1,5-Cyclooctadiene as a Bis-Homodiene Partner in a Metal-Catalyzed [4 + 2]Cycloaddition

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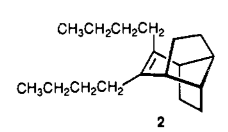
1,5-Cyclooctadiene (COD) is a very common ligand in a broad array of transition-metal organometallic complexes.[1] In spite of the vast number of complexes, remarkably few reactions of the double bonds outside of hydrogenation are described except for normal polar reactions represented by the Pd(2+) additions of nucleophiles.[2] While the individual double bonds have participated in normal olefin chemistry in the presence of transition metals (e.g., metathesis),[3] no cycloadditions deriving from the special spatial relationship that presumably imparts its excellent coordinating properties exists. In contrast to COD, norbornadiene, which is also a good ligand for transition metals, serves as a Diels–Alder-like diene in both thermal and metal-catalyzed cycloadditions.[4] In fact, even though up to 30 mol % $(COD)_2Ni$ is employed as catalyst in such reactions, adducts involving COD are not reported. All reported examples of thermal Diels–Alder reactions record COD participating as the dienophile.[5] To our knowledge, no cycloadditions—thermal or metal-catalyzed—wherein it serves as a diene partner have been recorded. (Cycloocta-1,3,5-triene)(cycloocta-1,5-diene)ruthenium[6] undergoes cycloadditions with acetylenes at the COT ligand. Extensive interest in metal catalyzed cycloadditions[7] leads us to record the first examples of the equivalent of a bis-homo-like Diels-Alder reaction of COD catalyzed by ruthenium that correlates to the unusual coordinating ability of this unique diene. Considering COD's widespread importance as a ligand in organometallic complexes, such an observation opens up fundamental questions into the factors that make it such a good ligand and provide access to a novel class of tricyclo[4.2.2.$0^{2,5}$]dec-7-enes.[8]

Except for catalytic hydrogenation, COD is generally believed to participate as a dummy ligand in a catalytic cycle, wherein it exchanges with one of the reactants. In conjunction with a recent study of the ruthenium-catalyzed intermolecular Alder ene reaction between simple olefins and acetylenes,[9] we explored the reactions of CpRu(COD)Cl (**1**)[10] with an olefin and an alkyne. Whereas the former led to no additions to COD, the reactivity of the latter prompted its further exploration.

Heating a 0.1 M solution of 5-decyne and a 2-fold excess of COD in degassed methanol at reflux in the presence of 5 mol% of ruthenium complex **1** produces an 83% distilled yield of a 1:1 adduct, as established by mass spectroscopy. The highly symmetrical nature and the number and type of olefins, as established by the appearance of nine signals in the ^{13}C NMR spectrum, only one of which was olefinic (δ 137.9), and by the absence of vinylic protons in the ^1H NMR spectrum, indicated structure **2**, **3**, or **4**. Differentiation between **2** and **3** or **4** stems from the symmetry properties since the two faces of the double bond of **2** are enantiotopic but are diastereotopic in either **3** or **4**. Thus, epoxidation of **2** can lead to only one epoxide but of **3** or **4** to two. The fact that exposure of the cycloadduct to MCPBA in methylene chloride at room temperature produces a 1:1 mixture of two epoxides in 94% yield demands structure **3** or **4**. Since there should be appreciable differences in steric shielding of the two diastereotopic faces of **3** but not of **4**, the lack of stereochemical discrimination in the epoxidation suggests that **4**,[11] not **3**, is the cycloadduct. Correlations using 2D NMR spectroscopy allow assignment of H_a (δ 2.06) and H_b (δ 1.88). A NOESY spectrum reveals a NOE between them, substantiating **4** as the correct structure.



