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Ti^{IV}-Catalyzed Asymmetric Sulfenylation of 1,3-Dicarbonyl Compounds

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Abstract: The electrophilic enantioselective sulfenylation of 1,3-dicarbonyl compounds with phenylsulfenyl chloride is effectively catalyzed by [Ti(TADDOLato)] complexes. The corresponding products are obtained in moderate to high yields. The highest *ee* values (up to 97%) are obtained in toluene at room temperature and with a typical catalyst loading of 5 mol%. Bulky ester groups and sterically undemanding substituents at the α-position were found to be crucial structural features of the starting materials in order to assure high enantioselectivity. The absolute configuration of one of the chiral products has been determined. The stereochemical course of the reaction is similar to that of analogous [Ti(TADDOLato)]-catalyzed atom-transfer reactions. A common side-reaction the sulfenylated products undergo is a deacylation leading to racemic α-sulfenylated esters.

Keywords: dicarbonyl compounds · asymmetric catalysis · sulfenylation · titanium

Introduction

Catalytic asymmetric processes involving molecules containing a carbonyl moiety are a rapidly expanding area in the field of enantioselective catalysis. Impetus for such an intensive research is the development of new reactions, but also the simplification of existing methods for the synthesis of optically active molecules bearing a stereogenic center adjacent to a carbonyl group, as it is often the case for biologically active molecules. Functionalized β-keto esters are very versatile building blocks and synthons in organic chemistry, therefore constituting an incentive for the development of new methods for the preparation of their optically active derivatives containing a carbon–heteroatom bond (C–E; E = that is, halogen, N, O and S). The enantioselective α-heterofunctionalization of carbonyl compounds has recently witnessed a boost based on organocatalytic approaches.[1] However, one of the turning points in this field has been the development of Ti^{IV}-catalyzed enantioselective fluorination of β-keto esters, as reported from our laboratory.[2] Catalytic asymmetric fluorination has been the subject of extensive research, undoubtedly because of the higher importance of fluorine, as compared to the other halogens.[3] Indeed, catalytic asymmetric chlorination, bromination and mixed-halogenation reactions have attracted less attention.[4] Asymmetric hydroxylation of β-keto esters has been accomplished by involving metal-catalyzed and organocatalytic approaches, respectively.[5] Direct formation of carbon–nitrogen bond in catalytic asymmetric processes has been a subject of exhaustive studies due to the potential biological activity of the products.[6] Optically active sulfur-containing molecules, as well, have been of wide interest since decades. Molecules bearing a thio ether functionality exhibit several different biological activities, especially as antibiotics.[7]

Numerous chiral sulfur-containing molecules, underestimated in the past, have been put forward as ligands with rapidly growing relevance in enantioselective catalysis.[8] Carbon–sulfur bond forming reactions and simultaneous generation of a stereogenic center were based on different strategies, the most popular being the application of chiral auxiliaries.[9] On the other hand, optically active sulfenylating reagents[10] and chiral phase-transfer catalysts[11] have been rarely employed. Indeed, there are also reports on catalytic asymmetric sulfenylation, but the known examples are mainly limited to conjugative addition of thiols to alkenes bearing electron-withdrawing substituents.[12] The first report on electrophilic sulfenylation based on organocatalysis was published not long ago.[13] Aldehydes and ketones in reactions catalyzed by L-proline derivative with *N*-(phenyl-

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thio)phthalimide furnished α-sulfenylated carbonyl derivatives in yields between 42 and 88%, but *ee* values were not reported. More recently, the organocatalytic formation of optically active products upon electrophilic sulfenylation of aldehydes was reported by Jørgensen.[14] In this case, the reaction with aldehydes gave the best results in toluene at room temperature and was accomplished using a reagent bearing the sulfur functionality protected by a heteroaromatic ring able to form a non-destructive leaving group, compatible with the reaction system.[15] The same group extended this study also to lactones, lactams and β-dicarbonyl molecules.[16] In cinchona-alkaloid-catalyzed reactions with the best reagent firstly reported,[14] that is, 1-benzylsulfanyl-[1.2.4]triazole, sulfenylated derivatives were obtained in high yields and with enantioselectivity up to 91%.

