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Synthesis of 4-Acetylbenzoxazolin-2(3*H*)-one Reported from *Zea mays*

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A three-step alternative synthesis of 4-acetylbenzoxazolin-2(3*H*)-one (**4**) is reported. Starting from inexpensive 3-hydroxyacetophenone (**1**) 3-hydroxy-2-nitroacetophenone (**2**) is prepared by nitration followed by catalytic hydrogenation to yield 2-amino-3-hydroxyacetophenone (**3**) in which a C═O unit is inserted by means of bis(trichloromethyl)carbonate (triphosgene) in the presence of triethylamine to afford **4** in 35% overall yield.

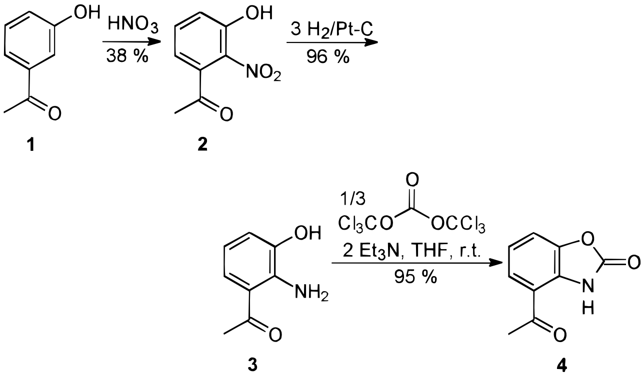
Recently, the isolation and characterization of 4-acetylbenzoxazolin-2(3*H*)-one (4-ABOA, **4**) was reported from kernels of a special *Zea mays* hybrid line.[1] This hybrid is tolerant to *Fusarium graminearum* and has insecticidal activity against *Sitophilus zeamais*.[2] A biosynthetic relationship of 4-ABOA to benzoxazolin-2(3*H*)-one (BOA) and 6-methoxybenzoxazolin-2(3*H*)-one (MBOA) known from gramineous plants[3] has been postulated.[2] We have shown that, at least synthetically, 4-ABOA (**4**) can indeed be prepared from a benzoxazinoid precursor, that is, by ether cleavage and subsequent hydrolysis of 5-acetyl-4-hydroxy-2-methoxy-2*H*-1,4-benzoxazin-3(4*H*)-one.[4] Therefore, we assume that the 4-ABOA isolated may have originated from the degradation of 5-acetyl-2,4-dihydroxy-2*H*-1,4-benzoxazin-3(4*H*)-one as the natural precursor. A four-step synthesis starting from the sensitive 3-hydroxyanthranilic acid has been reported[5] to produce 4-ABOA (**4**) in quantities sufficient for biological tests. We now report on an alternative synthesis of 4-ABOA (**4**) (Scheme 1) on the gram scale, based on an inexpensive starting material and avoiding the handling of phosgene and of light- and air-sensitive intermediates.

3-Hydroxy-2-nitroacetophenone (**2**) was prepared by nitration of 3-hydroxyacetophenone (**1**) with a mixture of 67% nitric acid and 96% sulfuric acid as described.[6] Compound **2** was hydrogenated over Pt−C in THF to yield 2-amino-3-hydroxyacetophenone (**3**) in 96% yield;[4] amine **3** is stable and storable. It was carbonylated by means of bis(trichloromethyl)carbonate (triphosgene) in the presence of a tertiary amine in THF in 95% yield. Triphosgene has been rediscovered as a solid, safe, and convenient phosgene substitute.[7] 4-ABOA (**4**) was finally obtained in 35% overall yield based on **1** by this procedure, which is similar to our synthesis of MBOA.[8]

Experimental Section

General Experimental Procedures. The crude product obtained by nitration[6] of 80 g (0.588 mol) commercial 3-hydroxyacetophenone (**1**) (Lancaster) was purified by crystallization from MeOH followed by column chromatography [Merck Si gel 0.063−0.200 mm, eluent toluene−EtOAc 5:1 (v/v)] to yield 3-hydroxy-2-nitroacetophenone (**2**) (41.0 g, 38%) of mp 134−136 °C (MeOH) (lit.[6] mp 131−132 °C), together with 3-hydroxy-4-nitroacetophenone (6.4 g, 6%) of mp 68−69 °C (MeOH) (lit.[6] mp 71.5−72.5 °C). 2-Amino-3-hydroxyacetophenone (**3**) obtained by hydrogenation[4] of **2** on the 20-mmol scale was used without recrystallization. Melting points were determined on a Boetius micro hot-stage apparatus and are corrected.

Scheme 1. Synthesis of 4-acetylbenzoxazolin-2(3*H*)-one (4-ABOA) (**4**)



4-Acetylbenzoxazolin-2(3*H*)-one (4). To a rapidly stirred solution of 2-amino-3-hydroxyacetophenone (**3**) (10 mmol, 1.51 g) in dry THF (150 mL) was added triethylamine (20 mmol, 2.02 g) and, in one portion, a solution of bis(trichloromethyl)carbonate (3.37 mmol, 1.00 g) in dry THF (10 mL) at 0 °C. After stirring at 0 °C for 1 h the solution was filtered, and the solvent was removed *in vacuo*. The remaining residue was recrystallized from H_2O (300 mL) to yield 4-acetylbenzoxazolin-2(3*H*)-one (**4**) (1.68 g, 95%) as pale yellow needles, pure according to TLC [Merck aluminum sheets Si gel 60 F_{254}, eluent toluene/EtOAc 1:1 (v/v), $R_f = 0.46$]: mp 202−204 °C (H_2O); mp 210−211° (MeOH) (lit.[1] mp 217−218 °C (Me_2CO-H_2O)]. Compound **4** proved to be identical with our synthetic sample previously reported by comparison of full spectroscopic data[4] and with the natural product described.[1]

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References and Notes

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