

Chiral derivatives of 1,2-benzenedisulfonimide as efficient Brønsted acid catalysts in the Strecker reaction†

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Two chiral derivatives of 1,2-benzenedisulfonimide, namely 4-methyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonimide and 4,5-dimethyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonimide, have been easily synthesized in good overall yields (respectively 34% and 41%) by means of an eleven-step synthetic protocol from commercially available 2-methyl-6-nitroaniline or 2,3-dimethyl-6-nitroaniline. 4,5-Dimethyl-3,6-bis(1-naphthyl)-1,2-benzenedisulfonimide was also synthesized, but the overall yield from 2,3-dimethyl-6-nitroaniline was lower (9%). The atropisomers of these compounds have been resolved and (–)atropisomers have been demonstrated to be efficient chiral catalysts in the Strecker reaction.

Introduction

Asymmetric catalysis is still one of the major challenges in modern organic chemistry,^{1,2} and chiral Brønsted organic acid catalysis, in particular, is an emerging area.³ In fact, asymmetric Brønsted acid catalysis has proved to be a very efficient tool for the synthesis of chiral molecules as it can boast of a number of impressive capabilities that contribute to obtaining the target products with very good enantioselectivity.

Currently, BINOL-derived phosphoric acids^{3c,d} (first proposed by Akiyama *et al.*⁴ and Terada *et al.*⁵) and the corresponding *N*-triflyl phosphoramides (first proposed by Yamamoto *et al.*⁶) are probably the most widely used chiral Brønsted acid catalysts, and this well established class of chiral Brønsted acid catalysts has been applied to an ever-increasing number of useful transformations.

Two different research groups have very recently reported that chiral binaphthyl sulfonimides are very effective chiral Brønsted acid catalysts. A number of binaphthyl sulfonimides have been synthesized by Lee *et al.* and tested in the asymmetric Friedel–Crafts alkylation of indoles with imines.⁷ List *et al.* developed chiral binaphthyl sulfonimide-catalyzed Mukaiyama aldol reactions, vinylogous and bisvinylogous Mukaiyama aldol reactions, hetero Diels–Alder reactions as well as Hosomi–Sakurai reactions.⁸ Both groups obtained excellent enantioselectivity results, especially when sulfonimides bore bulky aryl groups with electron-withdrawing substituents.

We have recently reported on the use of *o*-benzenedisulfonimide^{9a} (OBS; **1**; Fig. 1), in catalytic amounts, as a safe, non-volatile and noncorrosive Brønsted acid in several acid-catalyzed organic reactions under very mild and selective conditions.^{9b–m} The catalyst was easily recovered and purified, and was ready to be used in further reactions, giving economic and ecological advantages.

The results and advantages of using **1** are very promising considering its applications in the field of asymmetric catalysis. We have, therefore, proposed the synthesis of a 1,2-benzenedisulfonimide chiral derivative, namely 4-methyl-3-(*o*-tolyl)-

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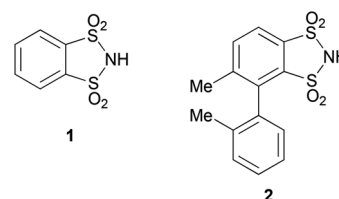


Fig. 1 OBS **1** and its chiral derivative **2**.

1,2-benzenedisulfonimide (**2**; Fig. 1).^{10a} Its chirality is due to the hindered rotation of the aryl group (atropisomerism). We used it as a chiral catalyst in the Strecker reaction and obtained unsatisfactory enantioselectivity results.^{10b}

Results and discussion

Synthesis of chiral derivatives of **1**

Our goal was now to synthesize a chiral derivative of **1** which can be more efficient than **2** in asymmetric catalysis.

The key to achieving good enantioselectivity results in the presence of strong chiral Brønsted acids as catalysts is the hydrogen bonding established between the protonated substrate and the conjugate chiral anion. Furthermore, a Brønsted acid should have the following attributes if it is to be considered a good chiral catalyst: adequate acidity^{11a} in order to catch up the substrate through hydrogen bonding without loose ion-pair formation,^{5b} type C_2 symmetry,^{11b,c} and the presence of bulky substituents closer to the acidic function that increase the stereochemical communication between the catalyst and the substrate.^{8a} Actually, **2** does not present type C_2 symmetry and has only one bulky group in the *ortho* position. In order to improve the chiral structure of **2**, we herein report the synthesis of 4-methyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonimide **3a** (Fig. 2) which has two bulky groups in the *ortho* positions but does not show C_2 symmetry, 4,5-dimethyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonimide **3b** and 4,5-dimethyl-3,6-bis-

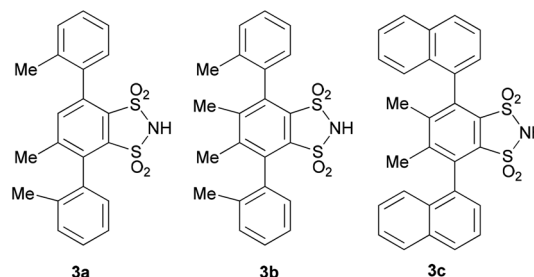


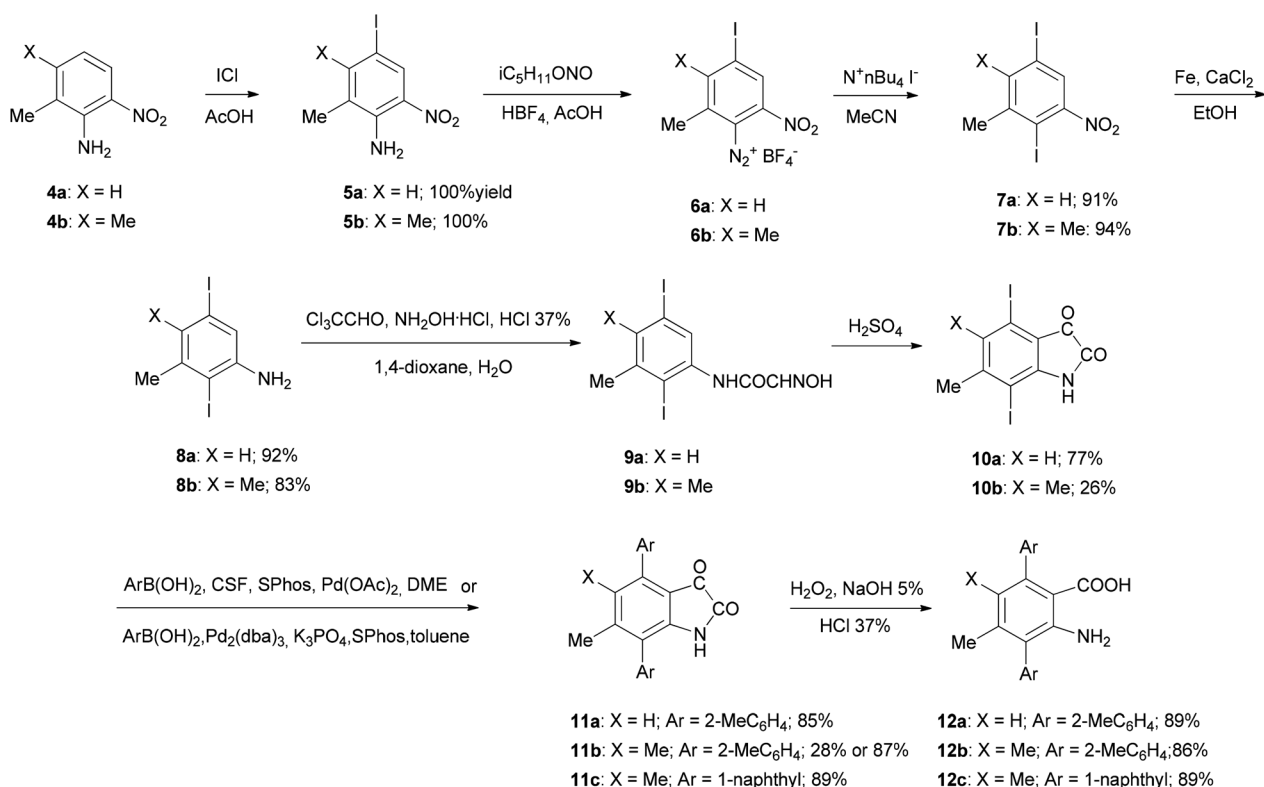
Fig. 2 Chiral adducts **3a**, **3b**, **3c**.

