

Palladium Inspired Activation of Hindered Anhydrides for the Acylation of Alcohols and Polyols

Background

The focus of our research is on protecting hydroxyl groups (or alcohols) against undesirable side reactions during organic synthesis. The traditional method of protecting hydroxyl groups uses acidic anhydride, DMAP, and pyridine. While this method is successful, it is a lengthy process and the key component pyridine is toxic. For these reasons, research continues to seek out different methods.

Current Methodologies

Current methodologies include using chemicals like scandium triflate and cobalt chloride as catalysts and while they are successful in protecting hydroxyl groups, they are very expensive, and therefore not feasible for furthering research.

Cationic Palladium as Catalysts in Organic Synthesis

In recent years, palladium has been used often in organic synthesis. Some instances include these glycosylation (linkage of two sugars) reactions (shown in the first three reactions). What's more, palladium has even demonstrated proficiency in activating simple anhydrides to protect hydroxyl groups (fourth reaction)!

Substrate Scope: With Isobutyric Anhydride

Therefore, we hypothesize that the same palladium can be used to activate more complex anhydrides, such as isobutyric anhydride (highly hindered). To pursue this, we tried palladium as a catalyst in *several* alcohols. Much to our surprise, *all* of the hydroxyl groups were protected quickly, sufficiently, and at room temperature!

Future Direction: With (Carbohydrate-Derived) Polyols and Other Hindered Anhydrides

After receiving these results, we are eager to expand our findings. We intend to determine the efficiency of palladium as a catalyst by using the same method, focusing on the protection of multiple polyols, using the very hindered pivalic anhydride.

Summary

Though other methods have been sufficient in hydroxyl group protection during organic synthesis, a more cost effective, less toxic, and time efficient solution is ideal. We have discovered a new method that complements previous advances in organic synthesis. Our research has proven that a new method, including the addition of palladium as a catalyst, is quicker, has a wider substrate scope, and is substantially more efficient than alternatives. We desire to continue our inquiry on palladium, to include activation of multiple polyols using more hindered anhydrides.