



Depósito de Investigación
Universidad de Sevilla

Depósito de investigación de la Universidad de Sevilla

<https://idus.us.es/>

“This is an Accepted Manuscript of an article published by Royal Society of Chemistry in *Organic and Biomolecular Chemistry* on Fernández, I., Alcudia, A., Gori, B., Valdivia, V., Recio, R., García, M. V. S., & Khiar, N. (2010). Chiral sulfur derivatives in the allylation of acyl hydrazones: C2-symmetric bis-sulfinamides as enhanced chiral organic promoters. *Organic and Biomolecular Chemistry*, 8(19), 4388.., available at: <https://doi.org/10.1039/c0ob00078g>”

Chiral sulfur derivatives in the allylation of acyl hydrazones: C₂-symmetric bis-sulfinamides as enhanced chiral organic promoters.†

Inmaculada Fernández,*^a Ana Alcudia,^a Beatrice Gori,^a Victoria Valdivia,^b Rocío Recio,^a María Victoria García^a and Nouredine Khiar*^b

Monosulfinamides and C₂-symmetric bis-sulfinamides are convenient neutral chiral promoters in the allylation of acyl hydrazones, the nature of the spacer and the substituent at the sulfinyl sulfur are key elements for the enantioselectivity of the process.

Introduction

The preparation of chiral amines, an important structure in drugs or drug candidates, is a standing area of interest in modern organic synthesis.¹ Even though a large variety of organometallic,² and organic³ catalysts were assayed in the hydrogenation of imines, up to now the best approach is the diastereoselective addition of organometallic reagents to sulfinamides chiral at sulfur.⁴ Among the recent methods developed so far, the use of organic Lewis bases to promote the enantioselective allylation of electrophilic imines, hold great promises for the development of an efficient and environmentally benign methods, for these industrially interesting and useful important molecules.⁵ Within a program directed toward the utilization of sulfur based ligand in organic and organometallic catalysis, we have found that ferrocenyl sulfoxides are good promoters of the allylation of hydrazones with allyl trichlorosilane,⁶ extending the pioneering work of Kobayashi, Malkov and Koc̆ovsky', and Rowlands.⁷ In order to determine the mechanism of the reaction and to develop a catalytic approximation of the process, we have recently shown that C₂-symmetric ethylene-bridged bis-sulfoxides, can catalyse the reaction with excellent enantioselectivities with only half equivalent than the corresponding monosulfoxides.⁸ Based on these findings, and taking into account that in comparison to sulfoxides ligands, the sulfinyl oxygen in sulfinamides is presumably more Lewis basic, in the present study we report our results on the allylation of acyl hydrazone type **I** with trichloroallyl silane **1**, using as promoters a wide range of enantiomerically pure sulfinamides and C₂-symmetric bis-sulfinamides⁹ (Fig. 1), prepared in a very convenient and rapid manner.

Results and discussion

In the first part of the present study we have evaluated the behaviour of free and alkylated monosulfinamides as potential

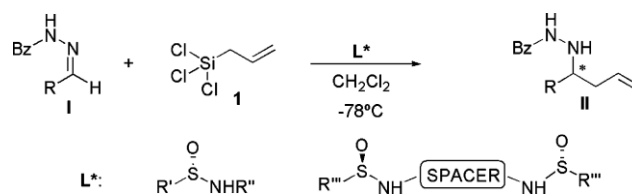
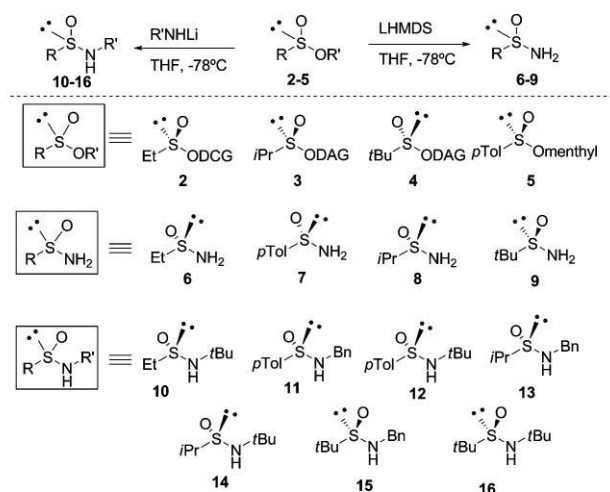


Fig. 1 Structure of monosulfinamides and C₂-symmetric bis-sulfinamides used as chiral promoters in allylation of benzoyl hydrazones.

