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ORCID® iDs	Cihangir Tanyeli - https://orcid.org/0000-0003-2270-8635

The Synthesis of Chiral β-Naphthyl-β-Sulfanyl Ketones via Enantioselective Sulfa-Michael Reaction in the Presence of a Bifunctional Cinchona/Sulfonamide Organocatalyst

Deniz Tözendemir[1], Cihangir Tanyeli*[1]

Address: [1]Department of Chemistry, Middle East Technical University, 06800 Ankara, Turkey

Email: Cihangir Tanyeli – tanyeli@metu.edu.tr

* Corresponding author

Abstract

Cinchona alkaloid derived organocatalysts are widely employed in various asymmetric transformations, yielding products with high enantiopurity. In this respect, a bifunctional quinine derived sulfonamide organocatalyst was developed to catalyze the asymmetric sulfa-Michael reaction of naphthalene-1-thiol with trans-chalcone derivatives. The target sulfa-Michael adducts were obtained with up to 96% ee under mild conditions and with a low (1 mol%) catalyst loading. Selected enantiomerically enriched SMA products were subjected to oxidation to obtain corresponding sulfones.

Keywords

asymmetric synthesis; organocatalysis; sulfa-Michael reaction; cinchona alkaloids; bifunctional catalysis

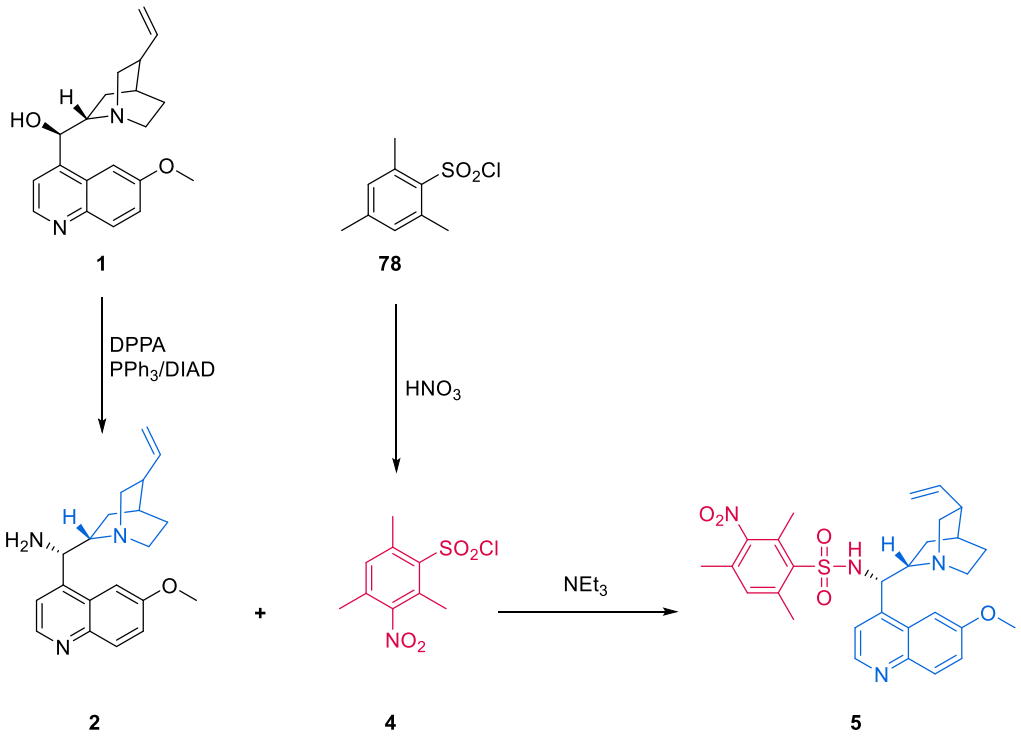
Introduction

Derivatives of the naturally occurring cinchona alkaloids have shown remarkable performance as organocatalysts for stereoselective synthesis in the past decade [1]. Among them, quinine derived organocatalysts make a noteworthy appearance in the formation of new stereogenic centres which can serve as valuable building blocks for the construction of more elaborate structures [2]. An outstanding class of quinine derived organocatalysts exhibit a bifunctional mode of activation by the incorporation of an acidic unit such as urea, thiourea, squaramide or sulfonamide moieties, giving rise to the simultaneous activation of both nucleophile and electrophile [3]. Quinine derived sulfonamides were first introduced to the literature by Song et al [4]. Since then, many contributions were made regarding their applications in a variety of reaction types [5]. However, sulfa-Michael addition (SMA) reactions remain a rather less explored reaction among asymmetric organocatalytic transformations, mainly because of the high nucleophilicity of thiols causing difficulties in controlling the stereoselectivity [6], despite C-S bond forming reactions are of great interest in synthetic organic chemistry [7]. Thus, the SMA with thiols and α,β-unsaturated ketones are generally carried out at low temperatures and with high catalyst loading [8]. The studies which employ mild conditions and low catalyst loading use thiophenol derivatives or simple alkyl thiols as nucleophiles [9]. Thionaphthols, however, are overlooked in sulfa-Michael addition reactions. And to our best knowledge, no study is present concerning SMA with naphthalene-1-thiol as the nucleophile for the addition to enones.

Encouraged by the good results obtained with enantioselective sulfa-Michael addition of thiols to chalcones with sulfonamide-type organocatalysts in the literature [9d,10], in this study, a new quinine sulfonamide derivative organocatalyst was developed to catalyse the enantioselective SMA of naphthalene-1-thiol to *trans*-chalcones under mild conditions and with a low (1 mol%) catalyst loading, to obtain enantiomerically enriched β-naphthyl-β-sulfanyl ketones with up to 96% ee. The target adducts are the core structure of *seco*-raloxifene derivatives, which are potent anti-breast cancer agents [11]. In addition, the same scaffold has also shown urease inhibitor activity [12]. Due to the shown biological attractiveness of those 1,3-biarylsulfanyl derivatives, the enantioenriched products can serve as important building blocks for new drugs. The sulphide moiety of β-naphthyl-β-sulfanyl ketones can be oxidized to form sulfones. Despite sulfones were outshined by sulphonamides in medicinal chemistry, they have a large array of biologic activities which show promising effects as potent anti-HIV-1 [13], anti-hepatitis C [14], antifungal [15], insecticidal/ acaricial [16] and antimalarial [17] agents.

Results and Discussion

We have previously reported the synthesis of new aminoDMAP based sulfonamides [18] and quinine based squaramide-type organocatalysts [19]. Motivated by the excellent results obtained with our aforementioned catalysts, we developed a new chiral bifunctional sulfonamide/quinine organocatalyst, which unites both classes. The synthesis of the basic part was initiated by converting quinine to quinine amine via Mitsunobu reaction, followed by Staudinger reduction [19]. Then it was coupled with the acidic part, which was obtained by the nitration of 2,4,6-trimethylbenzenesulfonyl chloride [18] to obtain organocatalyst **5** (Scheme 1).



Scheme 1: Synthesis of organocatalyst **5**

This new organocatalyst was employed in the model asymmetric sulfa-Michael reaction of naphthalene-1-thiol and *trans*-chalcone, in addition to the aminoDMAP and quinine based organocatalysts (**6**, **7a-c** and **8a-c**) in our library (Figure 1), as well as previously reported quinine derived organocatalysts **8d** and **9a-b** in the literature [9d,20].

Among the 11 screened organocatalysts, the ones with aminoDMAP cores gave unimpressive ee's (Table 1, entries 2-5). Quinine derived organocatalysts **8a-d** failed to attain striking stereoselectivity (25-43% ee). The popular urea/quinine and thiourea/quinine organocatalysts both gave the target compound with only 41% ee, which was well below satisfactory (entries 10 and 11). The best catalyst in terms of enantioselectivity proved to be the newly designed catalyst **5**, which gave desired product with 63% ee in 1 hour (Table 1, entry 1). After selecting the best working

catalyst, optimization studies were initiated on the model reaction to determine the conditions to achieve the best enantioselectivity.

