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George A. Kraus, Umayangani K. Wanninayake, Jashaun Bottoms

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George A. Kraus*, Umayangani K.Wanninayake and Jashaun Bottoms

Department of Chemistry, Iowa State University, Ames, IA 50011, United States
Iowa State University Center for Biorenewable Chemicals

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ABSTRACT

At ambient temperature, triacetic acid lactone reacts with amines to produce 4-amino-2-pyrones. If the temperature is raised to 100 °C, 4-hydroxy-2-pyridones are generated.

Triacetic acid lactone (**1**) is readily available either through the acid catalyzed deacetylation of dehydroacetic acid or through microbial transformation of glucose.[1] It is a useful intermediate for the synthesis of penstyrylpyrone (**3**)[2] and pogostone (**4**)[3], shown in Figure 1. A related synthetic compound PH797804 (**5**)[4] is a potent p38 MAPK inhibitor. As part of a program to expand the potential of **1** as a platform chemical[5], we studied the reaction of **1** and its tosylate **2** with amines. A number of groups have reported limited studies of **1** with primary amines and with glycine.[6-10]

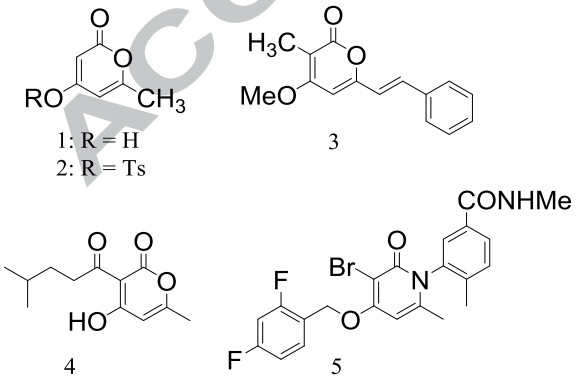
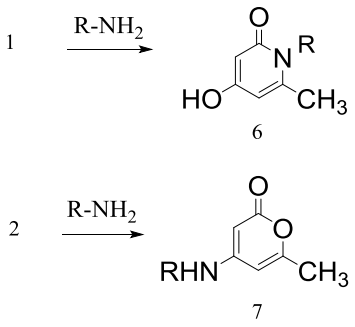


Figure 1. Triacetic acid lactone derivatives

Reaction of 1.1 equivalents of a primary amine with **1** at 100 °C in water afforded 2-pyridones **6**, as shown in Scheme 1. The structure assignment of **6a** was supported by a shift in the NMR resonance of the methyl group at C-6 and by a strong NOE interaction between the methyl group at C-6 and the methylene of the ethyl group.



Scheme 1. Reaction with amines

The products of primary amines with **1** are shown in Figure 2. Both aliphatic and aromatic amines react with **1**. The pyridones **6a**-**6g** were polar solids whose insolubility made them difficult to purify by silica gel chromatography.[19] Fortunately, the pyridones were readily separable from **1** by differential solubility in ethyl acetate.

*Corresponding author. Tel.: +1 515 294 7794; fax: +1 515 294 0105.
E-mail address: gakraus@iastate.edu (G.A. Kraus).