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Diastereoselective Synthesis of CF_3-Substituted Spiroisochromans by [1,5]-Hydride Shift/Cyclization/Intramolecular Friedel−Crafts Reaction Sequence

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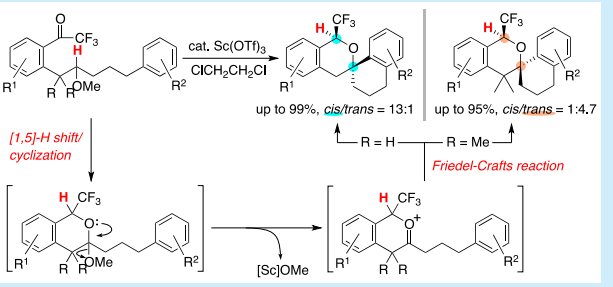
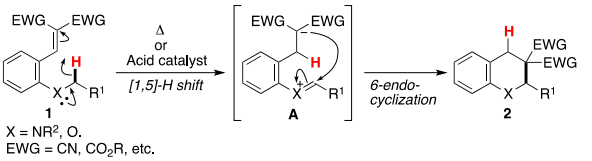
Supporting Information

ABSTRACT: Developed herein is a diastereoselective synthesis of CF_3-substituted spiroisochromans via C(sp^3)−H bond functionalization involving sequential transformations ([1,5]-hydride shift/cyclization/elimination of MeOH/intramolecular Friedel−Crafts reaction).



The direct transformation of C−H bonds has attracted much attention because it provides an efficient strategy for the synthesis of various organic molecules.[1] Hydride-shift-triggered C(sp^3)−H bond functionalization, also called the "internal redox process" (Scheme 1), has drawn a great deal of interest in the recent decade because of its unique features.[2] The key feature of this transformation is the [1,5]-hydride shift of the C(sp^3)−H bond α to a heteroatom, which is induced by the electronic assistance from the adjacent heteroatom. The subsequent *6-endo* cyclization affords fused heterocycle **2**.[3−7]

Scheme 1. C(sp^3)−H Functionalization by the Internal Redox Process



Recent efforts by us[3,4] and other groups[5−7] have revealed the high synthetic potential of this methodology, which has enabled the construction of various polyheterocycles, such as isoquinolines,[3e,g,6o] benzopyrans,[3b,6i] tetralins,[3c,d,h,i,k,6h,7m] spirooxindoles,[3i,6n,7n] and indoles.[3] The combination of this reaction system and another process would be a promising synthetic tool for the construction of complex polycyclic skeletons. To the best of our knowledge, there is no precedent for such a sequential system, and hence, the introduction of new methodology is required.

Our strategy is shown in the top portion of Scheme 2. The key point is the dual role of heteroatom X (shown in blue) as (1) a driving force for the hydride shift and (2) an activator of the resulting cyclized adduct by acting as a leaving group. We envisioned that a carbonyl (Y = O)[3j,4a,6l] or imine (Y = NR)[3a,e,g,6d,o] moiety with an *o*-phenethyl ether or amine moiety would be suited for this purpose in terms of the acceleration of the elimination of the XR group by the electron-donating ability of another heteroatom (Y). This would realize the further transformation of the cyclized adduct in the internal redox process, that is, the geminal functionalization of the carbon at the phenethyl position.

Herein we report the first realization of this concept in an intramolecular reaction, which has enabled the diastereoselective synthesis of CF_3-substituted spiroisochromans. This reaction is interesting in that the diastereoselectivity is affected by subtle structural differences in the starting materials. Whereas CF_3-ketones with a terminal nucleophilic aromatic ring (R = H) gave spiroisochromans in favor of the *cis* isomers, the *trans* isomers were favored in the case of substrates with two methyl groups at the benzylic position (R = Me).

