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A General Approach to Medium Ring Alkynes by Using Metathesis of Cobalt Hexacarbonyl Containing Dienes

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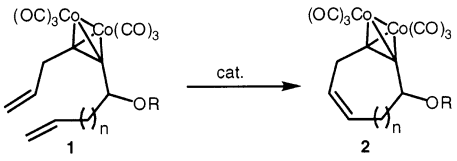
The assembly of medium sized rings (7−9) was achieved by using the metathesis of dienes linked by a cobalt hexacarbonyl complexed alkyne with either Grubbs' or Schrock's catalysts. The products of metathesis were subjected to transformations involving the dicobalt hexacarbonyl complexes, for example, decomplexation to liberate cyclic alkynes or Pauson−Khand reaction.

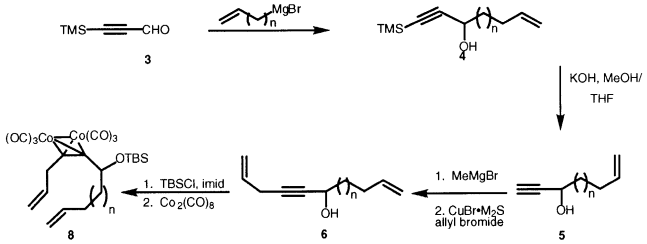
The ring-closing metathesis reaction has been incorporated into the synthetic chemists methods for synthesizing compounds containing rings.[1] This incorporation includes medium ring closures.[2] Our approach to the synthesis of strained ring compounds encompassed the synthesis of medium-sized rings that contained triple bonds as part of the superstructure.[3] However, because the triple bond would work against ring closure in a medium ring setting, it was decided to package the triple bond as a dicobalt hexacarbonyl complex. The increasing number of known transformations of cobalt complexes made the route attractive.

In an earlier paper, ring closure was demonstrated to be possible in the presence of a secondary organometallic group.[4] The present work revolves around ring size and functional group compatability (**1** → **2**, Scheme 1).

SCHEME 1



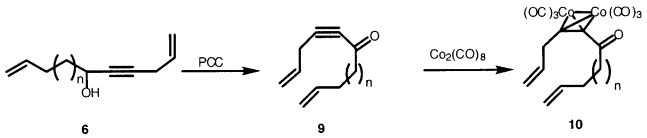
SCHEME 2



Substrate Preparation

Substrates **1** were synthesized following the published approach.[3] As shown in Scheme 2, trimethylsilyl propynal **3** was treated with 3-butenylmagnesium bromide, or 4-pentenylmagnesium bromide to furnish **4**, and then desilylated with potassium hydroxide/methanol to afford **5**.[5] The resulting alcohol was deprotonated with methylmagnesium bromide and the derived anion was subjected to allylation in the presence of copper bromide dimethyl sulfide complex to afford **6**.[6] The alcohol functional group was silylated to afford protected **7**.[7] This material was converted to the dicobalthexacarbonyl-protected alkyne **8** (92%), which completed formation of the metathesis precursor.[8] Alternatively, **6** was oxidized to the ketone using PCC to give **9**, and then complexed to afford metathetical ring closure precursor **10** (Scheme 3).[9]

SCHEME 3



The corresponding acetates were prepared through acylation of the alcohol (**6** → **11**) followed by preparation of the dicobalt hexacarbonyl (**12**, Scheme 4).[10]

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(7) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

(8) Greenfield, H.; Sternberg, H. W.; Friedel, R. A.; Wotiz, J. H.; Markby, R.; Wender, I. *J. Am. Chem. Soc.* **1956**, *78*, 120.

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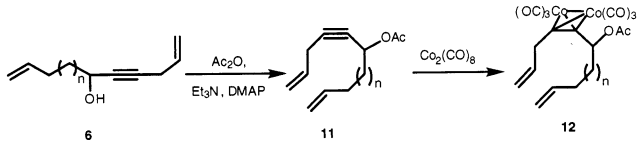
SCHEME 4



