Demethylation of Coordinated Hexamethylbenzene. Carbon−Carbon Bond Activation during Ruthenium-Mediated [3 + 2] Allyl Alkyne Cycloaddition Reactions

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Summary: The demethylation of coordinated hexamethylbenzene is integrated into [3 + 2] allyl/alkyne cycloaddition reactions mediated by (η^6-hexamethylbenzene)-Ru(η^3-allyl)OTf. The reaction proceeds in high yield at or below room temperature and yields methane and (η^6-pentamethylbenzene)ruthenium(1,2-dialkylcyclopentadienyl)$^+$OTf$^-$ complexes exclusively. Cycloaddition with carbon−carbon bond activation is general for a range of disubstituted alkynes.

Transition metals mediate the activation of carbon−carbon bonds in a range of contexts.[1] Both oxidative and nonoxidative (viz., β-alkyl elimination) processes are common, driven by various kinetic and thermodynamic effects: the relief of ring strain,[2] coordination-induced proximity,[3,4] ligand aromatization,[5] or in many cases, a combination of factors.[6]

In this communication, we report a general demethylation reaction that converts coordinated hexamethylbenzene into pentamethylbenzene in high yield under exceptionally mild conditions.[7] The demethylation process is integrated into an overall [3 + 2] cycloaddition reaction, which converts cationic (η^6-hexamethylbenzene)ruthenium η^3-allyl complexes and disubstituted alkynes into methane and (η^6-pentamethylbenzene)-ruthenium η^5-cyclopentadienyl complexes. This "unforced" carbon−carbon bond activation appears to be driven by relief of the cumulative steric strain experienced by the six mutually buttressed methyl substituents in hexamethylbenzene and by a surprisingly low kinetic barrier to the carbon−carbon bond scission.

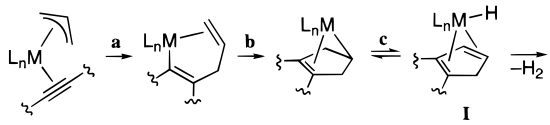

Figure 1.

Metal-mediated "oxidative" allyl/alkyne [3 + 2] cycloaddition reactions have been previously reported for half-sandwich η^5-cyclopentadienyl,[8] η^5-pentamethylcyclopentadienyl,[9,10] and η^6-arene[8] complexes of the late transition metals (Figure 1). The reaction represents an unexploited *convergent* synthesis of differentially substituted cyclopentadienyl ligands within the coordination sphere of a metal and is potentially attractive for the development of catalyst libraries and derivatizing alkyne-rich materials and polymers. The reaction proceeds via initial migratory coupling of allyl and alkyne ligands (**a**)[11a] and is *presumably* followed by migratory cyclization (**b**) and β-hydride elimination (**c**). Cyclopentadiene hydride complex **I** then transforms into the cyclopentadienyl complex by dehydrogenation or, as we demonstrate for the hexamethylbenzene ruthenium system, by an unexpected alternative pathway involving hexamethylbenzene dealkylation.

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(7) The dealkylation of hexaalkylbenzenes is also observed in $AlCl_3$-mediated exchange reactions of (cyclopentadienyl)metal complexes under very harsh conditions: Fischer, E. O.; Elschenbroich, C. *Chem. Ber.* **1970**, *103*, 162. Roman, E.; Astruc, D. *Inorg. Chim. Acta* **1979**, *11*, L465. Astruc, D. *Tetrahedron* **1983**, *39*, 4027.

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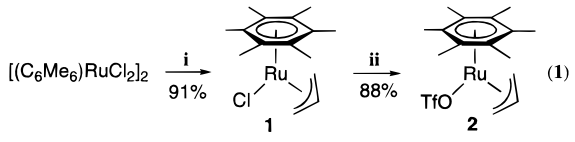
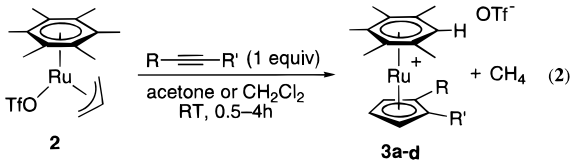
To support our investigation of allyl/alkyne [3 + 2 + 2] cycloaddition reactions,[11] the η^6-hexamethylbenzene ruthenium allyl complex **1** was prepared by modification of a literature procedure.[12] Thus, the reaction of Bennett's dimer[13] and tetraallyltin (1−2 equiv) in acetonitrile affords (η^6-C_6Me_6)Ru(allyl)Cl[14,15] (**1**) in near quantitative yield (eq 1).[16] Treatment with silver triflate provides inner-sphere triflate complex **2**, isolated from the reaction mixture as an analytically pure, thermally stable, mildly air-sensitive orange powder.[15]



Conditions: **i**. $(C_3H_5)_4Sn$, CH_3CN, RT, 12h; **ii**. AgOTf, acetone, RT, 2h.