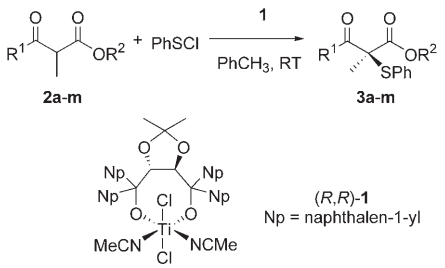
Chiral Ti^{IV} complexes have been extensively studied as they play an important role in a variety of catalytic asymmetric transformations.[17] In recent years, we studied the catalytic properties of such complexes in enantioselective fluorination,[2] bromination,[4e] chlorination,[4d–e] chloro-fluorination[4f] and hydroxylation.[5b] More recently, we reported the first metal-catalyzed asymmetric sulfenylation using chiral Ti(TADDOLato) complex and phenylsulfenyl chloride as the source of electrophilic sulfur.[18] β-Keto esters were efficiently transformed into their α-phenylsulfenyl derivatives with high enantioselectivity and good yields. Interestingly, the evolved hydrogen chloride did not hamper the reaction or the stereoselectivity. Very recently, we have developed another Ti-catalyzed asymmetric sulfenylation of β-keto esters.[19] The source of electrophilic sulfur was phthalimide-*N*-sulfenyl chloride. When the reaction was carried out in toluene, the reaction times were short and the products could be obtained in high yields, but the *ee* values did not go beyond about 60%.

Typical catalyst loading in asymmetric electrophilic atom-transfer reactions using the Ti(TADDOLato) catalyst **1** was 5 mol%, with a limiting value around 1 mol% in the case of the sulfenylation reaction. Therefore, for convenience, all experiments were carried out by using 5 mol% of complex **1** with toluene being the optimal solvent with respect to enantioselectivity. The top enantioselectivities (88% *ee*) were obtained with substrates bearing bulky ester group, that is, *t*Bu or *t*Am.[18]

Results and Discussion

Varying the substrate—Scope and limitations: Trying to extend the scope of the new [Ti(TADDOLato)]-catalyzed asymmetric sulfenylation reaction with phenylsulfenyl chloride (Scheme 1), we decided to study the role of the structure of β-keto esters as a selectivity determining factor. The results of this broader screening are collected in Table 1.

The neopentyl β-keto ester **2a** afforded only 52% *ee*, a value which is by 36% lower than the enantioselectivity observed with the corresponding *tert*-butyl ester. A remarkable drop of enantioselectivity down to the level of the ethyl β-keto ester (53% *ee*),[18] as caused by a single methylene spacer, reflects the subtle nature of the microenvironment of the ester group. We can therefore conclude that the vicinity of the bulky group to the reaction center is of prime importance for high enantioselectivity. This is also shown by the long, linear chain octyl ester **2b**, as well as by derivative **2c** having a yet bulky 2,2-diphenylethyl ester group (49% *ee*), both not contributing to a better enantioselectivity.

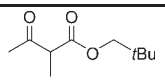
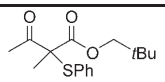
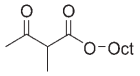
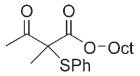
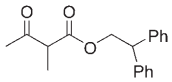
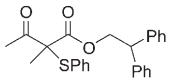
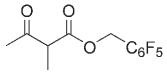
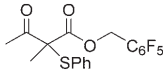
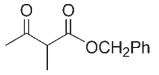
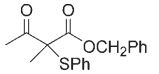
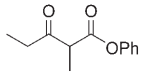
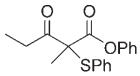
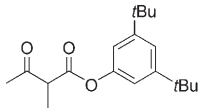
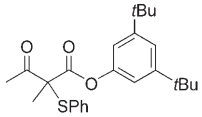
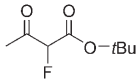
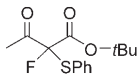
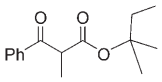
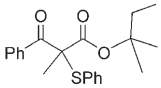
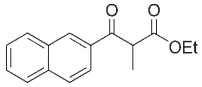
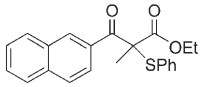
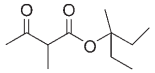
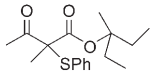
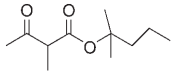
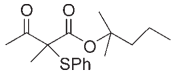
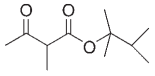
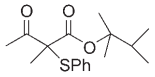


Scheme 1. Ti(TADDOLato)-catalyzed sulfenylation of β-keto esters with PhSCl.

The pentafluorophenyl group is a frequently used structural fragment and valuable marker due to its ability to dramatically modify molecular properties.[20] Because of this intriguing behavior, it was interesting to compare the two substrates **2d** and **2e**, the benzyl and pentafluorobenzyl ester, respectively, with respect to the enantioselectivity of the sulfenylation reaction. Indeed, the pentafluorobenzyl group has a beneficial influence on the enantioselectivity (73% *ee*) when compared to the corresponding non-fluorinated derivative **2e** (62% *ee*). This result can hardly be interpreted only on the basis of steric effects. We can speculate that the ability of the pentafluorobenzyl group to undergo additional weak π interactions[21] may contribute in stabilizing the major diastereoisomeric Ti(enolato) intermediate,[2c] thus leading to a relatively modest, but significant increase in enantioselectivity. The phenyl ester of 2-methyl-3-oxopentanoic acid (**2f**) was converted to 2-phenylsulfenyl derivative **3f** in good isolated yield and with 72% *ee*. On the other hand, the more crowded 3′,5′-di-*tert*-butylphenyl ester analogue **2g** was transformed into **3g** in good yield, but the *ee* dropped to 63%. All these observations taken together corroborate the intuitive notion that steric effects on enantioselectivity are not only a matter of size, but mainly of shape and position of corresponding substituents.

