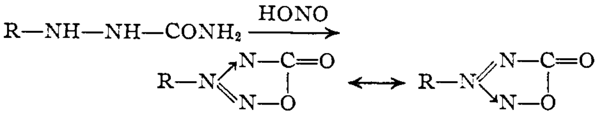
nitrous acid upon the corresponding semicarbazide, a reaction which parallels the preparation of sydnones from N-substituted glycines. Apparently the preparation of aryl ψ-oxatriazoles by this method is not applicable since N-nitrosoarylsemicarbazides readily undergo the loss of nitroxyl with the formation of an azocarboxamide.[7] The representation used here for the ψ-oxatriazoles has extended the use of a ring coördinate–covalent bond between nitrogen atoms as suggested by Earl.[3]



III

In agreement with similar observations on sydnones, the ψ-oxatriazoles gave no indication of the presence of either the nitroso or the isocyanate groups.

Experimental[8]

Preparation of Semicarbazones.—To a solution of 0.10 mole of a substituted cyclohexanone in 60 ml. of methanol was added just enough water to produce cloudiness. To this solution was added 18.0 g. of sodium acetate and 12.0 g. (0.108 mole) of semicarbazide hydrochloride. After vigorous shaking, the reaction mixture was placed in a 75° water-bath and allowed to come to room temperature. The solid was filtered off, washed with cold methanol, and dried overnight in a vacuum oven at 60°. Quantitative yields of 2-methylcyclohexanone semicarbazone, m.p. 185–187° and menthone semicarbazone, m.p. 189–191° were obtained.

Reduction of Semicarbazones.—The procedure of Poth and Bailey[9] for the reduction of menthone semicarbazone was followed. A solution of 100 ml. of water, 50 ml. of methanol, 0.2 g. of gum arabic and 5 ml. of 10% chloroplatinic acid solution was shaken under a hydrogen pressure of about 35 lb. per sq. in. until a black colloid developed. To this catalyst was added 0.132 mole of semicarbazone and 11 ml. (0.13 mole) of concentrated hydrochloric acid. The reaction mixture was shaken under a hydrogen pressure of about 30 to 40 lb. per sq. in. until hydrogen uptake had ceased (about 1.5 hours for 2-methylcyclohexanone semicarbazone, 6.5 hours for menthone semicarbazone). The reaction mixture was diluted to about twice its volume with acetone to break the platinum colloid. After the platinum had been filtered off, the filtrate was evaporated to about 100 ml. Addition of 10% sodium hydroxide solution until the solution was basic caused precipitation of a solid which was removed by filtration. Menthyl semicarbazide, m.p. 181–183° was obtained in 64% yield and 2-methylcyclohexyl semicarbazide, m.p. 162–165°, in 86% yield.

Preparation of Alkyl ψ-Oxatriazoles.—A solution or slurry of 0.030 mole of the semicarbazide in 10 ml. of water and 10 ml. of concentrated hydrochloric acid was cooled to 0° in an ice-bath. With stirring, 50 ml. of 10% sodium nitrite solution was added dropwise at such a rate that the temperature of the reaction did not rise above 5°. After all of the sodium nitrite had been added, there was a light yellow solid present (probably an intermediate nitroso compound). The ice-bath was replaced by a 50° water-bath and the material was stirred vigorously at this temperature for 30 minutes.

From the reaction on 2-methylcyclohexyl semicarbazide, there was a suspension of yellow oil droplets in the reaction mixture. The reaction mixture was poured into a separatory funnel and the bottom layer was separated. The aqueous layer was extracted with three 20-ml. portions of ether, the extracts being added to the organic layer. The combined organic solution was washed with dilute ammonium hydroxide and then washed with water. After the solution had been dried over magnesium sulfate, the ether was distilled at reduced pressure and gave 3.1 g. (57% yield) of ψ 5-keto-3-(2-methylcyclohexyl)-3,5-dihydro-1,2,3,4-oxatriazole, b.p. 103–106° (0.08 mm.), $n^{32}\mathrm{D}$ 1.4950, $d^{24.5}_{4}$ 1.1626.