SCHEME 5

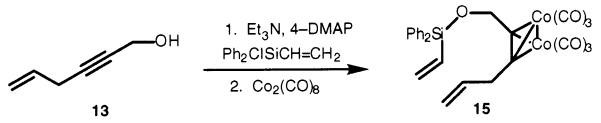
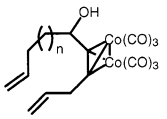
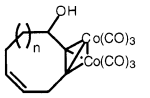
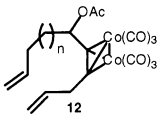
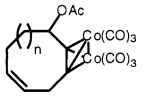
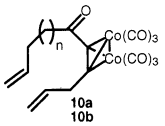
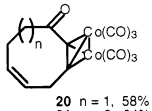
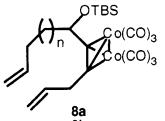
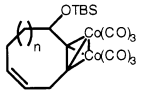
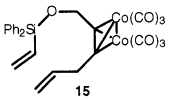
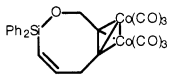


TABLE 1. Metathesis Ring Closure of Dicobalthexacarbonyl Dienes[a]

entry	substrate	product	conditions
1		 **16** n = 0, 11% **17** n = 1, 29% **18** n = 2, 43%	25 mol% a 30 mol% a 35 mol% b
2	 **12**	 **19** n = 1, 55%	25 mol% a
3	 **10a** **10b**	 **20** n = 1, 58% **21** n = 2, 64%	44 mol% a 25 mol% a
4	 **8a** **8b** **8c**	 **22** n = 0, 73% **23** n = 1, 87% **24** n = 2, 83%	25 mol% a 15 mol% a 25 mol% a
5	 **15**	 **25** n = 1, 48%	52 mol% c

[a] Reagents and conditions: (a) $(PCy_3)_2Cl_2Ru{=}CHPh$, CH_2Cl_2, rt; (b) $(PCy_3)_2Cl_2Ru{=}CHPh$, CH_2Cl_2, 37 °C; (c) 2,6-diisopropylphenylimidoneophylidene-molybdenum(VI) bis(hexafluoro-*tert*-butoxide), CH_2Cl_2.[11] All yields refer to isolated material.

A siloxane precursor was prepared from a known eneyne-ol as shown in Scheme 5. Silylation of the alcohol functional group in **13** with use of a vinylsilyl chloride produced the silyl ether **14** (not shown) that was complexed with dicobalt hexacarbonyl to afford **15** (Scheme 5).

Results

The results of ring closure are shown in Table 1. In general ring closure was effected with Grubbs' catalyst at room temperature. It is notable that ring sizes 7−9 were acquired in fair to good yield and a variety of functional groups were tolerated under metathesis conditions.

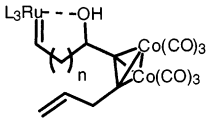


FIGURE 1.

A trend for the cyclization of alcohols (entries 1 a−c) is notable in that the yield of cyclic alcohol increased with increasing ring size. This may be an artifact of intramolecular complexation of the hydroxyl group to the intermediate metal alkylidene ruthenium center, which is produced after metathetical exchange (Figure 1). In this way as the tether length separating the OH and the metal increases, the yield of cyclic alcohol increases. This process may also be operative in the ketone series.[19]

The medium ring cyclic silyl ether required the use of Schrock's catalyst as a stoichiometric reagent in agreement with Denmark's findings.[12] This particular substrate gave 80% yield based on recovered starting material.

A six-membered-ring precursor was synthesized. Treatment of trimethylsilylpropynal with vinyl Grignard reagent gave allylic alcohol **26**. The alcohol was protected as the *tert*-butyldimethylsilyl ether by using *tert*-butyldimethylsilyl chloride and imidazole to afford **27**. The acetylene was unmasked using Haven's conditions to give **28** and then deprotonated with methylmagnesium bromide. The derived anion was reacted with allyl bromide in the presence of copper bromide to afford **29**, and then complexed with dicobalt octacarbonyl to complete a synthesis of **30**. It was found that metathesis of this structure did not occur with either catalyst at room temperature or at elevated temperature. Thus the seven-membered ring currently represents the lower limit for this type of ring closure.

Applications of the complexes were studied in preliminary form. Two medium ring structures were subjected to decomplexation employing ceric ammonium nitrate and acetone,[13] as shown in Scheme 7. Structures **18** and **21** gave rise to the cyclic alkynes **31** and **32** in modest yield.

