Highly Stereoselective, Molybdenum-catalysed [6 + 2]-Cycloadditions of α,β-Unsaturated Ketones to Cyclohepta-1,3,5-triene

Thomas Schmidt,* Frank Bienewald and Richard Goddard

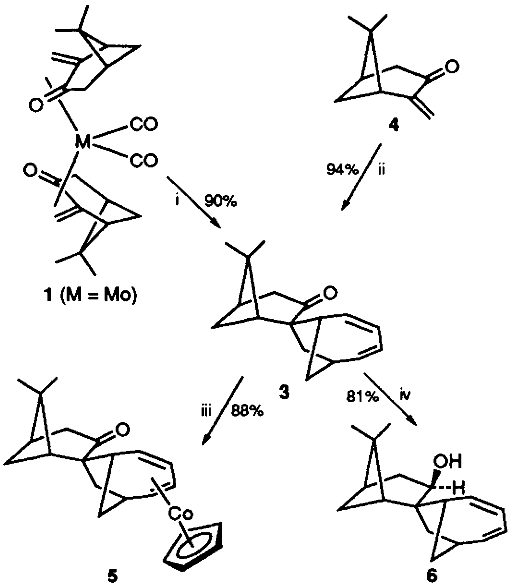
Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, D-45470 Mülheim an der Ruhr, Germany

Cycloheptatriene undergoes highly peri- and diastereo-selective [6 + 2]-cycloaddition reactions with 1-oxadienes in the presence of catalytic amounts of η^4-oxadiene molybdenum complexes under mild conditions; the stereochemistry of a cycloadduct derivative **6** and that of the corresponding tungsten oxadiene complex suggests that cycloheptatriene attacks the oxadiene from the metal free side.

The use of transition metal complexes as components in cycloaddition reactions is already well established, *e.g.* in [2 + 1]- or [4 + 2]-addition reactions of various carbene complexes.[1] Furthermore, tricarbonyl(η^6-cycloheptatriene)chromium has been shown to react with electron deficient alkenes or 1,3-dienes in [6 + 2]- and [6 + 4]-cycloadditions, respectively, after photochemical[2a] or thermal[2b] activation of the carbonyl complex. However, apart from stoichiometric reactions, very few examples of related catalytic reactions have recently been published.[3] Conditions for these reactions are also rather drastic, *i.e.* temperatures above 130 °C, and about 9–15 mol% of a chromium complex as catalyst are needed.

Using molybdenum η^4-oxadiene complexes, which can easily be obtained according to our procedure published[4] for the *R*-(+)-pulegone complex, we have found that metal catalysed [6 + 2]-cycloaddition reactions proceed smoothly at 50 °C or below. Analogous tungsten complexes exhibit a slightly lower catalytic activity. Bicyclo[4.2.1]nonadiene derivatives are obtained from cycloheptatriene and β-unsubstituted α,β-unsaturated ketones with extremely high peri- and diastereo-selectivity.

In a stoichiometric procedure, the molybdenum complex **1**[5] of the chiral terpene ketone (1*R*)-(+)-pinocarvone was treated with an excess of cycloheptatriene in benzene at room temp. under argon to yield the known tricarbonyl(η^6-cycloheptatriene)molybdenum **2** along with the cycloadduct **3** within 2 h. After oxidative decomposition of **2** and chromatography on silica gel, **3** was obtained in 90% yield as a colourless, crystalline compound.



Scheme 1 *Reagents and conditions*: i, 3 equiv. C_7H_8, benzene, 20 °C, argon, 2 h; ii, 5 mol % catalyst **1**, 1.1 equiv. C_7H_8, THF, 50 °C, argon, 12 h, then 1 h stirring under air; iii, 1 equiv. $(\eta^5\text{-}C_5H_5)Co(C_2H_4)_2$, hexane, 45 °C, 2 h; iv, 1.1 equiv. DIBALH in n-hexane, CH_2Cl_2, −78 to +20 °C, then 2N HCl, H_2O

The same compound can be prepared even more conveniently and on multigram scale from pinocarvone **4** and cycloheptatriene in the presence of only catalytic amounts (3–5 mol%) of complex **1** (M = Mo) at 50 °C in THF under argon. After stirring in air for 1 h and filtration using a pad of silica gel, analytically pure **3** (yield 94%) was obtained. It is worthy of note that none of any cycloadduct could be obtained by thermal activation (120 °C), in the presence of Lewis acids ($TiCl_4/AlCl_3$) or under high pressure (13 kbar) at temperatures up to 70 °C. In the first two of these cases, complete decomposition and/or polymerisation of the oxadiene occurred, whereas no reaction at all was observed in the last case.

