limation gave an analytical sample, mp 49–50.5°. The infrared spectrum (neat) showed absorption at 3300 cm^{-1} (OH); the nmr spectrum ($CDCl_3$) showed doublets at τ 2.70 and 3.21 (1 H doublets, J = 5 cps, aromatic), a broad absorption at 4.70–4.93 (1 H, OH), and a complex multiplet at 6.80–8.00 (5 H, aliphatic ring hydrogens).

Anal. Calcd for C_7H_8OS: C, 59.97; H, 5.75; S, 22.87. Found: C, 60.00, 59.97; H, 5.83, 5.85; S, 22.67, 22.53.

Registry No.—2,5-Dichlorothiophene, 3172-52-9; VII, 7687-77-6; VIII, 7695-30-9; IX, 7687-78-7; X, 7687-79-8; XI, 7687-82-3; XII, 7690-98-4; XIII, 7687-83-4; XIV, 7687-80-1; XV, 7690-97-3; XVI, 7687-81-2; XVII, 7687-84-5; XVIII, 5650-52-2; XVIII 2,4-dinitrophenylhydrazone, 7687-86-7; XIX, 5650-50-0; XX, 7687-88-9; acid chloride of IX, 7687-74-3; corresponding amide of IX, 7690-96-2.

Acknowledgment.—The authors gratefully acknowledge financial aid in the form of a grant by the Senate Research Committee of West Virginia University.

A Facile Cyclization of 4-(2-Chloroethyl)-3-methyl-2-pyrazolin-5-one to a Spirocyclopropane Derivative

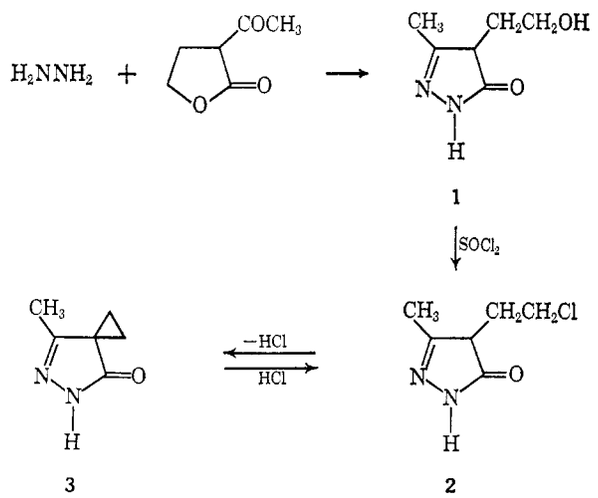
E. MAGNIEN AND W. TOM

Organic Research Department, U. S. Vitamin and Pharmaceutical Corporation, Yonkers, New York 10701

Received November 9, 1966

During the preparation of pyrazolin-5-one derivatives over the last few years it was noticed that one of the derivatives, 4-(2-chloroethyl)-3-methyl-2-pyrazolin-5-one (**2**), underwent a facile cyclization to 4-methyl-7-oxo-5,6-diazaspiro[2.4]hept-4-ene (**3**). A recent publication reporting similar findings[1] prompted us to report our results. The reaction path followed by us is outlined in Scheme I.

SCHEME I



Compound **2** was reported by Wamhoff and Korte[1] as an intermediate, but was not isolated. We have isolated **2** and its hydrochloride salt. Compound **3** was originally reported by von Rothenburg[2] who synthesized it from 1-acetyl-1-carbethoxycyclopropane and hydrazine. Von Rothenburg reported his melting point for **3** as 197°. The melting point as found by Wamhoff and Korte[1] and by us was 148–150°. We have attempted to repeat von Rothenburg's synthesis and were unable to isolate any pure material. The physical and chemical constants found by Korte and us are in agreement and indicate that the spiro structure assigned to **3** is the correct one.

The nmr spectrum of **3** using tetramethylsilane as an internal standard in $CDCl_3$ shows peaks at 9.75 (amide H) and 1.86 (CH_3), and a multiplet between 1.85 and 1.5 ppm (cyclopropyl) having an A_2B_2 spin-coupling pattern. These assignments were in agreement with those of Wamhoff and Korte.[1] The 0.2- to 0.3-ppm shift to higher field of the methyl protons can be explained by the shielding effects of the cyclopropyl ring which is fixed in a plane at right angle to the plane of the pyrazolinone ring. The spectrum was also run in pyridine in an attempt to separate methyl and methylene peaks; the resonances were shifted upfield, but the pattern remained unchanged.

