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Expanding the Scope of Cinchona Alkaloid-Catalyzed Enantioselective α-Aminations of Oxindoles: A Versatile Approach to Optically Active 3-Amino-2-oxindole Derivatives

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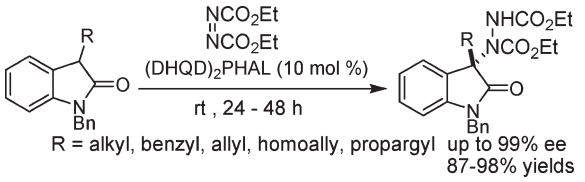

A cinchona alkaloid-catalyzed, highly enantioselective, α-amination of oxindoles has been developed. The reaction is general, operationally simple, and affords the desired products in high yields with good to excellent enantioselectivity. Significantly, this study provides a general catalytic method for the construction of a C−N bond at the C3 position of oxindoles as well as for the creation of a nitrogen-containing, tetrasubstituted chiral center.

Introduction

Oxindoles are important structural motifs found in a wide array of natural and biological active molecules.[1] Of particular interest are those that bear an oxygen or a nitrogen atom at the C3 position. These compounds exhibit important biological activities and are potential drug candidates.[2] Despite the biological relevance of these compounds, catalytic methods for their syntheses are still limited. Only a few recent reports have described the synthesis of 3-hydroxy-substituted oxindoles through the use of transition metal catalysis; in general, catalytic procedures that allow access to 3-amino-substituted oxindoles are lacking.[3−5] Although Chen et al. have recently reported cinchona alkaloid-catalyzed α-aminations of N-unprotected oxindoles, these reactions are highly limited in scope, working efficiently only with C3-benzyl-substituted oxindoles, and therefore, significant opportunities exist to develop a broadly applicable methodology.[5] In this communication, we describe a general organocatalytic approach to the creation of a nitrogen-containing tetrasubstituted center at C3 through cinchona alkaloid-catalyzed highly enantioselective electrophilic α-amination of oxindoles (Figure 1). Unlike Chen's method, this catalytic procedure is general with respect to oxindoles and aminating reagents. More importantly, we also detail in this report various factors that affect the reactivity and the enantioselectivity of oxindoles and their products, giving insight into the chemistry itself and providing a basic understanding for further development of asymmetric transformations involving oxindoles as nucleophiles.

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(2) (a) Hewawasam, P.; Erway, M.; Moon, S. L.; Knipe, J.; Weiner, H.; Boissard, C. G.; Post-Munson, D. J.; Gao, Q.; Huang, S.; Gribkoff, V. K.; Meanwell, N. A. *J. Med. Chem.* **2002**, *45*, 1487. (b) Suzuki, H.; Morita, H.; Shiro, M.; Kobayashi, J. I. *Tetrahedron* **2004**, *60*, 2489. (c) Leugn, C.; Tomaszewski, M.; Woo, S. (Astrazeneca AB, Sweden); U.S. Patent Appl. Publ. (**2007**), CODEN: USXXCO US 2007185179 A1 20070809; patent written in English, application US 2007-671153 20070205. Priority: US 2006-771119 20060207.

(3) Synthesis of 3-hydroxy-2-oxindoles using transition metal asymmetric catalysis: (a) Toullec, P. Y.; Jagt, R. B. C.; de Vries, J. G.; Feringa, B. L.; Minnaard, A. L. *Org. Lett.* **2006**, *8*, 2715. (b) Shintani, R.; Inoue, M.; Hayashi, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 3353. (c) Ishimaru, T.; Shibata, N.; Nagai, J.; Nakamura, S.; Toru, T.; Kanesmasa, S. *J. Am. Chem. Soc.* **2006**, *128*, 16488. (d) Tomita, D.; Yamatsugu, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 6946. (e) Grant, C. D.; Krische, M. J. *Org. Lett.* **2009**, *7*, 867. (f) Itoh, J.; Han, S. B.; Krische, M. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 6313. (g) Lai, H.; Huang, Z.; Wu, Q.; Qin, Y. *J. Org. Chem.* **2009**, *74*, 283.

