ORGANOMETALLICS

Volume 19, Number 9, May 1, 2000

Communications

Synthesis and Enantioselective Diels−Alder Reactions of Optically Active Cobalt(III) Salen-1,3-butadien-2-yl Complexes

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Received January 31, 2000

Summary: The syntheses of two optically active Co(salen)-1,3-butadien-2-yl complexes are reported. One of the dienyl complexes was characterized by X-ray crystallography. The dienyl complexes underwent Diels−Alder reactions with high enantioselectivity with dimethyl fumarate. A highlight of this chemistry is that Diels−Alder cycloadduct cobalt complexes were cleanly cleaved at the cobalt−carbon bond with concomitant optically active cobalt complex starting material and optically active cyclohexene cycloadduct recovery.

The preparation of enantiomerically pure complex molecules is a fundamental challenge of modern organic synthesis. The asymmetric Diels−Alder reaction is one of the most powerful synthetic methods for control of absolute stereochemistry. To date, unactivated dienes such as 1,3-butadiene have not been impressively employed in enantioselective Diels−Alder reactions.[1] We recently developed an efficient method for the preparation of cobalt(III) salen [Co(salen)]-1,3-butadien-2-yl complexes and demonstrated their utility as reactive, 1,3-butadiene synthons in numerous [4+2] cycloaddition reactions.[2] In a significant advance in this methodology, we now report the synthesis of optically active Co(salen)-1,3-butadien-2-yl complexes which undergo Diels−Alder reactions with dimethyl fumarate with high enantioselectivity. Many examples of chiral organic dienes have been reported,[3] but this is the first report of the use of optically active transition-metal-substituted dienyl complexes in enantioselective Diels−Alder reactions.[4] Wulff,[5] Barluenga,[6] and Dotz[7] have all independently reported the use of transition-metal carbene complexes as dienophiles in enantioselective Diels−Alder reactions.

Utilizing a modified literature procedure,[8] (*R*,*R*)-(−)

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(1) For a recent review see: (a) Corey, E. J.; Guzman-Perez, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 389. For some examples of related reactions with α-bromoacrolein as dienophile see: (b) Bruin, M. E.; Kundig, E. P. *Chem. Commun.* **1998**, 2635. (c) Hayashi, Y.; Rohde, J. J.; Corey, E. *J. Am. Chem. Soc.* **1996**, *110*, 5502.

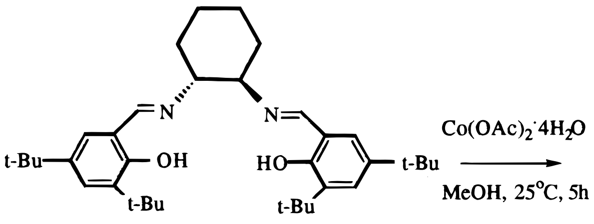
(2) Chapman, J. J.; Welker, M. E. *Organometallics* **1997**, *16*, 747. For a review of our related work in cobaloxime chemistry see: Wright, M. W.; Stokes, H. L.; Richardson, B. M.; Adams, T. A.; Smalley, T. L.; Vaughn, S. P.; Lohr, G. J.; Welker, M. E.; Liable-Sands, L.; Rheingold, A. L. In *Advances in Cycloaddition*; Lautens, M., Ed.; JAI Press: Greenwich, CT, 1997; Vol. 4, p 149.

(3) For a review of chiral, organic dienes see: (a) Enders, D.; Meyer, O. *Liebigs Ann.* **1996**, 1023. For some recent primary literature citations see: (b) Kozmin, S. A.; Rawal, V. H. *J. Am. Chem. Soc.* **1999**, *121*, 9562. (c) Hu, Y.-J.; Huang, X.-D.; Yao, Z.-J.; Wu, Y.-L. *J. Org. Chem.* **1998**, *63*, 2456. (d) Kozmin, S. A.; Rawal, V. H. *J. Am. Chem. Soc.* **1997**, *119*, 7165. (e) Aversa, M. C.; Barrattucci, A.; Bonaccorsi, P.; Giannetto, P.; Jones, D. N. *J. Org. Chem.* **1997**, *62*, 4376. (f) Barluenga, J.; Aznar F.; Ribas, C.; Valdes, C. *J. Org. Chem.* **1997**, *62*, 6746.

