代表性论文 7

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手性胍和双胍盐催化不对称合成 3,4-二氨基色酮：该论文利用胍类催化剂对吖内酯的活化和手性诱导作用，并结合该合成子的多个反应位点开展串联反应。采用水杨醛衍生的亚胺与吖内酯发生 Mannich-酰胺化反应，高对映和非对映选择性的一步合成了 3,4-二氨基苯并二氢吡喃-2-酮衍生物。有趣的是，当采用单胍-酰胺催化剂 G-PiPr$_2$ 时，产物主要以顺式为主；当采用双胍-酰胺形成的 HBAr$^F_4$ 盐催化剂 BGs-PiDPh$_2$ 时，产物主要以反式为主。证实了酰胺骨架对手性立体环境的调节作用。利用催化剂的对映异构体，可以很容易的得到该类二氨基苯并二氢吡喃酮的四个立体异构体。

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Asymmetric Synthesis of 3, 4-Diaminochroman-2-ones Promoted by Guanidine and Bisguanidium Salt

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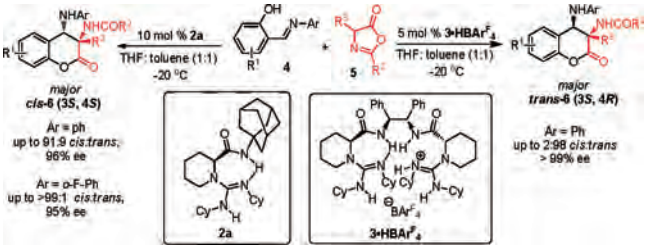
ABSTRACT



A highly enantioselective synthesis of 3,4-diaminochroman-2-ones has been realized *via* the domino reaction of *o*-hydroxy aromatic aldimines and azlactones. Notably, a *cis*-product was obtained as the major product by the use of guanidine 2a whereas a *trans*-product was the major product with bisguanidium salt 3•HBAr$^{F}_{4}$. In two cases, various substituted 3,4-dihydrocoumarins were obtained with high yields (up to 99%) as well as excellent enantioselectivities (up to 99% ee) and diastereoselectivities (up to >99:1 *cis*:*trans* and 98:2 *trans*:*cis*, respectively) under mild reaction conditions.

3,4-Dihydrocoumarins are one of the most privileged structural motifs frequently occurring in natural products,[1] and have been widely recognized as useful building blocks for the synthesis of various biologically active compounds.[2] As important variants, amino substituted 3,4-dihydrocoumarins exhibit intriguing biological activities,[3] such as **1a** with antihypertensive activity, **1b** as a potential inhibitor of TEM β-lactamase, and **1c** as an inhibitor of platelet aggregation (Figure 1). However,

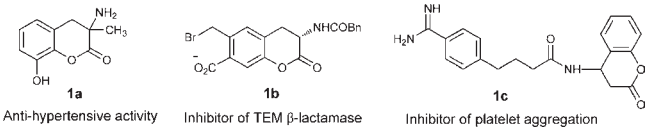


Figure 1. Examples of biologically active amino substituted 3, 4-dihydrocoumarins.

the methods[4] investigated thus far are limited to the construction of the racemates involving harsh conditions or multisteps. In view of the importance of amino substituted 3,4-dihydrocoumarin derivatives, catalytic enantioselective approaches to access this structure would be still challenging and in high demand.

(1) (a) Donnelly, D. M. X.; Boland, G. M. *Nat. Prod. Rep.* **1995**, 321. (b) Donnelly, D. M. X.; Boland, G. M. In *The Flavonoids: Advances in Research Since 1986*; Harborne, J. B., Ed.; Chapman and Hall: London, 1993; Chapter 6. (c) Matern, U.; Lüer, P.; Kreusch, D. In *Comprehensive Natural Products Chemistry*; Sankawa, U., Ed.; Pergamon: Oxford, 1999; Vol. 1, p 623.

