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A novel scandium *ortho*-methoxynitrosobenzene-dimer complex: mechanistic implications for the nitroso-Diels–Alder reaction

Andrew P. Lightfoot,[a] Robin G. Pritchard,[b] Hayley Wan,[c] John E. Warren[b] and Andrew Whiting*[c]
[a] *GlaxoSmithKline Pharmaceuticals, New Frontiers Science Park, Third Avenue, Harlow, Essex, UK CM19 5AW*
[b] *Department of Chemistry, UMIST, Faraday Building, PO Box 88, Manchester, UK M60 1QD*
[c] *Department of Chemistry, University Science Laboratories, University of Durham, South Road, Durham, UK DH1 3LE*

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Arylnitroso dienophiles exist in equilibrium with their dimeric counterparts, which in turn form stable bidentate complexes with scandium(III) triflate and react with cyclohexadiene to give the corresponding Diels–Alder adduct at the same rate as the normal thermal process.

Nitroso compounds are increasingly important as dienophiles for Diels–Alder cycloaddition reactions.[1] However, this class of dienophile has yet to succumb to asymmetric catalysis,[2] despite the many examples of chiral auxiliary-mediated asymmetric nitroso-Diels–Alder reactions reported.[3] As part of a programme aimed at developing new catalytic asymmetric processes, we have been studying the possibility of an asymmetric nitroso-dienophile-mediated catalytic asymmetric Diels–Alder reaction. In this communication, we report the lack of susceptibility of arylnitroso compounds towards Lewis acid mediated catalysis and asymmetric catalysis in Diels–Alder reactions, despite their ability to form stable Lewis acid complexes.

Table 1 Crystal structure data and parameters for compounds **1b** and **3**

	Nitroso dimer **1b**	Scandium complex **3**
Temperature/K	150	150
Crystal size/mm^3	0.30 × 0.3 0 × 0.13	0.30 × 0.25 × 0.20
Molecular formula	$C_{28}H_{28}N_4O_8$	$C_{21}H_{28}F_9N_20_{16}S_3Sc$
F_w	548.54	876.59
Crystal system	Monoclinic	Triclinic
Space group	*P*21/*c*	*P*1
a/Å	19.9465(3)	11.04780(10)
b/Å	8.98220(10)	11.35400(10)
c/Å	15.6262(2)	14.70440(10)
β/°	107.2590(10)	80.7060(10)
Z	4	2
λ/Å	0.71073	0.71073
Absorption coefficient/mm^{-1}	0.101	0.491
Reflections collected	43598	30643
Independent reflections	5959	7524
Reflections observed[a]	1332	2842
θ range for data collection/°	3.12–27.29	4.60–27.47
Restraints (parameters)	(0) 473	(0) 581
R_1 (observed reflections)	0.0463	0.0294
wR_2 (All reflections)[b]	0.1159	0.0721
Goodness-of-fit on F^2	1.021	1.052

[a] $I > 2\sigma(I)$. [b] $wR_2 = \{\sigma[w(F_0^2 - F_c^2)^2]/\sigma[w(F_0^2)^2]\}^{1/2}$.

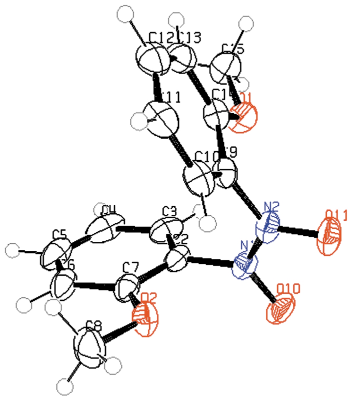
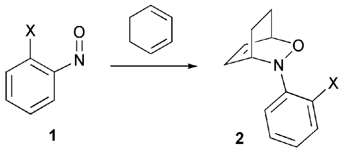