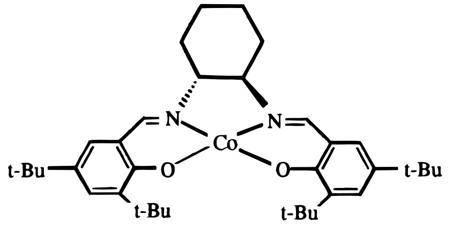
(4) Kundig has reported the use of an in situ generated chiral *o*-quinodimethane chromium complex (a diene rather than dienyl complex) that participates in Diels−Alder reactions: Kundig, E. P.; Leresche, J.; Saudan, L.; Bernardinelli, G. *Tetrahedron* **1996**, *52*, 7363.

(5) Powers, T. S.; Jiang, W.; Su, J.; Wulff, W. D. *J. Am. Chem. Soc.* **1997**, *119*, 6438.

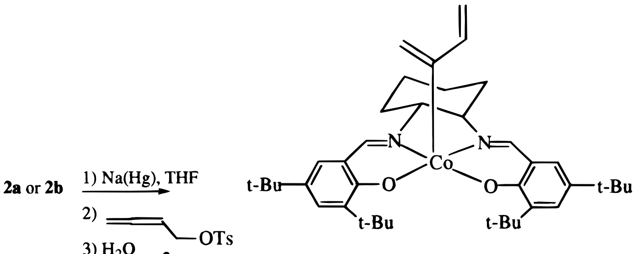
10.1021/om000074j CCC: $19.00 © 2000 American Chemical Society
Publication on Web 03/28/2000



99%, R, R shown
1a R, R $[\alpha]_D^{23}$ = -315° (c = 0.769, CH_2Cl_2)
1b S, S $[\alpha]_D^{23}$ = +315° (c = 0.425, CH_2Cl_2)



98%, R, R shown
2a R, R $[\alpha]_D^{23}$ = -1145.1° (c = 0.0324, $CHCl_3$)
2b S, S $[\alpha]_D^{23}$ = +1147.3° (c = 0.0319, $CHCl_3$)



R, R shown
4a R, R $[\alpha]_D^{20}$ = +3333.3° (c = 0.0105, CH_2Cl_2) (88%)
4b S, S $[\alpha]_D^{20}$ = -3325.0° (c = 0.0120, CH_2Cl_2) (91%)

(**1a**) and (*S*,*S*)-(+) (**1b**) salen ligands were both obtained in near quantitative yield starting originally from a single, large batch of the commercially available cis/trans mixture of 1,2-diaminocyclohexane. Optically active Co(II) salen complexes (**2a** and **2b**) were then obtained in quantitative yield by condensing cobalt acetate with the appropriate salen ligand (**1a** or **1b**) in methanol at 60 °C. The *R*,*R*-(−) enantiomer of this Co(salen) complex (**2a**) was characterized by X-ray crystallography by Leung et al. in 1996, but no optical rotation was reported.[9] Jacobsen and co-workers then reported the use of these Co(salen) complexes as catalysts for enantioselective epoxide ring opening.[10] Wu et al. reported the use of these Co(salens) as hetero Diels−Alder catalysts in 1998, and they reported a rotation of 1100° for the complexes (*c* = 0.01, CH_2Cl_2).[10] The preparation we report here uses a recrystallization from methanol, and the Co(salen) complexes obtained have slightly higher rotations [(*R*,*R*)-(−)-Co(II) salen, −1145.1°, and (*S*,*S*)-(+)-Co(II) salen, +1147.3° (*c* = 0.03, $CHCl_3$).