(1-naphthyl)-1,2-benzenedisulfonimide **3c** (Fig. 2) which have two bulky groups in *ortho* positions and C_2 symmetry. These new catalysts were tested in the Strecker reaction.

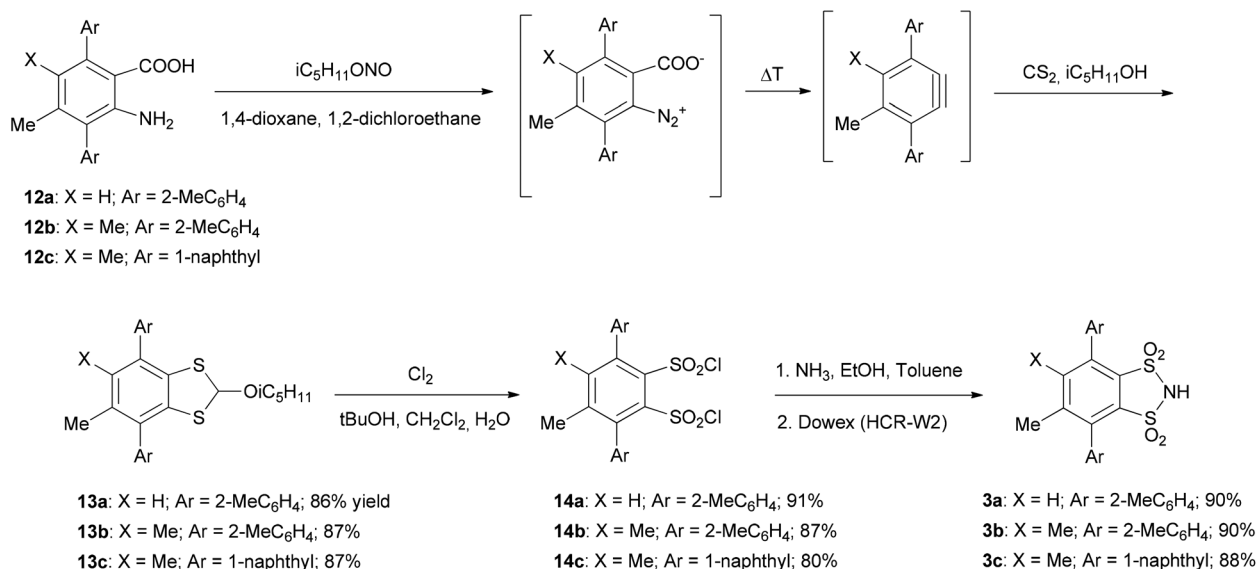
The precursor to **3a** is the corresponding anthranilic acid **12a** which was obtained from commercially available 2-methyl-6-nitroaniline (**4a**) as reported in Scheme 1.

12a was then converted into **3a**, using the same synthetic protocol^{10a} as that employed in the preparation of **2** (Scheme 2). The overall yield of **3a**, obtained with this synthetic sequence from **4a**, was 34%.

Conversely, the overall yield of imide **3b**, starting from 2,3-dimethyl-6-nitroaniline (**4b**), was very low (only 3%). In fact, the acid cyclization of **9b** mainly afforded a monodeiodinated adduct. Moreover, the Suzuki coupling of **10b** afforded the adduct **11b** in a low yield (28%). It was possible to increase the Suzuki coupling yield (89%) by reacting **10b** with *o*-tolylboronic



Scheme 1 Synthetic protocol for anthranilic acids **12**.

Scheme 2 Synthetic protocol for sulfonimides **3**.

in the presence of Pd₂(dba)₃, Sphos and K₃PO₄ and toluene as a solvent¹² and the overall yield increased by up to 10%. Furthermore, we modified the synthetic protocol to further increase the overall yield as described below (Scheme 3).

First of all, we carried out the Suzuki coupling on adduct **7b** and in the presence of Pd₂(dba)₃, Sphos and K₃PO₄.¹² In this way, we obtained the diarylated adduct **15** in a very good yield (95%).

The reduction of the nitro group allowed us to obtain amine **16** which was transformed into the corresponding isatine **11b** in good yields (89%).

It is worth noting that it was necessary to use MeSO₃H instead of H₂SO₄ to transform intermediate **17** into **11b**. It was then converted into anthranilic acid **12b**, which was converted

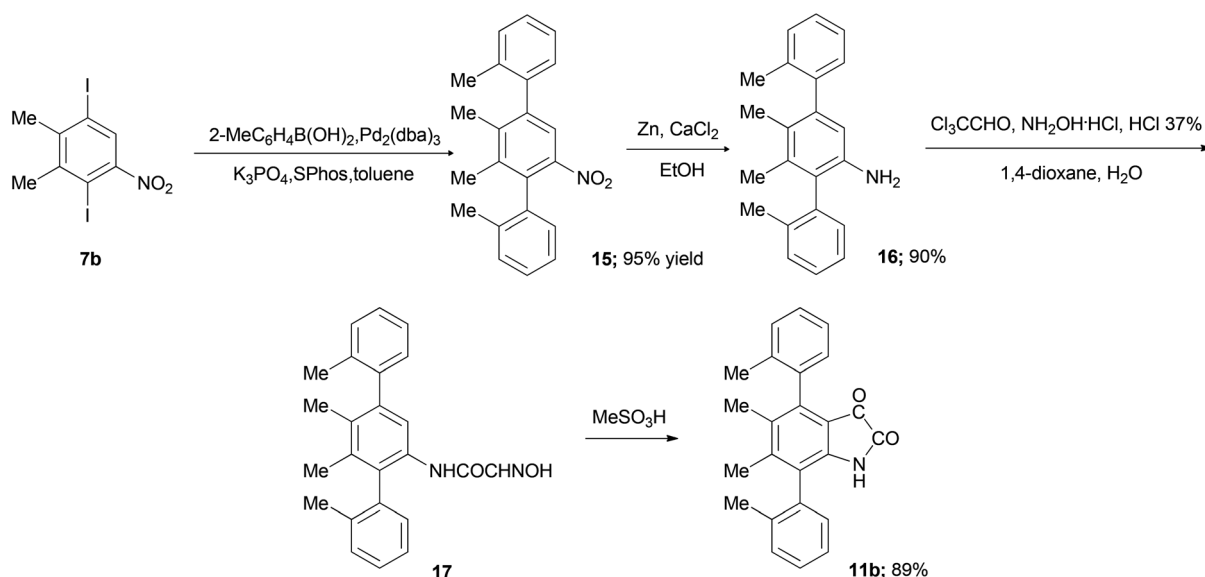
into **3b** (Scheme 2). The overall yield thus increased considerably (41%).