(2) (a) Still, W. C.; Goldsmith, D. J. *J. Org. Chem.* **1970**, *35*, 2282. (b) Loiodice, F.; Longo, A.; Bianco, P.; Tortorella, V. *Tetrahedron: Asymmetry* **1995**, *6*, 1001. (c) Biswas, B.; Sen, P. K.; Venkateswaran, R. V. *Tetrahedron* **2007**, *63*, 12026.

(3) (a) Reinhold, D. F.; North Plainfield, N. J.; Markillie. J. H.; Mich. K.; Sletzinger. M. U.S. Patent 3161655, 1964. (b) Rico, J. G. *Tetrahedron Lett.* **1994**, *35*, 6599. (c) Cabaret, D.; Adediran, S. A.; Garcia Gonzalez, M. J.; Pratt, R. F.; Wakselman, M. *J. Org. Chem.* **1999**, *64*, 713. (d) Bovy, P. R.; Miyano, M.; Rico, J. G.; Rogers, T. E. PCT Int. Appl. 9312103, 1993.

(4) (a) Ueda, S.; Naruto, S.; Yoshida, T.; Sawayama, T.; Uno, H. *J. Chem. Soc., Chem. Commun.* **1985**, 218. (b) Mohammed, S. M. *Orient. J. Chem.* **2004**, *20*, 283. (c) Abdel-Razik, H. H. *J. Chin. Chem. Soc.* **2005**, *52*, 141. (d) Tamam, G. H.; Bakeer, H. M.; Abdel-Motelab, R. M.; Arafa, W. A. *J. Chin. Chem. Soc.* **2005**, *52*, 1191.

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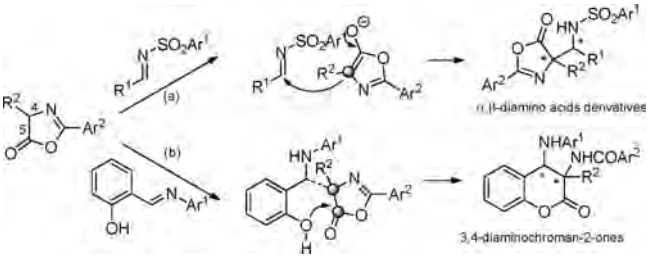
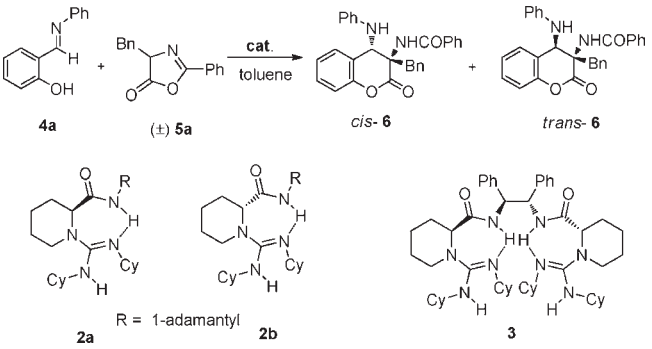
Azlactone, possessing both nucleophilic and electrophilic properities, enables a wide variety of synthetically important transformations.[5] For instance, the Mannich-type reaction[6] of aldimines with azlactones at the nucleophilic C-4 position has been well-studied to access the α-disubstituted α,β-diamino acid derivatives (Scheme 1, path a). Herein, taking advantage of both the nucleophilic site at C-4 and electrophilic site at C-5 of azlactones,[7]

Scheme 1. Reactions of Azlactones with Aldimines



we achieved the first asymmetric synthesis of optically active 3,4-diaminochroman-2-ones[8] from the domino reaction of azlactones with *o*-hydroxy aromatic aldimines (Scheme 1, path b).[9] An interesting switch of *cis*/*trans* selectivity was observed by the use of chiral guanidine[10] and bisguanidium salt[11] catalysts. Both *cis*- and *trans*-3,4-diaminochroman-2-ones were obtained in excellent yields (up to 99%) with excellent diastereo- and