Anal. Calcd. for $C_8H_{13}N_3O_2$: C, 52.45; H, 7.15; N, 22.93. Found: C, 52.53; H, 7.25; N, 22.65; M_D, 55.05.

From the reaction on menthyl semicarbazide a slightly yellow solid was filtered off and recrystallized from ethanol and water. After being dried for 3 hours in a vacuum oven at 60° there was 4.3 g. (64% yield) of ψ 5-keto-3-menthyl-3,5-dihydro-1,2,3,4-oxatriazole, m.p. 97–98°. Recrystallization from 95% ethanol gave material with constant m.p. at 94.8–95.3°. A portion of this material was submitted for analysis.

Anal. Calcd. for $C_{11}H_{19}N_3O_2$: C, 58.63; H, 8.50; N, 18.65. Found: C, 58.77; H, 8.37; N, 18.50.

Strong absorption by both of the alkyl ψ-oxatriazoles at 1790^{-1} cm. was indicative of the carbonyl group and was in close agreement with the carbonyl absorption of γ-lactones (1800–1760 cm.$^{-1}$)[10] and of sydnones (1752–1756 cm.$^{-1}$).[11] Lack of strong absorption by the ψ-oxatriazoles at 1400 cm.$^{-1}$ was indicative of the absence of the nitroso group and was in agreement with the failure of these compounds to give a positive test with the Liebermann nitroso reaction.

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[7] O. Widman, *Ber.*, **28**, 1925 (1895).

[8] Melting points are corrected. Elementary analyses by Microtech Laboratory, Skokie, Ill. Infrared analyses by Mr. J. E. Baudean, Perkin-Elmer Corp., New Orleans, La.

[9] E. J. Poth and J. R. Bailey, THIS JOURNAL, **45**, 3001 (1923).

[10] F. A. Miller, "Applications of Infrared-red and Ultraviolet Spectra to Organic Chemistry," in H. Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, 1953, p. 146.

[11] J. C. Earl, R. J. W. LeFevre, A. G. Pulford and A. Walsh, *J. Chem. Soc.*, 2207 (1951).

The Action of Acetic Anhydride on 4-Methylpyridine-N-oxide[1]

BY JEROME A. BERSON AND THEODORE COHEN

RECEIVED SEPTEMBER 7, 1954

The recent reports by Boekelheide and Linn[2] and by Bullitt and Maynard[3] on the rearrangements of alkylpyridine-N-oxides prompt us to communicate the results of similar experiments in this field which were completed before we were aware of the work of these authors. Our observations confirm the previous findings in part and, in addition, provide a basis for a mechanistic proposal.

Aromatic N-oxides, when heated with acetic anhydride or benzoic anhydride, rearrange to the corresponding 2-acyloxy heterocycles.[2,4–6] However, when an alkyl group is in the 2- or 4-position, rearrangement gives the corresponding 2- or 4-acyloxyalkyl derivative.[2,3] For example, pyridine-N-oxide gives 2-acetoxypyridine[4] and 3-methylpyridine-N-oxide gives 3-methyl-2-acetoxypyridine,[2] but 2-methylpyridine-N-oxide gives 2-pyridinemethanol acetate.[2,3]

We have investigated the action of acetic anhydride on 4-methylpyridine-N-oxide, previously reported[2,3] to give 4-pyridinemethanol acetate. Our procedure for working up the reaction mixture

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[1] This investigation was supported in part by a research grant, G-3149-CR, from the National Institutes of Health, Public Health Service.

[2] V. Boekelheide and W. J. Linn, THIS JOURNAL, **76**, 1286 (1954).

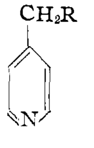
[3] O. H. Bullitt, Jr., and J. T. Maynard, *ibid.*, **76**, 1370 (1954).

[4] M. Katada, *J. Pharm. Soc. Japan*, **67**, 51 (1947).

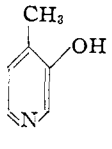
[5] E. Ochiai, *J. Org. Chem.*, **18**, 534 (1953).

