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James R. Green
University of Windsor

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James R. Green*

Chemistry and Biochemistry, School of Physical Sciences, University of Windsor, Windsor, Ontario, N9B 3P4, Canada

Fax (519)-973-7098; E-Mail: jgreen@uwindsor.ca

Abstract: Hexacarbonyldicobalt complexes of cycloheptenynes (**4**) may be prepared by the ring closing metathesis of the corresponding acyclic dienes (**2**) using Grubbs' catalyst, $(Cy_3P)_2Cl_2Ru$=CHPh. A cyclooctenyne complex (**8**) has also been prepared in the strictly analogous manner.

Key words: alkyne complexes, metathesis, ring closure, ruthenium, transition metals

The synthesis of cyclic alkynes of limited thermodynamic stability[1] has been facilitated by their availability in protected form as transition metal complexes, most notably the hexacarbonyldicobalt complexes.[2] This tactic has, in particular, been exploited in the preparation of cycloheptyne and cyclohexyne complexes [3,4] and their heterocyclic analogues. [5] We have been involved recently in the development of methods of rapid access to cycloheptenyne hexacarbonyldicobalt complexes,[4] and are particularly interested in the application of this class of compounds to terpenoid synthesis. Nevertheless, the types of approaches to these cycloheptyne systems is quite limited, relying largely on propargyl cation attack by allylsilanes[3a, 3c, 4] or other alkenes (carbocyclic),[3b] alcohols or silyl ethers (heterocyclic),[5b-d] or by lactonization (heterocyclic).[5a, 6] One subclass of this group of compounds that is particularly attractive is those bearing an oxygen atom in the propargylic position, due the ready ability to further functionalize at such sites. [7,8] Lewis acid mediated cyclization reactions with allylsilanes have not given us ready access to these compounds, and alternative routes for access to such compounds is therefore of interest. The mildness of conditions and functional group tolerance of ring-closing metathesis (RCM) reactions, particularly employing the Grubbs' catalyst, $(Cy_3P)_2Cl_2Ru$ =CHPh, has resulted in the rapid development of this approach to ring synthesis. [9,10] The process has in

many cases shown success in forming medium-sized rings. [11] As a result, we have addressed the viability of employing such olefin metathesis reactions of dienyne complexes **1** and **2**.

Suggested location for structures **1-4**

Initial work on **1a** was disappointing. Subjecting this compound to 10 mol% $(Cy_3P)_2Cl_2Ru$=CHPh in CH_2Cl_2 resulted in only ca. 10% conversion to the corresponding cycloheptenynol **3**, regardless of reaction temperature or time. Use of a disubstituted alkene in the allylic alcohol fragment, as in **1b**, resulted in some improvement in conversion, and **3** could be obtained in 55% yield (69% based on recovered starting material) (Table 1, entry 1). Acetylation of the alcohol function proved to be still more effective, as subjecting the resultant **2a** to 10 mol% of the Ru catalyst at room temperature for 3 h gave **4a** in 80% yield, with only a trace of starting material remaining (entry 2).

With a successful combination of substrate and reaction conditions in hand, several other dienyne complexes (**2**) were studied, including substrates (**2f, g, h**) without an oxygen function at the propargylic site. In the majority of cases the reactions would reach approximately 90-95% conversion at the 10% catalyst loading, with isolated yields of **4a** – **h** ≥ 80 %.[12,13] Longer reaction times resulted in no further conversion to cycloheptenyne.[14] The success of the reaction was not significantly affected by substitution at the other propargylic site, or in the cases with homoallylic versus allylic acetate functions. Despite the small amount of starting material recovered in most instances, in only two cases (**2c**, **2f**) (entries 6, 11) was the improvement upon employing 15 mol% of catalyst judged to warrant its use. The propargylic acetate/alcohol containing products (**3**, **4a-e**) could be separated from the starting materials by silica gel chromatography, whereas **4f-h** were isolated with the presence small amounts of unreacted starting material. The diastereomers of products **4b** and **4c** also could not be separated (1:1

diastereomeric ratios in each case), whereas the diacetate diastereomers of **4d** could be separated readily. In the case of this **2d-4d** conversion, the *syn-/anti-* mixture and the individual *syn-* diastereomer of **2d** transformed stereospecifically into the *trans-*/*cis-* diastereomeric mixture (entry 6) and pure *trans-* diastereomer (entry 7) of **4d**, respectively, with no sign of epimerization at the propargylic sites.[15] Geminally disubstituted substrates **5a** and **5b** did not undergo ring-closing metathesis, consistent with the known lower reactivity of 2- substituted alkenes. [16]

Suggested location for Table 1

Although our primary concern was the preparation of seven membered systems, approaches to both eight and six membered cases were briefly investigated. In the event, dienyne complexes **6a** and **6b** failed to react to afford any cyclohexenyne complex. Conversely, dienyne **7** gave eight membered complex **8** in good yield (76%, 79% based on recovered starting **7**) (entry 14) under directly analogous conditions. In none of the cases investigated has the Schrock catalyst, $Mo(C_{10}H_{12})(C_{12}H_{17}N)[OC(CH_3)(CF_3)_2]_2$, shown any ability to induce ring closing metathesis.