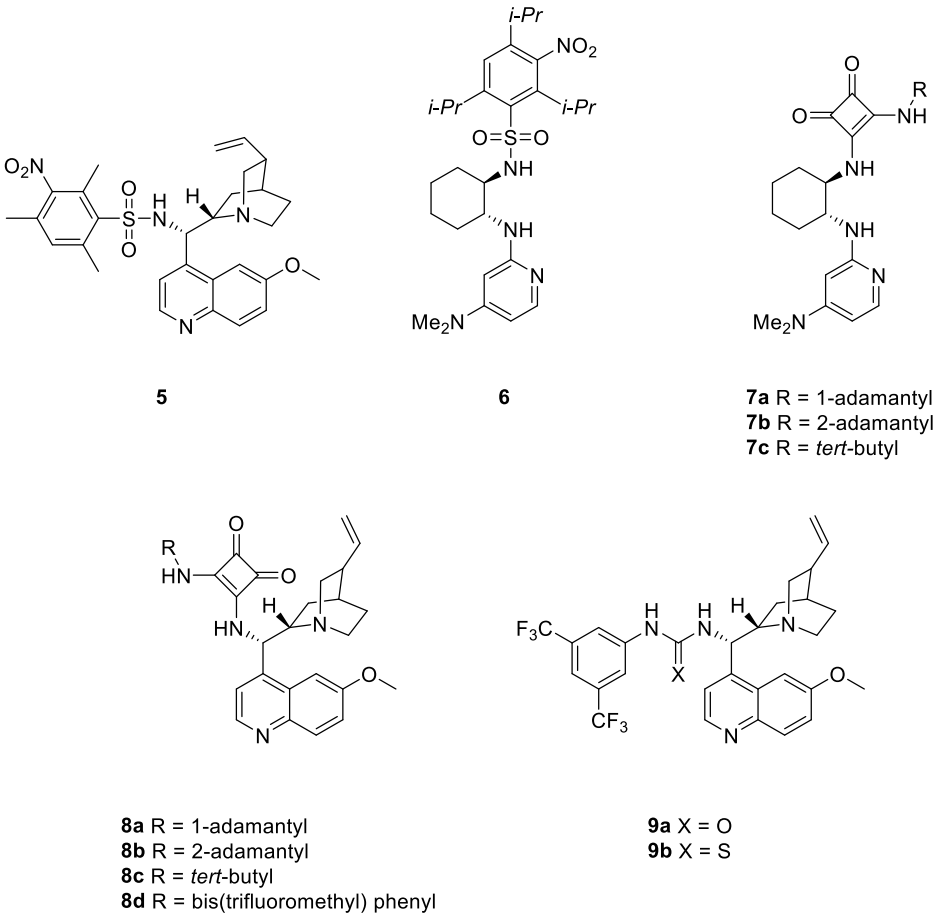
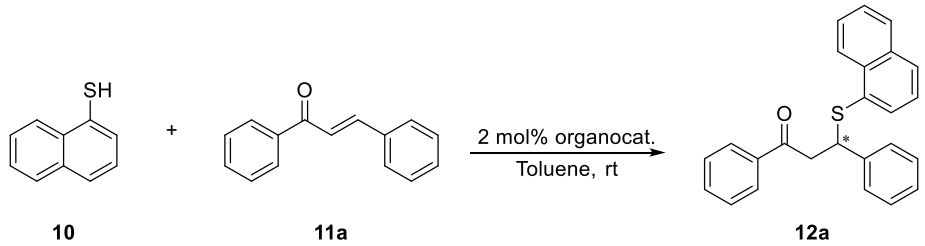


Figure 1: Structures of the screened organocatalysts

The first parameter screened was the effect of solvent. Using THF and dioxane (Table 1, entries 14 and 16, respectively) gave the two highest results, but the use of dioxane is best avoided due to its toxicity. Except for hexane (only 6% ee, entry 13), which resulted in almost racemic product presumably due to solubility issues, all other solvents afforded the target SMA adduct with similar moderate ee values. Thus, THF was selected as the best solvent despite the longer reaction duration.

Table 1: Catalyst and Solvent Screening



10 **11a** **12a**

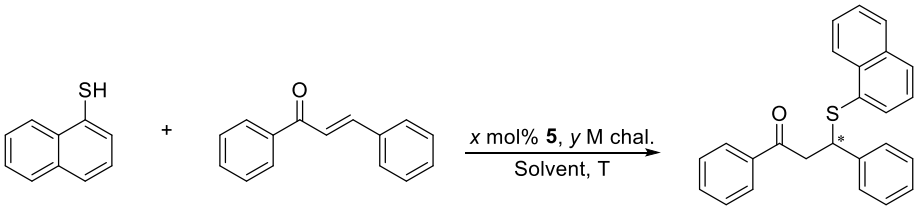
Entry[a]	Catalyst	Solvent	Time (h)	Yield[b] (%)	ee[c] (%)
1	**5**	Toluene	1	98	63
2	**6**	Toluene	2.5	>99	30
3	**7a**	Toluene	0.5	92	46
4	**7b**	Toluene	0.5	63	40
5	**7c**	Toluene	0.5	79	52
6	**8a**	Toluene	0.5	72	41
7	**8b**	Toluene	0.5	96	43
8	**8c**	Toluene	0.5	90	31
9	**8d**	Toluene	0.5	95	25
10	**9a**	Toluene	0.5	71	41
11	**9b**	Toluene	0.5	94	41
12	**5**	CH_2Cl_2	2.5	42	65
13	**5**	Hexane	1	>99	6
14	**5**	THF	4	85	79
15	**5**	$CHCl_3$	2	50	65
16	**5**	Dioxane	4	90	75
17	**5**	TBME	1	92	57
18	**5**	EtOAc	2	49	65
19	**5**	MeCN	1	81	55
20	**5**	Et_2O	3	28	57

[a] Unless stated otherwise, all reactions were performed with 0.10 mmol *trans*-chalcone and 0.20 mmol naphthalene-1-thiol in 0.5 mL of solvent, in the presence of 2 mol% organocatalyst at rt. [b] Isolated yields. [c] Determined by chiral HPLC analysis, AD-H column, 99:1 hexane/isopropanol, 0.8 mL/min, 220 nm.

Then, the catalyst loading was varied between 0.1 and 10 mol% to investigate its effect on enantioselectivity (Table 2, entries 1-6). At an extremely low catalyst loading as 0.1 mol%, the reaction was too sluggish; amount of the product was too small and was not isolated. Using 0.5 mol% of 5 gave rise to 82% ee (entry 2), however the outcome of the reaction with 1 mol% of 5 (83%, entry 3) was slightly better than the former and was completed in a shorter time (40 hours, compared to 23 hours, respectively). Thus, that part of the optimization was continued with 1 mol% catalyst loading.

The effect of concentration of the reaction mixture was investigated by changing the chalcone concentration gradually from 0.05 to 0.4 M (Table 2, entries 3 and 7-12). The best selectivity (83% ee) was obtained at 0.2 M chalcone concentration (Entry 3). Diluting the reaction mixture further than 0.15 M had decreased the rate of reaction considerably and the amounts of products were not appreciable to be isolated. Increasing the concentration leaded to a small decrease in ee. Using an equimolar mixture of chalcone and naphthalene-1-thiol had a similar outcome for the progress of the reaction as dilution (Table 2, entry 14). Changing the chalcone to naphthalene-1-thiol ratios to 1:1.5 or 1:3 resulted in small losses in enantioselectivity. Hence, the studies were continued with 2 molar equivalents of naphthalene-1-thiol to *trans*-chalcone.

Table 2: Further Screening Results on the Model Reaction



10 **11a** **12a**

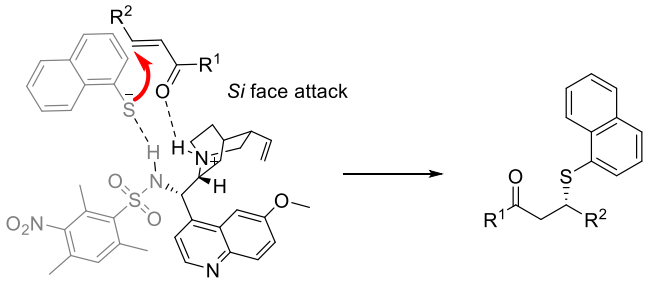
Entry[a]	Load	Conc. (M)	T (°C)	Time (h)	Yield[b] (%)	ee[c] (%)
1	0.1%	0.2	rt	72	-	-

2	0.5%	0.2	rt	40	81	82
3	1%	0.2	rt	23	93	83
4	2%	0.2	rt	4	85	79
5	5%	0.2	rt	6	95	76
6	10%	0.2	rt	3	83	69
7	1%	0.05	rt	72	-	-
8	1%	0.1	rt	72	-	-
9	1%	0.15	rt	26	>99	79
10	1%	0.25	rt	25	>99	78
11	1%	0.3	rt	20	91	79
12	1%	0.4	rt	19	>99	75
13[d]	1%	0.2	rt	72	-	-
14[e]	1%	0.2	rt	41	91	79
15[f]	1%	0.2	rt	19	90	78
16	1%	0.2	0	40	96	73
17	1%	0.2	-20	41	97	68
18	1%	0.2	-40	49	90	62

[a] Unless stated otherwise, all reactions were performed with 1:2 ratio of *trans*-chalcone to naphthalene-1-thiol in THF, in the presence of organocatalyst **5** at the indicated temperature. [b] Isolated yields. [c] Determined by chiral HPLC analysis, AD-H column, 99:1 hexane / isopropanol, 0.8 mL/min, 220 nm. [d] The reaction was carried out using 1:1 ratio of *trans*-chalcone to naphthalene-1-thiol. [e] The reaction was carried out using 1:1.5 ratio of *trans*-chalcone to naphthalene-1-thiol. [f] The reaction was carried out using 1:3 ratio of *trans*-chalcone to naphthalene-1-thiol.

