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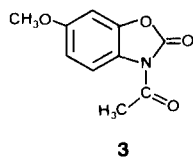
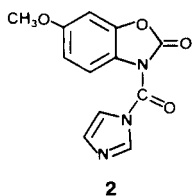
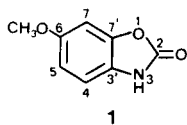
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Previously unknown 3-(1-imidazolyl)-6-methoxy-2-benzoxazolinone was isolated as a byproduct of the synthesis of reproductive-stimulant 6-methoxybenzoxazolinone (6-MBOA) with 1,1'-carbonyldiimidazole. Concomitant with byproduct formation was a 34% reduction in the yield of the desired 6-MBOA. A brief discussion of the formation of this byproduct and maximization of the yield of 6-MBOA is included.

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A previous communication from this laboratory reported [1] a much improved synthesis of 6-methoxy-2-benzoxazolinone (6-MBOA) and other benzoxazolinones from 2-aminophenols utilizing 1,1'-carbonyldiimidazole. Recently, much interest has been directed towards 6-MBOA, an isolate from corn, wheat and other grasses [2a-c], with reproductive stimulant activity in field rodents [3a-b] and the property [4] of modifying the binding affinity of auxins to their receptor sites in corn (*Zea mays*).

The purpose of this note is to report the isolation of a byproduct of the synthesis of 6-MBOA from 2-amino-5-methoxyphenol and to further define the conditions of the previously reported general procedure for the preparation of 2-benzoxazolinones to minimize its presence.



The crystallization of the relatively insoluble byproduct in the refluxing tetrahydrofuran reaction mixture was noted, among a few of the many repetitions of the 6-MBOA synthetic procedure conducted. A significant amount also remained in solution as a contaminant with the desired product, 6-MBOA. Concomitant with byproduct formation was a 34% reduction in the yield of 6-MBOA. This stable material when recrystallized was found to have a mp of 212-214° and molecular ion of m/z 259. Accurate mass data on the molecular ion was indicative of a $C_{12}H_9N_3O_4$ formula. Two single proton multiplets at δ 8.42 and 7.73

and a single proton multiplet at δ 7.13 suggested the presence of an 1-imidazolyl group. This was further supported by the loss of a $C_4H_2N_2O$ carbonylimidazole fragment from the molecular ion (m/z 259 to 165) and the presence of an imidazole acylium ion at m/z 95 in the mass spectrum. Coupled with the presence of a methoxy signal at δ 3.71 and a 1,2,4 aromatic substitution pattern in the pmr spectrum, these data suggested that the byproduct was the previously unknown 3-(1-imidazolyl)-6-methoxy-2-benzoxazolinone (**2**).

Treatment of **2** with acetic anhydride and pyridine in tetrahydrofuran effected the removal of the 1-imidazolyl moiety and led to a white crystalline compound that compared in all respects (mp, pmr, cmr, uv, ir) with **3** prepared *via* direct acylation of 6-MBOA. This transformation confirmed the presence of a 6-methoxy-2-benzoxazolinone ring system in byproduct **2**.

A review of the conditions employed in the various repetitions of the 6-MBOA synthetic procedure revealed that byproduct **2** appeared in significant amounts only in the few cases in which the precursor, 2-amino-5-methoxyphenol, was stored at 5° for a period of time before its utilization. It has been reported [5a-c] that 2-amino-5-methoxyphenol is air and light sensitive and subject to relatively rapid degradation. Degradation of this precursor over a period of time would lead to an overestimation of the amount of 1,1'-carbonyldiimidazole reagent required. This may account for the formation of byproduct **2** at the expense of the desired 6-MBOA in the reaction mixture. In conclusion, these data suggest that one should utilize the 2-amino-5-methoxyphenol immediately after preparation to prevent the formation of significant amounts of byproduct **2** and maximize the yield in the synthesis of 6-MBOA.

EXPERIMENTAL

The cmr, pmr, ir, uv and mass spectra were obtained using a JEOL JNM-PFT-100 (100 MHz), Nicolet 200 (200 MHz) or Varian EM-390 (90 MHz), Perkin-Elmer 727B, Hewlett-Packard 8451A Diode Array and a Micromass 7070F spectrometer respectively. Melting points are uncorrected.

