



Synthesis of α,β -diamino acid derivatives via asymmetric Mannich reactions of glycine imino esters catalyzed by a chiral phosphoramidite-silver complex



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ABSTRACT

AgOTf-phosphoramidite complexes efficiently catalyze the enantioselective Mannich-type reaction between benzophenone-imine glycine methyl ester and *N*-tosyl aldimines in the absence of a base. The corresponding *syn*-adducts, which are the direct precursors of α,β -diamino acids, are obtained with moderate to good *syn*-diastereoselectivities (up to 9:1) and high enantioselectivities (up to 99% ee).

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1. Introduction

The asymmetric Mannich reaction is a very useful methodology for the preparation of enantioenriched β -amino carbonyl compounds where the absolute configuration of two stereogenic centers can be defined simultaneously.^{1–3} There are many types of enolates which are able to add to imines by the intermediacy of chiral metal complexes or organocatalysts. In the case of using Schiff bases derived from α -amino esters **1** as nucleophiles and imines **2**, protected α,β -diamino esters **3** can be prepared straightforwardly. After deprotection, α,β -diamino acids **4** are easily generated, which are biologically relevant⁴ and also chemically attractive due to their use as chiral building blocks⁵ (Scheme 1). Apart from this Mannich-type reaction, the asymmetric amination of α,β -unsaturated acid derivatives, and the catalytic hydrogenation of bis-(amido)acrylates diamino are two additional routes.⁶

The enantioselective reaction of imino esters **1** with *N*-protected imines shown in Scheme 1 has been successfully performed in the presence of chiral organocatalysts **5**^{7a} and **6**^{7b} or chiral metal complexes **7–15**⁸ (Fig. 1). The reactions involving organocatalysts **5** and **6** afforded almost exclusively the *syn*-**3** diastereoisomer with excellent enantioselections.⁹ The *syn*-diastereoisomer was also the major product isolated when chiral copper complexes were employed. The unique exception was noted when the major *anti*-**3** diastereoisomer was isolated in good enantioselectivities after the reaction with copper(I) complexes **11** and **12**. In the case of aldimino esters **1** ($R^1 = H$, $R^2 = Ph$) the *anti*-**3**

diastereoisomers were isolated with excellent enantioselectivities, a bulky *N*-(8-quinolyl)sulfonyl protecting group being needed.⁸ⁱ Copper salts are mainly employed and only one contribution employed a chiral **15**-silver acetate complex affording the *syn*-diastereoisomers as major products.^{8k}

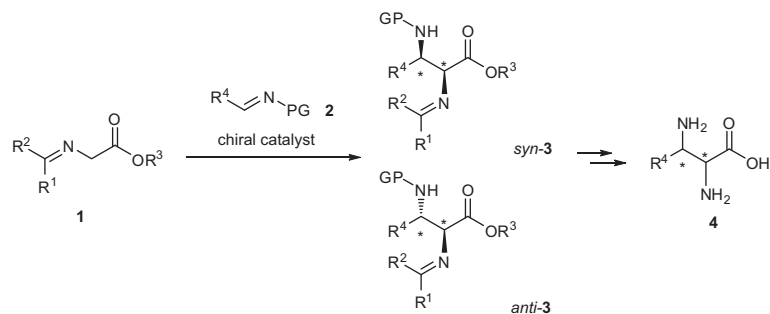
We have recently described that complexes formed by silver salts and privileged chiral ligands¹⁰ such as Binap **16**¹¹ and phosphoramidites **17** and **18**¹² are excellent catalysts for the enantioselective 1,3-dipolar cycloadditions^{13,14} of azomethine ylides derived from imino esters **1** in the construction of enantiomerically enriched highly substituted prolines.^{15,16} Herein we report the application of these silver chiral complexes¹⁷ in the Mannich type reaction of glycine benzophenone Schiff bases and protected aldimines (Fig. 2).

2. Results and discussion

The selected reaction for the optimization conditions involved the glycine benzophenone imine derivative **1a** ($R^1 = R^2 = Ph$, $R^3 = H$, and $R^4 = Me$), benzaldehyde *N*-tosylimine **2a** (PG = Ts), triethylamine (5 mol %) as the base, and AgOAc (5 mol %) in toluene as the solvent at room temperature for 1 day (Scheme 2). The reaction performed with (*S*)-Binap **16** was first evaluated in the presence and in the absence of triethylamine. High conversions and 67:33 *syn:anti* diastereomeric ratios of compound **3a** were obtained in both cases. The highest enantioselection was observed for the *syn*-diastereoisomer when no base was added (Table 1, entries 1 and 2). The same behavior was exhibited by the chiral catalyst formed by Monophos **17** and silver acetate. A higher 75:25 dr was observed but with lower enantioselection (Table 1,

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Scheme 1. General Mannich-type reaction between imino esters and *N*-protected imines.

entries 3 and 4). Phosphoramidite **18** and AgOAc gave a higher enantioselectivity (80% ee) and 80:20 dr when the reaction was carried out in the absence of a base (Table 1, compare entries 5 and 6). Copper(I) and copper(II) triflates were also tested (not shown in Table 1) giving a complex crude reaction mixture (¹H NMR) from complete. The reactions under the conditions shown in entries 5 and 6 were very slow at 0 °C.

Silver perchlorate was a suitable metal salt for phosphoramidite **18** and afforded the major *syn*-stereoisomer **3a** in high conversion but with lower diastereoselection (72:28) than that observed for the reaction run with AgOAc (Table 1, compare entries 5 with 6,

and 6 with 8). In light of all these tests, the reaction with different silver salts was next essayed without triethylamine. Thus, AgTfa (Tfa = trifluoroacetate), AgOBz, AgSbF₆, and Ag₂CO₃ did not improve the enantioselection generated by the employment of silver perchlorate (Table 1, entries 9–12). However, the best results were observed when AgOTf was employed as the silver salt (Table 1, entry 13).

In order to improve the diastereoselectivity of the process while also gaining some enantioselection, different nitrogen protecting groups for the imines such as nosyl (*p*-nitrophenylsulfonyl, Ns) and *N*-(8-quinolyl)sulfonyl (8-Q) were evaluated. In both cases