The optimization studies were concluded by investigating the effect of temperature on asymmetric induction (Table 2, entries 16-18). Lowering the temperature gradually to -40 °C caused a significant loss in ee, allowing the synthesis of the product **12a** with a final ee of 62% (entry 18). This unexpected phenomenon could be linked to an enthalpic factor that favors the formation of the major enantiomer at higher temperature. The most enantioenriched product was ultimately obtained at room temperature (83% ee).

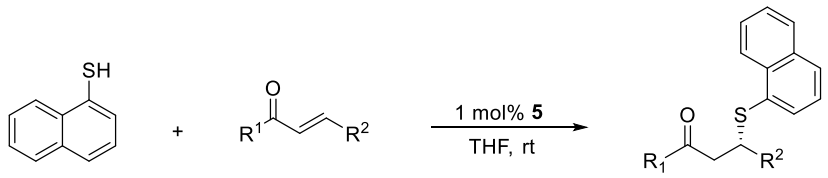
The absolute configuration of the product was assigned as "*S*" by comparing the obtained optical rotation value with the values in the literature for the organocatalytic SMA of thiols to trans-chalcone derivatives [9c,21]. A transition state model to explain the origin of stereoinduction was proposed (Scheme 2), according to the Houk's Brønsted acid−hydrogen bonding model, which was found to be the lowest-energy transition state for the SMA of thiols in the presence of cinchona alkaloid-type organocatalysts in Guo's work in 2017 [22].



Scheme 2: Proposed transition state for the SMA of 1-thionaphthol to *trans*-chalcones

The substrate scope was extended to substituted chalcones, under the optimized conditions (Table 3). The chalcone derivatives used in this work were obtained by Claisen-Schmidt condensation, using known procedures [23]. Among the chalcone derivatives employed in the model reaction, the best result in terms of enantioselectivity was attained with 4-methyl substituted chalcone, which allowed the synthesis of corresponding SMA adduct **12d** with an excellent ee of 91% (entry 4). Good to moderate results were obtained with chalcone derivatives possessing either electron donating or withdrawing substituents. Compared with the unsubstituted *trans*-chalcone, an unexpected and drastic decrease in enantioselectivity was observed with chalcone derivative **11c**, however (23% ee, entry 3).

Table 3: Results for the SMA of Naphthalene-1-thiol to Substituted *trans*-Chalcones in THF



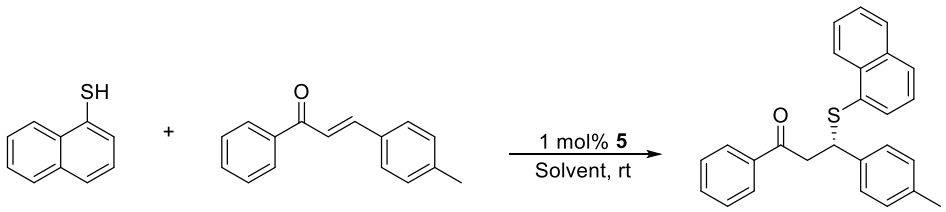
10 **11a** **12a**

Entry[a]	**11**	R^1, R^2	**12**	Time (h)	Yield[b] (%)	*ee*[c] (%)
1	**11a**	Ph, Ph	**12a**	23	93	83
2	**11b**	Ph, 3-MeC_6H_5	**12b**	46	87	78
3	**11c**	Ph, 4-MeC_6H_5	**12c**	20	>99	23
4	**11d**	4-MeC_6H_5, Ph	**12d**	42	>99	91
5	**11e**	Ph, 3-$OMeC_6H_5$	**12e**	42	83	58
6	**11f**	Ph, 4-$OMeC_6H_5$	**12f**	20	88	63
7	**11g**	Ph, 3,4,5-$(OMe)_3C_6H_5$	**12g**	21	94	50
8	**11h**	Ph, 2-ClC_6H_5	**12h**	23	84	66
9	**11i**	Ph, 3-ClC_6H_5	**12i**	22	79	85
10	**11j**	Ph, 4-ClC_6H_5	**12j**	21	>99	71
11	**11k**	Ph, 3-BrC_6H_5	**12k**	40	66	51
12	**11l**	4-BrC_6H_5, Ph	**12l**	23	>99	82
13	**11m**	Ph, 4-$CF_3C_6H_5$	**12m**	19	79	67
14	**11n**	2-$NO_2C_6H_5$, Ph	**12n**	21	84	82
15	**11o**	Ph, 4-$NO_2C_6H_5$	**12o**	21	81	68

[a] Unless stated otherwise, all reactions were performed with 0.20 mmol *trans*-chalcone and 0.40 mmol naphthalene-1-thiol in 1.0 mL of THF, in the presence of 1 mol% **5** at rt. [b] Isolated yields. [c] Determined by chiral HPLC analysis.

Intrigued by this unexpected result, we decided to revisit the solvent screening. For this purpose, the sulfa-Michael addition of naphthalene-1-thiol to **11c** was carried out again in toluene, dioxane and DCM, in addition to THF (Table 4).

Table 4: Solvent Screening Results for the SMA of Naphthalene-1-thiol to Chalcone Derivative **11c**



10 **11c** **12c**

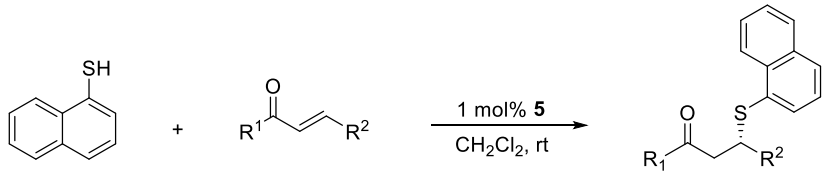
Entry[a]	Solvent	Time (h)	Yield[b] (%)	ee[c] (%)
1	THF	20	>99	23
2	Toluene	6	95	78
3	Dioxane	20	78	76
4	DCM	6	94	93

[a] Unless stated otherwise, all reactions were performed with 0.20 mmol **11c** and 0.40 mmol naphthalene-1-thiol in 1.0 mL of solvent, in the presence of 1 mol% **5** at rt. [b] Isolated yields. [c] Determined by chiral HPLC analysis.

In DCM, 93% ee was attained for adduct **12c**. In the light of this striking result, we decided to repeat the derivatization studies with DCM (Table 5).

Employing DCM as the solvent showed significant improvements in the asymmetric induction for chalcone derivatives having electron donating methyl and methoxy substituents (Table 5, entries 3-7), especially with 4-methyl and 3,4,5-trimethoxy substituted chalcones (23% to 94% ee and 50% to 96% ee; entries 3 and 7, respectively.) The only exception to this pattern was with 3-methyl derivative of chalcone, which resulted in a small decrease in enantioselectivity (78% to 70% ee, entry 2) when THF was switched to DCM. In the case of halogens and electron withdrawing substituents, an opposite behaviour was observed. The use of DCM instead of THF leaded to lower ee's for the chalcone derivatives having the aforementioned substituents (entries 8-15).

