Transition Metal Mediated *Exo* Selective Diels−Alder Reactions: Preparation of 2-Cobalt-Substituted 1,3-Dienes Containing C_2 Symmetric 2,3-Dibenzobicyclo[2.2.2]octanedione Dioxime Equatorial Ligands and Their Use in Thermal and Lewis Acid Catalyzed 4 + 2 Cycloadditions

Marcus W. Wright and Mark E. Welker*,†

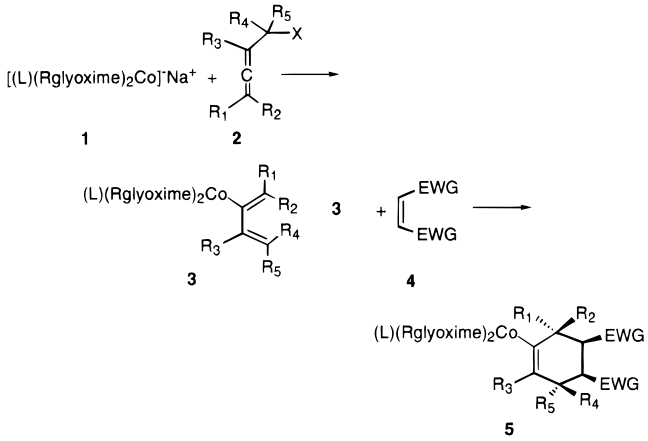
Department of Chemistry, Wake Forest University, P.O. Box 7486, Winston-Salem, North Carolina 27109

Received August 14, 1995[⊗]

The preparation of C_2 symmetric 2,3-dibenzobicyclo[2.2.2]octanedione dioxime is reported. This ligand is then used in the preparation of a (pyridine)(glyoxime)$_2$cobalt(III) chloride complex. The chloride is reduced to a cobaloxime anion which reacted with allenic electrophiles to produce (pyridine)(glyoxime)$_2$cobalt-1,3-dienyl complexes. Thermal and Lewis acid catalyzed Diels−Alder reactions of these dienyl complexes as well as the complexes with glyoxime = diphenylglyoxime and dimethylglyoxime are reported. In most cases these Diels−Alder reactions are *anti* (*exo*) selective, and in many cases diastereoselectivities are >20:1. Cycloadduct demetalation reactions are also reported which preserve cycloaddition stereochemistry and provide cobalt complexes which can be recycled into the starting dienyl complex.

Introduction

Recently, we have been preparing cobalt-substituted 1,3-dienes (**3**) and examining the rates, regioselectivities, and stereoselectivities of their reactions with dienophiles in Diels−Alder reactions.[1] Tada et al. have reported alternative preparations of some cobaloxime dienes as well as results of their cycloaddition reactions.[2] Several other groups have also recently reported that the alternate strategy of transition-metal substitution in the dienophiles can have a pronounced effect on cycloaddition diastereoselectivities.[3] We have found that for di- and trisubstituted dienophiles (**4**) the diastereoselectivities of these 4 + 2 cycloadditions range from about 5:1 *anti:syn* (*exo:endo* selectivity) for L = different pyridines and R = Me to >20:1 for L = DMAP and R = Ph. The diastereoselectivities seen are unusual for acyclic dienes in that products arising from *exo* transition states are the major products. In contrast, monosubstituted dienophiles reacted with these complexes with low diastereoselectivities (1:1 to 1:5, *anti:syn* (*exo:endo*)) with the major products always resulting from reaction through an *endo* transition state. In this paper, we report the synthesis of a cobalt-substituted diene with large C_2 symmetric equatorial ligands and the results of this ligand modification as well as Lewis acid catalysis on the diastereoselectivities of subsequent Diels−Alder reactions.



Experimental Section

General Methods. For a description of instrumentation and chromatographic adsorbents used, see ref 1b. Cobalt chloride hexahydrate and diisobutylaluminum chloride were purchased from Strem Chemicals and used as received. Trimethylaluminum, diethylaluminum chloride, and diisobutylaluminum hydride were purchased from Aldrich Chemicals and used as received. 4-Acetoxy-1,2-pentadiene (**20**),[1b] (3*E*)-1,3-pentadien-2-yl(pyridine)bis(dimethylglyoximato)cobalt(III) (**22a**),[1b] (3*E*)-1,3-pentadien-2-yl(pyridine)bis(diphenylglyoximato)cobalt(III) (**22b**),[1b] bicyclo[2.2.2]oct-5-ene-*cis*-2,3-diyl carbonate (**8**),[4] dibenzobicyclo[2.2.2]octane-*cis*-2,3-diyl carbonate (**15**),[5] and dibenzobicyclo[2.2.2]octane-*cis*-2,3-diol (**16**)[5] were prepared according to previously described methods.

Bicyclo[2.2.2]octane-*cis*-2,3-diyl Carbonate (9). Unsaturated carbonate **8**[4] was hydrogenated by modification of a literature procedure using Adam's catalyst.[6] Unsaturated carbonate **8** (3.125 g, 18.8 mmol) was dissolved in THF (20 mL). Adam's catalyst (PtO_2, 0.075 g, 0.331 mmol) was added, and the solution was degassed for 5 min with N_2. The reaction was shaken in a Parr hydrogenation apparatus at 47 psi of H_2 (24 h). Filtration followed, and removal of solvent yielded

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

[⊗] Abstract published in *Advance ACS Abstracts,* December 15, 1995.

(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**, 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) Sabat, M.; Reynolds, K. A.; Finn, M. G. *Organometallics* **1994**, *13*, 2084. (b) Gilbertson, S. R.; Zhao, X.; Dawson, D. P.; Marshall, K. L. *J. Am. Chem. Soc.* **1993**, *115*, 8517. (c) Anderson, B. A.; Wulff, W. D.; Powers, T. S.; Tribbitt, S.; Rheingold, A. L. *J. Am. Chem. Soc.* **1992**, *114*, 10784. (d) Barluenga, J.; Canteli, R.-M.; Florez, J.; Garcia-Granda, S.; Gutierrez-Rodriguez, A. *J. Am. Chem. Soc.* **1994**, *116*, 6949.

(4) Lambert, J. B.; Holcomb, A. G., *J. Am. Chem. Soc.* **1971**, *93*, 3952−3954.

(5) Newman, M. S.; Addor, R. W. *J. Am. Chem. Soc.* **1955**, *77*, 3789−3793.

(6) Vogel, A. I. *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; Wiley: New York, 1989; pp 64−7, 311−312, 320−321, 596.

0022-3263/96/1961-0133$12.00/0 © 1996 American Chemical Society

a tan-colored solid. Sublimation at 110 °C/5 mmHg yielded 3.092 g (18.38 mmol, 97.8%) of saturated carbonate (**9**): mp, this compound sublimes rather than melts; ^{1}H NMR ($CDCl_3$) 4.68 (s, 2H), 2.02 (s, 2H), 1.91−1.65 (m, 4H), 1.55−1.40 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, DEPT C (155.27), CH (76.74, 27.07), CH_2 (20.96, 17.61) ppm; IR ($CDCl_3$) 2946, 2875, 1862, 1780, 1373, 1359, 1168 cm^{-1}; EI LRMS 55 (33.2), 67 (56.3), 78 (100), 123 (0.94), 124 (1.3), 168 (M, 7.3), 169 (M + 1, 1.4), 170 (M + 2, 0.13). Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.02; H, 7.29.

Bicyclo[2.2.2]octane-*cis*-2,3-diol (10). A modification of a literature procedure was used to synthesize diol **10**.[4] Saturated carbonate **9** (3.773 g, 22.43 mmol) was added to 25% NaOH (35 mL) and refluxed (4 h). Cooling to 25 °C and adding 1.2 M HCl (50 mL) neutralized the solution. The aqueous solution was extracted with Et_2O (6 × 50 mL). The combined organic layers were washed with water (2 × 50 mL). The ether solution was dried with Na_2SO_4, and the solvent was removed by rotary evaporation. The crude solid was sublimed at 115 °C/5 mmHg to yield a white solid (**10**) (2.614 g, 18.38 mmol, 82.0%): mp, this compound sublimes rather than melts; ^{1}H NMR ($CDCl_3$) 3.75 (s, 2H), 2.90 (s, 2H), 1.90−1.76 (m, 2H), 1.73−1.65 (m, 2H), 1.63−1.52 (m, 2H), 1.51−1.40 (m, 2H) 1.34−1.25 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$) 68.43, 31.13, 23.03, 18.28 ppm; IR ($CDCl_3$) 3627, 3513, 2940, 2870, 1472, 1460, 1399, 1010 cm^{-1}. Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.54; H, 9.91.

