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Synthesis of Chiral Cyclic Nitrones by Asymmetric Addition of β-Ketosulfones to Nitroalkenes followed by Reductive Cyclization

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Abstract: The first organocatalytic addition of β-ketosulfones to nitroalkenes catalyzed by thiourea cinchona alkaloids is presented. The readily obtained addition products were selectively transformed into chiral nitrones by reduction of the nitro group and in situ cyclization (up to 99:1 e.r. and >98:2 d.r.). Moreover, the utility of this method has additionally been demonstrated by the further transformation to functionalized *N*-hydroxypyrrolidines that possess a quaternary center by addition of trimethylsilyl cyanide (TMSCN) to the C=N bond of the cyclic nitrones in the presence of a Lewis acid.

Keywords: asymmetric synthesis · ketosulfones · Michael addition · nitrones · organocatalysis

Introduction

An important target in organic chemistry is the stereoselective formation of C–C bonds. Recently, organocatalysis has especially provided different asymmetric strategies to reach this goal.[1] During the development of organocatalytic methodologies, asymmetric 1,4-conjugate addition reactions have emerged as a powerful strategy to obtain chiral organic compounds in an easy way.[2] There are two main organocatalytic activation modes for carrying out 1,4-addition reactions: 1) a covalent strategy, which often takes place after the formation of an iminium ion by the reaction of an unsaturated carbonyl compound with a chiral amine (aminocatalysis)[3] or 2) a noncovalent activation method, in which, for example, the cinchona alkaloids and thiourea catalysts represent a cornerstone in the functionalization of nitroalkenes.[4,5]

On the other hand, nitrones[6] are very useful intermediates in synthesis, especially five-membered cyclic nitrones,[6i] which have been used as starting materials for the construction of different natural products (e.g., pyrrolizidines or indolizine alkaloids[6k]). The main strategy for the preparation of these cyclic compounds typically implies a relatively long synthetic sequence that starts from different compounds of the chiral pool (e.g., D-malic acid esters). These methods usually incorporate only oxygen functionalities at 3- and/or 4-positions and generate the cyclic skeleton in the last steps through an amine or oxime cyclization followed by oxidation. Conversely, the syntheses of chiral cyclic nitrones with non-oxygenated substituents are scarce because most of them are non-asymmetric versions. For these reasons, the development of an alternative, more general, and straightforward synthesis of enantiomerically pure cyclic nitrones is highly desirable.

We focused our attention on the addition of β-ketosulfones to nitroalkenes for two main reasons: 1) the nitro function could later be reduced to a *N*-hydroxylamine, which can be cyclized in situ by condensation with the ketone moiety into a nitrone group and 2) the presence of the sulfone moiety in β-ketosulfones makes these nucleophiles especially attractive because it allows several further transformations. In addition, these β-ketosulfones have recently been used in some interesting nucleophilic addition reactions,[7] in which the iminium activation has been the main strategy for the Michael addition of these reagents

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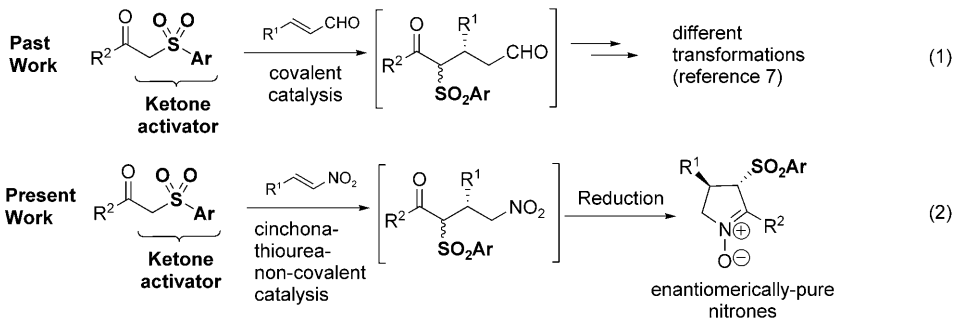
[Scheme 1, Eq. (1)]. We reasoned that the use of nitroalkenes and β-ketosulfones in this reaction would also be successful by employing the noncovalent approach under thiourea alkaloid catalysis.[8] A further partial reduction of the nitro function will provide the desired enantiomerically enriched cyclic nitrones [Scheme 1, Eq. (2)]. However, in most of the cases reported the addition of β-ketoesters and β-ketosulfones to different iminium intermediates[9] resulted in the formation of nonselective mixtures of epimers at the γ-position (the nucleophilic center), but with a high stereoselectivity control at the β-position (the electrophilic center) of the aldehyde [Scheme 1, Eq. (1)]. Bearing in mind that other previous studies solved this problem by taking advantage of the high acidity of the proton at the carbon atom, thus acting as nucleophile and permitting easy epimerization into the most stable isomer in the formation of cyclic compounds (obtained in a high diastereomeric ratio (d.r.)),[10] we envisioned that the construction of cyclic nitrones will also provoke the preferential formation of a single diastereoisomer [Scheme 1, Eq. (2)].



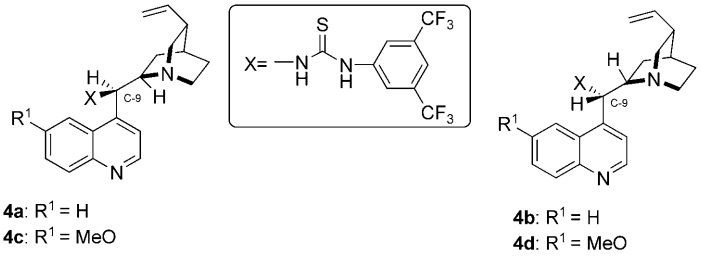
Scheme 1. Two different strategies for the addition of β-ketosulfones to activated alkenes.

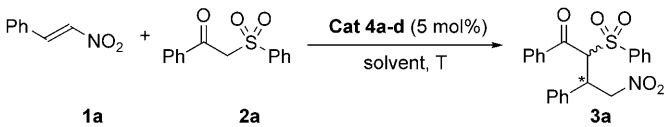
Results and Discussion

The screening of the appropriate conditions and catalysts for the model reaction between nitroalkene **1a** and β-ketosulfone **2a** is presented in Table 1. Initially, the reaction was carried out in dichloromethane at room temperature using 5 mol% of thiourea catalyst **4a**, which provided a nearly quantitative conversion. However, the enantioselectivity was moderate (enantiomeric ratio (e.r.)=77:23) and, as expected, a low diastereomeric ratio was obtained due to the high acidity at the α-position of the ketone group (d.r.=50:50; Table 1, entry 1). A similar low d.r. value was also observed for the rest of the entries in Table 1. As a result of the mixture of diastereosiomers of sulfone **3a**, the determination of the e.r. value was carried out on the final targeted nitrone **5a** (see below). Further exploration of thiourea catalysts **4b–d** (Table 1, entries 2–4, respectively) showed a significantly better performance of derivative **4c**, which improved the enantiomeric ratio up to 83:17 (Table 1, entry 3). Moreover, we observed that the stereochemistry at C-9 of the catalyst was responsible for the stereocontrol of the reaction. Thus, catalysts **4a** and **4c** lead preferentially to one enantiomer, whereas **4b** and **4d** to the opposite one (Table 1, entries 1–4).

We next examined other reaction temperatures with catalyst **4c**. Full conversion and good enantioselectivity were obtained at 0 and −20 °C after 18 h, with a slightly higher enantiomeric ratio at 0 °C (e.r.=90:10; Table 1, entry 6). The temperature effect was also observed with catalysts **4b** and **4d**, but the increase in the e.r. value was comparatively low (Table 1, entries 2, 4 and 7, 8). We studied the influence of the solvent, thus examining tol-

Table 1. Screening and optimization conditions for the addition of β-ketosulfone **2a** to nitroalkene **1a**.[a]





Entry	Catalyst [mol%]		Solvent	T [°C]	Conversion[b] [%]	e.r.[c] [%]
1	**4a**	(5)	CH_2Cl_2	RT	>99	77:23
2	**4b**	(5)	CH_2Cl_2	RT	>99	34:66
3	**4c**	(5)	CH_2Cl_2	RT	>99	83:17
4	**4d**	(5)	CH_2Cl_2	RT	>99	33:67
5	**4c**	(5)	CH_2Cl_2	−20	>99	89:11
6	**4c**	(5)	CH_2Cl_2	0	>99	90:10
7	**4d**	(5)	CH_2Cl_2	0	>99	29:71
8	**4b**	(5)	CH_2Cl_2	0	>99	36:64
9	**4c**	(5)	toluene	0	>99	81:19
10	**4c**	(5)	THF	0	>99	93:7
11	**4c**	(5)	C_6H_6	0	>99	90:10
12	**4c**	(5)	DCE	0	>99	82:18
13	**4c**	(5)	xylene	0	>99	95:5
14	**4c**	(5)	xylene	0	>99[d]	99:1[d]
15	**4c**	(2.5)	xylene	0	50	97:3
16	**4c**	(1)	xylene	0	15	nd[e]

[a] All the reactions were performed using β-ketosulfone **2a** (0.2 mmol), nitroalkene **1a** (0.4 mmol), and the indicated amount of catalyst **4** (1–5 mol%) in solvent (0.2 mL) and were stopped after 20 h. [b] Determined by ^{1}H NMR spectroscopic analysis. [c] The e.r. value was determined by transformation of product **3a** into nitrone **5a** (see Table 2). [d] This reaction was carried out on a 2.0 mmol scale. [e] Not determined.

