1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD) as a Lewis Base

Compiled by Aleksej Turočkin

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Introduction

1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD, 1) was first synthesized by McKay and Kreling in the laboratories of Monsanto Canada Limited in 1957. This bicyclic guanidine possesses a remarkably high Brønsted basicity (pKₐ = 28 in MeCN) and has found broad applications as an organic superbase. Moreover, the nucleophilic properties of guanidines have also been studied. Mayr and co-workers quantified the nucleophilicities for a series of guanidines, and TBD was by far the most powerful nucleophile among the investigated structures. In fact, TBD was found to be an even stronger nucleophile than the well-known Lewis base 4-dimethylaminopyridine (DMAP). In order to highlight the synthetic utility and usefulness of TBD as a Lewis base, a short overview of recent applications is presented.

Figure 1 Commercially available bicyclic guanidine base 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD, 1)

Abstracts

(A) Activation of carbon dioxide by TBD via formation of reactive carbamate adducts has been known for half a century. These intermediates can participate in various follow-up reactions, enabling metal-free CO₂ fixation. For instance, carboxylation of terminal alkenes 2 was reported by Wang and co-workers. The new method enables direct access to various propiolic acid derivatives.

(B) TBD was used for the synthesis of propylene carbonate (5) from carbon dioxide and propylene glycol (4). Other bases such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and Et₃N were also investigated, but TBD showed the highest catalytic activity.
TBD is an excellent acyl transfer catalyst, as demonstrated by the Waymouth group for the synthesis of amide 8 from ester 6 and primary amine 7. Related guanidines such as 1,4,6-triazabicyclo[3.3.0]oct-4-ene (TBO) showed significantly lower activity which was attributed to lower nucleophilicity and Bronsted basicity compared to TBD.

Baati and co-workers used TBD as an effective catalyst for intramolecular aldol reactions of various ketoaldehydes 9. Other guanidine bases, such as 1,1,3,3-tetramethylguanidine (TMG) and 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD), were much less active catalysts, despite similar Bronsted basicities. Therefore, a possible reaction mechanism was postulated in which TBD acts as a nucleophile.

TBD was found to be an exceptionally active catalyst for the cycloaddition of allenoate esters 11 and trifluoromethyl aryl ketones, enabling the preparation of very densely substituted oxtanes 12 in a diastereoselective manner. The reaction required only short reaction times and worked well with γ- and even with α,γ-disubstituted allenoates.

Selig et al. showed that TBD catalyzes the reaction between γ-alkyl allenoate esters 13 and aromatic aldehydes to give 4H-1,3-dioxin-6-yl-propanoates 14 with excellent diastereoselectivity. Mechanistic studies revealed that these complex heterocycles are obtained as a result of a four-step reaction cascade consisting of two consecutive Morita–Baylis–Hillman reactions on the α- and γ-position, an acetalization, and a final ring-closing intramolecular oxa-Michael reaction.

References

(6) For the crystallographic characterization of TBD-CO₂