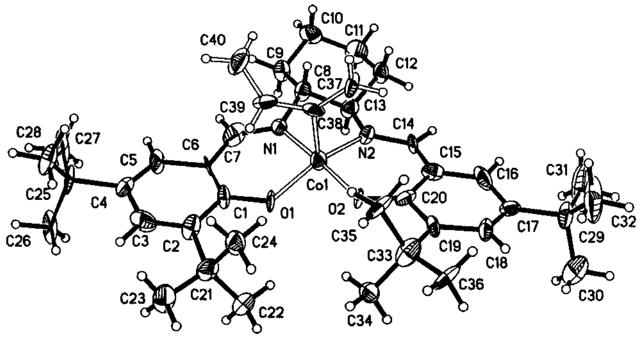
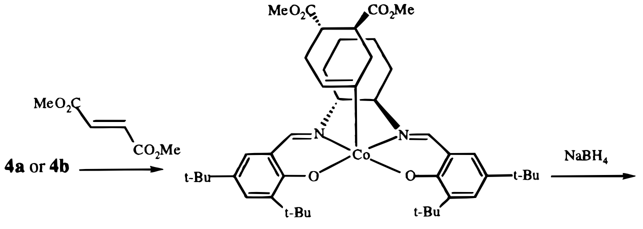
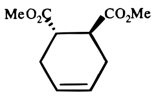


Figure 1. Perspective drawing of one of the two crystallographically independent molecules present in the solid state structure of **4a**.



R, R ligand shown
5a R, R ligand $[\alpha]_D^{20}$ = +3876.9° (c = 0.0130, $CHCl_3$) (96%)
5b S, S ligand $[\alpha]_D^{20}$ = -3880.0° (c = 0.0125, $CHCl_3$) (91%)



+ **2a** or **2b** (95%)
99% ee

S, S (+) cycloadduct (**6a**) obtained from **5a** shown
6a S, S (+) >98% ee at -20°C
6b R, R (−) >98% ee at -20°C

Lueng et al. reported that the Co(II) salens (**2a**, **2b**) could be reduced with sodium amalgam and that they treated the corresponding anion with unspecified alkyl halides.[9] They report that they could not isolate the presumably formed alkylation products. We found that Co(II) salen (**2a** or **2b**) was easily converted to the dark green Co(I) salen anion via Na(Hg) in THF. The dark green anion reacted with 4-tosyl-1,2-butadiene (**3**) to give the corresponding optically active (*R*,*R*)-(+)-(**4a**) and (*S*,*S*)-(−)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylideneaminato))-1,2-cyclohexanediamine)]-(1,3-butadien-2-yl)cobalt(III) (**4b**) complexes in high yield.

The dienyl complex **4a** from the *R*,*R* salen ligand was characterized by X-ray crystallography.[12] The solid-state structure showed two distinct conformers for this complex with equal solid state conformer populations (Figure 1 shows one of the two conformers). In solution, we saw no ^1H NMR evidence for hindered rotation about the cobalt−carbon bond over a temperature range of 25 to −63 °C, indicating conformer interconversion is facile over the temperature ranges we might employ for cycloadditions. These conformers have dihedral (torsion) angles around the C(38)−C(39) and C(88)−C(89) bonds

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(6) Barluenga, J.; Canteli, R.-M.; Florez, J.; Garcia-Granda, S.; Gutierrez-Rodriguez, A.; Martin, E. *J. Am. Chem. Soc.* **1998**, *120*, 2514.

(7) (a) Weyerhausen, B.; Nieger, M.; Dotz, K. H. *J. Org. Chem.* **1999**, *64*, 4206. (b) Dotz, K. H.; Bottcher, D.; Jendro, M. *J. Organomet. Chem.* **1999**, *583*, 34.

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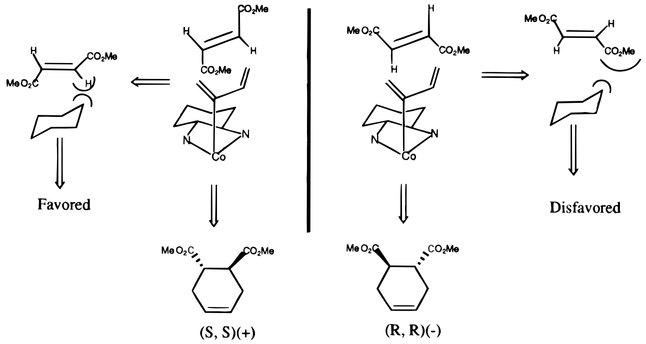
(11) Hu, Y. J.; Huang, X. D.; Yao, Z. J.; Wu, Y. C. *J. Org. Chem.* **1998**, *63*, 2456.