Table 5: Results for the SMA of Naphthalene-1-thiol to Substituted *trans*-Chalcones in DCM



10 **11a** **12a**

Entry[a]	**11**	R^1, R^2	Product	Time (h)	Yield[b] (%)	*ee*[c] (%)
1	**11a**	Ph, Ph	**12a**	21	90	66
2	**11b**	Ph, 3-MeC_6H_5	**12b**	22	77	70
3	**11c**	Ph, 4-MeC_6H_5	**12c**	6	94	94
4	**11d**	4-MeC_6H_5, Ph	**12d**	21	>99	86
5	**11e**	Ph, 3-$OMeC_6H_5$	**12e**	24	73	63
6	**11f**	Ph, 4-$OMeC_6H_5$	**12f**	23	93	84
7	**11g**	Ph, 3,4,5-$(OMe)_3C_6H_5$	**12g**	24	>99	96
8	**11h**	Ph, 2-ClC_6H_5	**12h**	23	85	44
9	**11i**	Ph, 3-ClC_6H_5	**12i**	21	71	15
10	**11j**	Ph, 4-ClC_6H_5	**12j**	21	86	51
11	**11k**	Ph, 3-BrC_6H_5	**12k**	23	84	26
12	**11l**	4-BrC_6H_5, Ph	**12l**	23	57	74
13	**11m**	Ph, 4-$CF_3C_6H_5$	**12m**	2	88	2
14	**11n**	2-$NO_2C_6H_5$, Ph	**12n**	21	91	74
15	**11o**	Ph, 4-$NO_2C_6H_5$	**12o**	23	92	6

[a] Unless stated otherwise, all reactions were performed with 0.20 mmol *trans*-chalcone and 0.40 mmol naphthalene-1-thiol in 1.0 mL of DCM, in the presence of 1 mol% **5** at rt. [b] Isolated yields. [c] Determined by chiral HPLC analysis.

The most dramatic decreases in selectivity were observed for derivatives **12m** and **12o**, for which the outcomes of the reactions were almost racemic (entries 13 and 15). The solvent effects on the SMA of chalcone derivatives and naphthalene-1-thiol was summarized in Figure 2. This behaviour might be related to the better stabilization of

the transition state of substrates containing electron withdrawing substituents or halogens with THF, or vice versa.

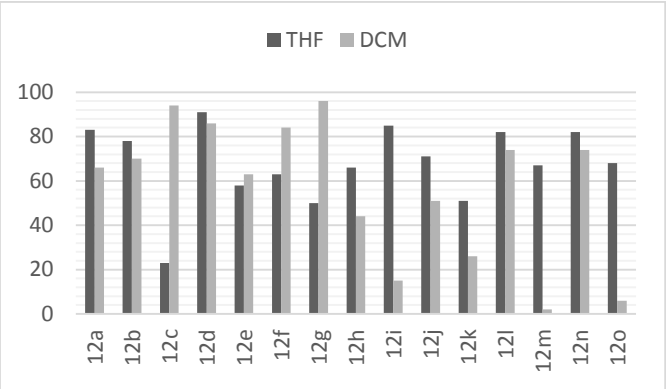
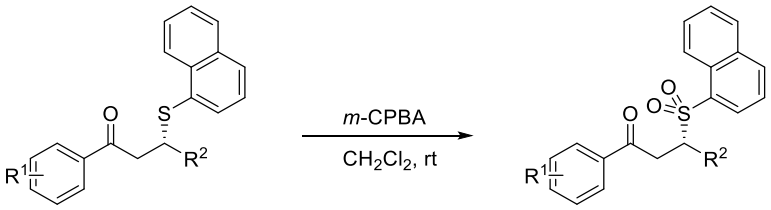


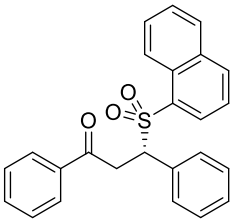
Figure 2: Comparison of the ee's of SMA in the presence of THF and DCM as solvent

In order to enhance the potential bioactivity of the obtained enantioenriched products, selected SMA adducts (β-naphthyl-β-sulfanyl ketones) was subjected to oxidation with *m*-CPBA [24]. (Table 6).

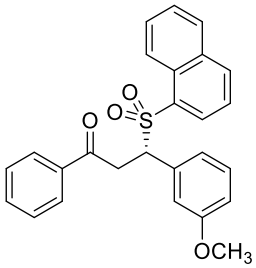
Table 6: Synthesis of enantioenriched sulfones from β-naphthyl-β-sulfanyl ketones[a]



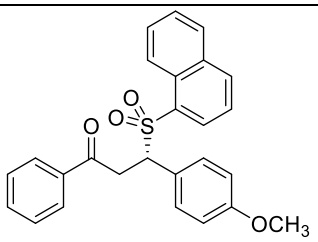
12 **13**



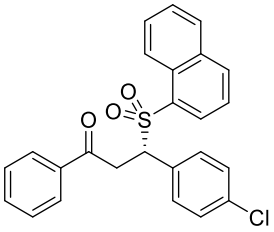
13a
43% yield, 86% ee



13e
45% yield, 68% ee



13f
62% yield, 86% ee



13j
28% yield, 66% ee

Unless stated otherwise, all reactions were performed with 1 eq β-aryl-β-sulfanyl ketone derivative and 2.2 eq *m*-CPBA in DCM.

During the oxidation reaction, it was seen that the enantioenriched sulfa-Michael adducts undergo retro-Sulfa-Michael reaction. The low yields of the oxidation and the fluctuations in enantioselectivity compared to the starting sulfa-Michael adducts can be attributed to this unpreventable retro-reaction. Despite this setback, the target sulfones were obtained with moderate to good ee's.

Conclusion

In conclusion, we report the enantioselective organocatalytic sulfa-Michael addition reaction of naphthalene-1-thiol to *trans*-chalcones, in the presence of a new bifunctional quinine derived sulfonamide organocatalyst. The adducts obtained with moderate to excellent ee's are β-naphthyl-β-sulfanyl ketones, which have potent activity against breast cancer. The easy access to the corresponding sulfones presents a versatile route for the implementation of a new biologically active moiety, the sulfone,

to the β-naphthyl-β-sulfanyl ketones. The enantioenriched products of both classes can be evaluated as building blocks of new potential drug molecules.

Experimental

Materials and methods

All chemicals were purchased from Sigma-Aldrich or Acros Organics. Column chromatographies were performed using silica gel 60 (200-300 mesh) as supporting material. All the eluents were distilled prior to use. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer, using $CDCl_3$ as solvent. Chemical shift values are reported in ppm with TMS a standard, *J* values are given in hertz. Optical rotations were determined by a polarimeter and reported as $[\alpha]_D^T$ (*c* in per 100 mL, solvent). Enantiomeric excess values were determined by chiral HPLC chromatography using Agilent instrument. All new products were further analyzed by LC/MS-HRMS-TOF or MALDI-ESI-TOF.

Synthesis of Organocatalyst 5

A solution of quinine amine **2** (226.40 mg, 0.70 mmol) and triethylamine (107 µL, 0.77 mmol) in CH_2Cl_2 was added to a screw-capped reaction vial. To this mixture, 2,4,6-trimethyl-3-nitrobenzenesulfonyl chloride **4** (184.59 mg, 0.70 mmol) was added at 0 °C. The mixture was then allowed to warm up to room temperature and stirred overnight. The crude product was directly loaded to a silica gel column, with ethyl acetate/triethylamine (98:2) as the eluent to afford the corresponding sulfonamide **5.**

N-((S)-(6-methoxyquinolin-4-yl)((1S,2S,4S,5R)-5-vinylquinuclidin-2-yl)methyl)-2,4,6-trimethyl-3-nitrobenzenesulfonamide (5)