Bicyclo[2.2.2]octane-2,3-dione (11). Oxidation of 2,3-diol **10** was accomplished by modification of a literature procedure.[7] DMSO (1.59 mL, 22.36 mmol) was added to freshly distilled CH_2Cl_2 (100 mL) under N_2, and the mixture was cooled to −60 °C. Trifluoroacetic anhydride (2.85 mL, 20.19 mmol) was added dropwise, and the mixture was stirred for 10 min. Diol **10** (1.00 g, 7.03 mmol) was dissolved in 2:1 CH_2Cl_2/DMSO (70 mL) and added dropwise over 10 min. The solution was colorless and homogeneous after 30 min of stirring. The reaction mixture was stirred for an additional 1 h, and Et_3N (6.50 mL, 46.6 mmol) was added dropwise. The solution turned yellow immediately and was stirred for 90 min at −60 °C and then warmed to about 5 °C. The mixture was then poured into 2 M HCl (260 mL) and stirred for 5 min (Caution: use a well-ventilated hood). The biphasic solution was shaken well, and the organic layer was separated. The aqueous layer was extracted with 6 × 20 mL of CH_2Cl_2. The combined organic layers were washed with 5 × 45 mL of water and then dried with $MgSO_4$. The solvent was removed by rotary evaporation in the hood to yield a yellow foul-smelling paste. The paste was dissolved in CH_2Cl_2 (10 mL) and cooled to 0 °C. Pentane was added until the solution was very pale yellow and almost all of the dione was precipitated. The yellow solid was collected by suction filtration and washed with 3 × 10 mL of pentane. The yellow solid was vacuum dried to yield **11** (0.818 g, 5.92 mmol, 84.2%) that was determined to be identical to previously reported data by ^{1}H NMR comparison.[8]

2,3-*β*-Bicyclo[2.2.2]octanedione Dioxime (12). Hydroxylamine hydrochloride (0.476 g, 6.85 mmol) and KOH (4.49 g, 67.94 mmol) were dissolved in water:EtOH (1:2, 15 mL). Dione **11** (0.383 g, 2.77 mmol) was added, and the solution was refluxed.[9a] After 2 days, the reaction mixture was cooled and extracted with 5 × 20 mL of Et_2O. After drying with $MgSO_4$, the solvent was removed by rotary evaporation to yield a white solid **12** (0.390 g, 2.55 mmol, 91.9%): mp 189 °C; ^{1}H NMR (C_3D_6O) 11.05 (s, 1H), 10.20 (s, 1H), 3.50 (m, 2H), 1.84−1.35 (m, 8H) ppm; EI LRMS 53 (44), 67 (71), 82 (100), 93 (89), 108 (36), 120 (52), 133 (77), 150 (40, $M^+ - H_2O$); CI LRMS 53 (67), 67 (80), 77 (82), 81 (100), 91 (84), 105 (31), 122 (44), 133 (51), 151 (33, $M^+ - OH$); LR FABMS calcd for $C_8H_{12}O_2N_2$ (168), found in 3-NBA + Li matrix 169.2 $(M + H)^+$, 175.2 $(M + Li)^+$ and in 3-NBA + Na matrix 191.2 $(M + Na)^+$, 213.2 $(M - H + 2Na)^+$. Anal. Calcd for $C_8H_{12}N_2O_2$: C, 57.13; H, 7.19; N, 16.66. Found: C, 57.79; H, 7.05; N, 16.91.

Dibenzobicyclo[2.2.2]octane-*cis*-2,3-diyl Carbonate (15). This compound was prepared as described previously, but ^{1}H NMR data was not previously reported:[5] ^{1}H NMR ($CDCl_3$) 7.41−7.34 (m, 4H), 7.30−7.20 (m, 4H), 4.89 (m, 2H), 4.60 (m, 2H) ppm.

Dibenzobicyclo[2.2.2]octane-*cis*-2,3-diol (16). This compound was prepared as described previously, but ^{1}H NMR data was not previously reported:[5] ^{1}H NMR ($CDCl_3$) 7.41−7.26 (m, 4H), 7.25−7.14 (m, 4H), 4.40 (m, 2H), 4.03 (m, 2H), 2.37 (s, 2H, OH) ppm.

Dibenzobicyclo[2.2.2]octane-2,3-dione (17). Oxidation of diol **16** to known dione[10] **17** was accomplished by an activated Swern oxidation.[11] A procedure analogous to that reported for **11** above was used with CH_2Cl_2 (133 mL), DMSO (2.30 mL, 32.34 mmol), trifluoroacetic anhydride (4.13 mL, 29.24 mmol), diol **16** (2.424 g, 10.17 mmol), and Et_3N (9.41 mL, 67.45 mmol) to yield **17** as a yellow solid (1.955 g, 8.35 mmol, 82.1%) that was determined to be identical to previously reported data by ^{1}H NMR comparison.[12]

2,3-Dibenzobicyclo[2.2.2]octanedione Dioxime (18α and 18*β*). Oximation following the previously reported procedure[12] yielded a 1:1 mixture of dioxime isomers. Starting with dione **17** (3.08 g, 13.15 mmol), we obtained after chromatography on silica (3:1 CH_2Cl_2/EtOAc) *β*-dioxime (**18***β*, 1.204 g, 4.56 mmol, 34.7%, R_f = 0.76). Elution with EtOAc yielded α-dioxime (**18**α, 1.180 g, 4.47 mmol, 34.0%, R_f = 0.36, 3:1 CH_2Cl_2/EtOAc). The following modification of the reported procedure[12] produced much more α-dioxime (**18**α). Dione **17** (3.394 g, 14.49 mmol) was dissolved in MeOH (200 mL) followed by hydroxylamine hydrochloride (6.044 g, 87.0 mmol) and K_2CO_3 (6.077 g, 43.5 mmol). The solution was heated for 3−5 min with a heat gun. TLC on silica (3:1 CH_2Cl_2/EtOAc) revealed that all the dione was consumed, and a spot at R_f = 0.36 corresponding to α-dioxime was very intense with the *β*-dioxime spot, R_f = 0.76, being very faint. Filtering the hot solution through Celite and removal of solvent yielded a white solid contaminated with some K_2CO_3. Triturating the solid with 3 × 40 mL THF and removal of solvent yielded a white powdery solid. The solid was vacuum dried and chromatographed on silica (3:1 CH_2Cl_2/EtOAc) yielding *β*-dioxime (**18***β*) followed by α-dioxime (**18**α). **18***β* (1.055 g, 27.5 mmol, 27.5%, R_f = 0.76, 3:1 CH_2Cl_2/EtOAc): mp 193 °C dec; ^{1}H NMR (THF-d_8) 11.39 (s, 1H), 11.13 (s, 1H), 7.55−7.30 (m, 4H), 7.25−7.00 (m, 4H), 6.01 (s, 1H), 5.06 (s, 1H) ppm; LR FABMS calcd for $C_{16}H_{12}O_2N_2$ 264, found in 3-NBA + Li matrix 271.3 $(M + Li)^+$, 277.3 $(M - H + 2Li)^+$. **18**α (2.684 g, 10.15 mmol, 70.1%, R_f = 0.36, 3:1 CH_2Cl_2/EtOAc) was determined to be identical to previously reported data by ^{1}H NMR comparison.[12]

Chloro(pyridine)bis(9,10-ethanoanthracene-11,12-dione dioxamato)cobalt(III) (19). Modification of a literature procedure was used to synthesize **19**.[12] Clean dioxime **18**α (0.500 g, 1.89 mmol) and $CoCl_2(H_2O)_6$ (0.225 g, 0.956 mmol) were dissolved in 95% EtOH (200 mL) and heated to about 70 °C. Pyridine (0.153 mL, 1.89 mmol) was added, and heating was stopped, but vigorous stirring open to air was continued. After cooling to 25 °C, air was bubbled through the solution for 45 min. After stirring for an additional 3 h, the reaction mixture was cooled to 0 °C, and water (50 mL) was added. The tan-colored precipitate was collected by vacuum filtration and washed with water (3 × 10 mL). Vacuum drying yielded the chloride complex **19** (1.03 g, 1.47 mmol, 78.2%) that was determined to be identical to previously reported data by ^{1}H NMR comparison.[12]

(3*E*)- and (3*Z*)-1,3-Pentadien-2-yl(pyridine)bis(9,10-ethanoanthracene-11,12-dione dioxamato)cobalt(III) (21*E* and 21*Z*). Synthesis of the AG diene **21** was accomplished via alkylation of the chloride complex **19**.[13] A representative synthesis follows: Chloride complex **19** (0.675g, 0.964 mmol) was added to 95% EtOH (300 mL). While being rapidly stirred and degassed, the solution was cooled to −20 °C. When the

(7) Amon, C. M.; Banwell, M. G.; Gravatt, G. L. *J. Org. Chem.* **1987**, *52*, 4851−4855.

(8) Rrebke, R.; Krieger, H.; Esser, H.; Schüfer, H. K.; Alder, V. K. *Chem. Ber.* **1955**, *88*, 23−35.