[6] F. Montanari and L. Pentimalli, *Gazz. chim. ital.*, **83**, 273 (1953).

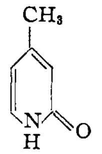
differed from that of the earlier studies[2,3] in that we removed the acetic anhydride, distilled the residue and *treated the distillate with an isopropyl alcohol solution of oxalic acid.* The precipitated salt, after recrystallization, melted at 138–139.5° and was the hydrogen oxalate of a liquid *base*, $C_8H_9O_2N$, identified as 4-pyridinemethanol acetate (Ia) by (i) its empirical composition, (ii) the similarity of its ultraviolet spectrum to that of 4-methylpyridine (Ib), (iii) the presence of an ester carbonyl band at 5.72 μ in its infrared spectrum and (iv) its smooth saponification to 4-pyridinemethanol (Ic).



Ia, R = OAc
b, R = H
c, R = OH



II

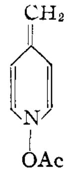


III

The mother liquor from the preparation of the 139.5° oxalate slowly deposited a neutral oxalate, m.p. 243°, of a *base*, C_6H_7ON, m.p. 120–121°, presumably arising from the corresponding acetate by ester interchange in the acidic alcoholic medium. The base was identified as 3-hydroxy-4-methylpyridine (II) by (i) the identity of its melting point with that reported for II prepared by alkali fusion of 4-methylpyridine-3-sulfonic acid,[7] (ii) the bright red ferric chloride reaction, (iii) the observation that the ultraviolet absorption behavior in neutral solution (λ_{max} 276 mμ, log ε 3.60) and in alkaline solution ($\lambda\lambda_{max}$ 244, 300 mμ, log ε 4.00, 3.69) paralleled that of 3-hydroxypyridine (neutral, λ_{max} 282.5 mμ, log ε 3.60; alkaline, $\lambda\lambda_{max}$ 234, 298 mμ, log ε 3.94, 3.63[8a]) and 2-methyl-5-hydroxypyridine (alkaline, $\lambda\lambda_{max}$ 239, 307.5 mμ, log ε 3.91, 3.53[8b]) and (iv) by the fact that the substance having the only alternative structure, 4-methyl-2-pyridone (III) is known,[9] its reported properties do not correspond to those observed, and it would not be expected[10,11] to exhibit the characteristic ultraviolet behavior of a 3-hydroxypyridine. Further, the infrared spectrum of II shows no absorption between 5.5 and 6.2 μ, in contrast to that of the model substance, α-pyridone, which has a strong carbonyl maximum at 6.06 μ.

Neither of the products (Ia and II) appears to be a precursor of the other, since interconversion of Ia to II or *vice versa* does not occur under the same conditions which give rise to both from 4-methylpyridine-N-oxide.

The mechanism of the rearrangements observed remains obscure. Our results do not eliminate the possibility of free radical processes of the type suggested previously,[2] but they are also consistent with a heterolytic mechanism involving the anhydrobase IV.[12]



IV

IV could suffer attack by external acetate ion at C_3, or at the methylene group, accompanied by extrusion of the acetoxy group bound to nitrogen (or could conceivably suffer internal rearrangement of the acetoxy group to C_3 by an SNi′-type mechanism) to give the observed products.[13]

Experimental[14]

Action of Acetic Anhydride on 4-Methylpyridine-N-oxide.—4-Methylpyridine-N-oxide was prepared in 82% yield from 4-methylpyridine by the method of Ochiai.[5] It had m.p. 179.8–180.2°, reported[15] m.p. 181°, reported[2] m.p. 185–186°. A solution of 10.2 g. of 4-methylpyridine-N-oxide in 60 cc. of acetic anhydride was heated at reflux for one hour. The acetic anhydride was removed *in vacuo* and the dark brown residue was distilled through a 12-inch Vigreux column. The distillate, a bright-yellow liquid, b.p. 82–85.5° at 3 mm., weighed 8.79 g.