Off-white colored solid, 135.3 mg, mp 101 °C, 35% yield. $[\alpha]_D^{30}$ = -134.95 (*c* 0.780, MeOH). ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ 8.58 (d, *J* = 4.2 Hz, 1H), 8.47 (d, *J* = 4.5 Hz, 1H), 7.97 (d, *J* = 9.1 Hz, 1H), 7.87 (d, *J* = 9.2 Hz, 1H), 7.74 – 7.53 (m, 1H), 7.50 – 7.45 (m, 1H), 7.44 – 7.31 (m, 1H), 7.20 (d, *J* = 4.2 Hz, 1H), 7.15 (d, *J* = 4.5 Hz, 1H), 6.54 (s, 1H), 6.44 (s, 1H), 5.78 – 5.56 (m, 1H), 5.31 (s, 1H), 5.10 (d, *J* = 10.6 Hz, 1H), 5.04 – 4.85 (m, 1H), 4.46 (d, *J* = 10.9 Hz, 1H), 3.99 (s, 1H), 3.94 (s, 1H), 3.46 (dd, *J* = 17.9, 9.4 Hz, 1H), 3.38 – 3.25 (m, *J* = 12.0 Hz, 1H), 3.22 – 3.09 (m, *J* = 13.5, 6.8 Hz, 1H), 3.09 – 2.92 (m, 1H), 2.90 – 2.71 (m, 1H), 2.41 (s, 1H), 2.39 (s, 1H), 2.34 (s, 1H), 2.13 (s, 1H), 2.12 (s, 1H), 1.96 (s, 1H), 1.75 (s, 1H), 1.71 – 1.59 (m, 2H), 1.48 – 1.19 (m, *J* = 30.9, 19.8 Hz, 1H), 1.06 – 0.79 (m, *J* = 28.0, 13.4, 7.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) (mixture of rotamers): δ 157.81, 156.81, 151.83, 151.22, 147.04, 146.51, 144.45, 144.18, 141.61, 140.97, 140.91, 140.75, 140.47, 138.89, 135.77, 134.82, 132.60, 132.40, 132.30, 132.13, 131.99, 131.89, 131.82, 131.79, 131.74, 131.33, 130.04, 129.81, 128.42, 128.30, 128.03, 126.34, 123.68, 121.35, 120.17, 119.72, 118.42, 114.72, 103.64, 100.68, 62.88, 61.06, 60.23, 55.76, 55.45, 55.28, 52.78, 40.27, 39.77, 39.42, 39.22, 27.74, 27.51, 27.21, 27.09, 26.06, 24.76, 23.22, 22.50, 16.83, 16.75, 15.88, 15.50, 14.06. IR (neat): 3077, 2934, 2871, 1619, 1589, 1530, 1506, 1475, 1429, 1359, 1262, 1238, 1168, 1138, 1103, 1032, 987, 912, 865, 840, 775, 717, 666, 563, 493 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd. for $C_{29}H_{35}N_4O_5S$ 551.2328; Found 551.2339.

General Procedure for the Synthesis of 12a-o

A screw-capped reaction vial was charged with *trans*-chalcone derivative (**11a-o**) (0.20 mmol) and organocatalyst **5** (1.10 mg, 0.0020 mmol) and 0.5 mL of THF or DCM. Then a solution of naphthalene-1-thiol (**10** (55.4 µL, 0.40 mmol) in 0.5 mL of the selected solvent was introduced slowly into the vial with stirring. The mixture was stirred at room

temperature and progress of the reaction was monitored with TLC. Upon the consumption of the chalcone derivative, the reaction mixture was directly subjected to flash column chromatography, using *n*-hexane/ethyl acetate mixture as eluent to yield products **12a-o**.

3-(Naphthalen-1-ylthio)-1,3-diphenylpropan-1-one (12a)

White solid, 68.61 mg, mp 99 °C, 93% yield. HPLC (AD-H, 99:1 *n*-Hexane/Isopropanol, 0.8 mL/min, 220 nm): t_{minor} = 33.445 min, t_{major} = 35.736 min, 83% ee, $[\alpha]_D^{23}$ = -70.25 (*c* 1.785, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (d, *J* = 8.6 Hz, 1H), 7.77 – 7.71 (m, 3H), 7.68 (d, *J* = 8.2 Hz, 1H), 7.48 – 7.38 (m, 4H), 7.31 (t, *J* = 7.7 Hz, 2H), 7.21 – 7.15 (m, 3H), 7.15 – 7.04 (m, 3H), 4.88 (dd, *J* = 7.9, 6.3 Hz, 1H), 3.61 (dd, *J* = 17.2, 8.0 Hz, 1H), 3.53 (dd, *J* = 17.2, 6.2 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$): δ 197.04, 141.18, 136.71, 134.45, 134.07, 133.26, 133.20, 131.34, 129.13, 128.63, 128.58, 128.47, 128.10, 127.82, 127.42, 126.82, 126.28, 125.81, 125.47, 48.89, 44.72. δ IR (neat): 3053, 3027, 2891, 2878, 1678, 1595, 1501, 1449, 1418, 1368, 1340, 1251, 1225, 1078, 1019, 1002, 981, 921, 801, 769, 750, 711, 689, 667, 642, 624, 599, 565, 549, 530, 419 cm^{-1}. MS (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{25}H_{20}NaOS$ 391.113; Found 391.133.

3-(Naphthalen-1-ylthio)-1-phenyl-3-(m-tolyl)propan-1-one (12b)

White solid, 66.79 mg, mp 56 °C, 87% yield. HPLC (OD-H, 99:1 *n*-Hexane/Isopropanol, 0.8 mL/min, 220 nm): t_{minor} = 16.063 min, t_{major} = 14.139 min, 78% ee, $[\alpha]_D^{24}$ = -111.4 (*c* 1.660, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 7.4 Hz, 3H), 7.69 (d, *J* = 8.2 Hz, 1H), 7.54 – 7.38 (m, 4H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 7.7 Hz, 1H), 7.02 (dd, *J* = 15.1, 7.7 Hz, 3H), 6.90 (d, *J* = 6.6 Hz, 1H), 4.95 – 4.76 (m, 1H), 3.62 (dd, *J* = 17.2, 8.1 Hz, 1H), 3.51 (dd, *J* = 17.2, 6.0 Hz, 1H), 2.17 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$): δ 197.12, 140.90, 138.03, 136.71, 134.41, 134.04, 133.19, 133.05, 131.47, 129.02, 128.58, 128.52, 128.31, 128.20, 128.07, 126.73, 126.22,

125.78, 125.43, 124.73, 48.29, 44.68, 21.38. IR (neat): 3054, 3022, 2920, 2852, 1681, 1594, 1502, 1448, 1415, 1363, 1334, 1249, 1216, 1055, 1019, 1000, 979, 877, 801, 784, 768, 754, 727, 713, 684, 638, 624, 602, 573, 534, 510, 443, 421 cm^{-1}. MS (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{26}H_{22}NaOS$ 405.129; Found 405.147.

3-(Naphthalen-1-ylthio)-1-phenyl-3-(p-tolyl)propan-1-one (12c)

White solid, 71.84 mg, mp 102 °C, 94% yield. HPLC (AD-H, 98:2 *n*-Hexane/Isopropanol, 0.8 mL/min, 254 nm): t_{minor} = 15.832 min, t_{major} = 14.441 min, 94% ee, $[\alpha]_D^{23}$ = -91.42 (*c* 0.480, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, *J* = 8.3 Hz, 1H), 7.77 – 7.70 (m, 3H), 7.68 (d, *J* = 8.2 Hz, 1H), 7.51 – 7.39 (m, 4H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.26 – 7.19 (m, 1H), 7.14 – 7.06 (m, 2H), 6.95 (d, *J* = 7.9 Hz, 2H), 4.87 (dd, *J* = 8.3, 5.9 Hz, 1H), 3.60 (dd, *J* = 17.1, 8.3 Hz, 1H), 3.49 (dd, *J* = 17.1, 5.9 Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.19, 138.06, 137.10, 136.73, 134.37, 134.09, 133.22, 132.89, 131.63, 129.21, 128.99, 128.61, 128.10, 127.68, 126.80, 126.27, 125.80, 125.51, 48.10, 44.86, 21.17. IR (neat): 3053, 3030, 2944, 2922, 2892, 2861, 1681, 1595, 1515, 1502, 1449, 1417, 1361, 1334, 1307, 1251, 1226, 1155, 1113, 1062, 1019, 1001, 978, 954, 918, 801, 770, 759, 733, 701, 684, 649, 623, 583, 564, 534, 521, 435, 417 cm^{-1}. MS (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{26}H_{22}NaOS$ 405.129; Found 405.190.

3-(Naphthalen-1-ylthio)-3-phenyl-1-(p-tolyl)propan-1-one (12d)

White solid, 76.31 mg, mp 110-112 °C, >99% yield. HPLC (AD-H, 98:2 *n*-Hexane/Isopropanol, 0.8 mL/min, 254 nm): t_{minor} = 22.531 min, t_{major} = 20.044 min, 91% ee, $[\alpha]_D^{24}$ = -74.25 (*c* 1.910, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, *J* = 8.3 Hz, 1H), 7.79 – 7.57 (m, 4H), 7.42 (dq, *J* = 15.4, 6.8 Hz, 3H), 7.27 – 6.98 (m, 8H), 4.88 (dd, *J* = 7.7, 6.4 Hz, 1H), 3.53 (qd, *J* = 17.1, 7.1 Hz, 2H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.64, 144.06, 141.25, 134.44, 134.31, 134.06, 133.11, 131.43, 129.29, 129.04, 128.53, 128.41, 128.22, 127.80, 127.35, 126.76, 126.22, 125.81, 125.43,

48.48, 44.57, 21.66. IR (neat): 3053, 3029, 2962, 2894, 1666, 1604, 1498, 1456, 1421, 1362, 1328, 1307, 1230, 118, 1019, 972, 942, 815, 800, 767, 698, 666, 594, 559, 524, 491, 456, 416 cm^{-1}. MS (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{26}H_{22}NaOS$ 405.129; Found 405.147.

