

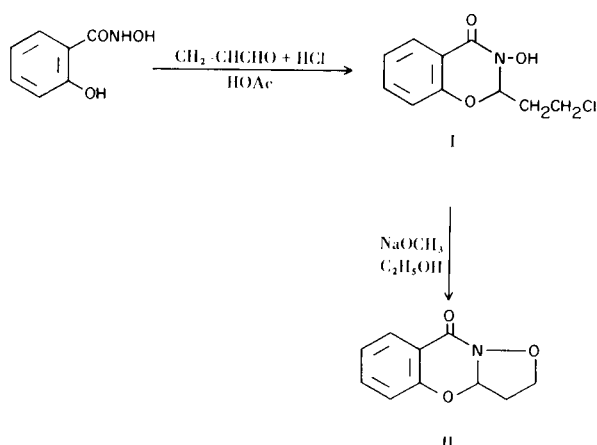
A New Heterocyclic Compound
3,3a-Dihydro-2*H*,9*H*-isoxazolo[3,2-*b*][1,3]benzoxazin-9-one

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Our interest in benzoxazines and in *N*-hydroxy heterocyclic compounds in general, as potential analgesic and anti-inflammatory agents, prompted us to prepare 2-(2-chloroethyl)-2,3-dihydro-3-hydroxy-4*H*-1,3-benzoxazin-4-one (I). It subsequently occurred to us that ring closure of this compound by elimination of hydrogen chloride would afford a heterocyclic compound which is a member of the hitherto unreported system C₃NO-C₄NO-C₆. Thus, I and sodium methoxide were heated in ethanol and the product of the reaction, after purification, gave elemental analysis data and spectral (ir and nmr) results which were consistent with those for the expected compound, 3,3a-dihydro-2*H*,9*H*-isoxazolo[3,2-*b*][1,3]benzoxazin-9-one (II).

The reactions employed to obtain II are shown below:



EXPERIMENTAL

Melting points were determined using a Thomas-Hoover melting point apparatus and are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. 37921. The nmr spectrum was obtained on a Varian T-60 spectrophotometer, and the infrared spectrum was recorded on a Perkin-Elmer 621 spectrophotometer.

2-(2-Chloroethyl)-2,3-dihydro-3-hydroxy-4*H*-1,3-benzoxazin-4-one (I).

Hydrogen chloride gas (8.8 g., 0.24 mole) was added to 90 ml. of glacial acetic acid with cooling. To one-half of this solution was added 15.3 g. (0.10 mole) of salicyloyl hydroxamic acid (Aldrich),

and then 6.1 g. (0.11 mole) of freshly distilled acrolein and the remaining half of the hydrogen chloride-acetic acid mixture were introduced simultaneously with stirring at a rate to maintain a temperature of 40-50°. The resulting mixture was stirred and heated at 50° for 1.5 hours and then poured into a mixture of ice and water with stirring. The tan solid was removed by filtration and washed successively with water, sodium bicarbonate solution, and water. The dried crude product weighed 15 g. (65.8%), m.p. 80-105°. A sample recrystallized from aqueous ethanol yielded analytically pure I, m.p. 113-114°.

Anal. Calcd. for C₁₀H₁₀ClNO₃: C, 52.79; H, 4.43; Cl, 15.57; N, 6.15. Found: C, 52.84; H, 4.31; Cl, 15.33; N, 6.15.

3,3a-Dihydro-2*H*,9*H*-isoxazolo[3,2-*b*][1,3]benzoxazin-9-one (II).

A solution of 4.56 g. (0.02 mole) of the crude 2-(2-chloroethyl)-2,3-dihydro-3-hydroxy-4*H*-1,3-benzoxazin-4-one and 1.08 g. (0.02 mole) of sodium methoxide in 60 ml. of ethanol was heated under reflux for 1.5 hours and filtered hot. The solid was washed with hot acetone and the combined filtrate and acetone washings were evaporated to dryness. The residue was washed with 10% sodium hydroxide, water, dilute hydrochloric acid, and again with water. The air-dried product weighed 2.5 g. (65.4%), m.p. 88.5-90.5°. A single recrystallization from ethyl acetate-pentane gave an analytically pure product, m.p. 89.5-90.5°; ir (potassium bromide) (1): 3010 (w), 2960 (w), 2900 (w), 1695 (s) and 1675 (s) doublet, 1615 (s), 1580 (w), 1468 (s), 1450 (s), 1430 (s), 1360 (m), 1330 (w), 1295 (m), 1275 (w), 1235 (w), 1210 (m), 1150 (m), 1125 (w), 1100 (s), 1090 (sh), 1030 (w), 1009 (s), 945 (m), 890 (w), 870 (w), 845 (w), 790 (s), 765 (s), 740 (w), 685 (s), 655 (m), 620 (w), 580 (w), 530 (m), 460 (w), 425 (w), 385 (w) cm⁻¹; nmr (deuteriochloroform with trimethylsilane as internal standard): δ 2.67-3.03 (q, 2H, CH₂ pos. 3), 4.20-4.50 (t, 2H, CH₂ pos. 2), 5.76-5.97 (t, 1H, CH pos. 3a), 6.94-8.05 ppm (m, 4H, aromatic).

Anal. Calcd. for C₁₀H₉NO₃: C, 62.82; H, 4.74; N, 7.33. Found: C, 62.80; H, 4.70; N, 7.28.

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REFERENCES

(1) The strong bands in the infrared spectrum, the doublet located at 1695 and 1675 cm⁻¹ are due to the amide carbonyl group. The strong band at 1615 cm⁻¹ is due to the aromatic ring.

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