Cyclotrimerisation of isocyanates catalysed by low-coordinate Mn(II) and Fe(II) *m*-terphenyl complexes

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Two- and three-coordinate *m*-terphenyl complexes of manganese and iron are efficient catalysts for the selective cyclotrimerisation of primary aliphatic isocyanates affording isocyanurates in short reaction times and under mild conditions.

The cyclotrimerisation of isocyanates is a direct and an atom-economical approach for the synthesis of isocyanurates. These compounds are commonly used as additives in polyurethane foams, coating materials and composites in order to enhance their physical properties.[1] They are also used as key components in applications such as microporous materials,[2] selective ion-bonding,[3] medicines and drug delivery.[4] Lewis bases (*e.g.* amines,[5] phosphines,[6] N-heterocyclic carbenes[7]), rare-earth[8] and main group complexes[9] have been used as precatalysts for the cyclooligomerisation of isocyanates. Less attention has been focused on the use of transition metal species for this purpose; an early example reported the use of copper(II) and nickel(II) halides,[10] and palladium(0) complexes have been traditionally more common for this chemistry.[11] Many existing cyclotrimerisation methodologies face issues such as low catalyst activity, by-product formation, long reaction times, high reaction temperatures or difficulty with product separation.

There is interest in the use of low-coordinate transition metal compounds as stoichiometric and catalyst precursors for diverse transformations, leading to unusual reactivity and unique mechanisms,[12] and two-[13] and three-coordinate[14] compounds have been investigated for their efficacy as catalyst precursors. As part of our research into low-coordinate transition metal *m*-terphenyl complexes, we are investigating the

efficacy of these species as precatalysts. Herein, we demonstrate that two-[15] and three-coordinate manganese(II) and iron(II) diaryl complexes stabilised by *m*-terphenyl ligands are efficient precatalysts for the cyclotrimerisation of isocyanates (Scheme 1). These complexes offer high activity, selectivity towards alkyl isocyanates, and high selectivity to the formation of isocyanurate products.

Ar = Tmp, *n* = 1, M = Mn (**1**), Fe (**2**)
Ar = Mes, *n* = 0, M = Mn (**3**), Fe (**4**)
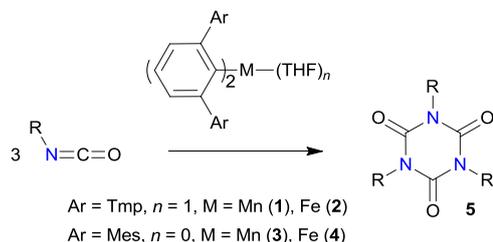
Scheme 1. Cyclotrimerisation of isocyanates catalysed by *m*-terphenyl Mn(II) (**1**, **3**) and Fe(II) (**2**, **4**) complexes, where Tmp = $2,4,5\text{-Me}_3\text{C}_6\text{H}_2$, Mes = $2,4,6\text{-Me}_3\text{C}_6\text{H}_2$ and R = Et (**5a**), ^{n}Pr (**5b**), ^{n}Hex (**5c**) or Bn (**5d**).

The reaction between $[2,6\text{-Tmp}_2\text{C}_6\text{H}_3\text{Li}]_2$ (**8**; Tmp = $2,4,5\text{-Me}_3\text{C}_6\text{H}_2$) and one equivalent of the corresponding metal dihalide $[\text{MnBr}_2$ or $\text{FeCl}_2(\text{THF})_{1.5}]$ in a mixture of toluene and THF at room temperature yields the three-coordinate diaryl complexes $(2,6\text{-Tmp}_2\text{C}_6\text{H}_3)_2\text{M}(\text{THF})$ [M = Mn (**1**), Fe (**2**)], with concomitant formation of the lithium halide. Complexes **1** and **2** were isolated as pale pink (**1**) or yellow (**2**) highly air- and moisture-sensitive crystals. They have been fully characterised and their solid state structures have been determined *via* X-ray crystallography. The molecular structures of **1** and **2** (Figure 1 and ESI) display a distorted trigonal planar geometry [Σ(angles at M): 360.0° (**1**) and 359.9° (**2**)] around the metal centre with the coordination sites occupied by two *m*-terphenyl ligands, both in a *syn* conformation, and a THF molecule. This is contrary to that observed for the related two-coordinate compounds $(2,6\text{-Ar}_2\text{C}_6\text{H}_3)_2\text{M}$ [Ar = $2,4,6\text{-Me}_3\text{C}_6\text{H}_2$ (Mes); $2,6\text{-}^i\text{Pr}_2\text{C}_6\text{H}_3$ (Dipp); M = Mn, Fe],[15,16] which feature the more sterically demanding Mes and Dipp substituents. Three-coordinate geometries have been observed previously when the *m*-terphenyl ligand features asymmetric flanking substituents.[17,18]