Optically active, fluorine-containing molecules are useful synthons in organic synthesis and, often due to increased biological activity, are indispensable as drugs for the treatment of various diseases and infections.[22] Reports on the preparation of chiral α-fluoro-α-sulfenylated β-keto esters are extremely rare,[23] and there is a complete lack of methods based on asymmetric catalysis for the preparation of this class of compounds. We tested the *tert*-butyl ester of 2-fluoro-3-oxobutanoic acid (**2h**) in the catalytic asymmetric sulfenylation reaction. We were pleased to find that the desired product was formed in 90% *ee*, although the isolated yield was only 60% despite the full conversion of the start-

Table 1. Ti-Catalyzed enantioselective sulfenylation of β-keto esters using PhSCl.[a]

Entry	Reactant **2**		Product **3**		Yield [%][b]	*ee* [%][c]
1		**2a**		**3a**	75	52
2		**2b**		**3b**	73	53
3		**2c**		**3c**	71	49
4		**2d**		**3d**	57	73
5		**2e**		**3e**	60	62
6		**2f**		**3f**	93	72
7		**2g**		**3g**	78	63
8		**2h**		**3h**	60	89
9		**2i**		**3i**	75	86
10		**2j**		**3j**	75	66
11		**2k**		**3k**	85	90
12		**2l**		**3l**	86	92
13		**2m**		**3m**	82	97

[a] Reaction conditions: 0.2 mmol β-keto ester **2**, 0.01 mmol **1**, 2 mL toluene and 0.25 mmol PhSCl, stirring at RT up to 14 h. [b] Isolated yield. [c] Determined by chiral stationary phase HPLC.

ing material **2h**. This is the consequence of the instability of the product, as indicated by the NMR spectrum of the crude reaction mixture already showing partial deacylation (10–15%). It is interesting to note the beneficial influence of the fluorine atom in substrate **2h** on enantioselectivity, as compared to the corresponding compound with a methyl group giving a slightly lower *ee* (88%).[18]

Furthermore, we varied the size of the α-substituent in order to ascertain its role on the course of the reaction. As a model substrate we chose the ethyl ester of 2-isopropyl-3-oxobutanoic acid and found that it was much less reactive than the analogous 2-methyl derivatives, the conversion to product not going beyond 10–15% (the *ee* has therefore not been determined). As discussed above, steric factors are of crucial importance and there is clearly a fundamental difference between the ester group and the α-substituent in this respect. The latter should be as sterically undemanding as possible.

We also examined the role of the structure of the group attached to ketone carbonyl moiety by comparing the 2-benzoyl and 2-naphthoyl propionates **2i** and **2j**. The *tert*-amyl ester **2i** was transformed to the sulfenylated derivative **3i** in 75% isolated yield and the *ee* reached 86%, thus showing that the replacement of the methyl by a phenyl group does not represent any significant advantage in terms of enantioselectivity. Additionally, the ethyl ester **2j**, containing the 2-naphthyl substituent, gave product **3j** in 75% isolated yield, but with an enantioselectivity not exceeding 66%. It is obvious that the structure of the ester functionality possesses a considerable higher impact on enantioselectivity that the keto group.

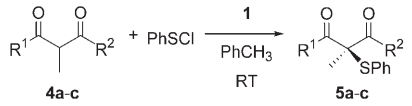
Finally, on the basis of the previous findings concerning the steric influence of the ester group, three isomeric β-keto esters **2k**, **2l** and **2m** were prepared and anticipated to afford high enantioselectivities. Indeed, they could be converted to their corresponding products in high yields and *ee* values up to 97% in the case of 1,1,2-trimethylpropyl ester **2m**. A closer examination of the structure of the three esters **2k**, **2l** and **2m** reveals that the branching of the ester group is crucial, thus being responsible for the most beneficial effect on enantioselectivity. Again, the positive steric effect of the ester group is here a matter of it being a bulky, rigid and compact aliphatic group.

We also explored benzylsulfenyl chloride as an electrophilic sulfur source. However, this reagent is less stable and therefore less convenient than the phenylsulfenyl chloride. Nevertheless, ethyl 2-methylacetoacetate was converted under the usual catalytic conditions into its benzylsulfenyl derivative **2n** with 56% *ee* and 82% isolated yield. We also tested two structurally different potential phenylsulfenyl group transfer reagents, that is, phenyl thiocyanate (PhSCN) and *N*,*N*-diethylbenzenesulfenamide ($PhSNEt_2$). Both were

found to be unsuited under Ti-catalytic conditions, since the starting material remained unreacted.