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(5) During the preparation of this paper, a related cinchona alkaloid-catalyzed α-amination of oxidoles was published online: Cheng, L.; Liu, Li.; Wang, D.; Chen, Y.-J. *Org. Lett.* **2009**, *11*, 3874.

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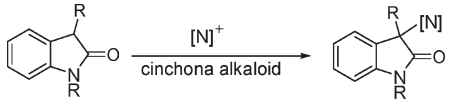
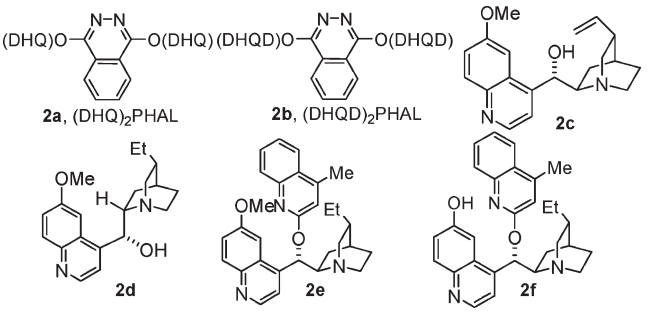


FIGURE 1. Synthesis of 3-amino-substituted oxindoles.

Over the past several years, electrophilic α-amination of carbonyl compounds using azodicarboxylates as a nitrogen source and amines or cinchona alkaloids as catalysts has drawn significant interest.[6] Carbonyl compounds such as aldehydes, ketones, β-ketoesters, and derivatives thereof are often employed as nucleophiles in these reactions.[7−11] We envisioned that the analogous transformation employing oxindoles as nucleophiles could be developed. This process would allow for the construction of a C−N bond at C3 in a catalytic fashion with the generation of a tetrasubstituted stereogenic center, a task that has not been accomplished to date by either organocatalysis or Lewis acid catalysis.[6,12] Success of the proposed transformation relies on deprotonating the C3 methine proton with a chiral amine base such that the resulting enolate is reactive enough to overcome the steric encumbrance at this position, while orchestrating the enantioselectivity of the addition. Therefore, judicious choice of chiral amine base in combination with finely tuned acidity of the oxindole methine proton is key to the development of this amination chemistry.[13]

SCHEME 1



Results and Discussion

Experimentally, the reaction of oxindole **1a** with diethyl azodicarboxylate was examined in the presence of commercially available catalyst **2a** (hydroquinine 1,4-phthalazinediyl diether $(DHQ)_2PHAL$, 10 mol %) (Scheme 1, Table 1). Gratifyingly, product **3a** was obtained in moderate yield and enantiomeric excess (ee) (entry 1).[14] Both yield and ee were improved notably when the reaction was performed at 4 °C (entry 2). Nonetheless, the low enantioselectivity warranted further optimization. A brief survey of other cinchona alkaloid-derived catalysts was conducted (entries 2−7). Catalyst **2b** (hydroquinidine 1,4-phthalazinediyl diether $(DHQD)_2PHAL$) was the most effective among cinchona alkaloids **2a** and **2c**−**2f** (entry 3 vs entry 2 and entries 4−7).

A subsequent solvent screen resulted in conditions in which good yield and enantioselectivity were obtained when the reaction was performed in diethyl ether (entry 12 vs entries 8−11 and entry 13). Finally, lowering the reaction temperature increased both yield and ee (entry 12 vs entry 14).[15] Like temperature, solvent affected ee significantly. For instance, with nonpolar solvents such as toluene, the reaction proceeded with only moderate yield and ee (entry 9).[16] In contrast, with more polar solvents such as ethyl acetate, diethyl ether, and dimethoxy ethane, notable improvement in yields and ee's was generally observed, although there was no simple correlation between ee and solvent polarity (entry 9 vs entries 10, 12, and 13). A loose correlation between solvent polarity and ee was noted in some cases (entry 9 vs entries 8, 11, and 12).[17] These results suggest that the polarity of solvent is not the sole factor that influences ee. The sensitivity of the amination reactions to solvent effects manifested itself in changes in ee's, yields, and perhaps reaction rates. We believe these solvent effects suggest that the reaction might involve a charged intermediate.