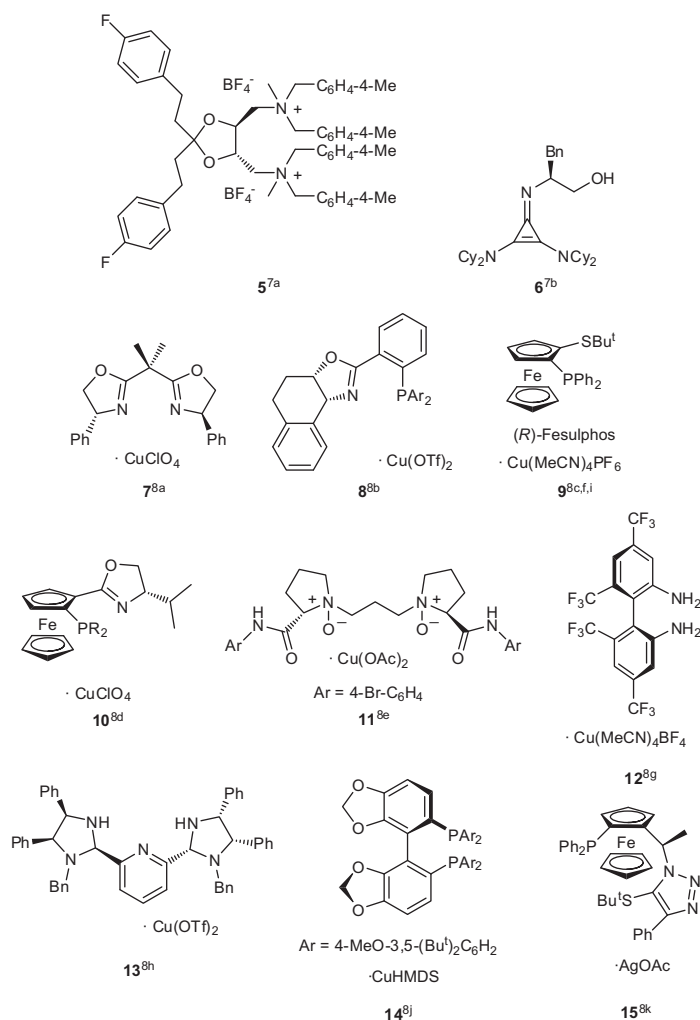


Figure 1. Chiral catalysts employed in the Mannich-type reaction between imino esters and *N*-protected imines.

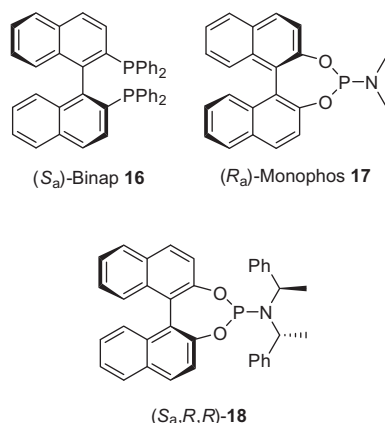
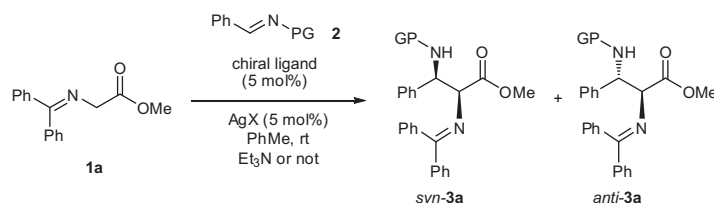


Figure 2. Chiral privileged ligands **16–18** employed herein.

conversions were high but the enantioselection was very poor (Table 1, entries 14 and 15), even when the *tert*-butyl (diphenylmethylene)glycinate was used (Table 1, entries 16–18).

The influence of the solvent was also noticeable. Toluene was the best solvent whereas THF, Et₂O, DCM, and MeCN furnished both lower dr and ee (Table 1, entries 19–22). The mechanism of this reaction is very similar to that reported for the asymmetric synthesis of polysubstituted prolines through a 1,3-dipolar cycloaddition reaction using the same catalytic system.^{12b}

The scope of the reaction was investigated under the optimized reaction conditions using toluene as the solvent at room temperature. When the reaction was catalyzed by the complex AgOTf·(*S_a,R_t,R_t*)-**18**, it gave the same results as those reported when using (*R_a,S_t,S_t*)-**18** ligand but with the opposite enantiomeric form *ent*-**3** (Table 2, entry 2). Different aldimines were prepared according to known methods and employed directly as electrophiles in the Mannich type reaction with imino ester **1a**. In general, if a comparison is established between product **3a** (Table 2, entry 1) and the different **3b–3l** molecules, the presence of a substituent at the *ortho*-position in the arene moiety decreased the enantioselection of the corresponding major *syn*-**3** diastereoisomers (Table 2, entries 3–5). However, halogenated aryl groups provided the highest ee in these series (Table 2, entries 4 and 5) with moderate diastereoselection. The *m*-substituted chloroarene in the imine **2** moiety afforded the best diastereoselection, but again very low



Scheme 2. Optimization reaction model.

Table 1
Optimization reactions

Ent.	AgX	Ligand	Base	PG	Yield ^a (%)	dr ^a (<i>syn:anti</i>)	ee ^b (<i>syn, anti</i>)
1	AgOAc	16	TEA	Ts	100	67:33	12, 20
2	AgOAc	16	—	Ts	100	67:33	24, 2
3	AgOAc	17	TEA	Ts	100	75:25	<10, <10
4	AgOAc	17	—	Ts	100	75:25	10, 6
5	AgOAc	18	TEA	Ts	90	80:20	12, 24
6	AgOAc	18	—	Ts	90	80:20	80, 10
7	AgClO ₄	18	TEA	Ts	100	86:14	12, <i>rac.</i>
8	AgClO ₄	18	—	Ts	75	72:28	92, 32
9	AgTfa	18	—	Ts	85	60:40	14, 12
10	AgOBz	18	—	Ts	100	75:25	78, 38
11	AgSbF ₆	18	—	Ts	85	60:40	64, 16
12	Ag ₂ CO ₃	18	—	Ts	92	84:16	8, 4
13	AgOTf	18	—	Ts	94	72:28	96, 58
14	AgOTf	18	—	Ns ^c	100	90:10	24, 18
15	AgOTf	18	—	8-Q ^d	90	72:28	6, 2
16	AgOTf ^e	18	—	Ts	95	80:20	4, 28
17	AgOTf ^e	18	—	Ns ^c	100	>96:4	56, <i>rac.</i>
18	AgOTf ^e	18	—	8-Q ^d	85	86:14	10, 6
19	AgOTf ^f	18	—	Ts	89	67:33	38, 6
20	AgOTf ^g	18	—	Ts	92	72:28	<i>rac., rac.</i>
21	AgOTf ^h	18	—	Ts	91	62:38	58, 86
22	AgOTf ⁱ	18	—	Ts	87	72:28	24, 40

^a Determined by ¹H NMR of the crude reaction mixture.

^b Determined by HPLC using chiral columns.

^c *p*-Nitrophenylsulfonyl group (nosyl).

^d *N*-(8-quinolyl)sulfonyl group.

^e The corresponding *tert*-butyl ester was employed.

^f Reaction run in the presence of THF as the solvent.

^g Reaction run in the presence of Et₂O as the solvent.

^h Reaction run in the presence of DCM as the solvent.