ligands. The synthesis of *S*-chiral sulfinamides in optically pure form has been carried out in high yields and enantioselectivities by rapid condensation of LHMDS¹⁰ with diastereomerically pure dicyclohexylidene- or diacetone-D-glucose alkanesulfinates **2–4**,¹¹ or (*S*)-menthyl *p*-toluenesulfinate **5**¹² at -78 °C. By simply suspending the crude reaction mixture in silica gel, followed by filtration and crystallization, the corresponding sulfinamides **6–9** were obtained with good yields and enantioselectivities (Scheme 1). On the other hand the preparation of *N*-alkylated sulfinamides **10–16** has been achieved by adding freshly prepared lithium benzyl- or *tert*-butylamide to diastereomerically pure sulfinate esters at -78 °C.¹³



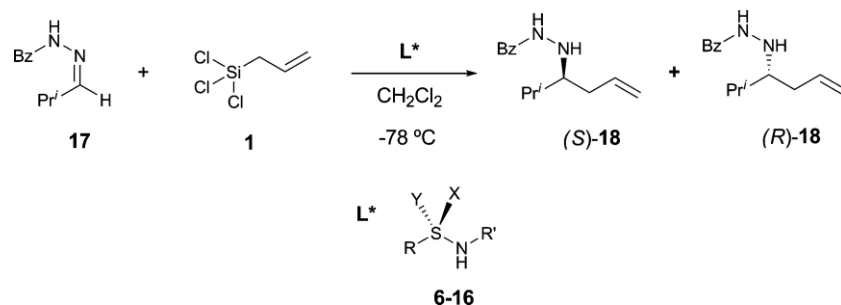
DAGOH: Diacetone-D-glucose
DCGOH: Dicyclohexylidene-D-glucose

Scheme 1 Asymmetric synthesis of sulfinamides used in this study.

^aDepartamento de Química Orgánica y Farmacéutica, Facultad de Farmacia, Universidad de Sevilla, 41012 Sevilla, Spain. E-mail: inmaff@us.es; Fax: (+) 34 95 455 67 37; Tel: (+)34 95 455 59 93

^bInstituto de Investigaciones Químicas, C.S.I.C.-Universidad de Sevilla, c/Americo Vespucio, s/n., Isla de la Cartuja, 41092 Sevilla, Spain. E-mail: khiar@iiq.csic.es; Fax: (+) 34 95 446 05 65; Tel: (+) 34 95 448 95 59

† Electronic supplementary information (ESI) available: Full experimental procedures, characterization data and copies of NMR spectra for all compounds. See DOI: 10.1039/c0ob00078g

Table 1 Enantioselective allylation of **17** using sulfinamides **6–16**.^a

Entry	L*	R	R _c	X	Y	ee.L* ^c (%)	(h)	Yield (%) ^b	ee 18 ^c (conf)
1	6	Et	H	Σ	O	99.9	0.5	50	7 (<i>S</i>)
2	7	<i>p</i> -Tol	H	Σ	O	96.0	0.5	60	74 (<i>S</i>)
3	8	<i>i</i> -Pr	H	Σ	O	94.0	0.6	80	56 (<i>S</i>)
4	9	<i>t</i> -Bu	H	∩	Σ	99.9	0.7	100	82 (<i>R</i>)
5	10	Et	<i>t</i> -Bu	Σ	O	96.0	0.5	73	30 (<i>S</i>)
6	11	<i>p</i> -Tol	Bn	Σ	O	98.0	0.5	81	6 (<i>S</i>)
7	12	<i>p</i> -Tol	<i>t</i> -Bu	Σ	O	98.0	0.5	91	0 (<i>S</i>)
8	13	<i>i</i> -Pr	Bn	Σ	O	100	1.0	76	72 (<i>S</i>)
9	14	<i>i</i> -Pr	<i>t</i> -Bu	Σ	O	—	1.5	92	70 (<i>S</i>)
10	15	<i>t</i> -Bu	Bn	O	Σ	90.0	0.5	90	80 (<i>R</i>)
11	16	<i>t</i> -Bu	<i>t</i> -Bu	O	Σ	—	24	84	84 (<i>R</i>)

^a Reactions were conducted in presence of 3.0 equiv. of L* and 0.5 equiv. of 2-methyl-2-butene in order to suppress ligand racemization. [L*] = 0.46 M.

^b Isolated yield. ^c Enantiomeric excesses were determined by HPLC (chiralpak column).