It was found by GLC and NMR spectroscopy of the crude reaction mixture that only a single diastereomer of compound **3**† [(1R,7S)-2,2-dimethyl-[1,3 : 7,12]-dimethanospiro[5,7]-trideca-8,10-dien-5-one] is formed. Its stereochemistry could not, however, be unambiguously derived from the complex NMR spectra. As it has not been possible to obtain crystals of **3** suitable for X-ray structure determination, two kinds of chemical derivatization have been performed. First, reaction with η^5-cyclopentadienylbis(η^2-ethene)cobalt(I)[6] in hexane diastereospecifically yields a cyclopentadienylcobalt diene complex **5**† with increased signal dispersion of the vinylic protons, thus allowing us to prove by ^{1}H-COSY experiments[7] that **5**, and implicitly also **3**, are conjugated dienes and that the latter therefore is a [6 + 2]-cycloadduct. Independently, ketone **3** can be reduced with diisobutyl aluminium hydride to yield the alcohol **6**,† again diastereospecifically. With alkyl and aryl Grignard reagents **3** undergoes enolization[8] instead of being alkylated at the carbonyl group. On recrystallization from methanol, clear, colourless crystals of **6** can be obtained and these were subjected to X-ray crystallographic investigation in order to clarify the stereochemistry.‡

The result is shown in Fig. 1(*a*), together with the structure of dicarbonylbis[η^4-(1*R*)-pinocarvone]tungsten [**1**, M = W, Fig. 1(*b*)]‡ which is isostructural with the molybdenum

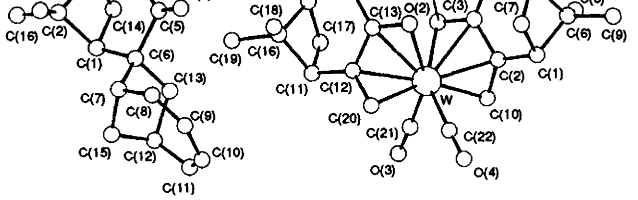


Fig. 1 Molecular structures of **6**(*a*) and **1** (M = W) (*b*). Selected bond distances (Å) and angles (°) for **6**, independent molecules averaged: O1–C5 1.431(5), C5–C6 1.566(6), C6–C13 1.544(6), O1–C5–C6 115.0(3), C5–C6–C13 110.0(7), O1–C5–C6–C13 89.1(8); and for **1** (M = W): W–O1 2.248(3), W–O2 2.217(4), W–C3 2.408(6), W–C13 2.367(5), W–C2 2.271(5), W–C12 2.280(5), W–C10 2.257(5), W–C20 2.262(5), O1–C3 1.298(6), O2–C13 1.260(6), C2–C3 1.399(7), C12–C13 1.409(7), C2–C10 1.442(8), C12–C20 1.439(7), O1–C3–C2 118.4(5), O2–C13–C12 120.7(5), C3–C2–C10 116.9(5), C13–C12–C20 114.1(5), C21–W–C22 87.1(2), O1–C3–C2–C10 16.0(10), O2–C13–C12–C20 15.8(9).

complex.[9] The two structures reveal important information about the mechanism of the cycloaddition. C_2-symmetrical complexes **1**, where only the sterically less hindered diastereotopic face of the oxadiene moiety is coordinated to the metal, are *exclusively* formed on complexation of pinocarvone **4**. This coordination mode is therefore also most likely to occur in intermediate structures of the catalytic reaction. As a result, the cycloheptatriene must have approached the coordinated oxadiene from the outside in order to yield compound **3**, *i.e.* away from where the metal was originally located in the complex. This makes it difficult to understand how a simultaneous activation of alkene and triene at the same metal centre could have taken place, as has previously been assumed for other metal-mediated [6 + 2]-cycloadditions.[2] It thus appears that a different mechanism is involved in the reactions reported here.