A preliminary experiment demonstrated the composition of the distillate and indicated a method of fractionation. A portion (2.36 g.) of the distillate was treated with considerably less than an equivalent amount of oxalic acid in isopropyl alcohol. Vigorous gas evolution occurred (*vide infra*). The mixture was heated on the steam-bath for 40 minutes and allowed to cool to give a mixture of oxalates A, 1.04 g., m.p. 120–235°. The mother liquor was treated with successive portions of oxalic acid in isopropyl alcohol until no further precipitation occurred. The precipitated solid B weighed 0.92 g., m.p. 128–140°. The compositions of fractions A and B were determined spectrophotometrically in 95% ethanol on the basis of the absorption spectra of the pure oxalates (*vide infra*) by determining the optical densities at two wave length maxima (256 and 276 mμ) and solving two simultaneous equations of the form $D = \epsilon_1 C_1 + \epsilon_2 C_2$. Fractions A and B consisted of 37.6 mole % and 96.1 mole % 4-pyridinemethanol acetate hydrogen oxalate, respectively, and 62.4 mole % and 3.9 mole % 3-hydroxy-4-methylpyridine oxalate, respectively. This corresponds in absolute yield to 20% of Ia and 14.4% of II in the total oxalates (A + B).

The pure oxalates were obtained (i) by recrystallization of the enriched fractions A and B, taking advantage of the relatively low solubility of the 243° oxalate in water or ethanol, or (ii) by the following procedure. The remainder of the original distillate (6.43 g.) was redistilled through a 12-inch vacuum-jacketed Vigreux column and the distillate treated with a large excess of a saturated solution of oxalic acid in isopropyl alcohol. The resulting precipitate weighed 3.18 g. and consisted of crude **4-pyridinemethanol-acetate hydrogen oxalate**, m.p. 126–142°. Recrystalliza-

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[7] O. Wulff, German Patent 563,373 (1929); *C. A.*, **24**, 5766 (1930).

[8] (a) E. Shaw, THIS JOURNAL, **71**, 67 (1949); (b) E. T. Stiller, J. C. Keresztesy and J. R. Stevens, *ibid.*, **61**, 1237 (1939).

[9] (a) R. Adams and A. W. Scbrecker, *ibid.*, **71**, 1186 (1949); (b) O. Seide, *Ber.*, **57**, 791 (1924).

[10] H. Specker and H. Gawroscb, *ibid.*, **75**, 1338 (1942).

[11] J. A. Berson, *ibid.*, **75**, 3521 (1953).

[12] The formation of IV would correspond to the anhydrobase intermediate postulated by I. J. Pachter, *ibid.*, **75**, 3026 (1953), in the change 2-methylquinoline-N-oxide → 2-quinolinemethanol benzoate. The possibility that anhydrobases may be intermediates in the formation of 2- or 4-acyloxyalkylpyridines from the corresponding N-oxides has been pointed out.[2,3]

[13] (a) The observation [M. Murakami and E. Matsumura, *J. Chem. Soc. Japan*, **70**, 393 (1949)] that pyrolysis (at 205–210°) of the product from the action of *p*-toluenesulfonyl chloride on pyridine-N-oxide gives a 3-hydroxypyridine derivative is not readily reconcilable with a simple mechanistic picture. We are indebted to Referee II for calling this reference to our attention. (b) Dr. V. Boekelheide has kindly informed us that results similar to ours have been reported for the case of 2-methylpyridine-N-oxide by Kobayashi and Furukawa, *Pharm. Bull. Japan*, **1**, 347 (1953). We have not yet been able to obtain a copy of this article.

[14] Melting points and boiling points are uncorrected. The analyses are by Mr. W. J. Schenck. The ultraviolet spectra were taken with the Beckman Spectrophotometer, model DU. The infrared spectra were taken with the Perkin–Elmer model 13 spectrometer, sodium chloride prism.

[15] E. Ochiai, M. Ishikawa and S. Zai-Ren, *J. Pharm. Soc. Japan*, **64**, 72 (1944).

tion from 95% ethanol gave white needles, m.p. 138–139.5°.