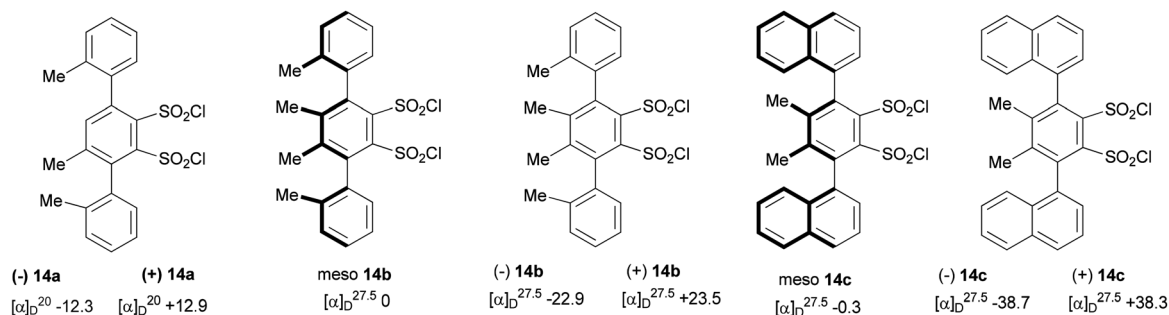
3c was also synthesized using the procedures reported in Schemes 1 and 2. The overall yield from **4b** was 9% when the Suzuki coupling was carried out in the presence of Pd₂(dba)₃, Sphos and K₃PO₄.

Unfortunately, it was impossible to obtain the adduct derived from the Suzuki coupling of **7b** with adequate purity in this case (Scheme 3).

Separation of atropisomers

After preparing chiral sulfonimides **3**, the next step was the resolution of their atropisomers. However, **3** are highly acidic (their pK_a value is most likely similar to that of parent OBS **1**

Scheme 3 Synthetic protocol for isatine **11b**.

Fig. 3 Atropisomers of **14**.

which, measured, was 6.09 in butanone¹³) and polar compounds, so their chromatographic separation can be considered extremely difficult. We preferred trying to separate the atropisomers of disulfonyl chlorides **14** that have the same chiral structure as **3**. Their separation was possible by semi-preparative chiral HPLC.

In particular, **14a** has only one structural motif that leads to atropisomerism and this is due to the hindered rotation of the aryl group bonded to the 3 position carbon. It is worth noting that no hindered rotation of the aryl group bonded to the 6 position carbon takes place due to the lack of a methyl group in the 5 position.^{10a}

The racemic mixture of **14a** (40 mg) was chromatographed on a semipreparative Chiralpak IC column. The two atropisomers (–)**14a** and (+)**14a**, eluted as single peaks, were collected (respectively 19.2 mg and 20.8 mg; ratio 1 : 1.08), after the solvents were removed under nitrogen flow (Fig. 3).

The situation is different for **14b** and **14c** for which there are two *identical* structural motifs that lead to the atropisomerism. For this reason, there is also a *meso* form in addition to the two atropisomers. Regarding **14b**, the mixture of atropisomers and *meso* form (40 mg) was chromatographed on a semipreparative Chiralpak IC column using an isocratic elution. We thus separated the *meso* form (the first eluted compound, 19.8 mg) from a racemic mixture of two atropisomers (the second eluted compound, 20.2 mg); ratio 1 : 1.02. Then, another run (20 mg) allowed us to separate the atropisomer (–)**14b** (Fig. 3; the first eluted compound, 9.5 mg), from the atropisomer (+)**14b** (Fig. 3; the second eluted compound, 10.5 mg); ratio 1 : 1.1. The same procedure was employed to separate the atropisomers of **14c** (40 mg). First, we separated the *meso* form (the first eluted compound, 20.4 mg) from a racemic mixture of two atropisomers (the second eluted compound, 19.6 mg); ratio 1.04 : 1. Then, another run (19 mg) allowed us to separate the atropisomer (–)**14c** (Fig. 3; the first eluted compound, 9.4 mg), from the atropisomer (+)**14c** (Fig. 3; the second eluted compound, 9.6 mg); ratio 1 : 1.02.

Finally, the separated atropisomers (–)**14a–c** were easily transformed into the corresponding (–)**3a–c** (Scheme 2).

Use of (–)atropisomers of **3** as catalysts

We reported that **2** catalyzed the Strecker reaction between acetophenone (**18a**), aniline (**19a**) and TMSCN (**20**) although it gave poor enantioselectivity (Table 1, entries 2 and 3).^{10b}

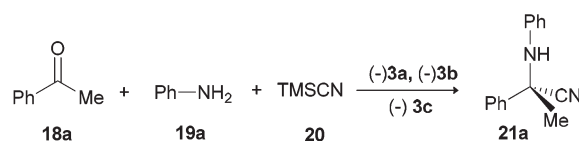
In the light of this, we decided to test the (–)atropisomer of **3** in this model reaction (Scheme 4), under the same conditions as those previously employed.^{10b}

The results are encouraging and are collected in Table 1. The use of (–)**3a** led to an increase in ee in 2-phenylamino-propanenitrile (**21a**; Table 1, entries 4 and 5). But the best results were obtained using (–)**3b**. The ee increased up to 84% when the reaction was carried out at 0 °C (Table 1, entry 6) and further cooling to –20° C increased it up to 94% (Table 1, entry 7). The yield, however, diminished as a small amount of the unreacted starting products was still present; **3c** was also a good chiral catalyst (Table 1, entries 8 and 9). From these data,

Table 1 Three-component Strecker reaction between **18a**, **19a** and **20** catalyzed by chiral catalysts (–)**2** and (–)**3**

Entry	Catalyst	Temp. (°C)	Time (min)	Yield ^{a,b} (%) of 21a	er in 21a	ee (%) in 21a
1 ^{10b}	1	rt	5	95	51 : 49	—
2 ^{10b}	2	rt	5	92	66 : 34	32
3 ^{10b}	2	0	180	88	78 : 22	56
4	3a	0	120	85	82 : 18	64
5	3a	–20	360	65	84 : 16	68
6	3b	0	120	86	92 : 8	84
7	3b	–20	360	70	97 : 3	94
8	3c	0	120	84	90 : 10	80
9	3c	–20	360	72	96 : 4	92

^a All the reactions were performed with 5 mol% of **3** (10 mg); reactants **18a** and **19a** were in equimolar amounts (see the Experimental section). TMSCN (**20**) was in slight excess (1.1 eq.). ^b Yields refer to the pure and isolated products.



Scheme 4 Strecker reaction with chiral catalysts **3**.

Table 2 Consecutive runs with recovered (–)**3b**

Entry	Time (min)	Yield (%) of 21 ^{a,b}	Recovery (%) of 3b	ee (%) in 21
1	120	86	95, 9.5 mg ^c	84
2	120	85	86, 8.2 mg ^d	82
3	180	89	82, 6.7 mg	81

^a Yields refer to the pure products. ^b The reaction was performed at 0 °C with 0.0468 mmol of **18a** and **19a**, 0.05148 mmol of **20** and 5 mol% of **3b** (10 mg, 0.0234 mmol). ^c Recovered **3b** was used as a catalyst in entry 2. ^d Recovered **3b** was used as a catalyst in entry 3.

it is evident that *C*₂ symmetry is essential for obtaining a good enantioselectivity.

Catalyst **3b** was easily recovered and used in another two consecutive catalytic cycles. The results are listed in Table 2. The enantiomeric excess was good in all cases.

The high enantiomeric excesses achieved encouraged us to further exploit catalyst **3b** in Strecker reactions. A selection (15 examples) of good results is presented in Table 3. The presence of electron-donating or electron-withdrawing groups on the aromatic ring of **18** or **19** did not affect the enantioselectivity of the reactions which generally provided excellent enantiomeric excess. Even with aliphatic **18l** and aldehydes **18m–p** very good results were obtained.

Theoretical calculations have allowed us to explain the mechanism of the Strecker reaction catalyzed by **1**.^{10b} The same mechanism should be used in the reactions catalyzed by **3b** (Scheme 5).

In particular, the intermediate **26a** should be crucial for carrying out this reaction in a highly enantioselective fashion. However, it must be stressed that this is only a hypothesis, and

in order to fully explain the role of **3b** as the chiral catalyst, depth mechanistic studies are planned.