Suggested location for structures **5-8**

To the best of our knowledge, there have no previous reports of ring closing metathesis reactions on alkyne-cobalt complexes. In related work, ring closing metathesis by the Grubbs' catalyst has been reported to be unaffected by the presence of a non-participating macrocyclic diyne-tetracobalt complex.[17] While the current work was in progress, Paley reported the ring-closing metathesis of η^4-(diene)iron tricarbonyl complexes to give a cycloheptadiene- and a cyclohexadiene complex.[18] A limited number of other substrates containing transition metal fragments have been shown to undergo RCM.[19] The vast majority of systems capable of undergoing ring-closing metathesis to afford medium sized rings possess a conformational

restraint to facilitate the cyclization. It is our contention that the large size of the $Co_2(CO)_6$ unit[20] and the ca. 140^o bond angles at the formal alkynyl carbon atoms in alkyne-$Co_2(CO)_6$ complexes serve as acyclic conformational constraints in the current case. Since older and unpurified samples of these dienyne complexes tended to undergo RCM to more limited conversions, it is our belief that trace amounts of decomposition products formed during reaction, perhaps Co(II) species, are responsible for the gradual consumption of the ruthenium alkylidene catalyst. Although the relative failure of allylic alcohol substrates may simply be the result of slower cyclization, Hoye has demonstrated recently the destructive consumption of the Grubbs' catalyst by secondary allylic alcohols in cases where the allyl alcohol double bond is clearly the initial site of metathesis.[21]

In summary, rapid access to cycloheptenyne-$Co_2(CO)_6$ complexes in good yield is available via ring closing metathesis chemistry. Work on subsequent chemistry of the propargylic acetate complexes, particularly as they apply to creating tethers for intramolecular Pauson-Khand reactions, and investigation into the suitability of the newer imidazolidene- based catalysts, [22] are in progress.

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Footnotes and References

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(12) **Typical Experimental Procedure**: To a solution of **2e** (0.1526 g) in CH_2Cl_2 (15 mL) was added a solution of $Cl_2(Cy_3P)_2Ru{=}CHPh$ (0.0270 g) in CH_2Cl_2. The solution was stirred for 3 h. Following removal of the solvents under reduced pressure, silica gel chromatography (20:1 petroleum ether : Et_2O) afforded sequentially recovered **2e** (0.0161 g, 11%) and **4e** (0.1177 g, 82%).

(13) (**3**) IR (neat, KBr) 3425 br, 3029, 2933, 2092, 2049, 2021 cm^{-1}; ^1H NMR δ 5.86 (br s, 2H), 5.62 (d, J = 3.3, 1H), 3.19 (dt, J = 17.0, 4.1, 1H), 2.98 (ddd, J = 3.5, 11.9, 17.0, 1H), 2.33 (m, 1H), 2.22 (m, 1H), 2.13 (d, J = 3.3, 1H); ^{13}C NMR δ 199.6, 138.5, 129.1, 97.8, 71.9, 33.3, 27.1. MS *m/e* 394 (M^+), 366 (M^+-1CO), 338 (M^+-2CO), 310 (M^+-3CO), 254 (M^+-5CO), 226 (M^+-6CO); HRMS *m/e* for $C_{13}H_8Co_2O_7$ calcd (M^+) 393.8934, found 393.8938. (**4a**) IR (neat, KBr) 3035, 2940, 2093, 2051, 2021, 1747 cm^{-1}; ^1H NMR δ 6.70 (br s, 1H), 5.94 (m, 1H), 5.78 (dt, J = 11.2, 2.2, 1H), 3.18 (dt, J = 17.1, 4.3, 1H), 3.00 (ddd, J = 3.7, 11.4, 17.1, 1H), 2.25 – 2.33 (m, 2H), 2.30 (s, 3H); ^{13}C NMR δ 199.3, 170.4, 134.3, 130.4, 98.0, 93.0, 73.9, 33.2, 27.2, 20.6. MS *m/e* 408 (M^+-1CO), 380 (M^+-2CO), 352 (M^+-3CO), 324 (M^+ - 4CO), 296 (M^+-5CO), 268 (M^+-6CO); HRMS *m/e* for $C_{15}H_{10}Co_2O_8$ calcd (M^+-1CO) 407.9090, found 407.9103. (**4b**) (1:1 diastereomeric mixture) IR (neat, KBr) 3036, 2962, 2021, 2048, 2021, 1747 cm^{-1}; ^1H NMR δ 6.67 (s) and 6.62 (s) (1H), 5.95 (m) and 5.84 (m) (1H), 5.78 (d, J = 11.0) and 5.73 (d, 11.7) (1H),