(9) (a) Becker, P. N.; Bergman, R. G. *Organometallics* **1983**, *2*, 787. (b) Bonner, M. P.; Thornton, E. R. *J. Am. Chem. Soc.* **1991**, *113*, 1299.

(10) Scharf, H. D.; Kuesters, W. *Chem. Ber.* **1972**, *105*, 564.

(11) The representative procedure presented in ref 7 was used except HCl was omitted during the aqueous workup.

(12) Stephenson, N. A.; Morales, L.; Warburton, P. R.; Chmielewski, P. J.; Busch, D. H. *J. Coord. Chem.* **1991**, *23*, 91−111.

(13) (a) Schrauzer, G. N.; Deutsch, E. *J. Am. Chem. Soc.* **1969**, *91*, 3341. (b) Schrauzer, G. N.; Kohnle, J. *Chem. Ber.* **1964**, *97*, 3056.

solution had reached −15 to −20 °C, $NaBH_4$ (0.182 g, 4.82 mmol) was added and an instant color change from brown to dark purple occurred. The solution was allowed to stir for 2 h at −20 °C. 4-Acetoxy-1,2-pentadiene[1b] (**20**) (0.134 g, 1.060 mmol) was added via syringe. The reaction mixture was allowed to warm to 25 °C slowly and stirred for 8 h. The volume of the bright orange solution was reduced by two-thirds via rotary evaporation (bath at 30 °C) and poured into H_2O (800 mL) containing pyridine (1 mL). The orange solid obtained was isolated via vacuum filtration and washed with H_2O (3 × 20 mL). The orange solid was vacuum dried to yield **21** (1.430 g, 1.954 mmol, 68%). The yield of the diene complex ranges from about 70 to 80%. The ratio of *trans*:*cis* isomers, however, varies considerably from batch to batch (>20:1 to 1:1). Rotary evaporation at 20−30 °C usually yields >20:1 *E*:*Z* diene complex **21**. The complex can be chromatographed on silica (3:1 CH_2Cl_2/EtOAc, 1% pyridine, $R_f = 0.65$); however, loading on silica with CH_2Cl_2 followed by removal of solvent caused isomerization: mp 215 °C dec; ^{1}H NMR ($CDCl_3$) 7.88 (t, J = 4.4 Hz, 2H), 7.42 (dd, J = 5.8, 3.3 Hz, 4H), 7.26−7.19 (m, 5H), 7.12 (dd, J = 5.8, 3.3 Hz, 4H), 7.01−6.92 (m, 4H), 6.76 (t, J = 6.6 Hz, 2H), *E* diene [5.82 (m, 1H), 5.52 (s, 4H), 4.46 (dq, J = 15.0, 6.6 Hz, 1H), 4.04 (s, 1H), 3.86 (s, 1H), 1.06 (dd, J = 6.6, 1.7 Hz, 3H)], *Z* diene [5.67 (m, 1H), 5.53 (s, 4H), 4.75 (dq, J = 11.0, 6.9 Hz, 1H), 4.29 (s, 1H), 3.75 (s, 1H), 0.65 (dd, J = 6.8, 1.8 Hz, 3H)] ppm; ^{13}C NMR ($CDCl_3$) *E* diene 151.70, 148.93, 140.12, 139.48, 137.91, 137.05, 127.14, 126.71, 124.88, 124.72, 124.58, 120.58, 113.05, 45.92, 17.92 ppm; IR ($CDCl_3$) 3692, 3606, 3074, 3025, 2912, 1702, 1604, 1494, 1460, 1249, 1229 cm^{-1}. Anal. Calcd for $C_{42}H_{34}O_4N_5Co$: C, 68.94; H, 4.68; N, 9.57. Found: C, 68.85; H, 4.70; N, 9.47.

(*anti*-4,4,7,7,8,9-Hexahydro-4-methyl-1,3-dioxoisobenzofuran-5-yl)(pyridine)bis(9′,10′-ethanoanthracene-11′,12′-dione dioximato)cobalt(III) (24c). A 2:1 and 16:1 (*E*:*Z*) mixture of diene **21** (1.40 g, 1.913 mmol) was added to degassed $CHCl_3$ (100 mL). Maleic anhydride (0.750 g, 7.653 mmol) was added to the heterogeneous solution. After stirring for 8 h, the homogeneous solution volume was reduced to about 20 mL by rotary evaporation. The orange solution was chromatographed on silica (CH_2Cl_2/1% pyridine). Elution of a single orange band (3:1 CH_2Cl_2/EtOAc containing 1% pyridine, $R_f = 0.81$) yielded one diastereomer (**24c**) as determined by ^{1}H NMR: mp 200 °C dec; ^{1}H NMR ($CDCl_3$) 7.98 (d, J = 5.0 Hz, 2H), 7.44−7.32 (m, 4H), 7.30−7.22 (m, 5H), 7.16−7.09 (m, 4H), 7.04−6.80 (m, 4H), 6.88 (t, J = 6.4 Hz, 2H), 5.53 (s, 2H), 5.51 (s, 2H), 5.05 (dd, J = 4.1, 1.6 Hz, 1H), 2.35−2.16 (m, 2H), 1.96 (m, 1H), 1.70−1.50 (m, 2H), 0.62 (d, J = 7.1 Hz, 3H) ppm; IR ($CDCl_3$) 3693, 3605, 3074, 2964, 1776, 1729, 1606, 1249, 1229 cm^{-1}; HRMS calcd for $C_{46}H_{37}O_7N_5Co$ 830.2024, found 830.1993 (M + H)$^+$. Anal. Calcd for $C_{46}H_{36}O_7N_5Co$: C, 66.59; H, 4.37. Found: C, 64.67; H, 4.59.

(*cis*- and *trans*-1-(1-Oxoethyl)-2-methyl-3-cyclohexen-4-yl)(pyridine)bis(9′,10′-ethanoanthracene-11′,12′-dione dioximato)cobalt(III) (26c and 27c). A 2:1 and 16:1 (*E*:*Z*) mixture of diene **21** (0.340 g, 0.465 mmol) was added to degassed $CHCl_3$ (75 mL) and cooled to −20 °C. Methyl vinyl ketone (0.773 g, 9.29 mmol) was added, and the solution was allowed to stand at −20 °C for 15 days. The solution was then cooled to −78 °C, and pentane was added (50 mL). The orange precipitate was collected by vacuum filtration and washed with pentane (3 × 10 mL). Vacuum drying yielded a 2:1 mixture of diastereomers (**26c:27c**) as determined by 200 MHz ^{1}H NMR (0.350 g, 0.437 mmol, 94%). Running the reaction at 25 °C for 8 h yielded a 1:1 mixture (99% yield) and 0 °C for 3 days yielded 1.4:1 ratio of **26c**:**27c** (93% yield): mp 190 °C dec; spectroscopic data for **26c** and **27c**. ^{1}H NMR ($CDCl_3$) 8.60−7.94 (m, 2H), 7.42−7.30 (m, 4H), 7.29−7.19 (m, 5H), 7.17−7.05 (m, 4H), 7.02−6.91 (m, 4H), 6.82 (apparent t, J = 5.3 Hz, 2H), 2.31−2.00 (m, 1H), 1.79−1.52 (m, 2H), 1.25−1.14 (m, 1H), 1.13−1.00 (m, 1H), 0.99−0.84 (m, 1H), major isomer **26c** [5.49 (s, 4H), 4.60 (d, J = 6.2 Hz, 1H), 1.85 (s, 3H), 0.02 (d, J = 6.8 Hz, 3H)], minor isomer **27c** [5.52 (s, 4H), 4.51 (s, 1H), 1.80 (s, 3H), 0.34 (d, J = 6.8 Hz, 3H)] ppm; IR ($CDCl_3$) 3196, 3074, 3046, 3026, 2959, 1700, 1605, 1460, 1449, 1228, 1070 cm^{-1}. HRMS calcd for (M + H$^+$) $C_{46}H_{41}O_5N_5Co$ 802.2440, found 802.2436.

