, *et al.*,[3] hydrogenated with Raney nickel both the oxime and the phenylhydrazone of I and obtained a mixture of inosamines. We have hydrogenated I oxime in 50% methanol with platinum oxide and have isolated 2-amino-2-desoxy-*myo*-inositol (inosamine SA) (II).[4]

Methylation of II with formaldehyde and formic acid produced the N,N-dimethyl derivative (III). This tertiary amine, its precursor (II) and the thiosemicarbazone of I have been tested for *in vitro* activity against tuberculosis (Dubos–Davis medium H37Rv).[5] They were not significantly active.

Experimental

Hydrogenation of 2-Keto-*myo*-inositol Oxime.—One gram of the oxime,[6] 0.1 g. of platinum oxide, 10 ml. of water and 10 ml. of methanol absorbed two moles of hydrogen during 10 to 15 hours. Addition of water, warming to solution, filtration and evaporation of the filtrate to one-fourth volume gave 0.5 g. (55%) of 2-amino-2-desoxy-*myo*-inositol (II), m.p. 277–279.5° (cor., evac. tube).

Anal. Calcd. for $C_6H_{13}NO_5$: C, 40.2; H, 7.3. Found: C, 40.7; H, 7.3.

The hydrochloride of II (NIH 3641) melted at 230–233° (Kofler) after undergoing transition at 187–195°, while the N-acetyl derivative melted at 245–248°.[3,4]

2-Dimethylamino-2-desoxy-*myo*-inositol (III) Hydrochloride.—Two grams of II, 2.0 ml. of 37% aqueous formaldehyde and 2.4 ml. of 98% formic acid, heated on the steam-bath for two hours, cooled, treated with a slight excess of concentrated hydrochloric acid and diluted with methanol, then ether, gave 1.7 g. (60%) of the hydrochloride of III. After three recrystallizations from methanol–ether (Norit), it melted at 218–220° (cor.)

Anal. Calcd. for $C_8H_{18}ClNO_5$: C, 39.4; H, 7.4. Found: C, 39.5; H, 7.3.

2-Keto-*myo*-inositol Thiosemicarbazone (NIH 3845).—One gram of I,[6] 0.6 g. of thiosemicarbazide and 15 ml. of water were kept on the steam-bath for 10 minutes and at 5° overnight to give 0.9 g. (70%) of thiosemicarbazone. Recrystallized from water (Norit) it melted at 194.5–196° (cor., dec.).

Anal. Calcd. for $C_7H_{13}N_3O_6S$: C, 33.5; H, 5.2. Found: C, 33.6; H, 5.1.

Acknowledgment.—We are indebted to Dr. Laura C. Stewart of this Institute for the biochemical preparation of 2-keto-*myo*-inositol. Microanalyses are from the Institutes service analytical laboratory under the direction of Dr. William C. Alford.

(1) The nomenclature used is that proposed by H. G. Fletcher, Jr., L. Anderson and H. A. Lardy, *J. Org. Chem.*, **16**, 1238 (1951). Trivial names used previously are also given.

(2) E. L. May and E. Mosettig, *ibid.*, **14**, 1137 (1949).

(3) H. E. Carter, R. K. Clark, B. Lytle and G. E. McCasland, *J. Biol. Chem.*, **175**, 683 (1948).

(4) After our work was completed L. Anderson and H. A. Lardy, THIS JOURNAL, **72**, 3141 (1950), reported the preparation of inosamine SA and assigned to it the structure of II. A recent study by G. E. McCasland, *ibid.*, **73**, 2295 (1951), supports the conclusions of these authors.

(5) Testing was done at the Tuberculosis Research Laboratory, Public Health Service, Cornell University Medical College, New York, N. Y., under the direction of Dr. Bernard D. Davis.

(6) H. E. Carter, C. Belinskey, R. K. Clark, E. H. Flynn, B. Lytle, G. E. McCasland and M. Robbins, *J. Biol. Chem.*, **174**, 415 (1948).

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PUBLIC HEALTH SERVICE
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The Reaction of Amines with Nitroguanyl Azide

BY EUGENE LIEBER,[1] CLAUDE C. HERRICK AND EDWARD SHERMAN

RECEIVED NOVEMBER 12, 1951

Nitroguanyl azide (I) cyclizes rapidly with a large variety of inorganic and organic bases to form a

(1) U. S. Naval Ordnance Test Station, Inyokern, China Lake, California, to whom all communications concerning this article should be addressed.