CF_3-ketone **3a** was selected as the suitable electrophilic portion because of its high electrophilic character and the high

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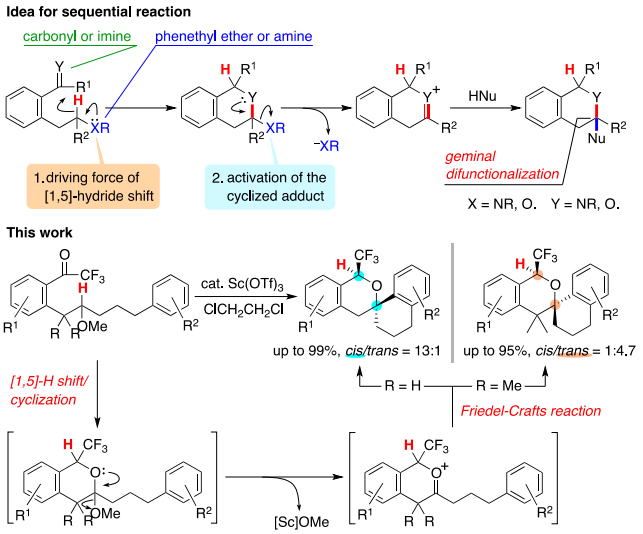
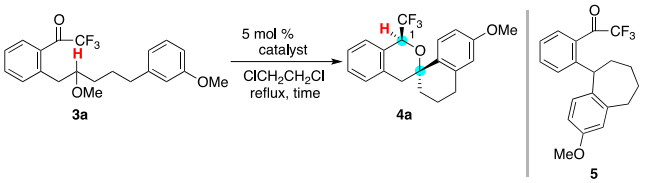
Scheme 2. Idea for Sequential Reaction and Diastereoselective Synthesis of CF_3-Substituted Spiroisochromans



utility of the resulting product. The latter point is intriguing. As far as we know, there have been no reports of the synthesis of CF_3-substituted spiroisochromans, despite their potentially high biological activities derived from the hybrid structure of a CF_3 group, a spiro structure, and an isochroman core. At first, **3a** was treated with 5 mol % $Sc(OTf)_3$, which exhibited excellent catalytic performance in a recently reported reaction of the substrate with a CF_3-ketone as the electrophilic portion (Table 1).[3j] Gratifyingly, the desired sequential reaction proceeded smoothly under the specified conditions (refluxing in $ClCH_2CH_2Cl$ for 24 h) to afford the desired CF_3-substituted spiroisochroman **4a** in excellent chemical yield with high diastereoselectivity (91% yield with *cis*:*trans* = 13:1; entry 1). The relative stereochemistry of the major isomer was determined to be *cis* by X-ray analysis.[8] Screening of catalysts revealed that $Sc(OTf)_3$ was the most effective catalyst, as shown in Table 1. Both $Yb(OTf)_3$ and $Hf(OTf)_4$[9] resulted in recovery of the starting material **3a** (entries 2 and 3). $TiCl_4$ was also ineffective (entry 4). Although $Gd(OTf)_3$ promoted the reaction, the chemical yield was moderate even with a longer reaction time (57%, 100 h), and the diastereomeric ratio also remained at a moderate level (*cis*:*trans* = 6.5:1) (entry 5). A stronger Brønsted acid (TfOH) afforded seven-membered-ring adduct **5** (17%),[10] and the desired spirocycle **4a** was not obtained. The selection of the solvent had a dramatic effect on the diastereoselectivity, and $ClCH_2CH_2Cl$ was the solvent of choice: although good chemical yields were achieved in aromatic solvents, such as toluene, benzene, and mesitylene, the diastereoselectivity remained at a moderate level in all cases (*cis*:*trans* = 5.0−7.8:1; entries 7−9). In the case of MeOH, the reaction failed to proceed, and **3a** was recovered (95%; entry 10). Importantly, this reaction could be performed on a 1.21 mmol scale while maintaining both the chemical yield and diastereomeric ratio (entry 11)

