A Diels-Alder Reaction Triggered by a [4 + 3] Metallacycloaddition

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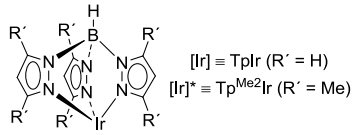
Supporting Information Placeholder

ABSTRACT: The Tp^{Me2}Ir(III) complex **1**-OH_2 (Tp^{Me2} = hydrotris(3,5-dimethylpyrazolyl)borate) that, in addition to a labile molecule of water, contains an iridium-bonded alkenyl moiety –C(R)=C(R)– (R = CO_2Me) as part of a benzo annulated five-membered iridacycle, reacts readily with the conjugated dienes butadiene and 2,3-dimethylbutadiene to afford the corresponding Diels-Alder products. Experimental and DFT studies are in accordance with an initial [4 + 3] cyclometallation reaction between the diene and the five-coordinated 16-electron organometallic fragment **1** (generated from **1**-OH_2 by facile water dissociation). The reaction can be extended to a related TpIr(III) complex (Tp = hydrotris(pyrazolyl)borate) that feature also a labile ligand (e.g. **2**-THF).

The Diels-Alder (DA) [4 + 2] cycloaddition, first reported in 1928,[1] is arguably one of the cornerstones of Organic Chemistry. The existence of different variants has allowed its application to a myriad of synthetic processes and has inspired, from the early days of its discovery, numerous experimental and theoretical studies.[2] Even if from a mechanistic point of view the [4 + 2] cycloaddition seems to be a simple reaction, an important breakthrough was the recognition of the accelerating effect caused by Lewis acids in hetero-DA reactions, as a consequence of their interaction with the heteroatom. Interestingly a recent study in this Journal has revealed a remarkable acceleration caused by a Li^+ cation enclosed in a fullerene cage, on the reaction of the latter species with cyclohexadiene.[3]

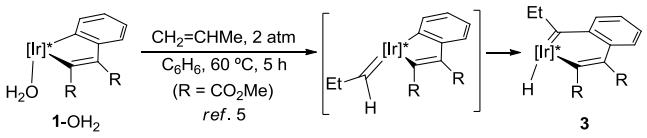
In this contribution, we wish to report on the striking reactivity of butadiene and 2,3-dimethylbutadiene toward an iridium-alkenyl terminus, [Ir–C(CO_2Me)=C(CO_2Me)–], that is part of two different, five-membered Ir(III) metallacyclic complexes, namely $[Tp^{Me2}Ir(C_6H_4\text{-}o\text{-}C(R)=C(R))(OH_2)]$, **1**-$OH_2$ and $[TpIr(CH_2CH_2C(R)=C(R))(THF)]$, **2**-THF ($Tp^{Me2}$ = hydrotris(3,5-dimethylpyrazolyl)borate; Tp = hidrotris(pyrazolyl)borate, Chart 1; R = CO_2Me). The outcomes of these reactions are DA products, but at variance with classical DA [4 + 2] cycloadditions, the success of our approach depends critically upon the facile generation of a vacant coordination site adjacent to the Ir-alkenyl linkage. As demonstrated by the experimental and DFT studies herein discussed, this allows for a [4 + 3] low-energy metallacycloaddition path[4] that greatly facilitates the formation of the DA adducts.

Chart 1. Tp-type ligands used in this study.



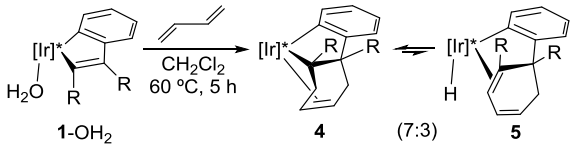
This reactivity clearly differs from other reactions experienced by compound **1**-OH_2. Thus, recent work from our group[5] dealt with the study of its reactivity toward α-olefins, R′CH=CH_2 and for instance propene (R′= Me) reacted with **1**-OH_2 to form (Scheme 1) the hydride-β-iridanaphthalene derivative **3**, as a consequence of an iridium promoted propene-to-propylidene isomerization,[6] followed by chemo- and stereo-selective carbene migratory insertion into the Ir–C_{aryl} bond and α-H elimination.