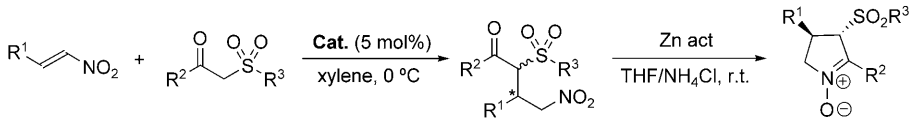
uene, THF, benzene, 1,2-dichloroethane (DCE), and xylene (Table 1, entries 9–13). The best results were obtained with xylene, which provided the addition product with a high e.r. value of 95:5. All the reactions were performed on a 0.2 mmol scale in 0.2 mL of xylene, except for entry 14 (Table 1), which was carried out on a 2.0 mmol scale. Under the latter conditions, **3a** was obtained with a significantly better enantioselectivity (e.r. = 99:1).[11] We decreased the amount of catalyst to 2.5 and 1 mol%; however, only moderate conversions were observed after 24 h (Table 1, entries 15 and 16, respectively).

With the optimized conditions (5 mol% of catalyst **4** in xylene at 0°C), we decided to investigate the scope of the reaction. However, to identify the optimal conditions under which to synthesize cyclic nitrones **5** from adducts **3**, a few different reducing reagents were initially investigated for the model substrate **3a**.[12] Nonselective reduction and desulfonylation reactions were carried out under most of the conditions tested. Thus, although the use of Raney nickel in EtOH or magnesium in MeOH gave complex mixtures of all the possible reduced cyclic compounds in which only traces of the desired product **5** could be identified, the combination of Pd–NH_2NH_2 or $NaBH_4$–$BiCl_3$ led, among other byproducts, to desulfonylated and reduced acyclic products.[13] Fortunately, the use of Zn/NH_4Cl[12,14,15] cleanly provided cyclic nitrone **5a** after 15 min at room temperature. Compound **5a** was isolated in 55% yield[16] as a unique diastereoisomer starting from a 1:1 diastereomeric mixture of **3a** (Table 2, entry 1). The reaction was also carried out on a 2.0 mmol scale and even better results were obtained (73% yield; Table 2, entry 2). The addition reaction of β-ketosulfone **2a** with different aryl (**1b–j**) and alkyl (**1k**) nitroalkenes was next explored (Table 2, entries 3–14). The reaction could be carried out with electron-donating groups (**1b,c**), thus obtaining good yields of the isolated products and e.r. values of 83:17 to 84:16 (Table 2, entries 3 and 4). Electron-withdrawing groups (**1d–i**) led to similar e.r. values (Table 2, entries 5–11), but interestingly the *para*-fluoro substitution gave an excellent e.r. value of 99:1 in a good yield of 89% (Table 2, entry 7).[11] In addition, heteroaromatic rings and alkyl chains were also tolerated, thus leading to the corresponding adducts **3j–k** in good yields and uniform enantioselectivities (Table 2, entries 12–14). β-Alkylketosulfone **2b** (R^2 = Me, R^3 = *p*-tol) was evaluated, thus giving **3l** with e.r. = 82:18 in 86% yield (Table 2, entry 15). Finally, a bulky aromatic ring at the sulfone group, such as 2-naphthyl, was also tolerated (Table 2, entry 16); however, the e.r. value decreased to 76:24.

The structure and the relative configuration of the model nitrone **5a** were determined by analysis of the X-ray structure of its crystals (Figure 1),[17] in which the relative configuration was *trans*. As pointed out before, the high diastereomeric ratio observed might be attributable to the easy enolization of the α-position of the ketone and obtention of the most stable *trans* compound. Therefore, reduction with Zn allowed the synthesis of cyclic nitrones and epimerization of the mixture to give a single diastereoisomer. Compounds **3b–m** showed a similar behavior when treated with Zn/NH_4Cl, thus leading to nitrones **5b–m** as single diastereoisomers in good yields, except for the more reactive alkylketone derivative **3l**. Under these reductive conditions, nitrone **5l** was further reduced to the corresponding cyclic deoxygenated ketimine **7l**, even when the reaction was stopped after only 2 min (Table 2, entry 15). Nitrones **5b–l** exhibited similar NMR signals relative to the model compound **5a**, thus suggesting an identical stereochemical reaction course. Therefore, the relative *trans* configuration was also assigned for the rest of the compounds **5**, though the absolute configuration of the products was determined through compound **6e** (see below, Figure 2).

Although in some cases the enantiomeric ratios were moderate, one of the major advantages of this method relates to the easy crystallization of prod-

Table 2. Reaction scope for the addition of β-ketosulfones to nitroalkenes and synthesis of nitrones **5**.[a]



1 **2** **3** **5** (d.r. >98:2)

Entry	R^1	R^2	R^3	Cat.	Yield of **3** [%]		Yield of **5** [%]		e.r.[b] [%]
1	Ph	Ph	Ph	**4c**	**3a**	84	**5a**	55	95:5 (>99:1)[c]
2	Ph	Ph	Ph	**4c**	**3a**	90[d]	**5a**	73[d]	99:1
3	*p*-$MeOC_6H_4$	Ph	Ph	**4d**	*ent*-**3b**	83	*ent*-**5b**	84	16:84
4	*p*-MeC_6H_4	Ph	Ph	**4c**	**3c**	95	**5c**	71	83:17
5	*p*-ClC_6H_4	Ph	Ph	**4c**	**3d**	85[e]	**5d**	85	80:20
6	*o*-ClC_6H_4	Ph	Ph	**4c**	**3e**	99	**5e**	87	82:18 (>99:1)[c]
7	*p*-FC_6H_4	Ph	Ph	**4a**	**3f**	89	**5f**	76	99:1
8	*p*-CNC_6H_4	Ph	Ph	**4c**	**3g**	50	**5g**	76	85:15
9	*p*-$CF_3C_6H_4$	Ph	Ph	**4c**	**3h**	85	**5h**	73	87:13
10	3,5-$(CF_3)_2C_6H_3$	Ph	Ph	**4c**	**3i**	68	**5i**	68	84:16 (99:1)[c]
11	3,5-$(CF_3)_2C_6H_3$	Ph	Ph	**4d**	*ent*-**3i**	68	*ent*-**5i**	48	15:85 (4:96)[c]
12	2-thienyl	Ph	Ph	**4c**	**3j**	80	**5j**	60	80:20 (99:1)[c]
13	2-thienyl	Ph	Ph	**4d**	*ent*-**3j**	90	*ent*-**5j**	86	19:81 (2:98)[c]
14	*n*Pr	Ph	Ph	**4c**	**3k**	82	**5k**	70	83:17
15	Ph	Me	*p*-MeC_6H_4	**4c**	**3l**	86	**5l** (**7l**)[f]	34 (56)	82:18
16	Ph	Ph	2-naphthyl	**4c**	**3m**	73[e]	**5m**	57	76:24

[a] Reaction conditions for the addition of β-ketosulfones: catalyst **4** (5 mol%), β-ketosulfone **2** (0.2 mmol), and nitroalkene **1** (0.4 mmol) in xylene (0.2 mL) at 0°C. Reaction conditions for the reductive cyclization: adduct **3** (0.1 mmol) and activated Zn (70 equiv) in THF/sat. NH_4Cl (1:1, 14 mL) at room temperature. [b] The e.r. values were determined by HPLC analysis on nitrone derivatives **5**. [c] The e.r. values were obtained after a single crystallization from CH_2Cl_2/pentane. [d] This reaction was carried out on a 2.0 mmol scale. [e] Reaction was carried out at room temperature. [f] In this case, the corresponding cyclic deoxygenated-ketimine **7l** was isolated as the major product (yield in parentheses).

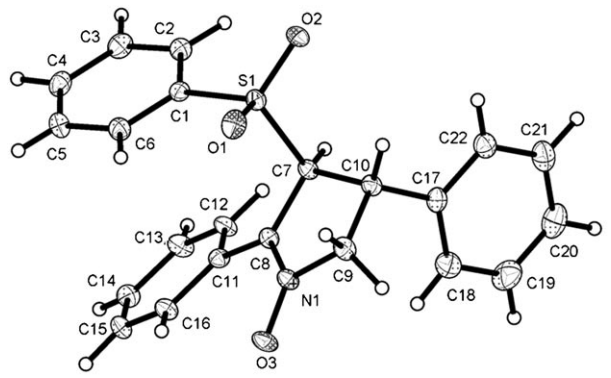
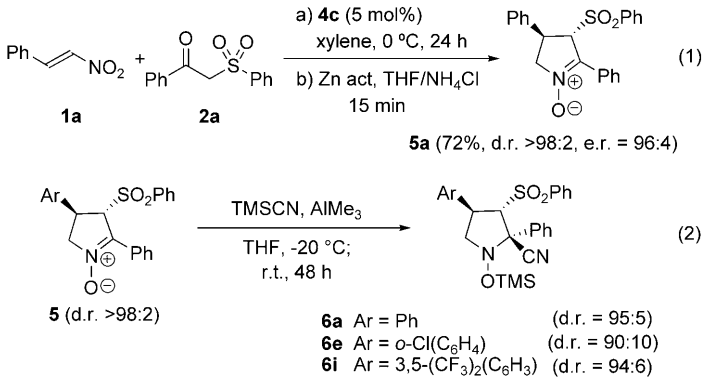


Figure 1. X-ray structure of compound *trans*-**5a**.

ucts **5**, which contain the sulfone moiety. We exemplified this feature with nitrones **5**, containing phenyl (**5a**), *o*-Cl-C_6H_4 (**5e**), 3,5-$(CF_3)_2$-C_6H_3 (**5i**), and thienyl (**5j**) groups, and obtained highly enantioenriched nitrones in all the cases with e.r. > 99:1 upon a single crystallization (Table 2, entries 1, 6, and 10–13). In addition, the reaction was performed with the diastereomeric catalyst of **4c**, **4d**, thus obtaining identical results with the opposite configuration at the new created chiral centers, allowing again the easy crystallization of sulfones *ent*-**5j** and *ent*-**5i** again (Table 2, entries 11 and 13).