Table 1. Examination of the Reaction Conditions[a]



entry	catalyst	time (h)	yield (%)	*cis*:*trans*[b]
1	$Sc(OTf)_3$	18.5	91	13:1
2	$Yb(OTf)_3$	42	0 (81)[c]	–
3	$Hf(OTf)_4$	70	0 (68)[c]	–
4	$TiCl_4$	45	0 (98)[c]	–
5	$Gd(OTf)_3$	100	57 (39)[c]	6.5:1
6	TfOH	23	– (**5**: 17%)	–
7[d]	$Sc(OTf)_3$	4	82	6.3:1
8[e]	$Sc(OTf)_3$	21	80	7.8:1
9[f]	$Sc(OTf)_3$	23	56	5.0:1
10[g]	$Sc(OTf)_3$	63	0 (95)[c]	–
11[h]	$Sc(OTf)_3$	24	81	11:1

[a]Unless otherwise noted, all reactions were conducted with 0.10 mmol of **3a** in the presence of 5 mol % catalyst in $ClCH_2CH_2Cl$ (1.0 mL) at refluxing temperature. [b]The diastereomeric ratio was determined by comparing the integration values for the methine proton at C-1 for each diastereomer in the ^1H NMR spectrum. [c]The recovery of **3a** is shown in parentheses. [d]In toluene. [e]In benzene. [f]In mesitylene at 120 °C. [g]In MeOH. [h]1.21 mmol scale.

Figure 1 shows the substrate scope of this reaction. At first, the effect of a terminal aromatic ring was investigated under

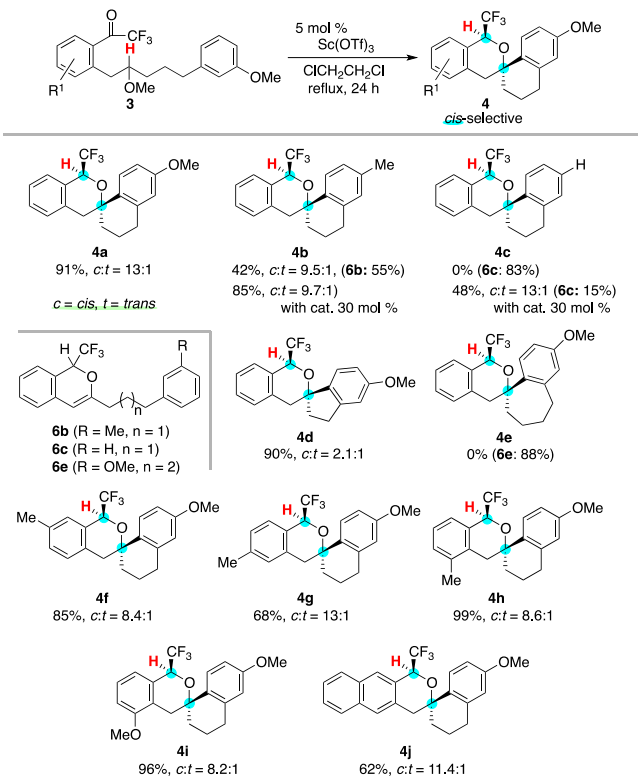


Figure 1. Substrate scope.

the optimized reaction conditions (entry 1, Table 1), which suggested that an electronic factor was found to play a significant role in promoting the desired sequential reaction, particularly the final Friedel−Crafts reaction. In the case of substrate **3b** bearing an *m*-tolyl group, the chemical yield of desired spirocycle **4b** was moderate (42%, *cis*:*trans* = 9.5:1), and a substantial amount of isochromene **6b**, which was produced by hydride shift/cyclization followed by the elimination of MeOH (not involving the intramolecular

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Friedel–Crafts reaction), was obtained (55%). This tendency became even more remarkable in substrate **3c** bearing a simple phenyl group. Isochromene **6c** was obtained exclusively (83%), and no spirocycle **4c** was generated. Increasing the catalyst loading to 30 mol % led to the formation of **4b** and **4c** (85% with *cis*:*trans* = 9.7:1 and 48% with *cis*:*trans* = 13:1, respectively), which revealed that isochromenes **6** also functioned as intermediates for the subsequent intramolecular Friedel–Crafts reaction.