Beside β-keto esters we also studied catalytic asymmetric sulfenylation reactions of other 1,3-dicarbonyl compounds (Table 2).

Table 2. Role of the structure of β-dicarbonyl compounds in the Ti-catalyzed enantioselective sulfenylation using PhSCl.[a]



Entry	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	Et	NHPh (**4a**)	75 (**5a**)	36
2	Et	NHCHPhMe (*S*) (**4b**)	79 (**5b**)	0[d]
3	EtO	O*t*Bu (**4c**)	87 (**5c**)	64

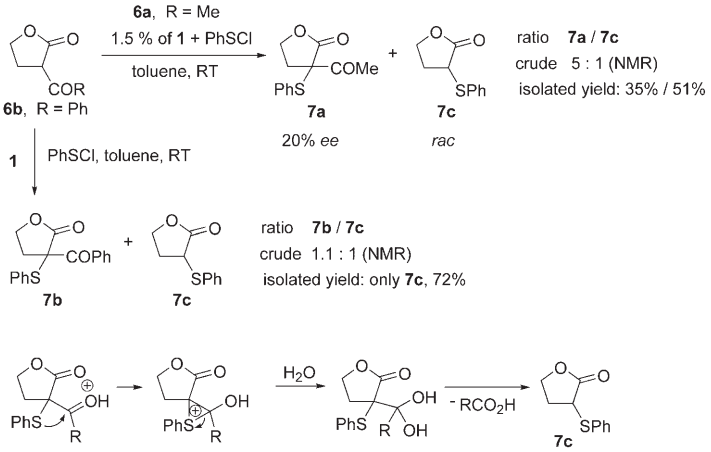
[a] Reaction conditions: 0.2 mmol substrate **4**, 2 mL toluene and 0.25 mmol PhSCl, stirring at RT up to 14 h. [b] Isolated yield. [c] Determined by chiral stationary phase HPLC. [d] 1:1 mixture of diastereoisomers.

β-Keto amides and β-keto lactams usually display a lower enol content than β-keto esters and are therefore less reactive in asymmetric electrophilic atom transfer reactions. To our surprise, we found that even unenolized β-keto amides react with phenylsulfenyl chloride instantaneously without the need of any catalyst. This was not the case for 3-acetyl-1-phenyl-2-pyrrolidone which, however, gave the sulfenylated product with low *ee*. The open-chain, non-enolized substrate **4a** reacts very rapidly in toluene giving the corresponding product with 36% *ee* and in good yield. The β-keto amide **4b**, derived from (*S*)-phenethylamine, is very reactive as well and the reaction in the presence of catalyst **1** yielded a 1:1 diastereoisomeric mixture of sulfenylated products. Malonate ester **4c**, similarly to β-keto amide **4a**, can hardly enolize and could be regarded as a tough substrate for catalytic reactions using complex **1**. Unexpectedly, the reaction of **4c** proceeded smoothly to completion with phenylsulfenyl chloride leading to the optically active sulfenylated derivative **5c** (64% *ee*) in high yield. The results observed with the three substrates **4a–c** had not been anticipated and reflect a somewhat anomalous behavior, at least in the context of our current understanding of this reaction system.

1,3-Diketones are usually highly enolized and therefore Ti[TADDOLato]-catalyzed transformation result in a product with negligible, or at best, low enantioselectivity.[5b] We tested 2-acetylcyclohexanone and isolated its 2-sulfenylated derivative, indeed in racemic form.

To complete the range of obvious 1,3-dicarbonyl substrates, we also examined the reactivity of β-keto lactones. Compounds **6a** and **6b** reacted completely when 1.5 mol% of **1** was used, as monitored by NMR spectroscopic analysis of the crude reaction mixture. However, some additional signals in the ^{1}H NMR spectrum that could not be assigned to the expected sulfenylated compound indicated the presence of another product.

Chromatographic separation in the case of **6a** gave, beside the expected **7a**, also the deacylated derivative **7c**. The optical yield of **7a** was a modest 21%, whereas **7c** was isolated in racemic form. The crude reaction mixture of **6b** contained, analogously to **6a**, both **7b** and **7c**. However, upon column chromatographic purification complete debenzoylation of **7b** took place yielding racemic **7c** as the only isolable product. A possible explanation for such a facile decomposition of the desired products is shown in Scheme 2.



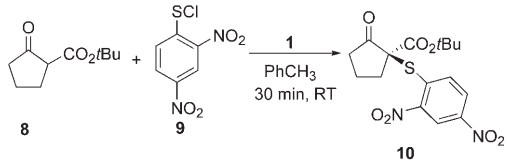
Scheme 2. Deacylation of sulfenylated lactones.

