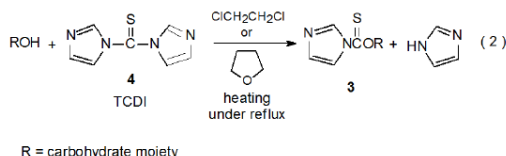
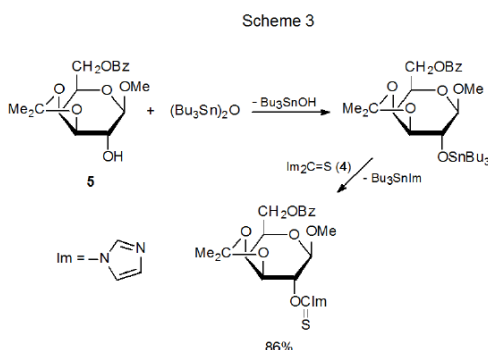


III. (Thiocarbonyl)imidazolides

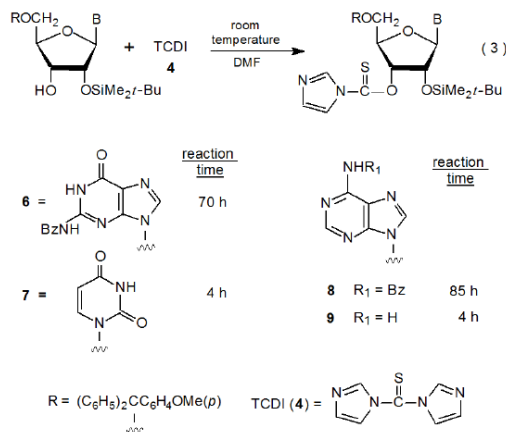
Formation of a (thiocarbonyl)imidazolidine (**3**) generally involves heating a partially protected carbohydrate with *N,N*-thiocarbonyldiimidazole (**4**, TCDI) under reflux in tetrahydrofuran (or 1,2-dichloroethane) and isolating the reaction product by chromatography (eq 2).^{1,11} Nearly every synthesis of a (thiocarbonyl)imidazolidine follows this procedure, although acetonitrile,^{12–14} toluene,^{15–17} and *N,N*-dimethylformamide^{18,19} occasionally are used as reaction solvents.



There are scattered reports of (thiocarbonyl)imidazolides forming more slowly than might be expected under typical reaction conditions. One such report concerns the methyl glycoside **5**, a compound that reacts so slowly that prior activation with bis(tributyltin)oxide is necessary to increase the nucleophilicity of **5** to the point that (thiocarbonyl)imidazolidine formation proceeds at an acceptable rate (Scheme 3).²⁰



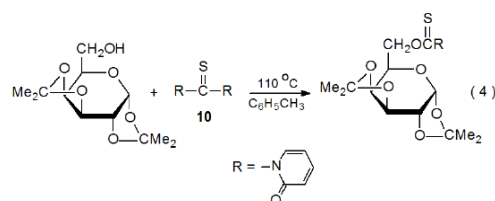
Reduced reactivity in nucleosides sometimes is brought about by *N*-benzoylation. The *N*-benzoylguanosine and adenosine derivatives **6** and **8** require treatment with TCDI (**4**) for 70 and 85 hours, respectively, for complete reaction to take place; in contrast, derivatives lacking the *N*-benzoyl group (**7** and **9**), need only four hours for reaction to reach completion (eq 3).²¹



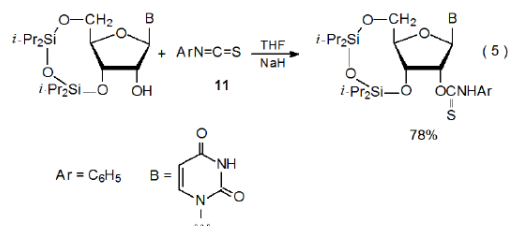
Even though (thiocarbonyl)imidazolides (**3**) can be prepared readily by the reaction shown in eq 2, this procedure has several minor drawbacks. One of these is that *N,N*-thiocarbonyldiimidazole (**4**, TCDI) needs to be kept in a dry atmosphere because it is unstable in the presence of atmospheric moisture.²² Another is that imidazole, produced as a byproduct in this reaction (eq 2), may catalyze unwanted transformation of some compounds.²² Finally, the cost of TCDI (**4**) is high enough to be a factor in deciding upon its use, particularly in large-scale reactions.

In an effort to overcome possible disadvantages associated with use of (thiocarbonyl)imidazolides, some researchers have proposed switching to related compounds. Thionocarbamates formed from 1,1'-thiocarbonyldi-2,2'-pyridone (**10**), a reagent stable to

atmospheric moisture, are effective replacements for (thiocarbonyl)imidazolides (eq 4),²² but detracting from the use of this new reagent (**10**) is its even greater cost than TCDI.



Some thionocarbamates synthesized from the inexpensive phenyl isothiocyanate (**11**) (eq 5) are capable of radical formation.^{23,24} Although producing a thionocarbamate by reacting a partially protected carbohydrate with phenyl isothiocyanate (**11**) solves the “cost problem”, it has the disadvantage that this reaction requires the presence of a strong base because hydroxyl group deprotonation is needed for this reaction to occur at an acceptable rate (eq 5). Also, not all thionocarbamates prepared from **11** form radicals under typical reaction conditions.²⁵ None of the alternatives to (thiocarbonyl)imidazolides have been widely adopted.



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