PREPARATION OF WHEAT ALLELOCHEMICALS AND THEIR DEGRADATION PRODUCTS

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2,4-Dihydroxy-7-methoxy-(2*H*)-1,4-benzoxazin-3(4*H*)-one (DIMBOA) and 2,4-Dihydroxy-(2*H*)-1,4-benzoxazin-3(4*H*)-one (DIBOA) have been described as important allelochemicals from *Gramineae* as well as *Acanthaceae*, *Rannunculaceae* and *Scrophulariaceae* plants. Several bioactivities have been described and evaluated for these compounds, including fungistatic, anti-feedant and phytotoxic. In our ongoing studies about allelochemicals as alternative herbicide models, the description of soil dynamics in phytotoxic agents has high importance, since the posible biotransformations developed by soil microorganisms could yield compounds with modified biologycal properties. Thus, different amounts of starting allelochemicals and degradation products were needed for the preparation of suitable analytical standards, and isolation and synthesis techniques have been optimized for them.

These compounds belong to three different structural families (Figure 1):

Type I: Compounds with (2*H*)-1,4-benzoxazin-3-(4*H*)-one moiety; Benzohydroxamic acids DIMBOA (R_1=R_2=OH, R_3=OCH_3) and DIBOA (R_1=R_2=OH, R_3=H), their glycosides (R_1=O-Glc) and degradation products 2,4-hydroxy-7-methoxy-(2*H*)-1,4-benzoxazin-3(4*H*)-one (HMBOA) and 2-hydroxy-(2*H*)-1,4-benzoxazin-3(4*H*)-one (HBOA) belong to this structural type.

Type II: N-[2-hydroxyphenyl]malonamic acids: These compounds are fungal degradation products from benzoxazolinones BOA and MBOA. N-[2-hydroxyphenyl] malonamic acid (R=H, **HPMA**) and N-[2-hydroxy-7-methoxyphenyl]malonamic acid (R=OH, **HMPMA**) have been synthesized in good yields and mild conditions.

Type III: 2-aminophenoxazin-3-ones and their derivatives: Some compounds, characterized by us like the final degradation materials from benzohydroxamic acids belong to this structure, and present different functionalization combinations. They have been synthesized in order to obtain analytical standards and to test their bioactivies. **APO** (R_1=R_2=R_3=H), **AAPO** (R_1=H, R_2=Oac, R_3=H), **AMPO** (R_1=R_2=H, R_3=OCH_3), **AAMPO** (R_1=H, R_2=Oac, R_3=OCH_3), **AHPO** (R_1=R_2=H, R_3=OH) and **AAHPO** (R_1=H, R_2=OAc, R_3=OH) have been produced as analytical standars and included in structure-activity relationships studies.

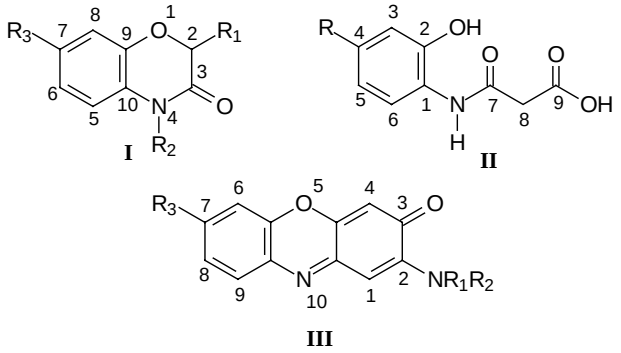

Figure 1: Structural types of isolated and synthesized compounds: 1,4-benzoxazin-3-one (I), N-[hydroxyphenyl]malonamic acid (II) and 2-aminophenoxazin-3-one (III)

DIMBOA, DIBOA and their glycosides have been obtained by isolation from corn (DIMBOA series) and rye (DIBOA series) seedlings. Their isolation procedures are modifications of previously described methods. Degradation products HBOA and HMBOA have been synthesized. HBOA have been produced by a new method in which a [3.3] sigmatropic acyl rearrangement allowed functionalization of C-2 position. (Figure 2) HMBOA have been prepared from DIMBOA by a selective reduction of N-OH moiety with samarium iodide (Figure 3).