3-(1-Imidazolyl)-6-methoxy-2-benzoxazolinone (**2**).

A solution of 2-amino-5-methoxyphenol (41.0 g, 0.29 mole) [5a], stored at 5° for 78 hours, and 1,1'-carbonyldiimidazole (51.7 g, 0.32 mole) in tetrahydrofuran (300 ml) was refluxed 4 hours. The crystalline insolubles were filtered, recrystallized from methylene chloride, and washed with small quantities of acetone to give 12.4 g (16%) of **2** as colorless needles, mp 212-214°; ir (potassium bromide): 1770 cm⁻¹ (C=O); ms: m/z (relative intensity), 259.0593 [Calcd. for C₁₂H₉N₃O₄: 259.0590], 165.0426 (M⁺-C₃H₂N₂CO, 100), 150 (165 -CH₃, 27), 95.0245 (C₄H₃N₂O, 1-imidazolyl ion, 13); uv (methanol): λ max 206, 262 and 286 nm; pmr (deuteriodimethyl sulfoxide): (200 MHz) δ 3.71 (s, OCH₃, 3H), 6.62 (d, H-4, 1H, J_{4,5} = 9 Hz), 6.68 (m, H-7, 1H), 6.94 (dd, H-5, 1H, J_{5,4} = 9 Hz, J_{5,7} = 2 Hz), 7.13 (m, imidazole moiety, 1H), 7.73 (m, imidazole moiety, 1H), 8.41 (m, imidazole moiety, 1H).

Anal. Calcd. for C₁₂H₉N₃O₄: C, 55.60; H, 3.50; N, 16.21. Found: C, 55.35; H, 3.60; N, 15.94.

Further workup [1] of the above reaction mixture led to the isolation of 6-MBOA (23.1 g, 48%) and additional **2** (2 g, 3%).

3-Acetyl-6-methoxy-2-benzoxazolinone (**3**) from **2**.

A suspension of 3-(1-imidazolyl)-6-methoxy-2-benzoxazolinone, (**2**) (2.5 g, 9.6 mmoles) in a solution of acetic anhydride (20 ml) and pyridine (2 ml) in tetrahydrofuran (150 ml) was refluxed for 4 hours. The resultant clear solution was evaporated to dryness, the solid residue crystallized and recrystallized from methylene chloride to yield **3** (1.1 g, 55%) as colorless crystals, mp 149-150.5°; ir (potassium bromide): 1735 cm⁻¹ (2-benzoxazolinone C=O) and 1780 cm⁻¹ (acetyl C=O); uv (methylene chloride): 224, 256 and 284 nm; ms: m/z (relative intensity) 207.0531 [Calcd. for C₁₀N₃NO₄: 207.0532], 165 (M⁺ -H₂C=C=O, 100), 150 (165

-CH₃, 32), 43 (CH₃H≡O⁺, 90); pmr (deuteriodimethylsulfoxide): (90 MHz) δ 2.57 (s, (CO)CH₃, 3H), 3.76 (s, OCH₃, 3H), 6.78 (dd, H-5, 1H, J_{5,4} = 9 Hz, J_{5,7} = 3 Hz), 7.02 (d, H-7, 1H, J_{7,5} = 3 Hz), 7.76 (d, H-4, 1H, J_{4,5} = 9 Hz); cmr (deuteriochloroform): (100 MHz) δ 24.8 ((CO)CH₃), 56.0 (OCH₃), 96.8 (C-7), 109.9 (C-5), 116.4 (C-4), 121.0 (C-3'), 142.9 (C-7'), 151.7 (C-2), 169.1 ((CO)CH₃).

These physical data and spectroscopic values matched those obtained from **3** prepared *via* treatment of **1** under the above acylating conditions.

Anal. Calcd. for C₁₀H₉NO₄: C, 57.97; H, 4.38; N, 6.76. Found: C, 57.93; H, 4.25; N, 6.77.

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