Alcohol **18** was also subjected to Nicholas' conditions involving the free hydroxyl group to afford the allyl ether **33** (Scheme 8).[14] This reaction was followed by the Pauson−Khand reaction, which occurred in straightforward fashion when conducted in *tert*-butyl methyl sulfide and 1,2-dichloroethane.[15]

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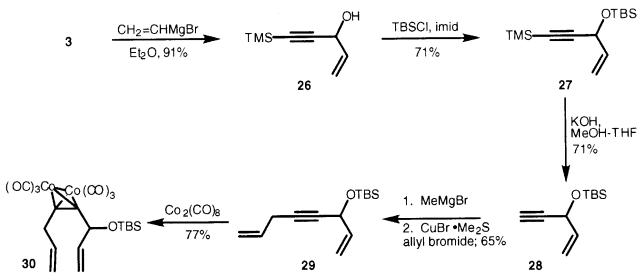
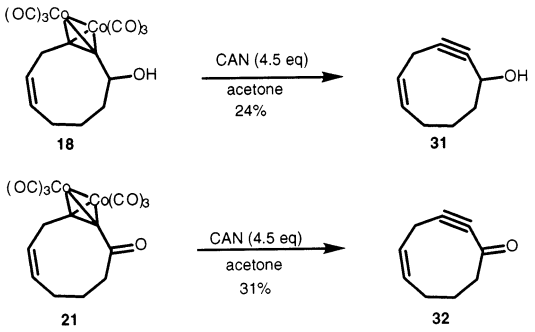
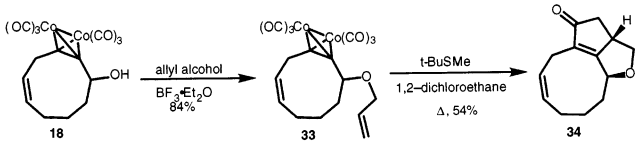
SCHEME 6



SCHEME 7



SCHEME 8



In conclusion, medium rings can be prepared in latent form by using the metathesis of cobalt hexacarbonyl complex linked alkenes. The further development of the chemistry surrounding these structures and their application in synthesis will be reported in due course.

Experimental Section

Hexacarbonyl-μ-[η4-4-nona-1,8-dien-5-yn-4-ol]dicobalt-(Co−Co) (Precursor to 16). To a stirred solution of 9.0 mg (66 μmol) of diene **5** in 0.5 mL of CH_2Cl_2 was added 24.8 mg (73 mmol) of dicobalt octacarbonyl. The reaction mixture was stirred at room temperature for 14 h, concentrated in vacuo, and directly chromatographed over 2 g of silica gel (eluted with 25:1, hexanes−ethyl acetate) to afford 25.8 mg (83%) as a red oil that was stored below 0 °C under nitrogen: IR (neat) 3466 (m, broad), 3083 (m), 3011 (m), 2983 (m), 2909 (m), 2475 (w), 2092 (s), 2049 (s), 2019 (s), 1859 (m), 1641 (m), 1606 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.04−5.86 (m, 2H), 5.28−5.14 (m, 4H), 4.86−4.79 (m, 1H), 3.58 (d, J = 7.1 Hz, 2H), 2.61−2.36 (m, 2H), 2.06 (d, J = 4.2 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 199.7 (s, 6C), 135.7 (d), 134.0 (d), 118.8 (t), 117.5 (t), 99.9 (s), 96.3 (s), 71.5 (d), 43.79 (t), 38.2 (t).

Hexacarbonyl-μ-[η4-5-cyclohepten-1-yn-3-ol]dicobalt-(Co−Co) (16). To a solution of 58.0 mg (137 μmol) of the above complex in 3 mL of CH_2Cl_2 was added 28.3 mg (34 μmol, 25 mol %) of bis(tricyclohexylphosphine)benzylidineruthenium-(IV) dichloride. The reaction mixture was stirred for 16 h, concentrated in vacuo, and chromatographed over 20 g of silica gel (eluted with 10:1, hexanes−ethyl acetate) to afford 6.0 mg of **16** (11%) as a red oil: IR (neat) 3417 (m, broad) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.92−5.75 (m, 2H), 4.95−4.87 (m, 1H), 3.68 (d, J = 2.2 Hz, 2H), 2.66−2.57 (m, 1H), 2.36−2.22 (m, 1H), 1.95 (d, J = 5.6 Hz, 1H); ^{13}C NMR (69.2 MHz, $CDCl_3$) δ 199.3 (s, 6C), 130.0 (d), 126.8 (d), 102.3 (s), 93.3 (s), 71.9 (d), 36.7 (t), 33.5 (t); exact mass calcd for $C_{13}H_8O_7Co_2$ ($M^{\bullet+}$) m/z 393.8934, found m/z 393.8936.