Table 1. Optimization of the Reaction Conditions[a]



entry	cat.	*t* (°C)	yield (%)[b]	*cis*:*trans*[c]	ee (%)[c] *cis*-**6a**	ee (%)[c] *trans*-**6a**
1	**2a**	0	90	80:20	89	−94
2[d]	**2a**	0	90	80:20	92	−94
3[d]	**2a**	−20	98	80:20	94[f]	−96
4[d]	**2b**	−20	98	80:20	−94	96
5	**3**	0	92	20:80	−15	40
6[e]	**3**·$HBAr^F_4$	0	92	25:75	−5	94
7[d,e]	**3**·$HBAr^F_4$	0	92	20:80	−10	95
8[d,e]	**3**·$HBAr^F_4$	−20	98	15:85	−15	96[f]

[a] Unless otherwise noted, all reactions were carried out with **2** (10 mol %) or **3** (5 mol %), **4a** (0.15 mmol), and **5a** (0.10 mmol) in toluene (1.0 mL) at 0 °C for 4−7 h. [b] Isolated yield of the two diastereomers. [c] Determined by chiral HPLC analysis. [d] THF/toluene (1/1, v/v) was used as the solvent. [e] $HBAr^F_4$ = $HB[3,5\text{-}(CF_3)_2C_6H_3]_4$. [f] The absolute configurations of *cis*-**6a** (3*S*, 4*S*) and *trans*-**6a** (3*S*, 4*R*) were both determined by X-ray analysis.[13]

enantioselectivities (up to >99:1 dr, 99% ee). This method could provide all optically active isomers, which is highly important and valuable in pharmaceutical and bioorganic chemistry due to the remarkable biological discrepancy of different enantiomers.[12]

Initially, catalytic amounts of a Brønsted base (for example, DABCO) were found to promote the domino reaction[8] of *o*-hydroxy benzaldimine **4a** with azlactone **5a** efficiently under mild reaction conditions to provide racemic diaminochroman-2-one **6a**. Then, a series of chiral guanidines were screened to access the optically pure product. It was found that (*S*)-pipecolic acid derived guanidine **2a** could catalyze the reaction smoothly, affording the major *cis*-**6a** with a moderate dr value and high enantioselectivity for both isomers (Table 1, entry 1). Using the mixed solvent of THF/toluene (v/v, 1:1) and lowering the reaction temperature further enhanced the enantioselectivity to 94% ee for *cis*-**6a** and 96% ee for *trans*-**6a**, but the diastereoselectivity did not increase (Table 1, entries 2 and 3). Notably, the *cis*-product with reversed enantioselectivity was dominantly obtained by (*R*)-pipecolic acid derived guanidine as expected (Table 1,

(5) For reviews, see: (a) Fisk, J. S.; Mosey, R. A.; Tepe, J. J. *Chem. Soc. Rev.* **2007**, *36*, 1432. (b) Mosey, R. A.; Fisk, J. S.; Tepe, J. J. *Tetrahedron: Asymmetry* **2008**, *19*, 2755. (c) Hewlett, N. M.; Hupp, C. D.; Tepe, J. J. *Synthesis* **2009**, 2825. (d) R. Alba, A.-N.; Rios, R. *Chem.—Asian J.* **2011**, *6*, 720.

(6) (a) Uraguchi, D.; Ueki, Y.; Ooi, T. *J. Am. Chem. Soc.* **2008**, *130*, 14088. (b) Liu, X. D.; Deng, L. J.; Jiang, X. X.; Yan, W. J.; Liu, C. L.; Wang, R. *Org. Lett.* **2010**, *12*, 876.

(7) (a) Jiang, J.; Qing, J.; Gong, L. Z. *Chem.—Eur. J.* **2009**, *15*, 7031. (b) Dong, S. X.; Liu, X. H.; Chen, X. H.; Mei, F.; Zhang, Y. L.; Lin, L. L.; Feng, X. M. *J. Am. Chem. Soc.* **2010**, *132*, 10650. (c) Terada, M.; Nii, H. *Chem.—Eur. J.* **2011**, *17*, 1760.

(8) Kumar, P.; Mukerjee, A. K. *Indian J. Chem., Sect. B* **1981**, *20B*, 418.