The synthesis of these cyclic nitrones was also achieved in a one-pot fashion [Scheme 2, Eq. (1)]. The 1,4-addition reaction between **1a** and **2a** was carried out under standard conditions and activated Zn, THF, and saturated NH_4Cl were added to the mixture after 24 h. Nitrone **5a** was isolated after 15 min in a good yield of 72% with a perfect diastereoisomeric ratio (d.r. > 98:2) and excellent enantiomeric ratio (e.r. = 96:4). In addition, we shortly investigated the use of these compounds as starting materials for further transformations. Consequently, the 1,3-addition of TMSCN to nitrones **5** in the presence of $AlMe_3$,[6,18] in which a quaternary carbon atom is generated, was explored. The resulting addition products **6** were obtained after 48 hours at room temperature in good yields (60–78%) with good selectivities [d.r. = 90:10–95:5; Scheme 2, Eq. (2)].



Scheme 2. One-pot synthesis and TMSCN addition to nitrones **5**. TMSCN = trimethylsilyl cyanide.

Finally, the absolute configuration of derivative **6e**, obtained after two steps from nitroalkane **1e** by using catalyst **4c**, was determined as 2*R*,3*S*,4*R* by X-ray crystallographic analysis (Figure 2).[19] By assuming that the initial and later addition reactions took place in the same manner, the configuration of adducts **3**, nitrones **5**, and nitriles **6** were accordingly assigned by analogy.

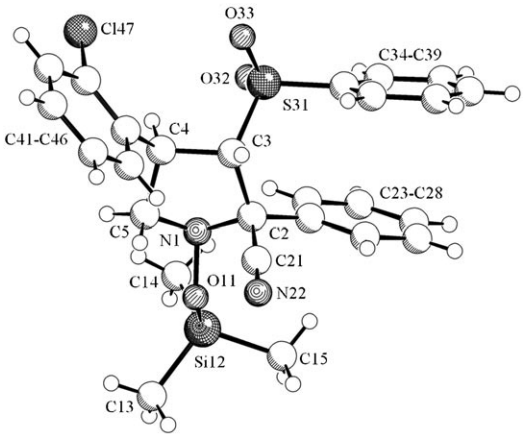


Figure 2. X-ray structure of compound (2*R*,3*S*,4*R*)-**6e**.

Conclusion

In conclusion, we have presented the first organocatalytic addition of β-ketosulfones to nitroalkenes catalyzed by thiourea cinchona alkaloids that lead to the formation of 1,4-addition products (e.r. up to 99:1). The obtained enantiomerically enriched active products were selectively transformed into cyclic nitrones by partial reduction of the nitro group. Moreover, the utility of this method has additionally been demonstrated by further transformation to functionalized *N*-hydroxypyrrolidines that possess a quaternary center.

Experimental Section

General methods: NMR spectra were acquired on Bruker 300, Varian 300, Varian 400, or Bruker 500 spectrometers at 300 and 75, 400 and 100, or 500 and 125 MHz for ^1H and ^{13}C NMR spectra, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CDCl_3$: $\delta = 7.26$ and 77.0 ppm for ^1H and ^{13}C NMR; $[D_6]$DMSO: $\delta = 2.50$ and 39.5 ppm for ^1H and ^{13}C NMR; $[D_6]$acetone: $\delta = 2.05$ and 29.8 ppm for ^1H and ^{13}C NMR). ^{13}C NMR spectra were acquired on a broad-band decoupled mode. Analytical TLC was performed on precoated aluminum-backed plates (Merck Kieselgel 60 F254) and visualized by UV irradiation or $KMnO_4$ dip. Purification of reaction products was carried out by column chromatography on silica gel (Merck-60). Exact masses (HRMS) were recorded on a Bruker Daltonics Micro TOF spectrometer with electrospray (ES^+) ionization. Elemental analyses were recorded on Vario EL III of Fa. Elementar Analysensysteme GmbH (Hanau). Optical rotations were measured on a Perkin–Elmer 241 polarimeter. The enantiomeric excess (*ee*) of the products was determined by chiral stationary-

phase HPLC (Daicel Chiralpak AD-H, AS-H, IB, or Chiralcel OD columns).

Materials: Analytical-grade solvents, nitroalkenes **1a–d,f** and β-ketosulfone **2a,b** were purchased by Aldrich and used as received. Nitroalkenes **1e,g,k** were prepared by a nitro aldol/dehydration reaction between nitromethane and the corresponding aldehyde.[20] β-Ketosulfone **2c** was obtained in two steps from 2-mercaptonaphthalene by condensation with 2-bromacetophenone[21] followed by oxidation with *meta*-chloroperbenzoic acid (*m*-CPBA). Column chromatography was performed on silica gel 60 (0.040–0.063 mm). Racemic samples were prepared with 1,4-diazobicyclo-[2.2.2]octane (DABCO) as the catalyst. Catalysts **4a–d** were obtained in a two-step synthesis from a commercially available Cinchona catalyst.[8]

General procedure for the addition of β-ketosulfones to nitroalkenes: In an ordinary vial, the corresponding catalyst **4** (e.g., **4c**; 6.0 mg, 0.001 mmol) was added to a stirred solution of nitroalkene **1** (0.4 mmol) and β-ketosulfone **2** (0.2 mmol) in xylene (0.2 mL) at 0 °C. After complete consumption of the β-ketosulfone (monitored by TLC analysis), the crude product was directly purified by column chromatography (eluent is indicated in each case) to afford pure product **3** as a mixture of diastereoisomers.

(2*R*/2*S*,3*R*)-4-Nitro-1,3-diphenyl-2-(phenylsulfonyl)butan-1-one (3a): According to the general procedure using catalyst **4c**, compound **3a** was obtained after purification by column chromatography (hexane/EtOAc 2:1) as a white solid and a 55:45 mixture of diastereoisomers (84% yield). ^{1}H NMR (300 MHz, $CDCl_3$) (major diastereoisomer): δ = 7.71 (d, J = 7.8 Hz, 2H), 7.52–6.94 (m, 13H), 5.58 (d, J = 11.1 Hz, 1H), 5.52 (dd, J = 13.5, 4.4 Hz, 1H), 5.12–4.98 (m, 1H), 4.39 ppm (dt, J = 10.7, 3.9 Hz, 1H); ^{1}H NMR (300 MHz, $CDCl_3$) (minor diastereoisomer): δ = 7.66 (d, J = 6.8 Hz, 2H), 7.52–6.94 (m, 13H), 5.41 (d, J = 5.0 Hz, 1H), 5.28 (dd, J = 13.8, 3.2 Hz, 1H), 5.12–4.98 (m, 1H), 4.49 ppm (ddd, J = 8.3, 4.8, 3.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of diastereoisomers): δ = 192.1, 191.0, 137.7, 137.0, 136.5, 136.4, 135.8, 134.8, 134.7, 134.5, 134.2, 133.7, 129.8, 129.3, 129.1, 129.0, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 128.1, 127.7, 77.9, 76.5, 71.2, 71.0, 43.2, 42.5 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{22}H_{19}NO_5S{\cdot}H^+$: 410.1056 [$M$+H]$^+$; found: 410.1054; elemental analysis calcd (%) for $C_{22}H_{19}NO_5S$ (409.45): C 64.53, H 4.68, N 3.42; found: C 64.94, H 4.34, N 3.05.

(2*R*/2*S*,3*S*)-3-(4-Methoxyphenyl)-4-nitro-1-phenyl-2-(phenylsulfonyl)butan-1-one (3b): According to the general procedure using catalyst **4d**, compound **3b** was obtained after purification by column chromatography (hexane/EtOA*c* = 3:1) as a white solid and a 80:20 mixture of diastereoisomers (83% yield). ^{1}H NMR (300 MHz, $CDCl_3$) (major diastereoisomer): δ = 7.78 (d, J = 6.0 Hz, 2H), 7.60–7.20 (m, 8H), 7.00 (d, J = 9.0 Hz, 2H), 6.62 (d, J = 9.0 Hz, 2H), 5.57 (d, J = 8.4 Hz,1H), 5.55 (dd, J = 13.2, 4.1 Hz, 1H), 5.07 (dd, J = 16.2, 10.6 Hz, 1H), 4.39 (dt, J = 10.9, 4.1 Hz, 1H), 3.63 ppm (s, 3H) ; ^{1}H NMR (300 MHz, $CDCl_3$) (minor diastereoisomer): δ = 7.73 (d, J = 7.3 Hz, 2H), 7.60–7.20 (m, 8H), 6.97 (d, J = 9.0 Hz, 2H), 6.69 (d, J = 6.5 Hz, 2H), 5.46 (d, J = 5.2 Hz, 1H), 5.25 (dd, J = 13.7, 3.4 Hz, 1H), 5.02 (dd, J = 13.7, 7.5 Hz, 1H), 4.52–4.46 (m, 1H), 3.72 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) (major diastereoisomer): δ = 190.1, 159.4, 136.7, 136.5, 134.7, 133.7, 129.9, 129.4, 129.1, 128.9, 128.6, 128.5, 128.2, 126.6, 114.5, 78.1, 71.3, 55.1, 42.6 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{23}H_{21}NO_6S{\cdot}H^+$: 440.1162 [$M$+H]$^+$; found: 440.1155.

(2*R*/2*S*,3*R*)-4-Nitro-1-phenyl-2-(phenylsulfonyl)-3-*para*-tolylbutan-1-one (3c): According to the general procedure using catalyst **4c**, compound **3c** was obtained after purification by column chromatography (hexane/EtOAc 3:1) as a yellow solid and a 60:40 mixture of diastereoisomers (95% yield), inseparable from the nitroalkene **1c**. ^{1}H NMR (300 MHz, $CDCl_3$) (major diastereoisomer): δ = 7.74–6.78 (m, 14H), 5.39 (d, J = 5.2 Hz, 1H), 5.21 (dd, J = 13.8, 3.4 Hz, 1H), 5.02 (dd, J = 10.5, 3.8 Hz, 1H), 4.43 (ddd, J = 8.6, 5.0, 3.4 Hz, 1H), 2.15 ppm (s, 3H); ^{1}H NMR (300 MHz, $CDCl_3$) (minor diastereoisomer): δ = 7.74–6.78 (m, 14H), 5.55 (d, J = 10.9 Hz, 1H), 5.485 (dd, J = 13.2, 3.8 Hz, 1H), 4.97 (dd, J = 14.6, 10.3 Hz, 1H), 4.34 (dt, J = 10.9, 4.1 Hz, 1H), 2.33 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of diastereoisomers and nitroalkene): δ = 192.0, 190.8, 142.9, 139.0, 138.3, 138.0, 137.7, 137.0, 136.5, 136.3, 136.2, 134.6, 134.3, 134.1, 133.5, 132.6, 131.6, 130.2, 130.0, 129.8, 129.7, 129.5, 129.1, 129.0 (2C), 128.9, 128.6, 128.4, 128.3, 128.0, 128.0, 127.5, 78.0, 76.6, 71.3, 71.0, 42.8, 42.1, 20.8, 20.7 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{23}H_{21}NO_5S{\cdot}H^+$: 424.1213 [$M$+H]$^+$; found: 424.1214.