3-(3-Methoxyphenyl)-3-(naphthalen-1-ylthio)-1-phenylpropan-1-one (12e)

White solid, 76.46 mg, mp 46-47 °C, >99% yield. HPLC (OD-H, 90:10 *n*-Hexane/Isopropanol, 1 mL/min, 230 nm): t_{minor} = 10.575 min, t_{major} = 9.406 min, 63% ee, $[\alpha]_D^{24}$ = -92.87 (*c* 2.100, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.42 (d, *J* = 8.2 Hz, 1H), 7.75 (t, *J* = 7.3 Hz, 3H), 7.69 (d, *J* = 8.2 Hz, 1H), 7.52 – 7.38 (m, 4H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.26 – 7.19 (m, 1H), 7.05 (t, *J* = 7.9 Hz, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.67 (d, *J* = 17.9 Hz, 1H), 6.62 (dd, *J* = 8.1, 2.0 Hz, 1H), 4.93 – 4.79 (m, 1H), 3.68 – 3.48 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.52, 158.04, 141.25, 135.25, 132.97, 132.57, 131.76, 131.73, 129.85, 127.96, 127.62, 127.14, 127.03, 126.62, 125.30, 124.76, 124.31, 123.98, 118.59, 111.92, 111.54, 53.69, 46.89, 43.17. IR (neat): 3055, 3001, 2959, 2918, 2836, 1710, 1685, 1597, 1489, 1448, 1359, 1260, 1221, 1157, 1090, 1042, 981, 873, 774, 692, 530 cm^{-1}. MS (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{26}H_{22}NaO_2S$ 421.124; Found 421.137.

3-(4-Methoxyphenyl)-3-(naphthalen-1-ylthio)-1-phenylpropan-1-one (12f)

White solid, 74.21 mg, mp 102 °C, 93% yield. HPLC (AD-H, 90:10 *n*-Hexane/Isopropanol, 1 mL/min, 220 nm): t_{minor} = 15.595 min, t_{major} = 13.816 min, 84% ee, $[\alpha]_D^{23}$ = -120.0 (*c* 1.845, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.42 (d, *J* = 8.3 Hz, 1H), 7.79 – 7.69 (m, 3H), 7.67 (d, *J* = 8.2 Hz, 1H), 7.51 – 7.37 (m, 4H), 7.29 (t, *J* = 7.7 Hz, 2H), 7.21 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.13 – 7.07 (m, 2H), 6.73 – 6.60 (m, 2H), 4.86 (dd, *J* = 8.3, 5.9 Hz, 1H), 3.63 (s, *J* = 6.0 Hz, 3H), 3.58 (dd, *J* = 17.1, 8.4 Hz, 1H), 3.47 (dd, J = 17.1, 5.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.17, 158.82, 136.76, 134.42, 133.17, 133.11, 133.04, 131.56, 128.98, 128.86, 128.58, 128.53, 128.06,

126.74, 126.22, 125.79, 125.46, 113.84, 55.23, 47.90, 44.90. IR (neat): 3051, 3006, 2953, 2931, 2891, 2834, 1681, 1609, 1594, 1512, 1448, 1415, 1363, 1334, 1293, 1247, 1223, 1176, 1107, 1060, 1029, 1000, 977, 954, 918, 850, 813, 800, 767, 736, 723, 699, 684, 667, 647, 621, 588, 564, 529, 427, 414 cm^{-1}. MS (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{26}H_{22}NaO_2S$ 421.124; Found 421.154.

3-(Naphthalen-1-ylthio)-1-phenyl-3-(3,4,5-trimethoxyphenyl) propan-1-one (12g)

White solid, 91.53 mg, mp 115-116 °C, >99% yield. HPLC (AD-H, 90:10 *n*-Hexane/Isopropanol, 1 mL/min, 230 nm): t_{minor} = 22.490 min, t_{major} = 16.387 min, 96% ee, $[\alpha]_D^{23}$ = -123.30 (*c* 2.410, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.36 (d, *J* = 8.1 Hz, 1H), 7.84 – 7.76 (m, 2H), 7.76 – 7.66 (m, 2H), 7.52 – 7.37 (m, 4H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 7.7 Hz, 1H), 6.27 (s, 2H), 4.80 (t, *J* = 7.1 Hz, 1H), 3.66 (s, 3H), 3.63 – 3.48 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.70, 151.59, 135.82, 135.43, 135.31, 133.32, 132.67, 132.39, 131.99, 129.83, 127.91, 127.33, 127.12, 126.76, 125.39, 124.92, 124.48, 124.14, 103.46, 59.47, 54.67, 47.61, 43.06. IR (neat): 3057, 3001, 2970, 2934, 2899, 2838, 2827, 1682, 1590, 1513, 1454, 1430, 1366, 1335, 1320, 1254, 1223, 1182, 1125, 1008, 899, 805, 768, 754, 722, 688, 647, 557, 522, 416 cm^{-1}. MS (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{28}H_{26}NaO_4S$ 481.145; Found 481.137.

3-(2-Chlorophenyl)-3-(naphthalen-1-ylthio)-1-phenylpropan-1-one (12h)

White solid, 67.65 mg, mp 54-55 °C, 84% yield. HPLC (OD-H, 90:10 *n*-Hexane/Isopropanol, 1 mL/min, 254 nm): t_{minor} = 7.968 min, t_{major} = 9.813 min, 66% ee, $[\alpha]_D^{24}$ = -4.622 (*c* 1.350, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.73 – 8.41 (m, 1H), 7.97 – 7.79 (m, 4H), 7.68 – 7.52 (m, 4H), 7.50 – 7.32 (m, 5H), 7.18 (dd, J = 8.8, 5.1 Hz, 2H), 5.54 (t, J = 7.1 Hz, 1H), 3.72 (qd, J = 17.3, 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ196.58, 138.47, 136.51, 134.66, 134.00, 133.91, 133.51, 133.26, 130.73, 129.80, 129.32, 128.61, 128.42, 128.41, 128.08, 126.90, 126.73, 126.24, 125.82, 125.40, 44.68, 44.15. IR (neat): 3052, 2916, 2894, 1687, 1581, 1502, 1472, 1447,

1357, 1312, 1264, 1243, 1202, 1160, 1061, 1032, 981, 911, 797, 770, 749, 732, 679, 650, 588, 557, 538, 503, 459, 418 cm^{-1}. MS (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{25}H_{19}ClNaOS$ 425.074; Found 425.131.

3-(3-Chlorophenyl)-3-(naphthalen-1-ylthio)-1-phenylpropan-1-one (12i)

White solid, 63.78 mg, mp 85 °C, 79% yield. HPLC (OD-H, 95:5 *n*-Hexane/Isopropanol, 1 mL/min, 220 nm): t_{minor} = 9.514 min, t_{major} = 8.199 min, 85% ee, $[\alpha]_D^{23}$ = -132.7 (*c* 1.590, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 8.3 Hz, 1H), 7.88 – 7.64 (m, 4H), 7.54 – 7.38 (m, 4H), 7.33 (t, *J* = 7.7 Hz, 2H), 7.26 – 7.19 (m, 1H), 7.17 (s, 1H), 7.10 – 6.92 (m, 3H), 4.82 (t, *J* = 7.1 Hz, 1H), 3.67 – 3.45 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.56, 143.36, 136.54, 134.49, 134.18, 134.08, 133.68, 133.38, 130.65, 129.55, 129.48, 128.67, 128.57, 128.07, 127.85, 127.49, 126.90, 126.31, 126.08, 125.68, 125.40, 47.89, 44.39. IR (neat): 3054, 3029, 2951, 2920, 2851, 1681, 1593, 1570, 1500, 1431, 1412, 1364, 1333, 1254, 1226, 1185, 1163, 1076, 1001, 984, 904, 834, 798, 769, 752, 729, 683, 64, 625, 604, 533, 508, 436, 419 cm^{-1}. MS (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{25}H_{19}ClNaOS$ 425.074; Found 425.087.