Fig. 1

It has long been established that nitroso compounds (blue or green as monomers) can exist in equilibrium with the dimeric form (usually colourless)[4] and there are a small number of examples of both monomeric[5] and dimeric metal complexes.[6] However, the fact that such metal complexes exist has failed to shed light upon the possible impact that such complexes could have upon prospective catalytic processes involving nitroso compounds. In order to explore the possible role of such complexes in arylnitroso Diels–Alder reactions, we therefore decided to examine the effect of different Lewis acids on the rate of a Diels–Alder reaction. For this purpose, two nitroso compounds, nitroso benzene **1a** and *ortho*-methoxy nitroso benzene (the latter compound was prepared according to literature methods[7] and was obtained as a highly crystalline, white solid dimer, as demonstrated by its crystal structure, shown in Fig. 1) (for crystal data, see Table 1) were employed by screening their reactivity with cyclohexadiene in the presence of a series of Lewis acidic metals, ligands and solvents [such as: Cu(OTf)$_2$, Sc(OTf)$_3$, Yb(OTf)$_3$, ZnCl$_2$, Ag(OTf)$_2$, CoCl$_2$·6H$_2$O, CuClO$_4$·MeCN, AgClO$_4$, Zn(OTf)$_2$, Cu(OTf)$_2$·C$_6$H$_6$; (*R*)-BINAP, (*R*)-PROPHOS, (*R*)-BINOL, (*R*,*R*)-diphenylethylenediamine, (*R*)-Box, (*S*)-1,1-diphenylpropane-1,2-diol, (*R*)-TolBINAP; MeOH, THF, MeCN; room temperature] and examining the reactions for approximate conversion and e.e. The highest level of enantiomeric excess detected by chiral HPLC on the crude reaction mixtures was only 15%, however, such figures were not significantly above the maximum estimated error for such crude reaction mixtures (*ca.* 10%). It was noteworthy that the reaction of either of the dienophiles **1** with cyclohexadiene [eqn. (1)] was sensitive to temperature; the reactions took approximately 1 hour to proceed to completion at room temperature, *versus* 24 hours at −78 °C to proceed to *ca.* 50% completion, as expected for a thermally allowed cycloaddition processes. It was therefore necessary to examine the rate of reaction of one of the dienophiles, *i.e.* **1b**, with cyclohexadiene under both thermal and Lewis acid-catalysed conditions. To our surprise, the rate of the thermal and Lewis acid catalysed reactions [10 mol % BF$_3$·OEt$_2$ and Yb(OTf$_3$)] were essentially identical, *i.e.* neither BF$_3$·OEt$_2$ nor Yb(OTf$_3$) showing evidence of either rate acceleration or



1
a; X = H
b; X = OMe

2
a; X = H
b; X = OMe

(1)

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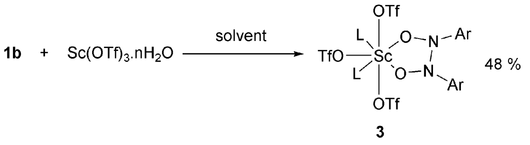
inhibition. These observations were even more confusing considering that attempts to prepare and isolate crystal structures of dienophiles **1** with several different Lewis acids (*vide supra*) had been unsuccessful, except for the complex resulting from treatment of scandium(III) triflate with *ortho*-methoxynitrosobenzene **1b**. Despite the intense green colour of the monomer form of nitroso dienophile **1b** in solution, only the dimer complex **3** could be isolated in 48% yield (eqn. 2) upon treatment of *o*-methoxynitrosobenzene with scandium(III) triflate as a crystalline solid which was readily amenable to X-ray crystallography. The X-ray structure of the 7-coordinate diaquo scandium complex is shown in Fig. 2) (for crystal data, see Table 1). Interestingly, the corresponding X-ray structure of the *o*-methoxynitrsosbenzene dimer, shown in Fig. 1,† illuminates the effect of bidentate metal coordination upon the N–O and N–N bonds. The N–N and N–O bond lengths of uncomplexed dimer, *i.e.* **4** (Ar = *o*-methoxyphenyl) (Fig. 1) are 1.316 and 1.260 or 1.277 Å, compared with 1.291 and 1.278 or 1.282 respectively in scandium complex **3** (Fig. 2).‡ Both the shortening of the N–N bond and lengthening of the N–O bonds upon bidentate metal coordination are exactly as in the corresponding iron-based system.[6] Taken together with the coplanarity of the O–N–N–O ligand system when coordinated to scandium, shows that there is substantial delocalisation of charge *via* sp^2-hyridisation of the ligand system.[6] Similar coplanarity and therefore sp^2-hybridisation also exists surprisingly in the uncomplexed dimer shown in Fig. 1. In this case, crystallisation occurs in the seemingly less favourable *cis*-geometry, *i.e.* with the N–O dipoles aligned and repulsion between the two aryl rings maximised.