ⁱ Reaction run in the presence of MeCN as the solvent.

enantiomeric excess was found for both the *syn*- and *anti*-isomers **3e** (Table 2, entry 6). The effect of the *para*-substitution was very similar to that observed in the examples run with *ortho*-substituted arenes, that is, low ee for the examples whose substituents were different from halogenated atoms (Table 2, entries 7–11). In this case 4-fluoro and 4-bromoarenes gave 99% ee and 80% ee, of the major *syn*-diastereoisomers **3h** and **3j**, respectively. Heterocyclic substituents bonded to the imino group were also good precursors for highly enantioselective Mannich-type additions. Thus, the 2-furyl derivative afforded 92% ee of **3k** and 2-*a*-thienyl surrogate furnished 78% ee of **3l** with a 75:25 dr in both cases (Table 2, entries 12 and 13). Despite the reaction being completed, chemical yields were moderate due to the instability of the final iminoesters **3** during purification using flash chromatography (Scheme 3).

Table 2
Scope of the Mannich-type reaction

Ent.	Ar	2	3	Yield ^a (%)	dr ^a (<i>syn</i> : <i>anti</i>)	ee ^b (<i>syn</i> , <i>anti</i>)
1	Ph	2a	3a	70	72:28	96, 58
2	Ph ^c	2a	3a	70	72:28	–96, –58
3	2-MeC ₆ H ₄	2b	3b	50	80:20	14, 4
4	2-ClC ₆ H ₄	2c	3c	55	56:44	46, <5
5	2-BrC ₆ H ₄	2d	3d	67	60:40	48, 34
6	3-ClC ₆ H ₄	2e	3e	42	90:10	14, 14
7	4-(CF ₃)C ₆ H ₄	2f	3f	30	75:25	15, 2
8	4-(NO ₂)C ₆ H ₄	2g	3g	47	70:30	20, 12
9	4-FC ₆ H ₄	2h	3h	48	70:30	99, 10
10	4-ClC ₆ H ₄	2i	3i	30	70:30	42, 16
11	4-BrC ₆ H ₄	2j	3j	35	50:50	80, 10
12	2-Furyl	2k	3k	45	75:25	92, 24
13	2-Thienyl	2l	3l	45	75:25	78, 38

^a Isolated yield after column chromatography.

^b Determined by HPLC using chiral columns.

^c Reaction performed in the presence of AgOTf(*R_aS,S*)-**18**.

This Mannich type reaction can be rationalized on the basis of the models proposed by different authors.^{8f} The freshly generated azomethine ylide is coordinated by a silver atom and the nucleophilic attack occurs at the tosyl imine whose arylsulfonyl group is placed far away from the benzylidene moiety of the dipole (Fig. 3). In this transition state, additional coordination between silver and sulfonamido group cannot be ruled out.

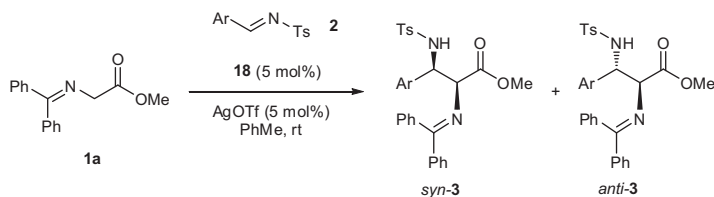
3. Conclusions

The chiral complex formed by phosphoramidite **18** and AgOTf (1:1 molar ratio) was the most effective catalyst in the Mannich-type reaction between imino esters derived from benzophenone and *N*-tosylimines. No extra base was needed for the reaction completion, meaning that it acted as a Lewis acid coordinating the imino ester and that the corresponding counteranion has the base role required for the α -deprotonation. Both chemical yields and diastereomeric ratios of the major *syn*-products were moderate to good. The *syn*-selectivity was in agreement with the data reported in the literature. The presence of heteroatoms and *para*-halogenated arenes in the aromatic part of the imine afforded the best enantioselection (up to 99% ee).

4. Experimental

4.1. General

N-Protected imines **2** were prepared according to the published methods.⁸ Anhydrous solvents were freshly distilled under an argon atmosphere and degassed by Freeze–Pump–Thaw methodology. Aldehydes were also distilled prior to use for the elaboration of the imino esters **1** and imines **2**. Melting points were determined with a Reichert Thermowar hot plate apparatus and are uncorrected. Only the structurally most important peaks of the IR spectra (recorded with a FT-IR 4100LE (JASCO) (PIKE MIRacle ATR) are listed. ¹H NMR (300 MHz) and ¹³C NMR (75 MHz) spectra were obtained with a Bruker AC-300 by using CDCl₃ as solvent and TMS as the internal standard, unless otherwise stated. Optical rotations were measured with a Perkin-Elmer 341 polarimeter. HPLC analyses were performed with a JASCO-2000 series equipped with a chiral column (detailed for each compound in the main text) by using mixtures of *n*-hexane/isopropyl alcohol as the mobile phase at 25 °C. Low-resolution electron impact (EI) mass spectra were obtained with a Shimadzu QP-5000 by injection or DIP, and high-resolution mass spectra were obtained with a Finnigan VG Platform or a Finnigan MAT 95S. Analytical TLC was performed on Schleicher & Schuell F1400/LS 254 silica gel plates and the spots were visualized under UV light ($\lambda = 254$ nm). Merck silica gel 60 (0.040–0.063 mm) was used for flash chromatography.



Scheme 3.

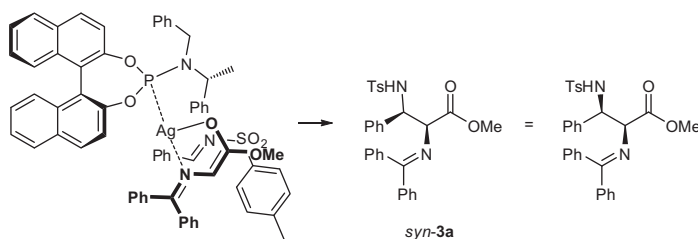


Figure 3. Proposed transition state leading to the *syn*-stereoisomer.

4.2. General procedure for the Mannich-type reaction

In a 10 ml vial covered by aluminum foil, was added AgOTf (1.54 mg, 0.006 mmol), phosphoramidite **18** (3.24 mg, 0.006 mmol) and toluene (2 ml), and the mixture was stirred at room temperature for 1 h. Benzophenone imine derivative **1** (0.120 mmol) and *N*-tosylimine **2** (0.144 mmol) were added. The reaction was stirred for 1 day at room temperature and the crude was analyzed by ¹H NMR spectroscopy to determine the diastereomeric ratio, and then purified by flash chromatography (*n*-hexane–EtOAc; 15% of EtOAc), affording the products *syn/anti*-**3**.

