J. Org. Chem. **1997,** *62,* 1299−1304 **1299**

Transition-Metal-Mediated *Exo*-Selective Diels−Alder Reactions for the Preparation of Octalones with Unusual Stereochemistries. Reactions of 2-Cobaloxime-Substituted 1,3-Dienes with Cyclohexenones in Thermal and Lewis Acid-Catalyzed [4 + 2] Cycloadditions

B. Matthew Richardson and Mark E. Welker*,†

Department of Chemistry, Wake Forest University, P.O. Box 7486, Winston-Salem, North Carolina 27109

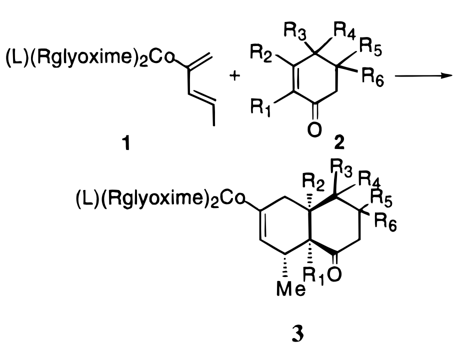
Received November 5, 1996⊗

2-Cobaloxime−(*E*)-1,3-pentadienyl complexes (cobaloxime = pyridine(dimethylglyoxime)$_2$cobalt(III)) react with a variety of cyclohexenones in [4 + 2] cycloaddition reactions. These cycloaddition reactions produce octalones with *cis* ring junctions through *exo* transition states. The octalones are removed from the cobalt via demetalation reactions that replace the cobalt with a hydrogen and provide pyr(dmg)$_2$CoMe, which can be recycled into the synthesis of the starting dienyl complex.

Introduction

Over the last 4 years, we have prepared cobalt-substituted 1,3-dienes (**1**) and examined the rates, regioselectivities, and stereoselectivities of their reactions with dienophiles in Diels−Alder reactions.[1] During this time, Tada and co-workers have reported alternative preparations of some cobaloxime-substituted dienes as well as results of their cycloaddition reactions;[2] other groups have also reported that the alternate strategy of transition-metal substitution in the dienophiles can have a pronounced effect on 4 + 2 cycloaddition diastereoselectivities.[3] The diastereoselectivities of the Diels−Alder reactions of these cobaloxime dienyl complexes (**1**) are unusual for acyclic dienes in that products arising from *exo* transition states are the major products. We have postulated that this *anti* (*exo*) selectivity is a result of metal ligand set−dienophile steric interactions that disfavor *endo* transition states.

Cyclohexenones (**2**) have traditionally been poor dienophiles in thermal and Lewis acid−catalyzed Diels−Alder reactions.[4] We were hopeful that our very reactive cobaloxime−substituted dienes (**1**) would react with these dienophiles under mild conditions to produce high yields of cycloadducts with excellent diastereoselectivity and without concomitant ring junction isomerization from *cis*- to *trans*-octalones.[4] Here, we report our results of thermal and Lewis acid−catalyzed Diels−Alder reactions of cobaloxime dienyl complexes (**1**) with cyclohexenones (**2**).



Experimental Section

General Methods. For a description of instrumentation and chromatographic adsorbents used see ref 1b. Cobalt chloride hexahydrate used in the preparation of dienyl complexes was purchased from Strem Chemicals and used as received. Trimethylaluminum, triethylaluminum, 2-cyclohexen-1-one, 4,4-dimethyl-2-cyclohexen-1-one, and all boron-containing Lewis acids were purchased from Aldrich Chemicals and used as received. (3*E*)-1,3-Pentadien-2-yl(pyridine)bis(dimethylglyoximato)cobalt(III) (**8b**),[1b,e] (3*E*)-1,3-pentadien-2-yl[4′-(dimethylamino)pyridine]bis(dimethylglyoximato)cobalt(III) (**8a**),[1b,e] 6-oxo-1-cyclohexene-1-carboxylic acid ethyl ester (**18**),[5] and 6-oxo-1-cyclohexene-1-carboxylic acid *tert*-butyl ester (**23**)[6] were prepared according to previously described methods. 3,5,5-Trimethyl-6-oxo-1-cyclohexene-1-carboxylic acid ethyl ester (**29**)[7] was prepared via a modification of a previously reported method as described below. All reactions were performed under an atmosphere of nitrogen unless specified otherwise.

8α-Methyl-3,4,4aα,5,8,8aα-hexahydro-1-oxo-(2*H*)-naphthalen-6-yl[4′-(*N*,*N*-dimethylamino)pyridine]bis(dimethylglyoximato)cobalt(III) (10). Diene **8a** (200 mg, 0.418 mmol) was dissolved in 2-cyclohexen-1-one (2.5 mL) in a sealed

---

* To whom correspondence should be addressed. FAX: (910) 759-4321. E-mail: welker@wfu.edu.

† Henry Dreyfus Teacher−Scholar Awardee (1994−99).

⊗ Abstract published in *Advance ACS Abstracts,* February 1, 1997.

(1) (a) Smalley, T. L.; Wright, M. W.; Garmon, S. A.; Welker, M. E.; Rheingold, A. L. *Organometallics* **1993**, *12*, 998. (b) Wright, M. W.; Smalley, T. L.; Welker, M. E.; Rheingold, A. L. *J. Am. Chem. Soc.* **1994**, *116*, 6777. (c) Stokes, H. L.; Richardson, B. M.; Wright, M. W.; Vaughn, S. P.; Welker, M.E.; Liable-Sands, L.; Rheingold, A. L. *Organometallics*, **1995**, *14*, 5520. (d) Wright, M. W.; Welker, M. E. *J. Org. Chem.* **1996**, *61*, 133. (e) Stokes, H. L., Welker, M. E., *Organometallics* **1996**, *15*, 2624. (f) Wright, M. W.; Stokes, H. L.; Richardson, B. M.; Adams, T. A.; Smalley, T. L.; Vaughn, S. P.; Lohr, G. J.; Welker, M. E.; Liable-Sands, L.; Rheingold, A. L. *Advances in Cycloaddition*; Lautens, M., Ed.; JAI Press: Greenwich, CT, 1997; Vol. 4, in press.