The X-ray study of **6** also reveals that the diene fragment is oriented towards the oxygen atom of alcohol and hence the preceding ketone **3**. This can be explained in terms of minimal steric hindrance during the approach of the cycloheptatriene. We may surmise that π-interaction between carbonyl and diene fragments of the molecule plays an additional role and could be responsible for the selectivity that is observed even in the absence of significant steric bulk.

Finally, it can be seen from Fig. 1(*a*) that the reduction of **3** has occurred by attack from the sterically less hindered face of the carbonyl group, *i.e.* opposite to the dimethylmethano bridge, as would be expected from steric bulk considerations.

The catalytic cycloaddition procedure described above has already been successfully applied to several β-unsubstituted α,β-unsaturated ketones, *e.g.* 2-methylenecycloheptanone and 3-phenylbut-3-en-2-one. With 1-oxadienes alkylated in the β-position, *e.g.* (*E*)-5-methylhex-3-en-2-one, only a stoichiometric reaction could be achieved hitherto starting from dicarbonylbis(oxadiene)molybdenum or tungsten complexes. Nevertheless, in all these cases, bicyclo[4.2.1]nona-2,4-dienes are formed exclusively and with high diastereoselectivity.[7]

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Footnotes

† Satisfactory analytical data including elemental analyses or high resolution mass spectra were obtained for compounds **3**, **5** and **6**. Spectral data supplied.

‡ *Crystal data*: **6**: $C_{17}H_{24}O$, $M = 244.4$ g mol^{-1}, crystal size 0.04 × 0.28 × 0.35 mm, $a = 15.037(2)$, $b = 16.465(2)$, $c = 12.702(2)$ Å, $\beta = 114.063(9)°$, $V = 2871.4$ Å^3, $T = 293$ K, $D_c = 1.13$ g cm^{-3}, $\mu = 4.85$ cm^{-1}, $F(000) = 1072$ e, $Z = 8$, monoclinic, space group *C*2 [No. 5], Enraf-Nonius CAD4 diffractometer, $\lambda = 1.54178$ Å, measuring method ω-2θ, 6135 measured reflections [$\pm h, \pm k, +l$], $[\sin\theta/\lambda]_{max} = 0.63$ Å^{-1}, 5867 independent and 3714 observed reflections [$I > 2\sigma(I)$], 324 refined parameters, hydrogen atom positions calculated and not included in least-squares refinement, $R = 0.060$, $R_w = 0.057$ [$w = 1/\sigma^2(F_0)$], final difference Fourier $\rho = 0.51$ e Å^{-3}. Fig. 1(*a*) shows one of the two similar independent molecules.

1 (M = W): $C_{22}H_{28}O_4W$, $M = 540.3$ g· mol^{-1}, crystal size 0.28 × 0.43 × 0.37 mm, $a = 24.422(6)$, $b = 6.733(1)$, $c = 14.429(4)$ Å, $\beta = 117.56(2)°$, $V = 2103.5$ Å^3, $T = 293$ K, $D_c = 1.71$ g· cm^{-3}, $\mu = 56.30$ cm^{-1}, $F(000) = 1064$ e, $Z = 4$, monoclinic, space group *C*2 (No. 5), empirical absorption correction, min. 0.786 max. 0.9997, Enraf-Nonius CAD4 diffractometer, $\lambda = 0.71096$ Å, measuring method ω-2θ, 7777 measured reflections [$\pm h, \pm k, +l$], $[\sin\theta/\lambda]_{max} = 0.75$ Å^{-1}, 6139 independent and 5181 observed reflections [$I > 2\sigma(I)$], 244 refined parameters, hydrogen atom positions calculated and not included in least-squares refinement, $R = 0.030$, $R_w = 0.020$ [$w = 1/\sigma^2(F_o)$], enantiopol parameter (Flack) 0.01, final difference Fourier $\rho = 1.61$ e Å^{-3}. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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