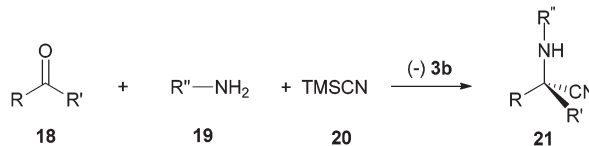
According to these data, this chiral Brønsted acid catalyzed reaction could be classified as ACDC.^{2a} In fact, List^{2a} has recently introduced the concept of asymmetric counteranion-directed catalysis (ACDC) in which the induction of enantioselectivity in a reaction *proceeds through a cationic intermediate by means of ion pairing with a chiral and enantiomerically pure anion provided by the catalyst*.

Conclusions

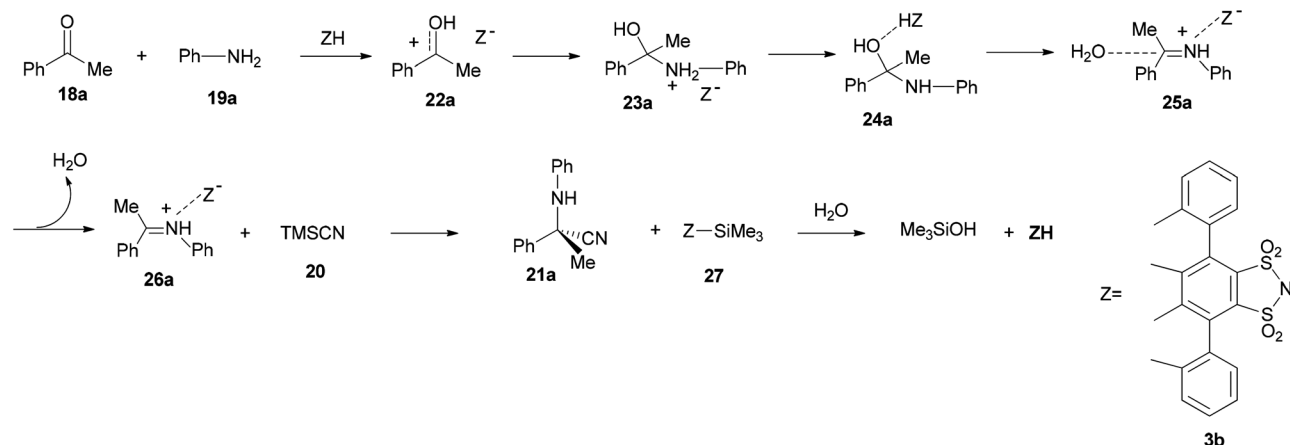
A protocol for the synthesis of three chiral derivatives of *o*-benzenedisulfonimide, namely **3a**, **3b** and **3c**, was developed under easy and moderate reaction conditions and with good overall yields.

In particular, the atropisomers (–)**3b** showed a good enantioselectivity in the Strecker reaction (16 examples, average ee 91%) and proved to be interesting chiral catalysts. In fact, *C*₂ symmetry^{11a,b} and the presence of aryl substituents on the sulfonimide ring (even without electron-withdrawing groups) created a chiral fashion allowing to have a high enantioselectivity. In order to confirm these good results, (–)**3b** will, of course, be tested in further reactions. Clearly, a shortcoming of this synthetic protocol is its lack of enantioselectivity. It is well known that chiral biaryl compounds have been easily synthesized in very good ee *via* catalytic asymmetric Suzuki coupling.¹⁴ In order to obtain enantiomerically pure **15** (one of the precursors to **3b**; Scheme 3), we could carry out this coupling in the presence of a chiral ligand. However, in the step in which **12** was converted into **13**, the formation of a

Table 3 Three-component Strecker reaction catalyzed by (–)**3b**

									
Entry	R in 18 , 21	R' in 18 , 21	R'' in 19 , 21	Products 21	Yield ^{a,b} (%)	Time (h)	ee in 21 (%)		
1	Ph	Me	18b	4-MeOC ₆ H ₄	19b	21b	69	6	95
2	Ph	Me	18c	4-NO ₂ C ₆ H ₄	19c	21c	65	6	93
3	Ph	Me	18d	4-BrC ₆ H ₄	19d	21d	61	7	92
4	Ph	Me	18e	4-FC ₆ H ₄	19e	21e	64	5	93
5	Ph	Me	18f	2-MeOC ₆ H ₄	19f	21f	68	6	82
6	Ph	Me	18g	3-MeOC ₆ H ₄	19g	21g	70	6	89
7	4-MeC ₆ H ₄	Me	18h	Ph	19h	21h	68	7	88
8	4-MeC ₆ H ₄	Me	18i	4-NO ₂ C ₆ H ₄	19j	21i	72	6	93
9	4-MeC ₆ H ₄	Me	18j	4-MeOC ₆ H ₄	19k	21j	68	5	97
10	4-NO ₂ C ₆ H ₄	Me	18k	4-MeOC ₆ H ₄	19l	21k	74	8	95
11	<i>n</i> Pr	Me	18l	Ph	19m	21l	71	8	87
12	Ph	H	18m	Ph	19n	21m	80	2	88
13	4-NO ₂ C ₆ H ₄	H	18n	Ph	19o	21n	85	2	95
14	4-MeC ₆ H ₄	H	18o	Ph	19p	21o	88	2	89
15	2-Thienyl	H	18p	Ph	19q	21p	84	2	89

^a All the reactions were performed at –20 °C with 5 mol% of **3b** (10 mg); the reactants **18** and **19** were in equimolar amounts (see the Experimental section). TMSCN (**20**) was in slight excess (1.1 eq.). ^b Yields refer to the pure and isolated products.



Scheme 5 Mechanism of the three-component acid-catalysed Strecker reaction catalyzed by **3b**.

benzyl intermediate occurred (Scheme 2). Most likely, this benzyne is not enough hindered to prevent rotation of the aryl group so that the previously achieved enantiomeric purity is lost.

Since (–)**3b** and (–)**3c** have proved to be (at least in the Strecker reaction) good chiral catalysts, we will dedicate our future research to developing an effective enantioselective synthetic protocol that allows strictly chiral derivatives of **1** to be obtained, without having to separate the various atropisomers. In addition, we will also evaluate the possibility of synthesizing derivatives with more bulky aromatic groups which may also bear electron-withdrawing substituents.

Experimental

General

Analytical grade reagents and solvents were used and the reactions were monitored by GC, GC-MS and TLC. Column chromatography and TLC were performed on Merck silica gel 60 (70–230 mesh ASTM) and GF 254, respectively. Petroleum ether (PE) refers to the fraction boiling in the range 40–70 °C. Room temperature (rt) is 20–25 °C. Mass spectra were recorded on an HP5989B mass selective detector connected to an HP 5890 GC with a cross-linked methyl silicone capillary column. ESI-MS spectra were obtained using a Waters micromass ZQ spectrometer equipped with an ESI ion source. Chiral analyses were performed on a Perkin-Elmer Autosystem GC connected to a J&W Scientific Cyclosil-B column; stationary phase: 30% heptakis (2,3-di-*O*-methyl-6-*O*-*t*-butyldimethylsilyl)- β -cyclodextrin in DB-1701. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker Avance 200 spectrometer at 200 and 50 MHz respectively. IR spectra were recorded on an IR Perkin-Elmer UATR-two spectrometer. HPLC separations were performed on HPLC Waters 1525 connected to a column Chiralpak IA-SFC. For the determination of optical rotations, a Jasco P-2000 polarimeter was used. All reagents were purchased from Sigma-Aldrich. Satisfactory microanalyses were performed for all new compounds. Syntheses and physical and spectral data

of compounds **5**, **7**, **8**, **10**, **11**, **12**, **13**, **15** and **16** precursors of **14a**, **14b** and **14c** are reported in ESI.†

Synthesis of 1,2-benzenedisulfonyl chlorides 14. 1,3-Benzo-dithiole (**13**; 2 mmol) was dissolved in *t*-butyl alcohol (20 mL), CH₂Cl₂ (16 mL) and H₂O (3 mL). The resulting mixture was cooled to 0 °C. Chlorine was bubbled through while the temperature was maintained at 0 °C and the reaction mixture vigorously stirred. The reaction was monitored on TLC (PE–EtOAc 7 : 3). After 1 h, when the spot of **13** disappeared and there was only one other spot, the reaction was complete. The reaction mixture was poured into CH₂Cl₂–H₂O (100 mL, 1 : 1). The aqueous layer was separated and extracted with CH₂Cl₂ (100 mL). The combined organic extracts were washed with a 5% NaOH solution (100 mL), dried over Na₂SO₄ and evaporated under reduced pressure. The crude residue, when purified in a chromatography column (PE–EtOAc 7 : 3), afforded pure **14**.