The M–C distances for **1** and **2** (Figure 1) are comparable to those for other three-coordinate M(II) complexes with aryl ligands.[19] The C–M–C angles [138.13(6)° and 133.89(8)° for **1** and **2**, respectively] are considerably larger than the value of 120° expected for a trigonal planar complex. This observation is consistent with the steric repulsion imposed by the two bulky *m*-terphenyl ligands. This angle is also similar to the related compound $(2,6\text{-Naph}_2\text{C}_6\text{H}_3)_2\text{CoOEt}_2$ (Naph = $1\text{-C}_{10}\text{H}_7$).[17] The torsion angle between the two central aryl rings for both **1** and **2** is slightly more acute than the corresponding interplanar angles in related two-coordinate *m*-terphenyl compounds.[15,16]
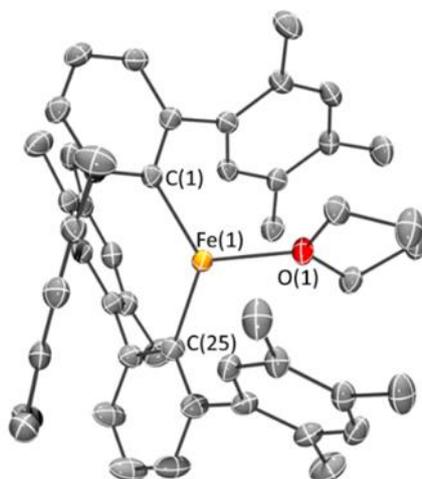
Figure 1. Molecular structure of **2** with anisotropic displacement ellipsoids set at 50% probability. Hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and angles (°) for **1** and **2**; **1**: Mn(1)–C(1) 2.1395(11), Mn(1)–O(1) 2.1303(13), C(1) –Mn(1)–C(1') 138.13(6), C(1) –Mn(1)–O(1) 110.93(3), Ar–Ar dihedral angle 78.77(6). **2**: Fe(1)–C(1)   2.073(2), Fe(1)–C(25) 2.0734(19), Fe(1)–O(1) 2.0583(14), C(1)–Fe(1)–C(25) 133.89(8), C(1)–Fe(1)–O(1) 115.22(7), C(25)–Fe(1)–O(1) 110.83(7), Ar–Ar dihedral angle 83.91(8).

An initial assessment of the catalytic activity of **1** and **2** for the cyclooligomerisation of isocyanates was carried out using ethyl isocyanate as a model substrate in C_6D_6 at room temperature with 5 mol% catalyst loading (Scheme 1, Table 1, entries 1 and 4). Remarkably, when using the manganese(II) species **1** as the precatalyst the reaction reaches completion in just an hour, but a significant decrease in the rate of the reaction was observed with the iron(II) complex **2**. Lowering the catalyst loading for **1** to 2 mol% and 0.5 mol% also affords high conversions in short times (entries 2 and 3).

The catalytic activity of **1** and **2** was compared with the related two-coordinate species (2,6-$Mes_2C_6H_3$)$_2$M [M = Mn (**3**), Fe (**4**)][15] (entries 5 and 6). Whilst the manganese(II) compounds **1** and **3** reached completion in comparable times, a notable difference was found between the two iron complexes. The two-coordinate iron(II) complex **4** reaches high conversion in shorter time for the cyclotrimerisation reaction compared to **2** (entries 6 and 4, respectively). Notably, no dimerisation of the isocyanates to form uretediones, a common by-product of cyclotrimerisation reactions,[7,8b,9c] was observed for any of the catalytic reactions. The scope of the reaction was evaluated for a variety of aliphatic and aromatic isocyanates using complexes **3** and **4** (Table 1 and Table S1, ESI), whereupon it was determined that the catalysis was only successful for primary aliphatic isocyanates (Table 1). No cyclotrimerisation was observed *via* NMR spectroscopy when aromatic isocyanates [phenyl-, *p*-tolyl- (*p*-Tol) and 3,5-dimethoxyphenyl isocyanate] were used as substrates, even when the reaction was heated to 60 °C for 48 h (entries 21-26, Table S1). Secondary and tertiary aliphatic isocyanates

(entries 27-32, Table S1) were not effective in this reaction possibly due to the incremented steric bulk of the substrates which could prevent access to the metal centre. This steric effect is illustrated in the notably longer reaction times observed for longer aliphatic chains (entries 1 and 7). The temperature also has an important effect on the catalytic transformation: for ^{n}PrNCO the catalytic activity improves significantly when raising the temperature from room temperature to 60 °C (entries 7 and 8). This exclusive reactivity towards the cyclotrimerisation of alkyl isocyanates is in contrast to that exhibited by other transition metal catalysts.