(9) For selected examples of domino reactions involving *o*-hydroxy aromatic aldimines, see: (a) Rueping, M.; Lin, M. Y. *Chem.—Eur. J.* **2010**, *16*, 4169. (b) Xie, P.; Huang, Y.; Chen, R. *Org. Lett.* **2010**, *12*, 3768. (c) Xie, Y. W.; Guan, X. Y.; Shi, M. *Org. Lett.* **2010**, *12*, 5664. (d) Alemán, J.; Núñez, A.; Marzo, L.; Marcos, V.; Alvarado, C.; Ruano, J. L. G. *Chem.—Eur. J.* **2010**, *16*, 9453.

(10) For reviews on chiral guanidine catalysts, see: (a) Ishikawa, T.; Isobe, T. *Chem.—Eur. J.* **2002**, *8*, 552. (b) Leow, D.; Tan, C. H. *Chem.—Asian J.* **2009**, *4*, 488. For selected examples, see:(c) Corey, E. J.; Grogan, M. J. *Org. Lett.* **1999**, *1*, 157. (d) Ishikawa, T.; Araki, Y.; Kumamoto, T.; Seki, H.; Fukuda, K.; Isobe, T. *Chem. Commun.* **2001**, 245. (e) Liu, H.; Leow, D.; Huang, K. W.; Tan, C. H. *J. Am. Chem. Soc.* **2009**, *131*, 7212. (f) Yu, Z. P.; Liu, X. H.; Zhou, L.; Lin, L. L.; Feng, X. M. *Angew. Chem., Int. Ed.* **2009**, *48*, 5195. (g) Ube, H.; Shimada, N.; Terada, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 1858. (h) Misaki, T.; Kawano, K.; Sugimura, T. *J. Am. Chem. Soc.* **2011**, *133*, 5695. (i) Chen, X. H.; Dong, S. X.; Qiao, Z.; Zhu, Y.; Xie, M. S.; Lin, L. L.; Liu, X. H.; Feng, X. M. *Chem.—Eur. J.* **2011**, *17*, 2583.

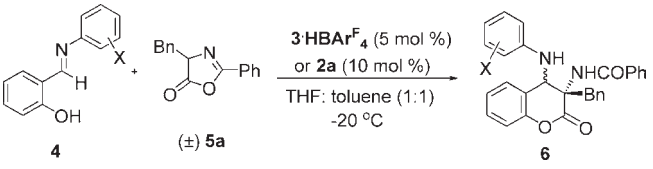
(11) (a) Uyeda, C.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2008**, *130*, 9228. (b) Fu, X.; Loh, W. T.; Zhang, Y.; Chen, T.; Ma, T.; Liu, H. J.; Wang, J. M.; Tan, C. H. *Angew. Chem., Int. Ed.* **2009**, *48*, 7387. (c) Tanaka, S.; Nagasawa, K. *Synlett* **2009**, 667. (d) Uyeda, C.; Rötheli, A. R.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2010**, *49*, 9753. (e) Uyeda, C.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2011**, *133*, 5062.

(12) For reviews, see: (a) Zanoni, G.; Castronovo, F.; Franzini, M.; Vidari, G.; Giannini, E. *Chem. Soc. Rev.* **2003**, *32*, 115. (b) Sibi, M. P.; Liu, M. *Curr. Org. Chem.* **2001**, *5*, 719.

entry 4). To our surprise, in the presence of bisguanidine **3**, *trans*-**6a** was obtained as the major product with moderate ee (Table 1, entry 5 vs 1). Encouraged by these interesting results, a number of chiral bisguanidium salts were evaluated.[14] Strikingly, the enantioselectivity of *trans*-**6a** was dramatically increased to 94% ee using bisguanidium salt with a large counterion $(BAr^{F}{}_{4})^{-}$ (Table 1, entry 6). Catalysts with other counterions were also tested, but no better results were obtained.[14] Similarly, up to 96% ee of *trans*-**6a** was achieved in the solvent of THF/toluene (v/v, 1:1) and at a lower reaction temperature in the presence of **3·HBAr$^{F}_{4}$** (Table 1, entries 7 and 8). The absolute configuration of the major products *cis*-**6a** (with **2a**) and *trans*-**6a** (with **3·HBAr$^{F}_{4}$**) were determined by single crystal X-ray analysis as (3*S*,4*S*) and (3*S*,4*R*), respectively.[13]