(2)

3

L = H_2O, Ar = *ortho*-MeOPh

Having isolated crystalline scandium complex **3**, it was treated with cyclohexadiene under stoichiometric conditions, resulting in the smooth formation of cycloadduct **2** in 31% yield after only 1 hour, *i.e.* the reaction proceeded with identical rate and outcome to both the thermal reaction of **1b** and **2** alone, and the scandium(III) triflate-'catalysed' reaction. Thus, not only does scandium complex **3** not interfere with the cycloaddition reaction of **1b** and **2**, it neither accelerates nor inhibits the reaction, reinforcing the fact that Lewis acids in general fail to significantly affect the rate of the arylnitroso cycloaddition reaction with cyclohexadiene. This therefore explains why the addition of Lewis acids fails to catalyse the nitroso-Diels–Alder reaction. Although arylnitroso compounds **1** exist as monomers in solution, they exist in rapid equilibrium with their dimer counterparts **4**, which in turn are reasonable bidentate ligands for transition metals (hence isolation of **3**). However, a rapid equilibrium exists between dimer **4** and the corresponding transition metal complex such as **3**. Hence, the rate determining step is the actual thermal cycloaddition reaction step (Scheme 1). These results suggest that hard and/or bidentate Lewis acids will cause neither rate acceleration, nor will they be applicable in obtaining asymmetric induction. Possible solutions are the use of softer Lewis acids, or Lewis acids which are only capable of monodentate coordination. Further studies are underway and will be reported in due course.

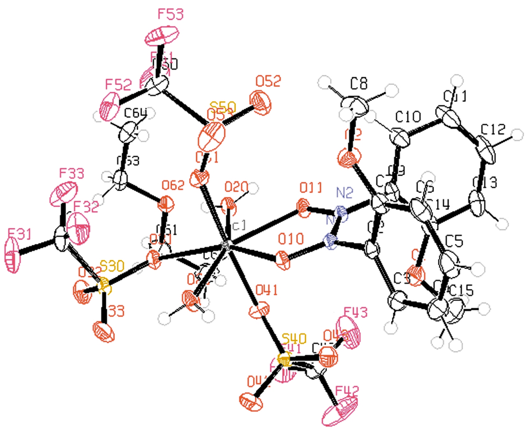
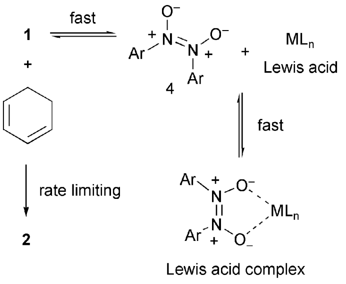


Fig. 2



Scheme 1

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Notes and references

† *Crystal structure* **1b**. T = 150 K, crystal size 0.30 × 0.30 × 0.13 mm^3, molecular formula $C_{28}H_{28}N_4O_8$, F_w 548.54, crystal system monoclinic, space group $P21/c$, a = 19.9465(3) Å, b = 8.98220(10) Å, c = 15.6262(2) Å, β = 107.2590(10)°, Z = 4, λ 0.71073 Å, absorption coefficient 0.101 mm^{-1}, reflections collected 43598, independent reflections 5959, reflections observed[a] 1332, θ range for data collection 3.12–27.29°, restraints (parameters) (0) 473, R_1 (observed reflections) 0.0463, wR_2 (all reflections)[b] 0.1159, goodness-of-fit on F^2 1.021. CCDC 176704. See http://www.rsc.org/suppdata/cc/b2/b206366b/ for crystallographic files in .cif or other electronic format.

‡ *Crystal structures* **3**. T = 150 K, crystal size 0.30 × 0.25 × 0.20 mm^3, molecular formula $C_{21}H_{28}F_9N_20_{16}S_3Sc$, F_w 876.59, crystal system triclinic, space group $P1$, a = 11.04780(10) Å, b = 11.35400(10) Å, c = 14.70440(10) Å, β = 80.7060(10)°, Z = 2, λ = 0.71073 Å, absorption coefficient 0.491 mm^{-1}, reflections collected 30643, independent reflections 7524, reflections observed[a] 2842, θ range for data collection 4.60–27.47°, restraints (parameters) (0) 581, R_1 (observed reflections) 0.0294, wR_2 (all reflections)[b] 0.0721, goodness-of-fit on F^2 1.052. CCDC 177523.

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