The ring size was just as important. In contrast to the excellent chemical yields of [6.6]-spirocycle **4a** and [5.6]-spirocycle **4d**, no [6.7]-spirocycle **4e** was obtained at all. This is ascribed to the difficulty of forming a middle-sized (seven-membered) ring even in the intramolecular reaction. No [6.7]-spirocycle **4e** was formed even when the catalyst loading was increased to 30 mol %.

The substituents on the mother nucleus were almost negligible. Spirocycles **4f–i** with various substituents on the aromatic ring (e.g., Me and OMe), and naphthyl-type spirocycle **4j** were obtained in good to high chemical yields with high diastereoselectivities (62–99%, *cis*:*trans* = 8.2–13:1). The relative stereochemistries of the major isomers were surmised as shown in Figure 1, Scheme 2, and Table 1 by analogy to **4a**, **4d**, and **4j**, whose relative stereochemistries were unambiguously established by X-ray crystallographic analysis.[8]

An investigation of the substituent effect at the benzylic position gave interesting information (Figure 2). Subjecting

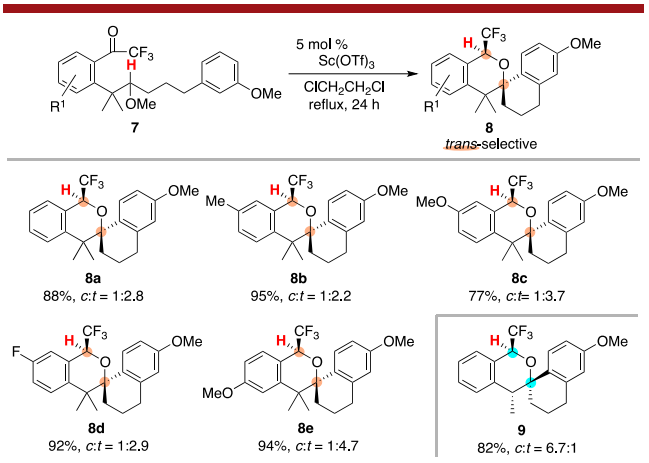

Figure 2. Scope of substrates with two methyl groups at the benzylic position.

substrate **7a** having two methyl groups at the benzylic position to the optimized reaction conditions afforded spirocycle **8a** in favor of the *trans* isomer (88% yield with *cis*:*trans* = 1:2.8; cf. *cis*:*trans* = 13:1 in **4a**). The relative stereochemistry of the minor isomer of **8a** was determined to be *cis* by X-ray analysis, and that of the major isomer was assigned as *trans*.[8] This stereochemical tendency was also observed with substrates **7b–e**, and the corresponding adducts **8b–e** were obtained in good chemical yields with a slight preference for the *trans* isomers (77–95%, *cis*:*trans* = 1:2.2–4.7). The reaction with a monomethyl group at the benzylic position resulted in high *cis* selectivity (*cis*:*trans* = 6.7:1), which suggested that the presence of two methyl groups was indispensable for achieving the *trans* selectivity.

We propose two mechanisms for the high diastereoselectivity (Figure 3): (1) the stereoselective Friedel–Crafts reaction

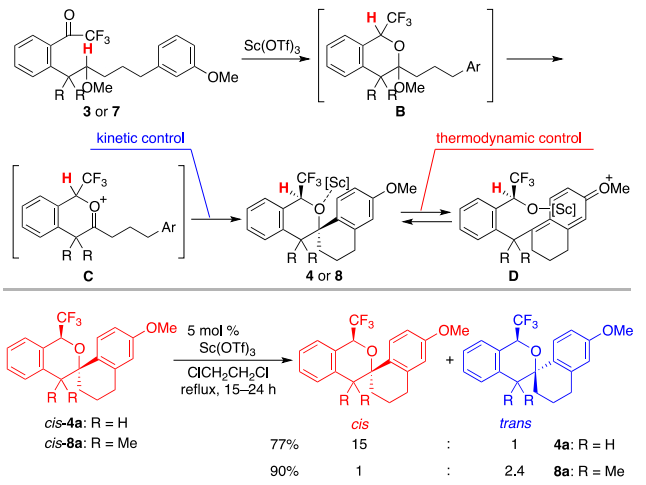

Figure 3. Plausible mechanism for the cyclization reaction.

to give oxonium cation **C** (kinetic control) and (2) the thermodynamic shift to a more stable isomer through the ring-opening and ring-closing equilibrium between **4** (or **8**) and **D** (thermodynamic control). In order to clarify the mechanism, isolated *cis* isomers **4a** and **8a** were subjected to the optimized reaction conditions. The observation of the *trans* isomers of **4a** and **8a** suggested the involvement of thermodynamic control in the reaction, although we could not completely rule out the kinetic control pathway.