Next, the scope of the reaction with respect to oxindole substrates was investigated. A major setback surfaced when we discovered that enantioselectivity notably decreased as

(6) Reviews on α-amination of carbonyl compounds: (a) Guillena, G.; Ramon, D. J. *Tetrahedron: Asymmetry* **2006**, *17*, 1465. (b) Janey, J. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 4292. (c) Erdick, E. *Tetrahedron* **2004**, *60*, 8747.

(7) Amine-catalyzed α-amination of aldehydes and ketones: (a) Kumaragurbaran, N.; Juhl, K.; Zhuang, W.; Bogevig, A.; Jorgensen, K. A. *J. Am. Chem. Soc.* **2002**, *124*, 6254. (b) Bogevig, A.; Juhl, K.; Kumaragurbaran, N.; Zhuang, W.; Jorgensen, K. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1790. (c) List, B. *J. Am. Chem. Soc.* **2002**, *124*, 5656. (d) Chowdari, N. S.; Barbas, C. F. III. *Org. Lett.* **2005**, *7*, 867. (e) Vogt, H.; Vanderheiden, S.; Brase, S. *Chem. Commun.* **2003**, 2448. (f) Dahlin, N.; Bogevig, A.; Adolfson, H. *Adv. Synth. Catal.* **2004**, *346*, 1101.

(8) Organocatalytic enantioselective α-amination of β-ketoesters and derivatives thereof: (a) Pihko, P. M.; Pohjakallio, A. *Synlett* **2004**, *12*, 2115. (b) Saaby, S.; Bella, M.; Jorgensen, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 8120. (c) Liu, X.; Li, H.; Deng, L. *Org. Lett.* **2005**, *7*, 167. (d) Terada, M.; Nakano, M.; Ube, H. *J. Am. Chem. Soc.* **2006**, *128*, 16044. (d) Liu, Y; Melgar-Fernandez, R.; Juaristi, E. *J. Org. Chem.* **2007**, *72*, 1522.

(9) For related C−C bond-forming reactions involving oxindoles as nucleophiles in organocatalysis, see: (a) Bui, T.; Syed, S.; Barbas, C. F. III. *J. Am. Chem. Soc.* **2009**, *131*, 8756. (b) He, R.; Ding, C.; Maruoka, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 4559. (c) Chen, X.-H.; Wei, Q.; Luo, S.-W.; Xiao, H.; Gong, L.-Z. *J. Am. Chem. Soc.* **2009**, *131*, 13819−13825. (d) Galzerano, P.; Bencivenni, G.; Pesciaioli, F.; Mazzanti, A.; Giannichi, B.; Sambri, L.; Bartoli, G.; Melchiorre, P. *Chem.—Eur. J.* **2009**, *15*, 7846. (e) Duffey, T. A.; Shaw, S. A.; Vedejs, E. *J. Am. Chem. Soc.* **2009**, *131*, 14. (f) Shaw, S. A.; Aleman, P.; Christy, J.; Kampf, J. W.; Va, P.; Vedejs, E. *J. Am. Chem. Soc.* **2006**, *128*, 925. Leading references for C−C bond-forming reactions of oxindoles involving transition metal catalysis: (g) Kato, Y.; Furutachi, M.; Chen, Z.; Mitsunuma, H.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 9168. (h) Ashimori, A.; Bachand, B.; Overman, L. E.; Poon, D. J. *J. Am. Chem. Soc.* **1998**, *120*, 6477. (i) Doumay, A. B.; Hatanaka, K.; Kodanko, J. J.; Oestreich, M.; Overman, L. E.; Pfeifer, L. A.; Weiss, M. M. *J. Am. Chem. Soc.* **2003**, *125*, 6261. (j) Trost, B. M.; Frederiksen, M. U. *Angew. Chem., Int. Ed.* **2005**, *44*, 308. (k) Trost, B. M.; Zhang, Y. *J. Am. Chem. Soc.* **2006**, *126*, 4590. (l) Trost, B. M.; Zhang, Y. *J. Am. Chem. Soc.* **2007**, *129*, 14548. (m) Lee, S.; Hartwig, J. F. *J. Org. Chem.* **2001**, *66*, 3402. (n) Hills, I. D.; Fu, G. C. *Angew. Chem., Int. Ed.* **2003**, *42*, 3921. (o) Kozlowski, M. C.; Linton, E. C. *J. Am. Chem. Soc.* **2008**, *130*, 16162.

