

Modelling of Lewis-Acid Catalyzed Ring Opening of Oxanorbornenes in the Synthesis of Azaheterocyclic Phosphonates

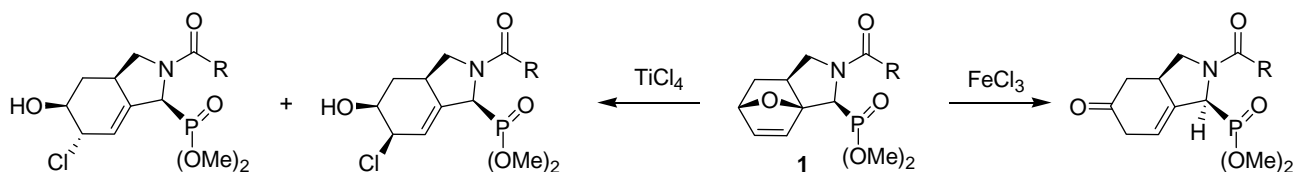
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Since the discovery of the biological activity of aminophosphonates, research started on the synthesis of more constraint azaheterocyclic phosphonates. We developed a route via an intramolecular Diels-Alder reaction towards α -aminophosphonates **1**. The obtained oxanorbornene skeleton is a valuable synthetic intermediate that has been used in various natural product syntheses. An important synthetic transformation involves the cleavage of the oxygen bridge, used to construct substituted arenes and cyclohexenes. We wanted to investigate the ring opening of adducts **1** using different Lewis acids experimentally and to get more insight in the reaction pathways towards the different products via molecular modelling. In this presentation the results obtained with TiCl_4 and FeCl_3 catalyst are shown.



One of the difficulties in studying transition metal catalysts is the determination of their proper spin state. The tetrahedral TiCl_4 monomer has spin zero. The FeCl_3 catalyst has a high-spin ground state. It prefers a half-filled d-shell and has multiplicity 6.

The complexation of the Lewis acids with different binding sites was investigated at a B3LYP level of theory with a LanL2DZ pseudopotential for the transition metals. Bidentate coordination towards the most electronegative phosphonate oxygen and the oxygen bridge is favoured for both catalysts.

The reaction pathways were evaluated at a TPSSh and a B3LYP level of theory. The role of dispersion interactions was evaluated using the Van der Waals correction term from B3LYP-D. The energy barrier for breaking the C-O bond with FeCl_3 is larger than with TiCl_4 . This corresponds with the experimental observation that the titanium catalyzed reaction completes at 0°C and the reaction with the iron catalyst requires reflux conditions in CH_2Cl_2 . The main difference between the TiCl_4 and FeCl_3 as Lewis acids in the opening of the oxanorbornene oxygen bridge is their way of stabilizing the oxide anion. When the C-O bond is broken, the bond between the alkoxide anion and the transition metal tightens. With TiCl_4 , the alkoxide replaces a chloride that adds to the allyl cation in a concerted way. With FeCl_3 , however, the carbocation is stabilized by the alkoxide anion itself and no chloride transfer occurs; instead, the bond with the phosphonate is broken. A plausible further reaction path towards the experimentally observed ketone involves a 1,2-hydride shift.

Reference: D. Claeys et al. *J. Org. Chem.*, **73**, 7921 (2008).