Using the best conditions previously reported for the reaction of allylation,⁸ we underwent a comparative study of the effect of the substituent at the sulfinyl sulfur and the amidic nitrogen on the stereoselectivity, the results are reported in Table 1. As already observed in previous studies, the concentration of the ligand in the reaction is critical, being 3 equivalents of the ligand in a 0.46 M solution, the best concentration for a good enantioselectivity. Any decrease in this concentration or in the number of equivalents of ligand led to a enantioselectivity drop.

From the analysis of the results summarized in Table 1, some general conclusions can be drawn. The first one is that simple sulfinamides **6–9** are able to catalyze the reaction affording the allylated product is in moderate to high chemical yields (Table 1, entries 1-4). Interestingly, the reaction takes place in short reaction times and the catalysts can be recovered from the crude reaction mixtures by column chromatography. The second observation is the clear significance of the substituent at the sulfinyl sulfur on the enantioselectivity of the process. Surprisingly, the influence the size difference between the substituents at the sulfinyl sulfur on the enantioselectivity is the opposite to that observed in the case of sulfoxides. Thus, while in the case of using sulfoxides as organic ligands, the highest ees were obtained with those having small sulfur substituents, in the case of sulfinamides sterically less demanding ethylsulfinamides **6** and **10** (Table 1, entries 1), afforded the allylated hydrazine with the lowest ees. On the contrary, the highest enantioselectivities (80–84% ee) were obtained with the bulkier *tert*-butylsulfinamides **9** (Table 1, entries 4). The same behaviour is maintained in the case N-substituted sulfinamides **10–16** (Table 1, entries 5–11), where sterically hindered sulfinamides **15** and **16** afforded the best enantioselectivities (Table 1, entries 10 and 11). On the other hand, there is no coherent relationship between the size or the electronic nature of the substituent on the

nitrogen and the enantioselectivity of the process (compare for instance in Table 1, entries 1 with 5, and 2 with 7).

We have recently presented compelling data indicating a dual pathway in the allylation of benzoyl hydrazones with allyl trichlorosilane using sulfoxide as organic ligands. The results summarized in Table 1 point out a similar behavior to that of sulfinamides ligands. Taking into account that a non-linear effect (NLE) is an important aspect in mechanistic studies,¹⁴ we decided to study the influence of the enantiopurity of the sulfinamide ligands on enantioselectivity of the allylated product. While non impressive, the reaction exhibits a small negative NLE with regard to enantiopurity of (*S*)-*N*-benzyl isopropylsulfinamide **13** used as ligand, as is shown in Fig. 2. This proves that other species