Scheme 1. Formation of the β-iridanaphthalene 3 from the reaction of the aquo adduct 1-OH_2 and propene



In contrast with this result, the analogous reaction of **1**-OH_2 and butadiene yielded, under similar conditions (Scheme 2), not the expected allyl substituted β-iridanaphthalene related to **3**, but a 7:3 equilibrium mixture of two isomeric species **4** and **5**, which were readily separated by chromatography on silica gel. All new compounds reported herein have been satisfactorily characterized by the usual techniques which included in many cases single-crystal X-ray crystallography (see SI).

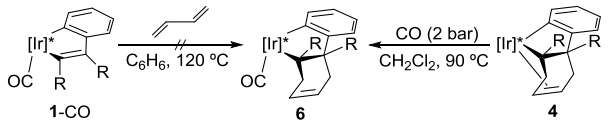
Scheme 2. Reaction of complex 1-OH_2 with butadiene



As represented in Scheme 2, complex **4** is the DA adduct of the diene and the alkenyl moiety of the iridacycle **1**-OH_2, in which the newly created C=C double bond has displaced the labile water ligand, whereas **5** is a closely related species that derives formally from **4** by olefin dissociation and β-H elimination.

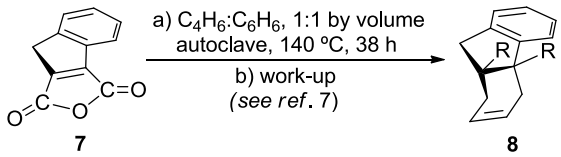
The stereochemistry of compound **4** is coherent with butadiene attacking the [Ir–C(R)=C(R)–] part of the metallacycle along the triangular face of the octahedron opposite to that occupied by the ancillary Tp^{Me2} ligand. Hence, an active role of the metal center in the reaction requires dissociation of the labile molecule of water. Indeed, in favor of such a role is the observation that the related carbonyl adduct **1**-CO, that would be electronically more favorable to undergo a classical [4 + 2] cycloaddition, but is reluctant to experience CO dissociation, did not react with butadiene even after prolonged heating at 120 ºC in benzene, even if the expected product could be prepared by carbonylation of **4** under milder conditions (Scheme 3).

Scheme 3. Two possible approaches to the synthesis of complex 6



As further compelling evidence for the key role of the unsaturated Ir(III) center in the formation of **4**, it should be mentioned that the indene compound **7**, which contains a CH_2 group isolobal with the [Tp^{Me2}Ir(R)(R′)] fragment of **1**, undergoes the DA cycloaddition with butadiene[7] only under the much harsher conditions specified in Scheme 4.

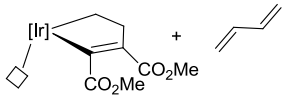
Scheme 4. Formation of the DA adduct 8 by the reaction of the indene 7 with butadiene



To gain further information on the mechanism of the reaction of **1**-OH_2 with butadiene, a kinetic investigation was performed employing an excess of the diene, whose results were in agreement with dissociation of H_2O being rate determining (CD_2Cl_2, 30 ºC, see Figure S1, SI). This proposal is in accordance with the observation that **1**-OH_2 reacts with propene (Scheme 1) and butadiene (Scheme 2) under very similar reaction conditions, as well as with previous studies from our group based on related [Tp′Ir(R)(R′)L] complexes with labile ligands L, like N_2.[8]

DFT calculations (wB97xD[9]/6-31+G(d,p) and lanl2dz) were also carried out using the simplified system shown in Chart 2 (butadiene + iridacycle **2** without fused benzene, parent Tp and unsubstituted butadiene).

Chart 2. Simplified system used for DFT calculations.