***anti*-4,4,7,7,8,9-Hexahydro-4-methyl-1,3-dioxoisobenzofuran (28).** Cycloadduct **24c** (0.300 g, 0.362 mmol) was dissolved in degassed CH_2Cl_2 (310 mL) and cooled to 0 °C in a Hanovia 450 W photolysis reactor equipped with a vycor filter. The solution was photolyzed for 5 h. The solvent was removed by rotary evaporation to yield a green powder. The powder was triturated with 1.7:1 pentane/ether (5 × 4 mL). The solvent was removed by rotary evaporation to yield a yellow oil. Kugelröhr distillation at 110 °C/1 mmHg yielded pure *anti* diastereomer **28** (0.0295 g, 0.178 mmol, 49.1%) that was determined to be identical to previously reported material which was enriched in this diastereomer[1b] by ^{1}H NMR comparison as well as the diastereomer from previously reported data on thermal reactions of *E* and *Z* piperylenes:[14] ^{1}H NMR ($CDCl_3$) of pure *anti* isomer not previously reported 5.83 (m, 2H), 3.32 (ddd, J = 9.6, 8.4, 5.5 Hz, 1H), 2.77 (dd, J = 9.6, 5.5 Hz, 1H), 2.64−2.34 (m, 3H), 1.25 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$) 173.90, 173.14, 132.67, 125.22, 46.04, 38.91, 29.74, 22.04, 19.89 ppm. The residual green powder (0.210 g, 0.319 mmol, 88%) was believed to be $(AG)_2CoCl_2^-(PyrH)^+$ [15] (**29**): ^{1}H NMR ($CDCl_3$) 7.83 (d, J = 5.0 Hz, 2H), 7.48−7.30 (m, 4H), 7.29−7.18 (m, 5H), 7.17−7.02 (m, 4H), 7.00−7.88 (m, 4H), 6.77 (apparent t, J = 5.0 Hz, 2H), 5.66 (s, 4H). This compound which was insoluble in the pentane/ether trituration step above was converted to the chloride complex **19** as described below.

Regeneration of (Pyridine)bis(9,10-ethanoanthracene-11,12-dione dioximato)cobalt(III) Chloride (19). The green salt **29** (0.152 g, 0.238 mmol) was suspended in methanol (10 mL). Pyridine (18.7 μL, 0.231 mmol) was added, and the solution was heated to about 60 °C and then allowed to stir for 8 h. The solution was then cooled to 0 °C, and after 20 min, water (20 mL) was added. The resulting brown solid was filtered to yield pyr(DBG)$_2$CoCl (**19**) (0.118 g, 0.169 mmol, 70%) which was identical to **19** reported above as determined by ^{1}H NMR comparison.

***cis*- and *trans*-1-(1-Oxoethyl)-2-methyl-3-cyclohexene (30 and 31).** A 1.4:1 ratio of an unknown diasteromeric mixture of **26c** and **27c** (0.330 g, 0.451 mmol) was dissolved in degassed CH_2Cl_2 (310 mL) and cooled to 0 °C in a Hanovia 450 W photolysis reactor equipped with a vycor filter. The solution was photolyzed for 6 h. The solvent was removed by rotary evaporation to yield a green residue. The residue was triturated with 1:1 pentane/ether (8 × 2 mL). The solvent was removed by rotary evaporation to yield a 1.4:1 mixture of **30**:**31** as a light yellow oil. Chromatography on silica with 1:1 ether/pentane failed to remove the yellow color. Kugelröhr distillation at 90 °C/30 mmHg yielded a 1.4:1 mixture of diastereomers **30:31** (0.054 g, 0.435 mmol, 86.6%) that was determined to be identical to authentic samples by ^{1}H NMR spectroscopic comparison.[16] The residual green powder $(pyrH)^+[(AG)_2CoCl_2]^-$ was collected and vacuum dried to yield **29** (0.267 g, 0.363 mmol, 80.5%) which was determined to be identical to the material reported in the other photolysis above by spectroscopic comparison.

Kinetics of *Z*:*E* Isomerization for the AG Dienyl Complex 21. These kinetics experiments were carried out in $CDCl_3$ with a 10-fold excess of dienophile, and rate constants were determined from the first-order decay of proton signals monitored by ^{1}H NMR. The appearance of cycloadduct **24c** was monitored by integrating the signal from the methyl protons at various times and correcting the observed value if necessary for any changes due to variations in instrument tuning using the integration of the signal from the methyl protons of the internal standard *tert*-butyl alcohol. More spectra were acquired early in the reaction (a spectrum every 600 s for six spectra and every 720 s for five spectra), and fewer at later time (a spectrum every 900 s for five spectra and then every 1200 s for three spectra). Monitoring of the methyl signal's appearance was carried out for almost 1 half-life. Analyses were carried out by graphic means; a linear plot on

(14) (a) Brocksom, T. J.; Constantino, M. G. *J. Org. Chem.* **1982**, *47*, 3450. (b) Brocksom, T. J.; Constantino, M. G. *An. Acad. Bras. Cienc.* **1982**, *54*, 655.

(15) Nakahara, A. *Bull. Chem. Soc. Jpn.* **1955**, *28*, 207.

(16) (a) Guner, O. F.; Ottenbrite, R. M.; Shillady, D. D.; Alston, P. V. *J. Org. Chem.* **1988**, *53*, 5348. (b) Bonnesen, P. V.; Puckett, C. L.; Honeychuck, R. V.; Hersh, W. H. *J. Am. Chem. Soc.* **1989**, *111*, 6070. c) Smith, D. A.; Sakan, K.; Houk, K. N. *Tetrahedron Lett.* **1986**, *27*, 4877.

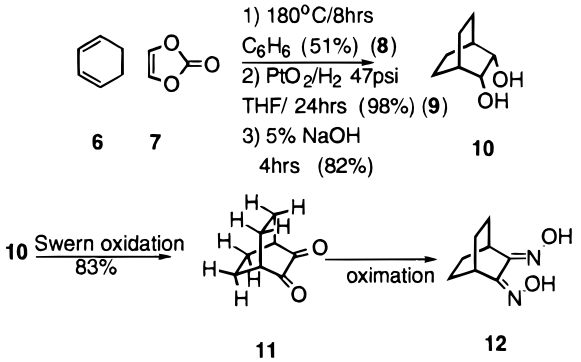
semilogarithmic paper of methyl peak integrals against time yielded the half-time $t_{1/2}$, and the rate constant was obtained from the equation $k_{obs} = 0.693/t_{1/2}$. A 2:1 (*E*:*Z*) mixture of AG diene **21** (0.016 g, 0.0218 mmol) was dissolved in 0.7 mL of $CDCl_3$. Maleic anhydride (0.0214 g, 0.218 mmol) was added and thoroughly mixed. Nineteen FIDs were taken at 26 °C. All of the *trans* diene **21** was consumed by the time the first spectrum was collected and transformed ($T = 3$ min). The rate constant for growth of the *anti* anhydride **24c** was determined to be $4.4 \times 10^{-5} \pm 1.3 \times 10^{-5}$ s^{-1} and $t_{1/2} = 4.4$ h.

NMR Titration Experiments with the DMG Diene 22a, MA, and $AlMe_3$. In a dry 5 mm NMR tube, DMG diene **22a**[1b] (0.010 g, 0.0229 mmol) was added under N_2, and 0.6 mL of dry, degassed $CDCl_3$ was added via syringe. After equilibration of the NMR probe and sample to −45 °C, a precooled solution of maleic anhydride was added (0.229 M, 0.1 mL, 0.0229 mmol). To determine the temperature where cycloaddition occurs thermally, the probe was warmed in 10 °C increments and held for 20 min. Cycloaddition occurred at −30 °C with an estimated half-life of 2 h. Both *anti* and *syn* diastereomers were seen. $AlMe_3$ reactions were carried out by successive additions of 2.0 M $AlMe_3$ in hexanes (0.012 mL, 0.0115 mmol equals 1 equiv) at −45 °C where no thermal uncatalyzed cycloaddition is taking place. Lewis acid additions started with 0.5 equiv and ended with 4 equiv in 0.5 equiv increments. Spectra were taken after each addition and then again after 15 min to observe any change. Changes in the pyridine resonances were monitored as well as the alkene H's on the diene.

