

Carbenoid transfer to imines: a new heterogeneous catalytic synthesis of aziridines

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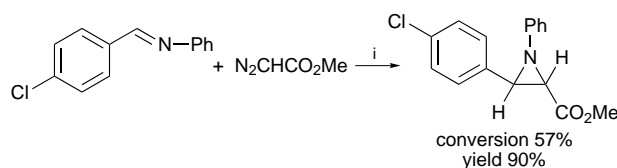
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A heterogeneous catalytic method for the preparation of *trans*-aziridines from imines and methyl diazoacetate is described using Rh^{III}- and Mn^{III}-exchanged montmorillonite K10 clays as catalysts.

The aziridine ring is a versatile building block for organic synthesis, not only because the ring opening of aziridines provides a convenient entry to the stereoselective preparation of functionalized amino compounds but also because the exocyclic N-substituent modulates the properties and reactivity of the 3-membered ring.¹ The chemistry and preparation of enantiomerically pure aziridine-2-carboxylates have been the targets of many synthetic efforts in recent years for the preparation of both α - and β -amino acids.² Classical methods³ for the synthesis of aziridines are ring closure of amino alcohols, ring opening of epoxides with sodium azide and addition of α -halo ester enolates to *N*-(trimethylsilyl)imines. Although potentially a very useful method for the preparation of aziridines, the cycloaddition of carbenes to imines has not been investigated extensively. In fact very few methods have been reported for the catalytic preparation of aziridines from aromatic imines and diazo esters. These methods employ catalysts such as copper complexes⁴ and methylrhodium trioxide⁵ under homogeneous conditions. More recently, BF₃·OEt₂-catalysed aziridination of imines with diazoacetate has been reported.⁶ The other important catalytic method, *viz.* the addition of [*N*-(toluene-*p*-sulfonyl)imino]phenyliodinane (PhI=NTs) as nitrene precursor onto alkenes, has been used for the direct synthesis of aziridines using soluble Cu^I and Cu^{II} complexes.⁷ However, the yields and selectivities reported are far from satisfactory. For example, Cu-catalysed addition of diazo esters to imines proceeds in low yields (15–30%) and is of limited use.⁸ Further, copper triflate-catalysed carbene addition to imines proceeds to give a mixture of *cis*- and *trans*-aziridines and shows poor selectivity in terms of product distribution. Recently Aggarwal *et al.*⁹ has also shown an effective asymmetric aziridination process mediated by sulfur ylides and working in a catalytic fashion.

Currently, acid catalysed organic transformations by transition metal-exchanged aluminosilicate clays is an area of considerable potential and interest due to ease of handling and workup, non-corrosiveness and low cost of clays.¹⁰ Here we report that the Rh^{III}-exchanged acid activated montmorillonite clay, K10, catalyses cycloaddition reactions between methyl diazoacetate and imines to form *trans*-aziridines with good conversion and yield (Scheme 1).

Rh- and Mn-exchanged montmorillonite K10 clay catalysts were prepared by exchanging the clay with dilute solutions of



Scheme 1 Reagents and conditions: i, Rh-clay (10% m/m), dry benzene, 353 K, 3 h

RhCl₃ and Mn(NO₃)₃, respectively. For example, a mixture containing RhCl₃ (0.3 g) and clay (25 g) in distilled water (600 ml) was stirred vigorously at room temperature for 24 h. It was centrifuged and the clay was washed repeatedly with distilled water until the discarded filtrate was free from Cl⁻ ions. Finally, the clay was dried at 110 °C for 12 h. A 5% Rh/C catalyst was obtained from Degussa. The 0.5 wt% Rh/Al₂O₃ and Rh/SiO₂ gel catalysts for comparison purpose were prepared using the incipient wetness impregnation technique.

In a typical experiment, a mixture of imine (R¹ = 4-ClC₆H₄, R² = Ph; 2.15 g, 10 mmol), methyl diazoacetate (1.2 g, 12 mmol) and Rh-clay (200 mg; 10% m/m) in dry benzene (30 ml) was heated under reflux for 5 h. The progress of the reaction was monitored by TLC. The catalyst was filtered off and the product purified by flash chromatography to afford the corresponding *trans*-aziridine[†] (1.63 g, 57%).

The results of aziridination of the imine (R¹ = 4-ClC₆H₄, R² = Ph) over various supported metal catalysts (Table 1) indicate that Rh^{III}-exchanged montmorillonite K10 clay exhibits significantly higher activity and selectivity than the Rh/SiO₂ and Rh/Al₂O₃ catalysts. However, it is to be noted that catalysts such as Cu-exchanged K10 and Rh/C failed to catalyse the reaction. Although Mn-clay also exhibited good conversion and yield in this case, it surprisingly failed to catalyse the aziridination reaction when applied to other types of imines.