To gain insights into the origin of the diastereoselectivity, we conducted DFT calculations. Consistent with the experimental results, *cis*-**4a** is more stable than *trans*-**4a** (Figure 4). After careful analysis of these structures, the preference for *cis*-**4a** is mainly attributed to stabilization by an intramolecular

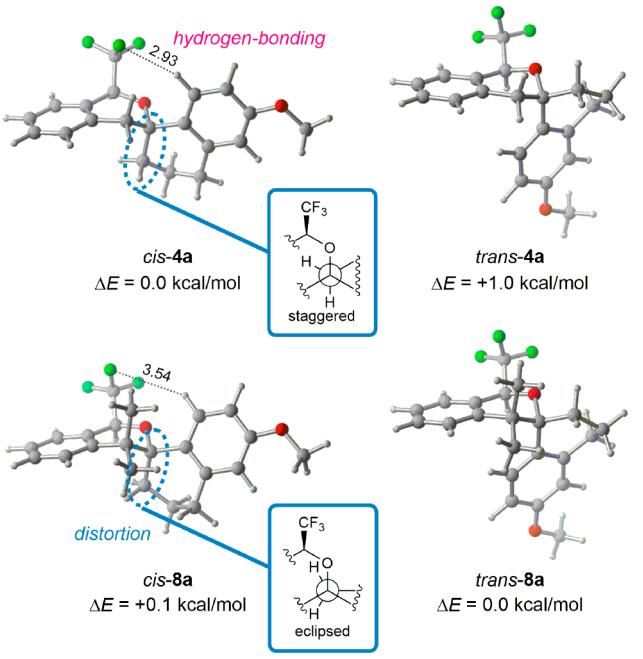

Figure 4. 3D structures and relative energies of *cis*-**4a**, *trans*-**4a**, *cis*-**8a**, and *trans*-**8a**. Bond lengths are in Å.

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hydrogen-bonding interaction between a fluorine atom of the CF_3 group and a hydrogen atom on the methoxyphenyl group. DFT calculations also revealed the key for the reversal of diastereoselectivity between **4** and **8**. Consistent with the experimental results, *trans*-**8a** is more stable than *cis*-**8a**. The reversal of the diastereoselectivity is ascribed to the greater distortion of the spiroisochroman core structure in *cis*-**8a** by the introduction of the two methyl groups at the benzylic position compared with that in *trans*-**8a** (see the Supporting Information for details).

In summary, we have developed an efficient diastereoselective synthesis of CF_3-substituted spiroisochromans via C(sp^3)−H bond functionalization involving sequential transformations ([1,5]-hydride shift/cyclization/elimination of MeOH/intramolecular Friedel−Crafts reaction). A range of substrates provided the desired CF_3-substituted spirocycles **4a−j** in good to excellent chemical yields with high *cis* selectivities. Interestingly, the introduction of two methyl groups at the benzylic position reversed the diastereoselectivity to furnish the *trans* isomers preferentially. Further investigation of the synthesis of useful polycyclic skeletons by the hydride shift/cyclization-initiated sequential reaction is underway in our laboratory

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b00668.