(10) Aldol and Mannich reactions involving oxindoles as nucleophiles: (a) Ogawa, S.; Shibata, N.; Inagaki, J.; Nakamura, S.; Toru, T.; Shiro, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 8666. (b) Tian, X.; Jiang, K.; Peng, J.; Du, W.; Chen, Y.-C. *Org. Lett.* **2008**, *10*, 3583.

(11) For related cinchona alkaloid-catalyzed α-fluorination of oxindoles: Ishimaru, T.; Shibata, N.; Horikawa, T.; Yasuda, N.; Nakamura, S.; Toru, T.; Shiro, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 4157.

(12) These optically active oxindoles are usually obtained through resolution or preparative HPLC separation; see ref 4.

(13) We previously observed that the acidity of the C3 methine proton could be affected greatly by changing the protecting group on the oxindole nitrogen atom; see ref 9a.

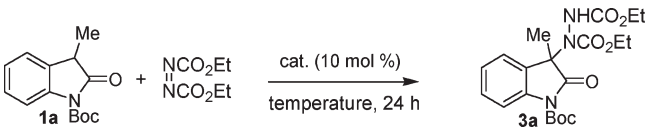
(14) Without a protecting group on the nitrogen atom and under identical conditions, **3a** was obtained in 78% yield with 11% ee.

(15) At −38 °C, with catalyst **2b**, product **3a** was obtained in 25% yield with 65% ee after 24 h reaction.

(16) The background reaction was significantly less in toluene than in methylene chloride, and this might, in part, account for the better ee observed in this solvent.

(17) Dielectric constants and solvent polarity: (a) Abboud, J-L. M.; Taft, R. W. *J. Phys. Org.* **1979**, *83*, 412. (b) Katritzky, A. R.; Fara, D. C.; Yang, H.; Tamm, K. *Chem. Rew.* **2004**, *104*, 175.

TABLE 1. Optimization Studies



entry	catalyst	solvent	temperature (°C)	yield[a](%)	ee[b](%)
1[c]	**2a**	THF	rt	70	29
2	**2a**	THF	4	86	49
3	**2b**	THF	4	84	81
4	**2c**	THF	4	87	60
5	**2d**	THF	−20	95	73[d]
6	**2e**	THF	4	77	74
7	**2f**	THF	4	62	66[d]
8	**2b**	CH_2Cl_2	4	80	2
9	**2b**	toluene	4	76	70
10	**2b**	EtOAc	4	81	70
11	**2b**	MeCN	4	90	35
12	**2b**	Et_2O	4	86	87
13	**2b**	$(MeOCH_2CH_2)_2O$	4	83	78
14	**2b**	Et_2O	−20	96	91

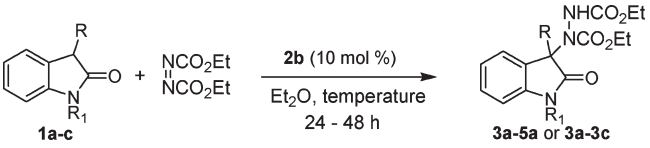
[a]Isolated yields. [b]Determined by chiral HPLC analysis. [c]Reaction run for 13 h. [d]The opposite enantiomer was obtained.

the steric bulk of the alkyl substituents at the C3 position increased, especially with *N*-Boc-protected oxindoles. Specifically, ee dropped from 91 to 82% as the alkyl substituent was changed from methyl to benzyl (Table 2, entries 1−3).[18] Fortunately, this selectivity problem was circumvented by changing the Boc group to a benzyl protecting group (entry 4). This change of protecting groups on the nitrogen atom may significantly attenuate the acidity of the methine proton at C3, thereby minimizing the background reaction. This might account for the enhanced ee and the attenuated reactivity observed in the reaction described in entry 4 compared to entry 2. Finally, the amination reaction proceeded smoothly at room temperature to afford the desired product with excellent yield and enantioselectivity (entry 5). More importantly, the yield and ee remained high with larger alkyl substituents (entry 5 vs entry 6).