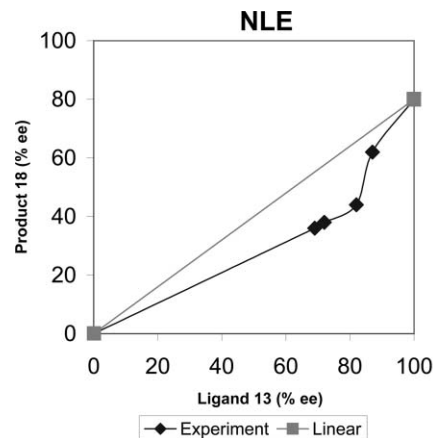
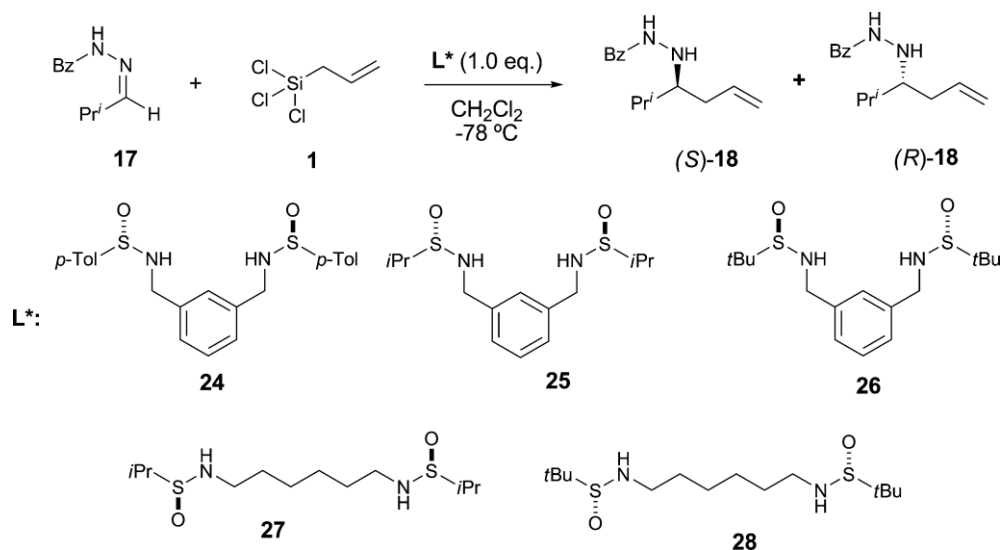
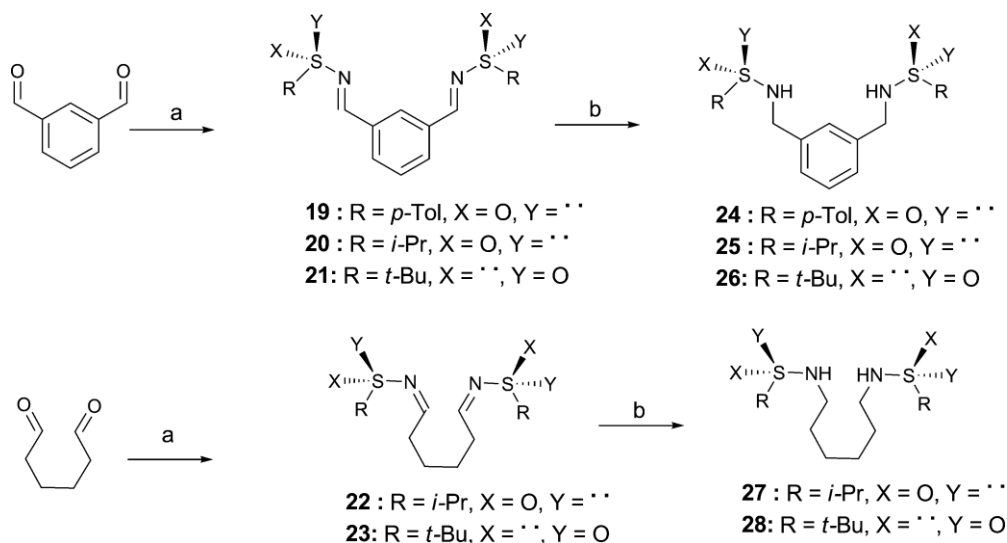


Fig. 2 Graph of allylated product **18** enantioselectivity vs. ligand **13** enantiopurity.

Table 2 Enantioselective allylation of **17** using sulfinamides **24–28**

Entry ^a	L*	Time/h	Yield (%) ^b	18S:18R ^c (%)	%e.e. 18 (conf.)
1	24	1	63	54 : 47	7 (<i>S</i>)
2	25	72	67	73 : 27	46 (<i>S</i>)
3	26	36	49	13 : 87	74 (<i>S</i>)
4	27	1	50	75 : 25	50 (<i>S</i>)
5	28	72	70	5 : 95	90 (<i>R</i>)
6	28^d	36	50	15 : 85	70 (<i>R</i>)

^a Reactions were conducted in presence of 0.5 equivalent of 2-methyl-2-butene in order to suppress ligand racemisation. ^b Isolated yield. ^c Enantiomeric excesses were determined by chiral HPLC analysis using Daicel chiralpack AD-column. ^d Reaction conducted in the presence of 0.5 equivalent of ligand.



Scheme 2 Synthesis of C₂-symmetric bis-sulfinamides **24–28**. Reagents and Conditions: a) RS(O)NH₂ (**7–9**), Ti(OEt)₄, THF [**19** (77%); **20** (60%); **21** (72%); **22** (64%); **23** (60%)]. b) NaBH₄, MeOH [**24** (91%); **25** (85%); **26** (85%); **27** (82%); **28** (79%)].

beside a simple monomeric species are present under the reaction conditions, producing different chiral entities.

Based on these precedents, we decided to assay in the same reaction a range of differently substituted C₂-symmetric bis-sulfinamides with two different spacers between the sulfinyl sulfurs. Condensation of sulfinamides **7–9** with isophthalaldehyde or with adipaldehyde using Ti(OEt)₄ as dehydrating reagent in THF,

afforded the corresponding bis-sulfinylimines **19–23** in moderate to good yields, Scheme 2. The reduction of the imine function with sodium borohydride in methanol yields the corresponding bidentate neutral ligands **24–28** in excellent yields, Scheme 2.¹⁵

The ability of the obtained bisulfinamides to act as chiral Lewis base was assayed in the allylation of benzoyl hydrazone **7**, and the results are compiled in Table 2.