We think that the scission of the strong carbon–carbon bond is an acid-catalyzed process, relying on the nucleophilic assistance of the sulfur atom adjacent to the acyl group, thereby increasing the basicity of the carbonyl oxygen. The protonated form of **7b** is stabilized as an episulfonium which is then attacked by a water molecule leading to a tetrahedral intermediate, readily decomposing to **7c** and benzoic acid.

Mechanistic considerations: We previously put forward a stereochemical model for the electrophilic sulfenylation reaction.[18] This model is based on an analogy with the related electrophilic asymmetric halogenation and hydroxylation processes using the same catalyst **1**.[2b,c,5b] Thus, despite the lack of final experimental evidence, the current mechanistic interpretation takes into account the formation of a mixture of diastereoisomeric Ti(carbonylenolato) complexes undergoing external attack by the electrophile.[2c] Derivatization of *tert*-butyl 2-oxocyclopentanecarboxylate (**8**) with 2,4-dinitrophenylsulfenyl chloride (**9**) produces *tert*-butyl 1-(2,4-dinitrophenylsulfanyl)-2-oxocyclopentanecarboxylate (**10**), a crystalline compound whose absolute configuration had previously been determined.[16] The optical rotation of a sample of **10**, obtained using (*R*,*R*)-**1** as catalyst, was compared with the literature value, thus establishing the *S* absolute configuration. This is consonant to the proposed stereochemical model governing the previously reported reactions.[2b,5b] The *Re* enantioface of the enolate in the prevalent diastereoisomeric intermediate is shielded by one of the two face-on naphthyl groups of the (*R*,*R*)-configured TADDOL. The

bond-forming interaction with the electrophile takes place at the *Si* side, thus yielding the *S* enantiomer of the product preferentially.

The reaction of *tert*-butyl 2-oxocyclopentanecarboxylate (**8**) with 2,4-dinitrophenylsulfenyl chloride (**9**) is more rapid than the one with phenylsulfenyl chloride and was completed in less than 30 min (Scheme 3). Similarly, phthalimide-*N*-



Scheme 3. Synthesis of compound **10** whose absolute configuration is known.

sulfenyl chloride also displays a higher reactivity. Electron-withdrawing groups make the sulfur atom more electron deficient, that is, more electrophilic. In principle, this would make it more prone to undergo ionic transformations, but it makes it also a better electron acceptor which, in turn, would possibly implicate a single-electron-transfer (SET) mechanism. The free-radical trap TEMPO was shown in the reaction of ethyl 2-methylacetoacetate with phenylsulfenyl chloride to decrease the *ee* from 49 to 38%, while the yield remained unchanged at 94%. We also conducted experiments with ethyl 2-methylacetoacetate in toluene that was previously purged with molecular oxygen and found that both enantioselectivity and yield are only moderately diminished. While both experiments seem to indicate that free radicals are not involved in the process, they cannot be considered as evidence against SET, as SET does not necessarily imply the formation of free radicals with a discrete life time. Thus, the intimate nature of the carbon–sulfur bond-forming process remains a debatable issue.

Conclusion

We have reported a Ti asymmetric sulfenylation of 1,3-dicarbonyl compounds using phenylsulfenyl chloride. Reactions proceed with good yields and enantioselectivity up to 97%. The best results were obtained in toluene at room temperature, the by-product hydrogen chloride not affecting the stereoselectivity. The proposed stereochemical model for this reaction involves diastereoisomeric intermediates containing the β-keto ester enolate coordinated to the Ti^{IV} center in a bidentate fashion. This leads to a preferential shielding of one of the enolate enantiofaces by a face-on naphthyl group of the ligand, as previously demonstrated for the analogous halogenation and hydroxylation reactions. This Ti(TADDOLato) catalyst remains the only highly effective transition-metal system for a sulfenylation reaction and maintains a unique character in view of the rather broad scope of applicable electrophiles.

Experimental Section

General methods: Reactions with air- or moisture-sensitive materials were carried out under an argon atmosphere using Schlenk techniques. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on Bruker AVANCE spectrometers AC 200, DPX 250, and DPX 300. ^{1}H and ^{13}C spectra were recorded in $CDCl_3$, chemical shifts are reported in ppm relative to the residual chloroform peak (7.26 ppm) for ^{1}H NMR and to the central line of $CDCl_3$ (77.0 ppm) for ^{13}C NMR. IR spectra were recorded on a Perkin Elmer FT-IR Paragon 1000. Optical rotations were measured by using a Perkin Elmer 341 polarimeter with a 1-dm cell. Column chromatography was carried out using Fluka silica gel 60 (230–400 mesh). Elemental analyses were carried out by the Laboratory of Microelemental Analysis (ETH Zürich). HRMS measurements were performed by the MS-service of the Laboratorium für Organische Chemie der ETH Zürich. Enantiomeric excesses were determined by HPLC with Agilent (Palo Alto, CA) HPLC 1100 or HPLC 1050 Series systems.

