



Pergamon

Tetrahedron: Asymmetry 9 (1998) 2023–2026

TETRAHEDRON:  
ASYMMETRY

# Enantioselective cycloadditions catalyzed by face resolved arene chromium carbonyl complexes

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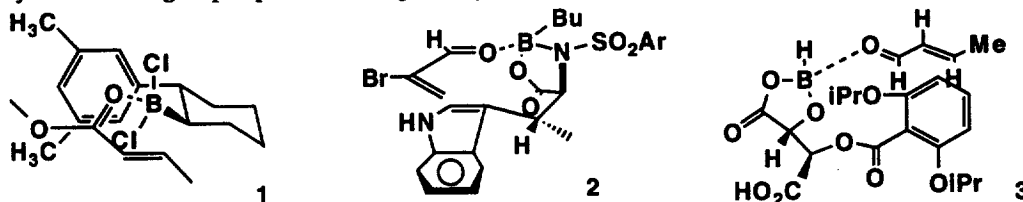
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Received 15 April 1998; accepted 7 May 1998

## Abstract

A new class of readily accessible enantioselective catalysts has been developed, and examined in the Diels–Alder cycloaddition of methacrolein. Analysis of potential transition state influences provides an insight for future modification and refinement. © 1998 Elsevier Science Ltd. All rights reserved.

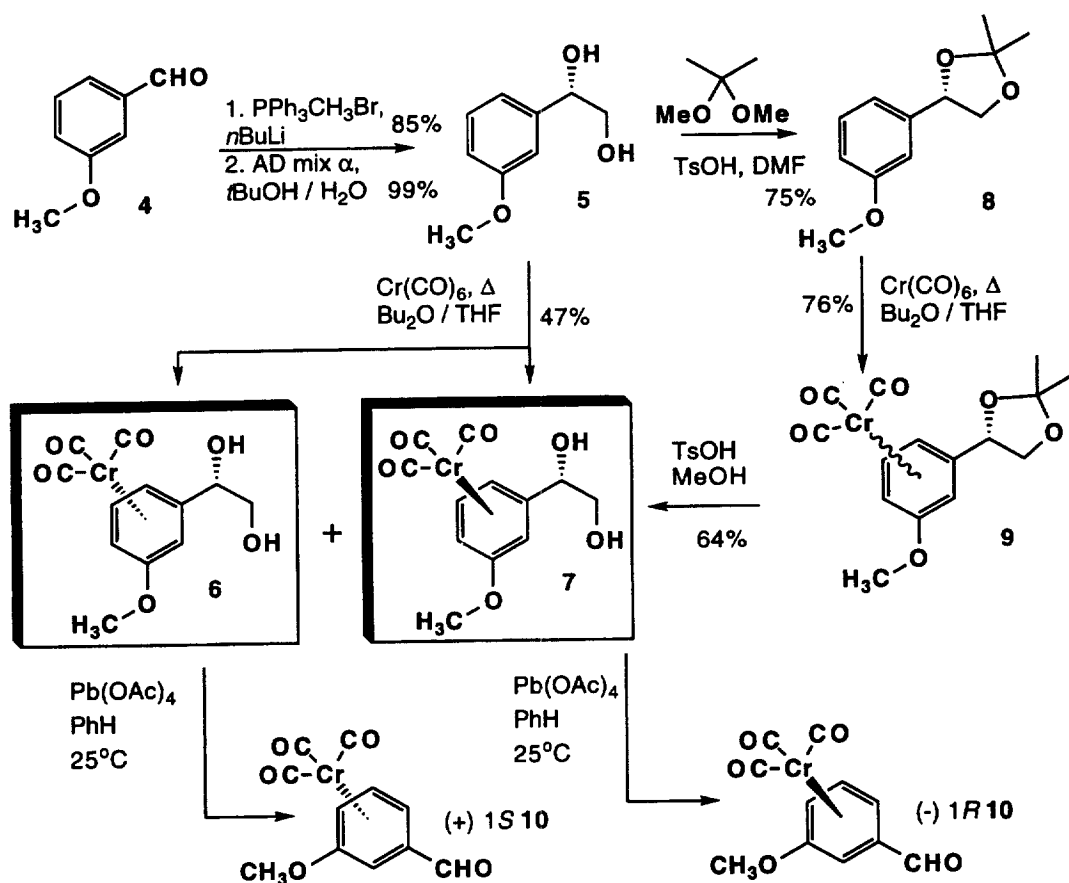
The rapid evolution of enantioselective Diels–Alder catalysts has resulted in many systems capable of mediating these cycloadditions with extremely high selectivity.<sup>1</sup> Particularly impressive are dual point binding catalysts, wherein conjugated substrates engage in primary coordination to a Lewis acidic site via a carbonyl group of the dienophile, with secondary interaction achieved via overlap of the dienophile vinyl group with an arene moiety of the catalyst. These secondary interactions range from  $\pi$ -shielding effects to attractive  $\pi$ -stacking interactions and have been described in a number of systems.<sup>2</sup> Pertinent examples include dichloroborane **1**,<sup>3</sup> oxazaborolidine **2**,<sup>4</sup> and acyloxyboronate **3**,<sup>5</sup> each depicted as 1:1 complexes with a coordinated dienophile. Additional interactions of the substrate formyl H atom with proximal lone pairs of oxygen atoms of the catalyst have also been suggested in the case of **2** and **3**, effectively establishing triple point binding catalyst–substrate assemblies.<sup>6</sup>