Table 3 Asymmetric allylation of hydrazones **17**, **29–32** using bisulfonamide **28** as ligand.^a

$$\text{R-NH-N(R')-C(=O)-H} + \text{Cl}_3\text{Si-CH}_2\text{CH=CH}_2 \xrightarrow[\text{-78 }^\circ\text{C}]{\text{CH}_2\text{Cl}_2, \text{L}^*} \text{R-NH-NH-CH(R')-CH}_2\text{CH=CH}_2 \text{ (S)} + \text{R-NH-NH-CH(R')-CH}_2\text{CH=CH}_2 \text{ (R)}$$

$$\text{L}^*: \text{tBu-S(=O)(NH-CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH-S(=O)tBu)}$$

28

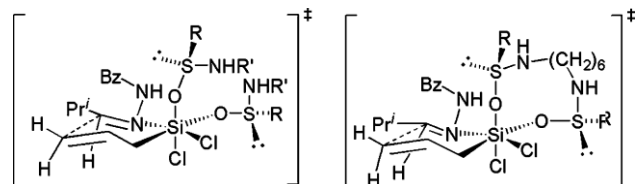
Entry	Hydrazone (R, R')	Hydrazine	Yield ^b (%)	[L*]/M	S:R' (%)	% ee
1	29 (Ac, Ph)	—	—	0.20	—	—
2	17 (Bz, <i>i</i> Pr)	18	70	0.42	5 : 95	90
3	17 (Bz, <i>i</i> Pr)	18	77	0.20	7 : 93	86
4	30 (Bz, <i>c</i> Hex)	33	78	0.20	17 : 83	66
5	31 (Bz, Ph)	34	70	0.15	82 : 18	64
6	32 (Bz, <i>p</i> ClC ₆ H ₄)	35	11	0.20	62 : 38	24

^a Reactions were conducted in presence of 0.5 equivalent of 2-methyl-2-butene in order to suppress ligand racemisation. ^b Isolated yield. ^c Enantiomeric excesses were determined by chiral HPLC analysis using Daicel chiralpak column.

Firstly, regarding the enantioselectivity of the process, the same behaviour previously observed with the monosulfonamide is conserved in the case of bis-sulfonamides. Less sterically demanding ligands, lead to the allylated product with low ees, while enhancing the steric hindrance of the sulfonamide induces an increase in the enantioselectivity. This trend is observed with both kind of ligands, those with an aromatic spacer (Table 2, compare entries 1, 2 and 3), and those with the aliphatic one (Table 2, compare entries 4, and 5). Secondly, the more flexible ligands, namely the bis-sulfonamides with the aliphatic spacer, **27** and **28**, give better results than the aromatic analogs (Table 2, compare entries 3 and 5). Finally, all the bis-sulfonamides gave the allylated product in moderate to good yields and in the case of bis-sulfonamide **28** with an excellent 90% ee (Table 2, entry 5) using only one equivalent of ligand, in contrast to monosulfonamides where 3 equivalents were necessary.

To determine the scope of the reaction, other hydrazones **29–32**¹⁶ were synthesized following the literature procedure, and tested in the allylation reaction using the best ligand **28**, under the optimized reaction conditions, and the results obtained are shown in Table 3. As can be seen from Table 3, both aliphatic and aromatic hydrazones provided good to high enantioselectivities, obtaining the best result in the case of the isopropyl derivative **17**. Interestingly, the allylation of the *p*-chlorophenyl hydrazone **32** gave the corresponding hydrazine **35** in a very low chemical yield and poor stereoselectivity. The acetyl derivative **29** did not react, probably due to stereoelectronic factors.

Taken all together, the results obtained so far can give some insights on the mechanism of the organocatalytic allylation of hydrazones with neutral sulfonamide, unknown for the moment. Firstly, the erosion of the enantioselectivity upon reducing the catalyst loading and upon diluting the reaction medium, suggest the possibility that the reaction could proceed through a dicoordinate transition state, as indicated in Fig. 3. Dicoordinated intermediate can be formed intramolecularly specially in the case

**Fig. 3** Possible dicoordinate transition states for the organocatalytic allylation of hydrazones with sulfonamides.

of bis-sulfonamides with the aliphatic spacer. The observed (-)-NLE point out in the same direction, with several molecules of the chiral ligand involved in the intermediate transition state.