Table 2 lists the results of the various imines which have been successfully aziridinated with N₂CHCO₂Me catalysed by the Rh^{III}-clay. The yield in the process is in the range 30–75%; products other than aziridine are not formed. A novel feature of this catalytic system is that only a single isomer of the aziridine was obtained as determined by GC-MS and ¹H and ¹³C NMR spectroscopy. The coupling constant for the aziridine ring protons for these products are in the range 3.6–3.8 Hz, which confirms that the only product is the isomer with *trans* configuration (*E*-isomer) with respect to the C–C bond. This *trans*-selective aziridination is therefore complementary to the earlier technique of Casarrubios *et al.*⁶ which is *cis*-selective. A variety of aromatic imines and one aliphatic imine have undergone cycloaddition with N₂CHCO₂Me over the Rh^{III}-clay to give aziridines in good yields and excellent selectivity. It is noteworthy that the product survives the acidic environment and does not yield side products arising out of cleavage by protonation of the aziridine ring nitrogen because of its poor

Table 1 Aziridination of aryl imine (R¹ = 4-ClC₆H₄, R² = Ph) with N₂CHCO₂Me over various catalysts^a

| Entry | Catalysts | <i>t</i> /h | Yield ^b (%) |
|-------|-----------------------------------|-------------|------------------------|
| 1 | Rh-clay | 5 | 57 |
| 2 | Mn-clay | 10 | 46 |
| 3 | Cu-clay | 10 | 0 |
| 4 | Rh/SiO ₂ gel | 12 | 52 |
| 5 | Rh/Al ₂ O ₃ | 12 | 40 |
| 6 | Rh/C ^c | 12 | 0 |

^a Reaction conditions: imine (10 mmol), diazo ester (12 mmol), catalyst (10% m/m), dry benzene, reflux. ^b Isolated and purified yield. ^c Commercial catalyst from Degussa.

basicity (aromatic amine). Also this result contrasts with that using methylrhodium trioxide, which is effective only for aromatic imines.⁵ The catalyst, recovered by filtration, was reused at least three times without affecting the reactivity and selectivity of the process.

In conclusion, this study was demonstrated that Rh^{III}-montmorillonite K10 is an efficient and reusable solid catalyst

for imine aziridination using methyl diazoacetate as the carbene precursor.

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Footnotes

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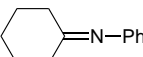
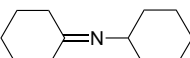
† Selected data for **2** (R¹ = 4-ClC₆H₄, R² = Ph): ¹H NMR (200 MHz, CDCl₃): δ 3.2 (1 H, d, *J* 3.8 Hz), 3.6 (3 H, s), 3.8 (1 H, d, *J* 3.8 Hz), 7.0 (2 H, d, *J* 8 Hz), 7.3 (5 H, m) and 7.6 (2 H, d, *J* 8 Hz); ¹³C NMR (50 MHz, CDCl₃): δ 45.52, 45.65, 51.96, 119.82, 122.95, 123.62, 128.17, 128.29, 128.65, 128.96, 129.91, 130.83, 130.83, 133.72, 133.83, 152.0 and 167.65; *m/z* 286 (M⁺, 25%), 256 (30), 228 (90), 193 (55), 165 (35), 155 (20), 150 (15), 125 (35), 104 (50), 89 (55), 77 (100), 63 (25) and 59 (15).

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Table 2 Rh-clay catalysed aziridination of imines^a

| Entry | R ¹ | R ² | <i>t</i> /h | Yield ^b (%) |
|-------|---|--|-------------|------------------------|
| 1 | 4-ClC ₆ H ₄ | Ph | 5 | 57 |
| 2 | 4-MeOC ₆ H ₄ | Ph | 3 | 32 |
| 3 | 3,4-(OMe) ₂ C ₆ H ₃ | Ph | 7 | 42 |
| 4 | 3,4,5-(OMe) ₃ C ₆ H ₂ | Ph | 10 | 75 |
| 5 | 4-ClC ₆ H ₄ | 2,5-Cl ₂ C ₆ H ₃ | 6 | 40 |
| 6 | 4-ClC ₆ H ₄ | 3-NO ₂ -4-MeC ₆ H ₃ | 9 | 50 |
| 7 | 2-Furyl | Ph | 7 | 38 |
| 8 | 2-Furyl | Cyclohexyl | 5.5 | 48 |
| 9 | Bn | Ph | 8 | 30 |
| 10 | Pr ⁱ | Ph | 8 | 48 |
| 11 |  | | 10 | 41 |
| 12 |  | | 6 | 37 |

^a Reaction conditions: imine (10 mmol), diazo ester (12 mmol), Rh-clay (10% m/m), dry benzene, reflux. ^b Isolated and purified yield; the selectivity was nearly 100% and no other product could be seen by TLC.