Table 1. Catalytic cyclotrimerisation of isocyanates using **1**-**4**.[a]

Entry	Isocyanate	Cat (mol%)	Product	T (°C)	Time (h)	Conv. (%)[b]
1	EtN=C=O	**1** (5)	**5a**	rt[c]	1	97
2	EtN=C=O	**1** (2)	**5a**	rt	2.8	98
3	EtN=C=O	**1** (0.5)	**5a**	rt	5	98
4	EtN=C=O	**2** (5)	**5a**	rt	24	97
5	EtN=C=O	**3** (5)	**5a**	rt	2.5	98
6	EtN=C=O	**4** (5)	**5a**	rt	6.5	99
7	^{n}PrN=C=O	**1** (5)	**5b**	rt	19	96
8	^{n}PrN=C=O	**1** (5)	**5b**	60	14	98
9	^{n}PrN=C=O	**2** (5)	**5b**	60	14	88
10	^{n}PrN=C=O	**3** (5)	**5b**	60	14	94
11	^{n}PrN=C=O	**4** (5)	**5b**	60	14	>99
12	^{n}HexN=C=O	**1** (5)	**5c**	60	14	97
13	^{n}HexN=C=O	**2** (5)	**5c**	60	14	98
14	^{n}HexN=C=O	**3** (5)	**5c**	60	14	99
15	^{n}HexN=C=O	**4** (5)	**5c**	60	14	99
16	BnN=C=O	**1** (5)	**5d**	60	14	99
17	BnN=C=O	**2** (5)	**5d**	60	14	65
18	BnN=C=O	**3** (5)	**5d**	60	14	>99
19	BnN=C=O	**4** (5)	**5d**	60	14	>99

[a] Reaction conditions: 0.6 mL of C_6D_6. [b] Determined by ^{1}H NMR spectroscopy. [c] rt = room temperature (20°C ± 2).

To investigate the reactivity towards aryl isocyanates, a stoichiometric reaction between complex **4** and one equivalent of 3,5-dimethoxyphenyl isocyanate was performed in toluene. Due to the paramagnetic

nature of the compound precluding useful NMR studies the reactions were monitored by IR spectroscopy. No reaction was observed after 12 h at room temperature, but raising the temperature to 60 °C for 16 h resulted in a colour change from yellow to a dark red solution, which is accompanied by the appearance of new peaks in the IR spectra. Whilst no peaks were observed in the aromatic isocyanurate region of the spectrum, the appearance of a strong peak at 1676 cm⁻¹ is consistent with formation of an Fe-amido species resulting from the insertion of the 3,5-dimethoxyphenyl isocyanate into the Fe–C bond.[20] Although this species could not be isolated, it was hydrolysed with water affording anilide derivative **6** (Scheme 2) which was characterised via spectroscopy and single-crystal X-ray diffraction studies (see ESI). That there is no reaction towards isocyanates indicates that this putative Fe-amido species is deactivated towards further insertion.
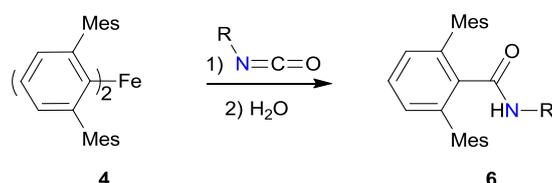
Scheme 2. Insertion of one equivalent of R-NCO (R = 3,5-(OMe)2C6H3) into an Fe-C bond of complex **4** followed by hydrolysis.

Experimental observations indicate that the cyclotrimerisation most likely proceeds through a homogeneous mechanism; no induction period is observed when monitoring the reaction by ¹H NMR. In addition, the rate of the catalysis is unaffected by the presence of a drop of mercury.[21] Moreover, the reaction does not appear to be radical-mediated as performing the reaction in the presence of a radical trap leads to no decrease in the reaction rate.[22] Kinetic experiments were performed at varying concentrations of precatalyst (**3**) and isocyanate (EtNCO). Analysis of the rate order reveals first-order behaviour with respect to both the precatalyst and the isocyanate (Figures S1-S4, ESI).