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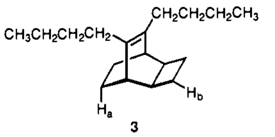

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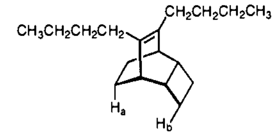

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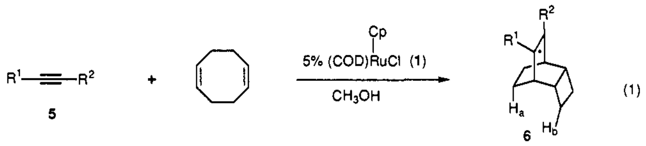
Having established the feasibility of the cycloaddition, its generality with respect to the acetylene partner was established. Using a standard protocol wherein a 0.1 M methanolic solution of 1 equiv of acetylene and 1.1 equiv of COD was treated with 5 mol% of the ruthenium complex **1**, a series of disubstituted acetylenes **5a–g** were reacted to give cycloadducts **6a–g**[11] (eq 1).



a)	$R^1 = CH_3$	$R^2 = CH_2OH$	78%
b)	$R^1 = CH_3$	$R^2 = CH_2OTIPS$	90%
c)	$R^1 = C_2H_5$	$R^2 = CH_2CH_2OH$	99%
d)	$R^1 = TIPSOCH_2$	$R^2 = CH_2OTIPS$	100%
e)	$R^1 = PMBOCH_2$	$R^2 = CH_2OPMB$	22%
f)	$R^1 = CH_3$	$R^2 = CO_2CH_3$	97%
g)	$R^1 = H$	$R^2 = CH_2CH_2CH_2CO_2CH_3$	91%

The reaction exhibits good chemoselectivity. A propargyl alcohol cycloadds well (**5a**), although silylation (**5b**) improves the yield from 78% to 90%. Moving the hydroxyl group to the homopropargylic position (**5c**) removes the small compromise in yield observed with the propargyl alcohol. Aromatic rings do pose a problem. Thus, the *p*-methoxybenzyl protected 2-butyne-1,4-diol **5e** gives a 22% isolated (65% yield brsm[12]) yield, with the

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[1] Wilkinson, G.; Stone, F. G. A.; Abel, E. W., Eds. *Comprehensive Organometallic Chemistry* Pergamon Press: Oxford, 1982.

[2] Tsuji, J.; Takahashi, H. *J. Am. Chem. Soc.* **1965**, *87*, 3275. Takahashi, H.; Tsuji, J. *J. Am. Chem. Soc.* **1986**, *90*, 2387.

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[7] For some overviews, see: Noyori, R. *Acc. Chem. Res.* **1979**, *12*, 61. Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 539. Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1. Binger, P.; Buch, H. M. *Top. Curr. Chem.* **1987**, *135*, 77.

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[9] Trost, B. M.; Indolese, A. *J. Am. Chem. Soc.* **1993**, *115*, 4361.

[10] Albers, M. O.; Robinson, D. J.; Shaver, A.; Singleton, E. *Organometallics* **1986**, *5*, 2199.

[11] This compound has been fully characterized.

[12] The abbreviation brsm = based on recovered starting material.

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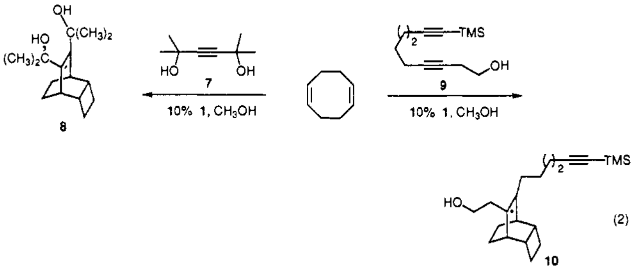
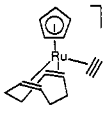
remainder largely being unreacted starting material, whereas the triisopropylsilyl protected derivative **5d** provides a quantitative yield of cyclodduct. A NOESY experiment with cycloadduct **6e** also reveals a NOE between H_a (δ 2.14) and H_b (δ 1.86), confirming the stereochemical assignment as unchanged, even with the presence of the aryl rings in the acetylenic partner (see supplementary material). Presumably, the formation of an arene ruthenium complex[13] generates a much less catalytically active species. There is also a significant rate retardation effect of electron-withdrawing groups. Whereas reaction is normally complete in 20 h, substrate **5f** required 90 h for completion, although the yield was still excellent. On the other hand, dimethyl acetylenedicarboxylate fails to react.

