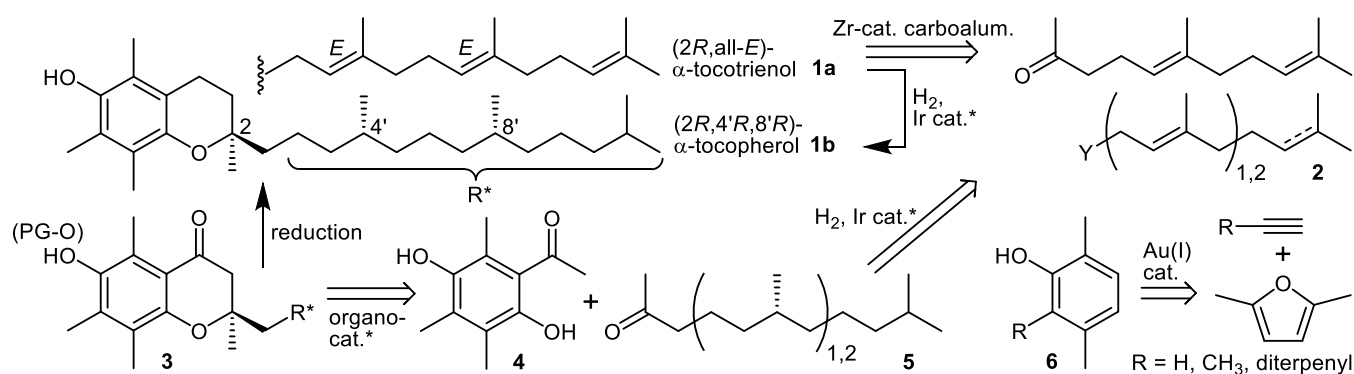


## Catalysis with and without Metals towards the Total Synthesis of Tocopherols

Thomas Netscher

Research and Development, DSM Nutritional Products, P.O. Box 2676, 4002 Basel, Switzerland  
 thomas.netscher@dsm.com

(2*R*,4'*R*,8'*R*)- $\alpha$ -Tocopherol (**1b**) is an industrially important target due to its highest biological potency of all vitamin E compounds.[1] Novel routes by total synthesis including the creation of the quaternary chroman stereocenter [2] will be presented. In continuation of our efforts together with academic partners [3-9] we discovered an enamine-based organocatalytic condensation to chromanone **3** [10] from hydroxyacetophenone **4** with chiral isoprenyl ketones of type **5** accessible from olefins **2** via asymmetric hydrogenation with highly selective and active iridium complexes.[11]



Alternative strategies will also be discussed.[12-14] An additional topic deals with the synthesis of aryl key building blocks **6** by Hashmi's gold-catalyzed furan-yne-cycloisomerization addressing the replacement of fossil resources by bio-renewables.[15]

[1] M. Eggersdorfer, D. Laudert, U. Letinois, T. McClymont, J. Medlock, T. N., W. Bonrath, *Angew. Chem. Int. Ed.* **2012**, *51*, 12960. [2] T. N., *Angew. Chem. Int. Ed.* **2014**, *53*, 14313, cit. lit.. [3] C. Rein, P. Demel, R.A. Outten, T. N., B. Breit, *Angew. Chem. Int. Ed.* **2007**, *46*, 8670. [4] M. Fuchs, Y. Simeo, B.T. Ueberbacher, B. Mautner, T. N., K. Faber, *Eur. J. Org. Chem.* **2009**, 833. [5] T. N., R.K. Müller, H. Schneider, E.-i. Negishi, *Int. Electron. Conf. Synth. Org. Chem.*, **2011**, a69/1-a69/4. [6] S. Bell, B. Wüstenberg, S. Kaiser, F. Menges, T. N., A. Pfaltz, *Science* **2006**, *311*, 642. [7] A.O. Termath, H. Sebode, W. Schlundt, R.T. Stemmler, T. N., W. Bonrath, H.-G. Schmalz, *Chem. Eur. J.* **2014**, *20*, 12051. [8] T. Rosenau, E. Kloser, L. Gille, F. Mazzini, T. N., *J. Org. Chem.* **2007**, *72*, 3268. [9] H. Klein, R. Jackstell, T. N., W. Bonrath, M. Beller, *ChemCatChem* **2011**, *3*, 1273. [10] See e.g.: U. Letinois, T. N., *WO 2015001029*, **2015**; U. Letinois, T. N., S. Ackermann, *WO 2015001030*, **2015**. [11] See e.g.: W. Bonrath, T. N., J.A. Medlock, G.K.M. Verzijl, A.H.M. De Vries, *US 20160185683*, **2016**. [12] U. Letinois, T. N., R.T. Stemmler, *WO 2015028463*, **2015**. [13] G. Schiefer, T. N., A.L.L. Duchateau, *WO 2012152779*, **2012**. [14] D. Burger, T. N., G. Schiefer, *WO 2016188945*, **2016**. [15] W. Bonrath, U. Letinois, T. N., *WO 2015110654*, **2015**; *WO 2015110655*, **2015**; U. Letinois, T. N., *WO 2016096566*, **2016**.