Anal. Calcd. for $C_{10}H_{11}O_6N$: C, 49.81; H, 4.60; N, 5.81. Found: C, 50.23; H, 4.81; N, 5.89.

The isopropyl alcohol mother liquor from the preparation of the above oxalate was heated at reflux for two hours. A white precipitate, 1.66 g., gradually appeared, m.p. 150–200°. After recrystallization from water, 0.87 g. of **3-hydroxy-4-methylpyridine oxalate**, was obtained as white prisms, m.p. 243° dec. An additional 0.20 g. was obtained by working up the mother liquors.

Anal. Calcd. for $C_{14}H_{16}N_2O_6$: C, 54.54; H, 5.23; N, 9.09. Found: C, 55.04; H, 5.61; N, 9.38.

The precipitation of the oxalates was attended by considerable gas evolution. This appears to be due to decomposition of oxalic acid induced by a combination of acetic anhydride and pyridine bases. We have found that solutions of oxalic acid vigorously evolve gas at room temperature in the presence of pyridine (or piperidine) and acetic anhydride, but the decomposition does not occur with pyridine, 2-pyridone, Ia, Ic, II or acetic anhydride alone. The nature of the reaction remains to be elucidated.

4-Pyridinemethanol acetate (Ia) was obtained by treating a solution of its oxalate with excess sodium carbonate and extracting the resulting oil with chloroform. The dried (sodium sulfate) solution was evaporated to give a pale yellow oil, $\lambda^{\mathrm{EtOH}}_{\mathrm{maxm}}$ 257 mμ, log ϵ 3.05; $\lambda^{\mathrm{chf}}_{\mathrm{max}}$ 5.72 μ. The model substance 4-methylpyridine shows λ_{max} 252 mμ, log ϵ 3.37 (in isoöctane).[16] The base was reconverted to the oxalate, m.p. 137–139°, alone or mixed with a sample isolated as above, or with an authentic sample prepared by acetylating 4-pyridinemethanol[17] and treating the product with oxalic acid.

4-Pyridinemethanol (Ic) was prepared by treating an aqueous suspension of the above acetate with an excess of 20% potassium hydroxide. The oil dissolved and the clear solution was extracted with ten portions of chloroform, the extracts dried over sodium sulfate and evaporated. The residue was a flaky, buff solid, m.p. 52–53.5°. Recrystallization from benzene gave white needles, m.p. 57.8–58.8° alone or mixed with an authentic sample[17]; reported for 4-hydroxymethylpyridine, m.p. 57–60°,[2] 57°,[18] 47–50°,[19] 58–60°.[17] The **hydrochloride** had m.p. 175–179°, reported 176–178°,[2] 176–180°,[19] 176°.[20]

The picrate, was obtained as yellow needles from ethanol, had m.p. 155° dec.

Anal. Calcd. for $C_{12}H_{10}O_8N_4$: C, 42.61; H, 2.98; N, 16.57. Found: C, 42.88; H, 3.01; N, 16.76.

When Ic was boiled in acetic anhydride for one hour, the acetic anhydride evaporated, the residue distilled and the distillate treated with oxalic acid, only the oxalate of Ia, m.p. 139.5°, was obtained.

3-Hydroxy-4-methylpyridine (II) was liberated from its oxalate with sodium carbonate, extracted with chloroform and recrystallized from benzene to give white needles, m.p. 120–121.2°; reported[7] m.p. 118–120°.

Anal. Calcd. for C_6H_7NO: C, 66.03; H, 6.47; N, 12.84. Found: C, 66.36, 65.95; H, 6.00, 6.58; N, 12.74.

The substance gave an immediate bright red color with ferric chloride. It was reconverted to the neutral oxalate, m.p. 243° dec., alone or mixed with a sample isolated as above. Its ultraviolet behavior in neutral ethanol and in ethanol which was 1.02×10^{-3} *M* in potassium hydroxide has been reported in the theoretical section.

II was not converted to Ia under the rearrangement conditions. It was recovered as its oxalate, m.p. 243° dec., after being boiled in acetic anhydride for one hour and worked up in the same manner as the rearrangement runs.

