

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

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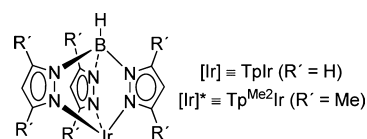
S Supporting Information

ABSTRACT: The $\text{Tp}^{\text{Me}_2}\text{Ir}(\text{III})$ complex $\mathbf{1-OH}_2$ (Tp^{Me_2} = hydrotris(3,5-dimethylpyrazolyl)borate), which contains a labile molecule of water and an iridium-bonded alkenyl moiety ($-\text{C}(\text{R})=\text{C}(\text{R})-\text{C}(\text{R})-\text{C}(\text{R})-$) as part of a benzoannulated 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] cyclometalation reaction between the diene and the five-coordinated 16-electron organometallic fragment $\mathbf{1}$ (generated from $\mathbf{1-OH}_2$ by facile water dissociation). The reaction can be extended to a related $\text{TpIr}(\text{III})$ complex (Tp = hydrotris(pyrazolyl)borate) that also features a labile ligand (i.e., 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

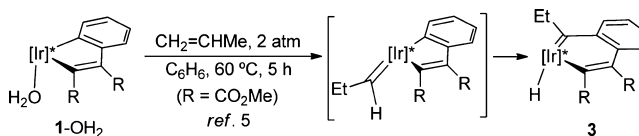
In this contribution, we wish to report on the striking reactivity of butadiene and 2,3-dimethylbutadiene toward an iridium-alkenyl terminus, $[\text{Ir}-\text{C}(\text{CO}_2\text{Me})=\text{C}(\text{CO}_2\text{Me})-]$, that is part of two different five-membered $\text{Ir}(\text{III})$ metallacyclic complexes, namely, $[\text{Tp}^{\text{Me}_2}\text{Ir}(\text{C}_6\text{H}_4\text{-}o\text{-C}(\text{R})=\text{C}(\text{R}))(\text{OH}_2)]$, $\mathbf{1-OH}_2$, and $[\text{TpIr}(\text{CH}_2\text{CH}_2\text{C}(\text{R})=\text{C}(\text{R}))(\text{THF})]$, $\mathbf{2-THF}$, (Tp^{Me_2} = hydrotris(3,5-dimethylpyrazolyl)borate, Tp = hydrotris(pyrazolyl)borate, Chart 1; $\text{R} = \text{CO}_2\text{Me}$). 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 path⁴ 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 $\mathbf{1-OH}_2$. Thus, recent work from our group⁵ dealt with the study of its reactivity toward α -olefins, $\text{R}'\text{CH}=\text{CH}_2$; for instance, propene ($\text{R}' = \text{Me}$) reacted with $\mathbf{1-OH}_2$ to form the hydride- β -iridanaphthalene derivative $\mathbf{3}$ (Scheme 1) as a

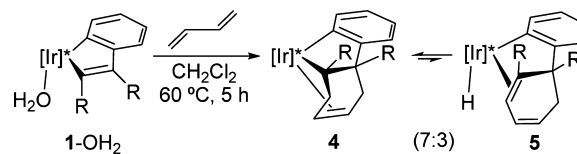
Scheme 1. Formation of β -Iridanaphthalene $\mathbf{3}$ from the Reaction of Aquo Adduct $\mathbf{1-OH}_2$ and Propene



consequence of an iridium-promoted propene-to-propylidene isomerization,⁶ followed by chemo- and stereoselective carbene migratory insertion into the Ir– C_{aryl} bond and α -H elimination.

In contrast with this result, the analogous reaction of $\mathbf{1-OH}_2$ and butadiene under similar conditions yielded not the expected allyl substituted β -iridanaphthalene related to $\mathbf{3}$, but a 7:3 equilibrium mixture of two isomeric species $\mathbf{4}$ and $\mathbf{5}$ (Scheme 2),

Scheme 2. Reaction of Complex $\mathbf{1-OH}_2$ with Butadiene



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 (Supporting Information).