4.3. Methyl 2-[(diphenylmethylene)amino]-3-(4-methylphenyl-sulfonamide)-3-phenylpropanoate *syn*-**3a** and *anti*-**3a**^{8k}

42.9 mg; 70% yield; HPLC: (Daicel Chiralpak AD-H), hexane/*i*-PrOH 90/10, flow rate 1 ml/min, *t*_R: 23.7 min (*syn*), 36.4 min (*anti*), 42.2 min (*anti*) and 45 min (*syn*), 254 nm; IR *v*_{max}: 3297, 1736, 1628, 1328, 1157 cm⁻¹; ¹H NMR *δ*_H: 2.27 (s, 3H, Me_{anti}), 2.34 (s, 3H, Me_{syn}), 3.49 (s, 3H, OMe_{anti}), 3.51 (s, 3H, OMe_{syn}), 4.14 (d, *J* = 2.2 Hz, 1H_{syn}), 4.36 (d, *J* = 5.9 Hz, 1H_{anti}), 4.71 (dd, *J* = 7.6, 5.8 Hz, 1H_{anti}), 5.16 (dd, *J* = 8.4, 2.0 Hz, 1H_{syn}), 5.78 (d, *J* = 7.1 Hz, NH_{anti}), 6.37 (t, *J* = 8.4 Hz, 2H_{syn} + NH_{syn}); 6.88–7.72 (m, 19H_{syn}, 19H_{anti}, Ar H); ¹³C NMR *δ*_C: 21.4 (Me), 52.3 (C_{syn}NH), 59.4 (C_{syn}N=), 60.0 (C_{anti}N=), 69.4 (OMe_{anti}), 69.9 (OMe_{syn}), 126.8, 126.9, 127.1, 127.3, 127.4, 128.1, 128.3, 128.6, 128.9, 129.2, 130.9, 135.5, 138.2, 138.5, 139.0, 142.8 (ArC), 169.6_{syn}, 173.1_{syn} (CO, CN). MS (EI) *m/z* (%): 512 (0.12), 259 (12), 194 (40), 155 (33), 91 (100), 65 (10).

4.4. Methyl 2-[(diphenylmethylene)amino]-3-(4-methylphenyl-sulfonamide)-3-(*o*-methylphenyl)propanoate *syn*-**3b** and *anti*-**3b**^{8k}

31.6 mg; 50% yield; HPLC: (Daicel Chiralpak AD-H), hexane/*i*-PrOH 85/15, flow rate 1 ml/min, *t*_R: 9.7 min (*syn*), 14.0 min (*anti*), 15.4 min (*anti*) and 19.9 min (*syn*), 254 nm; IR *v*_{max}: 2987, 1725, 1334, 1265, 1159, 1093, 733, 700 cm⁻¹; ¹H NMR *δ*_H: 1.97 (s, 3H, Me_{anti}), 2.04 (s, 3H, Me_{syn}), 2.26 (s, 3H, Me_{anti}), 2.33 (s, 3H, Me_{syn}), 3.51 (s, 3H, OMe_{syn}), 3.53 (s, 3H, OMe_{anti}), 4.06 (d, *J* = 2.1 Hz, 1H_{syn}), 4.31 (d, *J* = 6.5 Hz, 1H_{anti}), 4.87 (d, *J* = 6.5 Hz, 1H_{anti}), 5.40 (dd, *J* = 8.5, 2.0 Hz, 1H_{syn}), 6.21 (d, *J* = 7.5 Hz, 2H_{syn}), 6.42 (d, *J* = 8.4 Hz, NH_{syn}), 6.79–7.89 (m, 16H_{syn}, 16H_{anti}, Ar H); ¹³C NMR *δ*_C: 21.5 (Me), 52.4 (C_{syn}NH), 55.9 (C_{syn}N=), 125.6, 126.5, 126.8, 127.0, 128.3, 128.5, 128.9, 129.2, 129.7, 130.1, 132.4, 169.7_{syn}; 172.9_{syn} (CO, CN); MS (EI) *m/z* (%): 526 (0.23), 194 (42), 165 (12), 118 (78), 117 (13), 91 (100), 65 (15).

4.5. Methyl 2-[(diphenylmethylene)amino]-3-(4-methylphenyl-sulfonamide)-3-(*o*-chlorophenyl)propanoate *syn*-**3c** and *anti*-**3c**^{8k}

36.1 mg; 55% yield; HPLC: (Daicel Chiralpak IB), hexane/*i*-PrOH 95/5, flow rate 1 ml/min, *t*_R: 17.4 min (*syn*) and 21.7 min (*syn*), 254 nm; IR *v*_{max}: 1739, 1597, 1443, 1332, 1159, 1088, 764, 697 cm⁻¹; ¹H NMR *δ*_H: 2.23 (s, 3H, Me_{anti}), 2.36 (s, 3H, Me_{syn}), 3.44 (s, 3H, OMe_{syn}), 3.47 (s, 3H, OMe_{anti}), 4.30 (d, *J* = 2.1 Hz, 1H_{syn}), 4.48 (d, *J* = 5.9 Hz, 1H_{anti}), 4.85 (t, *J* = 5.8 Hz, 1H_{anti}), 5.54 (dd, *J* = 8.3, 2.0 Hz, 1H_{syn}), 6.28 (d, *J* = 7.3 Hz, 2H_{syn}), 6.32 (d, *J* = 6.0 Hz, NH_{syn}), 6.46 (d, *J* = 8.3 Hz, NH_{anti}), 6.78–7.73 (m, 18H_{syn}, 18H_{anti}, Ar H); ¹³C NMR *δ*_C: 21.4 (Me), 52.0 (C_{syn}NH), 56.2 (C_{syn}N=), 66.6 (OMe_{syn}), 126.7, 127.1, 127.5, 127.9, 128.3, 128.6, 129.0, 129.3, 129.7, 130.0, 130.9, 132.4, 135.3, 136.4, 137.8, 138.5, 143.0, 169.9_{syn}, 172.6_{syn} (CO, CN); MS (EI) *m/z* (%): 547 (0.15), 258 (33), 194 (35), 165 (10), 155 (33), 91 (100), 65 (10).

4.6. Methyl 2-[(diphenylmethylene)amino]-3-(4-methylphenyl-sulfonamide)-3-(*o*-bromophenyl)propanoate *syn*-**3d** and *anti*-**3d**^{8k}

47.6 mg; 67% yield; HPLC: (Daicel Chiralpak OD-H), hexane/*i*-PrOH 90/10, flow rate 0.6 ml/min, *t*_R: 15.2 min (*syn*), 16.9 min (*anti*), 22.7 min (*anti*), and 37.8 min (*syn*), 254 nm. IR *v*_{max}: 3285, 2987, 1738, 1333, 1159, 1081, 765, 697 cm⁻¹; ¹H NMR *δ*_H: 2.24 (s, 3H, Me_{anti}), 2.36 (s, 3H, Me_{syn}), 3.45 (s, 3H, OMe_{anti}), 3.46 (s, 3H, OMe_{syn}), 4.33 (d, *J* = 2.1 Hz, 1H_{syn}), 4.49 (d, *J* = 5.7 Hz, 1H_{anti}), 4.80 (t, *J* = 5.5 Hz, 1H_{anti}), 5.50 (dd, *J* = 8.2, 2.0 Hz, 1H_{syn}), 6.26 (d, *J* = 6.7 Hz, 2H_{syn}), 6.39 (d, *J* = 8.4 Hz, NH_{anti}), 6.49 (d, *J* = 8.2 Hz, NH_{syn}), 6.79–7.87 (m, 18H_{syn}, 18H_{anti}, Ar H); ¹³C NMR *δ*_C: 21.4 (Me), 51.9 (C_{syn}NH), 58.4 (C_{syn}N=), 66.5 (OMe_{syn}), 126.7, 127.2, 127.3, 127.5, 127.7, 128.0, 128.6, 129.0, 129.3, 129.7, 130.0, 130.9, 132.6, 135.3, 138.5, 143.1, 169.8_{syn}, 172.6_{syn} (CO, CN); MS (EI) *m/z* (%): 591 (0.36), 258 (38), 194 (36), 165 (11), 155 (33), 91 (100), 65 (10).