(2*R*/2*S*,3*R*)-3-(4-Chlorophenyl)-4-nitro-1-phenyl-2-(phenylsulfonyl)butan-1-one (3d): According to the general procedure using catalyst **4c** at room temperature, compound **3d** was obtained after purification by column chromatography (hexane/EtOAc 5:1) as a white solid and a 67:33 mixture of diastereoisomers (85% yield). ^{1}H NMR (300 MHz, $CDCl_3$) (major diastereoisomer): δ = 7.77 (d, J = 8.8 Hz, 2H), 7.62–7.02 (m, 12H), 5.61 (d, J = 11.2 Hz, 1H), 5.56 (dd, J = 12.6, 4.0 Hz, 1H), 5.08 (dd, J = 19.1, 10.4 Hz, 1H), 4.44 ppm (dt, J = 10.8, 4.0 Hz, 1H); ^{1}H NMR (300 MHz, $CDCl_3$) (minor diastereoisomer): δ = 7.69 (d, J = 8.7 Hz, 2H), 7.02–7.62 (m, 12H), 5.47 (d, J = 5.5 Hz, 1H), 5.24 (dd, J = 13.9, 3.4 Hz, 1H), 5.04 (dd, J = 19.5, 10.4 Hz, 1H), 4.54 ppm (ddd, J = 9.4, 5.5, 3.5 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) (mixture of diastereoisomers): δ = 191.8, 190.6, 137.7, 136.9, 136.3, 134.8, 134.7, 134.5, 134.4, 134.2, 134.0, 133.5, 129.8, 1296, 129.5, 129.3 129.2 (2C), 129.1 (2C), 128.9, 128.8, 128.6 (2C), 128.2, 77.7, 77.2, 71.0, 70.7, 42.6, 42.0 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{22}H_{18}ClNO_5S{\cdot}H^+$: 444.0665 [$M$+H]$^+$; found: 444.0644.

(2*R*/2*S*,3*R*)-3-(2-Chlorophenyl)-4-nitro-1-phenyl-2-(phenylsulfonyl)butan-1-one (3e): According to the general procedure using catalyst **4c**, compound **3e** was obtained after purification by column chromatography (dichloromethane/pentane 2:1) as a white solid and a 80:20 mixture of diastereoisomers (99% yield). ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of diastereoisomers): δ = 7.83 (d, J = 7.6 Hz, 2H), 7.78 (br d, J = 8.4 Hz, 1H), 7.65–7.60 (m, 1H), 7.59–7.39 (m, 7H), 7.34–7.27 (m, 3H), 7.16–7.09 (m, 2H), 7.08–6.97 (m, 2H), 6.07 (br s, 1H), 5.66–5.44 (m, 3H), 5.39 (dd, J = 14.4, 10.4 Hz, 1H), 4.98 ppm (ddd, J = 10.3, 4.8, 3.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (mixture of diastereoisomers): δ = 191.8, 190.8, 137.7, 137.2, 136.4, 135.0, 134.8, 134.5, 134.2, 133.7, 130.7, 130.0, 129.6, 129.7, 129.2, 128.71, 128.6, 127.8, 127.5, 74.5, 68.7, 39.0 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{22}H_{18}ClNO_5S{\cdot}Na^+$: 466.0492 [$M$+Na]$^+$; found: 466.0494.

(2*R*/2*S*,3*R*)-3-(4-Fluorophenyl)-4-nitro-1-phenyl-2-(phenylsulfonyl)butan-1-one (3f): According to the general procedure using catalyst **4a**, compound **3f** was obtained after purification by column chromatography (hexane/EtOAc 2:1) as a white solid and a 53:47 mixture of diastereoisomers (89% yield). ^{1}H NMR (300 MHz, $CDCl_3$) (mixture of diastereoisomers): δ = 7.70 (d, J = 7.5 Hz, 2H), 7.64 (d, J = 7.5 Hz, 2H), 7.53–7–32 (m, 11H), 7.26 (t, J = 7.8 Hz, 2H), 7.19–6.89 (m, 7H), 6.81 (t, J = 8.5 H, 2H), 6.72 (t, J = 8.5 Hz, 2H), 5.52–5.47 (m, 2H), 5.39 (d, J = 5.4 Hz, 1H), 5.05–4.92 (m, 2H), 4.51–4.45 (m, 1H), 4.37 ppm (td, J = 10.9, 4.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of diastereoisomers): δ = 191.9, 190.8, 164.0 (d, J_{C-F} = 73.4 Hz), 160.8 (d, J_{C-F} = 72.3 Hz), 137.7, 136.9, 136.4, 136.3, 134.8, 134.5, 134.4, 134.0, 131.6 (d, J_{C-F} = 15.0 Hz), 130.7 (d, J_{C-F} = 13.4 Hz), 130.11, 130.0, 129.8, 129.7, 129.6, 129.3, 129.2, 129.0, 128.8, 128.6, 128.1, 116.5 (d, J_{C-F} = 81.0 Hz), 116.0 (d, J_{C-F} = 75.8 Hz), 77.9, 76.7, 71.3, 71.0, 42.6, 42.0 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{22}H_{18}FNO_5S{\cdot}H^+$: 428.0962 [$M$+H]$^+$; found: 428.0962.

(2*R*/2*S*,3*R*)-3-(4-Cyanophenyl)-4-nitro-1-phenyl-2-(phenylsulfonyl)butan-1-one (3g): According to the general procedure using catalyst **4c**, compound **3g** was obtained after purification by column chromatography (dichloromethane/pentane 2:1) as a white solid and a 66:34 mixture of diastereoisomers (50% yield). ^{1}H NMR (300 MHz, $(CD_3)_2CO$) (major diastereoisomer): δ = 7.87–7.83 (m, 2H,), 7.72–7.43 (m, 11H), 7.35–7.30 (m, 2H), 6.33 (d, J = 11.2 Hz, 1H), 5.83 (dd, J = 13.7, 4.2 Hz, 1H), 5.19–5.07 (m, 1H), 4.51 ppm (td, J = 11.3, 4.2 Hz, 1H); ^{1}H NMR (300 MHz, $(CD_3)_2CO$) (minor diastereoisomer): δ = 7.87–7.83 (m, 2H), 7.72–7.43 (m, 11H), 6.23 (d, J = 8.7 Hz, 1H), 5.30 (dd, J = 13.7, 11.5 Hz, 1H), 5.19–5.07 (m, 1H), 4.73–4.66 ppm (m, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2CO$) (mixture of diastereoisomers): δ = 192.3, 191.6, 142.4, 139.5, 138.1, 137.6, 137.3, 135.7, 135.2, 135.1, 134.9, 133.3, 133.2, 131.1, 130.8, 130.5, 130.1, 130.0, 129.8, 129.5, 129.4, 129.3, 118.7, 118.5, 112.9, 112.7, 78.4, 77.8, 70.4, 70.2, 44.3, 44.2 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{23}H_{18}N_2O_5S{\cdot}Na^+$: 457.0834 [$M$+Na]$^+$; found: 457.0832.

(2*R*/2*S*,3*R*)-4-Nitro-1-phenyl-2-(phenylsulfonyl)-3-(4-(trifluoromethyl)-phenyl) butan-1-one (3h): According to the general procedure using catalyst **4c**, compound **3h** was obtained after purification by column chromatography (dichloromethane/pentane 2:1) as a white solid and a 50:50 mixture of diastereoisomers (85% yield). ^{1}H NMR (300 MHz, $CDCl_3$)

(mixture of diastereoisomers): $\delta = 7.80–7.77$ (m, 2H), 7.68–7.63 (m, 4H), 7.60–7.53 (m, 3H), 7.47–7.42 (m, 8H), 7.40–7.34 (m, 6H), 7.28–7.22 (m, 5H), 5.66 (d, $J = 7.9$ Hz, 1H), 5.60 (dd, $J = 13.7$, 4.0 Hz, 1H), 5.54 (d, $J = 5.9$ Hz, 1H), 5.24 (dd, $J = 14.1$, 3.5 Hz, 1H), 5.15 (dd, $J = 13.7$, 10.4 Hz, 1H), 5.07 (dd, $J = 14.1$, 9.6 Hz, 1H), 4.65 (ddd, $J = 9.4$, 5.9, 3.5 Hz, 1H), 4.54 ppm (td, $J = 10.7$, 4.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of diastereoisomers): $\delta = 191.8$, 190.8, 139.9, 139.4, 137.8, 136.9, 136.4, 136.2, 135.1, 134.8, 134.8, 134.3, 130.8 (q, $J = 32.7$ Hz), 130.8 (q, $J = 32.7$ Hz), 129.5, 129.4, 129.1, 129.0, 128.9, 128.8, 128.8, 128.6, 128.3, 126.4 (q, $J = 3.7$ Hz), 126.1 (q, $J = 3.7$ Hz), 123.7 (q, $J = 272.3$ Hz), 123.6 (q, $J = 272.7$ Hz), 77.7, 76.6, 70.8, 70.7, 43.0, 42.5 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): $\delta = -62.90$ (s), -63.00 ppm (s); HRMS (TOF-MS ES$^+$): calcd for $C_{23}H_{18}F_3NO_5S{\cdot}Na^+$: 500.0755 $[M+Na]^+$; found: 500.0742.