4-Methyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonyl chloride (14a). Couple of atropisomers. White waxy solid (0.86 g, 91% yield). Found: C 53.76; H 3.92; Cl 15.07; S 13.71. C₂₁H₁₈Cl₂O₄S₂ requires: C 53.74; H 3.87; Cl 15.11; S 13.66%. ¹H NMR (200 MHz, CDCl₃): δ = 7.51 (s, 1H), 7.32–7.15 (m, 8H), 2.24 (s, 3H), 2.09 (s, 3H), 2.01 (s, 3H). ¹³C NMR (50 MHz, CDCl₃): δ = 147.9, 147.5, 145.8, 145.2, 143.5, 141.2, 140.5, 138.2, 137.0, 136.0, 135.8, 130.9, 130.5, 129.7, 129.5, 128.7, 126.2, 125.6, 21.2, 21.1, 20.5. MS (ESI+) m/z : 469.12 (M + H)⁺. IR (neat) ν (cm^{–1}): 1383, 1175 (SO₂).

Compound **14a** (40 mg) was chromatographed on a semi-preparative Chiralpak IC column (F 10 × 250 mm, Daicel, Osaka, Japan) using an isocratic elution with heptane–CH₂Cl₂ (4 : 1) at a flow rate of 3.0 mL min^{–1}. The compounds eluted from the column were monitored using a photodiode array detector. Two compounds (respectively 19.2 mg and 20.8 mg), eluted as single peaks at 7.90 and 11.97 min, were collected, after removing the solvents under nitrogen flow.

The first one was (–)-4-methyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonyl chloride (**14a**; waxy white solid). [α]_D²⁰ –12.3 (c 0.18, CH₂Cl₂). Spectral data were identical to what had been reported for the couple of two atropisomers.

The second one was (+)4-methyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonyl chloride (**14a**; waxy white solid). $[\alpha]_{\text{D}}^{20} +12.9$ (*c* 0.18, CH₂Cl₂). Spectral data were identical to what had been reported for the couple of two atropisomers.

Circular dichroism studies are in progress to determine the absolute configuration of the atropisomers (–)**14a**.

4,5-Dimethyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonyl chloride (14b). Mixture of diastereomers (*meso* isomer and a couple of atropisomers). Waxy white solid (0.84 g; 87% yield). Found: C 54.61; H 4.21; Cl 14.78; S 13.19. C₂₂H₂₀Cl₂S₂O₄ requires: C 54.66; H 4.17; Cl 14.67; S 13.26%. ¹H NMR (200 MHz, CDCl₃): δ = 7.39–7.10 (m, 8H), 2.09, 2.03, 1.98 and 1.96 (4 s, 12H). ¹³C NMR (50 MHz, CDCl₃): δ = 146.8, 144.6, 144.3, 137.8, 136.7, 136.3, 135.7, 130.7, 130.4, 130.2, 129.5, 129.4, 125.9, 125.8, 20.6, 20.4, 19.0, 18.6. MS (ESI+) *m/z*: 483.24 (M + H)⁺. IR (neat) ν (cm^{–1}): 1380, 1173 (SO₂).

Compound **14b** (40 mg) was chromatographed on a semi-preparative Chiralpak IC column (F 10 × 250 mm, Daicel, Osaka, Japan) using an isocratic elution with heptane–CH₂Cl₂ (3 : 2) at a flow rate of 5.0 mL min^{–1}. The compounds eluted from the column were monitored using a photodiode array detector. Two compounds (respectively 19.8 mg and 20.2 mg), eluted as single peaks at 5.12 and 6.57 min, were collected after removing the solvents under nitrogen flow.

The first one was the *meso* isomer. ¹H NMR (200 MHz, CDCl₃): δ 7.39–7.10 (m, 8H), 2.09 (s, 3H), 1.98 (s, 3H). ¹³C NMR (50 MHz, CDCl₃): δ = 146.8, 144.6, 137.8, 136.7, 135.7, 130.7, 130.4, 129.5, 125.9, 20.6, 19.0. $[\alpha]_{\text{D}}^{27.5}$ 0.0 (*c* 0.10, CH₂Cl₂). The second one was a couple of atropisomers. ¹H NMR (200 MHz, CDCl₃): δ = 7.35–7.10 (m, 8H), 2.03 (s, 3H), 1.96 (s, 3H). ¹³C NMR (50 MHz, CDCl₃): δ 146.6, 144.3, 137.8, 136.3, 135.7, 130.7, 130.2, 129.4, 125.8, 20.4, 18.6). $[\alpha]_{\text{D}}^{27.5}$ +0.1 (*c* 0.10, CH₂Cl₂).

The second eluted compound (20 mg) was again chromatographed on a semipreparative Chiralpak IC column (F 10 × 250 mm, Daicel, Osaka, Japan) using an isocratic elution with heptane–CH₂Cl₂ (4 : 1) at a flow rate of 3.0 mL min^{–1}. The compounds eluted from the column were monitored with a photodiode array detector. Two compounds (respectively 9.5 mg and 10.5 mg), eluted as single peaks at 10.44 and 14.42 min, were collected, after removing the solvents under nitrogen flow.

The first one was (–)4,5-dimethyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonyl chloride (**14b**; waxy white solid). $[\alpha]_{\text{D}}^{27.5}$ –22.9 (*c* 0.15, CH₂Cl₂). Spectral data were identical to what had been reported for the couple of atropisomers.

The second one was (+) 4,5-dimethyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonyl chloride (**14b**; waxy white solid). $[\alpha]_{\text{D}}^{27.5}$ +23.5 (*c* 0.15, CH₂Cl₂). Spectral data were identical to what had been reported for the couple of atropisomers.

Circular dichroism studies are in progress to determine the absolute configuration of the atropisomers (–)**14b**.

4,5-Dimethyl-3,6-bis(1-naphthyl)-1,2-benzenedisulfonyl chloride (14c). Mixture of diastereomers (*meso* isomer and a couple of atropisomers). Waxy white solid (0.89 g; 80% yield). Found: C 60.51; H 3.67; Cl 12.80; S 11.52. C₂₈H₂₀Cl₂S₂O₄ requires: C 60.54; H 3.63; Cl 12.76; S 11.54%. ¹H NMR

(200 MHz, CDCl₃): δ = 7.68–7.44 (m, 10H), 1.98 (s, 6H). ¹³C NMR (50 MHz, CDCl₃): δ = 137.8, 137.6, 134.6, 134.2, 133.9, 133.8, 133.6, 132.5, 132.0, 131.8, 131.7, 128.4, 128.1, 127.5, 127.1, 126.9, 126.6, 126.2, 126.1, 125.2, 125.1, 19.2, 19.0. MS (ESI+) *m/z*: 555.31 (M + H)⁺. IR (neat) ν (cm^{–1}): 1384, 1171 (SO₂).