3-(4-Chlorophenyl)-3-(naphthalen-1-ylthio)-1-phenylpropan-1-one (12j)

White solid, 80.50 mg, mp 121-122 °C, >99% yield. HPLC (AD-H, 90:10 *n*-Hexane/Isopropanol, 1 mL/min, 220 nm): t_{minor} = 11.144 min, t_{major} = 9.939 min, 71 ee, $[\alpha]_D^{24}$ = -125.2 (*c* 2.090, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.40 (d, *J* = 8.2 Hz, 1H), 7.88 – 7.72 (m, 3H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.55 – 7.38 (m, 4H), 7.33 (t, *J* = 7.7 Hz, 2H), 7.21 (dd, *J* = 14.7, 6.8 Hz, 1H), 7.13 – 7.03 (m, 4H), 4.83 (dd, *J* = 7.7, 6.5 Hz, 1H), 3.70 – 3.42 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.69, 139.85, 136.58, 134.45, 134.09, 133.53, 133.38, 133.00, 130.81, 129.40, 129.14, 128.68, 128.62, 128.54, 128.07, 126.93, 126.33, 125.70, 125.46, 77.42, 77.10, 76.78, 47.75, 44.52. IR (neat): 3050, 3028, 2926, 2897, 1679, 1595, 1493, 1450, 1418, 1359, 1332, 1226, 1154, 1091, 1015, 976, 954, 917, 853, 815, 799, 769, 751, 732, 683, 656, 619, 571, 531, 505, 430

cm^{-1}. MS (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{25}H_{19}ClNaOS$ 425.074; Found 425.086.

3-(3-Bromophenyl)-3-(naphthalen-1-ylthio)-1-phenylpropan-1-one (12k)

White solid, 59.28 mg, mp 84 °C, 66% yield. HPLC (OD-H, 90:10 *n*-Hexane/Isopropanol, 1 mL/min, 254 nm): t_{minor} = 8.699 min, t_{major} = 7.584 min, 51% ee, $[\alpha]_D^{24}$ = -145.1 (*c* 1.480, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 8.2 Hz, 1H), 7.82 – 7.63 (m, 4H), 7.43 (dd, *J* = 15.1, 7.6 Hz, 4H), 7.37 – 7.27 (m, 3H), 7.29 – 7.11 (m, 2H), 7.03 (d, *J* = 7.6 Hz, 1H), 6.94 (t, *J* = 7.8 Hz, 1H), 4.80 (t, *J* = 7.0 Hz, 1H), 3.55 (d, *J* = 7.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.46, 142.56, 135.43, 133.42, 133.00, 132.66, 132.32, 129.68, 129.53, 129.33, 128.77, 128.44, 127.60, 127.51, 127.00, 125.84, 125.47, 125.25, 124.61, 124.34, 121.33, 46.78, 43.28. IR (neat): 3056, 3041, 2927, 2892, 1680, 1594, 1565, 1501, 1475, 1448, 1429, 1415, 1357, 1329, 1219, 1151, 1061, 983, 953, 918, 878, 811, 795, 768, 753, 716, 685, 667, 638, 604, 570, 533, 508, 445, 433, 419 cm^{-1}. MS (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{25}H_{19}BrNaOS$ 469.024; Found 469.024.

1-(4-Bromophenyl)-3-(naphthalen-1-ylthio)-3-phenylpropan-1-one (12l)

White solid, 78.24 mg, mp 162-163 °C, >99% yield. HPLC (AD-H, 98:2 *n*-Hexane/Isopropanol, 1 mL/min, 254 nm): t_{minor} = 16.944 min, t_{major} = 17.723 min, 82% ee, $[\alpha]_D^{24}$ = -53.21 (*c* 1.260, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.40 (d, *J* = 8.2 Hz, 1H), 7.70 (dd, *J* = 23.8, 8.0 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.51 – 7.31 (m, 5H), 7.27 – 6.99 (m, 6H), 4.84 (t, *J* = 7.0 Hz, 1H), 3.65 – 3.31 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.26, 139.14, 133.59, 132.64, 132.26, 131.53, 130.11, 129.36, 127.79, 127.43, 126.79, 126.70, 126.65, 125.95, 125.71, 125.05, 124.50, 123.94, 123.65, 46.60, 42.89. IR (neat): 3055, 3030, 2899, 1682, 1583, 1500, 1452, 1396, 1365, 1331, 1220, 1177, 1070, 1007, 983, 823, 799, 774, 721, 699, 661, 626, 601, 557, 524, 470,

448, 419 cm^{-1}. MS (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{25}H_{19}BrNaOS$ 469.024; Found 469.058.

3-(Naphthalen-1-ylthio)-1-phenyl-3-(4-(trifluoromethyl)phenyl) propan-1-one (12m)

White solid, 79.57 mg, mp 118 °C, 91% yield. HPLC (AD-H, 90:10 *n*-Hexane/Isopropanol, 1 mL/min, 254 nm): t_{minor} = 8.847 min, t_{major} = 7.195 min, 67% ee, $[\alpha]_D^{23}$ = -74.02 (*c* 1.730, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, *J* = 7.8 Hz, 1H), 7.88 – 7.68 (m, 4H), 7.54 – 7.30 (m, 8H), 7.28 – 7.16 (m, 3H), 4.89 (t, *J* = 7.1 Hz, 1H), 3.78 – 3.50 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.41, 144.34, 135.38, 133.42, 133.01, 132.74, 132.41, 129.34, 128.55, 128.33 (q, *J* = 32.3 Hz), 127.64, 127.54, 127.02, 126.99, 125.89, 125.29, 124.54, 124.34, 124.25 (dd, *J* = 7.5, 3.8 Hz), 46.87, 43.15. IR (neat): 3050, 2939, 2902, 1677, 1618, 1596,1503, 1450, 1426, 1365, 1328, 1226, 1157, 1123, 1072, 1018, 986, 954, 918, 860, 821, 797, 769, 758, 708, 684, 647, 634, 620, 601, 563, 529, 425 cm^{-1}. MS (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{26}H_{19}F_3NaOS$ 459.101; Found 459.123.

3-(Naphthalen-1-ylthio)-1-(2-nitrophenyl)-3-phenylpropan-1-one (12n)

White solid, 73.61 mg, mp 112 °C, 89% yield. HPLC (AD-H, 99:1 *n*-Hexane/Isopropanol, 0.8 mL/min, 254 nm): t_{minor} = 64.775 min, t_{major} = 68.571 min, 82% ee, $[\alpha]_D^{24}$ = -1.545 (*c* 1.165, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.52 – 8.22 (m, 1H), 8.07 – 7.82 (m, 1H), 7.78 – 7.60 (m, 2H), 7.55 – 7.31 (m, 5H), 7.20 (t, J = 7.7 Hz, 1H), 7.16 – 7.00 (m, 5H), 6.94 – 6.81 (m, 1H), 4.75 (t, J = 7.3 Hz, 1H), 3.41 (t, J = 8.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 198.21, 143.90, 138.96, 136.14, 132.76, 132.67, 132.51, 131.58, 129.39, 129.05,127.05, 126.96, 126.27, 126.08, 126.05, 125.31, 124.74, 124.09 123.93, 122.74, 47.22, 46.93. IR (neat): 3058, 3029, 2923, 2910, 2856, 1709, 1573, 1529, 1499, 1455, 1403, 1367, 1343, 1218, 1142, 1019, 987, 935, 856,

790, 767, 747, 732, 715, 697, 668, 634, 618, 572, 547, 508, 451, 420 cm^{-1}. (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{25}H_{19}NNaO_3S$ 436.098; Found 436.139.

3-(Naphthalen-1-ylthio)-3-(4-nitrophenyl)-1-phenylpropan-1-one (12o)

Yellow solid, 67.23 mg, mp 129-130 °C, 81% yield. HPLC (AD-H, 90:10 *n*-Hexane/Isopropanol, 1 mL/min, 210 nm): t_{minor} = 26.461 min, t_{major} = 24.532 min, 68% ee, $[\alpha]_D^{23}$ = -153.6 (*c* 1.665, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, *J* = 8.1 Hz, 1H), 7.92 (d, *J* = 8.7 Hz, 2H), 7.83 – 7.68 (m, 4H), 7.54 – 7.40 (m, 3H), 7.37 (t, *J* = 7.6 Hz, 3H), 7.26 – 7.15 (m, 3H), 4.90 (t, *J* = 7.1 Hz, 1H), 3.74 – 3.55 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.06, 148.01, 145.81, 135.24, 133.43, 133.12, 133.05, 132.59, 128.90, 128.76, 127.73, 127.66, 127.54, 127.01, 126.05, 125.40, 124.47, 124.36, 122.50, 46.75, 42.93. IR (neat): 3073, 3048, 2962, 2900, 2851, 1673, 1595, 1515, 1449, 1260, 1227, 1107, 1016, 975, 956, 918, 857, 798, 796, 751, 716, 682, 647, 618, 566, 536, 514, 427 cm^{-1}. MS (MALDI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{25}H_{19}NNaO_3S$ 436.098; Found 436.151.