(2) (a) Tada, M.; Shimizu, T. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1252. (b) Tada, M.; Mutoh, N.; Shimizu, T. *J. Org. Chem.* **1995**, *60*, 550.

(3) (a) For a recent review of transition-metal-mediated cycloaddition reactions see: Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49. (b) Sabat, M.; Reynolds, K. A.; Finn, M. G. *Organometallics* **1994**, *13*, 2084. (c) Gilbertson, S. R.; Zhao, X.; Dawson, D. P.; Marshall, K. L. *J. Am. Chem. Soc.* **1993**, *115*, 8517. (d) Anderson, B. A.; Wulff, W. D.; Powers, T. S.; Tribbitt, S.; Rheingold, A. L. *J. Am. Chem. Soc.* **1992**, *114*, 10784. (e) Barluenga, J.; Canteli, R.-M.; Florez, J.; Garcia-Granda, S.; Gutierrez-Rodriguez, A. *J. Am. Chem. Soc.* **1994**, *116*, 6949.

(4) For recent reviews of thermal and Lewis acid-catalyzed Diels−Alder reactions of 2-cyclohexenones see: (a) Fringuelli, F.; Minuti, L.; Pizzo, F.; Taticchi, A. *Act. Chem. Scand.* **1993**, *47*, 255. (b) Fringuelli, F.; Taticchi, A.; Wenkert E. *Org. Prep. Proc. Int.* **1990**, *22*, 131.

(5) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434.

(6) Kato, M.; Kamat, V. P.; Yoshikoshi, A. *Synthesis* **1988**, *9*, 699.

(7) Andreeva, L. N.; Perlova, T. G.; Negrebetskii, V. V.; Dymova, S. F.; Koroleva, T. I.; Shvetsova-Shilovaskaya, K. D.; Promonenkov, V. K. *J. Org. Chem. USSR* **1981**, *17*, 1800.

S0022-3263(96)02076-2 CCC: $14.00

tube. The mixture was heated (75 °C) for 24 h and then cooled to 25 °C. CH_2Cl_2 (5 mL) was added, and the crude product was purified on silica, first eluting with Et_2O to remove unreacted dienophile followed by EtOAc to remove cycloadduct **10**. Solvent was removed by rotary evaporation, and the resultant precipitate was vacuum dried to give a bright yellow powder (**10**) (130 mg, 0.226 mmol, 54%). Mp: 151−154 °C dec. ^1H NMR ($CDCl_3$): δ 8.07 (d, $J = 7.0$ Hz, 2H), 6.37 (d, $J = 7.0$ Hz, 2H), 4.93 (d, $J = 2.4$ Hz, 1H), 2.94 (s, 6H), 2.57−2.45 (m, 2H), 2.20−2.11 (m, 1H), 2.08 (s, 6H), 2.06 (s, 6H), 2.02−1.81 (m, 3H), 1.80−1.46 (m, 4H), 1.39−1.20 (m, 1H), 0.77 (d, $J = 6.9$ Hz, 3H) ^{13}C NMR ($CDCl_3$): δ 214.85, 154.2, 149.3, 149.1, 148.9, 127.5, 107.5, 57.8, 39.0, 38.7, 38.2, 36.5, 31.6, 25.6, 22.7, 20.9, 14.1, 12.1. IR ($CDCl_3$): 2956, 2928, 1691, 1622, 1537, 1390, 1232, 1013 cm^{-1}. HRFABMS: *m/z* calcd for $C_{26}H_{39}N_6O_5Co$ 574.2314, found 574.2314.

8*β*-Methyl-3,4,4a*β*,5,8,8a*β*-hexahydro-1-(2*H*)-naphthalenone (11) from 10. Cycloadduct **10** (51 mg, 0.089 mmol) was dissolved in dry THF (5 mL). The solution was cooled to 0 °C, and then $AlMe_3$ (100 μL of a 2 M solution in hexanes, 0.20 mmol) was added. The solution was warmed to 25 °C after 0.5 h and stirred for 5 h. The solution was cooled to 0 °C, and H_2O (2 mL) was added. The water was extracted with CH_2Cl_2 (2 × 25 mL), and the organic layers were combined and dried over $MgSO_4$. The solvent was removed by rotary evaporation, and the product was purified on silica using 1:1 Et_2O/hexane to elute **11** as a pale yellow oil (12 mg, 0.073 mmol, 82%). ^1H NMR ($CDCl_3$): δ 5.64−5.39 (m, 2H), 2.61 (broad m, 1H), 2.41 (ddd, $J = 14.3, 3.2, 3.2$ Hz, 1H), 2.31 (d, $J = 4.6$ Hz, 1H), 2.28 (m, 2H), 2.02 (m, 2H), 1.83 (m, 2H), 1.70 (m, 2H), 0.95 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 213.1, 130.4, 124.0, 56.2, 39.6, 34.4, 28.2, 28.0, 27.8, 24.8, 20.1. IR ($CDCl_3$): 3155, 2961, 2929, 2872, 1705, 1460, 1380, 1093 cm^{-1}. EIHRMS: *m/z* calcd for $C_{11}H_{16}O$ 164.1201, found 164.1199. For spectroscopic data on closely related cycloadducts see ref 8. Further elution with EtOAc yielded a bright yellow powder (**12**) (12 mg, 0.028 mmol, 32%) after solvent removal by rotary evaporation and high vacuum, which proved identical to material previously reported[1c] by spectroscopic comparison.