Experimental procedures, analytical and spectroscopic data for new compounds, computational details, and Cartesian coordinates (PDF)

^1H, ^{13}C, and ^{19}F NMR spectra of new compounds (PDF)

Accession Codes

CCDC 1881483−1881486 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For recent reviews of C−H activation, see: (a) Godula, K.; Sames, D. *Science* **2006**, *312*, 67. (b) Bergman, R. G. *Nature* **2007**, *446*, 391. (c) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (d) Davies, H. M. L.; Manning, J. R. *Nature* **2008**, *451*, 417. (e) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (f) Jazzar, R.; Hitce, J.; Renaudat, A.; Sofack-Kreutzer, J.; Baudoin, O. *Chem. - Eur. J.* **2010**, *16*, 2654. (g) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (h) Davies, H. M. L.; Du Bois, J.; Yu, J.-Q. *Chem. Soc. Rev.* **2011**, *40*, 1855. (i) Brückl, T.; Baxter, R. D.; Ishihara, Y.; Baran, P. S. *Acc. Chem. Res.* **2012**, *45*, 826. (j) Qin, Y.; Lv, J.; Luo, S. *Tetrahedron Lett.* **2014**, *55*, 551. (k) Davies, H. M. L.; Morton, D. J. *J. Org. Chem.* **2016**, *81*, 343. Also see the highlight on visible-light photocatalysis: (l) Hu, X.-Q.; Chen, J.-R.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2017**, *56*, 1960.

(2) For recent reviews of the internal redox process, see: (a) Tobisu, M.; Chatani, N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1683. (b) Pan, S. C. *Beilstein J. Org. Chem.* **2012**, *8*, 1374. (c) Wang, M. *ChemCatChem* **2013**, *5*, 1291. (d) Peng, B.; Maulide, N. *Chem. - Eur. J.* **2013**, *19*, 13274. (e) Wang, L.; Xiao, J. *Adv. Synth. Catal.* **2014**, *356*, 1137. (f) Haibach, M. C.; Seidel, D. *Angew. Chem., Int. Ed.* **2014**, *53*, 5010. (g) Kwon, S. J.; Kim, D. Y. *Chem. Rec.* **2016**, *16*, 1191.

(3) For the internal redox reaction developed by our group, see: (a) Mori, K.; Ohshima, Y.; Ehara, K.; Akiyama, T. *Chem. Lett.* **2009**, *38*, 524. (b) Mori, K.; Kawasaki, T.; Sueoka, S.; Akiyama, T. *Org. Lett.* **2010**, *12*, 1732. (c) Mori, K.; Sueoka, S.; Akiyama, T. *J. Am. Chem. Soc.* **2011**, *133*, 2424. (d) Mori, K.; Sueoka, S.; Akiyama, T. *Chem. Lett.* **2011**, *40*, 1386. (e) Mori, K.; Kawasaki, T.; Akiyama, T. *Org. Lett.* **2012**, *14*, 1436. (f) Mori, K.; Kurihara, K.; Akiyama, T. *Chem. Commun.* **2014**, *50*, 3729. (g) Mori, K.; Umehara, N.; Akiyama, T. *Adv. Synth. Catal.* **2015**, *357*, 901. (h) Yoshida, T.; Mori, K. *Chem. Commun.* **2017**, *53*, 4319. (i) Machida, M.; Mori, K. *Chem. Lett.* **2018**, *47*, 868. (j) Yokoo, K.; Mori, K. *Chem. Commun.* **2018**, *54*, 6927. (k) Hisano, N.; Kamei, Y.; Kansaku, Y.; Yamanaka, M.; Mori, K. *Org. Lett.* **2018**, *20*, 4223. (l) Yoshida, T.; Mori, K. *Chem. Commun.* **2018**, *54*, 12686. For an asymmetric version of the internal redox reaction catalyzed by a chiral phosphoric acid, see: (m) Mori, K.; Ehara, K.; Kurihara, K.; Akiyama, T. *J. Am. Chem. Soc.* **2011**, *133*, 6166.

(4) For double C(sp^3)−H bond functionalization by sequential utilization of the internal redox reaction developed by our group, see: (a) Mori, K.; Kurihara, K.; Yabe, S.; Yamanaka, M.; Akiyama, T. *J. Am. Chem. Soc.* **2014**, *136*, 3744. Also see: Wang, L.; Xiao, J. *Org. Chem. Front.* **2016**, *3*, 635. (b) Mori, K.; Umehara, N.; Akiyama, T. *Chem. Sci.* **2018**, *9*, 7327. For an enantioselective version catalyzed by a chiral magnesium bisphosphate, see: (c) Mori, K.; Isogai, R.; Kamei, Y.; Yamanaka, M.; Akiyama, T. *J. Am. Chem. Soc.* **2018**, *140*, 6203.