4.7. Methyl 2-[(diphenylmethylene)amino]-3-(4-methylphenyl-sulfonamide)-3-(*m*-chlorophenyl)propanoate *syn*-**3e** and *anti*-**3e**^{8d}

27.6 mg; 42% yield; HPLC: (Daicel Chiralpak AD), hexane/*i*-PrOH 90/10, flow rate 1 ml/min, *t*_R: 40.8 min (*syn*) and 78.1 min (*syn*), 254 nm. IR *v*_{max}: 2987, 1739, 1657, 1597, 1159, 1076, 701, 665 cm⁻¹; ¹H NMR *δ*_H: 2.30 (s, 3H, Me_{anti}), 2.36 (s, 3H, Me_{syn}), 3.50 (s, 3H, OMe_{anti}), 3.51 (s, 3H, OMe_{syn}), 4.15 (d, *J* = 2.3 Hz, 1H_{syn}), 4.42 (d, *J* = 5.4 Hz, 1H_{anti}), 4.78 (dd, *J* = 7.7, 5.5 Hz, 1H_{anti}), 5.16 (dd, *J* = 8.3, 2.3 Hz, 1H_{syn}), 5.77 (d, *J* = 7.7 Hz, NH_{anti}), 6.44 (t, *J* = 8.4 Hz, 2H_{syn} + NH_{syn}), 6.89–7.69 (m, 16H_{syn}, 16H_{anti}, Ar H); ¹³C NMR (75 MHz, CDCl₃) *δ*_C: 21.4 (Me), 29.7, 52.5 (C_{syn}NH), 57.4 (C_{syn}N=), 69.5 (OMe_{syn}), 123.0, 126.6, 127.0, 128.3, 128.6, 128.9, 129.4, 129.5, 130.0, 131.2, 132.4, 134.6, 134.7, 143.2, 148.4, 148.6, 169.2_{syn}, 173.8_{syn} (CO, CN); MS (EI) *m/z* (%): 547 (0.21), 260 (17), 233 (16), 194 (38), 155 (20), 91 (100), 65 (10).

4.8. Methyl 2-[(diphenylmethylene)amino]-3-(4-methylphenyl-sulfonamide)-3-(*p*-trifluoromethylphenyl) propanoate *syn*-**3f** and *anti*-**3f**^{8k}

20.9 mg; 30% yield; HPLC: (Daicel Chiralpak AD-H), hexane/*i*-PrOH 90/10, flow rate 0.8 ml/min, *t*_R: 13.5 min (*syn*), 16.4 min (*anti*), 27.8 min (*syn*) and 30.5 min (*anti*), 254 nm; IR *v*_{max}: 3288, 2360, 1743, 1324, 1159, 1119, 1067, 700 cm⁻¹; ¹H NMR *δ*_H: 2.29 (s, 3H, Me_{anti}), 2.36 (s, 3H, Me_{syn}), 3.52 (s, 3H, OMe_{anti}), 3.54 (s, 3H, OMe_{syn}), 4.17 (d, *J* = 2.2 Hz, 1H_{syn}), 4.43 (d, *J* = 5.5 Hz, 1H_{anti}), 4.81 (dd, *J* = 7.6, 5.6 Hz, 1H_{anti}), 5.20 (dd, *J* = 8.3, 1.9 Hz, 1H_{syn}), 5.83 (d, *J* = 7.6 Hz, NH_{anti}), 6.39 (d, *J* = 7.1 Hz, 2H_{syn}), 6.46 (d, *J* = 8.3 Hz, NH_{syn}), 6.87–7.70 (m, 18H_{syn}, 18H_{anti}, Ar H); ¹³C NMR *δ*_C: 21.3 (Me), 52.5 (C_{syn}NH), 59.1 (C_{syn}N=), 69.5 (OMe_{syn}), 126.7, 127.1, 127.3, 128.2, 128.3, 128.5, 128.8, 128.9, 129.3, 130.0, 131.2, 137.8, 138.1, 143.1, 143.2, 169.3_{syn}, 173.6_{syn} (CO, CN); MS (EI) *m/z* (%): 580 (0.25), 252 (10), 194 (35), 165 (10), 155 (46), 91 (100), 65 (10).

4.9. Methyl 2-[(diphenylmethylene)amino]-3-(4-methylphenyl-sulfonamide)-3-(*p*-nitrophenyl)propanoate *syn*-**3g** and *anti*-**3g**^{8d}

31.4 mg; 47% yield; HPLC: (Daicel Chiralpak OD-H), hexane/*i*-PrOH 85/15, flow rate 0.6 ml/min, *t*_R: 17.4 min (*syn*), 21.0 min (*anti*), 23.0 min (*syn*), and 39.1 min (*anti*), 254 nm; IR *v*_{max}: 3273, 1734, 1624, 1519, 1344, 1159, 851, 697 cm⁻¹; ¹H NMR *δ*_H: 2.28 (s, 3H, Me_{anti}), 2.37 (s, 3H, Me_{syn}), 3.48 (s, 3H, OMe_{syn}), 3.49 (s, 3H, OMe_{anti}), 4.18 (d, *J* = 2.2 Hz, 1H_{syn}), 4.38 (d, *J* = 5.5 Hz, 1H_{anti}), 4.78 (dd, *J* = 7.5, 5.6 Hz, 1H_{anti}), 5.20 (dd, *J* = 8.0, 2.1 Hz, 1H_{syn}), 5.91 (d, *J* = 7.0 Hz, NH_{anti}), 6.45 (d, *J* = 7.1 Hz, 2H_{syn}), 6.51 (d, *J* = 8.1 Hz, NH_{syn}), 6.82–8.12 (m, 18H_{syn}, 18H_{anti}, Ar H); ¹³C NMR

δ_C : 21.4 (Me_{syn}), 25.3 (Me_{anti}), 52.3 (C_{anti}NH), 52.5 (C_{syn}NH), 58.9 (C_{syn}N=), 59.2 (C_{anti}N=), 64.4 (OMe_{anti}), 69.2 (OMe_{syn}), 123.2, 123.3, 126.6, 127.0, 127.2, 127.8, 128.2, 128.3, 128.6, 128.7, 128.8, 128.9, 129.4, 131.3, 135.1, 137.7, 137.9, 143.4, 145.1, 146.7, 147.1, 169.1_{syn}, 169.4_{anti}, 173.9_{syn} (CO, CN); MS (EI) m/z (%): 557 (0.13), 194 (44), 165 (12), 155 (36), 91 (100), 65 (10).

