

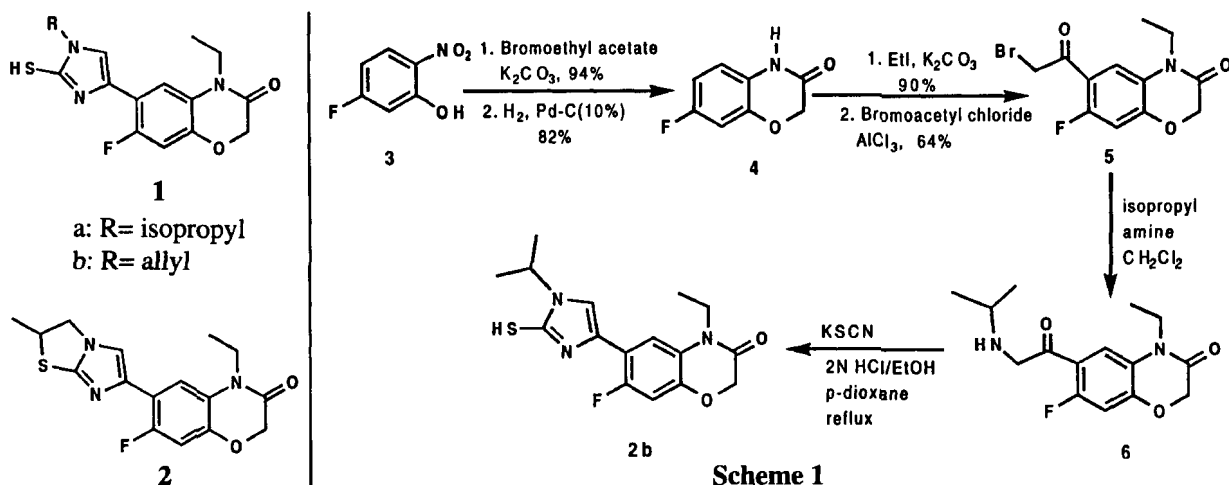
Synthesis of substituted imidazoles and uracils as herbicides

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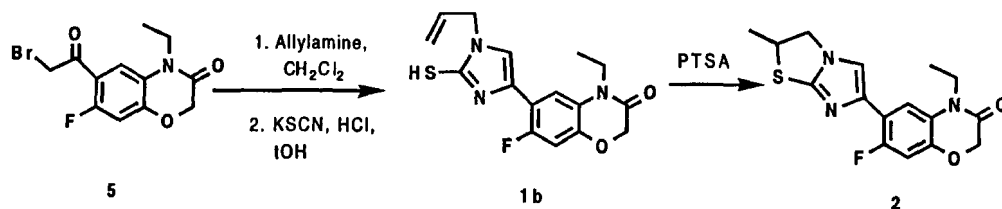
Abstract: Compounds **1** and **2** represent a new class of herbicides which demonstrate activity against several agriculturally important weed species. The mechanism of action has been found to involve inhibition of Protoporphyrinogen Oxidase (Protox) which results in the accumulation of Protoporphyrin IX. With light, Protoporphyrin IX acts as a photosensitizer in the formation of singlet oxygen which causes lipid peroxidation and membrane disruption.

We have been interested in the development of new classes of compounds with low use rates to control unwanted vegetation in crops. One of the areas we have been working for some time is the inhibition of Protoporphyrinogen Oxidase (Protox) as a herbicidal target. The enzyme Protoporphyrinogen Oxidase involved in the chlorophyll biosynthesis has been an interesting target for herbicide discovery (1) to many agricultural companies. Inhibition of Protox leads to the accumulation of Protoporphyrin IX in the outer cell membrane which in the presence of light acts as a photosensitizer in the formation of singlet oxygen (2). This causes the cell necrosis and ultimately plant death. The inhibition of this enzyme is one of the active areas of research by many agricultural companies and academic institutions which resulted in many patents and publications(1). The general structure of Protox inhibitors consists of a heterocycle moiety attached to an aromatic part either by a nitrogen or carbon bond. Here we describe a synthesis of imidazole compounds such as **1** and **2** as Protox inhibiting herbicidal compounds.