(12) Crystallographic data for **4a**: triclinic, P1-C (l/i) (No. 1), *a* = 10.3046(4) Å, *b* = 13.1485(5) Å, *c* = 14.4207(6) Å, α = 92.228(1)°, *β* = 99.969(1)°, *γ* = 107.988(1)°, volume = 1821.39(12) Å^3, *Z* = 2, R1 = 0.084, GOF = 1.090. Complete details of the crystallographic characterization of **4a** are included in the Supporting Information.

Table 1. Enantioselective Synthesis of Dimethyl Fumarate Cycloadducts

entry	diene	solv	Lewis acid	temp (°C)	time (h)	step 2	yield (%)	ee (%)	cycloadduct
1	**4a**	THF	none	40	6	$NaBH_4$ EtOH	81	36	**6a**
2	**4b**	THF	none	40	6	$NaBH_4$ EtOH	86	24	**6b**
3	**4a**	THF	5Å sieves	25	24	$NaBH_4$ EtOH	84	51	**6a**
4	**4a**	CH_2Cl_2	none	25	72	$NaBH_4$ MeOH	92	12	**6a**
5	**4b**	CH_2Cl_2	none	25	72	$NaBH_4$ MeOH	91	15	**6b**
6	**4a**	$CHCl_3$	none	25	24	$LiBH_4$ EtOH	87	29	**6a**
7	**4a**	CH_2Cl_2	Et_2AlCl	25	0.33	$NaBH_4$ EtOH	73	46	**6a**
8	**4a**	CH_2Cl_2	$EtAlCl_2$	25	0.33	$NaBH_4$ EtOH	75	64	**6a**
9	**4a**	CH_2Cl_2	$AlCl_3$	25	0.33	$NaBH_4$ EtOH	78	78	**6a**
10	**4b**	CH_2Cl_2	$AlCl_3$	25	0.33	$NaBH_4$ EtOH	79	76	**6b**
11	**4b**	CH_2Cl_2	$AlCl_3$	0−25	0.5	$Hg(OAc)_2$ $NaBH_4$ EtOH	65	82	**6b**
12	**4a**	CH_2Cl_2	$AlCl_3$	−20	18	$NaBH_4$ EtOH	55	>98	**6a**
13	**4b**	CH_2Cl_2	$AlCl_3$	−20	18	$NaBH_4$ EtOH	54	>98	**6b**



of 68−70°, similar to dienyl cobalt glyoxime complexes we have reported previously.[13] The cobalt(1)−C(38) and cobalt(2)−C(88) distances of 1.962(9) and 2.007(13) Å are also similar to those seen in the glyoxime ligand series.[13]

Optically active dienyl complexes **4a** and **4b** were then reacted with dimethyl fumarate in a series of thermal and Lewis acid-catalyzed Diels−Alder reactions (Table 1). Cobalt-containing cycloadducts (**5a** and **5b**) can be isolated and characterized if desired however; for most of the runs presented in Table 1, the cycloaddition and subsequent demetalation to yield *trans*-1,2-dicarbomethoxy-3-cyclohexene (**6**) were performed in the same flask. The cycloadduct **5** from a thermal reaction (Table 1, entry 1) was also characterized by X-ray crystallography, confirming its formulation as shown.[14]