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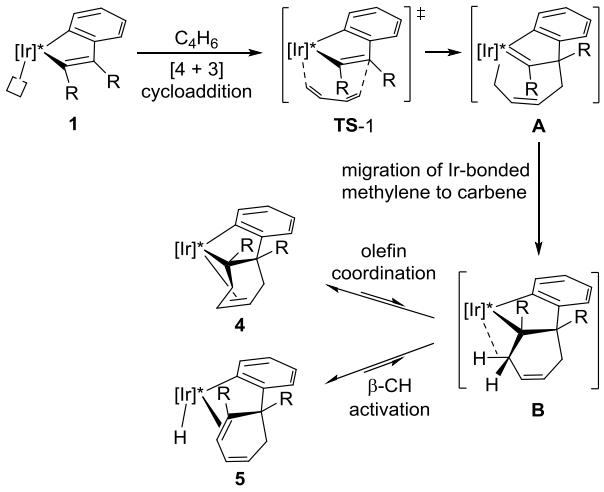
These studies led to the mechanism depicted in Scheme 5, with transition state **TS**-1 connecting **1** and the alkylidene intermediate **A**,[10] which corresponds to a [4 + 3] cycloaddition.[11]

Scheme 5. Proposed mechanism (DFT) for the formation of the equilibrated mixture of complexes 4 and 5



Detailed calculations with the model system of Chart 2 (Figure 1), failed to locate a transition state for a [4 + 2] cycloaddition and energy scans (PES) for such a process suggested that the energy barriers would be larger than 40 kcal·mol^{-1}. It was the examination of the frontier orbitals of the metal fragment which led to a [4 + 3] cycloaddition mechanism, with participation of Ir, for which a transition state, **TS**-1, was found (Figure 1 and Scheme 5). The energy barrier (Zero-Point-corrected Energy in the gas phase) associated with the formation of **A**[12] from **2**·η^2-*cis*-C_4H_6 is 19.6 kcal·mol^{-1}. An electronic description of this step based on localized orbitals[13] can be found in the Supplementary Information.

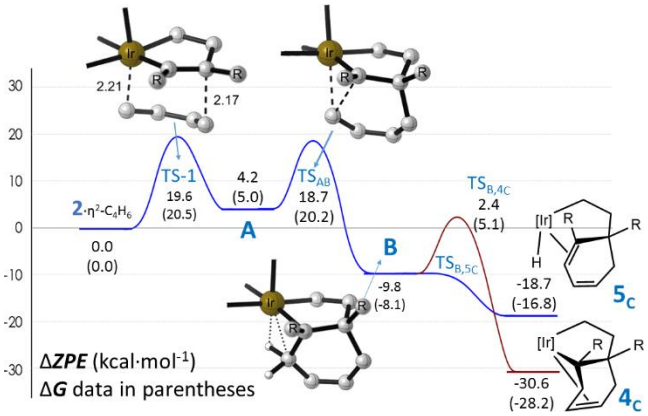


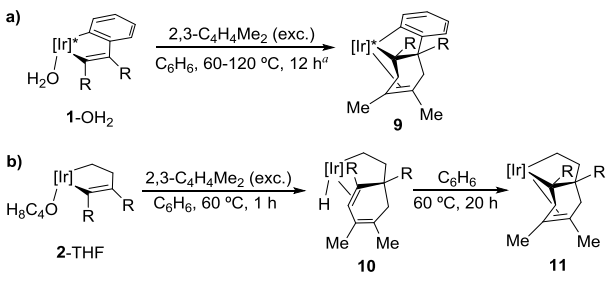
Figure 1. DFT-calculated Zero Point-Corrected Energy profile for the formation of $\mathbf{5}_C$ and $\mathbf{4}_C$. Fragments of relevant DFT-optimized structures are also shown. Subscript C indi-

cates calculated species without an experimental counterpart. Energy values are relative to **2**·η²-C_4H_6.