Further optimization to improve the diastereoselectivity was made by examining the protective groups of aldimines **4**. The results suggested that the position of the substituent on the *N*-aryl group of the aldimine had a significant impact on the diastereoselectivity of the reaction catalyzed by guanidine **2a**. The *cis*-product was dominantly obtained with the diastereoselectivity increased to 86:14 using 4-Cl-substituted aldimine and to 96:4 using the 2-Cl-substituted one, while the ee values were slightly decreased (Table 2, entries 1−3). The size of the substituent was also found to affect the stereoselectivity of the reaction (Table 2, entries 1, 4, and 5). 2-Bromoaniline-derived aldimine gave the highest dr (97:3), and 2-fluoroaniline-derived aldimine gave the highest ee value (94% ee). Considering both ee and dr values, 2-fluoroaniline-derived aldimine was the better candidate. For the bisguanidium salt catalyst, changing the protecting group of aldimines gave no better stereoselectivity for the major *trans*-product (Table 2, entries 6−8).[14]

Table 2. Effect of the Protective Groups of Aldimines[a]

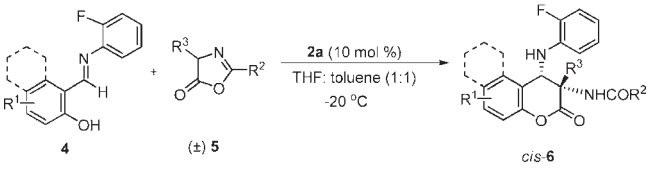


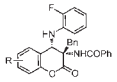
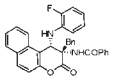
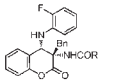
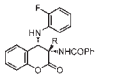
entry	cat.	X	yield (%)[b]	*cis*:*trans*[c]	ee (%)[c] *cis*-**6**	ee (%)[c] *trans*-**6**
1	**2a**	2-Cl	94 (**6a$_1$**)	96:4	90	−94
2	**2a**	3-Cl	93 (**6a$_2$**)	90:10	94	−99
3	**2a**	4-Cl	96 (**6a$_3$**)	86:14	94	−99
4	**2a**	2-Br	95 (**6a$_4$**)	97:3	88	−80
5	**2a**	2-F	98 (**6b**)	93:7	94	−98
6	**3·HBAr$^{F}_{4}$**	2-Cl	93 (**6a$_1$**)	90:10	−44	75
7	**3·HBAr$^{F}_{4}$**	3-Cl	95 (**6a$_2$**)	30:70	−31	99
8	**3·HBAr$^{F}_{4}$**	4-Cl	95 (**6a$_3$**)	24:76	−31	98

[a] Unless otherwise noted, all reactions were carried out with **2a** (10 mol %) or **3·HBAr$^{F}_{4}$** (5 mol %), **4** (0.15 mmol), and **5a** (0.10 mmol) in THF/toluene (1/1, v/v, 1.0 mL) at −20 °C for 4−7 h. [b] Isolated yield of the two diastereomers. [c] Determined by chiral HPLC analysis.

Under the optimized reaction conditions (Table 2, entry 5), various *o*-fluorophenyl-protected aldimines **4** and azlactones **5** were evaluated with guanidine **2a**, giving a wide range of diaminochroman-2-ones **6** with high diastereomeric ratios (up to >99:1 *cis*:*trans*) and excellent ee values (90−95% ee).