Preparative Lewis Acid Catalyzed Reactions. The following is a representative procedure for the Lewis acid catalyzed reactions of cobalt dienes **22a**, **22b**, and **22c** with MVK or MA. A small vial with a stir bar was flame dried and cooled under a stream of N_2. Diene **22a** (100 mg, 0.230 mmol) was introduced into the vial and purged with nitrogen for 2−3 min. The vial was then capped by crimping on a septa-containing top, and dry CH_2Cl_2 (3.2 mL) was added followed by cooling to −45 °C. Precooled $AlMe_3$ (2.0 M in hexanes, 0.230 mL, 0.460 mmol) was added slowly via a dry syringe and allowed to stir 10 min. Next, precooled BCl_3 (1.0 M in CH_2Cl_2, 58 μL, 0.058 mmol), or other Lewis acids as described in the text were then added slowly. A stock solution of the dienophile was prepared in another flame-dried vial as follows: MA (25 mg/mL) in dry CH_2Cl_2 and MVK (16 mg/mL or 21 μL/mL) in dry CH_2Cl_2. The stock dienophile solution was cooled to −45 °C, and the MVK solution (1.0 mL, 0.253 mmol) was added slowly. The reaction mixture was left at −50 °C for 2.7 days. A 50% aqueous solution of 2-propanol was cooled to −10 to −20 °C. Slowly, the 50% aqueous solution (1 mL) was added and stirred for 20 min at 0 °C. With vigorous stirring, $MgSO_4$ was slowly added at 0 °C. The reaction mixture was filtered, and the $MgSO_4$ was washed with (3×8 mL) CH_2Cl_2. The solvent was removed by rotary evaporation, and the residue was vacuum dried. Crude ^1H NMRs were taken at this point to establish *anti*:*syn* ratios and compare to previously reported data.[1b] Purification of cycloadducts was accomplished by chromatography on silica (dmg complexes require EtOAc as the elutent, dpg complexes require CH_2Cl_2, and AG complexes require 3:1 CH_2Cl_2:EtOAc containing 1% pyridine). The reaction of the dmg complex **22a** with MVK described above yielded a 1.6:1 mixture of **27a:26a** (80.2% yield). Reactions using 2.0 equiv of DIBALH required an aqueous workup. The reactions were first quenched with 50% aqueous 2-propanol (1.0 mL) and warmed to 25 °C. Saturated aqueous NH_4Cl (1.5 mL) was added and stirred vigorously for 10 min. The biphasic solution was poured into a separatory funnel and shaken well. The aqueous layer was washed with CH_2Cl_2 (3×5.0 mL). The combined organic layers were dried with $MgSO_4$, and solvent was removed by rotary evaporation. The residue was then vacuum dried and purified as mentioned above.

Results and Discussion

***C_2* Symmetric Glyoxime Preparation.** We knew from our previous studies[1b] that switching from dimethylglyoxime (dmg) to diphenylglyoxime (dpg) as the equatorial ligand for our dienyl complexes had improved *anti* (*exo*) selectivities of subsequent Diels−Alder reactions. If we stayed with the glyoxime ligand set, we thought bicyclic glyoximes offered the best chance to present steric bulk to incoming dienophiles. Bicyclic glyoximes derived from readily available bicyclo[2.2.1]heptanes were known, but since these ligands are not C_2 symmetric, they produce mixtures of geometrical isomers when two of them are coordinated to a transition-metal center.[17] Therefore, we decided to prepare glyoximes derived from bicyclo[2.2.2]-octane precursors since they offered the advantage of being C_2 symmetric. We first attempted to prepare the simplest glyoxime of this framework, 2,3-bicyclo[2.2.2]-octanedione dioxime. Dione **11** had been prepared previously[8] from commercially available but expensive bicyclo-[2.2.2]octene. We chose a somewhat lengthier strategy utilizing readily available 1,3-cyclohexadiene (**6**) and vinylene carbonate (**7**).[4,5] Diels−Alder reaction of **6** and **7** was followed by hydrogenation of the resulting unsaturated bicyclic carbonate **8** to yield the saturated bicyclic carbonate **9**.[6] Hydrolysis of the carbonate was easily accomplished with 5% NaOH[4] to produce the diol **10** which was oxidized via an activated Swern oxidation[7] to the known dione **11**.[8] Many attempts were made to convert dione **11** to the α-dioxime. Standard procedures using NH_2OH−HCl and KOH yielded only β-dioxime (**12**).[9a] Procedures previously reported to oximate sterically hindered ketones were also used without success.[18] Refluxing **11** with NH_2OH−HCl and NaOAc in H_2O/EtOH[9b] also produced **12**. The β isomer is a poor ligand for the type of chemistry we wanted to do so we had to look for other C_2 symmetric glyoximes which could be prepared as the α isomer.

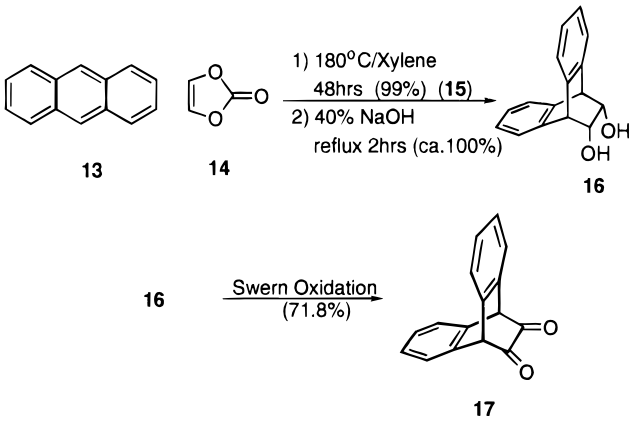


The preparation of 2,3-dibenzobicyclo[2.2.2]octanedione dioxime (**18**) had been reported previously by Busch et al.[12] so we picked this C_2 symmetric dioxime as our next target. The Busch group referred to this ligand as anthraglyox, and we will simply abbreviate it as AG. The dione **17** required for the preparation of AG had been reported previously by Scharf and Kuesters.[10] Their route required the preparation of tetrachloroethylene carbonate as well as dichlorovinylene carbonate, both of which are strong lachrymators. We chose instead to do

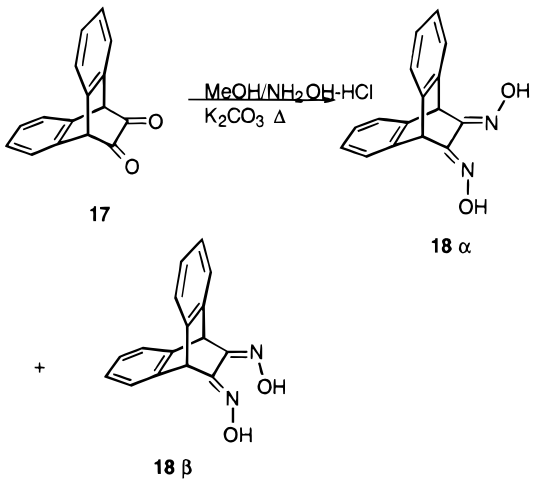
(17) (a) Nakamura, A. *Pure Appl. Chem.* **1978**, *50*, 37. (b) Nakamura, A.; Konishi, A.; Tatsuno, Y.; Otsuka, S. *J. Am. Chem. Soc.* **1978**, *100*, 3443. (c) Nakamura, A.; Konishi, A.; Tsujitani, R.; Kudo, M.; Otsuka, S. *J. Am. Chem. Soc.* **1978**, *100*, 3449. (d) Ma, M. S.; Angelici, R. J. *Inorg. Chem.* **1980**, *19*, 363.

(18) (a) Bari, S. S.; Bose, A. K.; Chaudhary, A. G.; Manhas, M. S.; Raju, V. S.; Robb, E. W. *J. Chem. Ed.* **1992**, *69*, 938−939. (b) Puciová, M.; Toma, S. *Collect. Czech. Chem. Commun.* **1992**, *57*, 1507−1512.

a Diels−Alder reaction between commerically available vinylene carbonate **14** and anthracene[5] (**13**) followed by carbonate hydrolysis[5] and activated Swern oxidation[7] to produce dione **17**.

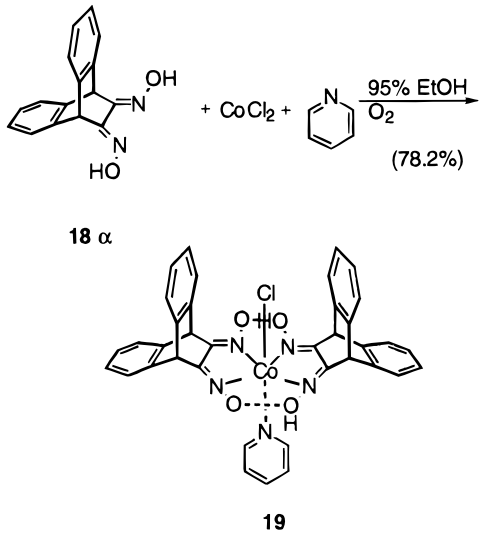


Oximation of **17**, following the reported procedure,[12] yielded a 1:1 mixture of α- and *β*-dioxime isomers (**18**α and **18***β*). Heating **17** with NH_2OH−HCl and K_2CO_3 for only 3−5 min with a heat gun rather than refluxing for 30 h[12] yielded a 4:1 mixture of **18**α:**18***β*. The α and *β* isomers were easily separated by chromatography, and the α isomer produced in abundance at short reaction times proved to be identical to that reported by Busch et al.[12] It was determined by TLC that heat and K_2CO_3 in MeOH had no effect on isomerization. *p*-Toluenesulfonic acid (PTSA) or hydroxylamine hydrochloride in MeOH did cause isomerization of pure *β*-dioxime (**18***β*) or α-dioxime (**18**α) to about a 1:1 mixture of α:*β*.