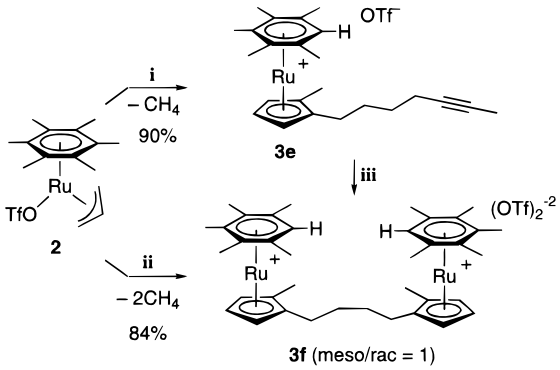
Either chloride complex **1** or triflate complex **2** can be used for subsequent allyl/alkyne cycloaddition reactions, the former in conjunction with in situ ionization using silver salts or highly polar solvents (e.g., CF_3CH_2-OH). The reactions of triflate complex **2**, however, generally proceed more cleanly and provide [3 + 2] cycloadducts in higher isolated yields. Treatment of the triflate complex at room temperature with 1 equiv[17] of a range of disubstituted alkynes provides the disubstituted cyclopentadienyl complexes **3a**−**d** in yields of 72−96% after purification by recrystallization (eq 2).[15,18] The



a. R, R' = Me 79%
b. R, R' = Ph 96%
c. R, R' = $-(CH_2)_6-$ 72%
d. R = Me, R' = ^{t}Bu 91%

new cyclopentadienyl ligands were identified by characteristic signatures in both the ^{1}H and ^{13}C NMR spectra: very small vicinal coupling constants ($^3J_{HH}$ = 2−3 Hz) for the methine hydrogen atoms and, where determined, large one-bond carbon−hydrogen coupling constants ($^1J_{CH}$ = 170−180 Hz) for the methine carbon atoms. NMR spectroscopic analysis, however, also reveals that in each case the symmetry of the hexamethylbenzene ligand is broken and a downfield singlet (^{1}H NMR: δ 5.9−6.1, 1H) is observed, consistent with the presence of a η^6-pentamethylbenzene ligand.

Scheme 1



Conditions: **i**. 2,8-decadiyne (1.6 equiv), acetone (high dilution), RT, 12h; **ii**. 2,8-decadiyne, CH_2Cl_2, 0 °C→RT, 2.5h; **iii**. Complex **3** (1 equiv), acetone, RT.

To confirm the dealkylation and determine the ultimate fate of the methyl group, the reaction with 2-butyne was carried out in a sealed NMR tube and monitored by ^{1}H NMR spectroscopy. The formation of methane was detected (0.15 ppm in acetone-d_6) and confirmed by comparison with an authentic sample.[15] In addition, photolysis of dimethylcyclopentadienyl complex **3a** (450W Hanovia lamp, Pyrex filter) in the presence of 3 equiv of trimethylphosphine leads to the liberation of pentamethylbenzene, identified by comparison to an authentic sample, and formation of the tentatively identified tris(phosphine) complex, [(η^5-$Me_2C_5H_3$)Ru(PMe_3)$_3$]$^+$OTf$^-$ (**4**).[15,19]

Exclusive dealkylation is also observed in the reactions of 2,8-decadiyne with triflate complex **3**, which can be converted with high selectivity into either mono(cyclopentadienyl) complex **3e** or tethered bis(cyclopentadienyl) complex **3f**, depending on reaction stoichiometry and conditions (Scheme 1).[15] The latter complex is formed as the expected inseparable 1:1 diastereomeric mixture.

The mechanism of the dealkylation process remains under investigation, but it is reasonable to posit the intermediacy of a diene hydride complex analogous to **I** in Figure 1 (Scheme 2). After that, we suggest that (reversible) migration of the hydride to the arene ligand[20] (Scheme 2) is more kinetically facile than dehydrogenation, providing hexamethylcyclohexadienyl intermediate **II** bearing an *exo*-methyl substituent. This species may, in principle, suffer direct radical scission (path **a**), as postulated by Chaudret to explain related ruthenium-mediated *exo*-methyl dealkylations.[5f] The significantly milder reaction conditions required for the present demethylation (below room temperature vs >100 °C), however, render such a radical mechanism

(12) Allylation of [(η^6-C_6H_6)$RuCl_2$)]$_2$ using tetraallyltin in acetonitrile: Baird, M. C. Zelonka, R. A. *J. Organomet. Chem.* **1972**, *44*, 383. The reported use of a large excess of the tin reagent unnecessarily complicates isolation and purification of the allylated product.

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(14) Bennett, M. A. Huang, T.-N.; Turney, T. W. *J. Chem. Soc., Chem. Commun.* **1979**, 312.

(15) Complete experimental, spectroscopic, and analytical data are provided as Supporting Information.