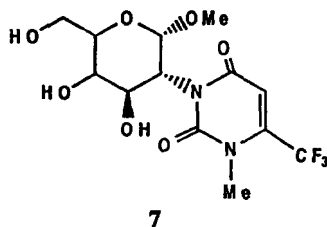


Initially, we prepared the acyclic thioimidazoles **1** (R=allyl and isopropyl) which we extended to the preparation of cyclic compound **2** from **1b**. The compound **1a** was prepared starting from the phenol **3** (Scheme 1). Phenol **3** on reaction with bromoethyl acetate followed by hydrogenation of the nitro compound gave the benzoxazinone **4**. The compound **4** on treatment with ethyl iodide in acetone in the presence of K_2CO_3 gave the corresponding N-ethyl compound, Friedel-Crafts reaction of which with bromoacetyl chloride and AlCl_3 gave the bromo derivative **5** in good yield. Compound **5** on condensation with isopropylamine gave the amino compound **6**, which on heating with potassium thiocyanate (**3**) afforded the thioimidazole **1a**. Alternatively, the N-allyl thioimidazole **1b** was also prepared from compound **5** and allylamine following reaction conditions described for the preparation of **1a** from **5**.

Scheme 2



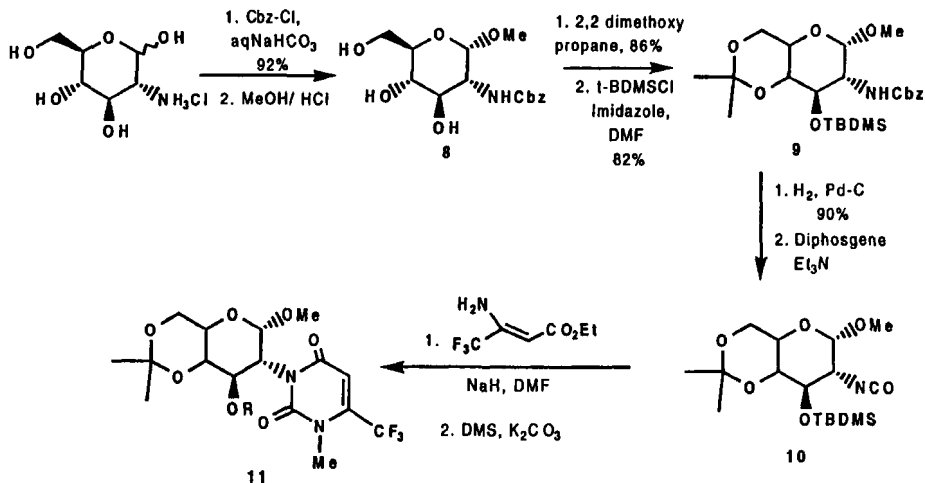
The allyl derivative **1b** was used for preparing the cyclic compound **2** (Scheme 2). When the compound **1b** was exposed to acidic reaction conditions using PTSA in xylene at reflux it gave exclusively **1**.



The other area of interest is designing new herbicidal compounds containing a carbohydrate moiety such as **7**. Here we describe a synthesis of compound **7** starting from D-glucosamine (Scheme 3).

N-Cbz glucosamine (**3**) was heated at reflux with methanolic HCl to give the anomeric mixture of methyl glycosides. The major α -anomer **8** was separated and was converted to the acetonide by reaction with 2,2-dimethoxypropane in the presence of PTSA, and the resulting acetonide was reacted with tBDMS-chloride in DMF in the presence of imidazole to give the silyl acetonide **9**. The Cbz group of compound **9** was removed by catalytic hydrogenation using Pd-C (10%) to give the corresponding amino compound which on reaction with diphosgene in the presence of triethylamine afforded the corresponding isocyanate **10**. The isocyanate **10** was reacted with ethyl 3-amino-4,4,4-trifluorocrotonate to afford the uracil compound which on methylation with dimethyl sulfate gave the corresponding N-methyl compound **11**. The compound **11** can be converted to **7** via deprotection of the acetonide and silyl groups by standard methods.

Scheme 3



REFERENCES

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