Table 3. Substrate Scope for the Domino Reaction of *o*-Fluorophenyl-Protected Aldimines **4** with Azlactones **5** Catalyzed by Guanidine **2a**[a]



entry	pro.	R	yield (%)[b]	*cis*:*trans*[c]	ee(%)[c] *cis*-**6**
1		5-Cl	85 (**6c**)	90:10	90
2		5-Br	90 (**6d**)	90:10	91
3		5-MeO	91 (**6e**)	90:10	92
4		4-MeO	95 (**6f**)	90:10	93
5		5-Me	94 (**6g**)	90:10	93
6			96 (**6h**)	75:25	91
7		2-ClC_6H_4	80 (**6i**)	85:15	92
8		3-ClC_6H_4	96 (**6j**)	90:10	93
9		4-ClC_6H_4	94 (**6k**)	90:10	93
10		4-MeC_6H_4	95 (**6l**)	90:10	94
11		4-MeOC_6H_4	98(**6m**)	93:7	94
12		Me	99 (**6n**)	96:4	95
13		*i*-Pr	88 (**6o**)	>99:1	91
14		4-OHBn	90 (**6p**)	90:10	90
15		$(CH_2)_2SCH_3$	95 (**6q**)	93:7	94

[a] Unless otherwise noted, all reactions were carried out with **2a** (10 mol %), **4** (0.15 mmol), and **5** (0.10 mmol) in THF/toluene (1/1, v/v, 1.0 mL) at −20 °C for 5−12 h. [b] Isolated yield of the two diastereomers. [c] Ee value of *cis*-**6** was determined by chiral HPLC analysis.

As shown in Table 3, N-aryl aromatic aldimines with both electron-withdrawing and -donating groups at different positions were well tolerated in terms of the diastereo- and enantioselectivities (Table 3, entries 1−5). Notably, a fused ring aldimine was also a suitable substrate (Table 3, entry 6), affording the desired adduct with 91% ee and a slightly lower diastereoselectivity (75:25 dr). Furthermore, the scope of the domino reaction of various azlactones with *o*-fluorophenyl-protected aldimine was also surveyed. Regardless of the electronic nature and steric hindrance of the substituents on the aromatic ring at the C2-position of azlactones, high diastereoselectivities (up to 93:7) and enantioselectivities (up to 94% ee) could be obtained (Table 3, entries 7−11). It was noteworthy that the substrates could be extended to azlactones with variety at the C-4 site synthesized from other amino acids with excellent results (Table 3, entries 12−15).

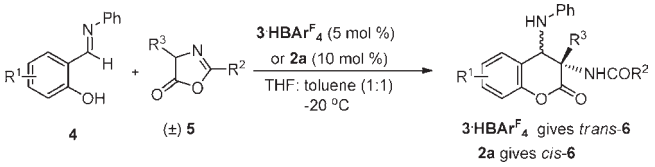
(13) CCDC 805263 (*cis*-**6a**) and CCDC 805353 (*trans*-**6a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/datarequest/cif.

(14) For details, see Supporting Information.

Unfortunately, 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde derived aldimine failed to give the desired products propably due to the large steric hindrance.

Due to the remarkably different biological properties of optical isomers, we then turned our attention to the preparation of *trans*-diaminochroman-2-ones **6** in the presence of 5 mol % of biguanidium salt **3·HBAr$^F_4$**. As presented in Table 4, *N*-phenylaldimines with a 5-chloro- or 5-bromo-substituent gave the desired adducts with a slightly lower dr value (75:25) than other substituents such as a methyl or methoxyl group (Table 4, entries 1 and 2 vs entries 3−5). The position of the substituent also had an effect on the results, and the 5-methoxyl substituted aldimine was better than the 4-methoxyl substituted one (Table 4, entry 3 vs 4). High yields with excellent diastereoselectivities (up to 98:2) and enantioselectivities (93−99% ee) could be obtained for various azlactones (Table 4, entries 6−11). Moreover, using 10 mol % of guanidine **2a** as the catalyst, the *cis*-adducts **6** were obtained as the major product with comparable results (Table 4, entries 12−18).