4.10. Methyl 2-[(diphenylmethylene)amino]-3-(4-methylphenyl-sulfonamide)-3-(*p*-fluorophenyl)propanoate syn-3h and anti-3h^{8e}

30.6 mg; 48% yield; HPLC: (Daicel Chiralpak OD-H), hexane/*i*-PrOH 90/10, flow rate 0.6 ml/min, t_R : 13.4 min (syn), 14.8 min (anti), 17.1 min (anti), and 32.6 min (syn), 254 nm; IR ν_{max} : 3289, 2971, 1753, 1628, 1509, 1428, 1328, 1156, 1081, 736, 697 cm⁻¹; ¹H NMR δ_H : 2.29 (s, 3H, Me_{anti}), 2.36 (s, 3H, Me_{syn}), 3.50 (s, 3H + 3H, OMe_{syn+anti}), 4.12 (d, J = 2.3 Hz, 1H_{syn}), 4.34 (d, J = 5.8 Hz, 1H_{anti}), 4.71 (dd, J = 7.1, 6.1 Hz, 1H_{anti}), 5.13 (dd, J = 8.1, 2.0 Hz, 1H_{syn}), 5.80 (d, J = 7.5 Hz, NH_{anti}), 6.42 (t, J = 7.5 Hz, 2H_{syn} + NH_{syn}), 6.74–7.90 (m, 18H_{syn}, 18H_{anti}, Ar H); ¹³C NMR δ_C : 21.4 (Me), 52.4 (C_{syn}NH), 58.8 (C_{syn}N=), 69.9 (OMe_{syn}), 114.9, 126.5, 126.8, 127.0, 128.2, 128.4, 128.9, 129.2, 129.7, 130.0, 131.0, 132.4, 138.0, 142.9, 169.5_{syn}, 173.4_{syn} (CO, CN); MS (EI) m/z (%): 530 (0.32), 277 (10), 194 (37), 155 (35), 91 (100), 65 (10).

4.11. Methyl 2-[(diphenylmethylene)amino]-3-(4-methylphenyl-sulfonamide)-3-(*p*-chlorophenyl)propanoate syn-3i and anti-3i^{8k}

46.2 mg; 70% yield; HPLC: (Daicel Chiralpak OD-H), hexane/*i*-PrOH 90/10, flow rate 0.6 ml/min, t_R : 16.3 min (syn), 17.6 min (anti), 21.1 min (syn), and 37.4 min (anti), 254 nm; IR ν_{max} : 3260, 2923, 1754, 1597, 1288, 1157, 1088, 698, 662 cm⁻¹; ¹H NMR δ_H : 2.30 (s, 3H, Me_{anti}), 2.37 (s, 3H, Me_{syn}), 3.50 (s, 3H + 3H, OMe_{syn+anti}), 4.13 (d, J = 2.3 Hz, 1H_{syn}), 4.35 (d, J = 5.7 Hz, 1H_{anti}), 4.69 (dd, J = 7.3, 5.8 Hz, 1H_{anti}), 5.11 (dd, J = 8.3, 2.1 Hz, 1H_{syn}), 5.79 (d, J = 7.6 Hz, NH_{anti}), 6.41 (d, J = 9.1 Hz, NH_{syn}), 6.44 (d, J = 7.4 Hz, 2H_{syn}), 6.93–7.88 (m, 18H_{syn}, 18H_{anti}, Ar H); ¹³C NMR δ_C : 21.4 (Me), 52.4 (C_{syn}NH), 58.9 (C_{syn}N=), 69.7 (OMe_{syn}), 126.4, 126.8, 127.0, 128.2, 128.5, 128.9, 129.3, 129.7, 130.0, 131.1, 133.2, 135.3, 137.5, 138.2, 143.1, 169.5_{syn}, 173.5_{syn} (CO, CN); MS (EI) m/z (%): 547 (0.18), 194 (36), 155 (40), 91 (100), 65 (10).

4.12. Methyl 2-[(diphenylmethylene)amino]-3-(4-methylphenyl-sulfonamide)-3-(*p*-bromophenyl)propanoate syn-3j and anti-3j^{8h}

24.8 mg; 35% yield; HPLC: (Daicel Chiralpak OD-H), hexane/*i*-PrOH 90/10, flow rate 0.6 ml/min, t_R : 13.3 min (syn), 14.7 min (anti), 16.8 min (syn), and 29.7 min (anti), 254 nm; IR ν_{max} : 3296, 2971, 1754, 1630, 1328, 1157, 1075, 698 cm⁻¹; ¹H NMR δ_H : 2.31 (s, 3H, Me_{anti}), 2.37 (s, 3H, Me_{syn}), 3.50 (s, 3H + 3H, OMe_{syn+anti}), 4.13 (d, J = 2.3 Hz, 1H_{syn}), 4.35 (d, J = 5.6 Hz, 1H_{anti}), 4.67 (dd, J = 7.5, 5.7 Hz, 1H_{anti}), 5.08 (dd, J = 8.3, 2.1 Hz, 1H_{syn}), 5.74 (d, J = 7.4 Hz, NH_{anti}), 6.37 (d, J = 8.3 Hz, NH_{syn}), 6.45 (d, J = 7.1 Hz, 2H_{syn}), 6.85–7.69 (m, 18H_{syn}, 18H_{anti}, Ar H); ¹³C NMR δ_C : 21.4 (Me), 29.7, 52.4 (C_{syn}NH), 58.9 (C_{syn}N=), 69.6 (OMe_{syn}), 126.8, 127.1, 128.2, 128.5, 128.6, 128.9, 129.3, 130.0, 131.2, 138.2, 143.1, 169.4_{syn}; MS (EI) m/z (%): 591 (0.48), 194 (36), 155 (47), 91 (100), 65 (10).