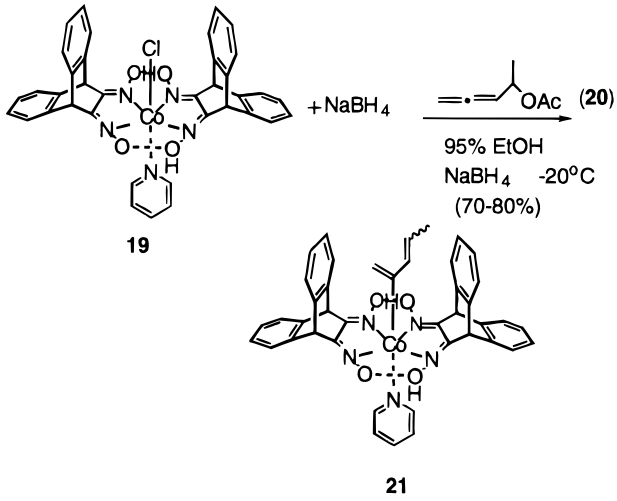


Time	Ratio(α:β)	%yield (18)
30hrs	1:1	34% (α) 34.7% (β)
5min	4:1	70.1% (α) 27.5% (β)

Preparation of Cobalt Chloride and Cobalt Diene Complexes. Using clean α-dioxime (**18**α), cobalt chloride complex **19** was synthesized using a modification of Busch's procedure in significantly higher yield than previously reported.[12] The *β*-dioxime isomers (**12** and **18***β*) failed to produce a cobalt chloride complex in this reaction.



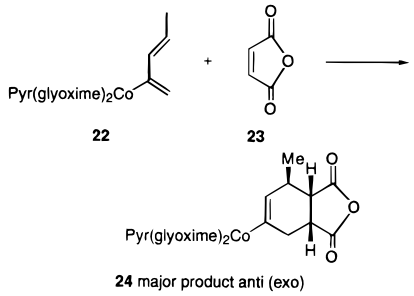
Synthesis of AG dienyl complex **21** was accomplished via reduction of the chloride complex **19** in EtOH with $NaBH_4$[13] followed by the addition of allenic acetate **20**.[1b] The ratio of *trans*:*cis* (**21*E***:**21*Z***) can vary considerably from batch to batch (>20:1 to 1:1), depending on the workup procedure used (due to facile thermal isomerization of **21**). Working with **21** at 20−30 °C results in the isolation of **21*E*** cleanly. The overall yield for production of **21** via six steps is about 30%. Additional observations about this *E*:*Z* isomerization and its possible effects on the outcome of 4 + 2 cycloadditions are presented below.



Thermal 4 + 2 Cycloadditions and Subsequent Demetalation Reactions. Previously, we had shown that *anti* (*exo*) selectivity of thermal Diels−Alder reactions of cobalt-substituted dienes with maleic anhydride improved as the size of the equatorial ligands increased (Table 1, entries 1−4).[1b] We had been able to get selectivity for the *anti* (*exo*) diastereomer **24** up to 8.4:1 using commercially available glyoximes, but we hoped that the bulky AG glyoxime complex **21** would be significantly better than this. We were gratified to see that **21** condensed with maleic anhydride to produce exclusively the *anti* product **24c**. The relative stereochemistry of this cycloadduct was proven by the demetalation reaction described below. We also found that we could condense 16:1 and 2:1 (*E*:*Z*) mixtures of **21** with MA and obtain the same diastereomeric ratio in the product **24c**.

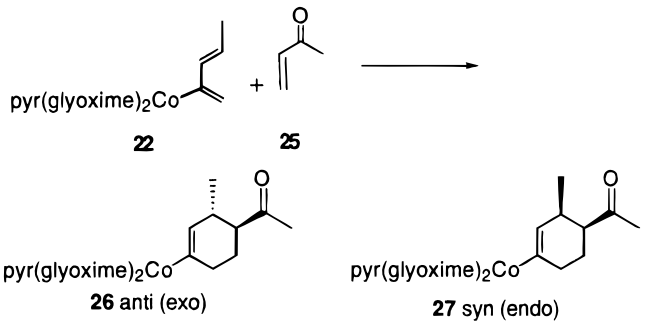
We next turned to methyl vinyl ketone as a dienophile. This small dienophile had reacted with our dmg diene

Table 1. Thermal Reactions of Cobalt Diene Complexes with Maleic Anhydride



entry	glyoxime	conditions	ratio (*anti*:*syn*)	yield, %	no.
1	DMG	THF, reflux	2.3:1	78	**24a**
2	DPG	THF, reflux	6.0:1	87	**24b**
3	DPG	$CHCl_3$, 25 °C	4.9:1	76	**24b**
4	DPG	$CHCl_3$, −22 °C	8.4:1	98	**24b**
5	AG	$CHCl_3$, 25 °C	>20:1	98	**24c**

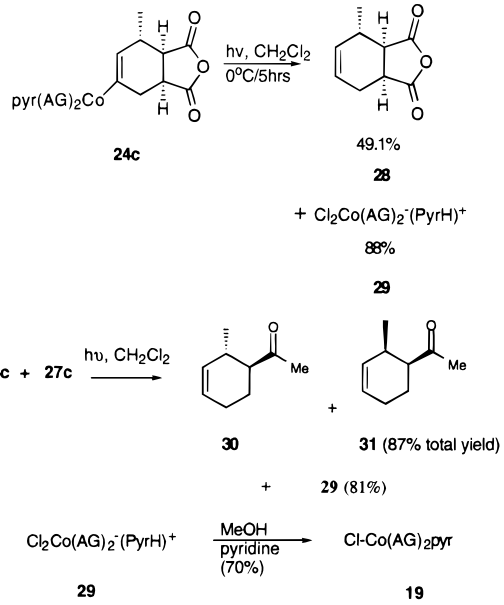
Table 2. Thermal Reactions of Cobalt Diene Complexes with Methyl Vinyl Ketone



entry	glyoxime	conditions	ratio (*anti*:*syn*)	yield, %	no.
1	DMG	THF, reflux	1:5.0	95	**26a**
2	DPG	THF, reflux	1.0:1	90	**26b**
3	DPG	$CHCl_3$, 25 °C	1.0:1	82	**26b**
4	AG	$CHCl_3$, 25 °C	1.0:1	70	**26c**
5	AG	$CHCl_3$, 0 °C	1.4:1	93	**26c**
6	AG	$CHCl_3$, −20 °C	2.0:1	94	**26c**

(Table 2, entry 1) with a modest *syn* (*endo*) preference, and the best we had been able to do for *anti* (*exo*) selectivity with a commercially available glyoxime (dpg) (Table 2, entries 2 and 3) was 1:1 (**26b**:**27b**). The dpg dienyl complex **22b** proved unreactive toward MVK in $CHCl_3$ at −20 °C. We had high hopes for **21** in this reaction, but they proved unwarranted. This dienyl complex (**21**) did prove to be more reactive than the dpg complex, but *anti* (*exo*) selectivity improved only slightly to 2.0:1 (Table 2, entry 6). Once again, the relative stereochemistry of the major cycloadduct **26c** was proven by demetalation as described below.

Demetalation of complexes **24c** and **26c** was accomplished with concomitant cobalt recovery using procedures we have described previously.[1b] Initially we tried $AlMe_3$-mediated cobalt−carbon bond cleavage, but these Lewis acid conditions, which had worked for dmg and dpg cycloadducts, were extremely slow (>24 h) and resulted in isomerization and decomposition of the organic products. Photochemical cobalt−carbon bond homolysis proved to be much more successful. The recovered anhydride **28** from adduct **24c** corresponded to the *anti* diastereomer only. We had prepared **28** in diastereomerically enriched form with the *syn* isomer previously.[1b,14] This cleavage reaction established the *exo* selective addition of MA to diene **21** and also yielded the pyridinium salt of the cobalt dichloride **29** which was easily converted back into chloride **19**, the complex we used to prepare **21**. The MVK cycloadducts **26c** and **27c** were cleaved in the same manner to yield **30** (which was determined to be identical to previously reported data by ^{13}C NMR spectroscopic comparison)[16] and **31** in addition to **29**. This cleavage reaction also established the *exo* selective nature of the cycloaddition between **21** and methyl vinyl ketone.

