Chiral ruthenium complexes as catalysts in enantioselective Diels–Alder reactions. Crystal structure of the Lewis acid–dienophile adduct

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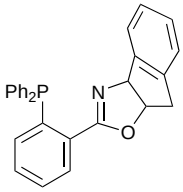
On the basis of spectroscopic and structural studies a full catalytic cycle is proposed for the Diels–Alder reaction between methacrolein and cyclopentadiene when the new chiral aquo-complexes (R_{Ru}, S_{Ru})-[(η^6-*p*-cymene)Ru(PN)(H_2O)][SbF_6]$_2$ {PN = (3a*S*, 8a*R*)-2-(2-diphenylphosphinophenyl)-3a,8a-dihydroindane[1,2-d]oxazole} are used as catalysts.

The Diels–Alder reaction is one of the most important reactions owing to its synthetic relevance and to its mechanistic implications.[1] For these reasons, considerable efforts have been devoted to the development of its enantioselective versions.[2] Among them the use of chiral transition-metal Lewis acids is one of the most recent and versatile variants.[3] It is commonly assumed that for activated alkenes, such as acroleins, the catalytic activity implies an η^1-coordination mode through the oxygen atom followed by subsequent attack of the diene.



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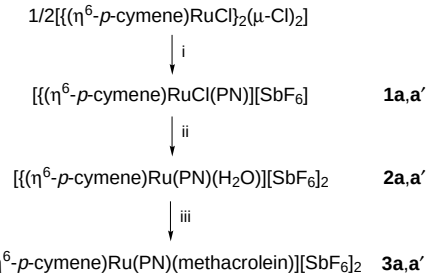
However, studies supporting this assumption in transition metal catalyzed enantioselective Diels–Alder reactions are very scarce.[4] Following our studies on transition metal complexes with chiral metal centres,[5] we report here spectroscopic and crystallographic evidence that supports the aforementioned path for the Diels–Alder reaction between methacrolein and cyclopentadiene (HCp) catalyzed by the new aquo-complexes (R_{Ru}, S_{Ru})-[(η^6-*p*-cymene)Ru(PN)(H_2O)][SbF_6]$_2$, including the X-ray crystal structure determination of the Lewis acid–dienophile adduct (S_{Ru})-[(η^6-*p*-cymene)Ru(PN)(methacrolein)][SbF_6]$_2$. The new enantiopure phosphinoxazoline ligand **I**, prepared from (1*S*,2*R*)-1-aminoindan-2-ol according to the Williams' procedure,[6] was used as a chiral auxiliary. The methacrolein complex was prepared following the sequence of reactions depicted in Scheme 1. Complexes **1** were prepared as a 70 : 30 mixture of epimers at ruthenium in essentially quantitative chemical yield. Enantiopure **1a** and **1a′** can be obtained by fractional crystallization from methanol and CH_2Cl_2–Et_2O, respectively.† NOE difference spectra support an *S* configuration at ruthenium[7] for **1a**.‡

The aquo-complexes **2** were obtained as a mixture of epimers at the metal.† The water molecule proceeds from the solvents. The epimeric composition is independent from the composition of the starting chloride compound **1**, but it depends on the solvent. ^{1}H NMR spectra of aliquots of the same solid sample reveal 65 : 35 and 82 : 18 epimeric ratios in $(CD_3)_2CO$ and CD_2Cl_2, respectively. ROESY experiments indicated that the configuration at the metal for the major diastereomer is *S*.§



Scheme 1 *Reagents*: i, PN, $NaSbF_6$, MeOH; ii, $AgSbF_6$, CH_2Cl_2–acetone (95 : 5, v/v); iii, methacrolein (excess)

At room temp., dichloromethane solutions of **2** catalyse rapidly the Diels–Alder reaction of methacrolein with HCp (91% conversion in 20 min), the system operating with low loading (5% mol), good *exo* : *endo* selectivity (92 : 8) and moderate enantioselectivity {46% in the *exo* adduct (1*R*,2*S*,4*R*)-2-methylbicyclo[2.2.1]hept-5-ene-2-carbaldehyde}.¶

In order to probe the mechanism of the Diels–Alder catalysis, **2** was combined separately with HCp and methacrolein (**2**: methacrolein or HCp, 1 : 20 molar ratio). While no interaction with HCp was detected by either ^{1}H or ^{31}P NMR, immediate adduct formation with methacrolein occurred to give **3** in 73% chemical yield as a 90 : 10 mixture of epimers at the metal† along with 27% of unreacted **2**. From the NMR solution single-crystals of complex **3** were obtained. An X-ray difraction study‖