4.13. Methyl 2-[(diphenylmethylene)amino]-3-(4-methylphenyl-sulfonamide)-3-(2-furyl)propanoate syn-3k and anti-3k^{8d}

27.1 mg; 45% yield; HPLC: (Daicel Chiralpak AD), hexane/*i*-PrOH 90/10, flow rate 1 ml/min, t_R : 15.0 min (syn), 25.1 min (anti), 40.5 min (anti), and 65.5 min (syn), 254 nm; IR ν_{max} : 3267, 2971, 2360, 1739, 1277, 1158, 1075, 812, 700, 665 cm⁻¹; ¹H NMR δ_H : 2.37 (s, 3H, Me_{anti}), 2.37 (s, 3H, Me_{syn}), 3.52 (s, 3H, OMe_{anti}), 3.58

(s, 3H, OMe_{syn}), 4.26 (d, J = 2.3 Hz, 1H_{syn}), 4.58 (d, J = 4.3 Hz, 1H_{anti}), 5.24 (dd, J = 9.1, 4.2 Hz, 1H_{anti}), 5.45 (dd, J = 8.8, 1.9 Hz, 1H_{syn}), 6.35 (d, J = 9.1 Hz, NH_{anti}), 6.75 (m, 4H_{syn} + NH_{syn}), 7.03–7.94 (m, 14H_{syn}, 14H_{anti}, Ar H); ¹³C NMR δ_C : 21.4 (Me), 52.5 (C_{syn}NH), 55.9 (C_{syn}N=), 69.9 (OMe_{syn}), 125.3, 126.2, 127.0, 128.2, 128.3, 128.5, 128.8, 129.1, 129.2, 130.1, 131.0, 132.4, 142.8; MS (EI) m/z (%): 502 (0.56), 194 (40), 155 (23), 92 (11), 91 (100), 65 (10).

4.14. Methyl 2-[(diphenylmethylene)amino]-3-(4-methylphenyl-sulfonamide)-3-(2-thienyl)propanoate syn-3l and anti-3l^{8h}

28.0 mg; 45% yield; HPLC: (Daicel Chiralpak AS-H), hexane/*i*-PrOH 85/15, flow rate 1 ml/min, t_R : 15.3 min (syn) and 22.7 min (syn), 254 nm; IR ν_{max} : 3269, 2357, 1742, 1572, 1329, 1156, 1089, 812, 734, 700 cm⁻¹; ¹H NMR δ_H : 2.34 (s, 3H, Me_{anti}), 2.38 (s, 3H, Me_{syn}), 3.51 (s, 3H + 3H, OMe_{syn+anti}), 4.37 (d, J = 2.5 Hz, 1H_{syn}), 4.47 (d, J = 6.0 Hz, 1H_{anti}), 5.20 (dd, J = 9.3, 2.0 Hz, 1H_{syn}), 6.07 (dd, J = 2.5, 0.8 Hz, 1H_{syn}), 6.15 (dd, J = 3.2, 1.9 Hz, 1H_{syn}), 6.22 (d, J = 9.3 Hz, 1H_{syn}), 6.75 (d, J = 1.6 Hz, 1H_{syn}), 6.77 (d, J = 1.2 Hz, NH_{syn}), 7.08–7.89 (m, 14H_{syn}, 14H_{anti}, Ar H); ¹³C NMR δ_C : 21.4 (Me), 52.5 (C_{syn}NH), 55.9 (C_{syn}N=), 69.9 (OMe_{syn}), 107.8, 110.4, 125.3, 125.5, 126.2, 126.4, 127.0, 127.9, 128.1, 128.5, 128.8, 129.0, 129.2, 129.3, 129.7, 131.0, 136.7, 139.0, 162.2, 169.3_{syn}, 173.8_{syn} (CO, CN); MS (EI) m/z (%): 518 (0.47), 194 (40), 165 (10), 155 (22), 91 (100), 65 (10).

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References

- Subramaniapillai, S. G. *J. Chem. Sci.* **2013**, *125*, 467–482.
- (a) Bhadury, P. S.; Yang, S.; Song, B.-A. *Curr. Org. Synth.* **2012**, *9*, 695–726; (b) Kiss, L.; Fulop, F. *Chem. Rev.* **2014**, *114*, 1116–1169.
- For recent general reviews, see: (a) Karimi, B.; Enders, D.; Jafari, E. *Synthesis* **2013**, 45, 2769–2812; (b) Córdova, A. In *Stereoselective Organocatalysis*; Ríos-Torres, R., Ed.; Wiley: Weinheim, 2013; (c) Gómez-Arrayás, R.; Carretero, J. C. *Chem. Soc. Rev.* **2009**, *38*, 1940–1948.
- This structural arrangement is very common in Nature: (a) Viso, A.; Fernández de la Pradilla, R.; García, A.; Flores, A. *Chem. Rev.* **2005**, *105*, 3167–3196; (b) This strategy has been used for the synthesis of antibacterial agents: Patterson, B. D.; Lu, Q.; Aggen, J. B.; Dozzo, P.; Kasar, R. A.; Linsell, M. S.; Kane, T., R.; Glied, M. J.; Hildebrandt, D. J.; McEnroe, G. A. *PCT Int. Appl.* **2013**, WO 2013170030 A1 20131114. CAN: 159:731375.
- For a recent example, see: Callebaut, G.; Mangelinckx, S.; Kiss, L.; Sillanpää, R.; Fülöp, F.; De Kimpe, N. *Org. Biomol. Chem.* **2012**, *10*, 2326–2338.
- Wang, J.; Zhang, L.; Jiang, H.; Liu, H. *Curr. Pharm. Des.* **2010**, *16*, 1252–1259.
- (a) Okada, A.; Shibuguchi, T.; Ohshima, T.; Masu, H.; Yamaguchi, K.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 4564–4567; (b) Bandar, J.; Lambert, T. H. *J. Am. Chem. Soc.* **2013**, *135*, 11799–11802.
- (a) Juhl, K.; Gathergood, N.; Jorgensen, K. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 2995–2997; (b) Bernardi, L.; Gothelf, A. S.; Hazell, R. G.; Jorgensen, K. A. *J. Org. Chem.* **2003**, *68*, 2583–2591; (c) Hernández-Toribio, J.; Gómez-Arrayás, R.; Carretero, J. C. *J. Am. Chem. Soc.* **2008**, *130*, 16150–16151; (d) Yan, X.-X.; Peng, Q.; Li, Q.; Zhang, K.; Yao, J.; Hou, X.-L.; Wu, Y.-D. *J. Am. Chem. Soc.* **2008**, *130*, 14362–14363; (e) Shang, D.; Liu, Y.; Zhou, X.; Liu, X.; Feng, X. *Chem. Eur. J.* **2009**, *15*, 3678–3681; (f) Hernández-Toribio, J.; Gómez-Arrayás, R.; Carretero, J. C. *Chem. Eur. J.* **2010**, *16*, 1153–1157; (g) Liang, G.; Tong, M.-C.; Tao, H.; Wang, C.-J. *Adv. Synth. Catal.* **2010**, *352*, 1851–1855; (h) Arai, T.; Mishiho, A.; Matsumura, E.; Awata, A.; Shirasugi, M. *Chem. Eur. J.* **2012**, *18*, 11219–11222; (i) Hernandez, E.; Gómez-Arrayás, R.; Carretero, J. C. *Chem. Commun.* **2012**, 9622–9624; (j) Yamashita, Y.; Yoshimoto, S.; Masuda, K.; Kobayashi, S. *Asian J. Chem.* **2012**, *1*, 327–330; (k) Imae, K.; Shimizu, K.; Ogata, K.; Fukuzawa, S.-I. *J. Org. Chem.* **2011**, *76*, 3604–3608; (l) Yamashita, Y.; Yoshimoto, S.; Masuda, K.; Kobayashi, S. *Asian J. Chem.* **2012**, *1*, 327.
- Imino nitriles have been also tested as dipole precursors: Yamashita, Y.; Matsumoto, M.; Chen, Y.-J.; Kobayashi, S. *Tetrahedron* **2012**, *68*, 7558–7563.

