Anomalous role of molecular sieves 4A in the preparation of a binaphthol-derived active μ_3-oxo titanium catalyst

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The active species of binaphthol-derived titanium catalyst 1, which is used as an efficient catalyst for glyoxylate–ene reactions, is primarily composed of a μ_3-oxo (Ti_3O) species, for which the molecular sieves 4A employed in the catalyst preparation act as a H_2O donor.

Recently, much attention has been focused on the development of chiral Lewis-acid catalysts for a variety of carbon–carbon bond forming reactions.[1] We have already reported the asymmetric glyoxylate–ene reaction catalysed by the chiral titanium complex **1** prepared from optically pure binaphthol (BINOL) and $[TiCl_2(OPr^i)_2]$ in the presence of molecular sieves (MS) 4A [Scheme 1, eqn. (1)].[2] The MS 4A employed in the catalyst preparation has been proven to serve as a catalyst for the ligand-exchange reaction.[2a] Thus, the structure of the active titanium catalyst is assumed to be the BINOL-derived titanium dichloride **2**. Herein we report that, by elucidating the significant role of MS 4A,[3,4] the active species of the chiral titanium catalyst **1** is not the dichlorotitanium complex **2** but a μ_3-oxo species (Ti_3O) on the basis of ^{17}O NMR and elemental analyses (Scheme 1).

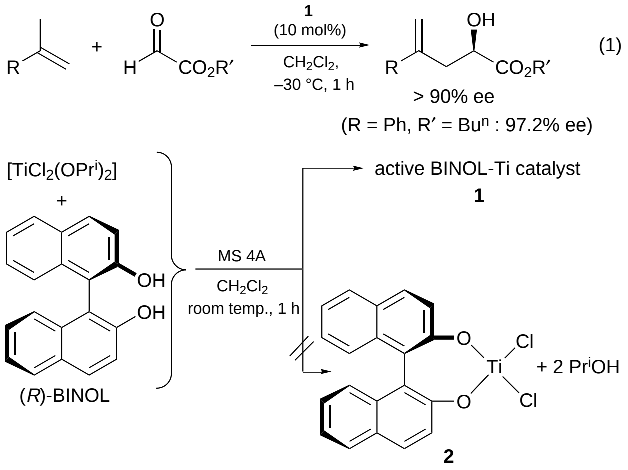
As shown in Scheme 2, it can be confirmed that the dichlorotitanium complex **2**, prepared from $TiCl_4$ and BINOL dilithium salt in dichloromethane according to the preparative procedure of dichlorotitanium 3,3′-dimethylbinaphthoxide,[5] is probably not the active species in the glyoxylate–ene reaction; the dichlorotitanium complex **2** only gives the ene product in low yield along with a low % ee.† By contrast, treatment of **2** with commercially available MS 4A‡ without activation significantly increases the chemical yield along with a higher level of % ee. These results reveal that the MS 4A converts the pre-catalyst **2** into the active BINOL–Ti catalyst **1**.

In order to elucidate the role of MS 4A to give the active catalyst **1**, the chiral titanium catalyst was prepared from BINOL and $[TiCl_2(OPr^i)_2]$ in the presence of highly activated (320 °C, < 0.05 mmHg, 12 h) and, hence, dehydrated MS 4A (< 0.2% m/m H_2O).[7] Inspection of the data in Scheme 3 reveals, in turn, a significant role of an 'unactivated' MS 4A; a quite low chemical yield is observed by using activated MS 4A. In contrast, titanium complex prepared in the presence of commercially available and unactivated MS 4A following our original procedure[2a,c] gives the ene product in high chemical yield with a high level of enantioselectivity. From gravimetric analysis of the H_2O content in the unactivated MS 4A, the commercially available MS 4A employed in the catalyst preparation[2] is found to contain 5.3% m/m H_2O.§ These results, coupled with the catalytic activity, imply that H_2O thus contained in MS 4A is important in giving the active BINOL–Ti catalyst **1**.¶