Conclusion

In summary, we have demonstrated that bis-sulfonamides are effective promoters for the allylation of benzoyl hydrazones with allyl trichlorosilane, in highly concentrated conditions. These preliminary studies done in order to rationalize the mechanism of the allylation of benzoyl hydrazones with trichloroallyl silane using chiral sulfur ligands, confirm that a dicoordinate transition is likely to be responsible for the high enantioselectivity observed especially in the case of C₂-symmetric ligands.

Experimental

All reactions were run under an atmosphere of dry argon using oven-dried glassware and freshly distilled and dried solvents over activated molecular sieves. TLC was performed on Silica Gel GF254 (Merck) with detection by charring with phosphomolybdic acid/EtOH. For flash chromatography, silica Gel (Merck 230–400 mesh) was used. Columns were eluted with positive air pressure. Chromatographic eluents are given as volume to volume ratios

(v/v). NMR spectra were recorded with a Bruker AMX500 (^1H , 500 MHz) and Bruker Avance DRX500 (^1H , 500 MHz) spectrometers. Chemical shifts are reported in ppm, and coupling constants are reported in Hz. Routine spectra were referenced to the residual proton or carbon signals of the solvent. High-resolution mass spectra were recorded on a Kratos MS-80RFA 241-MC apparatus. Optical rotations were determined with a Perkin-Elmer 341 polarimeter. The organic extracts were dried over anhydrous sodium sulfate and concentrated *in vacuo*.

Sulfinyl chlorides were obtained by the method reported by Hermann.¹⁷ Optically pure alkanesulfinates were prepared as previously described following DAG methodology.¹¹

Menthyl *p*-toluenesulfinate was prepared as described by Soladie¹² and used as starting material for the synthesis of *N*-alkyl-*p*-toluenesulfonamides **11** and **12** as previously described.¹³

General procedure for the synthesis of *N*-alkyl alkanesulfonamides, **10**, **13–16**.

To a solution of the corresponding amine (2.2 eq.) in THF at $-78\text{ }^\circ\text{C}$, *n*-BuLi (in hexane, 2.0 eq.) was added. The solution was stirred at $-78\text{ }^\circ\text{C}$ for 30 min. and then it was added on a solution of the corresponding alkanesulfinate 2–4 (1 eq.) in THF, and it was stirred until all the starting material is consumed (observed by TLC, AcOEt–CH₂Cl₂, 1 : 4), from 0.5 to 1 h. Then it was quenched with saturated NH₄Cl aqueous solution, extracted with AcOEt, washed with saturated NaHCO₃ aqueous solution and brine. The organic layer was dried over Na₂SO₄ and the solvent evaporated. The residue was purified by flash chromatography.

(*R*)-*N*-*tert*-Butyl *tert*-butylsulfonamide, **16**.

Prepared from *tert*-butylamine and (*R*)-DAG *tert*-butylsulfinate **4**. Time of reaction: 45 min. Purified by cc: AcOEt : Hexane, 1 : 1, to AcOEt. 50% Yield, white solid. M.p. $79\text{--}81\text{ }^\circ\text{C}$. $[\alpha]_{\text{D}}^{20}$: -38 (c 2.0, CHCl₃). $^1\text{H-NMR}$ (500 MHz, CDCl₃) δ : 3.01 (brs, 1H), 1.31 (s, 9H), 1.20 (s, 9H). $^{13}\text{C-NMR}$ (125 MHz, CDCl₃) δ : 55.1, 53.1, 31.0, 22.4. HRMS Calc. for C₈H₂₀NOS (M+H)⁺: 178.1266, Found 178.1265.

General procedure for the synthesis of C₂-symmetric bis-(sulfinyl)hexanediamines, **22**, **23**.

To a solution of the corresponding sulfinamide, **4–7**, (2 eq.) in THF was added Ti(O*i*Pr)₄ (4 eq.), and then 1,6-hexanedialdehyde (1 eq.). When the starting material is consumed (24 h), the reaction is poured into water, and after stirring, filtered through a plug of celite, and the filter cake was washed with AcOEt. The solvent is removed *in vacuo* and the residue purified by flash chromatography (AcOEt:Hexane, 1 : 1, to AcOEt).

(*R,R*)-*N,N* ϵ -Bis-(*tert*-butylsulfinyl)-1,6-hexanediamine, **23**.