10. (a) Teichert, J. F.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2010**, *49*, 2486–2528; (b) *Privileged Chiral Ligands and Catalysts*; Zhou, Qi-Lin, Ed.; Wiley-VCH: New York, 2011.
11. (a) Martín-Rodríguez, M.; Nájera, C.; Sansano, J. M.; Costa, P. R. R.; Crizanto de Lima, E.; Dias, A. G. *Synlett* **2010**, 962–966; (b) Martín-Rodríguez, M.; Nájera, C.; Sansano, J. M.; de Cózar, A.; Cossío, F. P. *Chem. Eur. J.* **2011**, *17*, 14224–14233; (c) Mancebo-Aracil, J.; Martín-Rodríguez, M.; Nájera, C.; Sansano, J. M.; Costa, P. R. R.; Crizanto de Lima, E.; Dias, A. G. *Tetrahedron: Asymmetry* **2012**, *23*, 1596–1606.
12. (a) Nájera, C.; Retamosa, M. G.; Sansano, J. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 6055–6058; (b) Nájera, C.; Retamosa, M. G.; Martín-Rodríguez, M.; Sansano, J. M.; de Cózar, A.; Cossío, F. P. *Eur. J. Org. Chem.* **2009**, 5622–5634; (c) Castelló, L. M.; Nájera, C.; Sansano, J. M.; Larrañaga, O.; de Cózar, A.; Cossío, F. P. *Org. Lett.* **2013**, *15*, 2902–2905.
13. (a) Padwa, A.; Pearson, W. H. *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*; John Wiley & Sons: New Jersey, 2003; (b) Nájera, C.; Sansano, J. M. *Curr. Org. Chem.* **2003**, *7*, 1105–1150; (c) Eberbach, W. *Sci. Synth.* **2004**, *27*, 441–498. chp. 11; (d) Coldham, I.; Hufton, R. *Chem. Rev.* **2005**, *105*, 2765–2810; (e) Nair, V.; Suja, T. D. *Tetrahedron* **2007**, *63*, 12247–12275; (f) Padwa, A.; Bur, S. K. *Tetrahedron* **2007**, *63*, 5341–5378; (g) Hashimoto, T.; Maruoka, K. In *Handbook of Cyclization Reactions*; Ma, S., Ed.; Wiley-VCH: Weinheim, 2010.
14. For more specific recent reviews of asymmetric 1,3-DC, see: (a) Pellissier, H. *Tetrahedron* **2007**, *63*, 3235–3285; (b) Nájera, C.; Sansano, J. M. In *Topics in Heterocyclic Chemistry*; Hassner, A., Ed.; Springer-Verlag: Berlin-Heidelberg, 2008; vol. 12, pp 117–145; (c) Stanley, L. M.; Sibi, M. P. *Chem. Rev.* **2008**, *108*, 2887–2902; (d) Álvarez-Corral, M.; Muñoz-Dorado, M.; Rodríguez-García, I. *Chem. Rev.* **2008**, *108*, 3174–3198; (e) Naodovic, M.; Yamamoto, H. *Chem. Rev.* **2008**, *108*, 3132–3148; (f) Nájera, C.; Sansano, J. M.; Yus, M. *J. Braz. Chem. Soc.* **2010**, *21*, 377–412; (g) Kissane, M.; Maguire, A. R. *Chem. Soc. Rev.* **2010**, *39*, 845–883; (h) Adrio, J.; Carretero, J. C. *Chem. Commun.* **2011**, 6784–6794; (i) Nájera, C.; Sansano, J. M. *J. Organomet. Chem.* **2014**, *771*, 78–92.
15. Recent references using chiral copper complexes: (a) Pascual-Escudero, A.; González-Esguevillas, M.; Padilla, S.; Adrio, J.; Carretero, J. C. *Org. Lett.* **2014**, *16*, 2228–2231; (b) Tong, M.-C.; Chen, X.; Tao, H. Y.; Wang, C.-J. *Angew. Chem., Int. Ed.* **2014**, *39*, 12377–12380; (c) Tao, H. Y.; He, Z.-H.; Yang, Y.; Wang, C. J. *RSC Adv.* **2014**, *4*, 16899–16905; (d) Castelló, L. M.; Nájera, C.; Sansano, J. M.; Larrañaga, O.; de Cózar, A.; Cossío, F. P. *Org. Lett.* **2013**, *15*, 2902–2905; (e) Li, Q.-H.; Liu, T.-L.; Wei, L.; Zhou, X.; Tao, H.-Y.; Wang, R. *Chem. Commun.* **2013**, 9642–9644; (f) Narayan, R.; Bauer, J. O.; Strohmann, C.; Antonchick, A. P.; Waldmann, H. *Angew. Chem., Int. Ed.* **2013**, *38*, 12892–12896; (g) Watanabe, S.; Tada, A.; Tokoro, Y.; Fukuzawa, S.-I. *Tetrahedron Lett.* **2014**, *55*, 1306–1309; Recent references using chiral silver complexes: (h) González-Esguevillas, M.; Adrio, J.; Carretero, J. C. *Chem. Commun.* **2013**, *49*, 4649–4651; (i) Yamashita, Y.; Kobayashi, S. *Chem. Eur. J.* **2013**, *19*, 9420–9427; (j) Imae, K.; Konno, T.; Ogata, K.; Fukuzawa, S.-I. *Org. Lett.* **2012**, *14*, 4410–4413; Recent references using chiral gold complexes: (k) Martín-Rodríguez, M.; Nájera, C.; Sansano, J. M.; de Cózar, A.; Cossío, F. P. *Chem. Eur. J.* **2011**, *17*, 14224–14233.
16. For recent examples of organotolyzed processes, see: (a) Wang, L.; Shi, X.-M.; Dong, W.-P.; Zhu, L.-P.; Wang, R. *Chem. Commun.* **2013**, 3458–3460; (b) Guo, C.; Song, J.; Gong, L.-Z. *Org. Lett.* **2013**, *15*, 2676–2679; (c) Shi, F.; Xing, G.-J.; Tan, R.; Zhu, R.-Y.; Tu, S. *Org. Biomol. Chem.* **2013**, *11*, 1482–1489; (d) Tian, L.; Hu, X.-Q.; Li, Y.-H.; Xu, P.-F. *Chem. Commun.* **2013**, 7213–7215; (e) Reboredo, S.; Reyes, E.; Vicario, J. L.; Badía, D.; Carrillo, L.; de Cózar, A.; Cossío, F. P. *Chem. Eur. J.* **2012**, *18*, 7179–7188.
17. Chen, Q.-A.; Zeng, W.; Wang, D.-W.; Zhou, Y.-G. *Synlett* **2009**, 2236–2241.