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[16] R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1951.

[17] H. S. Mosher and J. E. Tessieri, THIS JOURNAL, **73**, 4925 (1951).

[18] M. Protiva, *Chem. Listy*, **45**, 20 (1951); *C. A.*, **45**, 8997 (1951).

[19] P. Rabe, O. Spechelsen, L. Wilhelm and H. Höter, *J. prakt. Chem.*, **151**, 65 (1938).

[20] F. Šörm and L. Sědivy, *Collection Czech. Chem. Communs.*, **13**, 289 (1948).

5-Aza-2,8,10-trithiaadamantan or Trithiotrimorpholine

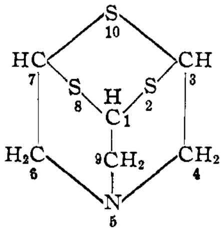
BY DAVID CRAIG, J. J. SHIPMAN, A. HAWTHORNE AND RAY FOWLER

RECEIVED OCTOBER 18, 1954

A recent review[1] of compounds having the cage structure of adamantan called our attention to an impurity (I), m.p. 147–148°, which we had isolated from crude 4-thiazoline-2-thione[2] prepared from the reaction of chloroacetaldehyde with excess ammonium dithiocarbamate. The excess of the ammonium salt was subsequently found to be essential apparently because this assured the presence of hydrogen sulfide as well as ammonia. Carbon disulfide was found to be a by-product. Analysis and molecular weight determination showed I to be $C_6H_9NS_3$. We can therefore write the equations

$$
\begin{gathered}
H_2NCS_2NH_4 \longrightarrow NH_4CNS + H_2S \\
N_2NCS_2NH_4 \longrightarrow NH_3 + CS_2 \\
NH_3 + 3ClCH_2CHO \longrightarrow N(CH_2CHO)_3 + 3HCl \\
3H_2S + N(CH_2CHO)_3 \longrightarrow \underset{\mathrm{I}}{N(CH_2CHS)_3} + 3H_2O
\end{gathered}
$$

The infrared absorption spectrum of I was essentially transparent up through seven microns except for strong bands at 3.44 and 6.99 μ. These are due to the stretching and wagging vibrations of hydrogen atoms on carbon. Thus SH, NH, C═C, C═S and C═N groups are shown to be absent and we can infer that the method of synthesis and the absorption spectrum of I show the structure to be



A Stuart type scale model of this structure was made easily. It was slightly strained due to the sulfur atoms being a little too large for close packing with the smaller nitrogen and carbon atoms. The structure is seen to have a trithiane grouping on one side and on the opposite side an exposed nitrogen atom.

Experimental

The crude "thiazolethiol" (60 g.) of Mathes and Beber was extracted serially with 200-, 100- and 50-ml. portions of boiling alcohol. The extracts were united and cooled to give 7.2 g. of crystals, m.p. 145–146°. The filtrate was used to re-extract the insoluble part and a further 2.4 g. of the 145–146° melting compound was isolated. The yield of I thus is 16% of the crude "thiazolethiol." Recrystallized from alcohol the compound came down as cream colored needles, m.p. 147–148°.

Anal. Calcd. for $C_6H_9NS_3$: C, 37.66; H, 4.74; N, 7.32; S, 50.27; mol. wt., 191. Found: C, 37.76, 37.76, 37.56; H, 4.93, 4.97, 4.76; N, 7.26, 7.31; S, 50.02, 49.82; mol. wt. in boiling benzene, 186, 186.

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[1] H. Stetter, *Z. angew. Chem.*, **66**, 217 (1954).

[2] R. A. Mathes and A. J. Beber, THIS JOURNAL, **70**, 1452 (1948). According to these authors and most usage, this compound, m.p. 79 to 80°, is called 2-thiazolethiol in spite of the fact that methods which are suitable for distinguishing the thioamide form from the thiol isomer disclose the presence of only the thioamide isomer. Compare M. G. Ettlinger, *ibid.*, **72**, 4701 (1950).