8aα-Carbethoxy-8α-methyl-3,4,4aα,5,8-pentahydro-1-oxo-(2*H*)-naphthalen-6-yl[4′-(*N*,*N*-dimethylamino)pyridine]bis(dimethylglyoximato)cobalt(III) (19). Diene **8a** (65 mg, 0.136 mmol) was dissolved in dry THF (4 mL). 1-Cyclohexene-1-carboxylic acid 6-oxoethyl ester (**18**) (91.5 mg, 5.45 mmol) was added, and the solution was refluxed (72 h). The solvent was removed by rotary evaporation, and the product was dissolved in CH_2Cl_2 (1 mL). Cold hexane (10 mL) was added slowly, and the resulting yellow solid (**19**) was collected by vacuum filtration and then dried under vacuum (77 mg, 0.121 mmol, 89%). Mp: 168 °C dec. ^1H NMR ($CDCl_3$): δ 8.09 (d, $J = 7.0$ Hz, 2H), 6.38 (d, $J = 7.0$ Hz, 2H), 5.06 (d, $J = 5.1$ Hz, 1H), 4.08 (q, $J = 7.3$ Hz, 2H), 2.95 (s, 6 H), 2.80 (m, 1H), 2.59 (m, 1H), 2.18 (m, 2H), 2.10 (s, 6H), 2.05 (s, 6H), 1.98−1.46 (m, 6H), 1.17 (t, $J = 7.3$ Hz, 3 H), 0.70 (d, $J = 7.0$ Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 206.5, 171.9, 161.0, 154.2, 149.3, 149.1, 127.9, 107.5, 64.0, 60.5, 40.0, 39.0, 36.5, 33.5, 26.4, 25.6, 23.4, 17.6, 14.1, 12.1, 12.0. IR ($CDCl_3$): 3155, 2960, 1707, 1622, 1559, 1472, 1385, 1093 cm^{-1}. Anal. Calcd for $CoN_6O_7C_{28}H_{43}$; C, 52.99; H, 6.83. Found: C, 52.73; H, 6.63.

8aα-Carbethoxy-8α-methyl-3,4,4aα,5,8-pentahydro-1-(2*H*)-naphthalenone (20). Cycloadduct **19** (230 mg, 0.362 mmol) was dissolved in dry THF (10 mL). The solution was cooled to 0 °C, and then $AlMe_3$ (362 μL of a 2 M solution in hexanes, 0.725 mmol) was added. The solution was warmed to 25 °C after 0.5 h and stirred for 5 h. The solution was cooled to 0 °C, and H_2O (2mL) was added. The water was extracted with CH_2Cl_2 (2 × 25 mL), and the organic layers were combined and dried over $MgSO_4$. The solvent was removed by rotary evaporation, and the product was purified on silica using 1:1 Et_2O/hexane to elute **20** as a light yellow oil (60 mg, 0.254 mmol, 70%). ^1H NMR ($CDCl_3$): δ 5.62 (m, 1H), 5.50 (m, 1H), 4.18 (q, $J = 7.2$ Hz, 2H), 2.94−2.84 (m, 1H), 2.82−2.68 (m, 1H), 2.41−2.29 (m, 2H), 2.28−2.14 (m, 1H), 2.10−1.80 (m, 4 H), 1.63−1.48 (m, 1H), 1.24 (t, $J = 7.2$ Hz, 3H), 0.85 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 206.27, 170.79, 130.32, 122.58, 63.44, 60.95, 40.08, 33.46, 30.93, 26.12, 23.16, 17.32, 14.01, 0.97. IR ($CDCl_3$): 2969, 2935, 1709, 1469, 1383, 1247, 1221, 1085 cm^{-1}. HREIMS: *m/z* calcd for $C_{14}H_{20}O_3$ 236.1412, found 236.1412. Further elution with ethyl acetate, followed by solvent removal, yielded **12** as a yellow solid (79 mg, 0.185 mmol, 51%) identical by spectroscopic comparison to material prepared and characterized previously.[1c]

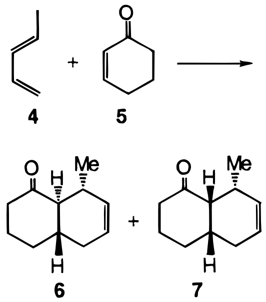
General Procedure for Lewis Acid-Catalyzed Reactions. Diene complex **8b** (100 mg, 0.23 mmol) was dissolved in CH_2Cl_2 (3.2 mL) and cooled to the desired temperature (−45 or −78 °C). $AlMe_3$ (230 μL of a 2.0 M solution in hexanes, 0.46 mmol), which had been cooled to 0 °C, was added, and gas evolution as well as a color change from light to dark orange were noted. A standard stock solution of dienophile (1.0 mL, 0.254 M (0.254 mmol) in CH_2Cl_2) that had been cooled to 0 °C was then added quickly. The "active" Lewis acid (0.115 mmol) (see Table 1 for specific ones used) was then added and allowed to stir under N_2 for 2−24 h depending on the boron Lewis acid used (see Table 1 for specific times). 2-Propanol/water (1:1, 1.5 mL) was then added, and the mixture was allowed to warm to 25 °C and then CH_2Cl_2 (10 mL) added. The solution was dried with $MgSO_4$, and then the solution was vacuum filtered and the salts were washed with CH_2Cl_2. The product was purified on silica gel (ethyl acetate). The solvent was removed by rotary evaporation, and the resultant orange powder was vacuum dried.