(2*R*/2*S*,3*S*)-3-[3,5-Bis(trifluoromethyl)phenyl]-4-nitro-1-phenyl-2-(phenylsulfonyl)butan-1-one (3i). According to the general procedure using catalyst **4d**, compound **3i** was obtained after purification by column chromatography (dichloromethane/pentane 2:1) as a white solid and a 77:23 mixture of diastereoisomers (68% yield). ^{1}H NMR (300 MHz, $CDCl_3$) (major diastereoisomer): $\delta = 7.86–7.20$ (m, 13H), 5.57 (d, $J = 6.7$ Hz, 1H), 5.16 (dd, $J = 14.0$, 3.2 Hz, 1H), 5.00 (dd, $J = 14.1$, 9.2 Hz, 1H), 4.75–4.70 ppm (m, 1H); ^{1}H NMR (300 MHz, $CDCl_3$) (minor diastereoisomer): $\delta = 7.86–7.20$ (m, 13H), 5.7 (d, $J = 11.2$ Hz, 1H), 5.6 (dd, $J = 14.1$, 3.8 Hz, 1H), 4.61 ppm (td, $J = 10.4$, 3.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of diastereoisomer): $\delta = 192.1$, 192.1, 140.6, 139.8, 139.8, 139.6, 138.1, 138.1, 137.9, 137.4, 137.4, 135.9, 135.4, 135.3, 135.1, 132.3 (q, $J = 33.5$ Hz), 132.17 (q, $J = 33.3$ Hz), 131.3, 131.3, 130.8, 130.7, 130.6, 130.3, 130.1, 129.7, 129.2, 128.6, 124.1 (q, $J = 272.3$ Hz,), 124.0 (q, $J = 272.2$ Hz), 123.2 (sept, $J = 3.7$ Hz), 122.9 (sept, $J = 3.7$ Hz), 78.2, 78.1, 78.0, 44.4, 44.3, 44.1, 44.0 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): $\delta = -63.00$ (s), -63.20 ppm (s); HRMS (TOF-MS ES$^+$): calcd for $C_{24}H_{17}F_6NO_5S{\cdot}Na^+$: 568.0629 $[M+Na]^+$; found: 568.0627.

(2*R*/2*S*,3*S*)-4-Nitro-1-phenyl-2-(phenylsulfonyl)-3-(thiophen-2-yl)butan-1-one (3j): According to the general procedure using catalyst **4d**, compound **3j** was obtained after purification by column chromatography (dichloromethane/pentane 2:1) as a white solid and a 50:50 mixture of diastereoisomers (90% yield). ^{1}H NMR(300 MHz, $CDCl_3$): (mixture of diastereoisomers): $\delta = 7.76–7.73$ (m, 4H), 7.61–7.57 (m, 3H), 7.55–7.49 (m, 4H), 7.45–7.38 (m, 5H), 7.32 (t, $J = 7.8$, 2H), 7.24, (dd, $J = 10.6$, 4.9 Hz, 2H), 7.11 (br d, $J = 5.0$ Hz, 1H), 7.03 (br d, $J = 5.1$ Hz, 1H), 6.82 (br d, $J = 3.3$ Hz, 2H), 6.79 (dd, $J = 5.0$, 3.6 Hz, 1H), 6.70 (dd, 5.1, 3.6 Hz, 1H), 5.75 (d, $J = 11.1$ Hz, 1H), 5.56 (d, $J = 4.8$ Hz, 1H), 5.50 (dd, $J = 13.8$, 3.8 Hz, 1H), 5.42 (dd, $J = 14.1$, 3.0 Hz, 1H), 5.18 (dd, $J = 7.9$, 5.9 Hz, 1H), 5.12 (dd, $J = 8.2$, 5.9 Hz, 1H), 4.90 (ddd, $J = 9.8$, 4.6, 3.1 Hz, 1H), 4.82 ppm (ddd, $J = 11.0$, 9.7, 3.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of diastereoisomers): $\delta = 192.0$, 190.8, 138.4, 137.8, 137.2, 137.1, 136.5, 136.4, 135.0, 134.8, 134.5, 134.0, 129.9, 129.5, 129.3, 129.1, 128.9, 128.7, 128.6, 128.5, 128.4, 127.4, 127.2, 126.2, 126.1, 78.5, 77.7, 71.7, 71.1, 38.9, 38.1 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{20}H_{17}NO_5S_2{\cdot}Na^+$: 438.0446 $[M+Na]^+$; found: 438.0437.

(2*R*/2*S*,3*R*)-3-Nitromethyl-1-phenyl-2-(phenylsulfonyl)hexan-1-one (3k): According to the general procedure using catalyst **4c**, compound **3k** was obtained after purification by column chromatography (hexane/EtOAc 3:1) as a yellow gum and a 63:27 mixture of diastereoisomers (82% yield). ^{1}H NMR (300 MHz, $CDCl_3$) (major diastereoisomer): $\delta = 7.76$ (d, $J = 7.3$ Hz, 2H), 7.66–7.20 (m, 8H), 5.26 (d, $J = 4.4$ Hz, 1H), 5.19 (dd, $J = 14.3$, 3.1 Hz, 1H), 4.46 (dd, $J = 14.3$, 8.1 Hz, 1H), 3.15–3.00 (m, 1H), 1.54–1.34 (m, 2H), 1.28–1.15 (m, 2H), 0.73 ppm (t, $J = 7.2$ Hz, 3H); ^{1}H NMR (300 MHz, $CDCl_3$) (minor diastereoisomer): $\delta = 7.68$ (d, $J = 7.2$ Hz, 2H), 7.66–7.20 (m, 8H), 5.59 (d, $J = 9.1$ Hz, 1H), 5.08 (dd, $J = 14.5$, 5.1 Hz, 1H), 4.89 (dd, $J = 14.5$, 4.2 Hz, 1H), 3.15–3.00 (m, 1H), 1.54–1.34 (m, 2H), 1.28–1.15 (m, 2H), 0.72 ppm (t, $J = 6.7$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of diastereoisomers): $\delta = 192.1$, 192.0, 137.6, 137.4, 137.0, 136.7, 134.7, 134.5, 134.4, 134.3, 129.5, 129.4, 129.2, 129.1, 129.0, 128.8, 128.7, 128.5, 76.4, 74.7, 69.1 (2C), 36.9, 36.5, 33.1, 31.5, 19.8, 19.7, 13.7, 13.4 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{19}H_{21}NO_5S{\cdot}H^+$: 376.1213 $[M+H]^+$; found: 376.1212.

(2*R*/2*S*,3*R*)-5-Nitro-4-phenyl-3-(4-tolylsulfonyl)pentan-2-one (3l): According to the general procedure using catalyst **4c**, compound **3l** was obtained after purification by column chromatography (dichloromethane/pentane 3:1) as a white solid and a 60:40 mixture of diastereoisomers (86% yield). ^{1}H NMR (300 MHz, $CDCl_3$) (major diastereoisomer): $\delta = 7.72$ (d, $J = 4.9$ Hz, 2H), 7.41 (d, $J = 8.0$ Hz, 2H), 7.36–7.20 (m, 3H), 7.16–7.10 (m, 2H), 5.47 (dd, $J = 13.2$, 4.1 Hz, 1H), 4.91 (dd, $J = 13.2$, 10.7 Hz, 1H), 4.67–4.59 (m, 1H), 4.22–4.08 (m, 1H), 2.49 (s, 3H), 1.79 ppm (s, 3H); ^{1}H NMR (300 MHz, $CDCl_3$) (minor diastereoisomer): $\delta = 7.64$ (d, $J = 4.9$ Hz, 2H), 7.36–7.20 (m, 3H), 7.16–7.10 (m, 2H), 7.01–6.94 (m, 2H), 5.06–5.00 (m, 2H), 4.67–4.59 (m, 1H), 4.22–4.08 (m, 1H), 2.46 (s, 3H), 2.27 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of diastereoisomers): $\delta = 200.0$, 198.3, 146.5, 146.0, 135.7, 134.8, 134.6, 133.2, 130.1, 129.5, 129.4, 129.3, 129.0, 128.8, 128.6, 128.2, 127.5, 125.9, 78.0, 76.5, 76.4, 76.2, 42.3, 42.2, 34.2, 32.1, 21.8, 21.7 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{18}H_{19}NO_5S{\cdot}Na^+$: 384.0882; found: 384.0876 $[M+Na]^+$; elemental analysis (%) calcd for $C_{18}H_{19}NO_5S$ (361.41): C 59.82, H 5.30, N 3.88; found: C 59.41, H 4.98, N 3.71.

(2*R*/2*S*,3*R*)-2-(Naphthalen-2-ylsulfonyl)-4-nitro-1,3-diphenylbutan-1-one (3m): According to the general procedure using catalyst **4c** at room temperature, compound **3m** was obtained after purification by column chromatography (dichloromethane/pentane 2:1) as a white solid and a 58:42 mixture of diastereoisomers (73% yield). ^{1}H NMR (300 MHz, [D$_6$]DMSO) (major diastereoisomer): $\delta = 8.51$ (s, 1H), 8.09 (d, $J = 8.2$ Hz, 2H), 8.06–7.89 (m, 2H), 7.83–7.55 (m, 4H), 7.50 (t, $J = 7.5$ Hz, 2H), 7.32–7.17 (m, 3H), 7.12–7.01 (m, 3H), 6.58 (d, $J = 11.1$ Hz, 1H), 5.87–5.72 (m, 1H), 5.21 (t, $J = 12.5$ Hz, 1H), 4.16 ppm (td, $J = 11.1$, 3.9 Hz, 1H); ^{1}H NMR (300 MHz, [D$_6$]DMSO) (minor diastereoisomer): $\delta = 8.17$ (d, $J = 7.9$ Hz, 2H), 8.06–7.89 (m, 2H), 7.83–7.55 (m, 5H), 7.38 (t, $J = 7.2$ Hz, 2H), 7.32–7.17 (m, 3H), 7.01–6.90 (m, 3H), 6.25 (d, $J = 9.3$ Hz, 1H), 5.04–4.83 (m, 2H), 4.41 ppm (td, $J = 9.3$, 5.2 Hz, 1H); ^{13}C NMR (75 MHz, [D$_6$]DMSO): $\delta = 191.9$, 191.1, 136.9, 136.1, 135.7, 135.5, 135.1, 134.6, 134.5, 133.9, 133.4, 131.8, 131.4, 131.2, 130.4, 130.0, 129.7, 129.3, 129.2, 129.1, 128.7, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 123.7, 122.4, 78.5, 77.8, 69.3, 68.9, 43.6, 43.3 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{26}H_{21}NO_5S{\cdot}Na^+$: 482.1038 $[M+Na]^+$; found: 482.1033.