General Procedure for the Synthesis of Sulfones

A solution of β-naphthyl-β-sulfanyl ketone (0.1 mmol) in 0.8 mL DCM was cooled to 0°C. *m*-CPBA (0.22 mmol, 37.97 mg) was added to this stirred solution portionwise in 15 minutes. Then the mixture was allowed to warm up to room temperature and stirred for a total of 30 minutes. After the completion of the reaction, the reaction mixture was diluted with 0.8 mL of DCM. Then washed with 3 x 0.8 mL of 5% K_2CO_3 (aq) and 3 x 1 mL of 5% $NaHCO_3$ (aq) to remove the excess *m*-CPBA. The aqueous layer was extracted with DCM (3 x 1 mL). The organic layers were then combined, dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on silica with using *n*-hexane/ethyl acetate as eluent to afford the target sulfones.

3-(Naphthalen-1-ylsulfonyl)-1,3-diphenylpropan-1-one (13a)

White solid, 17.22 mg, mp 135 °C, 43% yield. HPLC (IA, 95:5 *n*-Hexane/Isopropanol, 1 mL/min, 220 nm): t_{minor} = 44.650 min, t_{major} = 47.501 min, 86% ee, $[\alpha]_D^{22}$ = -156.9 (*c* 1.140, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.74 (d, *J* = 8.6 Hz, 1H), 7.92 (dd, *J* = 28.8, 7.8 Hz, 4H), 7.75 (d, *J* = 7.3 Hz, 1H), 7.69 – 7.62 (m, 1H), 7.59 – 7.48 (m, 2H), 7.44 – 7.36 (m, *J* = 7.7 Hz, 2H), 7.25 (t, *J* = 7.8 Hz, 1H), 7.13 – 6.90 (m, *J* = 28.3, 13.6, 7.1 Hz, 5H), 5.22 (dd, *J* = 9.2, 3.8 Hz, 1H), 4.15 (dd, *J* = 17.9, 3.8 Hz, 1H), 3.94 (dd, *J* = 18.0, 9.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.99, 136.16, 135.25, 133.87, 133.68, 132.56, 131.98, 129.41, 129.36, 139.13, 128.84, 128.75, 128.70, 128.33, 128.16, 126.97, 124.32, 123.93, 65.74, 36.79. IR (neat): 3034, 2957, 2915, 2852, 1685, 1596, 1505, 1449, 1420, 1363, 1341, 1303, 1235, 1196, 1150, 1025, 981, 921, 826, 801, 768, 750, 699, 686, 629, 594, 573, 555, 525, 506, 476 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{25}H_{20}NaO_3S$ 423.1031; Found 423.1022.

3-(3-Methoxyphenyl)-3-(naphthalen-1-ylsulfonyl)-1-phenylpropan-1-one (13e)

White solid, 19.41 mg, mp 93 °C, 45% yield. HPLC (IA, 95:5 *n*-Hexane/Isopropanol, 1 mL/min, 254 nm): t_{minor} = 18.229 min, t_{major} = 20.872 min, 68% ee, $[\alpha]_D^{23}$ = -115.5 (*c* 1.313, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ. ^{13}C NMR (100 MHz, $CDCl_3$): δ 8.74 (d, *J* = 8.7 Hz, 1H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.88 (t, *J* = 7.5 Hz, 3H), 7.80 (d, *J* = 7.4 Hz, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.58 – 7.48 (m, 2H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.8 Hz, 1H), 6.91 (t, *J* = 8.0 Hz, 1H), 6.65 – 6.51 (m, 2H), 6.41 (s, *J* = 9.9 Hz, 1H), 5.18 (dd, *J* = 9.3, 3.8 Hz, 1H), 4.12 (dd, *J* = 17.9, 3.9 Hz, 1H), 3.93 (dd, *J* = 18.0, 9.3 Hz, 1H), 3.42 (s, *J* = 10.6 Hz, 3H).. ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.87, 157.18, 134.08, 133.07, 131.84, 131.73, 131.54, 129.96, 129.86, 127.34, 127.17, 126.94, 126.69, 126.63, 126.06, 124.84, 122.24, 121.88, 119.52, 112.64, 112.59, 63.71, 52.88, 34.58. IR (neat): 3053, 2960, 2918, 2849, 1726, 1685, 1594, 1493, 1447, 1362, 1305, 1258, 1231, 1149, 1121, 1035, 883, 792, 770, 688, 679, 633, 619, 593, 552, 528, 504, 486 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M]^+$ Calcd. for $C_{26}H_{22}O_4S$ 430.1239; Found 439.1239.

3-(3-Methoxyphenyl)-3-(naphthalen-1-ylsulfonyl)-1-phenylpropan-1-one (13f)

White solid, 26.61 mg, mp 146 °C, 62% yield. HPLC (IA, 90:10 *n*-Hexane/Isopropanol, 1 mL/min, 254 nm): t_{minor} = 40.307 min, t_{major} = 45.189 min, 86% ee, $[\alpha]_D^{22}$ = -173.1 (*c* 1.773, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 8.73 (d, *J* = 8.6 Hz, 1H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.87 (d, *J* = 7.7 Hz, 3H), 7.78 (d, *J* = 7.3 Hz, 1H), 7.66 (t, *J* = 7.8 Hz, 1H), 7.59 – 7.49 (m, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.29 (t, *J* = 7.8 Hz, 1H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.53 (d, *J* = 8.7 Hz, 2H), 5.16 (dd, *J* = 9.4, 3.7 Hz, 1H), 4.09 (dd, *J* = 17.9, 3.8 Hz, 1H), 3.90 (dd, *J* = 17.9, 9.5 Hz, 1H), 3.61 (s, 3H), 1.51 (s, *J* = 19.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.08, 158.82, 135.20, 134.14, 132.87, 132.61, 131.13, 130.94, 129.55, 128.35, 128.08, 127.74, 127.71, 127.13, 125.90, 123.37, 123.31, 123.00, 112.79, 64.17, 54.14, 35.82. IR (neat): 3061, 3004, 2962, 2916, 2850, 1684, 1610, 1580, 1511, 1457, 1421, 1361, 1303, 1254, 1229, 1179, 1154, 1120, 1025, 979, 910, 852, 800, 768, 729, 711, 679, 639, 621, 600, 572, 552, 529, 505, 484, 440 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd. for; $C_{26}H_{22}NaO_4S$ 453.1136; Found 453.1164.

3-(4-Chlorophenyl)-3-(naphthalen-1-ylsulfonyl)-1-phenylpropan-1-one (13j)

White solid, 12.28 mg, mp 134 °C, 28% yield. HPLC (IA, 90:10 *n*-Hexane/Isopropanol, 1 mL/min, 254 nm): t_{minor} = 25.206 min, t_{major} = 31.435 min, 66% ee, $[\alpha]_D^{23}$ = -135.7 (*c* 1.040, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$):): 8.71 (d, *J* = 8.7 Hz, 1H), 8.00 – 7.93 (m, *J* = 6.3 Hz, 1H), 7.90 – 7.82 (m, 3H), 7.77 (d, *J* = 7.4 Hz, 1H), 7.71 – 7.64 (m, 1H), 7.64 – 7.42 (m, 3H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.35 – 7.27 (m, *J* = 15.3, 7.7 Hz, 1H), 6.93 (dd, *J* = 35.0, 8.5 Hz, 4H), 5.17 (dd, *J* = 9.6, 3.6 Hz, 1H), 4.01 (ddd, *J* = 27.6, 18.0, 6.6 Hz, 2H) . ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.63, 134.88, 134.30, 133.67, 132.75, 132.65, 130.89, 130.61, 130.05, 129.50, 128.43, 128.09, 127.80, 127.64, 127.42, 126.98, 125.92, 123.00, 122.87, 63.96, 49.26, 35.60. IR (neat): 3059, 2917, 2849, 1681, 1658, 1593, 1492, 1447, 1420, 1363, 1329, 1142, 1119, 1094, 1015, 979, 924, 858, 798,

772, 775, 707, 689, 631, 620, 598, 564, 533, 507, 481, 456 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{25}H_{19}ClNaO_3S$ 457.0641; Found 457.0666.

Supporting Information

Supporting Information File 1:

Copies of ^1H and ^{13}C NMR spectra and HPLC chromatograms of products

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