8α-Methyl-3,4,4aα,5,8,8aα-hexahydro-1-oxo-(2*H*)-naphthalen-6-yl(pyridine)bis(dimethylglyoximato)cobalt(III) (31). The procedure outlined above using 1 M *B*-chlorocatecholborane (120 μL, 0.115mmol) as the active Lewis acid produced **31** (121mg, 0.228 mmol, 99%). Mp: 138−140 °C dec. ^1H NMR ($CDCl_3$): δ 8.62 (d, $J = 6.6$ Hz, 2H), 7.68 (t, $J = 6.6$ Hz, 1 H), 7.30 (t, $J = 6.6$ Hz, 2 H), 4.94 (d, $J = 1.6$ Hz, 1H), 2.60−2.45 (m, 3H), 2.45−2.25 (m, 2 H), 2.20−1.85 (m, 2 H), 2.09, (s, 6H), 2.06, (s, 6H), 1.7−1.5 (m, 4 H), 0.79, (d, $J = 7.0$ Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 214.4, 150.1, 149.7, 149.5, 137.4, 127.8, 125.1, 57.6, 38.5, 38.2, 36.5, 31.5, 26.7, 25.4, 20.8, 12.1. IR ($CDCl_3$): 3155, 2984, 2902, 1700, 1506, 1473, 1382, 1093 cm^{-1}. Anal. Calcd for $CoN_5O_5C_{24}H_{34}$: C, 54.24; H, 6.45. Found: C, 54.27; H, 6.64.

8α-Methyl-3,4,4aα,5,8,8aα-hexahydro-1-(2*H*)-naphthalenone (11) from 31. Cycloadduct **31** (200 mg, 0.376 mmol) was dissolved in dry THF (10 mL). The mixture was cooled to 0 °C, and $AlMe_3$ (235 μL of a 2.0 M solution in hexanes, 0.470 mmol) was added via syringe. After 0.5 h, the solution was warmed to 25 °C and allowed to stir for 2.0 h. H_2O (2.0 mL) was added and the solution stirred for 10 min. CH_2Cl_2 (25 mL) was added, and then the solution was dried over $MgSO_4$. The Mg salts were removed by vacuum filtration and washed with CH_2Cl_2 (10 mL). The solvent was removed by rotary evaporation, and the resulting orange oil was purified by chromatography on silica using 1:1 Et_2O/hexane to give **11** as a pale yellow oil after solvent removal (44 mg, 0.268 mmol, 71%). This yellow oil was identical by spectroscopic comparison to **11** reported above. Further elution with EtOAc, followed by removal of solvent with rotary evaporation and high vacuum, gave an orange solid (**32**) (108 mg, 0.282 mmol, 75%) identical by spectroscopic comparison to pyr(DMG)$_2$CoMe reported and characterized previously.[1b]

Results and Discussion

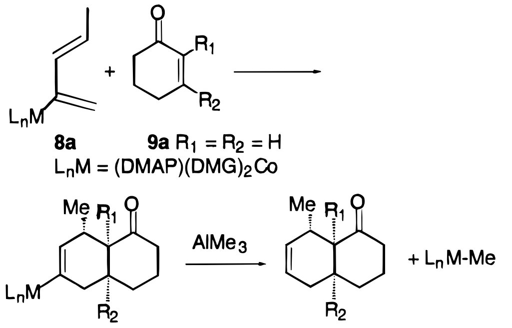
Thermal 4 + 2 Cycloadditions and Subsequent Demetalations. Cyclohexenone and alkyl-substituted cyclohexenones are notoriously poor dienophiles in Diels−Alder reactions with simple acyclic dienes. For example, the thermal Diels−Alder reaction between (*E*)-piperylene and cyclohexenone requires 142 h at 150 °C to produce a 1:1 mixture of *cis*- (**7**) and *trans*-octalones (**6**) in 46% yield. The use of aluminum chloride as a Lewis acid improved the yield (81%) and lowered the reaction temperature (40 °C) and time (96 h) but still produced a poor ratio of *cis*- (**7**) and *trans*-octalones (**6**).[8]



4 **5**

6 **7**

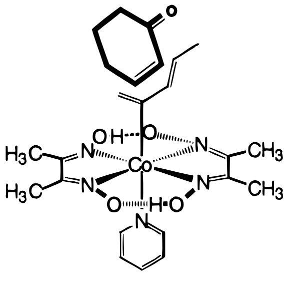
We have previously demonstrated that cobaloxime-substituted dienes participate in thermal and Lewis acid-catalyzed Diels–Alder reactions with dramatic rate enhancements compared to their acyclic organic diene counterparts.[1] Using 4-{dimethylamino}pyridine (DMAP) as an axial ligand in bis(dimethylglyoxime) (DMG) dienyl complexes rather than pyridine provided an additional 2–3-fold rate enhancement, so we picked the DMAP pentadienyl complex (**8a**) for our thermal Diels–Alder reactions with cyclohexenones.[1] DMAP dienyl complex (**8a**) was only about 20% reacted with cyclohexenone (**9a**) after 24 h at reflux in THF, so this reaction was performed in a sealed tube at 75 °C to produce octalone **11** after demetalation.



8a **9a** $R_1 = R_2 = H$
$L_nM = (DMAP)(DMG)_2Co$

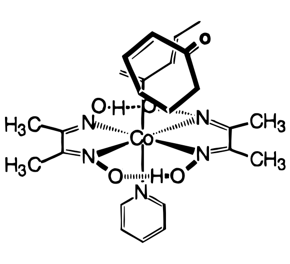
10 (54%) **11** (82%) **12** (32%)

The single diastereomer (**11**) reported is the product of the *exo* transition state with a *cis* ring junction, the *cis* ring junction being implicated by the $R_1 = H$, ^1H NMR resonance at δ 2.31 ($CDCl_3$, d, $J = 4.6$ Hz, 1H).[9] The ^1H NMR methyl resonance ($CDCl_3$, δ 0.95, d, $J = 7.2$ Hz, 3H) did not match the resonance reported previously for the *endo/cis* ring juncture (**6**) or the *endo/trans* (**7**) ring juncture,[8] which left *exo/cis* ring junction product (**11**) as the only possibility consistent with the observed ring junction coupling constant. Given our earlier observations of cobaloxime dienyl Diels–Alder products resulting from *exo* transition states,[1] we expected that the cyclohexenone would adopt a conformation where the bulk of the dienophile would be away from the dienyl complex's equatorial ligands (**13**).