(16) The use of the more convenient allyltriphenyltin reagent is also effective, but the yield is somewhat lower (70−80%) and separation of the byproduct Ph_3SnCl requires chromatography.

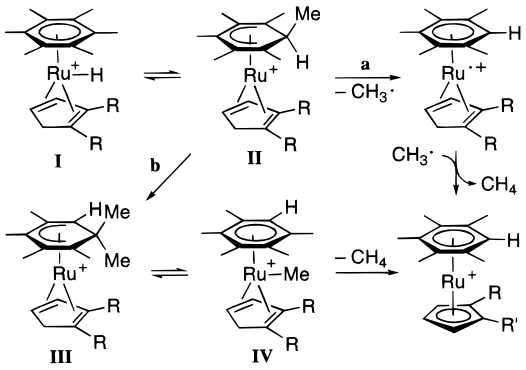
(17) For most disubstituted alkynes, the presence of excess alkyne has no significant effect on the course of the reaction. In the presence of excess 2-butyne, however, a more complicated reaction manifold is accessed. The reactions of terminal acetylenes and dimethylacetylene dicarboxylate also proceed via alternative reactivity patterns. These reactions will be discussed separately: Older, C. M.; Stryker, J. M. Manuscript in preparation.

(18) Demethylation occurs cleanly using either acetone or dichloromethane as reaction solvent.

(19) Tris(phosphine) complex **4** was not isolated from the photolysis mixture, but is spectroscopically very similar[15] to the known complex, [(η^5-C_5H_5)Ru(PMe_3)$_3$]$^+$$PF_6^-$: Bruce, M. I.; Wong, F. S.; Skelton, B. W.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1981**, 1398.

(20) Alkyl or hydride migration to a coordinated arene ring is rare, but documented: (a) Beard, L. K.; Silvon, M. P.; Skell, P. S. *J. Organomet. Chem.* **1981**, *209*, 245. (b) Brookhart, M.; Pinhas, A. R.; Lukacs, A. *Organometallics* **1982**, *1*, 1730. (c) Rush, P. K.; Noh, S. K.; Brookhart, M. *Organometallics* **1986**, *5*, 1745. (d) Kowalski, A. S.; Ashby, M. T. *J. Am. Chem. Soc.* **1995**, *117*, 12639.

Scheme 2



less attractive.[21] A more interesting and, perhaps, reasonable alternative involves 1,2-migration[22] of the *exo*-methyl group to form geminal dimethyl complex **III** (path **b**), which now projects an *endo*-methyl group into the coordination sphere of the unsaturated metal. The carbon−carbon bond activation then belongs to a relatively common class of β-carbon elimination reactions,[3,5] although such transformations also often require significantly harsher reaction conditions.[23] Itoh et al., however, have demonstrated that a similarly mild demethylation pathway exists in (C_5Me_5)Ru-mediated [4 + 2] diene/alkyne cycloaddition reactions, where it is suggested that the *endo*-methyl minor isomer of a ruthenium η^5-1-methylcyclohexadienyl intermediate undergoes carbon−carbon bond activation under conditions where the concomitantly formed *exo*-isomer does not.[5g] While it is not yet possible to rigorously exclude bimolecular dealkylation mechanisms, we note that the reaction of triflate complex **2** with diphenylacetylene proceeds slowly but exclusively to demethylated product **3b** even at high dilution (<0.0003 M in ruthenium). No intermediates were detected in a reaction monitored at room temperature by ^{1}H NMR spectroscopy.

The steric origin of the driving force for this general demethylation process is supported by allyl/alkyne cycloaddition in the corresponding η^6-pentamethylbenzene series: the reaction of (η^6-pentamethylbenzene)-Ru(η^3-allyl)OTf[15,24] and diphenylacetylene provides mainly η^6-*penta*methylbenzene product **3b** (>80%), accompanied by trace amounts of several unidentified, but presumably demethylated byproducts.[15] Further mechanistic investigations are in progress.

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Supporting Information Available: Experimental procedures and complete spectroscopic and analytical data for all new compounds (8 pages). Ordering information is given on any current masthead page.

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(21) The Chaudret mechanism was developed to rationalize ruthenium-mediated angular methyl dealkylations observed in stereochemically defined unsaturated steroidal substrates, reactions for which various alternative mechanisms can be discounted.[5f]

(22) A sigmatropic shift on the *exo*-face of a coordinated ligand was proposed by Crabtree[5c] to account for rearranged products observed from the reactions of 1,1-dialkylcyclopentanes with an unsaturated iridium complex.

(23) The closely related complex [(dppe)Ru(1,1-dimethylcyclohexadienyl)$(CH_2Cl_2)]^+PF_6^-$, bearing a labile ligand and both *endo*- and *exo*-methyl substituents, nonetheless requires 12 h at 90 °C to induce methyl migration to the metal center.[5h]

(24) This complex was prepared by the same methodology used to synthesize triflate complex **2**.[15]