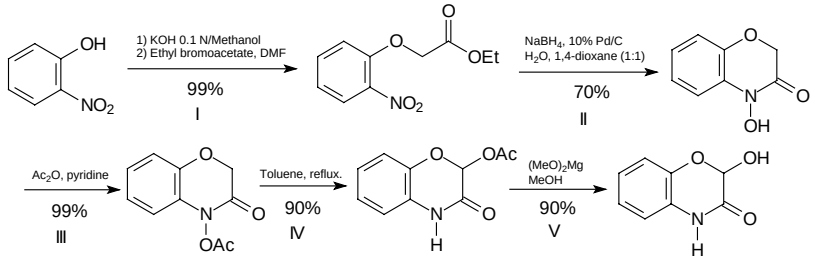

Figure 2. Reaction conditions and yields for HBOA synthesis.

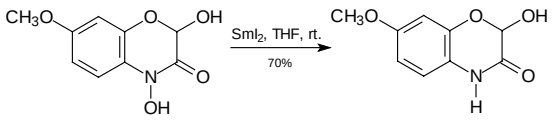

Figure 3. Reduction of HMBOA with samarium iodide.

Malonamic acids have been obtained from their corresponding nitrophenols (2-nitrophenol for HPMA and 5-methoxy-2-nitrophenol for HMPMA) by reaction sequences in which protection of aromatic hydroxyl group, reduction of nitro moiety; side chain introduction and final deprotection are included. The transformation were quick and in high yield. Protection and deprotection steps have been included to avoid dimerization to aminophenoxazines and to provide new source materials for the synthesis of other new derivatives (Figure 4).

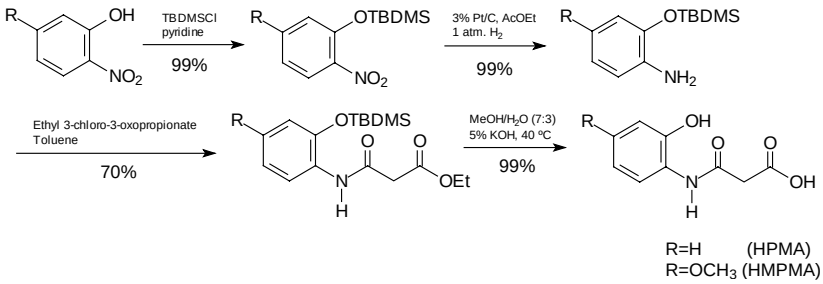

Figure 4. Synthesis of N-hydroxyphenyl malonamic acids

We took advantage of those dimerization processes to get access to the aminophenoxazin skeleton and all their derivatives. Dimerization of 2-aminophenol has been previously described, as well as acetylation method to obtain AAPO. 7-methoxyaminophenoxazin skeleton has been synthesized by a novel reductive dimerization method which afforded AMPO in high yield (70%), mild conditions and one reaction step. From APO and AMPO, the acylamino and 7-hydroxy derivatives have been obtained directly by using common chemical methods (Figure 5).

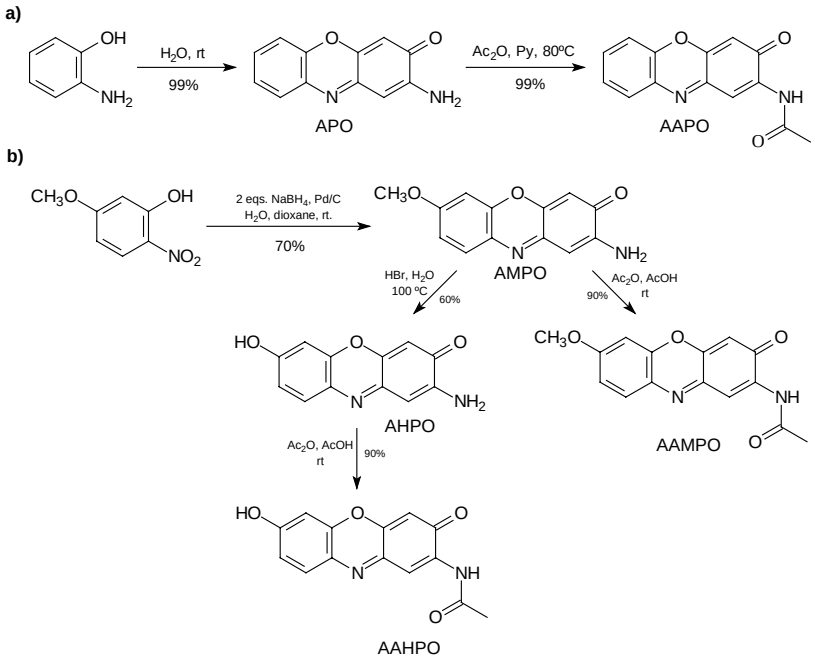

Figure 5. Synthesis of aminophenoxazinone derivatives

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