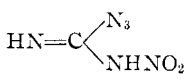
TABLE I

AMINE SALTS OF 5-NITROAMINOTETRAZOLE

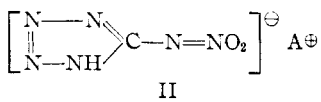
Amine	Yield, %	M.p., °C.[a]	Formula	Analyses,[b] % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
(1) Monoacid salts									
Pyridine[c]	70[d]	133	$C_6H_7N_7O_2$	34.55	34.20	3.37	3.57	46.18	47.07
Quinaldine[c]	60[e]	136	$C_{11}H_{12}N_7O_2$	48.35	48.36	4.04	4.28	35.89	35.90
Quinoline[c]	39[f]	142	$C_{10}H_9N_7O_2$	46.33	46.35	3.50	3.63	37.83	37.44
α-Picoline[c]	78[f]	99	$C_7H_{10}N_7O_2$	37.67	37.65	4.07	4.40	43.92	43.60
N-Dimethylaniline[c]	63[g]	109	$C_9H_{13}N_7O_2$	42.84	42.43	5.19	5.34	38.87	39.43
N-Diethylaniline[c]	37[g]	109	$C_{11}H_{17}N_7O_2$	47.30	47.50	6.13	6.16	35.11	35.08
Phenylguanidine[h]	67[i]	200	$C_8H_{11}N_9O_2$	36.22	35.96	4.18	4.30	47.53	47.67
2-Aminopyridine[c]	73[j]	183	$C_6H_8N_8O_2$	32.14	32.20	3.60	4.05	49.99	50.21
8-Aminoquinoline[c]	85[g]	155	$C_{10}H_{10}N_8O_2$	43.79	43.24	3.68	3.55	40.86	41.22
(2) Acid salts									
Piperidine[c]	73[k]	107	$C_{11}H_{24}N_8O_2$	43.98	43.97	8.05	8.22	37.31	37.34
Morpholine[c]	53[j]	166	$C_9H_{20}N_8O_4$	35.53	34.96	6.62	6.83	36.83	37.05
n-Amylamine[c]	84[f]	162	$C_{11}H_{28}N_8O_2$	43.40	43.40	9.27	9.28	36.82	36.65
Isoamylamine[c]	71[f]	157	$C_{11}H_{28}N_8O_2$	43.40	42.73	9.27	9.10	36.82	36.35
s-Butylamine[c]	56[f]	122	$C_9H_{24}N_8O_2$	39.12	39.52	8.76	8.81	40.56	40.71
n-Propylamine[c]	61[f]	161	$C_7H_{20}N_8O_2$	33.88	33.68	8.12	8.35	45.42	45.13
Allylamine[c]	72[f]	142	$C_7H_{16}N_8O_2$	34.41	33.86	6.60	6.44	45.89	45.81
Dibenzylamine[c]	65[l]	202	$C_{29}H_{32}N_8O_2$	66.41	65.96	6.15	6.51	21.37	21.30
Cyclohexylamine[c]	87[f]	162	$C_{13}H_{28}N_8O_2$	47.54	47.21	8.59	8.66	34.12	33.97
Ethylenediamine[m]	92[n]	239	$C_3H_{10}N_8O_2$	18.95	18.65	5.30	5.40	58.93	59.42
Hydrazine[o]	85[p]	165	$CH_{10}N_{10}O_2$	6.22	6.03	5.19	5.07	72.14	72.03

[a] All melting points were carried out on a Fisher–Johns block and are corrected. [b] Micro-analyses by Micro Tech Laboratories, Skokie, Illinois. [c] Reaction carried out in anhydrous ethyl ether as solvent. [d] Recryst. from acetone. [e] Recryst. from mixture of ethyl alcohol and ether. [f] Recryst. from isopropyl alcohol. [g] Recryst. from ethyl acetate. [h] Reaction carried out in isopropyl alcohol as solvent. [i] Recryst. from water. [j] Recryst. from 1:1 isopropyl and ethyl alcohols. [k] Recryst. from methyl alcohol–water. [l] Recryst. from acetone–water. [m] Reaction carried out in anhydrous ethyl alcohol. [n] Recryst. from isopropyl alcohol–water. [o] As 100% N_2H_5OH, reaction carried out in methyl alcohol. [p] Recryst. from ethyl alcohol–water.