The synthesis of **3** by Wamhoff and Korte[1] was carried out by treatment of **1** with either sulfuric acid or thionyl chloride followed by basification and extraction. We have instead, isolated **2** and its hydrochloride salt by reaction of **1** with thionyl chloride. Compound **2** was stable in refluxing water, alcohol, and pyridine. In water, the pH of a suspension of **2** dropped from 6 to about 3.2. Apparently an equilibrium was set up in water: $2 \rightleftarrows 3 + HCl$. The liberation of HCl prevents further conversion to **3** since **2** can be recovered almost quantatively from refluxed aqueous suspensions. When **2** was suspended in water, addition of aqueous sodium hydroxide brought the pH up momentarily after which it dropped again. After 1 equiv had been added, all of **2** was converted to **3** and the pH remained stable at 5.9. During the addition, the pH was never allowed to go higher than 6.0. In one attempt to convert **2** (HCl salt) to its base, 2 equiv of sodium hydroxide solution was added in error. In the time it took to bring the pH back to 7, all the material had cyclized. Compound **3** could be reconverted to **2** by heating in concentrated hydrochloric acid. Wamhoff and Korte[1] claim that the formation of **3** from **1** on treatment with concentrated sulfuric acid proceeds by dehydration. We have tried heating at 190° and also treatment with dicyclohexylcarbodiimide in an attempt to convert **1** to **3**. In both cases starting material was recovered. Bachman and Heisey[3] also attempted dehydration of **1** by treatment with potassium hydroxide and with disodium hydrogen phosphate in an attempt to make vinyl compounds, but were unable to isolate any identifiable material. We believe, therefore, that the reaction of **1** with sulfuric acid produces a 4-(2-hydrogensulfato)ethyl compound which on treatment with base undergoes γ elimination of sulfuric acid to give **3**.

(1) H. Wamhoff and F. Korte, *Chem. Ber.*, **99**, 2962 (1966).

(2) R. von Rothenburg, *J. Pract. Chem.*, [2] **51**, 60 (1895).

(3) G. B. Bachman and L. V. Heisey, *J. Am. Chem. Soc.*, **71**, 1985 (1949).

Experimental Section[4]

4-(2-Hydroxyethyl)-3-methyl-2-pyrazolin-5-one (1).—This compound was prepared by a modification of the Bachman and Heisey procedure.[3] To 10.0 g (0.078 mole) of 2-acetylbutyrolactone in 20 ml of acetonitrile was added dropwise 4.0 g (0.078 mole) of hydrazine hydrate (99–100%). The reaction was very exothermic and Dry Ice–acetone cooling was required. After addition, the colorless product was filtered off to yield 10.3 g (93%) of product having a melting point of 181–182°.[3]

4-(2-Chloroethyl)-3-methyl-2-pyrazolin-5-one (2).—To 20.0 g (0.141 mole) of **1** was added all at once 120 ml of thionyl chloride. An exothermic reaction ensued and after 2.5 hr the thionyl chloride was removed *in vacuo*. The viscous residue was dissolved in water and just neutralized to pH 7. The gray precipitate which formed was filtered to yield 16.1 g of crude **3** (76%). Crystallization from ethanol gave material of mp 170–171°.

Anal. Calcd for $C_6H_9ClN_2O$: C, 44.87; H, 5.64; N, 17.44. Found: C, 44.92; H, 5.82; N, 17.07.

The hydrochloride could be obtained by crystallizing the residue obtained after removal of thionyl chloride from acetonitrile–ether (79%), mp 108–113°.

Anal. Calcd: Cl, 18.05. Found: Cl, 18.2 (by titration).

Cyclization of 2 to 4-Methyl-7-oxo-5,6-diazaspiro[2.4]hept-4-ene (3).—Cyclization of **2** could be accomplished by adding an excess of aqueous sodium hydroxide to a suspension of **2** in water, followed by neutralization. Alkaline conditions were not necessary to effect cyclization as shown in the following example. To a suspension of 30.0 g (0.25 mole) of **2** in 200 ml of water was added with stirring a solution of 11 g of sodium hydroxide in 400 ml of water over a 4-hr period. The pH was never allowed to go above 6 and the final pH was 5.9. The solution was filtered from a small amount of insoluble material and evaporated to dryness and the residue was crystallized from acetonitrile to yield 20.0 g of **3**, mp 140–141°. Recrystallization from ethanol raised the melting point to 148–149°.

Anal. Calcd for $C_6H_8N_2O$: C, 58.05; H, 6.50; N, 22.57. Found: C, 58.09; H, 6.57; N, 22.50.

Ring Opening of 3 to 2.—A solution of 1.0 g (0.005 mole) of **3** in 2 ml of concentrated hydrochloric acid was refluxed for 5 min. The solution was cooled and neutalized with aqueous sodium hydroxide. The solid was filtered off to give 1.2 g of product **2** having the identical infrared spectrum and melting point with those of the product prepared above.