60% Yield, colourless oil. $[\alpha]_{\text{D}}^{20}$: -262 (c 0.3, CHCl₃). $^1\text{H-NMR}$ (500 MHz CDCl₃) δ : 8.10 (t, $J = 4.5$ Hz, 2H), 2.61–2.58 (m, 4H), 1.77–1.74 (m, 4H), 1.22(s, 18H). $^{13}\text{C-NMR}$ (125 MHz, CDCl₃) δ : 168.8, 56.5, 35.7, 24.9, 22.3.

General procedure for the synthesis of C₂-symmetric bis-sulfonamides, **24–28**.

To a solution of the corresponding C₂-symmetric bis-sulfinylimine, **19–23**, in MeOH is added at $0\text{ }^\circ\text{C}$, sodium borohydride (2 eq.). After stirring for 30 min, acetone is added and the reaction is stirred another 5 min. The solvent is removed *in vacuo* and the residue is purified by flash chromatography.

(*R,R*)-*N,N* ϵ -Bis-(*tert*-butylsulfinyl)-1,6-hexanediamine, **28**.

79% Yield, white solid. M.p.: $79\text{--}82\text{ }^\circ\text{C}$. $^1\text{H-NMR}$ (500 MHz, CDCl₃) δ : 3.25–3.06 (m, 6H), 1.59 (m, 4H), 1.35 (m, 4H), 1.20 (s, 18H). $^{13}\text{C-NMR}$ (125 MHz, CDCl₃) δ : 55.6, 45.6, 30.9, 26.3, 22.6. HRMS Calc. for C₁₄H₃₃N₂O₂S₂ (M+H)⁺: 325.2064. Found: 325.1985.

Enantioselective allylation of *N*-(benzoyl)isobutylhydrazone.

General method: (Kobayashi conditions) To a solution of *N*-(benzoyl)isobutylhydrazone **17** (20.5 mg, 0.108 mmol), the chiral sulfonamide **6–16** (0.324 mmol) or chiral C₂-symmetric bisulfonamide **24–28** (0.108 mmol), and 2-methyl-2-butene (27 mL, 0.054 mmol) in dichloromethane (0.7 mL) was added allyltrimethylsilane **2** (23 mL, 0.162 mmol) at $-78\text{ }^\circ\text{C}$. After stirred at $-78\text{ }^\circ\text{C}$ for the time indicated in Tables 1 and 2, the reaction was quenched by adding saturated aqueous NaHCO₃ (1 mL). After warmed to room temperature, saturated NaCl aqueous solution was added, and the mixture was extracted with dichloromethane (three times). The combined organic layers were dried over Na₂SO₄, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (AcOEt: hexanes, 1 : 4) to afford the corresponding *N* ϵ -(1-isopropylbut-3-enyl)benzohydrazide **18** in high chemical yields as a white solid, mp $73\text{--}74\text{ }^\circ\text{C}$.

Acknowledgements

We thank the DGICYT for financial support (grant No. CTQ2010-21755-C02-01 and CTQ2010-21755-C02-02) and The Junta de Andalucía (grant P06-FQM-01852 and P07-FQM-2774), B. Gori, M. V. García, V. Valdivia and R. Recio thank respectively, Fundació'n Ramón Areces, CDCH Universidad Central de Venezuela, CSIC and the Junta de Andalucía for predoctoral grants.

References

- (a) D. Enders and V. Reinhold, *Tetrahedron: Asymmetry*, 1997, **8**, 1895; (b) S. Kobayashi and H. Ishitani, *Chem. Rev.*, 1999, **99**, 1069; (c) C. H. Senanayake and D. Krishnamurthy, *Curr. Opin. Drug Discovery Dev.*, 1999, **2**, 590.
- (a) H.-U. Blaser, F. Spindler, in *Comprehensive Asymmetric Catalysis*, E. N. Jacobsen, H. Yamamoto, Eds; Springer Berlin, 1999, **vol. 1**, Chap. 6.2; (b) C. J. Cobley and J. P. Henschke, *Adv. Synth. Catal.*, 2003, **345**, 195; (c) Q. Yang, G. Shang, W. Gao, J. Deng and X. Zhang, *Angew. Chem., Int. Ed.*, 2006, **45**, 3832.
- (a) M. Rueping, C. Azap, E. Sugiono and T. Theissmann, *Synlett*, 2005, **2367**; (b) D. Pei, Z. Wang, S. Wei, Y. Zhang and J. Sun, *Org. Lett.*, 2006, **8**, 5913; (c) S. G. Ouellet, A. M. Walji and D. W.-C. Macmillan, *Acc. Chem. Res.*, 2007, **40**, 1327.
- (a) J. A. Ellman, T.-D. Owens and T. P. Tang, *Acc. Chem. Res.*, 2002, **35**, 984; (b) P. Zhou, B. C. Chen and F. A. Davis, *Tetrahedron*, 2004, **60**, 8003.
- S. Kobayashi, M. Sugiura and C. Ogawa, *Adv. Synth. Catal.*, 2004, **346**, 1023.