While tuning of the primary Lewis acidic  $\sigma$  coordination sites of such catalysts is usually accomplished via metal ligand variation, modulation of the aryl–substrate vinyl  $\pi$ -shielding/ $\pi$ -stacking interactions is not generally possible without drastically changing the catalyst architecture. Based on previous experience with chiral arene chromium tricarbonyl complexes,<sup>7–9</sup> we became interested in empowering

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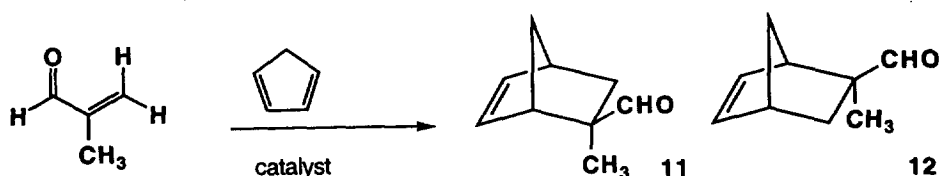
the planar chirality of these complexes to direct face selective cycloaddition reactions.<sup>10</sup> Electronic interactions between the substrate and arene could in principle be modulated by appropriate selection of ligand combinations about chromium to render the arene either  $\pi$ -basic or  $\pi$ -acidic.<sup>9,11</sup> To provide proof of principal, *m*-disubstituted arene diol complexes were selected since they; (i) can be accessed from readily available precursors, (ii) possess requisite planar chirality, (iii) asymmetry can be introduced via versatile asymmetric dihydroxylation technology and (iv) the *m*-substituent should not present a significant steric entity to metallocycles derived from these diols, allowing the effects of the metal complex to be highlighted more effectively.<sup>10</sup> Accordingly, *m*-anisaldehyde was subjected to olefination followed by Sharpless dihydroxylation to give *S*-diol **5** in >99% e.e. (Scheme 1).<sup>12</sup> Complexation at this point using conventional conditions<sup>8</sup> gave a moderate yield of a 1:1 mixture of diastereomers **6** and **7**, which were separable using chromatographic methods.<sup>13</sup> Protection of the hydroxyl functions in the form of ketal **8** followed by complexation gave a higher yield of complex **9**, but in a ratio of 5:1 in favor of the *S,S*-complex confirmed on deprotection to give **6**. The identity of facial diastereomers **6/7** was established via oxidative cleavage to give the known aldehydes **10**.<sup>14</sup>



Scheme 1. Preparation and stereochemical assignment of catalyst precursors

The diols were then exposed to a variety of Lewis acids, and the corresponding metallocycles/chelates examined in the catalytic enantioselective cycloaddition of 2-methacrolein with cyclopentadiene, using catalysts derived from **5** as controls. Though *exo*-preference was observed with every Lewis acid combination examined, *R* enantiomeric cycloaddition product **11** was favored with both the boron

and titanium metallocycles and the *S*-enantiomer **12** predominated with the aluminum metallocycles (Scheme 2, Table 1).