Anal. Calcd for $C_{13}H_8O_7Co_2$: C, 39.62; H, 2.05. Found: C, 39.50; H, 2.33.

1-(Trimethylsilyl)hept-6-en-1-yn-3-ol (4a). To a stirred solution of 6 mL of ether was added 408 mg (16.8 mmol) of magnesium, a catalytic amount of iodine, and then 1.5 mL (2.0 g, 15 mmol) of 4-bromo-1-butene as a solution in 10 mL of ether dropwise over 10 min. The reaction mixture was allowed to briefly reflux and then stirred for 40 min at room temperature. The resulting solution was transferred dropwise via syringe to another vessel charged with 1.324 g (10.5 mmol) of **3** as a solution in 8 mL of ether at −78 °C over 10 min. The reaction mixture was stirred for 20 h at room temperature, and then was quenched by dropwise addition of 13 mL of an aqueous solution of saturated NH_4Cl. The aqueous layer was extracted with three 30-mL portions of ether. The combined organic layers were washed with 15 mL of brine, dried ($MgSO_4$), and concentrated in vacuo to afford 1.73 g (91%) of **4a** as a colorless oil that was suitable for use in further reations without purification: IR (neat) 3336 (s, broad) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.84 (ddt, J = 17.1, 10.3, 6.7 Hz, 1H), 5.11−4.97 (m, 2H), 4.44−4.35 (m, 1H), 2.28−2.19 (m, 2H), 2.00 (d, J = 4.0 Hz, 1H), 1.81 (m, 2H), 0.18 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 137.6 (d), 115.2 (t), 106.5 (s), 89.7 (s), 62.3 (d), 36.7 (t), 29.4 (t), −0.2 (q, 3C); exact mass calcd for $C_9H_{15}SiO$ ($M^{\bullet+}$− CH_3) m/z 167.0892, found m/z 167.0899 ($M^{\bullet+}$ not observed).

Anal. Calcd for $C_{10}H_{18}SiO$: C, 65.87; H, 9.95. Found: C, 65.80; H, 9.99.

Deca-1,9-dien-6-yn-5-ol (6a). To a solution of 628 mg of alcohol **5a** (5.70 mmol) in 26 mL of THF at 0 °C was added 4.6 mL (13.7 mmol) of a 3 M solution of methylmagnesium bromide in ether. The mixture was heated to 50 °C for 40 min, cooled to −20 °C, followed by addition of 294 mg (1.43 mmol) of copper(I) bromide−dimethyl sulfide complex and 0.60 mL (830 mg, 6.8 mmol) of allyl bromide. The resulting solution was heated under reflux for 15 h, cooled to room temperature, and quenched with 6.0 mL of water, followed by 22 mL of saturated aqueous NH_4Cl and 6 mL of 10% (v/v) HCl. The blue aqueous layer was extracted with three 30-mL portions of ether and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product was chromatographed over 30 g of silica gel (eluted with 10:1, hexanes−ethyl acetate) and distilled (80 °C/15 Torr) to afford 647 mg (76%) of **6a** as a colorless oil: IR (neat) 3350 (s, broad), 3080 (m), 2979 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.90−5.74 (m, 2H), 5.32 (dd, J = 17.0, 1.7 Hz, 1H), 5.15−4.97 (m, 3H), 4.46−4.38 (m, 1H), 3.03−2.96 (m, 2H), 2.28−2.19 (m, 2H), 1.90 (d, J = 5.4 Hz, 1H), 1.84−1.75 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 137.7 (d), 132.3 (d), 116.2 (t), 115.2 (t), 83.4 (s), 82.2 (s), 62.1 (d), 37.1 (t), 29.4 (t), 23.0 (t); exact mass calcd for $C_{10}H_{13}O$ ($M^{\bullet+}$ − H) m/z 140.0966, found m/z 140.0969 ($M^{\bullet+}$ not observed).