General procedure for the synthesis of nitrones 5: Activated Zn[15] (450 mg) and saturated NH_4Cl (7.0 mL) were added at room temperature to an ordinary flask equipped with a magnetic stirring bar charged with sulfone **3a–m** (0.1 mmol) and THF (7.0 mL). The reaction was followed by TLC analysis (usually 1–30 min), and the crude reaction mixture was filtered through celite and washed with dichloromethane (30 mL). The organic phase was separated and the aqueous phase was extracted with dichloromethane (20 mL). The organic phases are collected, dried over anhydrous Na_2SO_4, filtered, and the solvent was removed under reduced pressure. The residue was purified by column chromatography, thus leading to the corresponding nitrone **5** as a single diastereoisomer (d.r. > 98:2).

(3*R*,4*S*)-3,5-Diphenyl-4-(phenylsulfonyl)-3,4-dihydro-2*H*-pyrroline-1-oxide (5a): According to the general procedure, compound **5a** was obtained after purification by column chromatography (hexane/EtOAc 3:1) as a white solid and a single diastereoisomer (55% yield). Upon a single recrystallization from CH_2Cl_2/pentane of a sample (e.r. = 97:3, 300 mg), compound **5a** was obtained with e.r. > 99.5:0.5 (231 mg, 77%). M.p. 157–159 °C; $[\alpha]^{20}_D = +16.7$ ($c = 0.21$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.94$ (d, $J = 8.7$ Hz, 2H), 7.68 (d, $J = 8.5$ Hz, 2H), 7.54 (t, $J = 7.5$ Hz, 1H), 7.38–7.17 (m, 10H), 4.86 (s, 1H), 4.68 (br dd, $J = 14.3$, 7.8 Hz, 1H), 4.28 (d, $J = 7.7$ Hz, 1H), 4.40 ppm (br d, $J = 14.5$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 141.0$, 137.0, 134.4, 133.7, 130.2, 129.6, 129.2, 120.0, 128.2, 128.1, 127.4, 126.1, 69.9, 37.7, 29.6 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{22}H_{19}NO_3S{\cdot}H^+$: 378.1158 $[M+H]^+$; found: 378.1142; elemental analysis (%) calcd for $C_{22}H_{19}NO_3S$ (377.46): C 70.00, H 5.07, N 3.71; found: C 69.77, H 4.79, N 3.53; HPLC analysis on a Chiralcel IB column (hexane/*i*PrOH 90:10); flow rate = 1.0 mL min^{-1}; $\tau_{major} = 35.4$, $\tau_{minor} = 47.9$ min (e.r. > 99.5:0.5).

(3*S*,4*R*)-3-(4-Methoxyphenyl)-5-phenyl-4-(phenylsulfonyl)-3,4-dihydro-2*H*-pyrroline-1-oxide (*ent*-5b): According to the general procedure, compound ***ent*-5b** was obtained after filtration through a short pad of silica gel as a yellow solid and a single diastereoisomer (84% yield). M.p. 166–168 °C; $[\alpha]^{20}_D = +6.8$ ($c = 0.10$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$

8.10 (d, $J=7.3$ Hz, 2H), 7.83 (d, $J=7.90$ Hz, 2H), 7.72–7.35 (m, 6H), 7.26 (d, $J=8.6$ Hz, 2H), 6.97 (d, $J=8.5$ Hz, 2H), 4.98 (s, 1H), 4.82 (dd, $J=14.2$, 7.9, Hz, 1H), 4.39 (d, $J=7.7$ Hz, 1H), 4.27 (d, $J=15.3$ Hz, 1H), 3.93 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=160.3$, 137.0, 134.4, 134.2, 133.0, 130.3, 129.2, 129.0, 128.2, 127.7, 127.6, 127.3, 114.9, 70.0, 55.2, 37.0, 30.1 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{23}H_{21}NO_4S\cdot H^+$: 408.1264 $[M+H]^+$; found: 480.1267; HPLC analysis on a Chiralcel IB column (hexane/*i*PrOH 90:10); flow rate = 1.0 mL min^{-1}; $\tau_{minor}=52.3$, $\tau_{major}=71.7$ min (e.r. = 16:84).

(3*R*,4*S*)-5-Phenyl-4-(phenylsulfonyl)-3-*para*-tolyl-3,4-dihydro-2*H*-pyrroline-1-oxide (5c): According to the general procedure, compound **5c** was obtained after filtration through a short pad of silica gel as a brown oil and a single diastereoisomer (71% yield). $[\alpha]^{20}_D=-6.2$ ($c=0.10$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.93$ (d, $J=7.2$ Hz, 2H), 7.67 (br d, $J=8.1$ Hz, 2H), 7.54 (t, $J=7.5$ Hz, 1H), 7.38–6.98 (m, 9H), 4.83 (s, 1H), 4.66 (br dd, $J=14.4$, 7.9 Hz, 1H), 4.23 (d, $J=7.7$ Hz, 1H), 4.13 (br d, $J=14.5$ Hz, 1H), 2.30 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$ 138.0, 17.8, 136.9, 134.4, 134.3, 130.2, 130.1, 129.1, 128.9, 128.0, 127.5, 125.9, 69.8, 53.3, 29.6, 21.0 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{23}H_{21}NO_3S\cdot Na^+$: 414.1134 $[M+Na]^+$; found: 414.1137; HPLC analysis on a Chiralcel IB column (hexane/*i*PrOH 90:10); flow rate = 1.0 mL min^{-1}; $\tau_{major}=35.4$, $\tau_{minor}=50.7$ min (e.r. = 83:17).

(3*R*,4*S*)-3-(4-Chlorophenyl)-5-phenyl-4-(phenylsulfonyl)-3,4-dihydro-2*H*-pyrroline-1-oxide (5d): According to the general procedure, compound **5d** was obtained after purification by column chromatography (hexane/EtOAc 3:1) as a yellow oil and a single diastereoisomer (85% yield). $[\alpha]^{20}_D=-1.0$ ($c=0.10$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.90$ (d, $J=8.7$ Hz, 2H), 7.64 (br d, $J=8.0$ Hz, 2H), 7.50–7.07 (m, 10H), 4.78 (s, 1H), 4.68 (dd, $J=9.1$, 8.0 Hz, 1H), 4.27 (d, $J=7.6$ Hz, 1H), 7.07 ppm (br d, $J=15.0$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=139.0$, 136.4, 135.4, 134.1, 133.8, 129.9, 129.4, 128.8, 128.6, 127.3, 127.2, 126.9, 125.1, 69.3, 36.8, 28.8 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{22}H_{18}ClNO_3S\cdot H^+$: 412.0768 $[M+H]^+$; found: 412.0758; HPLC analysis on a Chiralcel IB column (hexane/*i*PrOH 90:10); flow rate = 1.0 mL min^{-1}; $\tau_{major}=45.7$, $\tau_{minor}=69.4$ min (e.r. = 80:20).

(3*R*,4*S*)-3-(2-Chlorophenyl)-5-phenyl-4-(phenylsulfonyl)-3,4-dihydro-2*H*-pyrroline-1-oxide (5e): According to the general procedure, compound **5e** was obtained after purification by column chromatography (pentane/EtOAc 3:1) as a white solid and a single diastereoisomer (87% yield). Upon a single crystallization from CH_2Cl_2/pentane of a sample (e.r. = 82:18, 98 mg), compound **5e** was obtained with e.r. > 99:1 (58.7 mg, 60%). M.p. > 190 °C (decomp); $[\alpha]^{20}_D=+7.3$ ($c=0.11$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.03$–8.01 (m, 2H), 7.75–7.73 (m, 2H), 7.66 (t, $J=1.6$ Hz, 1H), 7.59–7.55 (m, 1H), 7.35 (dd, $J=7.9$, 1.5 Hz, 1H), 7.32 (br d, $J=6.9$ Hz, 1H), 7.26–7.25 (m, 1H), 7.22 (dd, $J=6.6$, 1.7 Hz, 1H), 7.18 (dd, $J=7.5$, 1.5 Hz, 1H), 7.09 (dd, $J=7.7$, 1.7 Hz, 1H), 4.96 (s, 1H), 4.78–4.72 (m, 2H), 4.02 ppm (dt, $J=7.9$, 6.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=138.0$, 137. 2, 134.7, 133.4, 130.6, 130.5, 129.7, 129.5, 129.3, 128.4, 128.2, 127.7, 127.6, 127.0, 75.1, 69.8, 69.6, 35.2 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{22}H_{18}ClNO_3S\cdot Na^+$: 434.0594 $[M+Na]^+$; found: 434.0581; HPLC analysis on a Chiralpack AD-H column (hexane/*i*PrOH 80:20); flow rate = 0.9 mL min^{-1}; $\tau_{minor}=43.1$, $\tau_{major}=46.0$ min (e.r. > 99:1).