Materials: All solvents were distilled prior to use. Complex [$TiCl_2$((*R*,*R*)-1-Np-TADDOLato)$(MeCN)_2$] (**1**, bis(acetonitrile)dichloro [(4*R*,5*R*)-2,2-dimethyl-α,α,α′,α′-tetra(naphthalene-1-yl)-1,3-dioxolane-4,5-dimethanolato(2-)-κ*O*,κ*O*′]titanium),[24] phenylsulfenyl chloride[25] and benzylsulfenyl chloride[26] were prepared following published procedures. 2,4-Dinitrophenylsulfenyl chloride was obtained from Aldrich. Starting β-dicarbonyl compounds **2a**,[27] **2b**,[27] **2c**,[28] **2d**,[29] **2e**,[27] **2f**,[30] **2i**,[28] **2j**,[4e] **4a**,[31] **4c**[32] and **8**[33] were prepared according to the published procedures. β-Keto lactones **6a**[34] and **6b**[34] were prepared from γ-butyrolactone by deprotonation and subsequent quenching with acetyl or benzoyl chloride, respectively, according to standard procedures.

General procedure for the enantioselective catalytic sulfenylation of β-dicarbonyl compounds: β-Keto ester **2a** (29 mg, 0.2 mmol) and catalyst **1** (2.4 mg, 0.003 mmol, to 7.6 mg, 0.01 mmol) were placed in a heat-gun dried Schlenk tube containing freshly distilled toluene (2 mL). After 10 min of stirring, phenylsulfenyl chloride (0.25 mL, 0.25 mmol) solution in toluene (0.25 mL) was added via syringe. After stirring for 12–14 h at room temperature, the reaction mixture was diluted with *t*BuOMe and filtered over a pad of alumina. The solvent was evaporated and the product was purified by column chromatography (SiO_2, hexane/*t*BuOMe mixtures).

2,2-Dimethylpropyl 2-methyl-3-oxo-2-(phenylsulfanyl)butanoate (3a): The *ee* was determined by HPLC using a ReproSil Chiral-DP column (hexane/*i*PrOH 99.5:0.5); flow rate 0.6 mL min^{-1}; τ_{major} = 22 min; τ_{minor} = 24 min); $[\alpha]_D^{RT}$ = −29.5 (*c* = 0.5 in CH_2Cl_2, 50% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 0.95 (s, 9H; CMe_3), 1.51 (s, 3H; CH_3), 2.39 (s, 3H; CH_3), 3.82 (d, *J*(H,H) = 10.5 Hz, 1H; C*H*H), 3.92 (d, *J*(H,H) = 10.5 Hz, 1H; CH*H*), 7.26–7.46 ppm (m, 5H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25°C): δ = 20.7, 26.1, 26.3, 31.5, 65.8, 75.7, 129.0, 129.3, 129.8, 136.9, 169.9, 199.2 ppm; IR (KBr): $\tilde{\nu}$ = 2961, 1715, 1475, 1440, 1368, 1247, 1124, 976, 751, 693 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{16}H_{22}O_3S$: 294.1285; found 294.1282 $[M]^+$.

Octyl 2-methyl-3-oxo-2-(phenylsulfanyl)butanoate (3b): The *ee* was determined by HPLC using a Daicel Chiralcel AD-H column (hexane/*i*PrOH 99:1); flow rate 0.5 mL min^{-1}; τ_{major} = 16.5 min; τ_{minor} = 15 min); $[\alpha]_D^{RT}$ = −30.5 (*c* = 0.51 in CH_2Cl_2, 56% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 0.88 (m, 3H; CH_3), 1.20–1.39 (m, 10H; 5×CH_2), 1.50 (s, 3H; CH_3), 1.65 (m, 2H; CH_2), 2.37 (s, 3H; CH_3), 4.18 (t, *J*(H,H) = 6.3 Hz, 2H; OCH_2), 7.27–7.46 ppm (m, 5H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25°C): δ = 14.1, 20.7, 22.6, 25.8, 26.0, 28.3, 29.1, 31.7, 65.7, 66.6, 128.9, 129.4, 129.8, 136.9, 170.0, 199.3 ppm; IR (neat): $\tilde{\nu}$ = 2929, 2857, 1715, 1440, 1246, 1120, 749, 693 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{19}H_{28}O_3S$: 336.1754; found 336.1752 $[M]^+$.