Reactions between dimethyl fumarate and both enantiomers of Co(III) salen-1,3-butadiene (**3a** and **3b**) were carried out in polar and nonpolar solvents between −78 and 68 °C. Chloroform, THF, and methylene chloride were evaluated initially as reaction solvents for thermal Diels−Alder reactions. Tetrahydrofuran required heating to 40 °C or the addition of molecular sieves to proceed with reasonable rates (Table 1, entries 1−3). Reactions in CH_2Cl_2 and $CHCl_3$ proceeded slowly at 25 °C, but the chemical yields were excellent (Table 1, entries 4−6). The solubility characteristics of CH_2Cl_2 and the ability to screen a variety of Lewis acids led us to investigate catalyzed Diels−Alder reactions in CH_2Cl_2. $BF_3{\cdot}Et_2O$, $AlCl_3$, $EtAlCl_2$, Et_2AlCl, $SnCl_4$, and $TiCl_4$ were evaluated as potential catalysts. $BF_3{\cdot}Et_2O$, $SnCl_4$, and $TiCl_4$ all appeared to destroy the diene (**4a**, **4b**) when employed as catalyst. Alkyl aluminum chlorides reacted under mild conditions but resulted in lower ee's than aluminum chloride (Table 1, entries 7, 8). Aluminum chloride-catalyzed reactions gave ee's > 75% at 0−25 °C (Table 1, entries 9−11) and ee's approaching 100% at −20 °C (Table 1, entries 12, 13). Reactions attempted with aluminum chloride were too slow to monitor below −20 °C. A highlight of this chemistry is that Diels−Alder cycloadducts **5a** and **5b** were cleanly cleaved at the cobalt−carbon bond using sodium borohydride in ethanol with concomitant optically active cobalt complex **2a**,**b** and cycloadduct **6a**,**b** recovery. Optical purities of cleaved cycloadducts were established via chiral GC, and specific rotations of cleaved cycloadducts were compared to the chemical literature to derive the absolute stereochemistry of the cycloadducts.[15] Corey has previously noted that these esters (**6**) cannot be obtained in high optical purity from the Diels−Alder reaction of 1,3-butadiene with dimenthyl fumarate followed by menthyl ester transesterification.[16] However

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[13] (a) Wright, M. W.; Smalley, T. L.; Welker, M. E.; Rheingold, A. L. *J. Am. Chem. Soc.* **1994**, *116*, 6777. (b) Stokes, H. L.; Richardson, B. M.; Wright, M. W.; Vaughn, S. M.; Welker, M. E.; Liable-Sands, L.; Rheingold, A. L. *Organometallics* **1995**, *14*, 5520.

[14] This X-ray structure determination will be reported in a forthcoming full paper.

[15] Walborsky, H. M.; Barash, L.; Davis, T. C. *Tetrahedron* **1963**, *19*, 2333.

[16] Corey, E. J.; Su, W. *Tetrahedron Lett.* **1988**, *29*, 3423.

[17] (a) Backer, H. J.; Blaas, T. A. H. *Rec. Trav.* **1942**, *61*, 785. (b) Sample, T. E.; Hatch, L. F. *Organic Syntheses*; Wiley: New York, Collect. Vol. VI; 1988; p 454.

[18] Brandsma, L.; Verkruijsse, H. D. *Synthesis of Acetylenes, Allenes, and Cumulenes*; Elsevier Publishing Co.: New York, 1981; pp 65, 171, 188.

this chiral diene rather than chiral dienophile approach does provide these compounds (**6**) in high enantiomeric purity.

At this point we do not know what effect, if any, the conformer population (noted in the solid-state structure of **4a** above) has on Diels–Alder cycloaddition outcomes. In the case studied here, the observed enantioselectivities can be rationalized through an analysis of dienophile–diene steric interactions which are independent of reactive conformer. Using the (*R*,*R*)-(+) dienyl complex conformer calculated to be most stable (Spartan Plus PM3 calculation) (**4a**, Figure 1b) as an example, cyclohexadienyl–dienophile steric interactions predict a selectivity for the observed (*S*,*S*)-(+) cycloadduct. A detailed explanation of the observed enantioselectivity awaits our investigation of additional dienyl complexes and dienophiles in the future. In summary, we report the synthesis and X-ray crystallographic characterization of the first chiral transition-metal-substituted 1,3-dienes with σ bonds from the transition metal to the dienyl fragment. These dienes participate in enantioselective Diels–Alder reactions from which cyclohexenes and Co(II) salen complexes can be recovered in high enantiomeric purity.

Acknowledgment. We thank the National Science Foundation (CHE-9726172) 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) and Duke University Mass Spectrometry Facility performed high-resolution mass spectral analyses.

Supporting Information Available: Tables giving details of the X-ray structure determinations, atomic coordinates and isotropic thermal parameters, bond lengths and bond angles, and anisotropic displacement parameters and an ORTEP for the second conformer for **4a**, in addition to spectroscopic and characterization data on all new compounds reported. This material is available free of charge via the Internet at http://pubs.acs.org.

OM000074J