Migratory insertion of the electrophilic alkylidene of **A** into the Ir–CH_2 bond has a barrier of 14.5 kcal·mol^{-1} and affords the tertiary alkyl derivative **B**, stabilized by a β-agostic C–H interaction.[14] **B** is the common intermediate from which the reaction products arise. In a kinetically controlled, almost barrier-less and reversible process, the β-C–H activated bond of **B** completes the transfer of its agostic hydrogen atom to iridium with formation of the hydride product **5**$_C$ (a model for experimental species **5** and **10**, see below). Notwithstanding, **B** can also undergo cleavage of the weak agostic interaction concomitant with a torsion of the cyclohexene ring that permits the stronger, thermodynamically preferred Ir-olefin coordination found in **4**$_C$ ($\Delta E^{\ddagger}$ = 12.2 kcal·mol^{-1} from **B**). In accordance with the experimental data (see below), the last step is more or less reversible depending on the nature of the organometallic and diene reagents under consideration. Thus the energy difference between the thermodynamic and kinetic products of the reaction with the smaller system **2** + butadiene (**4**$_C$ and **5**$_C$) is 11.9 kcal·mol^{-1}, whereas the calculated (see SI) energy difference of the corresponding reaction products of the reaction with the real system **1** + butadiene (**4** and **5**) is 1.7 kcal·mol^{-1}, and the calculated overall barrier for the equilibrium **4** ⇌ **5** is 19.8 kcal·mol^{-1} (see Figure S8, SI).

To study the scope of the newly discovered transition metal-mediated reactions that lead to DA products, other related systems were investigated. The bulkier and more electron rich substituted diene 2,3-dimethylbutadiene, that usually undergoes faster DA cycloadditions than butadiene, reacted less cleanly with complex **1**-OH_2 to give the corresponding adduct **9** (Scheme 6a) in yields of *ca.* 60%. An isomeric hydride related to **5** was not detected. Similarly, O´Connor's complex, [Tp$^{\prime}$Ir(CH$_2$CH$_2$C(R)=C(R))(THF)], **2**-THF,[15] which contains the less bulky, unsubstituted Tp ligand and a labile molecule of THF, reacted also with an excess of 2,3-dimethylbutadiene to generate quantitatively (by ^{1}H NMR) the corresponding hydride **10** and DA **11** products (Scheme 6b), in sequential, well-differentiated chemical events (60 ºC, 1 h and 20 h reaction times, respectively). Once again in agreement with rate-determining ligand dissociation (THF), the formation of complex **10** was clearly disfavored when THF was utilized as the reaction solvent (no reaction after 2 h at 60 ºC).

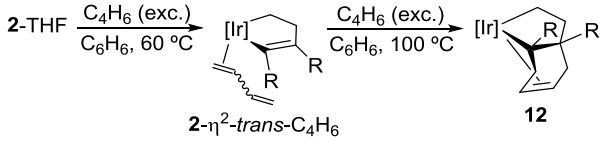
Scheme 6. Reaction of the complexes 1-OH_2 (a) and 2-THF (b) with 2,3-dimethylbutadiene



[a]The reaction was cleaner at 120 ºC.

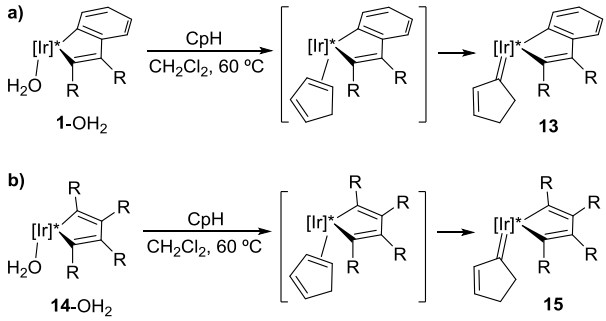
Compound **2**-THF reacted with excess of butadiene under similar conditions (C_6H_6, 60 ºC), but the reaction yielded the butadiene adducts **2**-η²-*trans*-C_4H_6 (Scheme 7) in the form of a 3:1 kinetic mixture of two diastereomers with both featuring η² coordination of a molecule of *trans*-C_4H_6 (NOESY evidence). Prolonged heating of this mixture at 100 ºC converted these species into the desired DA adduct **12** ($t_{1/2}$ = 20 h), but no evidence for a hydride related to **5** could be obtained.