Exo-Transition State

13

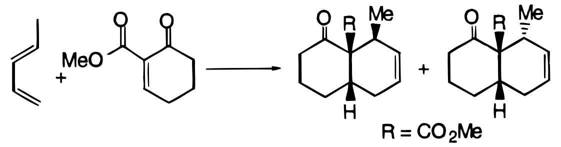


Endo-Transition State

14

2- and 3-Methylcyclohexenones are even poorer substrates than cyclohexenone in thermal Diels–Alder reactions.[4] 3-Methyl-2-cyclohexenone will not react with (*E*)-piperylene under a variety of thermal or Lewis acid-catalyzed conditions.[10] 3-Methyl-2-cyclohexenone is reported to require 25% $EtAlCl_2$, 4 equiv of (*E*)-piperylene, and heating at 50 °C under 12 kbar pressure for 16 h to produce a 60% yield of a 4.9:1 mixture of *cis* to *trans*-decalones.[10] 3-Methyl-2-cyclohexenone (**9b**, $R_1 = H$, $R_2 = Me$) proved unreactive toward **8b** ($L_nM = pyr(dmg)_2Co$) after 48 h at 75 °C in a sealed tube in THF, and we also noted significant diene decomposition. Likewise, 2,4,4-trimethylcyclohexenone (**9c**, $R_1 = Me$, $R_2 = H$, 4, 4 = Me) proved unreactive toward **8b** ($L_nM = pyr(dmg)_2Co$) with significant decomposition noted under identical thermal conditions. 3-Methyl-2-cyclohexenone did react thermally with DMAP dienyl complex (**8a**) when heated in a sealed tube at 100 °C for 24 h. Unfortunately, the temperature required for this cycloaddition caused significant decomposition of **8a**, and the mass balance for this reaction was repeatedly poor so the cycloadduct was not characterized.

Addition of an electron-withdrawing group such as a carbalkoxy group on the 2-position of 2-cyclohexenones was known to increase their reactivity in thermal Diels-Alder reactions, but these dienophiles were still problematic. For example, (*E*)-piperylene (**4**) is reported to react with 2-carbomethoxy-2-cyclohexen-1-one (**15**) ($SnCl_4$, −78 °C, 6 h, 34%) to produce a 5:3 mixture of the *exo* (with respect to the cyclohexenone) (**16**) and *endo* (with respect to the cyclohexenone) (**17**) products.[11] We first tried the analogous carboethoxy dienophile (**18**)[5] in a thermal cycloaddition with dienyl complex **8**. The cycloaddition proceeded in high yield and was highly diastereoselective for the *exo* (with respect to cyclohexenone) product **19**. This stereochemical assignment was confirmed by cobalt–carbon bond cleavage to produce **20**, which had a ^1H NMR spectrum analogous to **16**.[11] The methyl ^1H NMR doublet in **16** occurs at δ 0.83 ($CDCl_3$), whereas the same signal in **17** is at δ 1.17. The methyl doublet of **20** appears at δ 0.85 ($CDCl_3$), and we have previously observed that methyl doublets for all other related bicyclic *anti* (*exo*) products we have prepared are always upfield of the *syn* (*endo*) diastereomers. Attempts to shorten the reaction time by use of a sealed tube (75 °C, 24 h) resulted in an almost 1:1 mixture of diastereomers (**19** and its Me epimer) in 80% yield.



4 **15** **16** **17**

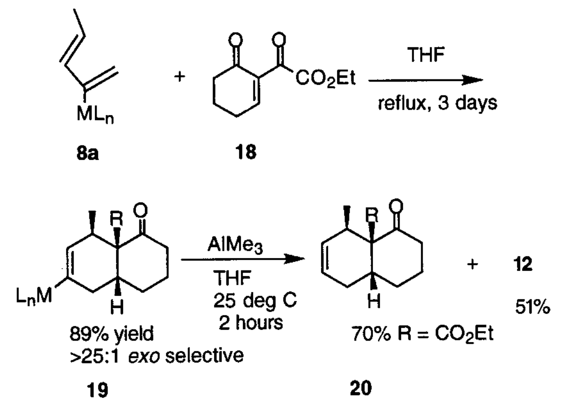
---

[8] Fringuelli, F.; Pizzo, F.; Taticchi, A.; Halls, T. D. J.; Wenkert, E. *J. Org. Chem.* **1982**, *47*, 5056.

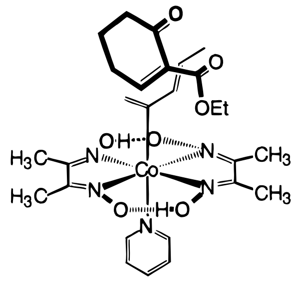
[9] Liu, H. J.; Browne, E. N. C. *Can. J. Chem.* **1987**, *65*, 1262.

[10] Aben, R. W. M.; Minuti, L.; Scheeren, H. W.; Taticchi, A. *Tetrahedron Lett.* **1991**, *32*, 6445.