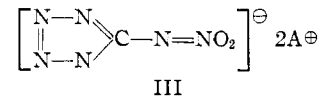
series of mono- (II) and diacid (III) salts of 5-nitroaminotetrazole.[2]



I



II



III

The structure of the monoacid salts (I) as the *aci-nitro* form has been demonstrated by ultraviolet absorption spectroscopy.[3] Of the organic bases, the reaction of aniline, β-naphthylamine, *n*-butylamine, diethylamine and guanidine have been reported.[2] The question as to whether a mono- or diacid salt of 5-nitroaminotetrazole resulted from the reaction of an organic amine with (I) appeared to depend upon the relative basicities of the amines involved, although with the limited amount of data available[2] notable exceptions occurred. Roughly, it appeared that organic bases whose basic dissociation constants were less than about 10^{-5} formed monoacid salts (II). In order to pursue this question further, the reaction of (I) with a large variety of organic bases was studied. This paper reports upon the results of that investigation.

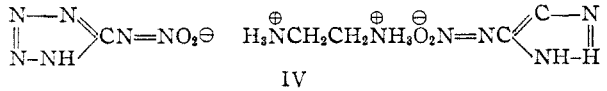
Twenty new salts of 5-nitroaminotetrazole were prepared and characterized during the course of this study. These are presented in Table I. The experimental section describes in detail the preparation of typical mono- and diacid salts. In general, the data obtained supported the general conclusion of our previous investigation[2] in that the more basic organic amines yield diacid salts (II), however, with some exceptions. This also extends to the crystalline form of the salts obtained, the large majority of the monoacid salts being well defined needles, while the diacid salts were largely in plate form. Due to the exceptions, however, the crystalline form cannot be taken as a criterion as to which series the salt will fall in. The reaction of the organic amine with (I) proceeds quite rapidly with evolution of considerable heat of reaction. In general the yield on recovery of the salt is fairly good, although recrystallization difficulties occur and proper choice of solvent for purification must be sought. The reaction of (I) with *o*- and *p*-phenylenediamine, *o*-anisidine and *p*-aminodiethylaniline yielded dark colored intractable tars which could not be recrystallized. Tertiary aliphatic amines appear to yield oils as were obtained with tri-*n*-butyl- and triethylamine. Oils were also obtained with N-ethylaniline and β-dimethylaminoethanol.

The structure given for the ethylenediamine salt (Table I) is not unambiguous, although the ultimate analysis demonstrates that the compounds

(2) E. Lieber, E. Sherman, R. A. Henry and J. Cohen, THIS JOURNAL, **73**, 2327 (1951).

(3) E. Lieber, E. Sherman and S. H. Patinkin, *ibid.*, **73**, 2329 (1951).

have combined in a 1:1 stoichiometric ratio. This precludes a bis-monoacid structure (IV), although one cannot distinguish the salt as being mono- or



IV

diacid. Since 5-nitroaminotetrazole does form salts with very weakly basic amines it has been assumed that the salt is diacidic.

Experimental

Nitroguanyl Azide.—This was prepared as previously described.[2] The product obtained by evaporation of the combined ether extracts, m.p. 79°, was sufficiently pure and was not recrystallized further.

Amines.—C.P. grade reagents were purified by distillation or recrystallization until they met the reported values for physical constants.

General Procedure for Reaction of Amines with Nitroguanyl Azide.—Specific illustrative examples for the preparation of the mono- and diacid salts of 5-nitroaminotetrazole have been described elsewhere.[2] In general the compounds noted in Table I were prepared by dissolving the nitroguanyl azide in ether (15 ml. for 0.01 mole) and adding the amine, in two molar proportions, also dissolved in ether (10 to 15 ml. for 0.02 mole of amine). Deviations from the use of anhydrous ether as solvent are noted in Table I. The amine salt of 5-nitroaminotetrazole, generally, immediately precipitates. However, the reaction mixture may be allowed to stand, at room temperature, for periods from 30 minutes or overnight. The crystals are removed by filtration, washed with anhydrous ethyl ether and recrystallized. The choice of solvent for recrystallization varies with the individual preparation. This has been noted in Table I.

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S-Benzylthiuronium Salts of Nitroalkyl Hydrogen Sulfates

BY A. C. MCINNIS, JR., AND L. G. TOMPKINS

RECEIVED APRIL 9, 1951

We have prepared as derivatives for the characterization of several low molecular weight nitroalcohols the crystalline S-benzylthiuronium salts of their sulfate esters. The latter are prepared by the addition of the nitroalcohol to a mixture of chlorosulfonic acid and dioxane.[1]

The 3,5-dinitrobenzoates of two of these nitroalcohols also have been prepared. Benzenesulfonates, *p*-toluenesulfonates[2,3] and α-naphthylurethans[4] have previously been used to characterize nitroalcohols.

Pertinent data are tabulated herewith. Melting points were determined with a Fisher–Johns apparatus which was calibrated over the 50–160° range.