Scheme 2. Metallo-dioxolane catalyzed [4+2] cycloadditions

A key feature of these catalysts is the geometric flexibility of the Lewis acidic metal center. Boronates were in general less selective than the aluminates, and within this class, aluminates capable of forming *bona fide* metallocycles [entries 8–11] less discriminating than the dihaloaluminates [entries 12–15]. As noted above, the coordinative geometry of the metal center itself also has a profound effect on the product enantiomer distribution. Though selectivity is modest (<65% e.e.), catalysts derived from **6** are routinely superior to **7** which are in turn superior to uncomplexed analogs **5**. However, since the same enantiomeric product predominates using either **6** or **7** it is suggestive that the entire arene metal–carbonyl appendage is functioning as a stand alone stereodirective element, a function of its planar chirality. Ongoing investigations, using mixed ligand arene chromium carbonyl complexes of this class<sup>15,16</sup> are designed to delineate the relative importance of; (i)  $\pi$ – $\pi$  interactions between the catalyst aryl group and methacrolein vinyl group,<sup>17,18</sup> (ii) formyl substrate–catalyst hydrogen bonds<sup>6</sup> and (iii) the Lewis basicity of the chiral *sec*-alcohol function.

In summary, a new family of enantioselective catalysts has been developed, utilizing the planar chirality of *m*-disubstituted arene chromium carbonyl complexes. The ready accessibility of the catalysts, and the potential for both refinement and application in a number of catalytic processes renders their study an important objective.

Table 1  
Enantioselective cycloaddition of 2-methacrolein using diol catalysts<sup>a</sup>

Entry	diol	mol% LA	prod. (%) <sup>b</sup>	exo:endo <sup>c</sup>	%e.e. <sup>d</sup>	
1	<b>5</b>	20	BH <sub>2</sub> Br	<b>11</b> (99)	92:8	19
2	<b>7</b>	20	BH <sub>2</sub> Br	<b>11</b> (83)	95:5	20
3	<b>6</b>	20	BH <sub>2</sub> Br	<b>11</b> (91)	96:4	39
4	<b>6</b>	20	BCl <sub>3</sub>	<b>11</b> (95)	90:10	0
5	<b>6</b>	20	BHCl <sub>2</sub>	<b>11</b> (95)	81:9	44
6	<b>6</b>	20	BHBr <sub>2</sub>	<b>11</b> (87)	86:14 <sup>e</sup>	43
7	<b>6</b>	20	BF <sub>3</sub> OEt <sub>2</sub>	<b>11</b> (75)	99:1	0
8	<b>5</b>	20	Et <sub>2</sub> AlCl	<b>12</b> (98)	66:34	21
9	<b>7</b>	20	Et <sub>2</sub> AlCl	<b>12</b> (82)	99:1	31
10	<b>6</b>	20	Et <sub>2</sub> AlCl	<b>12</b> (83)	98:2	41
11	<b>6</b>	80	Et <sub>2</sub> AlCl	<b>12</b> (82)	99:1	41
12	<b>5</b>	20	EtAlCl <sub>2</sub>	<b>12</b> (67)	85:15	29
13	<b>7</b>	20	EtAlCl <sub>2</sub>	<b>12</b> (92)	96:4	53
14	<b>6</b>	20	EtAlCl <sub>2</sub>	<b>12</b> (99)	95:5	61
15	<b>6</b>	100	EtAlCl <sub>2</sub>	<b>12</b> (83)	96:4	62
16	<b>5</b>	20	TiCl <sub>2</sub> OiPr <sub>2</sub>	<b>11</b> (91)	64:36	28
17	<b>6</b>	20	TiCl <sub>2</sub> OiPr <sub>2</sub>	<b>11</b> (87)	73:27	46

(a) All reactions employed 0.5 mmol substrate in CH<sub>2</sub>Cl<sub>2</sub> (-78°C / 24h); (b) isolated yields following SGC; (c) determined by <sup>1</sup>H NMR of crude isolates; (d) determined by chiral shift analysis using Eu(hfc)<sub>3</sub>; (e) conducted in THF.

## Acknowledgements

We thank the GHS, Elsa U. Pardee Foundation and the Donors of the Petroleum Research Fund (Administered by the American Chemical Society) for financial support of this work (28706-AC1).