[11] (a) Liu, H.-J.; Ngooi, T. K.; Browne, E. N. C. *Can. J. Chem.* **1988**, *66*, 3143. (b) Liu, H.-J.; Ngooi, T. K. *Can. J. Chem.* **1984**, *62*, 2676.

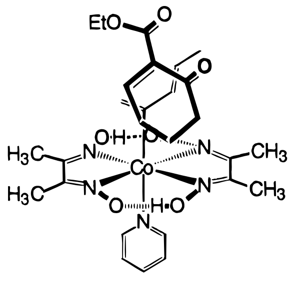


Production of diastereomer **19** arising from a *exo* transition state with respect to the cyclohexenone **21** would be expected on steric grounds. The *endo* (with respect to cyclohexenone) transition state **22** would place the bulk of the cyclohexenone ring close to the metal's equatorial ligand set. This observed reactivity of a dienyl complex (**8a**), which exhibits complete *exo* selectivity with respect to the cyclohexenone, is much better than the 5:3 selectivity for this product (**20**), which was noted for Lewis acid catalyzed Diels–Alder reactions of (*E*)-piperylene.[11]



Exo-Transition State

21



Endo-Transition State

22

If the transition state arguments presented by structures **21** and **22** are correct, then bulkier ester substituents should produce more *endo* product (with respect to the cyclohexenone portion of the dienophile). Indeed, carbo-*tert*-butoxy dienophile **23**[6] reacted with **8a** to produce a 1:2 mixture of *exo* (**24**) and *endo* (**25**) products. The stereochemical assignments were again made after AlMe$_3$-mediated cobalt carbon bond cleavage to yield **26** and **27**, which had ^{1}H NMR methyl doublets at δ 0.90 and 0.95 (CDCl$_3$), respectively. The most downfield methyl doublet is assigned to **27** by analogy to **16** and **17**.[11]

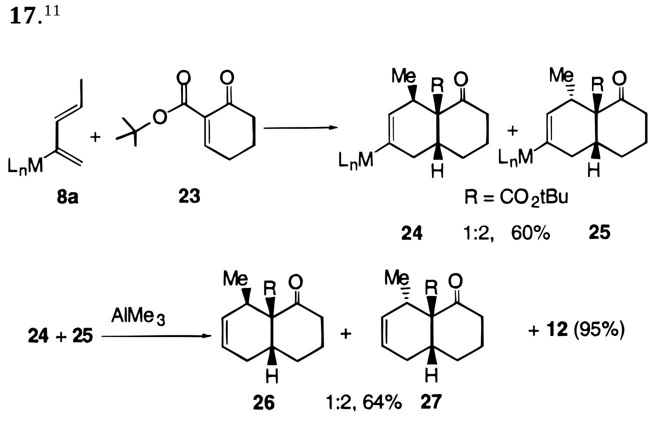
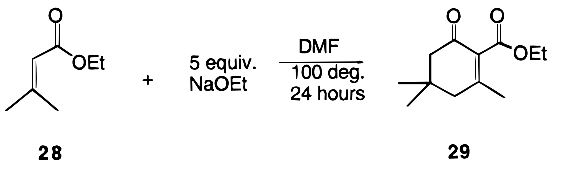
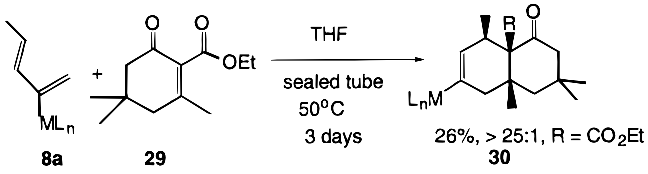


Table 1. Lewis acid Catalyzed Reactions of Cobalt Dienyl Complex 8b with Cyclohexenone (5)

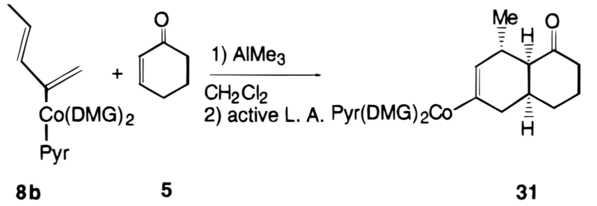
active Lewis acid	time (h)	T (°C)	% yield
(1) BCl$_3$	96	−45	80
(2) BF$_3$·Et$_2$O	24	−45	98
(3) BPhCl$_2$	2	−45	95
(4) *B*-Chlorocatecholborane	2	−78	99

To test a tetrasubstituted double bond in a dienophile, we prepared cyclohexenone **29**[7] (31%) and treated it with dienyl complex **8a**. The diastereoselectivity for product **30** was excellent, and the stereochemical assignment shown is based on analogy to compounds reported above since **30** exhibits the characteristic upfield methyl ^{1}H NMR doublet at δ 0.58 (CDCl$_3$). The yield of **30** is quite good and the conditions quite mild when one considers that heating a 2-(*tert*-butyldimethylsiloxy)-1,3-butadiene with 2-carbomethoxy-3-methyl-2-cyclohexenone at 140 °C (neat) in a sealed tube for 66 h reportedly produced only a 20% yield of *syn*/*endo* product.[12]





