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Pyridineamidoximes

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In a recent publication,[1] Buu-Hoï, *et al.* reported that the 5-chloro-, 3,5-dichloro-, 5-bromo- and 5-iodo-salicylamidoximes inhibited the *in vitro* growth of *Mycobacterium tuberculosis* $H_{37}Rv$ at a concentration of the order of one microgram per milliliter. In view of the above findings, an investigation of the amidoximes derived from the pyridine monocarboxylic acids was undertaken.

The pyridineamidoximes were prepared according to the procedure of Tiemann and Krüger,[2] which involves the heating of the appropriate cyanopyridine at 80–85° with an aqueous solution of hydroxylamine. In the case of 3-pyridineamidoxime, the reaction was carried out in a sealed tube at 70°.[3] If the cyanopyridine was not soluble in water, as was the case with 2-cyanopyridine, sufficient ethyl alcohol was added to effect solution.

The pyridineamidoximes reported here were tested for *in vitro* tuberculostatic activity but were found to be inactive.

EXPERIMENTAL[4,5]

2-Pyridineamidoxime. A solution of 2.1 g. (0.030 mole) of hydroxylamine hydrochloride and 1.9 g. (0.015 mole) of sodium carbonate monohydrate in 10 ml. of water was heated to 60°. Three grams (0.029 mole) of 2-cyanopyridine was added in one portion, followed by sufficient ethyl alcohol (approximately 7 ml.) to dissolve the 2-cyanopyridine. The temperature of the mixture was raised to 85° and maintained for 2 hr. The alcohol was removed under reduced pressure and a tan oil separated from solution. On cooling to 0°, the oil solidified. The crystalline solid was filtered, washed twice with 10 ml. of ice-cold water, and dried in a vacuum desiccator over calcium chloride. The crude product (3.9 g.; 98%) melted at 114–116°. A sample recrystallized from water and dried *in vacuo* at 110° melted at 115.5–116°.

Anal. Calcd. for $C_6H_7N_3O$: C, 52.5; H, 5.1; N, 30.6. Found: C, 52.9; H, 5.0; N, 30.4.

3-Pyridineamidoxime. Prepared according to the procedure of Michaelis[3] in 70% yield, m.p. 127.5–128°.

4-Pyridineamidoxime. A solution of 2.1 g. (0.030 mole) of hydroxylamine hydrochloride and 1.9 g. (0.015 mole) of sodium carbonate monohydrate in 10 ml. of water was heated to 60°. Three grams (0.029 mole) of 4-cyanopyridine was added in one portion. An exothermic reaction took place causing the temperature to rise to 75°. Almost immediately a mass of colorless crystals separated from solution. Heating was continued at 80° for 0.5 hr. to complete the reaction. The suspension was cooled to 0°, filtered and dried in a vacuum desiccator over calcium chloride. The crude product (3.6. g.; 90%) melted at 175–177°. Recrystallization from ethyl alcohol gave colorless needles, m.p. 178–179°.

Anal. Calcd. for $C_6H_7N_3O$: C, 52.5; H, 5.1; N, 30.6. Found: C, 52.9; H, 5.1; N, 30.4.

Acknowledgment. The author wishes to thank Irene Melvin for performing the *in vitro* testing of compounds reported in this paper.

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[1] N. P. Buu-Hoï, M. Welsch, N. D. Xuong, and K. V. Thang, *Experientia*, **10**, 169 (1954).

[2] F. Tiemann and P. Krüger, *Ber.*, **17**, 1685 (1884).

[3] L. Michaelis, *Ber.*, **24**, 3439 (1891).

[4] All melting points are uncorrected.

[5] Carbon and hydrogen analyses by Schwarzkopf Microanalytical Laboratory.

Kinetics of the Thermal Isomerization of 2-*tert*-Butyl-3-Phenyloxazirane

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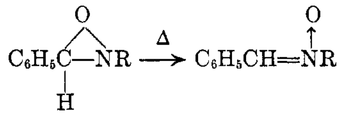
The observation[1] that 2-*tert.*-alkyl-3-phenyloxaziranes (I) isomerize on heating to the corresponding nitrones (II) and the novelty of the oxazirane ring system prompted the immediate investigation of the kinetices of this reaction. This kinetic study was primarily designed to determine the enthalpy and entropy of activation for the rearrangement of 2-*tert.*-butyl-3-phenyloxazirane, III, in diethyleneglycol diethyl ether (diethyl carbitol) solvent over a 40° temperature range.



I II

R = *tert*-alkyl

Preliminary experiments showed that the rearrangement of III to *N-tert.*-butyl benzaldoxime, IV, proceeded quantitatively in the 60–100° temperature range and that the ultraviolet absorption spectra of these two materials were sufficiently different in acetonitrile to afford an analytical method for IV in the presence of III. The nitrone (IV) has an extinction coefficient of 1.68×10^4 at λ_{max} 298 mμ while III has an extinction coefficient of only 92 at this same wave length.

The isomerization of III to IV was carried out in diethyl carbitol solvent at 60, 85, and 100° and the

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[1] W. D. Emmons, *J. Am. Chem. Soc.*, **78**, 6208 (1956).