(5) This type of reaction is classified as the "*tert*-amino effect." For reviews, see: (a) Meth-Cohn, O.; Suschitzky, H. *Adv. Heterocycl. Chem.* **1972**, *14*, 211. (b) Verboom, W.; Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas* **1990**, *109*, 311. (c) Meth-Cohn, O. *Adv. Heterocycl. Chem.* **1996**, *65*, 1. (d) Quintela, J. M. *Recent Res. Dev. Org. Chem.* **2003**, *7*, 259. (e) Mátyus, P.; Éliás, O.; Tapolcsányi, P.; Polonka-Bálint, A.; Halász-Dajka, B. *Synthesis* **2006**, 2625.

(6) For selected examples of internal redox reactions, see: (a) Pastine, S. J.; McQuaid, K. M.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 12180. (b) Pastine, S. J.; Sames, D. *Org. Lett.* **2005**, *7*, 5429. (c) Polonka-Bálint, A.; Saraceno, C.; Ludányi, K.; Bényei, A.; Mátyus, P. *Synlett* **2008**, 2846. (d) Zhang, C.; Murarka, S.; Seidel, D. *J. Org. Chem.* **2009**, *74*, 419. (e) McQuaid, K. M.; Sames, D. *J. Am. Chem. Soc.* **2009**, *131*, 402. (f) Shikanai, D.; Murase, H.; Hata, T.; Urabe, H. *J. Am. Chem. Soc.* **2009**, *131*, 3166. (g) Ruble, J. C.; Hurd, A. R.; Johnson, T. A.; Sherry, D. A.; Barbachyn, M.; Toogood, R. P. L.; Bundy, G. L.; Graber, D. R.; Kamilar, G. M. *J. Am. Chem. Soc.* **2009**, *131*, 3991. (h) Mahoney, M. J.; Moon, D. T.; Hollinger, J.; Fillion, E. *Tetrahedron Lett.* **2009**, *50*, 4706. (i) McQuaid, K. M.; Long, J. Z.; Sames, D. *Org. Lett.* **2009**, *11*, 2972. (j) Vadola, P. A.; Sames, D. *J. Am. Chem. Soc.* **2009**, *131*, 16525. (k) Zhou, G.; Zhang, J. *Chem. Commun.* **2010**, *46*, 6593. (l) Jurberg, I. D.; Peng, B.; Wöstefeld, E.; Wasserloos, M.; Maulide, N. *Angew. Chem., Int. Ed.*