Steric hindrance plays a role. The butynediol **7** (eq 2) reacts slowly to give cycloadduct **8** in 51% yield (98% brsm) after 80 h at reflux. Such steric factors may provide good chemoselectivity with polyacetylenes. Thus, the diyne **9** cycloadds exclusively to the sterically more accessible acetylene (63% yield, 72% brsm) to give cycloadduct **10** (eq 2). Surprisingly, even terminal acetylenes participate normally (CH_3OH, 70 °C, 20 h, eq 1g), as illustrated by formation of the cycloadduct **6g** in 91% yield.



The special nature of COD is clearly revealed in the failures of 1,5-hexadiene and 2,6-octadiene to cycloadd under identical conditions. Whether steric or electronic effects are responsible for this dramatic effect remains to be established. ZINDO calculations[14] on **12, 13** and **14** indicate that the latter two have HOMO–LUMO orbitals that are very similar in both energy and electron distribution with the electron distribution centered on ruthenium and the acetylene in the HOMO. The HOMO of COD complex **12** lies higher in energy, and the electron distribution of this orbital extends to the olefinic linkages as well. Furthermore, these calculations suggest that the two double bonds of **13** and **14** are twisted such that a mechanism invoking a direct tautomerization comparable to **15** going to **17** (see Scheme I) is not feasible. While these results are suggestive, more sophisticated calculations are required before any definite conclusions can be reached. It is possible that a correlation between the source of the unique ligating properties of COD and its reactivity as a bis-homodiene in this cycloaddition exists. Thus, a more detailed understanding of the ligating properties of COD may shed light on this cycloaddition. Scheme I outlines a reasonable mechanistic rationale which also accounts for the stereochemistry and regioselectivity. Other potentially highly coordinatively unsaturated ruthenium compounds like ruthenium chloride also catalyze the reaction but with low reactivity and significant byproduct formation. The remarkable facility of these Ru catalyzed reactions suggests that there may be a wealth of metal-catalyzed reactions of COD yet to unfold and that the coordinating properties of COD may derive from more than entropic effects resulting from spatial proximity. Perhaps some of the electronic interactions that account for the high reactivity of norbornadiene may also exist in an attenuated fashion in COD.



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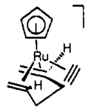

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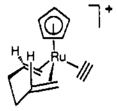

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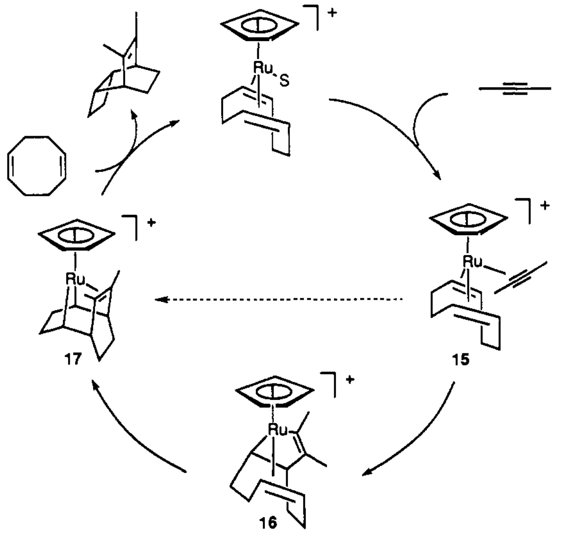
Scheme I. Mechanistic Rationale for a Ru-Catalyzed Diels–Alder Reaction with a Bis-Homodiene



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Supplementary Material Available: Experimental details and characterization data for **4**, **6a–g**, **8**, and **10**; NOESY spectrum of **6e** (4 pages). Ordering information is given on any current masthead page.

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[13] Bennett, M. A.; Bruce, M. I.; Matheson, T. W. in *Comprehensive Organometallic Chemistry*; Wilkinson, G.; Stone, F. G. A.; Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 4, p 796. Le Bozec, H.; Touchard, D.; Dixneuf, P. H. *Adv. Organomet. Chem.* **1989**, *29*, 163.

[14] ZINDO calculations were performed using a CAChe Scientific Work System.