

SYNLETT Spotlight 464

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

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This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Aleksej Turočkin was born in 1986 in Nizhny Tagil, Russian Federation. He studied chemistry at Technische Universität München and carried out his master's thesis under the supervision of Professor Dr. Lukas Hintermann in 2011. After a research internship at Priaxon AG, he started his PhD in 2012 in the research group of Dr. Philipp Selig at RWTH Aachen University. His research focuses on the investigation of nucleophilic properties of guanidines and on the syntheses of chiral bicyclic guanidine organocatalysts.

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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 1957.¹ This bicyclic guanidine possesses a remarkably high Brønsted basicity ($pK_a = 28$ in MeCN)² and has found broad applications as an organic superbases.³ Moreover, the nucleophilic properties of guanidines have also been studied.⁴ Mayr and co-workers quantified the nucleophilicities for a series of guanidines,⁵ 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.

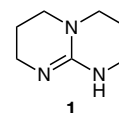
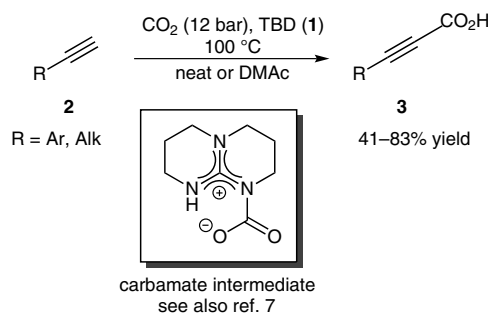


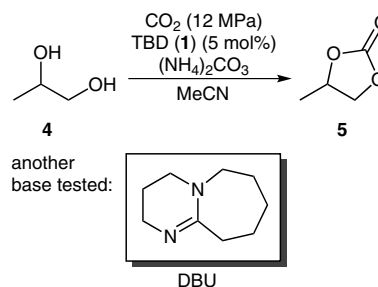
Figure 1 Commercially available bicyclic guanidine base 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD, **1**)

Abstracts

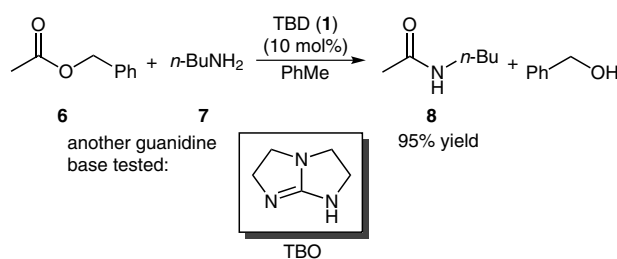
(A) Activation of carbon dioxide by TBD via formation of reactive carbamate adducts has been known for half a century.^{1,6} These intermediates can participate in various follow-up reactions, enabling metal-free CO₂ fixation. For instance, carboxylation of terminal alkynes **2** was reported by Wang and co-workers.⁷ The new method enables direct access to various propiolic acid derivatives **3**.



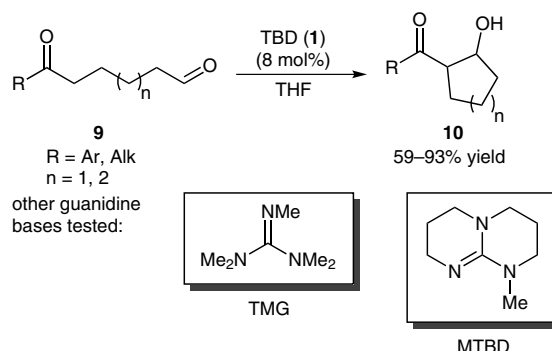
(B) TBD was used for the synthesis of propylene carbonate (**5**) from carbon dioxide and propylene glycol (**4**). Other bases such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and Et₃N were also investigated, but TBD showed the highest catalytic activity.⁸



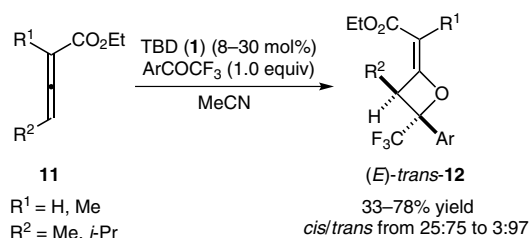
(C) TBD is an excellent acyl transfer catalyst, as demonstrated by the Waymouth group for the synthesis of amide **8** from ester **6** and primary amine **7**.⁹ Related guanidines such as 1,4,6-triazabicyclo[3.3.0]oct-4-ene (TBO) showed significantly lower activity which was attributed to lower nucleophilicity and Brønsted basicity compared to TBD.



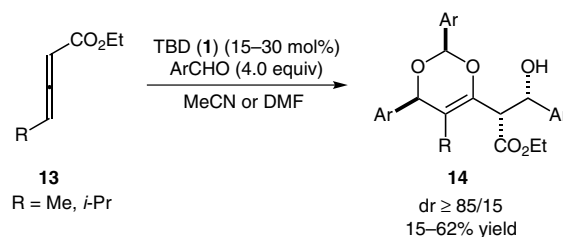
(D) Baati and co-workers used TBD as an effective catalyst for intramolecular aldol reactions of various ketoaldehydes **9**. Other guanidine bases, such as 1,1,3,3-tetramethylguanidine (TMG) and 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD), were much less active catalysts, despite similar Brønsted basicities. Therefore, a possible reaction mechanism was postulated in which TBD acts as a nucleophile.¹⁰



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



(F) Selig et al. showed that TBD catalyzes the reaction between γ -alkyl allenolate esters **13** and aromatic aldehydes to give 4*H*-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.¹²



References

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