(3*R*,4*S*)-3-(4-Fluorophenyl)-5-phenyl-4-(phenylsulfonyl)-3,4-dihydro-2*H*-pyrroline-1-oxide (5f): According to the general procedure, compound **5f** was obtained after purification by column chromatography (hexane/EtOAc 3:1) as a yellow oil and a single diastereoisomer (76% yield). $[\alpha]^{20}_D=-2.2$ ($c=0.10$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.91$ (d, $J=7.3$ Hz, 2H), 7.66 (d, $J=7.3$ Hz, 2H), 7.55–6.98 (m, 10H), 4.80 (s, 1H), 4.68 (dd, $J=14.5$, 7.9 Hz, 1H), 4.28 (d, $J=7.7$ Hz, 1H), 4.08 ppm (d, $J=15.5$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=164.0$, 160.7, 136.8, 136.7 (d, $J_{C-F}=13.5$ Hz), 134.5, 133.8, 130.3, 129.2, 129.0, 128.5, 128.1, 127.9, 127.8, 127.5, 127.4, 116.5 (d, $J_{C-F}=86.0$ Hz), 76.7, 69.9, 37.1 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{22}H_{18}FNO_3S\cdot H^+$: 396.1064 $[M+H]^+$; found: 396.1064; HPLC analysis on a Chiralcel IB column (hexane/*i*PrOH 90:10); flow rate = 1.0 mL min^{-1}; $\tau_{minor}=38.8$, $\tau_{major}=42.7$ min (e.r. = 99:1).

(3*R*,4*S*)-3-(4-Cyanophenyl)-5-phenyl-4-(phenylsulfonyl)-3,4-dihydro-2*H*-pyrroline-1-oxide (5g): According to the general procedure, compound **5g** was obtained after purification by column chromatography (pentane/EtOAc 1:1) as a white solid and a single diastereoisomer (76% yield). $[\alpha]^{20}_D=+5.7$ ($c=0.21$, $CHCl_3$); M.p. > 200 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.89$–7.86 (m. 2H), 7.67–7.64 (m, 4H), 7.58–7.52 (m, 1H), 7.37–7.32 (m, 4H), 7.30–7.26 (m, 1H), 7.24–7.18 (m, 2H), 4.79 (s, 1H), 4.76–4.71 (m, 1H), 4.41–4.35 (m, 1H), 4.15–4.08 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=146.0$, 136.7, 134.9, 133.6, 130.7, 129.5, 129.2, 128.4, 127.4 127.4, 118.2, 112.7, 76.3, 69.4, 37.8 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{23}H_{18}N_2O_3S\cdot Na^+$: 425.0936 $[M+Na]^+$; found: 425.0930; HPLC analysis on a Chiralpack AS-H column (hexane/*i*PrOH 80:20); flow rate = 0.9 mL min^{-1}; $\tau_{major}=13.8$, $\tau_{minor}=17.8$ min (e.r. = 85:15).

(3*R*,4*S*)-5-Phenyl-4-(phenylsulfonyl)-3-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2*H*-pyrroline-1-oxide (5h): According to the general procedure, compound **5h** was obtained after purification by column chromatography (pentane/EtOAc 1:3) as a white solid and a single diastereoisomer (73% yield). M.p. > 174 °C (decomp); $[\alpha]^{20}_D=+8.0$ ($c=0.05$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=7.91$–7.88 (m, 2H), 7.68–7.62 (m, 2H), 7.58–7.52 (m, 1H), 7.38–7.27 (m, 5H), 7.24–7.18 (m, 2H), 4.81 (s, 1H), 4.74 (dd, $J=14.6$, 7.9 Hz, 1H), 4.38 (d, $J=7.7$ Hz, 1H), 4.14 ppm (br d, $J=14.6$ Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=144.9$, 136.9, 134.8, 134.1, 130.9 (q, $J=33.0$ Hz), 130.7, 129.5, 129.2, 128.4, 127.6, 127.5, 126.9 (q, $J=3.8$ Hz), 123.8 (q, $J=271.7$ Hz), 76.6, 76.5, 49.5, 37.7 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): $\delta=-62.77$ ppm (s); HRMS (TOF-MS ES$^+$): calcd for $C_{23}H_{18}F_3NO_3S\cdot Na^+$: 468.0857 $[M+Na]^+$; found: 468.0853; HPLC analysis on a Chiralpack AD-H column (hexane/*i*PrOH 90:10); flow rate = 1.0 mL min^{-1}; $\tau_{minor}=38.6$, $\tau_{major}=40.8$ min (e.r. = 87:13).

(3*R*,4*S*)-3-[3,5-Bis(trifluoromethyl)phenyl]-5-phenyl-4-(phenylsulfonyl)-3,4-dihydro-2 H-pyrroline-1-oxide (5i): According to the general procedure, compound **5i** was obtained after purification by column chromatography (pentane/EtOAc 2:1) as a white solid and a single diastereoisomer (68% yield). Upon a single crystallization from CH_2Cl_2/pentane of a sample (e.r. = 84:16, 114.0 mg, **4c**), compound **5i** was obtained with e.r. = 99:1 (58.7 mg, 51%). (3*R*,4*S*)-**5i**: $[\alpha]^{20}_D=+11.4$ ($c=0.11$, $CHCl_3$). Upon a single crystallization from CH_2Cl_2/pentane of a sample (e.r. = 15:85, 23 mg, **4d**), compound *ent*-**5i** was obtained with e.r. = 4:96 (9.2 mg, 40%). (3*S*,4*R*)-**5i**: $[\alpha]^{20}_D=-7.2$ ($c=0.10$, $CHCl_3$). M.p. > 213 °C (decomp); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=7.89$ (d, $J=7.8$ Hz, 2H), 7.86 (s, 1H), 7.67 (d, $J=7.7$ Hz, 2H), 7.64 (s, 2H), 7.57 (t, $J=7.4$ Hz, 1H), 7.37 (t, $J=7.7$ Hz, 2H), 7.31 (t, $J=7.3$ Hz, 1H), 7.23 (t, $J=7.6$ Hz, 2H), 4.83 (s, 1H), 4.79 (dd, $J=14.7$, 8.2 Hz, 1H), 4.48 (d, $J=7.9$ Hz, 1H), 4.18 ppm (d, $J=15.6$ Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=143.4$, 136.6, 135.0, 133.6, 133.3 (q, $J=33.8$ Hz), 130.8, 129.5, 129.5, 129.3, 129.3, 128.5, 128.5, 127.5, 127.3, 126.9 (br q, $J=3.5$ Hz), 122.9 (q, $J=273.1$ Hz), 122.7 (sept, $J=3.8$ Hz), 76.3, 69.2, 37.5 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): $\delta=-62.89$ ppm (s); HRMS (TOF-MS ES$^+$): calcd for $C_{24}H_{17}F_6NO_3S\cdot Na^+$: 536.0731 $[M+Na]^+$; found: 536.0726; HPLC analysis on a Chiralpack AD-H column (hexane/*i*PrOH 80:20); flow rate = 0.5 mL min^{-1}; $\tau_{major}=12.2$, $\tau_{minor}=15.6$ min (e.r. = 99:1).

(3*R*,4*S*)-5-Phenyl-4-(phenylsulfonyl)-3-(thiophen-2-yl)-3,4-dihydro-2*H*-pyrroline- 1-oxide (5j): According to the general procedure, compound **5j** was obtained after purification by column chromatography (pentane/EtOAc 2:1) as a white solid and a single diastereoisomer (86% yield). Upon a single crystallization from CH_2Cl_2/pentane of a sample (e.r. = 80:20, 65.0 mg, **4c**), compound **5j** was obtained with e.r. = 99:1 (34.8 mg, 54%). (3*R*,4*S*)-**5j**: $[\alpha]^{20}_D=-43.3$ ($c=0.12$, $CHCl_3$). Upon a single crystallization from CH_2Cl_2/pentane of a sample (19:81% *ee*, 15 mg, **4d**), compound *ent*-**5j** was obtained with e.r. = 2:98 (6.5 mg, 43%). (3*S*,4*R*)-**5j**: $[\alpha]^{20}_D=+33.0$ ($c=0.14$, $CHCl_3$); M.p. > 158 C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.97$–7.93 (m, 2H), 7.69–7.66 (m, 2H), 7.55 (br t, $J=7.6$ Hz, 1H), 7.38–7.33 (m, 2H), 7.32–7.27 (m, 1H), 7.25–7.18 (m, 3H), 6.96–6.92 (m, 2H), 4.97 (s, 1H), 4.72 (br dd, $J=14.1$, 7.6 Hz, 1H), 4.60 (d, $J=7.6$ Hz, 1H), 4.12 ppm (br d, $J=14.1$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=143.5$, 137.0, 134.7, 133.7, 130.4, 129.4, 129.2, 128.4, 127.8, 127.5, 125.3, 124.9, 110.1, 76.8, 70.9, 34.2 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{22}H_{20}NO_3S\cdot Na^+$: 406.0548 $[M+Na]^+$; found: 406.0542; elemental analysis (%) calcd for $C_{20}H_{17}NO_3S_2$ (383.48): C 62.64, H 4.47, N 3.65; found: C 62.23, H 4.16, N 3.33; HPLC analysis on a Chiralpack

AD-H column (hexane/*i*PrOH 70:30); flow rate = 0.8 mL min^{-1}; τ_{minor} = 40.2, τ_{major} = 53.4 min (e.r. = 99:1).

(3*R*,4*S*)-3-Phenyl-4-(phenylsulfonyl)-5-propyl-3,4-dihydro-2*H*-pyrroline-1-oxide (5k): According to the general procedure, compound **5k** was obtained after purification by column chromatography (hexane/EtOAc 3:1) as a yellow oil and a single diastereoisomer (70% yield). $[\alpha]^{20}_D = -2.1$ ($c = 0.10$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.30$ (d, $J = 7.9$ Hz, 2H), 7.56 (d, $J = 7.1$ Hz, 2H), 7.50–7.10 (m, 6H), 4.58 (s, 1H), 4.17 (dd, $J = 14.3$, 8.6 Hz, 1H), 3.65 ppm (d, $J = 14.1$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 137.0$, 134.5, 134.3, 130.2, 129.1, 128.8, 127.9, 127.5, 125.4, 74.1, 68.6, 37.0, 29.5, 19.3, 13.5 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{19}H_{20}NO_3S{\cdot}H^+$: 343.1242 [*M*+H]$^+$; found: 344.1260; HPLC analysis on a Chiralcel OD column (hexane/*i*PrOH 90:10); flow rate = 1.0 mL min^{-1}; τ_{minor} = 45.5, τ_{major} = 49.5 (e.r. = 83:17).