3.00 (m) and 2.79 (m) (1H), 2.45 (m) and 2.34 (m) (1H), 2.18 (s) and 2.16 (s) (3H), 1.92 (m, 1H of one diastereomer), 1.45 – 1.75 (4H of one diastereomer, 5H of remaining diastereomer), 0.95 – 1.03 (m, 3H); ^{13}C NMR δ 199.6, 170.5 and 170.4, 134.3 and 131.2, 130.1 and 130.0, 104.1 and 103.7, 94.0 and 91.9, 74.1 and 73.1, 42.8 and 41.1, 41.0 and 39.2, 33.5 and 32.7, 20.9 and 20.73, 20.67 and 20.6, 14.01 and 13.99. MS *m/e* 478 (M^+), 450 (M^+-CO), 422 (M^+-2CO), 394 (M^+ - 3CO), 366 (M^+-4CO), 338 (M^+-5CO); (**4c**) (1:1 diastereomeric mixture) IR (neat, KBr) 3034, 2930, 2091, 2048, 2017, 1747 cm^{-1}; ^{1}H NMR δ 6.67 (s) and 6.61 (s) (1H), 5.82 – 6.00 (m, 1H), 5.77 (d, J = 10.9) and 5.73 (d, J = 11.9) (1H), 2.98 (m) and 2.77 (m) (1H), 2.45 (m) and 2.37 (m) (1H), 2.18 (s) and 2.16 (s) (3H), 1.90 (m, 1H of one diastereomer), 1.25 – 1.70 (m, 8H of one diastereomer, 9H of remaining diastereomer), 0.92 (br t, J = 6.6, 3H); ^{13}C NMR δ 199.5, 170.4 and 170.3, 134.3 and 131.1, 130.1 and 130.0, 104.1 and 103.6, 94.0 and 91.9, 74.1 and 73.1, 43.1 and 41.4, 38.8 and 37.1, 33.6 and 32.8, 31.9 and 31.8, 27.5 and 27.4, 22.59 and 22.56, 20.62 and 20.58, 14.0. MS *m/e* 478 (M^+-1CO), 450 (M^+-2CO), 394 (M^+ - 4CO), 366 (M^+-5CO), 338 (M^+-6CO); HRMS *m/e* for $C_{20}H_{20}Co_2O_8$ calcd (M^+-2CO) 449.9924, found 407.9927. (***trans*-4d**) IR (neat, KBr) 3038, 2929, 2098, 2057, 2029, 1743 cm^{-1}; ^{1}H NMR δ 6.61 (s, 1H), 5.94 (dt, J = 11.1, 4.3, 1H), 5.88 (m, obscured, 1H), 5.86 (dd, J = 11.3, 4.3, 1H), 2.61 (m, 1H), 2.34 (m, 1H), 2.18 (s, 3H), 2.15 (s, 3H); ^{13}C NMR δ 198.6, 170.3, 170.0, 136.9, 125.6, 95.3, 91.8, 73.8, 72.7, 33.2, 20.8, 20.6. MS *m/e* 466 (M^+-1CO), 438 (M^+-2CO), 410 (M^+-3CO), 382 (M^+-4CO), 354 (M^+-5CO), 326 (M^+-6CO); HRMS *m/e* for $C_{17}H_{12}Co_2O_{10}$ calcd (M^+-2CO) 437.9196, found 437.9195. (***cis*-4d**) IR (neat, KBr) 3025, 2926, 2099, 2063, 2015 cm^{-1}; ^{1}H NMR δ 6.55 (s, 1H), 6.10 (dd, J = 4.4, 8.2, 1H), 5.7 – 5.8 (m, 2H), 2.64 (m, 1H), 2.50 (m, 1H), 2.17 (s, 3H), 2.12 (s, 3H); ^{13}C