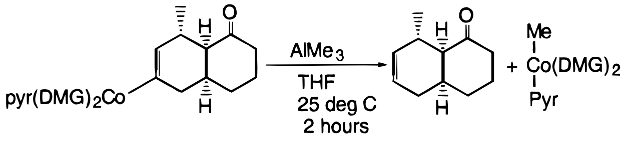
Lewis Acid-Catalyzed 4 + 2 Cycloadditions and Subsequent Demetalations. We next turned our attention to Lewis acid-catalyzed Diels–Alder reactions of 2-cyclohexenone. We had already demonstrated that we could perform these types of reactions for other dienophiles as long as we add 2 equiv of AlMe$_3$ (which exchanges with the dmg hydroxyl hydrogens) before we add a catalytic amount of the Lewis acid we wish to use as a catalyst.[1d] Since we ultimately want to be able to perform enantioselective as well as *exo*-selective Diels–Alder reactions, we surveyed a variety of Lewis acid types in the cycloaddition with cyclohexenone (Table 1). All of these reactions were performed by first adding 2 equiv of AlMe$_3$ to the pyridine dienyl complex (**8b**) at low temperature followed by 0.5 equiv of the active Lewis acid listed in Table 1. The reactions were kept for the prescribed times at low temperature and then quenched by the addition of 1:1 iPrOH:H$_2$O at low temperature. Boron Lewis acid BCl$_3$ had proven most effacious in our earlier studies using cobalt dienyl complex **8b**,[1d] so we investigated a variety of boron Lewis acids here. Several of these Lewis acids proved synthetically useful, with



---

(12) Orban, J.; Turner, J. V. *Tetrahedron Lett.* **1983**, *24*, 2697.

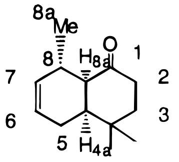
B-chlorocatecholborane being particularly fast and high yielding (Table 1, entry 4). Several comments on these cyclizations are in order. $BF_3{\cdot}Et_20$ was initially run at 96 h like BCl_3, and in that case we isolated decalone **11** (58%) and cobalt methyl complex **32** (87%). At long reaction times at low temperature or if allowed to warm to 25 °C, BF_3 has catalyzed the Diels−Alder reaction and cleaved the cobalt carbon bond in the cycloadduct so isolation of **31** prior to cobalt carbon bond cleavage is not required. If *B*-chlorocatecholborane was used at −45 °C rather than −78 °C, we saw a 4:3 mixture of *anti/exo* and *syn/endo* cycloadducts (92%). Several milder boron Lewis acids (BMe_2Br, $B(OtBu)_3$, BPh_3, $B(OiPr)_3$) proved unreactive as catalysts over 2 h at −45 °C. Zinc chloride also proved unreactive as a catalyst at −78 and −45 °C. $TiCl_4$ did not catalyze the reaction over 2.5 h at −78 °C, but at −45 °C the cycloaddition was about 2/3 complete after 4.5 h. However, the crude product was a 1.25:1 mixture of *anti/exo* (**31**) and *syn/endo* adducts so purification and isolation was not attempted. The stereochemistry of the product (**31**) was determined following demetalation to yield **11** (as described above). Cobalt was also again recovered in a reuseable form as the cobalt methyl complex **32**.



31 **11** (71%) **32** (75%)

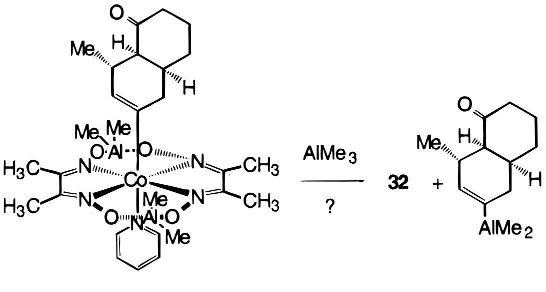
A few comments on a possible mechanism of this $AlMe_3$-mediated cobalt carbon bond cleavage are also in order. We knew from our earlier ^{1}H NMR studies that 2 equiv of $AlMe_3$ reacted rapidly with cobaloximes at −45 °C to replace the DMG hydroxyl hydrogens with $AlMe_2$ (**33**).[1d] Addition of more $AlMe_3$ at low temperature has no effect, but as the solution is warmed to −10 to 0 °C, we start to see cleavage product. Initially, we assumed a transmetalation probably produced cobalt methyl (**32**) and a vinyl dimethylalane (**34**). If this were true, we would assume that a D_2O quench would produce **11** with a deuterium on alkene carbon 6. However, treating cycloadduct **31** with $AlMe_3$ in THF, warming to 25 °C for 2 h, and quenching with D_2O showed no deuterium incorporation in **11** (isolated yield 69%) or **32** (isolated yield 52%). Likewise, performing the cleavage reaction in $CDCl_3$ and quenching with D_2O/iPrOH-d_8 also produced **11** (84%) and **32** (54%) with no deuterium incorporation. Starting with complex **8b** and performing a Lewis acid catalyzed Diels−Alder reaction in $CDCl_3$ followed by warming to effect cobalt carbon bond cleavage and D_2O/iPrOH-d_8 quench also produced **11** (71%) and **32** (75%) with no deuterium incorporation. These experiments suggested that the proton that replaced the cobalt in the cycloadduct **31** came from $AlMe_3$ or the DMG methyls rather than from solvent. Since the number of DMG protons is so large (12), we checked for deuterium incorporation on the DMG methyls in **32** using ^{13}C NMR and saw no splitting of the DMG carbon signal. We now think the proton that replaces cobalt in the cycloadduct (**11**) comes from the $AlMe_3$, possibly via a radical cobalt carbon bond homolysis.[13] This would produce a vinyl radical that rapidly abstracts the adjacent hydrogen of a bound AlMe. The methyl that ends up on cobalt then apparently comes from the other bound $AlMe_2$ fragment since the methyl bound to cobalt in the cobalt methyl complex (**32**) isolated shows no deuterium incorporation. If cobalt carbon bond homolysis is the rate-limiting step leading to cleavage products, that reaction should be slowed by steric congestion in the metal's coordination sphere. Consistent with that hypothesis is our observation that **31** cleaved more slowly when $AlEt_3$ (3 h at 25 °C required, 84% yield of **11**) and $Al(iBu)_3$ (cleavage 59% complete after 3 h at 25 °C) were used as Lewis acids to replace $AlMe_3$.