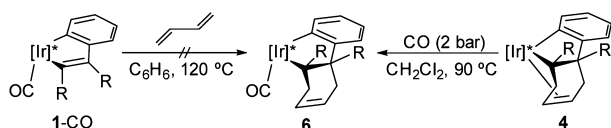
Received: February 11, 2015

Published: March 18, 2015

As represented in Scheme 2, complex **4** is the DA adduct of the diene and the alkenyl moiety of iridacycle **1-OH₂**, 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.

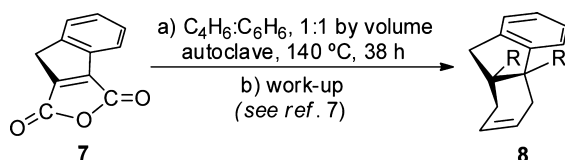
The stereochemistry of compound **4** is coherent with butadiene attacking the [Ir-C(R)=C(R)-] part of the metallacycle along the triangular face of the octahedron opposite that occupied by the ancillary Tp^{Me₂} ligand. Hence, an active role of the metal center in the reaction requires dissociation of the labile molecule of water. Indeed, in favor of such a role is the observation that the related carbonyl adduct **1-CO**, which 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 °C 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 indene compound **7**, which contains a CH₂ group isolobal with the [Tp^{Me₂}Ir(R)(R')] fragment of **1**, undergoes the DA cycloaddition with butadiene⁷ only under the much harsher conditions specified in Scheme 4.

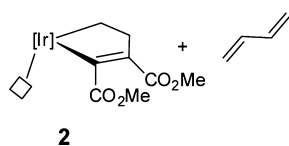
Scheme 4. Formation of DA Adduct **8** by the Reaction of Indene **7** with Butadiene



To gain further information on the mechanism of the reaction of **1-OH₂** with butadiene, a kinetic investigation was performed by employing an excess of the diene; the results were in agreement with dissociation of H₂O being rate-determining (CD₂Cl₂, 30 °C; see Figure S1, Supporting Information). This proposal is in accordance with the observation that **1-OH₂** 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^{Me₂}Ir(R)(R')L] complexes with labile ligands, L, such as N₂.⁸

DFT calculations (wB97xD⁹/6-31+G(d,p) and lanl2dz) were also carried out using the simplified system shown in Chart 2

Chart 2. Simplified System Used for DFT Calculations



(butadiene + iridacycle **2** without fused benzene, parent Tp, and unsubstituted butadiene).

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**

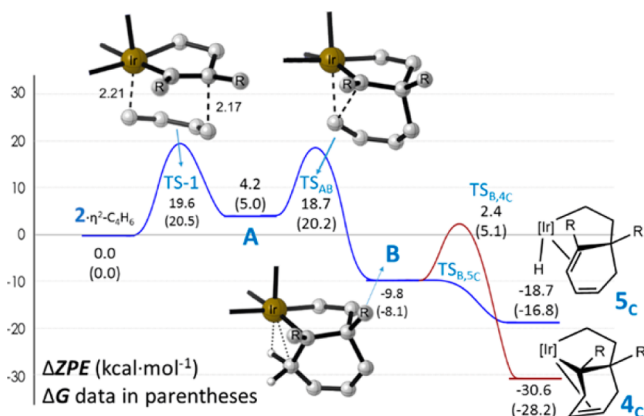
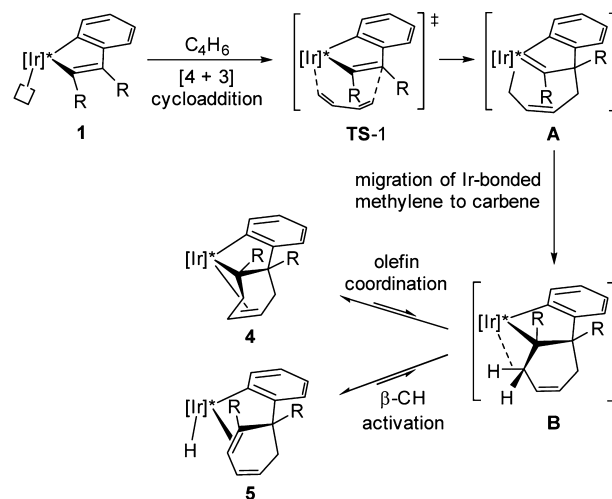