Compound **14c** (40 mg) was chromatographed on a semi-preparative Chiralpak IC column (F 10 × 250 mm, Daicel, Osaka, Japan) using an isocratic elution with heptane–CH₂Cl₂ (3 : 2) at a flow rate of 5.0 mL min^{–1}. The compounds eluted from the column were monitored with a photodiode array detector. Two compounds (respectively 20.4 mg and 19.6 mg), eluted as single peaks at 12.11 and 17.23 min, were collected, after removing the solvents under nitrogen flow.

The first one was the *meso* isomer. ¹H NMR (200 MHz, CDCl₃): δ = 7.68–7.44 (m, 10H), 1.98 (s, 3H). ¹³C NMR (50 MHz, CDCl₃): δ = 137.8, 134.6, 134.2, 133.9, 133.6, 132.5, 131.7, 128.4, 127.5, 127.1, 126.6, 126.2, 125.2, 19.2. $[\alpha]_{\text{D}}^{27.5}$ –0.3 (*c* 0.15, CH₂Cl₂). The second one was a couple of atropisomers. ¹H NMR (200 MHz, CDCl₃): δ = 7.68–7.40 (m, 10H), 1.98 (s, 6H). ¹³C NMR (50 MHz, CDCl₃): δ = 137.6, 134.6, 134.2, 133.8, 133.6, 132.0, 131.7, 128.1, 127.5, 126.9, 126.6, 126.1, 125.1, 19.0. $[\alpha]_{\text{D}}^{27.5}$ –0.1 (*c* 0.15, CH₂Cl₂).

The second eluted compound (19 mg) was again chromatographed on a semipreparative Chiralpak IC column (F 10 × 250 mm, Daicel, Osaka, Japan) using an isocratic elution with heptane–MeOH (9 : 1) at a flow rate of 3.0 mL min^{–1}. The compounds eluted from the column were monitored with a photodiode array detector. Two compounds (respectively 9.4 mg and 9.6 mg), eluted as single peaks at 9.33 and 14.27 min, were collected, after removing the solvents under nitrogen flow.

The first one was (–)4,5-dimethyl-3,6-bis(1-naphthyl)-1,2-benzenedisulfonyl chloride (**14c**; waxy white solid). $[\alpha]_{\text{D}}^{21.5}$ –38.7 (*c* 0.10, CH₂Cl₂). Spectral data were identical to what had been reported for the couple of atropisomers.

The second one was (+)4,5-dimethyl-3,6-bis(1-naphthyl)-1,2-benzenedisulfonyl chloride (**14c**; waxy white solid). $[\alpha]_{\text{D}}^{21.5}$ +38.3 (*c* 0.10, CH₂Cl₂). Spectral data were identical to what had been reported for the couple of atropisomers.

Circular dichroism studies are in progress to determine the absolute configuration of the atropisomers (–)**14c**.

Synthesis of 1,2-benzenedisulfonimides 3. 1,2-Benzenedisulfonyl chloride (**14**; 2 mmol) was dissolved in toluene (8 mL) and EtOH (12 mL). The resulting mixture was cooled to 0 °C. Ammonia was bubbled through while the temperature was maintained at 0 °C and the reaction mixture was vigorously stirred. The reaction was monitored by TLC (PE–EtOAc 7 : 3). After 30 min, the reaction was complete. The mixture was first filtered in order to eliminate NH₄Cl and then solvent was evaporated under reduced pressure. The crude residue, when dissolved in H₂O and passed through a Dowex (HCR-W2) column (H₂O), afforded pure **3**.

4-Methyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonimide (3a). Grey waxy solid (0.75 g, 90%). Found: C 61.02; H 4.68; N 3.33; S 15.54. C₂₁H₁₉NO₄S₂ requires: C 61.00; H 4.63; N 3.39; S 15.51%. ¹H NMR (200 MHz, CDCl₃): δ = 7.49 (s, 1H), 7.32–7.18

(m, 8H), 2.15 (s, 3H), 2.12 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (50 MHz, CDCl_3): δ = 145.9, 145.7, 138.4, 138.0, 137.4, 136.7, 136.5, 136.3, 135.4, 134.2, 132.7, 130.5, 129.8, 129.6, 126.4, 126.3, 125.9, 125.8, 20.5, 20.4, 19.9. MS (ESI+) m/z : 414.63 ($\text{M} + \text{H}$) $^+$. IR (neat) ν (cm^{-1}): 3004 (NH), 1362, 1151 (SO_2).

(-)-4-Methyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonimide (3a). The title compound (grey waxy solid; 32 mg, 77% yield) was obtained from (-)-4-methyl-3,6-bis(2-tolyl)-1,2-benzenedisulfonyl chloride (**14a**; 0.1 mmol, 47 mg) as reported above.

$[\alpha]_{\text{D}}^{21}$ -14.8 (c 0.15, CH_2Cl_2). Spectral data were identical to what had been reported for the mixture of two atropisomers.

4,5-Dimethyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonimide (3b). Mixture of diastereomers (*meso* isomer and a couple of atropisomers). Grey waxy solid (0.77 g; 90% yield). Found: C 61.77; H 4.92; N 3.33; S 15.04. $\text{C}_{22}\text{H}_{21}\text{NO}_4\text{S}_2$ requires: C 61.81; H 4.95; N 3.28; S 15.00%. ^1H NMR (200 MHz, CDCl_3): δ = 7.39–7.14 (m, 8H), 2.05 (s, 12H). ^{13}C NMR (50 MHz, CDCl_3): δ = 144.9, 137.1, 136.9, 136.7, 135.4, 133.6, 130.5, 129.9, 129.8, 126.3, 126.2, 20.1, 19.9, 17.6. MS (ESI+) m/z : 428.01 ($\text{M} + \text{H}$) $^+$. IR (neat) ν (cm^{-1}): 3001 (NH), 1360, 1156 (SO_2).

(-)-4,5-Dimethyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonimide (3b). The title compound (pale grey waxy solid; 35 mg, 82% yield) was obtained from (-)-4,5-dimethyl-3,6-bis(2-tolyl)-1,2-benzenedisulfonyl chloride (**14b**, 0.1 mmol, 48 mg) as reported above.

$[\alpha]_{\text{D}}^{27}$ -18.4 (c 0.12, CH_2Cl_2); ^1H NMR (200 MHz, CDCl_3): δ = 7.39–7.18 (m, 8H), 2.05 (s, 12H). ^{13}C NMR (50 MHz, CDCl_3): δ = 144.9, 137.1, 136.9, 136.7, 135.4, 133.6, 130.5, 129.8, 126.3, 19.9, 17.6.

4,5-Dimethyl-3,6-bis(1-naphthyl)-1,2-benzenedisulfonimide (3c). Mixture of diastereomers (*meso* isomer and a couple of atropisomers). Grey waxy solid (0.98 g; 88% yield). Found: C 67.40; H 4.21; N 2.74; S 12.84. $\text{C}_{28}\text{H}_{21}\text{NO}_4\text{S}_2$ requires: C 67.32; H 4.24; N 2.80; S 12.83%. ^1H NMR (200 MHz, CDCl_3): δ = 8.43–8.29 (m, 2H), 7.92–7.29 (m, 8H), 2.05 (s, 6H). ^{13}C NMR (50 MHz, CDCl_3): δ = 140.1, 140.0, 137.5, 137.4, 135.7, 135.5, 135.4, 135.1, 133.1, 130.2, 128.6, 128.2, 128.1, 128.0, 127.0, 126.3, 120.3, 120.2, 19.3, 19.2. MS (ESI+) m/z : 500.11 ($\text{M} + \text{H}$) $^+$. IR (neat) ν (cm^{-1}): 2998 (NH), 1357, 1159 (SO_2).