2,2-Diphenylethyl 2-methyl-3-oxo-2-(phenylsulfanyl)butanoate (3c): The *ee* was determined by HPLC using a Daicel Chiralcel AD-H column (hexane/*i*PrOH 99:1); flow rate 0.6 mL min^{-1}; τ_{major} = 44 min; τ_{minor} = 35 min); $[\alpha]_D^{RT}$ = −21.0 (*c* = 0.50 in CH_2Cl_2, 49% *ee*); ^{1}H NMR (200 MHz, $CDCl_3$, 25°C): δ = 1.34 (s, 3H; CH_3), 1.96 (s, 3H; CH_3), 4.39 (t, *J*(H,H) = 7.6 Hz, 1H; CH), 4.73 (m, 2H; CH_2), 7.10–7.40 (m, 15H; 3×Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25°C): δ = 20.5, 25.6, 49.7, 65.7,

68.4, 127.0, 127.1, 128.1, 128.7, 128.9, 129.3, 129.8, 136.9, 140.3, 169.7, 199.1; IR (neat): $\tilde{\nu}$ = 2930, 1714, 1245, 1122, 750, 701 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{25}H_{24}O_3S$: 404.1437; found 404.1439 $[M]^+$.

Pentafluorobenzyl 2-methyl-3-oxo-2-(phenylsulfanyl)butanoate (3d): The *ee* was determined by HPLC using a Daicel Chiralcel AD-H column (hexane/*i*PrOH 99:1); flow rate 0.6 mL min^{-1}; τ_{major} = 25 min; τ_{minor} = 22 min); $[\alpha]_D^{RT}$ = −37.0 (*c* = 0.50 in CH_2Cl_2, 74% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 1.51 (s, 3H; CH_3), 2.34 (s, 3H; CH_3), 5.27 (s, 2H, CH_2), 7.24–7.44 ppm (m, 5H, Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25°C): δ = 20.7, 25.8, 54.8, 65.5, 108.4, 129.0, 130.0, 135.5, 136.8, 139.7, 143.7, 147.7, 169.4, 198.9 ppm; ^{19}F NMR (188.3 MHz, $CDCl_3$, 25°C): δ = −160.9 (m, 2F), −151.2 (tt, *J*(F,H) = 21, 2.2 Hz, 1F), −141.6 ppm (m, 2F); IR (neat): $\tilde{\nu}$ = 2936, 1716, 1524, 1508, 1440, 1310, 1233, 1133, 1056, 940, 751, 693 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{18}H_{13}F_5O_3S$: 404.0501; found 404.0504 $[M]^+$.

Benzyl 2-methyl-3-oxo-2-(phenylsulfanyl)butanoate (3e): The *ee* was determined by HPLC using a Daicel Chiralcel AD-H column (hexane/*i*PrOH 99:1); flow rate 0.6 mL min^{-1}; τ_{major} = 39 min; τ_{minor} = 31 min); $[\alpha]_D^{RT}$ = −46.0 (*c* = 0.50 in CH_2Cl_2, 63% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 1.51 (s, 3H; CH_3), 2.28 (s, 3H; CH_3), 5.22 (s, 2H; CH_2), 7.24–7.43 ppm (m, 5H; Ar-H); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25°C): δ = 20.7, 26.0, 65.7, 67.9, 128.5, 128.6, 128.9, 129.2, 129.8, 134.8, 136.9, 169.7, 199.2 ppm; IR (neat): $\tilde{\nu}$ = 2934, 1713, 1234, 1115, 750, 693 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{18}H_{18}O_3S$: 314.0972; found 314.0971 $[M]^+$.

Phenyl 2-methyl-3-oxo-2-(phenylsulfanyl)pentanoate (3f): The *ee* was determined by HPLC using a Daicel Chiralcel AD-H column (hexane/*i*PrOH 99:1); flow rate 0.6 mL min^{-1}; τ_{major} = 22 min; τ_{minor} = 26 min); $[\alpha]_D^{RT}$ = −25.5 (*c* = 1 in CH_2Cl_2, 71% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 1.19 (t, *J*(H,H) = 7.2 Hz, 3H; CH_3), 1.67 (s, 3H; CH_3), 2.76 (dq, *J*(H,H) = 17.8 Hz, *J*(H,H) = 7.2 Hz, 1H; C*H*H), 2.98 (dq, *J*(H,H) = 17.8 Hz, *J*(H,H) = 7.2 Hz, 1H; CH*H*), 7.08 (m, 2H; Ar-H), 7.22–7.53 ppm (m, 8H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25°C): δ = 8.5, 21.1, 31.7, 65.5, 121.0, 126.3, 129.0, 129.2, 129.6, 130.0, 137.1, 150.4, 168.7, 202.5 ppm; IR (neat): $\tilde{\nu}$ = 2935, 1754, 1716, 1592, 1493, 1191, 1162, 1086, 749, 689 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{18}H_{18}O_3S$: 314.0972; found 314.0974 $[M]^+$.