After having established the optimal reaction conditions, we began to examine the scope of the α-amination reaction. A wide variety of oxindoles bearing different alkyl substituents were investigated (Table 3). Remarkably, the amination reaction tolerated various oxindole substrates and afforded the desired products in good yields with good to excellent ee (Table 3, entries 1−4). Even with a branched allyl substituent, the yield and ee of the desired product were still high (Table 3, entry 5). Synthetically, the allyl groups in compounds **3b** and **3e**, for example, are useful handles for further functional group manipulation. These results showed the synthetic advantages of our method over Chen's, which works well only with C3-benzyl-substituted oxindoles and requires the use of a rather uncommon halogenated solvent instead of diethyl ether. The requirement of benzyl-substituted oxindoles in order to obtain high ee in Chen's method precludes its broad synthetic utility. The synthetic advantages of the current procedure

(18) Attempts to solve this selectivity problem by changing the diethyl azodicarboxylate reagent failed. Specifically, 39 and 63% ee were obtained when dibenzyl azodicarboxylate and diisopropyl azodicarboxylate were used, respectively.

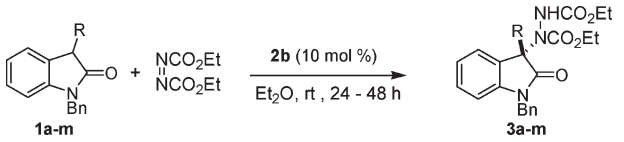
TABLE 2. Substituent Effects on Enantioselectivities



entry	R_1	R	temperature (°C)	product	yield[a](%)	ee[b](%)
1	Boc	Me	−20	**3a**	96	91
2	Boc	allyl	−20	**4a**	89	87
3	Boc	Bn	−20	**5a**	85	82
4[c]	Bn	allyl	−20 to 4	**3b**	41	97
5	Bn	allyl	rt	**3b**	95	94
6	Bn	Bn	rt	**3c**	96	99

[a]Isolated yields. [b]Determined by chiral HPLC analysis. [c]Reaction performed at −20 °C for 24 h, then warmed to 4 °C for 48 h.

TABLE 3. Scope of α-Amination



entry	R	product	yield[a](%)	ee[b]
1[c]	Me	**3a**	96	91
2	allyl	**3b**	95	94
3	benzyl	**3c**	96	99
4	4-Br-benzyl	**3d**	90	89
5	2-methylallyl	**3e**	98	98
6[d]	cinnamyl	**3f**	87	91
7	homoallyl	**3g**	96	96
8	$-CH_2CCSiMe_3$	**3h**	95	97
9[d]	$-(CH_2)_3-Ph$	**3i**	94	97
10	Et	**3j**	90	90
11	Me	**3k**	97	76
12[e]	2-methylallyl	**3l**	93	95
13[c]	4-Br-benzyl	**3m**	91	96

[a]Isolated yields. [b]Determined by chiral HPLC analysis. [c]*N*-Boc-protected oxindole as a substrate and the reaction performed at −20 °C for 24 h. [d]Et_2O/THF (5/1) as solvent. [e]Use of di-*tert*-butyl azodicarboxylate as an aminating reagent.