(3*R*,4*S*)-5-Methyl-3-phenyl-4-(4-tolylsulfonyl)-3,4-dihydro-2*H*-pyrroline-1-oxide (5l): According to the general procedure (2 min), compound **5l** and cyclic imine **7l** were obtained after purification by column chromatography (pentane/EtOAc 3:1) as a white solid and a single diastereoisomer (**5l**: 34%, **7l**: 56%). M.p. 109–110 °C; $[\alpha]^{20}_D = -15.6$ ($c = 0.20$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.75$ (d, $J = 8.3$ Hz, 2H), 7.34 (d, $J = 8.0$ Hz, 2H), 7.21–7.14 (m, 3H), 6.81–6.72 (m, 2H), 4.23 (d, $J = 3.3$ Hz, 1H), 3.99–3.91 (m, 2H), 3.70–3.60 (m, 1H), 2.45 (s, 3H), 2.37 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 145.4$, 142.2, 134.4, 130.0, 129.0, 128.7, 127.2, 126.2, 83.4, 67.5, 46.4, 21.7, 20.3 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{18}H_{19}NO_3S{\cdot}Na^+$: 352.0983 [*M*+Na]$^+$; found: 352.0978; HPLC analysis on a Chiralpack AD-H column (hexane/*i*PrOH 85:15); flow rate = 0.9 mL min^{-1}; τ_{minor} = 10.9, τ_{major} = 11.7 min (e.r. = 82:18).

(3*R*,4*S*)-5-Methyl-3-phenyl-4-(4-tolylsulfonyl)-3,4-dihydro-2*H*-pyrrole (7l): M.p. 161–163 °C; $[\alpha]^{20}_D = -2.4$ ($c = 0.32$, $CHCl_3$); ^{1}H NMR(300 MHz, $CDCl_3$): $\delta = 7.72$ (d, $J = 8.3$ Hz, 2H), 7.35 (d, $J = 8.0$ Hz, 2H), 7.27–7.16 (m, 3H), 6.98–6.86 (m, 2H), 4.18 (s, 1H), 4.07–3.94 (m, 1H), 3.89–3.75 (m, 2H), 2.42 (s, 3H), 2.07 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 146.3$, 140.6, 136.2, 133.6, 130.4, 129.5, 128.8, 128.1, 126.0, 78.6, 67.2, 38.6, 21.8, 12.9 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{18}H_{19}NO_2S{\cdot}Na^+$: 336.1034 [*M*+Na]$^+$; found: 336.1029.

(3*R*,4*S*)-4-(Naphthalen-2-ylsulfonyl)-3,5-diphenyl-3,4-dihydro-2*H*-pyrroline-1-oxide (5m): According to the general procedure, compound **5m** was obtained after purification by column chromatography (pentane/EtOAc 2:1) as a white solid and a single diastereoisomer (57% yield). M.p. >190 °C (decomp); $[\alpha]^{20}_D = +1.0$ ($c = 0.14$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.19$ (br s, 1H), 7.82–7.66 (m, 5H), 7.77–7.51 (m, 3H), 7.40–7.29 (m, 3H), 7.24–7.17 (m, 2H), 7.02–6.94 (m, 3H), 4.91 (s, 1H), 4.76 (br dd, $J = 14.4$, 7.9 Hz, 1H), 4.37 (d, $J = 7.7$ Hz, 1H), 4.19–4.08 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 141.1$, 135.4, 133.9, 133.6, 131.8, 131.7, 129.9, 129.7, 129.6, 129.5, 129.4, 128.3, 127.9, 127.8, 127.7, 127.6, 127.2, 126.2, 122.9, 76.8, 70.1, 37.6 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{26}H_{21}NO_3S{\cdot}Na^+$: 450.1140 [*M*+Na]$^+$; found: 450.1134; HPLC analysis on a Chiralpack AD-H column (hexane/*i*PrOH 90:10); flow rate = 1.0 mL min^{-1}; τ_{major} = 80.0, τ_{minor} = 85.4 min (e.r. = 76:24).

General procedure for the addition of TMSCN to nitrones 5:[18] TMSCN (60 μL, 0.48 mmol) and $AlMe_3$ (90 μL, 0.18 mmol) were added to a dried Schlenk flask charged with nitrone **5** (0.15 mmol) and THF (2.5 mL), filled with argon, and cooled to −20 °C. The reaction mixture was stirred for 5–10 min at −20 °C and then allowed to reach room temperature. After stirring for 2 days, water was added, the organic phase was separated, and the aqueous phase was extracted with EtOAc (3 × 3 mL). The organic phases were collected, dried over anhydrous Na_2SO_4, filtered, and the solvent was removed under reduced pressure, thus obtaining the corresponding products **6** after purification by column chromatography.

(2*R*,3*S*,4*R*)-2,4-Diphenyl-3-(phenylsulfonyl)-1-(trimethylsilyloxy)pyrrolidine-2-carbonitrile (6a): According to the general procedure, compound **6a** was obtained from **5a** (e.r. > 99:1, **4c**) after purification by column chromatography (pentane/EtOAc 10:1) as a white solid and a 95:5 mixture of diastereoisomers (78% yield). M.p. 173–175 °C; $[\alpha]^{20}_D = +120.0$ ($c = 0.10$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) (major isomer): $\delta = 7.72$–7.66 (m, 2H), 7.40–7.28 (m, 6H), 7.28–7.12 (m, 7H), 4.48 (d, $J = 8.1$ Hz, 1H), 4.06 (dt, $J = 10.5$, 7.9 Hz, 1H), 3.85 (dd, $J = 9.9$, 7.7 Hz, 1H), 3.34 (t, $J = 10.3$ Hz, 1H), 0.06 ppm (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 138.6$, 138.5, 133.2, 130.8, 129.7, 129.6, 128.9, 127.8, 127.8, 127.6, 127.6, 117.9, 75.4, 63.9, 42.1, 0.00 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{26}H_{28}N_2O_3SSi{\cdot}Na^+$: 499.1488 [*M*+Na]$^+$; found: 499.1482.

(2*R*,3*S*,4*R*)-4-(2-Chlorophenyl)-2-phenyl-3-(phenylsulfonyl)-1-(trimethylsilyloxy)pyrrolidine-2-carbonitrile (6e): According to the general procedure, compound **6e** was obtained from **5e** (e.r. > 99:1, **4c**) after purification by column chromatography (pentane/EtOAc 10:1) as a white solid and a 90:10 mixture of isomers (67% yield). M.p. 153–156 °C; $[\alpha]^{20}_D = +78.2$ ($c = 0.11$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) (major isomer): $\delta = 7.78$ (dd, $J = 7.9$, 1.7 Hz, 2H), 7.42–7.09 (m, 11H), 7.04 (td, $J = 7.6$, 1.7 Hz, 1H), 4.70–4.50 (m, 2H), 3.82 (dd, $J = 9.6$, 7.1 Hz, 1H), 3.11 (t, $J = 10.0$ Hz, 1H), 0.00 ppm (s, 9H); ^{1}H NMR (300 MHz, $CDCl_3$) (minor isomer): $\delta = 7.51$ (t, $J = 6.9$ Hz, 2H), 7.42–7.09 (m, 12H), 4.90–4.80 (m, 1H), 4.45 (d, $J = 8.7$ Hz, 1H), 3.80–3.70 (m, 1H), 3.42 (dd, $J = 10.0$, 3.0 Hz, 1H), −0.29 ppm (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of diastereoisomers): $\delta = 138.4$, 135.5, 133.8, 133.4, 130.8, 130.3, 129.8, 129.7, 129.2, 128.8, 128.7, 128.7, 128.6, 128.5, 127.9, 127.8, 127.6, 127.5, 127.3, 117.8, 74.2, 62.7, 38.4, −0.1, −0.8 ppm; HRMS (TOF-MS ES$^+$): calcd for $C_{26}H_{27}{}^{35}ClN_2O_3SSi{\cdot}Na^+$: 533.1098 [*M*+Na]$^+$; found: 533.1092.

(2*R*,3*S*,4*R*)-4-(3,5-Bis(trifluoromethyl)phenyl)-2-phenyl-3-(phenylsulfonyl)-1-(trimethylsilyloxy) pyrrolidine-2-carbonitrile (6i): Compound **6i** was obtained from **5i** (e.r. = 99:1, **4c**) according to the general procedure as a white solid and a 94:6 mixture of isomers (60% yield) after purification by column chromatography (pentane/EtOAc 10:1). M.p. 60–64 °C; $[\alpha]^{20}_D = +28.0$ ($c = 0.35$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) (major isomer): $\delta = 7.82$–7.70 (m, 5H), 7.44–7.28 (m, 6H), 7.24–7.16 (m, 2H), 4.51 (d, $J = 8.5$ Hz, 1H), 4.24 (dd, $J = 17.5$, 8.5 Hz, 1H), 3.90 (dd, $J = 10.8$, 8.1 Hz, 1H), 3.29 (dd, $J = 10.8$, 9.4 Hz, 1H), 0.11 ppm (s, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 141.6$, 138.5, 133.8, 132.3 (q, $J_{C-F} = 32.0$ Hz), 132.0, 130.5, 129.9, 129.4, 129.1, 128.3 (q, $J_{C-F} = 3.7$ Hz), 128.2, 127.6, 123.0 (q, $J_{C-F} = 273.0$ Hz), 121.7 (sept, $J_{C-F} = 3.6$ Hz), 117.7, 77.2, 75.7, 63.5, 42.7, −0.2 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): $\delta = -62.9$ ppm (s); HRMS (TOF-MS ES$^+$): calcd for $C_{28}H_{26}F_6N_2O_3SSi{\cdot}Na^+$: 635.1235 [*M*+Na]$^+$; found: 635.1230.

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