NMR δ 198.3, 170.23, 170.17, 131.6, 126.5, 94.7, 91.8, 73.0, 72.7, 32.9, 20.7, 20.6. MS *m/e* 466 (M^+-1CO), 438 (M^+-2CO), 410 (M^+-3CO), 382 (M^+-4CO), 354 (M^+-5CO), 326 (M^+-6CO); HRMS *m/e* for $C_{17}H_{12}Co_2O_{10}$ calcd (M^+-1CO) 465.9145, found 465.9143. (**4e**) IR (neat, KBr) 3022, 2929, 2095, 2063, 2015, 1747 cm^{-1}; ^1H NMR δ 5.99 (dd, J = 3.8, 10.9, 1H), 5.93 (m, 1H), 5.82 (m, 1H), 3.69 (apparent d, J = 3.4, 2H), 2.60 (m, 1H), 2.40 (m, 1H), 2.13 (s, 3H); ^{13}C NMR δ 199.3, 170.3, 130.7, 126.0, 97.7, 93.6, 73.4, 33.6, 33.2, 20.7. MS *m/e* 408 (M^+-1CO), 380 (M^+-2CO), 352 (M^+-3CO), 324 (M^+ - 4CO), 296 (M^+-5CO), 268 (M^+-6CO); HRMS *m/e* for $C_{15}H_{10}Co_2O_8$ calcd (M^+-2CO) 379.9141, found 379.9139. (**4f**) IR (neat, KBr) ν_{max} 3026, 2935, 2090, 2045, 2014 cm^{-1}; ^1H NMR δ 5.97 (m, 1H), 5.87 (m, 1H), 3.69 (d, J = 4.8, 2H), 3.10 (dd, J = 6.5, 5.5, 2H), 2.32 (ddd, J = 6.5, 6.5, 5.5, 2H); ^{13}C NMR δ 200.0, 132.0, 129.7, 100.6, 95.5, 34.0, 33.5, 27.2. MS *m/e* 378 (M^+), 350 (M^+-1CO), 322 (M^+-2CO), 294 (M^+-3CO), 266 (M^+-4CO), 238 (M^+-5CO), 210 (M^+-6CO); HRMS *m/e* for $C_{13}H_8Co_2O_6$ calcd (M^+) 377.8985, found 377.8988. (**4g**) IR (neat, KBr) ν_{max} 3026, 2962, 2088, 2045, 2014 cm^{-1}; ^1H NMR δ 5.95 (m, 1H), 5.85 (m, 1H), 3.69 (apparent d, J = 5.0, 2H), 2.89 (m, 1H), 2.33 (m, 1H), 2.01 (m, 1H), 1.66 (m, 1H), 1.40-1.65 (m, 3H), 1.00 (t, J = 7.1, 3H); ^{13}C NMR δ 200.3, 131.2, 129.0, 106.5, 95.1, 43.0, 40.3, 33.7, 33.2, 20.9, 14.0. MS *m/e* 392 (M^+-1CO), 364 (M^+-2CO), 336 (M^+-3CO), 308 (M^+ - 4CO), 280 (M^+-5CO), 252 (M^+-6CO); HRMS *m/e* for $C_{16}H_{14}Co_2O_6$ calcd (M^+-1CO) 391.9505, found 391.9505. (**4h**) IR (neat, KBr) ν_{max} 3026, 2928, 2089, 2049, 2015 cm^{-1}; ^1H NMR δ 5.95 (m, 1H), 5.86 (m, 1H), 3.68 (apparent d, J = 5.1, 2H), 2.86 (m, 1H), 2.33 (m, 1H), 1.98 (m, 1H), 1.65 (m, 1H), 1.30-1.60 (m, 7H), 0.93 (m, 3H); ^{13}C NMR δ 200.1, 131.3, 129.0, 106.4, 95.1, 43.3, 38.2, 33.7, 33.3, 31.9, 27.5, 22.6, 14.0. MS *m/e* 420 (M^+-1CO), 392 (M^+-2CO), 364 (M^+-3CO), 336 (M^+ -

4CO), 308 (M^+-5CO). (**8**) IR (neat, KBr) ν_{max} 3019, 2935, 2087, 2044, 2016 cm^{-1}; ^1H NMR δ5.93 (br s, 2H), 3.14 (apparent t, J = 5.0, 4H), 2.43 (m, 4H); ^{13}C NMR δ 200.3, 131.6, 98.8, 38.0, 27.3. MS *m/e* 392 (M^+), 364 (M^+-1CO), 336 (M^+-2CO), 308 (M^+-3CO), 280 (M^+-4CO), 252 (M^+-5CO), 224 (M^+-6CO); HRMS *m/e* for $C_{14}H_{10}Co_2O_6$ calcd (M^+) 391.9141, found 391.9140.

(14) Conversion of **2a** to **4a** ceased at approximately 1.5 h. Use of 5 mol% catalyst gave only 60% conversion of starting material.

(15) The stereochemical assignments for **2d** and **4d** rest on the assignment of *trans*- **4d** based on its NOESY cross-peak between the allylic methine (δ 6.61) and the methylene proton (δ 2.34) *trans*- diaxial to the remaining methine (δ 5.86).

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