TABLE I

Nitroalcohol	S-Benzylthiuronium salt M.p., °C.	Nitrogen, % Calcd.	Found
2-Nitro-1-propanol	114–115	11.96	11.81
2-Nitro-1-butanol	100–101	11.50	11.54
2-Nitro-2-methyl-1-propanol	145–146	11.50	11.46
3-Nitro-2-butanol	105–106	11.50	11.69
3-Nitro-2-pentanol	127–128	11.08	11.15
3-Nitro-3-methyl-2-butanol	119–120	11.08	11.05

(1) R. K. Bair and C. M. Suter, THIS JOURNAL, **64**, 1978 (1942).
(2) P. J. Baker, U. S. Patent 2,395,386 (Feb. 26, 1946).
(3) J. L. Riebsomer, *J. Org. Chem.*, **11**, 182 (1946).
(4) D. Nightingale and J. R. Janes, THIS JOURNAL, **66**, 352 (1944).

Experimental

2-Nitro-2-methylpropyl 3,5-Dinitrobenzoate.—One gram of 2-nitro-2-methyl-1-propanol was dissolved in 3 ml. of anhydrous pyridine and 0.5 g. of 3,5-dinitrobenzoyl chloride was added to the stirred solution. The mixture was heated on the steam-bath for 15 minutes and then poured into 10 ml. of distilled water and stirred vigorously. The solid was collected on a filter and washed with 5 ml. of 5% sodium carbonate solution. It was recrystallized twice from 95% ethanol: m.p. 126–127°; N calcd., 13.42; N found, 13.39.

3-Nitro-3-methyl-2-butyl 3,5-Dinitrobenzoate.—Two milliliters of 3-nitro-3-methyl-2-butanol was added to 0.5 g. of 3,5-dinitrobenzoyl chloride contained in a dry test-tube. Dry pyridine was added dropwise to the mixture, allowing about five minutes for the addition of ten drops. The resulting mixture was heated over a steam-bath for 15 minutes. The reaction mixture was cooled to room temperature, and 10 ml. of distilled water was added with stirring. The product was collected and washed with 10 ml. of 2% sodium carbonate solution. Three recrystallizations from 50% aqueous ethanol gave a flaky product which melted sharply at 140°; N calcd., 12.48, N found, 12.79.

S-Benzylthiuronium 2-Nitro-1-propyl Sulfate.—Five drops of 2-nitro-1-propanol was added to a mixture of 5 drops of dry dioxane and 4 drops of chlorosulfonic acid. Hydrogen chloride was evolved immediately on shaking the test-tube. After standing 10 to 15 minutes the mixture was diluted with 1 ml. of water and added to 1 ml. of saturated aqueous S-benzylthiuronium chloride. After five minutes in an ice-bath the product precipitated, and was recrystallized three times from 10% ethanol and dried in a vacuum desiccator. The fine white needles melted at 114–115°. Analysis is given in Table I.

Acknowledgment.—The authors express their appreciation to The Commercial Solvents Corporation for supplies of nitroalkanes used in this work.

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Some Diels–Alder Reactions of Chloroprene[1]

BY JOHN S. MEEK AND WALTER B. TRAPP

Chloroprene has been condensed with acrolein,[2] methyl vinyl ketone,[2] methyl ethynyl ketone,[2] acrylonitrile,[3] methacrylic acid[4] and methyl methacrylate.[4]

Methyl methacrylate and methacrylic acid gave mixtures which were not separated.[4] The structure of the chloroprene–methyl ethynyl ketone adduct was shown by dehydrogenation to be *p*-chloroacetophenone.[2] The structures of the remaining adducts were not proven. However, the adducts of acrylonitrile and acrolein were converted into the same acid which was believed by Petrov and Sopov to be 4-chloro-1,2,5,6-tetrahydrobenzoic acid (I) by analogy with the chloroprene–methyl ethynyl ketone adduct.

In our work, we have shown this to be correct. This same acid, 4-chloro-1,2,5,6-tetrahydrobenzoic acid, was prepared by condensing chloroprene with acrylic acid. The adduct was brominated with N-bromosuccinimide and then dehydrohalogenated with triethylamine to give *p*-chlorobenzoic acid. Compound I was also synthesized in low yield from

(1) This work was supported by the Office of Naval Research.
(2) A. A. Petrov and N. P. Sopov, *J. Gen. Chem.* (*U. S. S. R.*), **17**, 1295 (1947).
(3) A. A. Petrov and N. P. Sopov, *ibid.*, **17**, 2228 (1947).
(4) A. A. Petrov and N. P. Sopov, *ibid.*, **18**, 1781 (1948).