## References

1. For review see Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994.
2. Jones, G. B.; Chapman, B. J. *Synthesis* **1995**, 475.
3. Hawkins, J. M.; Loren, S. *J. Am. Chem. Soc.* **1991**, *113*, 7794; Hawkins, J. M.; Loren, S.; Nambu, M. *J. Am. Chem. Soc.* **1994**, *116*, 1657.
4. Corey, E. J.; Loh, T.-P. *J. Am. Chem. Soc.* **1991**, *113*, 8966; Corey, E. J.; Loh, T.-P.; Roper, T. D.; Azimioara, M. D.; Noe, M. C. *J. Am. Chem. Soc.* **1992**, *114*, 8290.
5. Ishihara, K.; Gao, Q.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 10412.
6. Corey, E. J.; Rhode, J. J. *Tetrahedron Lett.* **1997**, *38*, 37.
7. Jones, G. B.; Heaton, S. B. *Tetrahedron Lett.* **1992**, *33*, 1693; Jones, G. B.; Heaton, S. B. *Tetrahedron: Asymmetry* **1993**, *4*, 261; Jones, G. B.; Huber, R. S. *Synlett* **1993**, 367; Jones, G. B.; Chapman, B. J.; Huber, R. S.; Beaty, R. *Tetrahedron: Asymmetry* **1994**, *5*, 1199; Jones, G. B.; Huber, R. S.; Chapman, B. J. *Tetrahedron: Asymmetry* **1997**, *8*, 1797; Jones, G. B.; Guzel, M.; Chapman, B. J. *Tetrahedron: Asymmetry* **1998**, *9*, 901.
8. Jones, G. B.; Heaton, S. B.; Chapman, B. J.; Guzel, M. *Tetrahedron: Asymmetry* **1997**, *8*, 3625.
9. Jones, G. B.; Chapman, B. J. *Synlett* **1997**, 439.
10. Solladie-Cavallo, A.; *Advances in Metal–Organic Chemistry*, Liebeskind, L. S. Ed; JAI Press, CT, 1989, Vol. 1, pp. 99–133.
11. Jaouen, G.; Dabard, R. *J. Organometal. Chem.* **1974**, *72*, 377.
12. Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, *57*, 2768.
13. Key data: (6)  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  6.92 (s, 1H), 5.58 (t, 1H,  $J$  9 Hz), 5.42 (s, 1H), 5.09 (s, 1H), 5.05 (s, 1H), 4.79 (s, 1H), 4.53 (s, 1H), and 3.70 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  232.2, 128.3, 113.8, 94.9, 83.8, 82.9, 72.8, 67.8, 55.7; (7)  $^1\text{H}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  6.94 (s, 1H), 5.53 (t, 1H,  $J$  6 Hz), 5.41 (s, 1H), 5.12 (s, 1H), 4.81 (s, 1H), 4.29 (s, 1H), 4.18 (s, 1H), and 3.79 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  233.1, 127.8, 113.1, 94.7, 83.8, 82.7, 70.4, 68.6, and 55.6.
14. Dabard, R.; Jaouen, G. *Tetrahedron Lett.* **1969**, 3391.
15. For other examples of catalysts incorporating the arene chromium carbonyl moieties see: Uemura, M.; Miyake, R.; Nakayama, K.; Shiro, M.; Hayashi, Y. *J. Org. Chem.* **1993**, *58*, 1238; Pasquier, C.; Naili, S.; Pelinski, L.; Brocard, J.; Mortreux, A.; Agbossou, F. *Tetrahedron: Asymmetry* **1988**, *9*, 193.
16. Jones, G. B.; Chapman, B. J.; Mathews, J. E. *J. Org. Chem.* **1998**, *63*, 2928.
17. The  $\pi$ -donor ability of an arene chromium tricarbonyl complex has been reported: see Kaneta, N.; Mitamura, F.; Uemura, M.; Murata, Y.; Komatsu, K. *Tetrahedron Lett.* **1996**, *37*, 5385.
18. For an example of a chromium tricarbonyl  $\pi$ -complexed borabenzene–acrolein adduct see: Amendola, M. C.; Stockman, K. E.; Hoic, D. A.; Davis, W. M.; Fu, G. C. *Angew. Chem. Intl. Ed.* **1997**, *36*, 267.