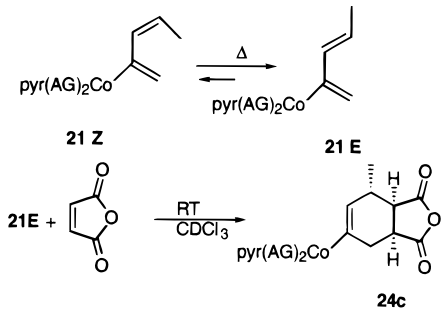


We next wanted to investigate the effect (if possible) of Lewis acid catalysis on the stereochemical outcome of these cycloadditions; however, some additional comments on the *E*:*Z* isomerization of **21** are in order. We knew that with MA only one diastereomer (**24c**) was formed from any *E*:*Z* mixture of dienes (**21**). One explanation for this could be that *E* diene **21** reacted via a completely *exo* transition state much faster than *Z* diene **21**. The *Z* diene then isomerized to produce more *E* diene which is removed by rapid *exo* selective cycloaddition much faster than Z diene cycloadds with MA. As long as the *E* diene reacted in a completely stereoselective fashion much faster than the *Z* diene, we would observe only one product. Another possible explanation for the stereochemical outcome of this reaction is that the *E* diene reacted via only an *exo* transition state and the *Z* diene reacted via only an *endo* transition state. The *E*:*Z* isomerization of diene complex (**21**) and subsequent cycloaddition with MA were observed at 25 °C by ^1H NMR spectroscopy. By monitoring the Diels−Alder reaction of *E*:*Z* mixtures of **21** with maleic anhydride under pseudo-first-order conditions in $CDCl_3$, we observed complete disappearance of the *E* diene between mixing and acquisition of the first free induction decay (FID). We then observed first-order disappearance of the *Z* diene and first-order appearance of only the *anti* cycloadduct **24c** with a rate constant of 4.4×10^{-5} s^{-1} ± 1.3×10^{-5} and $t_{1/2} = 4.4$ h. Given our earlier observations that pyr(dmg)$_2$Co-substituted *Z* dienes react with maleic anhydride (under conditions where *Z*:*E* isomerization is not occurring) with half-lives on the order of 5 days,[1c] it would appear that the latter possible explanation for our observed results is highly unlikely and the rate constant

Table 3. ^{1}H NMR Resonances of $AlMe_3$−21 Complexes

resonance	chemical shift (ppm)	species
ortho ^{1}H on pyridine	8.69 (app d)	**21**
	8.30 (app d)	**32**
	7.81 (app d)	**33**
	7.64 (app d)	**34**
vinyls	4.49 (s), 4.39 (s)	**21**
	4.33 (s), 4.20 (s)	**32**
	4.33 (s), 4.25 (s)	**33**
	5.35 (d)	**34**
OH	18.21 (s)	**21**
	18.53 (s)	**32**

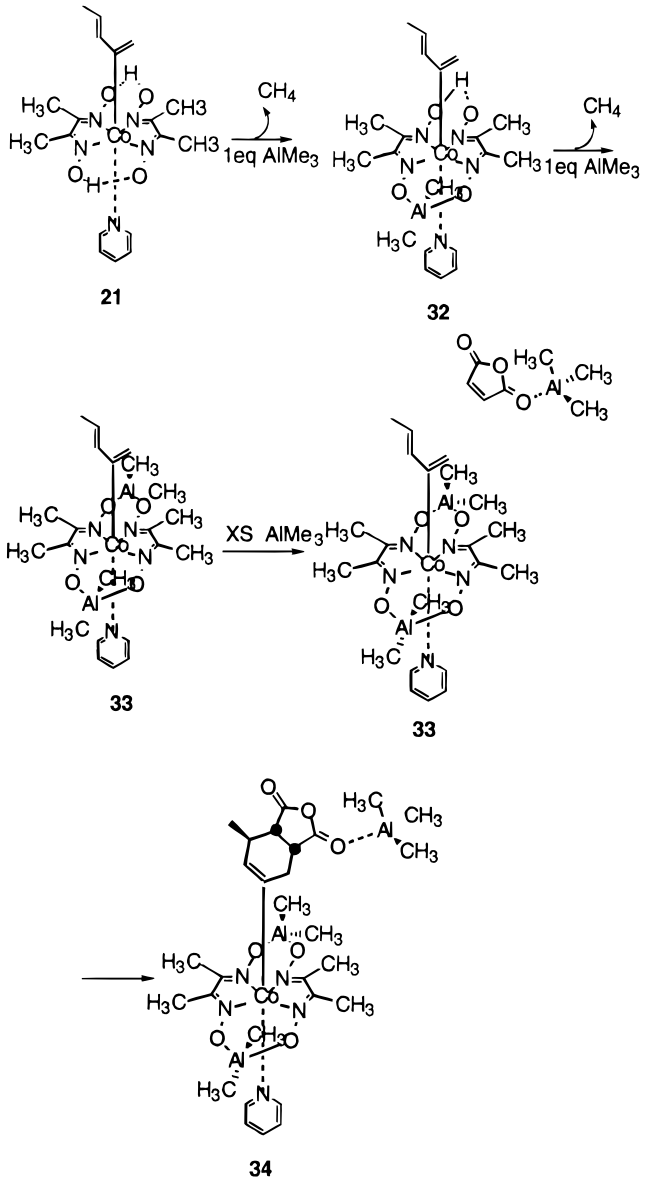
reported here is the rate constant for *Z*:*E* isomerization of diene complex **21**.



In summary, cycloaddition of AG diene **21** (regardless of the *E*:*Z* ratio) with MA increased the *anti* (*exo*) selectivity of the thermal Diels−Alder reaction to >20:1, confirming our earlier postulate that larger equatorial ligands do aid with *exo* dienophile approach. However, the thermal cycloaddition of **21** with MVK was disappointing, 2:1 *anti* (*exo*) selectivity. The pursuit of even larger equatorial ligands was possible, but we thought that the effective size of the complexes and the dienophiles might be increased more easily through the careful use of Lewis acids.

Lewis Acid Catalyzed 4 + 2 Cycloadditions of Cobalt Dienyl Complexes. From our observation, the main obstacle to the use of Lewis acids to promote Diels−Alder reactions of these cobalt dienyl complexes (regardless of equatorial ligand) was that cobalt−carbon bonds in cycloadducts as well as dienyl complexes are cleaved by a variety of mild Lewis acids at −10 to 0 °C.[1] Any Lewis acid selected would have to be capable of catalyzing 4 + 2 cycloadditions at temperatures significantly lower than −10 °C without effecting concomitant cobalt−carbon bond cleavage.

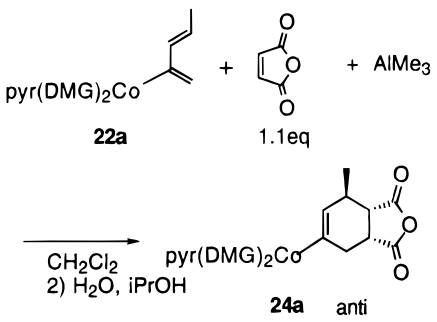
We first established by NMR tube reactions that dmg diene **22a** was unreactive toward MA in $CDCl_3$ at −45 °C and that it reacted very slowly with 1 equiv of MA at −30 °C with a half-life of about 2 h. With this information in hand, we first proceeded to answer the question of how the equatorial ligands' Lewis base sites participate in the complexation of Lewis acids. In an NMR tube containing 1 equiv of MA and **22a** in $CDCl_3$ at −45 °C, we introduced 0.5 equiv of $AlMe_3$ and observed two cobalt species as determined by the ^{1}H NMR *o*-pyridine protons, OH, and vinyl resonances (Table 3). Control spectra were carried out to confirm that signal changes were not due to $AlMe_3$−pyridine adducts. The two species present were the original diene **22a** and what is postulated to be the diene with a $AlMe_2$ in place of one of the bridging ligand OH protons **32**. At 1 equiv of $AlMe_3$, we see only one species corresponding to the monocomplexed diene **32** indicating that **21** reacts much quicker with $AlMe_3$ than **32**.



With the addition of 1.5 equiv of $AlMe_3$, two species were seen again. One species was the monocomplex diene **32**, and the new species was presumed to be the bis-complexed diene **33**. At 2.0 equiv of $AlMe_3$, only bis-complexed diene **33** was seen (i.e. no oxime OH resonances were present). Up to this point there was no consumption of MA, indicating that Lewis acid reaction with the diene is much faster than dienophile activation. With 2.5 equiv of $AlMe_3$, another set of peaks appeared, corresponding to the single cycloadduct **34** (cycloaddition approximately 50% complete). Holding the temperature at −45 °C for 15 min revealed no further increase in the amount of **34** present. This implied that all the Lewis acid added over 2 equiv activated MA for cycloaddition but probably remained complexed to the cycloadduct rather than dissociating and activating more MA. This observation is consistent with reports that Lewis acid promoted Diels−Alder reactions involving α,β-unsaturated esters many times are not catalytic in Lewis acid.[19] As the amount of $AlMe_3$ was increased to 3 equiv, all MA was consumed and only the single cycloadduct **34** was observed.

(19) Keay, B. A.; Rauk, A.; Woo, W.; Rogers, C.; Hunt, I. R. *J. Am. Chem. Soc.* **1995**, *117*, 1049.