A catalytic cycle for the cyclotrimerisation reaction is proposed in Scheme 3. Taking into account the inherent coordinative unsaturated nature and the +II oxidation states of the metals in complexes **1**-**4**, it is reasonable to assume that the catalysts act as Lewis acids,[23] in a similar manner to that postulated for Yb complexes.[8c] Initially, the isocyanate coordinates to the metal centre to give **A**. Previous calculations on a Pd(0) cyclotrimerisation catalyst have found that the C=N coordination mode is slightly more stable than C=O, but both states lie close in energy.[11b] This coordination renders the carbon atom more electrophilic. Following this, an outer-sphere attack of the nucleophilic nitrogen of the incoming isocyanate at the electropositive carbon yields intermediate **B**.[11a,24] Subsequently, nucleophilic attack of a free isocyanate on the coordinated linear dimer results in the formation of intermediate **C**. Finally, ring closure to give the cyclotrimer, which is displaced by a new isocyanate moiety, regenerates the catalyst. An alternative reaction pathway has been

proposed by Paul *et al.* where the coordination of the isocyanate to the metal centre results in an increase of the nucleophilic character of the coordinated isocyanate.[11b] Therefore, the stepwise formation of the cyclotrimer would take place by nucleophilic attack of the coordinated isocyanate onto free isocyanate.
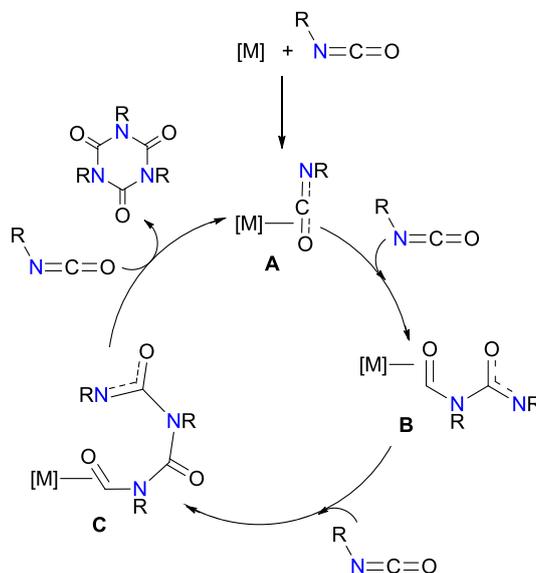
Scheme 3. Proposed catalytic cycle for the cyclotrimerisation of isocyanates catalysed by *m*-terphenyl Mn(II) (**1**, **3**) and Fe(II) (**2**, **4**) complexes.

The proposed mechanism is consistent with the substantial difference in the catalytic activity of the manganese and iron complexes which is most probably due to the more Lewis acidic manganese(II) centre compared to the iron(II) centre. The proposed mechanism suggests that the steric demands decrease as the linear chain grows further away from the sterically encumbered metal centre. Therefore it should be possible for the unreactive isocyanates (featuring aryl and secondary alkyl substituents, for example) to react after the coordination of the first or second isocyanate (intermediates **A** and **B**) producing mixed cyclotrimers. In fact, when preliminary cross coupling reactions were carried out with isocyanate mixtures (Table S2, ESI) we observed the formation of mixed trimers by ^{1}H NMR and GC-MS. Especially interesting is the reaction between EtNCO and *p*-TolNCO (1:2 ratio) where the possible isocyanurate isomers are obtained with a degree of selectivity [ratios are 21:50:29 for (EtNCO)$_3$:(EtNCO)$_2$(*p*-TolNCO):(EtNCO)$_2$(*p*-TolNCO)]. Furthermore, we do not observe a promoting effect within our monomer mixture; the presence of the more reactive monomer (in our case EtNCO) does not promote the formation of (*p*-TolNCO)$_3$ or (^{i}PrNCO)$_3$. The synthesis of asymmetrically-substituted isocyanurates is of interest as they are an important class of molecules with pharmaceutical and agricultural utility;[4a,b] this reactivity offers the possibility of obtaining these compounds through an atom economical one-pot reaction using only isocyanate precursors.

In summary, we have shown that an *m*-terphenyl ligand (2,6-Tmp$_2$C$_6$H$_3$$^-$) can be used to access three-coordinate manganese(II) and iron(II) complexes. Low-coordinate *m*-terphenyl species **1**-**4** were found to be

efficient precatalysts for the cyclotrimerisation of primary aliphatic isocyanates under mild conditions. These precatalysts show a selectivity towards aliphatic monomers not generally exhibited by other catalysts, with preliminary results offering the possibility of the selective synthesis of cross-coupled isocyanurates. These results highlight the potential of two- and three-coordinate *m*-terphenyl complexes as precursors for catalytic transformations.

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