Table 4. Substrate Scope for the Domino Reaction of Phenyl-Protected Aldimines **4** with Azlactones **5** Catalyzed by **3·HBAr$^F_4$** or **2a**[a]



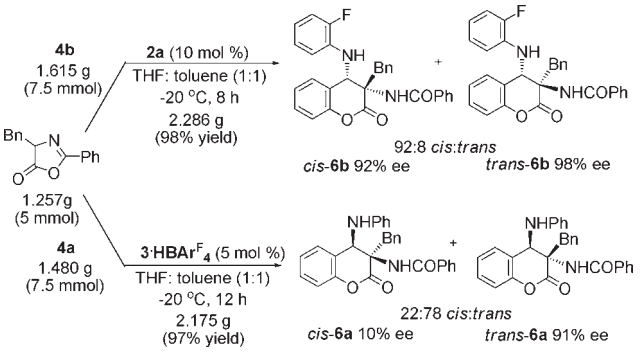
entry	pro.	R	yield(%)[b]	*cis*:*trans*[c]	ee (%)
1		5-Cl	93 (**6r**)	25:75	94(−20)
2		5-Br	85 (**6s**)	25:75	91(−20)
3		5-MeO	89 (**6t**)	15:85	99(−25)
4		4-MeO	80 (**6u**)	13:87	88(−55)
5		5-Me	87 (**6v**)	20:80	96(−55)
6		2-ClC_6H_4	92(**6w**)	2:98	99(0)
7		3-ClC_6H_4	89 (**6x**)	17:83	97(−30)
8		4-ClC_6H_4	91 (**6y**)	6:94	97(−30)
9		4-MeC_6H_4	83 (**6z**)	18:82	98(−27)
10		4-MeOC_6H_4	98 (**6aa**)	18:82	98(−31)
11			85 (**6ab**)	11:89	93(−27)
12		5-Br	88 (**6s**)	82:18	90(−88)
13		5-MeO	85 (**6t**)	88:12	93(−90)
14		4-MeO	96 (**6u**)	83:17	96(−93)
15		5-Me	93 (**6v**)	70:30	96(−97)
16		4-Cl C_6H_4	87(**6y**)	78:22	94(−88)
17		4-MeO C_6H_4	98 (**6aa**)		94(−90)
18			82 (**6ab**)	91:9	96(−99)

[a] Unless otherwise noted, all reactions were carried out with **3•HBAr$^F_4$** (5 mol %; entries 1−11, *trans*-**6** as major products) or **2a** (10 mol %; entries 12−18, *cis*-**6** as major products), **4** (0.15 mmol), and **5** (0.10 mmol) in THF/toluene (1/1, v/v, 1.0 mL) at −20 °C for 7−24 h. [b] Isolated yield of the two diastereomers. [c] Ee values were determined by chiral HPLC analysis, and the data in parentheses correspond to the minor product.

In all cases, the *cis*- and *trans*-adducts could be separated through silica gel chromatography.

For the purpose of examining the synthetic potential of the present approach, a gram-scaled synthesis of 3,4-diaminochroman-2-one was performed for both catalytic systems (Scheme 2). As shown in Scheme 2, in the presence of 10 mol % of guanidine **2a**, 5 mmol of azlactone **5a** reacted with 1.5 equiv of aldimine **4b** to provide *cis*-**6b** as the major product in a total yield of 98% (2.286 g) with 92:8 dr and 92% ee. Similarly, subgram quantities of product **6a** with the *trans*-isomer as the major product (2.175 g, 97% total yield, 22:78 dr and 91% ee) were obtained using 5 mol % of guanidium **3·HBAr$^F_4$**.

Scheme 2. Scaled-up Version of the Domino Reaction



In summary, the first example of a catalytic asymmetric domino reaction of *o*-hydroxy aromatic aldimines and azlactones has been developed. By the use of the catalyst guanidine **2a** or bisguanidium salt **3•HBAr$^F_4$** derived from the same amino acid, either *cis*- or *trans*-3,4-diaminochroman-2-ones were obtained in high yields (up to 99%) with excellent diastereoselectivities (up to >99:1) and enantioselectivities (up to 99% ee). More endeavors to understand the mechanism of the reaction and using azlactones in other asymmetric domino reactions are in progress.

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Supporting Information Available. Experimental procedures, spectral and analytical data for the products. This material is available free of charge via the Internet at http://pubs.acs.org.