Table 4. $AlMe_3$−22a Promoted Cycloadditions

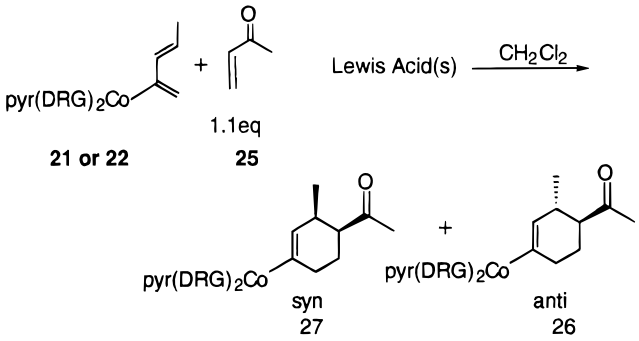


entry	$AlMe_3$ (equiv)	conditions	24 *anti*:*syn* (% yield)
1	0.0	25 °C, 8 h	1:1 (81.3)
2	3.0	−50 °C, 19 h	9.4:1 (66)
3	4.0	−50 °C, 19 h	>20:1 (78.9)
4	2.0	−78 °C, 22 h	1:1 (95.3)
5	3.0	−78 °C, 26.5 h	9.0:1 (74.1%
6	4.0	−78 °C, 26.5 h	>20:1 (72.6)

The preparative scale reactions of MA and **22a** with $AlMe_3$ produced largely expected results as determined by NMR experiments (Table 4). One surprise was that the diastereoselectivities, while good when 3 equiv of Lewis acid was used, were not as high as those seen in the NMR tube experiments. Complete *anti* (*exo*) selectivity required the addition of more Lewis acid. If the cycloaddition is slow at 3 equiv of $AlMe_3$ on the preparative scale or there are slight inaccuracies in Lewis acid molarity, there could still be unreacted diene (**22a**) and MA present upon quenching and warm up. A purely thermal Diels−Alder reaction (entry 1, Table 4) between the remaining diene and MA would then decrease the *anti* (*exo*) selectivity seen in the cycloadduct (entry 2, Table 4). At 4 equiv of $AlMe_3$ (entries 3 and 6, Table 4), we saw that there was complete *exo* addition to produce only *anti* diastereomer (**24a**). Entry 4, Table 4, confirmed our NMR observation that we would expect the first 2 equiv of Lewis acid to react with the diene with no Lewis acid catalysis. If this occurred, the Diels−Alder reaction would simply occur after aqueous quenching and warming, and we would expect the same diastereoselectivity that was observed in the absence of Lewis acid. By just adding 4 equiv of $AlMe_3$, we have accelerated the reaction at −50 °C and induced a totally *anti* (*exo*) selective addition of MA with the dmg diene. Unfortunately, this observation means that attempts at using a chiral aluminum Lewis acid to induce an enantioselective and *exo* selective Diels−Alder reaction may be stoichiometric in Lewis acid for this dienophile.

Since α,β-unsaturated ketones are known to participate in catalytic Lewis acid mediated Diels−Alder reactions,[19] we decided to investigate Lewis acid catalyzed reactions of cobalt dienes (**22a**−**c**) with MVK. We could anticipate that the first 2 equiv of Lewis acid would complex the diene and then any excess would promote the Diels−Alder reaction. Using 2.25 equiv of $AlMe_3$ with cobalt dmg diene (**22a**) we saw no product, which indicated that $AlMe_3$ was not strong enough to promote the Diels−Alder reaction (Table 4), and the use of 2.25 equiv of a stonger Lewis acid such as BCl_3 caused significant complex decomposition even at −50 °C. We thought that since the first 2 equiv of Lewis acid bind irreversibly to the diene complex, we could then use the first 2 equiv to both increase the steric bulk of the diene and protect the diene from stronger Lewis acids that would otherwise decompose it (i.e. BCl_3). We tried using 2.0 equiv of $AlMe_3$ followed by 0.25 equiv of a stronger Lewis acid, $AlEt_2Cl$. Cycloaddition occurred but only 20% after 2.7 days. Using 0.25 equiv of BCl_3 following 2.0 equiv of $AlMe_3$ did promote the desired catalytic reaction at −50 °C with a 1.6:1 *syn*:*anti* (*endo*:*exo*) selectivity (entry 3, Table 5). This reaction was significantly more

Table 5. Lewis Acid Catalyzed Diels−Alder Reactions of 21 or 22 with MVK



entry	Lewis acid(s)	conditions	*syn*:*anti* (% yield)
	DMG (22a)		
1	2.25 equiv of $AlMe_3$	−50 °C, 11 h	*a*
2	2.0 equiv of $AlMe_3$, 0.25 equiv of $AlEt_2Cl$	−50 °C, 11 h	*b*
3	2.0 equiv of $AlMe_3$, 0.25 equiv of BCl_3	−50 °C, 2.7 h	1.6:1 (80.2%)
	DPG (22b)		
4	0.0 equiv	−22 °C, 14 d	*a*
5	2.25 equiv of $AlMe_3$	−50 °C, 12 h	*a*
6	2.0 equiv of $AlMe_3$, 0.25 equiv of $AlEt_2Cl$	−50 °C, 12 h	1:1.3 (81.7)
7	2.0 equiv of DIBALH, 0.25 equiv of Et_2Cl	−50 °C, 1.5 d	1:1.3 (83.4)
8	2.0 equiv of DlBALH, 0.25 equiv of DlBALCl	−50 °C, 1.5 d	1:1.6 (90.1)
	AG (21)		
9	2.0 equiv of $AlMe_3$, 0.25 equiv of BCl_3	−50 °C	*a*
10	2.0 equiv of DlBALH, 0.25 equiv of BCl_3	−50 °C	*c*
11	2.0 equiv of DiBALH, 0.25 equiv of DlBAlCl	−50 °C	*c*

[a] Unreacted diene. [b] 10% complete after 11 h and 20% after 2.7 days. [c] 10% comlete after 5 d with a 1:1 ratio of diastereomers.

exo selective than the purely thermal cycloaddition result (5:1 *endo*:*exo*). This result indicated that we should try using larger ligand sets on the first 2 equiv of Lewis acid to see if this produced even more *exo* addition.

Increasing the size of the equatorial ligand using Lewis acids was next pursued with the larger equatorial ligand dienyl complexes **22b** and **21**. We knew that dpg diene (**22b**) failed to cyclize with 20 equiv of MVK in the absence of Lewis acids at −22 °C (entry 4, Table 5). Once again, using $AlMe_3$ alone with a dienyl complex, this time **22b**, failed to promote any cycloaddition (entry 5, Table 5). Using 2 equiv of $AlMe_3$ and 0.25 equiv of $AlEt_2Cl$ promoted cycloaddition, but the selectivity (1.3:1 *anti: syn* (*exo*: *endo*), entry 6, Table 5 was only slightly better than the thermal result at 25 °C (1:1). Adding a larger Lewis acid (2.0 equiv of DIBALH) followed by 0.25 equiv of $AlEt_2Cl$ (entry 7, Table 5) had virtually no additional effect. Using an even larger commercially available Lewis acid combination (2.0 equiv of DIBALH followed by 0.25 equiv of DIBAlCl), we saw a slight increase in *exo* selectivity (entry 8, Table 5). Unfortunately, the very sterically hindered AG dienyl complex **21** proved to be essentially unreactive toward MVK under these low-temperature Lewis acid catalyzed conditions (entries 9−11, Table 5).

Conclusions

Table 6 summarizes our results to date for thermal and Lewis acid catalyzed Diels−Alder reactions of cobalt-substituted dienes with tri-, di-, and monosubstituted dienophiles. We have been able to achieve >20:1 *anti* (*exo*) selectivity for the tri- or disubstituted dienophiles. The monosubstituted dienophile, MVK, has proven to be the toughest case for us, and our best *anti* (exo) selective Diels−Alder reaction for this dienophile produces the *anti* (*exo*) diastereomer in 2:1 excess over the *syn* (*endo*) diastereomer. In all cases following cycloaddition, we have developed cobalt−carbon bond cleaving reactions which allow recovery of the organic cycloadduct with stereochemistry intact as well as a cobalt complex that is easily converted back into our starting cobalt dienes **21** and **22**.

Table 6. Best Selectivities *Anti*:*Syn* (*Exo*:*Endo*) Obtained for a Variety of Dienophiles

pyr(R)$_2$Co		BQ	MA	CA	MVK
DMG **22a**	thermal	**>20:1**	2.3:1		1:5
	Lewis Acid		**>20:1**		1:1.6
DPG **22b**	thermal		8.4:1	**>20:1**	1:1
	Lewis Acid				1.6:1
AG **21**	thermal		**>20:1**		2:1
	Lewis Acid				NR

Acknowledgment. We thank the National Science Foundation (CHE-9321454), the donors of the Petroleum Research Fund administered by the American Chemical Society, 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. M.W.W. acknowledges Sigma Xi for a student grant-in-aid.

JO951505O