Figure 1. DFT-calculated zero-point-corrected energy profile for the formation of **5_c** and **4_c**. Fragments of relevant DFT-optimized structures are also shown. Subscript C indicates calculated species without an experimental counterpart. Energy values are relative to 2- η^2 -C₄H₆.

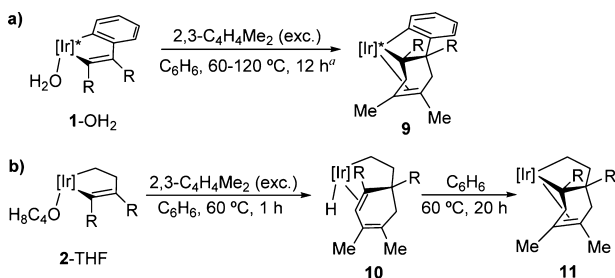
Detailed calculations with the model system of Chart 2 (Figure 1) failed to locate a transition state for a [4 + 2] cycloaddition and energy scans (PES) for such a process suggested that the energy barriers would be greater than 40 kcal·mol⁻¹. It was the examination of the frontier orbitals of the metal fragment that led to a [4 + 3] cycloaddition mechanism with participation of Ir for which 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*-C₄H₆ is 19.6 kcal·mol⁻¹. An electronic description of this step that is based on localized orbitals¹³ can be found in the Supporting Information.

Migratory insertion of the electrophilic alkylidene of **A** into the Ir-CH₂ 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 barrierless, 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** ($\Delta E^\ddagger = 12.2 \text{ kcal}\cdot\text{mol}^{-1}$ 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 $11.9 \text{ kcal}\cdot\text{mol}^{-1}$, whereas the calculated energy difference (Supporting Information) of the corresponding reaction products of the reaction with the real system **1** + butadiene (**4** and **5**) is $1.7 \text{ kcal}\cdot\text{mol}^{-1}$, and the calculated overall barrier for the equilibrium $4 \rightleftharpoons 5$ is $19.8 \text{ kcal}\cdot\text{mol}^{-1}$ (see Figure S8, Supporting Information).

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, which usually undergoes faster DA cycloadditions than butadiene, reacted less cleanly with complex **1-OH₂** to give the corresponding adduct **9** (Scheme 6a) in yields of ca. 60%. An isomeric hydride

Scheme 6. Reaction of Complexes (a) **1-OH₂** and (b) **2-THF** with 2,3-Dimethylbutadiene

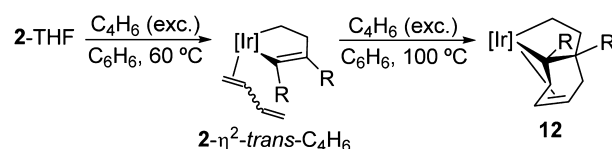


^aThe reaction was cleaner at 120 °C.

related to **5** was not detected. Similarly, O'Connor's complex, $[\text{TpIr}(\text{CH}_2\text{CH}_2\text{C}(\text{R})=\text{C}(\text{R}))(\text{THF})]$, **2-THF**,¹⁵ which contains the less bulky, unsubstituted Tp ligand and a labile molecule of THF, also reacted with an excess of 2,3-dimethylbutadiene to generate quantitatively (by ¹H NMR) corresponding hydride **10** and DA product **11** (Scheme 6b) in sequential, well-differentiated chemical events (60 °C, 1 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 °C).