(-)-4,5-Dimethyl-3,6-bis(1-naphthyl)-1,2-benzenedisulfonimide (3c). The title compound (pale grey waxy solid; 36 mg, 72% yield) was obtained from (-)-4,5-dimethyl-3,6-bis(1-naphthyl)-1,2-benzenedisulfonyl chloride (0.1 mmol, 55 mg) as reported above.

$[\alpha]_{\text{D}}^{21}$ -45.4 (c 0.15, CH_2Cl_2); ^1H NMR (200 MHz, CDCl_3): δ = 8.36–8.29 (m, 2H), 8.36–8.29 (m, 2H), 7.92–7.29 (m, 8H), 2.05 (s, 6H). ^{13}C NMR (50 MHz, CDCl_3): δ = 140.0, 137.5, 135.7, 135.4, 135.1, 133.1, 130.2, 128.6, 128.2, 128.0, 127.0, 126.3, 120.2, 19.3.

Chiral sulfonimides 3 as catalysts in the Strecker reaction

(-)-4-Methyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonimide (3a) as a catalyst. 1. TMSCN (**20**, 53 mg, 0.53 mmol) was added to a mixture of (-)-4-methyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonimide (**3a**; 5 mol%; 10 mg, 0.0242 mmol), acetophenone (**18a**, 58 mg, 0.484 mmol) and aniline (**19a**, 45 mg, 0.484 mmol)

that had been cooled to 0 °C. The mixture was stirred at 0 °C for 3 hours until GC and GC-MS analyses showed complete disappearance of the starting compounds and complete formation of 2-phenyl-2-phenylaminopropanenitrile (**21a**). Cold H_2O (2 ml) was added to the reaction mixture under vigorous stirring. The resulting solid was filtered on a Hirsch funnel and washed with additional cold H_2O (2×1 ml) and a small amount of PE (1 ml). It was virtually pure (GC, GC-MS, ^1H NMR, and ^{13}C NMR), 2-phenyl-2-phenylaminopropanenitrile (**21a**; white solid; 89 mg, 83% yield). Spectral and physical data were identical to what had been reported in the literature.¹⁵ After analyzing **21a** on a GC with a chiral column, the presence of two enantiomers was found; the enantiomeric ratio (er) was 82 : 18; the enantiomeric excess (ee) was 64%.

2. The reaction was carried out at -20 °C and small amounts of **18a** and **19a** were detected by GC and GC-MS analyses after 6 hours. However, the reaction had stopped. The yield of **21a** was 65% (70 mg).

After analyzing **21a** on a GC with a chiral column, the presence of two enantiomers was found; er was 87 : 12; ee was 75%.

(-)-4,5-Dimethyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonimide (3b) as a catalyst. 1. (-)-4,5-Dimethyl-3,6-bis(*o*-tolyl)-1,2-benzenedisulfonimide (**3b**; 5 mol%; 10 mg, 0.0234 mmol). The amounts of **18a**, **19a** and **20** were, respectively, 56 mg (0.0468 mmol), 43 mg (0.0468 mmol), and 51 mg (0.0515 mmol). At 0 °C the yield of **21a** was 86% (88 mg). After analyzing **21a** on a GC with a chiral column, the presence of two enantiomers was found; er was 92 : 8; ee was 84%. The aqueous washings were collected and evaporated under reduced pressure. After the removal of H_2O , a virtually pure (^1H NMR) **3b** was recovered (9.5 mg, 95% yield). The recovered **3b** was employed in another two catalytic cycles under the conditions described above. Table 2 reports the yields of **21a** and the yields of recovered **3b**.

2. The reaction was carried out at -20 °C and small amounts of **18a** and **19a** were detected by GC and GC-MS analyses after 6 hours. However, the reaction had stopped. The yield of **21a** was 70% (73 mg). After analyzing **21a** on a GC with a chiral column, the presence of two enantiomers was found; er was 97 : 3; ee was 94%.

Under the same conditions, 2-(4-methoxyphenyl)-2-phenylaminopropanenitrile (**21b**),¹⁶ 2-(4-nitrophenyl)-2-phenylaminopropanenitrile (**21c**),^{10b} 2-(4-bromophenylamino)-2-phenylaminopropanenitrile (**21d**),^{10b} 2-(4-fluorophenylamino)-2-phenylaminopropanenitrile (**21e**),^{10b} 2-(2-methoxyphenyl)-2-phenylaminopropanenitrile (**21f**),^{10b} 2-(3-methoxyphenylamino)-2-phenylaminopropanenitrile (**21g**),¹⁶ 2-phenylamino-2-(4-tolyl)propanenitrile (**21h**),¹⁷ 2-(4-nitrophenylamino)-2-(4-tolyl)propanenitrile (**21i**),^{10b} 2-(4-methoxyphenylamino)-2-(4-tolyl)propanenitrile (**21j**),^{10b} 2-(4-methoxyphenylamino)-2-(4-nitrophenyl)propanenitrile (**21k**),¹⁶ 2-methyl-2-phenylaminopentanenitrile (**21l**), 2-phenyl-2-phenylaminoacetoneitrile (**21m**),¹⁸ 2-(4-nitrophenyl)-2-phenylaminoacetoneitrile (**21n**),¹⁹ 2-(4-tolyl)-2-phenylaminoacetoneitrile (**21o**)²⁰ and 2-(2-thienyl)-2-phenylaminoacetoneitrile (**21e**)²¹ were obtained. The yields and the ee of each of these compounds are reported in Table 3. Their

spectral and physical data (reported in ESI†) are identical to those reported in the literature, with the only exception of **21l**, unknown in the literature.

2-Methyl-2-phenylaminopentanenitrile (21l). Viscous oil (65 mg, 71%). Found: C 76.51; H 8.55; N 14.92. $C_{12}H_{16}N_2$ requires: C 76.56; H 8.57; N 14.88%. 1H NMR (200 MHz, $CDCl_3$): δ = 7.24–7.10 (m, 2H), 6.88–6.82 (m, 3H), 3.58 (br s, 1H), 1.97–1.75 (m, 2H), 1.64–1.44 (m, 2H), 1.58 (s, 3H), 0.95 (t, J = 7.2 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 144.1, 129.5, 121.9, 120.6, 117.4, 53.0, 42.7, 25.8, 17.7, 14.1. MS (EI) m/z : (%) 188 [M^+] (5), 161 (35), 146 (45), 118 (100), 77 (55). IR ($CHCl_3$) ν (cm^{-1}): 3431 (NH), 2249 (CN).

(–)-4,5-Dimethyl-3,6-bis(1-naphthyl)-1,2-benzenedisulfonimide (3c) as a catalyst. 1. 4,5-Dimethyl-3,6-bis(1-naphthyl)-1,2-benzenedisulfonimide (**3c**; 5 mol%; 10 mg, 0.02 mmol). The amounts of **18a**, **19a** and **20** were, respectively, 48 mg (0.04 mmol), 37 mg (0.04 mmol), and 44 mg (0.044 mmol). At 0 °C the yield of **21a** was 84% (75 mg). After analyzing **21a** on a GC with a chiral column, the presence of two enantiomers was found; er was 90 : 10; ee was 80%.

2. The reaction was carried out at –20 °C and small amounts of **18a** and **19a** were detected by GC and GC-MS analyses after 6 hours. However, the reaction had stopped. The yield of **21a** was 72% (64 mg). After analyzing **21a** on a GC with a chiral column, the presence of two enantiomers was found; er was 96 : 4; ee was 92%.