-
- 6 (a) I. Fernández, V. Valdivia, B. Gori, F. Alcudia, E. Alvarez and N. Khiar, *Org. Lett.*, 2005, **7**, 1307; (b) For leading references on organocatalytic asymmetric allylation see: F. García-Flores, L.-S. Flores-Michel and E. Juaristi, *Tetrahedron Lett.*, 2006, **47**, 8235; (c) S. B. Jagtap and S. B. Tsogoeva, *Chem. Commun.*, 2006, 4747; (d) P. M. A. Rabbat, S. C. Valdez and J. L. Leighton, *Org. Lett.*, 2006, **8**, 6119; (e) M. Sugiura and S. Kobayashi, *Angew. Chem., Int. Ed.*, 2005, **44**, 5176; (f) C. Ogawa, M. Sugiura and S. Kobayashi, *Angew. Chem., Int. Ed.*, 2004, **43**, 6491; (g) C. Baudequin, D. Chaturvedi and S. B. Tsogoeva, *Eur. J. Org. Chem.*, 2007, 2623; (h) D. Pei, Z. Wang, S. Wei, Y. Zhang and J. Sun, *Org. Lett.*, 2006, **8**, 5913.
- 7 (a) S. Kobayashi, C. Ogawa, H. Konishi and M. Sugiura, *J. Am. Chem. Soc.*, 2003, **125**, 6610; (b) A. Massa, A. V. Malkov, P. Koc̆ovsky' and A. Scettri, *Tetrahedron Lett.*, 2003, **44**, 7179; (c) G. J. Rowlands and W. K. Barnes, *Chem. Commun.*, 2003, 2712; (d) J. R. Fulton, L. M. Kamara, S. C. Morton, J. R. Gareth and G. J. Rowlands, *Tetrahedron*, 2009, **65**, 9134.
- 8 I. Fernández, V. Valdivia, M. Pern'ia and N. Khiar, *Org. Lett.*, 2007, **9**, 2215.
- 9 D. Pei, Y. Zhang, S. Wei, M. Wang and J. Sun, *Adv. Synth. Catal.*, 2008, **350**, 619.
- 10 F. A. Davis, R. E. Reddy, J. M. Szewczyk, G. V. Reddy, P. S. Portonovo, H. Zhang, D. Fanelli, T. R. Reddy, P. Zhou and P. J. Carroll, *J. Org. Chem.*, 1997, **62**, 2555.
- 11 (a) For leading references on sulfinate synthesis using "The DAG methodology" see: I. Fernández and N. Khiar, *Chem. Rev.*, 2003, **103**, 3651; (b) I. Fernández, N. Khiar, J. M. Llera and F. Alcudia, *J. Org. Chem.*, 1992, **57**, 6789; (c) N. Khiar, I. Fernández and F. Alcudia, *Tetrahedron Lett.*, 1994, **35**, 5719; (d) N. Khiar, C. S. Araujo, F. Alcudia and I. Fernández, *J. Org. Chem.*, 2002, **67**, 345.
- 12 G. Solladie', *Synthesis*, 1981, 185.
- 13 J. L. García-Ruano, R. Alonso, M. M. Zarzuelo and P. Noheda, *Tetrahedron: Asymmetry*, 1995, **6**, 1133.
- 14 H. B. Kagan, in *New Frontiers in Asymmetric Catalysis* (ed.: K. Mikami, M. Lautens, John Wiley and Sons) 2007, Chap. 7, pp. 207.
- 15 T. D. Owens, A. J. Souers and J. A. Ellman, *J. Org. Chem.*, 2003, **68**, 3.
- 16 (a) S. Kobayashi and R. Hirabayashi, *J. Am. Chem. Soc.*, 1999, **121**, 6942; (b) R. Hirabayashi, C. Ogawa, M. Sugiura and S. Kobayashi, *J. Am. Chem. Soc.*, 2001, **123**, 9493.
- 17 (a) J.-H. Yoon and R. Hermann, *Tetrahedron Lett.*, 1986, **27**, 1493; (b) J.-H. Yoon and R. Hermann, *Synthesis*, 1987, **72**.
-