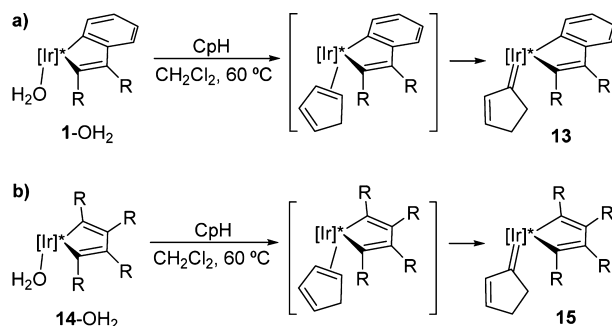
Compound **2-THF** reacted with excess of butadiene under similar conditions (C_6H_6 , 60 °C), but the reaction yielded butadiene adducts **2- η^2 -trans-C₄H₆** (Scheme 7) in the form of a 3:1 kinetic mixture of two diastereomers with both featuring η^2 coordination of a molecule of *trans*-C₄H₆ (NOESY evidence). Prolonged heating of this mixture at 100 °C converted these species into the desired DA adduct **12** ($t_{1/2} = 20 \text{ h}$), 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 the outcome of the reaction of complex **1-OH₂** 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-OH₂** combined with C_5H_6 but generated carbene complex **13** instead of the corresponding DA adduct (Scheme 8a). Therefore, C_5H_6

Scheme 8. Reaction of Complexes **1-OH₂** and **14-OH₂** with Cyclopentadiene



behaved as an olefin rather than as a diene, and this result is of interest in its own right because 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 reactions¹⁷ (for instance, Scheme 1 for the reaction of **1-OH₂** 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 °C). A similar outcome was observed with the symmetrically related iridacyclopentadiene $[\text{Tp}^{\text{Me}_2}\text{Ir}(\text{C}(\text{R})=\text{C}(\text{R})\text{C}(\text{R})=\text{C}(\text{R}))(\text{OH}_2)]$, **14-OH₂** ($\text{R} = \text{CO}_2\text{Me}$),¹⁹ Scheme 8b).

In conclusion, we have demonstrated that two different five-membered $\text{Tp}'\text{Ir}(\text{III})$ metallacycles ($\text{Tp}' =$ an anionic ligand of the tris(pyrazolyl)borate family), both containing an $[\text{Ir}-\text{C}(\text{R})=\text{C}(\text{R})-]$ ($\text{R} = \text{CO}_2\text{Me}$) functionality and a labile coligand (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 $[4 + 3]$ cyclo-metallation process as the key step in the reaction path that leads to these products.

■ ASSOCIATED CONTENT

Supporting Information

Details on the synthesis and spectroscopic characterization of compounds **4**, **5**, **1-CO**, **8–11**, **2- η^2 -trans-C₄H₆**, **12**, **13**, and **15**;

computational and X-ray details; and crystallographic data for CCDC-1035123 (4), -1035124 (5), and -1035126 (15). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

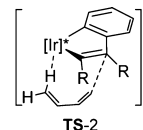
The authors declare no competing financial interests.

ACKNOWLEDGMENTS

Financial support (FEDER contribution) from the Spanish Ministerio de Economía y Competitividad (project CTQ2014-51912-REDC) and the Junta de Andalucía (grant FQM-119 and project P09-FQM-4832) is acknowledged. The use of computational facilities of the Supercomputing Center of Galicia (CESGA) is also acknowledged. J.L.-S thanks the MICINN and the European Social Fund for a Ramón y Cajal contract.

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



(12) Two $2-\eta^2$ -*cis*-C₄H₆ adducts were located regarding the relative orientation of the diene; see Figure S7 in the Supporting Information. Each adduct evolves through parallel pathways with similar energy barriers, and these converge in intermediate **B**. Thus, only one of the pathways is discussed in the main text.

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(17) See ref 5 and references therein.

(18) The overall calculated energy barrier for methylene migration (TS_{AB}) from $2-\eta^2$ -CpH is more than 10 kcal·mol⁻¹ higher than the corresponding barrier from $2-\eta^2$ -*cis*-C₄H₆ (>30 kcal·mol⁻¹). See the Supporting Information for details.

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