5-(*tert*-Butyldimethylsiloxy)-deca-1,9-dien-6-yne (7a). To a solution of 229 mg (1.53 mmol) of alcohol **6a** in 9.0 mL of CH_2Cl_2 was added 277 mg (1.84 mmol) of *tert*-butyldimethylsilyl chloride and 168 mg (2.45 mmol) of imidazole. The reaction mixture was stirred for 15 h at room temperature. The crude product was directly chromatographed over 40 g of silica gel (eluted with 200:1, hexanes−ethyl acetate) to afford 362 mg (90%) of **7a** as a colorless oil: IR (neat) 3081 (m), 2953 (s) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.92−5.74 (m, 2H), 5.32 (dd, J = 17.0, 1.6 Hz, 1H), 5.10−4.93 (m, 3H), 4.37 (t, J = 6.4 Hz, 1H), 3.03−2.96 (m, 2H), 2.24−2.15 (m, 2H), 1.81−1.70 (m, 2H), 0.91 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 138.1 (d), 132.5 (d), 116.0 (t), 114.8 (t), 84.1 (s), 81.0 (s), 62.5 (d), 38.1 (t), 29.5 (t), 25.8 (q, 3C), 23.0 (t), 18.2 (s), −4.4 (q), −5.0 (q); exact mass calcd for $C_{12}H_{19}OSi$ ($M^{\bullet+}$ − C_4H_9) m/z 207.1205, found m/z 207.1214 ($M^{\bullet+}$ not observed).

Anal. Calcd for $C_{16}H_{28}OSi$: C, 72.66; H, 10.67. Found: C, 72.79; H, 10.62.

Hexacarbonyl-μ-[η4-5-(*tert*-butyldimethylsiloxy)deca-1,9-dien-6-yne]dicobalt(Co−Co) (8a). To a solution of 101 mg (383 μmol) of silyl ether **7a** in 2.5 mL of CH_2Cl_2 was added 144 mg (421 μmol) of dicobalt octacarbonyl at room temperature. The reaction mixture was stirred for 16 h and directly chromatographed over 40 g of silica gel (eluted with pentane) to afford 194 mg (92%) of **8a** as a red oil: IR (neat) 3083 (m), 2954 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.02−5.75 (m, 2H), 5.24−4.99 (m, 4H), 4.84 (t, J = 7.1 Hz, 1H), 3.56 (d, J = 6.8 Hz, 2H), 2.18 (q, J = 7.2 Hz, 2H), 1.97−1.74 (m, 2H), 0.92 (s, 9H), 0.15 (s, 3H), 0.13 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 200.1 (s, 6C), 137.5 (d), 135.7 (d), 117.4 (t), 115.0 (t), 101.5 (s), 96.8 (s), 72.5 (d), 40.3 (t), 38.5 (t), 29.6 (t), 25.8 (q, 3C), 18.1 (s), −4.1 (q), −4.3 (q); exact mass calcd for $C_{20}H_{28}O_5SiCo_2$ ($M^{\bullet+}$ − 2CO) m/z 494.0370, found m/z 494.0356 ($M^{\bullet+}$ not observed).

Hexacarbonyl-μ-[η4-3-(*tert*-butyldimethylsiloxy)-6-cycloocten-1-yne]dicobalt(Co−Co) (23). To a solution of 111 mg (201 μmol) of silyl ether **8b** in 9.0 mL of CH_2Cl_2 was added 24.8 mg (30.2 μmol, 15 mol %) of bis(tricyclohexylphosphine)-benzylidineruthenium(IV) dichloride. The reaction mixture was stirred for 17 h, concentrated in vacuo, then directly chromatographed over 40 g of silica gel (eluted with pentane) to afford 93.1 mg (87%) of **23** as a red oil: IR (neat) 3026 (m), 2953 (s), 2933 (s), 2889 (m), 2860 (s), 2473 (w), 2089 (s), 2050 (s), 1600 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.02−5.94 (m, 1H), 5.79 (q, J = 8.8 Hz, 1H), 4.82 (dd, J = 9.9, 5.0 Hz, 1H), 3.59 (d, J = 5.9 Hz, 2H), 2.29−2.05 (m, 3H), 1.64−1.52 (m, 1H), 0.92 (s, 9H), 0.13 (s, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 200.40 (s, 6C), 133.40 (d), 130.12 (d), 101.67 (s), 98.12 (s), 74.72 (d), 34.94 (t), 32.36 (t), 25.86 (q, 3C), 23.40 (t), 18.14 (s), −4.51 (q 2C); exact mass calcd for $C_{20}H_{24}O_7SiCo_2$ ($M^{\bullet+}$) m/z 521.9955, found m/z 521.9973.

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Supporting Information Available: Spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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