Registry No.—**1**, 7721-54-2; **2**, 7721-55-3; hydrochloride of **2**, 7721-56-4; **3**, 7721-57-5.

Acknowledgment.—We wish to thank Dr. Eugene A. Pier of Varian Associates for running and interpreting the nmr spectra.

(4) Melting points were determined on a calibrated Fisher-Johns apparatus and are corrected. Elemental analyses were performed by Midwest Microlab, Inc., Indianapolis, Ind. 46226. Proton nmr spectra were obtained using a Varian HA-100 spectrometer in $CDCl_3$ solution using tetramethylsilane as internal standard.

The Resolution of 3-Amino-3-methylhexane[1]

DON C. IFFLAND AND NGUYEN T. BUU

Department of Chemistry, Western Michigan University, Kalamazoo, Michigan 49001

Received October 17, 1966

A search of the chemical literature has revealed no resolution of simple completely aliphatic tertiary carbinylamines. An interest in the stereochemistry at the tertiary carbon atom has lead us to prepare and resolve 3-amino-3-methylhexane as described in the Experimental Section.

(1) (a) Support of this study by Grant GP 1943 from the National Science Foundation is gratefully acknowledge. (b) Abstracted from a portion of the M.A. thesis of N. T. B., Western Michigan University, 1965.

This amine was repeatedly prepared in 75% yields by the Ritter method.[2] Hydrogen cyanide was alkylated with 3-methyl-3-hexanol and the resulting N-substituted formamide was hydrolyzed in aqueous alkali to form the amine.

Resolution of the racemic amine was realized by the fractional crystallization of the diastereoisomeric monoamine (+)-tartaric acid salts. It was noteworthy that even though successive recrystallizations of this salt provided an amine of successively greater specific rotation, neither the melting points nor the specific rotations of the tartrate salts correlated with the activity of the isolated amine.

The amine isolated after four crystallizations of the salt showed a low specific rotation, $[\alpha]^{25}D$ −0.096°. Although it was possible that this amine was not fully resolved, further recrystallizations were not obtained because of the limited amount of salt at this point. Nevertheless, there is reason to believe that this *t*-alkylamine possesses a low specific rotation when optically pure. Following the conformational analysis and empirical rules described by Brewster,[3] the predicted specific rotation[4] for this amine is 0°. Furthermore, a comparison of the maximum specific rotations reported for the isoelectronic *sec*-alkylamines and *sec*-carbinols shows that the amines commonly have specific rotations 0.4 to 0.8 the values for the related alcohols as indicated in Table I. If this relationship is valid in the *t*-alkyl series, a specific rotation as great as 0.152° would be anticipated for the 3-amino-3-methylhexane based on the $[\alpha]D$ 0.19° reported for 3-methyl-3-hexanol.[5]

TABLE I

SPECIFIC ROTATIONS OF RELATED *sec*-ALKYLAMINES AND *sec*-CARBINOLS

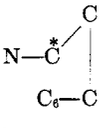
R	$[\alpha]D$, deg RNH_2	$[\alpha]D$, deg ROH	Ratio of RNH_2/ROH
2-Butyl	+7.80[a]	+13.83[b]	0.55
2-Hexyl	+4.3[c]	+10.7[c]	0.40
3-Heptyl	+4.15[c]	+5.12[c]	0.79
4-Octyl	+0.45[c]	+0.74[d]	0.61
3-Nonyl	+4.61[c]	+7.08[d]	0.65

[a] W. Leithe, *Ber.*, **63**, 804 (1930). [b] J. Kenyon, H. Phillips, and V. P. Pittman, *J. Chem. Soc.*, 1077 (1935). [c] P. A. Levine, A. Rothen, and M. Kuna, *J. Biol. Chem.*, **120**, 759 (1937). [d] P. A. Levine and R. E. Marker, *ibid.*, **91**, 418 (1931).

The conversion of the active amine to the N-methylene derivative introduced a group of greater refractivity than present in the amine and accordingly an increase in specific rotation was observed. In a consistent manner, reduction of the N-methylene derivative to 3-methylamino-3-methylhexane resulted in a decrease in the specific rotation.

Resolution of the 3-amino-3-methylhexane was attempted using the following active acids: (+)-

(2) J. J. Ritter and T. Kalisch, *J. Am. Chem. Soc.*, **70**, 4048 (1948).
(3) J. H. Brewster, *ibid.*, **81**, 5475 (1959).
(4) Including, at equal weight, the five-atom strained comformations



leads to a predicted value of 0.5°.
(5) A. G. Davies, J. Kenyon, and L. W. F. Salame, *J. Chem. Soc.*, 3148 (1957).