Table 2. ^{1}H and ^{13}C NMR Assignments for 37



37

no.	^{13}C	^{1}H
1	212.12	
2	37.90	2.41 (ddd, J = 14.3, 13.5, 7.0 Hz) 2.19 (ddd, J = 14.3, 5.3, 2.2 Hz)
3	35.71	1.82 (dd, J = 13.7, 5.4 Hz) 1.55 (m)
4	32.83	
4a	42.49	1.88 (m)
5	24.59	2.00 (app dt, J = 10.7, 3.1 Hz) 1.62 (m)
6	123.54	5.51 (m)
7	130.81	5.60 (m)
8	27.29	2.76 (m)
8a	50.86	2.68 (d, J = 4.6 Hz)
8α	20.46	0.95 (d, J = 7.3 Hz)



33 **34**

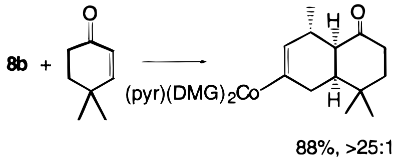
Given the success of the Lewis acid-catalyzed cycloaddition reactions of 2-cyclohexenone, we next surveyed other more highly substituted cyclohexenones. 2,4,4-Trimethylcyclohexenone and 3-methyl-2-cyclohexenone unfortunately proved unreactive toward **8b** under a variety of the Lewis acid conditions reported in Table 1: BCl_3, −45 °C, 1 day; $BF_3{\cdot}Et_2O$, −45 °C, 3 days; *B*-chlorocatecholborane, −45 °C, 4 days. Unreacted **8b** (73−99%) was recovered in all cases. These results indicate that the second electron-withdrawing group on the dienophile is a requirement for 3-substituted cyclohexenones (**29**) and that we are limited to electron-withdrawing groups as the initial substitutent in the 2 position (**18**). Similarly, 2,6,6-trimethyl-2-cyclohexene-1,4-dione (which could react in Diels−Alder reactions like a 2- or 3-methylcyclohexenone) failed to react with **8b** in Lewis acid-catalyzed 4 + 2 cycloadditions.

Cyclohexenone substituents at positions other than 2 or 3 can be accommodated. 4,4-Dimethyl-2-cyclohexen-

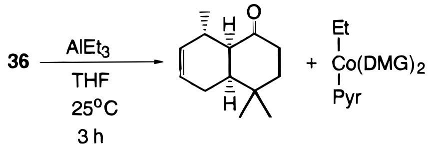
---

(13) Branchaud, B. P.; Meier, M. S.; Malekzadeh, M. N. *J. Org. Chem.* **1987**, *52*, 212.

1-one (**35**) reacted with **8b** under *B*-chlorocatecholborane catalysis to produce **36** in high yield. Liu and Browne had reported very low yields of Diels–Alder reactions of **35** with acyclic dienes in both thermal and Lewis acid catalyzed reactions.[9] However, Wenkert *et al.* report that (*E*)-piperylene reacts with **35** at 40 °C for 48 h with a very strong Lewis acid (25% $AlCl_3$) to produce the Diels–Alder adduct in 90% yield.[8]



35 **36**



37 (90%) **38** (45%)

The relative stereochemistry of **37** and hence **36** was determined after demetalation. The ^1H NMR methyl resonance of **37** was not identical to the *cis* ring junction *endo* or *trans* ring junction *endo* product, thereby leaving *exo* products as the only alternatives.[8,9] The *cis* ring junction for this *exo* product was indicated by the $J_{H8a-H4a}$ coupling constant of 4.6 Hz.[9,14] ^1H and ^{13}C NMR assignments for **37** were made using a combination of COSY, HETCOR, and HMQC spectra and are presented in Table 2. The ^1H NMR resonance at δ 2.68 ($CDCl_3$, d, $J = 4.6$ Hz, 1H) was rigorously proven to be ring junction proton H_{8a} using long-range $^1H-^{13}C$ correlations seen in the HMBC spectrum of **37** where H_{8a} showed cross peaks to C_1, C_{4a}, C_5, C_7, C_8, and $C_{8\alpha}$.

Conclusions

We have demonstrated that a variety of 2-cyclohexenones participate in [4 + 2] cycloaddition reactions with cobaloxime dienyl complexes under thermal and Lewis acid-catalyzed conditions. The thermal cycloadditions are notable for the mildness of the reaction conditions compared to reactions of other acyclic 1,3-dienes with cyclohexenones. Both the thermal and Lewis acid-catalyzed Diels–Alder reactions are also unusual in that the major and in most cases exclusive diastereomer produced resulted from an *exo* rather than *endo* transition state. Demetalation reactions then yield the diastereomerically pure octalones in addition to recovery of cobalt in a form that can be recycled into the synthesis of the dienyl complexes.

Acknowledgment. We thank the National Science Foundation (CHE-9321454), the Exxon Education Foundation, and the Camille and Henry Dreyfus Foundation (Henry Dreyfus Teacher–Scholar Award to M.E.W, 1994–99) for their support. Low-resolution mass spectra were obtained on an instrument purchased with the partial support of NSF (CHE-9007366). The Nebraska Center for Mass Spectrometry (NSF DIR9017262) performed high-resolution mass spectral analyses. B.M.R. acknowledges the North Carolina Academy of Science for a student grant-in-aid of research. We thank Greg Young of the UNC Biomolecular NMR Laboratory for obtaining 500 MHz ^1H NMR, HMQC, and HMBC spectra of **37**.

Supporting Information Available: Complete details of the preparation and characterization of compounds **24**–**27**, **29**, **30**, **36**, and **37** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO962076C

---

(14) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*, 5th ed.; John Wiley: New York, 1991; p 197.