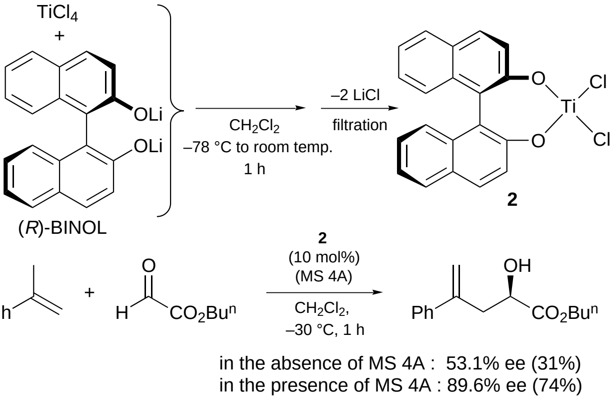
In order to obtain evidence for the involvement of H_2O in the active catalyst **1**, we next turned our attention to the ^{17}O NMR analysis of the active BINOL–Ti catalyst **1**. An analytical sample of **1** was prepared from BINOL and $[TiCl_2(OPr^i)_2]$ in the presence of MS 4A doped with $H_2{}^{17}O$ [5.3% m/m $H_2{}^{17}O$ (10 atom% enriched)]. The ^{17}O NMR spectrum of the active BINOL–Ti catalyst **1** in $[^2H_8]$toluene reveals peaks only in the μ_3-oxo (Ti_3O) region (δ 520–590).‖

Furthermore, elemental analysis of **1** reveals only a low amount of Cl (Found: Ti, 11.4; Cl, 0.6%; Cl/Ti = 0.07. Calc. for **2**: Ti, 11.9; Cl; 17.6%). These results strongly suggest that the MS 4A not only serves as an H_2O donor to hydrolyse the titanium pre-catalyst but also as a base to trap HCl.

In summary, we have uncovered that the MS 4A, despite being a desiccant, serves anomalously as a H_2O donor towards

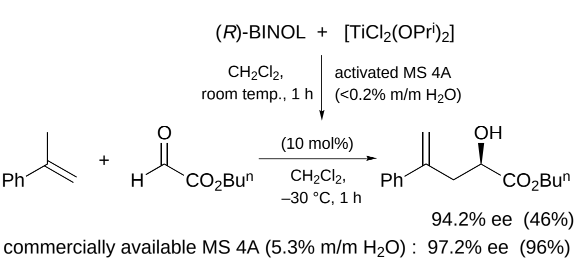


Scheme 1



in the absence of MS 4A : 53.1% ee (31%)
in the presence of MS 4A : 89.6% ee (74%)

Scheme 2



94.2% ee (46%)
commercially available MS 4A (5.3% m/m H_2O) : 97.2% ee (96%)

Scheme 3

a titanium pre-catalyst and also acts as a base to trap HCl to give the active BINOL–Ti catalyst **1**. We have further disclosed by ^{17}O NMR spectroscopy that the active BINOL–Ti catalyst **1** is composed of μ_3-oxo species.

Footnotes

† In our previous report,[2] the dichlorotitanium complex **2** prepared in ether according to Reetz's procedure[6] exhibits high levels of enantioselectivity (93% ee). However, in our hands, the reproducibility of the enantioselectivity is poor ranging from 37 to 93% ee.

‡ Molecular sieve 4A, powder (catalogue no. 23,366-8) was purchased from Aldrich.

§ Quite recently,[8] the amount of H_2O content externally introduced in MS 4A was reported to affect the % ee in an asymmetric Diels–Alder reaction catalysed by the BINOL-derived chiral titanium complex **1** prepared according to our modified procedure.[2d]

¶ Binaphthoxytitanium diisopropoxide **3**, which was prepared from $[Ti(OPr^i)_4]$ and BINOL with azeotropic removal of isopropyl alcohol and recrystallization, exhibited only low catalytic activity (12% yield), but after treatment with unactivated MS 4A, gives high chemical yield (98%) and enantioselectivity (97.3% ee) to suggest that MS 4A also acts as a H_2O donor for **3**.

∥ The oxygen chemical shifts of titanium(iv) polyoxo–alkoxides have been reported to be strongly dependent on the titanium bridging mode; μ_3-oxo (Ti_3O) and μ-oxo (Ti_2O) oxygens have chemical shifts at δ 450–650 and 650–850, respectively.[9]

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