DOI: 10.1021/acs.orglett.9b00668
Org. Lett. XXXX, XXX, XXX−XXX

2012, *51*, 1950. (m) Sugiishi, T.; Nakamura, H. *J. Am. Chem. Soc.* **2012**, *134*, 2504. (n) Han, Y.-Y.; Han, W.-Y.; Hou, X.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2012**, *14*, 4054. (o) Vadola, P. A.; Carrera, I.; Sames, D. *J. Org. Chem.* **2012**, *77*, 6689. (p) Gao, X.; Gaddam, V.; Altenhofer, E.; Tata, R. R.; Cai, Z.; Yongpruksa, N. A.; Garimallaprabhakaran, K.; Harmata, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 7016. (q) Chen, D.-F.; Han, Z.-Y.; He, Y.-P.; Yu, J.; Gong, L.-Z. *Angew. Chem., Int. Ed.* **2012**, *51*, 12307. (r) Shaaban, S.; Peng, B.; Maulide, N. *Synlett* **2013**, *24*, 1722. (s) Cera, G.; Chiarucci, M.; Dosi, F.; Bandini, M. *Adv. Synth. Catal.* **2013**, *355*, 2227. (t) Dieckmann, A.; Richers, M. T.; Platonova, A. Y.; Zhang, C.; Seidel, D.; Houk, K. N. *J. Org. Chem.* **2013**, *78*, 4132. (u) Alajarin, M.; Bonillo, B.; Marin-Luna, M.; Sanchez-Andrada, P.; Vidal, A. *Chem. - Eur. J.* **2013**, *19*, 16093. (v) Vidal, A.; Marin-Luna, M.; Alajarin, M. *Eur. J. Org. Chem.* **2014**, *2014*, 878. (w) Chang, Y.-Z.; Li, M.-L.; Zhao, W.-F.; Wen, X.; Sun, H.; Xu, Q.-L. *J. Org. Chem.* **2015**, *80*, 9620. (x) Suh, C. W.; Kwon, S. J.; Kim, D. Y. *Org. Lett.* **2017**, *19*, 1334. (y) Ramakumar, K.; Maji, T.; Partridge, J. J.; Tunge, J. A. *Org. Lett.* **2017**, *19*, 4014. (z) Zhu, S.; Chen, C.; Xiao, M.; Yu, L.; Wang, L.; Xiao, J. *Green Chem.* **2017**, *19*, 5653. (aa) Li, S.-S.; Zhou, L.; Wang, L.; Zhao, H.; Yu, L.; Xiao, J. *Org. Lett.* **2018**, *20*, 138.

(7) For examples of enantioselective internal redox reactions, see: (a) Murarka, S.; Deb, I.; Zhang, C.; Seidel, D. *J. Am. Chem. Soc.* **2009**, *131*, 13226. (b) Kang, Y. K.; Kim, S. M.; Kim, D. Y. *J. Am. Chem. Soc.* **2010**, *132*, 11847. (c) Cao, W.; Liu, X.; Wang, W.; Lin, L.; Feng, X. *Org. Lett.* **2011**, *13*, 600. (d) Zhou, G.; Liu, F.; Zhang, J. *Chem. - Eur. J.* **2011**, *17*, 3101. (e) He, Y.-P.; Du, Y.-L.; Luo, S.-W.; Gong, L. Z. *Tetrahedron Lett.* **2011**, *52*, 7064. (f) Chen, L.; Zhang, L.; Lv, Z.; Cheng, J.-P.; Luo, S. *Chem. - Eur. J.* **2012**, *18*, 8891. (g) Zhang, L.; Chen, L.; Lv, Z.; Cheng, J.-P.; Luo, S. *Chem. - Asian J.* **2012**, *7*, 2569. (h) Jiao, Z.-W.; Zhang, S.-Y.; He, C.; Tu, Y.-Q.; Wang, S.-H.; Zhang, F.-M.; Zhang, Y.-Q.; Li, H. *Angew. Chem., Int. Ed.* **2012**, *51*, 8811. (i) Kang, Y. K.; Kim, D. Y. *Adv. Synth. Catal.* **2013**, *355*, 3131. (j) Suh, C. W.; Woo, S. B.; Kim, D. Y. *Asian J. Org. Chem.* **2014**, *3*, 399. (k) Kang, Y. K.; Kim, D. Y. *Chem. Commun.* **2014**, *50*, 222. (l) Suh, C. W.; Kim, D. Y. *Org. Lett.* **2014**, *16*, 5374. (m) Yu, J.; Li, N.; Chen, D.-F.; Luo, S.-W. *Tetrahedron Lett.* **2014**, *55*, 2859. (n) Cao, W.; Liu, X.; Guo, J.; Lin, L.; Feng, X. *Chem. - Eur. J.* **2015**, *21*, 1632. Also see refs 3m and 4c.

(8) CCDC 1881483, 1881484, 1881485, and 1881486 contain the supplementary crystallographic data for **4a**, **4d**, **4j**, and *cis*-**8a**, respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk.

(9) Ishitani, H.; Suzuki, H.; Saito, Y.; Yamashita, Y.; Kobayashi, S. *Eur. J. Org. Chem.* **2015**, 5485.

(10) Compound **5** was generated by the following sequential process: elimination of MeOH from **3a**, protonation of the resulting styrene moiety, and subsequent intramolecular Friedel–Crafts reaction.

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