were illustrated further in the scope of the α-amination reaction with other oxindole substrates having different functionalities such as cinnamyl, homoallyl, and propargyl groups. No decrease in ee was observed in these cases (Table 3, entries 6−8). Moreover, oxindoles bearing saturated, aliphatic alkyl substituents also provided the corresponding products in good yields and ee's (Table 3, entries 9 and 10). Surprisingly, with *N*-benzyl-protected oxindoles having a methyl substituent at C3, the ee was lower than with the reaction employing *N*-Boc-protected oxindoles (Table 3, entry 11 vs entry 1). The yield and ee were high when di-*tert*-butyl azodicarboxylate was used in place of diethyl azodicarboxylate, thus broadening the scope of the reaction with respect to electrophiles (Table 3, entry 12 vs entry 5). Hydrazide **3l** was deprotected readily under acidic conditions.[19] Again, unlike Chen's procedure, which requires

(19) Use of di-*tert*-butyl azocarboxylate in Lewis acid catalyzed asymmetric amination: (a) Mashiko, T.; Hara, K.; Tanaka, D.; Fujiwara, Y.; Kumagai, N.; Shibasaki, M. *J. Am. Chem. Soc.* **2007**, *129*, 11342. (b) Mashiko, T.; Kumagai, N.; Shibasaki, M. *Org. Lett.* **2008**, *10*, 2725.

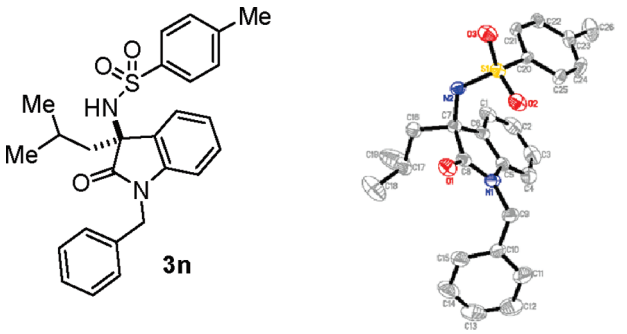
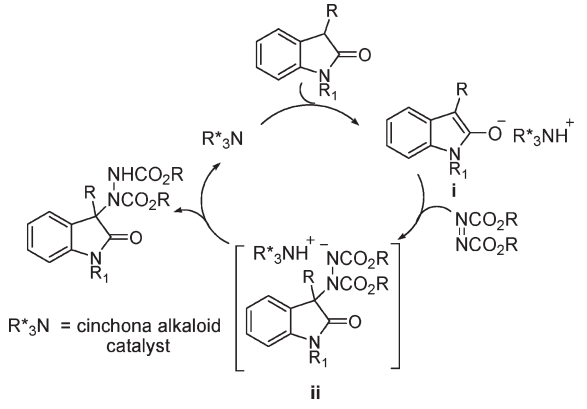


FIGURE 2. X-ray structure of **3n** (H atoms omitted for clarity).

the use of diisopropyl azodicarboxylates, the flexibility of our method in the choice of aminating reagents employed provides yet another synthetic advantage in addition to the aforementioned characteristics. Finally, oxindole **3m** was also obtained in high yield with excellent enantioselectivity.[20]

The absolute configuration at the newly created center was determined to be *S*. This was established by X-ray dispersion analysis of a sulfonamide derived from product **3l** (Figure 2).[20,21] Although details of the reaction mechanism have not been determined, our current hypothesis is that the α-amination reaction involves the generation of zwitterionic enolate (i) from the starting oxindole by deprotonation (Scheme 2). This species may exist as a contact ion pair such that the cinchona alkaloid catalyst relays its chirality to the reacting carbon center, thereby creating an asymmetric environment around the nucleophile. A subsequent C−N bond formation occurs and proceeds to provide an intermediate (ii), which, upon protonation, leads to the formation of the desired product and releases the catalyst back into the cycle.

SCHEME 2



Conclusions

In summary, we have developed new cinchona alkaloid-catalyzed enantioselective α-amination reactions involving oxindoles as nucleophiles. These addition reactions are general, broad in scope, and proceed under mild conditions to afford the desired products in excellent yields with good to excellent enantioselectivity. Significantly, these reactions provide a unique, catalytic approach to the construction of C−N bonds of oxindoles and also provide the first examples of general, catalytic, asymmetric procedures that allow the installation of a nitrogen atom at the C3 position. The investigations of the scope of this chemistry in other asymmetric transformations are underway, and the results will be reported in the near future.

