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Thiourea-Assisted Halogenation of Alcohols and Extension to a Direct Gabriel Synthesis

Alcohol activation for nucleophilic substitutions has been recently rated as one of the most important chemical reactions that needs to be further developed for a sustainable future. Classical reagents for halogenation of unreactive alcohols are well known, and most act in a similar fashion by converting the alcohol into an intermediate that can be readily displaced by the halide nucleophile. The halogenated compounds have numerous industrial and practical uses, and appear in a myriad of natural products. In this study, we developed a general pathway for the halogenation of alcohols by using thioureas and N-halosuccinimide (NXS) as the halogen source under very mild conditions and in a surprisingly facile manner. The reaction can be carried out on many different types of alcohols, including primary, secondary and tertiary alcohols and is compatible with several functional groups. The availability and low cost of the reagents, and the possibility to recycle the succinimide by-product, makes this reaction highly economic and atom efficient and could become a very important tool for this ubiquitous transformation both in academia and industry. Interestingly, N-bromophthalimide (NBP) can be used both as the bromine and imide source for a direct Gabriel synthesis from alcohols, plotting the pathway for the facile conversion of alcohols to primary amines. Hence, the reaction of alcohols with NBP in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and dimethyl thiourea readily afforded the desired imide product. Thus, the fact that alcohols are ubiquitous natural products coupled with the importance of both of these chemical transformations could make a strong impact on sustainable organic synthesis methodologies and may become the new paradigm for the transformation of alcohols to alkyl halides and amines.
References