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References

- Books: (a) *Enantioselective Organocatalysis*, ed. P. I. Dalko, Wiley-VCH, Weinheim, 2007; (b) *Organocatalysis*, ed. M. T. Reetz, B. List, S. Jaroch and H. Weinmann, Springer Verlag, Berlin, 2008.
- Reviews: (a) M. Mahlau and B. List, *Angew. Chem., Int. Ed.*, 2013, **52**, 518 and references cited therein; (b) F. Giacalone, M. Gruttadauria, P. Agrigento and R. Noto, *Chem. Soc. Rev.*, 2012, **41**, 2406; (c) M. Rueping, J. Dufour and F. R. Schoepke, *Green Chem.*, 2011, **13**, 1084; (d) S. Bertelsen and K. A. Jørgensen, *Chem. Soc. Rev.*, 2009, **38**, 2178; (e) D. W. C. MacMillan, *Nature*, 2008, **455**, 304; (f) H. Pellissier, *Tetrahedron*, 2007, **63**, 9267.
- (a) D. Kampen, C. M. Reisinger and B. List, *Top. Curr. Chem.*, 2009, **291**, 395 and references cited therein; (b) P. R. Schreiner, *Chem. Soc. Rev.*, 2003, **32**, 289; (c) A. J. Neel, J. P. Hehn, P. F. Tripet and F. D. Toste, *J. Am. Chem. Soc.*, 2013, **135**, 14044 and references cited therein; (d) M. Terada, *J. Synth. Org. Chem., Jpn.*, 2013, **71**, 480.
- (a) T. Akiyama, J. Itoh, K. Yokota and K. Fuchibe, *Angew. Chem., Int. Ed.*, 2004, **43**, 1566; (b) M. Yamanaka, J. Itoh, K. Fuchibe and T. Akiyama, *J. Am. Chem. Soc.*, 2007, **129**, 6756; (c) T. Akiyama, *Chem. Rev.*, 2007, **107**, 5744.
- (a) D. Uraguchi and M. Terada, *J. Am. Chem. Soc.*, 2004, **126**, 5356; (b) M. Terada, *Synthesis*, 2010, 1929; (c) M. Terada, *Curr. Org. Chem.*, 2011, **15**, 2227.
- D. Nakashima and H. Yamamoto, *J. Am. Chem. Soc.*, 2006, **128**, 9626.
- (a) H. He, L.-Y. Chen, W.-Y. Wong, W.-H. Chan and A. W. M. Lee, *Eur. J. Org. Chem.*, 2010, 4181; (b) L.-Y. Chen, H. He, W.-H. Chan and A. W. M. Lee, *J. Org. Chem.*, 2011, **76**, 7141.
- (a) P. Garcia-Garcia, F. Lay, P. Garcia-Garcia, C. Rabalakos and B. List, *Angew. Chem., Int. Ed.*, 2009, **48**, 4363; (b) L. Ratjen, P. Garcia-Garcia, F. Lay, M. E. Beck and B. List, *Angew. Chem., Int. Ed.*, 2011, **50**, 754; (c) J. Guin, C. Rabalakos and B. List, *Angew. Chem., Int. Ed.*, 2012, **51**, 754; (d) M. Mahlau, P. Garcia-Garcia and B. List, *Chem. – Eur. J.*, 2012, **18**, 16283; (e) S. Gandhi and B. List, *Angew. Chem., Int. Ed.*, 2013, **52**, 2573.
- (a) M. Barbero, S. Bazzi, S. Cadamuro and S. Dughera, *Curr. Org. Chem.*, 2011, **15**, 576; (b) M. Barbero, S. Cadamuro and S. Dughera, *Synth. Commun.*, 2013, **43**, 758; (c) M. Barbero, S. Cadamuro and S. Dughera, *ARKIVOC*, 2012, **ix**, 262; (d) M. Barbero, S. Cadamuro, S. Dughera, C. Magistris and P. Venturello, *Org. Biomol. Chem.*, 2011, **9**, 8393; (e) M. Barbero, S. Bazzi, S. Cadamuro, S. Dughera, C. Magistris, A. Smarra and P. Venturello, *Org. Biomol. Chem.*, 2011, **9**, 2192; (f) M. Barbero, S. Bazzi, S. Cadamuro and S. Dughera, *Tetrahedron Lett.*, 2010, **51**, 6356; (g) M. Barbero, S. Bazzi, S. Cadamuro and S. Dughera, *Tetrahedron Lett.*, 2010, **51**, 2342; (h) M. Barbero, S. Bazzi, S. Cadamuro, C. Piccinini and S. Dughera, *Synthesis*, 2010, 315; (i) M. Barbero, S. Bazzi, S. Cadamuro, S. Dughera and G. Ghigo, *Eur. J. Org. Chem.*, 2009, 4346; (j) M. Barbero, S. Cadamuro, A. Deagostino, S. Dughera, P. Larini, E. G. Occhiato, C. Prandi, S. Tabasso, R. Vulcano and P. Venturello, *Synthesis*, 2009, 2260; (k) M. Barbero, S. Bazzi, S. Cadamuro and S. Dughera, *Eur. J. Org. Chem.*, 2009, 430; (l) M. Barbero, S. Cadamuro, S. Dughera and P. Venturello, *Synthesis*, 2008, 3625; (m) M. Barbero, S. Cadamuro, S. Dughera and P. Venturello, *Synthesis*, 2008, 1379; (n) M. Barbero, S. Cadamuro, S. Dughera and P. Venturello, *Synlett*, 2007, 2209.
- (a) M. Barbero, S. Bazzi, S. Cadamuro, L. Di Bari, S. Dughera, G. Ghigo, D. Padula and S. Tabasso, *Tetrahedron*, 2011, **67**, 5789; (b) M. Barbero, S. Cadamuro, S. Dughera and G. Ghigo, *Org. Biomol. Chem.*, 2012, **10**, 4058.
- (a) K. Kaupmees, N. Tolstoluzhsky, S. Raja, M. Rueping and I. Leito, *Angew. Chem., Int. Ed.*, 2013, **52**, 11569; (b) S. Wu, M. He and X. Zhang, *Tetrahedron: Asymmetry*, 2004, **15**, 2177; (c) S. Basra, J. G. de Vries, D. J. Jyett, G. Harrison, K. M. Heslop, A. G. Orpen, P. G. Pringle and K. von der Luehe, *J. Chem. Soc., Dalton Trans.*, 2004, 1901.

- 12 T. E. Barder, S. D. Walker, J. R. Martinelli and S. L. Buchwald, *J. Am. Chem. Soc.*, 2005, **127**, 4685.
- 13 M. Barbero, S. Berto, S. Cadamuro, P. G. Daniele, S. Dughera and G. Ghigo, *Tetrahedron*, 2013, **69**, 3212.
- 14 J. Yin and S. L. Buchwald, *J. Am. Chem. Soc.*, 2000, **122**, 12051.
- 15 K. Matsumoto, J. C. Kim, H. Iida, H. Hamana, K. Kumamoto, H. Kotsuki and G. Jenner, *Helv. Chim. Acta*, 2005, **88**, 1734.
- 16 G.-W. Zhang, D.-H. Zheng, J. Nie, T. Wang and J.-A. Ma, *Org. Biomol. Chem.*, 2010, **8**, 1399.
- 17 A. Shaabani, A. Maleki, M. Reza Soudi and H. Mofakham, *Catal. Commun.*, 2009, **10**, 945.
- 18 Z. Li, Y. Ma, J. Xu, J. Shi and H. Cai, *Tetrahedron Lett.*, 2010, **51**, 3922.
- 19 A. Majhi, S. S. Kim and S. T. Kadam, *Appl. Organomet. Chem.*, 2008, **22**, 705.
- 20 J. S. Yadav, B. V. Subba Reddy, B. Eeshwaraiah and M. Srinivas, *Tetrahedron*, 2004, **60**, 1767.
- 21 K. Niknam, D. Saberi and M. N. Sefat, *Tetrahedron Lett.*, 2010, **51**, 2959.