Experimental Section

General Procedure for α-Aminations of Boc-Protected Oxindoles (Compound 3a). To a solution of oxindole **1a** (54.6 mg, 0.2 mmol, 1 equiv) and cinchona alkaloid catalyst **2b** (12.4 mg, 0.02 mmol, 0.1 equiv) in diethyl ether at −20 °C was added diethyl azodicarboxylate (40 μL, 0.22 mmol, 1.1 equiv). The resulting solution was stirred at −20 °C for 24 h. The reaction mixture was first diluted with ethyl acetate and then quenched with a saturated aqueous ammonium chloride solution. The aqueous layer was separated and extracted with ethyl acetate (three times). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude material was purified by flash column chromatography (hexanes/ethyl acetate) to afford 76 mg (96%) of **3a** as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (dd, J = 11.9, 8.2 Hz, 2H), 7.31 (t, J = 7.5 Hz, 1H), 7.18 (t, J = 7.4 Hz, 1H), 7.02 (s, 1H), 4.33−4.26 (m, 2H), 4.01−3.94 (m, 2H, J = 7.4 Hz), 1.65 (s, 9H), 1.55 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H), 1.00 (br t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.9, 157.0, 154.0, 149.1, 138.2, 131.1, 128.7, 124.9, 123.6, 114.6, 84.3, 66.0, 62.9, 62.3, 28.0, 23.7, 14.4, 13.7; HRMS calcd for $C_{20}H_{27}N_3O_7$ (MH^+) 422.1922, found 422.1925; HPLC (Chiralpak AD, hexane/*i*-PrOH = 90:10, flow rate = 1.00 mL/min, λ = 254 nm) t_R = 9.68 min (minor enantiomer), t_R = 15.44 min (major enantiomer).

General Procedure for α-Aminations of Benzyl-Protected Oxindoles (Compound 3b). To a solution of oxindole **1b** (52.7 mg, 0.2 mmol, 1 equiv) and cinchona alkaloid catalyst **2b** (15.6 mg, 0.02 mmol, 0.1 equiv) in diethyl ether at rt was added diethyl azodicarboxylate (46 μL, 0.24 mmol, 1.2 equiv). The resulting solution was stirred at rt for 48 h and then directly purified by flash column chromatography (hexanes/ethyl acetate, 3/1) to afford 83.1 mg (94%) of **3b** as oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J=7.2 Hz, 1H), 7.39−7.25 (m, 5H), 7.15 (t, J=8.7 Hz, 1H), 7.05 (t, J=7.4 Hz, 1H), 6.96 (s, 1H), 6.66 (d, J=7.7 Hz, 1H), 5.26−5.16 (m, 1H), 5.05−4.99 (m, 2H), 4.89 (d, J=9.96 Hz, 1H), 4.76 (d, J= 15.7 Hz, 1H), 4.21−4.37 (m, 2H), 4.02−3.88 (m, 2H), 2.84−2.71 (m, 2H), 1.33 (t, J=7.1 Hz, 5H). 0.95 (t, J=6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 157.1, 154.1, 142.5, 135.9, 130.0, 129.8, 128.6, 127.6, 127.5, 124.2, 123.1, 120.5, 120.4, 108.7, 68.7, 62.7, 62.7, 44.3, 40.4, 14.5, 14.0; HRMS calcd for $C_{24}H_{27}N_3O_5$ (MH^+) 438.2023, found 438.2019; HPLC (Chiralpak AD, hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, λ = 254 nm) t_R = 20.37 min (major enantiomer), t_R = 31.87 min (minor enantiomer).

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Supporting Information Available: Experimental procedures and compound characterization data as well as X-ray data for **3n**. This material is available free of charge via the Internet at http://pubs.acs.org.

(20) Occasionally, *N*-Boc-protected oxindoles gave products with high ee. However, they are not as general as *N*-benzyl-protected counterparts. Compounds **3m** and **3d** were made in an attempt to obtain crystals for X-ray analysis. Unfortunately, these compounds did not yield satisfactory crystals.

(21) See Supporting Information.