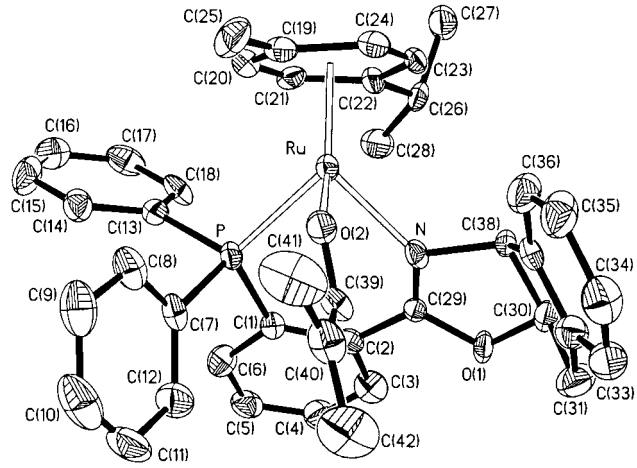
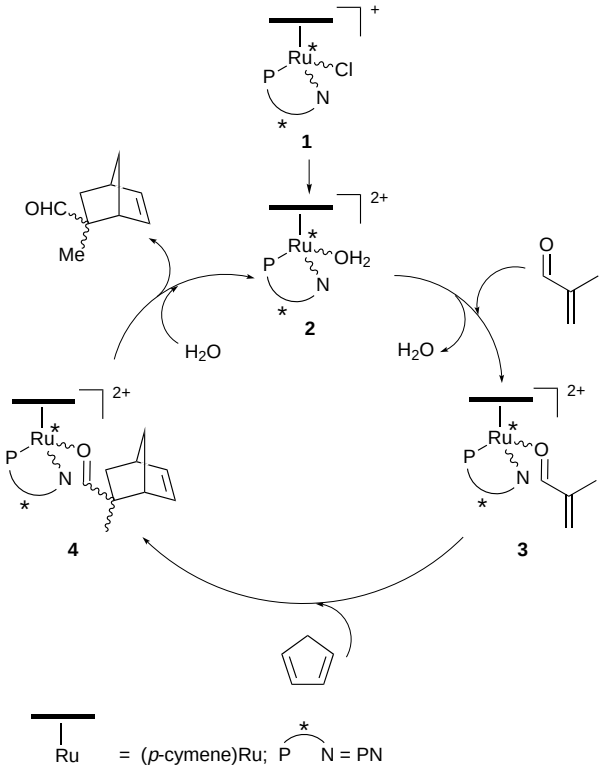


Fig. 1 Molecular representation of (S_{Ru})-**3**. Selected bond distances (Å) and angles (°): Ru–P 2.327(2), Ru—N 2.106(6), Ru–O(2) 2.110(5), O(2)–C(39) 1.219(8), C(39)–C(40) 1.448(11), C(40)–C(41) 1.475(13), C(40)–C(42) 1.329(13); P–Ru–N 89.0(2), P–Ru–O(2) 89.7(2), N–Ru–O(2) 85.7(2), Ru–O(2)–C(39) 131.2(5), O(2)–C(39)–C(40) 123.1(7), C(39)–C(40)–C(41) 118.3(8), C(39)–C(40)–C(42) 116.0(8), C(41)–C(40)–C(42) 125.7(8).



Scheme 2

showed an η^1-coordination mode through the oxygen atom for the methacrolein ligand which adopts an *S-trans* configuration. The methacrolein fragment maintains its planar structure upon coordination [O(2)–C(39)–C(40)–C(42) torsion angle −178.8(8)°], with the metal atom slightly out of this plane by 0.024(6) Å. The absolute configuration at the metal centre results to be *S*.[7] (Fig. 1).

Subsequent addition at 183 K of HCp to CH_2Cl_2 solutions of **3**, prepared as above, (**2** : methacrolein : HCp, 1 : 20 : 40 molar ratio) produced the appearance in the ^{31}P NMR spectrum of a new broad peak centred at δ 32.9 at the expense of the major epimer of **3**, the minor one and the aquo-complexes **2** retaining their relative intensities. At this temperature the Diels–Alder reaction was not observed and we assume that the new resonance would be due to one of several of the possible metal–complex diastereoisomers **4** in which the Diels–Alder adduct is still coordinated to the metal. On warming to 253 K the reaction starts and the sole species observed during the catalytic process are the aquo-complexes **2**. When the catalysis has been completed compounds **2** remain and, as expected, addition of methacrolein regenerates compounds **3** restarting the catalytic cycle.

In conclusion, the catalytic cycle depicted in Scheme 2 is proposed on the basis of spectroscopic data and of the X-ray molecular structure of the complex (S_{Ru})-[(η^6-*p*-cymene)Ru-(PN)(methacrolein)][SbF_6]$_2$. Further work in this area is in progress in order to optimise the catalytic conditions and to obtain information on the origin of the enantioselectivity.