Scheme 7. Reaction of complex 2-THF with butadiene at different temperatures



A final piece of information pertinent to the unprecedented reactivity reported in this paper concerns with the outcome of the reaction of complex **1**-OH_2 and cyclopentadiene, the diene *par* excellence in classical DA cycloadditions. Under experimental conditions identical to those of the butadiene and 2,3-dimethylbutadiene reactions, complex **1**-OH_2 combined with C_5H_6 but generated the carbene complex **13** instead of the corresponding DA adduct (Scheme 8a). Therefore, C_5H_6 behaved as an olefin rather than as a diene and this result is of interest in its own right, as it represents a most notable example of a rarely observed olefin-to-alkylidene rearrangement.[16] In fact we have often proposed this type of isomerization to take place as an intermediate step in different reactions[17] (see for instance Scheme 1 for the reaction of **1**-OH_2 with propene) but the alkylidene intermediate normally was not seen. The result reported in Scheme 8a is probably due to steric hindrance, a hypothesis that is supported by DFT calculations.[18] The same explanation could account for the lack of reactivity of complex **13** toward carbene migratory insertion even at high temperatures (120 ºC). A similar outcome was observed with the symmetrical related iridacyclopentadiene [Tp^{Me2}Ir(C(R)=C(R)C(R)=C(R))(OH$_2$)], **14**-OH_2,[19] (R = CO_2Me) (Scheme 8b).

Scheme 8. Reaction of complexes 1-OH_2 and 14-OH_2 with cyclopentadiene



In conclusion, we have demonstrated that two different five-membered Tp´Ir(III) metallacycles (Tp´ = symbolizes an anionic ligand of the tris(pyrazolyl)borate family), both containing an [Ir–C(R)=C(R)–] (R = CO_2Me) functionality and a labile co-ligand (H_2O or THF), react with butadiene and 2,3-dimethylbutadiene to give the corresponding Diels-Alder (DA) adducts as the main products. Experimental data and DFT calculations are in accordance with a [4 + 3] cyclometallation process as the key step in the reaction path that leads to these products.

ASSOCIATED CONTENT

Supporting Information

The synthesis and spectroscopic characterization of compounds **4**, **5**, **1**-CO, **8**, **9**, **10**, **11**, **2**-η^2-*trans*-C_4H_6, **12**, **13** and **15** are collected in the Supporting Information. Computational and X-ray details are also given in the SI; CCDC-1035123 (**4**), 1035124 (**5**) and 1035126 (**15**) contain the supplementary crystallographic data for this paper. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interests.

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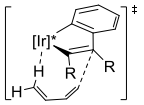
(11) The experimental results are also in accord with a mechanism of the type **1**-OH_2 ➔ **5** ⇌ **4** in which a regioselective C–H activation of butadiene by fragment **1** gives rise in the first place to complex **5** via the **TS**-2 shown below. However no such step was found by DFT calculations.



TS-2

(12) Two **2**-η^2-*cis*-C_4H_6 adducts were located regarding the relative orientation of the diene, see Figure S7 in the SI. Each adduct evolves through parallel pathways, with similar energy barriers and converge in intermediate **B**. Thus, only one of the pathways is discussed in the main text.

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(16) See reference 6c and references therein.

(17) See reference 5 and references therein.

(18)The overall calculated energy barrier for methylene migration (**TS**$_{AB}$) from **2**-η^2-CpH is more than 10 kcal·mol^{-1} higher than the corresponding barrier from **2**-η^2-*cis*-C_4H_6 (> 30 kcal·mol^{-1}). See the Supplementary Information for details.

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