Footnotes and References

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† *Selected spectroscopic data*: for **1a**: $^{31}P\{^1H\}$ NMR [121.4 MHz, $(CD_3)_2CO$, 20 °C, H_3PO_4] δ 27.5 (s). ^1H NMR [300 MHz, $(CD_3)_2CO$, 20 °C, $SiMe_4$] δ 3.58, 3.78 (2 H, AB part of an ABX system, J_{AB} 18.1, J_{AX} 6.9, J_{EX} 3.6 Hz, CH_2CHO); 5.95 (m, 2 H, CHO and CHN). For **1a′**: $^{31}P\{^1H\}$ NMR [121.4 MHz, $(CD_3)_2CO$, 20 °C, H_3PO_4] δ 37.3 (s). ^1H NMR [300 MHz, $(CD_3)_2CO$, 20 °C, Me_4Si] δ 3.52, 3.66 (2 H, AB part of an ABX system, J_{AB} 18.1, J_{AX} *ca.* 0, J_{BX} 4.5 Hz, CH_2CHO); 5.75 (dd, 1 H, J_{HH} 6.1, 4.5 Hz, CHO); 5.19 (d, 1 H, J_{HH} 6.1 Hz, CHN). For **2a** (major diastereomer): $^{31}P\{^1H\}$ NMR (121.4 MHz, CD_2Cl_2, 20 °C, H_3PO_4) δ 36.1 (s). ^1H NMR (300 MHz, CD_2Cl_2, 20 °C, $SiMe_4$) δ 3.54, 3.68 (2 H, AB part of an ABX system, J_{AB} 18.2, J_{AX} 5.9, J_{BX} *ca.* 0 Hz, CH_2CHO); 4.55 (br s, 2 H, H_2O); 5.90 (m, 2 H, CHO and CHN). For **2a′** (minor diastereomer): $^{31}P\{^1H\}$ NMR (121.4 MHz, CD_2Cl_2, 20 °C, H_3PO_4); δ 34.9 (s). ^1H NMR (300 MHz, CD_2Cl_2, 20 °C, $SiMe_4$) δ 4.26 (br s, 2 H, H_2O). For **3a** (major diastereomer): $^{31}P\{^1H\}$ NMR (121.4 MHz, CD_2Cl_2, −90 °C, H_3PO_4) δ 42.65 (s). For **3a′** (minor diastereomer): $^{31}P\{^1H\}$ NMR (121.4 MHz, CD_2Cl_2, −90 °C, H_3PO_4) δ 39.2 s.

‡ The X-ray crystal structure determination of **1a** confirm the assigned configuration: D. Carmona and F. J. Lahoz, unpublished work.

§ The priority orders for the chloride (**1**) and aquo-compounds (**2**) are *p*-cymene > Cl > P > N and *p*-cymene > P > O > N, respectively. Note that, comparing **1** to **2**, if the configuration at the metal is the same its descriptor changes and *vice versa*.

¶ *Catalytic Diels–Alder reaction*: a solution of the catalyst (0.025 mmol) in 2 ml of dry CH_2Cl_2 was prepared under argon. The dienophile (0.5 mmol in 2 ml of CH_2Cl_2) and freshly distilled cyclopentadiene (3 mmol in 2 ml of CH_2Cl_2) were added consecutively by syringe. The resulting solution was stirred until the dienophile was consumed (GC). Yields and *exo* : *endo* ratios were determined by GC analysis. The reaction mixture was concentrated and filtered through silica gel (CH_2Cl_2–hexane as eluent) before the determination of the enantiomeric purity. Ee values were determined by ^1H NMR spectroscopy in the presence of the chiral shift reagent Eu(hfc)$_3$. The configuration of the major adduct was assigned by comparing the sign of $[\alpha]_D$ with that in the literature.[9]

‖ *Crystal data* for (S_{Ru})-**3**: $C_{42}H_{42}F_{12}NO_2PRuSB_2$, M = 1196.32, orthorhombic, space group $P2_12_12_1$, a = 11.3401(8), b = 18.2209(12), c = 20.7142(13) Å (by least-squares refinement of the setting angles for 92 reflections within θ = 12.5–19.5°), U = 4280(1) Å^3, Z = 4, D_c = 1.857 g cm^{-3}, T = 200.0(2)K, μ = 1.73 mm^{-1}, F(000) = 2344, orange irregular block (0.69 × 0.48 × 0.38 mm). Data were collected on a Siemens P4 diffractometer with graphite-monochromated Mo-Kα radiation (λ = 0.710 73 Å) within a 2θ range 4–50°. 8444 reflections collected, 7508 unique. Absorption correction applied according to ψ-scan method. The structure was solved by direct methods (SHELXS-86)[8] and refined by full-matrix least squares on F^2 using all unique data. Anisotropic displacement parameters used for all atoms except for the disordered SbF_6^- groups. Hydrogens included in calculated (methyl groups) or found positions (all the remaining H atoms). Final R_1 = 0.0636; wR_2 = 0.0950 (SHELXL-93, all data) for 570 parameters. CCDC 182/640.

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