3,5-Di-*tert*-butylphenyl 2-methyl-3-oxobutanoate (2g): ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 1.31 (s, 18H; 2×CMe_3), 1.49 (d, *J*(H,H) = 7.2 Hz, 3H; CH_3), 2.38 (s, 3H; CH_3), 3.76 (q, *J*(H,H) = 7.2 Hz, 1H; CH), 6.90 (d, *J*(H,H) = 1.5 Hz, 2H; Ar-H), 7.29 ppm (t, *J*(H,H) = 1.5 Hz, 1H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25°C): δ = 12.8, 28.7, 31.3, 35.0, 53.7, 115.3, 120.1, 150.2, 152.4, 169.2, 203.4 ppm; IR (KBr): $\tilde{\nu}$ = 2968, 1763, 1709, 1362, 1195, 1144, 1091, 910, 707 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{19}H_{28}O_3$: 304.2033; found 304.2036 $[M]^+$.

3,5-Di-*tert*-butylphenyl 2-methyl-3-oxo-2-(phenylsulfanyl)butanoate (3g): The *ee* was determined by HPLC using a Daicel Chiralcel OD-H column (hexane/*i*PrOH 99.7:0.3); flow rate 0.1 mL min^{-1}; τ_{major} = 79 min; τ_{minor} = 72 min); $[\alpha]_D^{RT}$ = −34.0 (*c* = 0.61 in CH_2Cl_2, 63% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 1.31 (s, 18H; 2×CMe_3), 1.68 (s, 3H; CH_3), 2.52 (s, 3H; CH_3), 6.87 (d, *J*(H,H) = 1.3 Hz, 2H; Ar-H), 7.26–7.44 (m, 4H; Ar-H), 7.52 ppm (m, 2H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25°C): δ = 20.9, 26.3, 31.3, 35.0, 65.9, 114.9, 120.3, 129.1, 129.2, 130.0, 137.0, 150.2, 152.5, 168.6, 199.3 ppm; IR (KBr): $\tilde{\nu}$ = 2964, 1754, 1719, 1612, 1588, 1226, 1089, 749, 704, 692 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{25}H_{32}O_3S$: 412.2067; found 412.2072 $[M]^+$.

***tert*-Butyl 2-fluoro-3-oxobutanoate (2h)**: ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 1.51 (s, 9H; CMe_3), 2.32 (d, *J*(H,F) = 3.9 Hz, 3H; CH_3), 5.07 ppm (d, *J*(H,F) = 49.9 Hz, 1H; CH); ^{19}F NMR (188.3 MHz, $CDCl_3$, 25°C): δ = −191.6 ppm (qd, *J*(F,H) = 49.9 Hz, *J*(F,H) = 3.9 Hz; F).

***tert*-Butyl 2-fluoro-3-oxo-2-(phenylsulfanyl)butanoate (3h)**: The *ee* was determined by HPLC using a Daicel Chiralcel OJ column (hexane/*i*PrOH 99:1); flow rate 0.3 mL min^{-1}; τ_{major} = 66 min; τ_{minor} = 59.5 min); $[\alpha]_D^{RT}$ = −41.0 (*c* = 0.545 in CH_2Cl_2, 90% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 1.40 (s, 9H; CMe_3), 2.20 (d, *J*(H,H) = 3.2 Hz, 3H; CH_3), 7.30–7.42 (m, 3H; Ar-H), 7.53–7.60 ppm (m, 2H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25°C): δ = 26.0, 27.6, 85.3, 105.2 (d, *J*(C,F) = 243.7 Hz, CF), 127.4 (d, *J* = (C,F) = 1.5 Hz, CF), 129.2, 130.0, 135.7 (d, *J*(C,F) = 1.7 Hz, CF), 162.2 (d, *J*(C,F) = 28 Hz, CF), 196.6 ppm (d, *J*(C,F) = 28.8 Hz, CF); ^{19}F NMR (188.3 MHz, $CDCl_3$, 25°C): δ = −133.1 ppm (q, *J*(F,H) = 3.2 Hz; F); IR (neat): $\tilde{\nu}$ = 2981, 2932, 1737, 1371, 1258, 1153, 747, 691 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{14}H_{17}FO_3S$: 284.0877; found 284.0880 $[M]^+$.

2-Methyl-3-oxo-3-phenyl-2-phenylsulfanyl-propanoic acid-*tert*-amyl ester (3i): The *ee* was determined by HPLC using a Daicel Chiralcel AD-H column (hexane/*i*PrOH 99:1); flow rate 0.2 mL min^{-1}; τ_{major} = 40 min; τ_{minor} = 36 min); $[\alpha]_D^{RT}$ = +104 (*c* = 0.5 in CH_2Cl_2, 83% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 0.63 (t, *J*(H,H) = 7.5 Hz, 3H; CH_3), 1.19 (s, 3H; CH_3), 1.30 (s, 3H; CH_3), 1.47 (m, 2H; CH_2), 1.65 (s, 3H; CH_3), 7.24–7.37 (m, 5H; Ar-H), 7.40–7.49 (m, 2H; Ar-H), 7.51–7.59 (m, 1H; Ar-H), 8.15 ppm (m, 2H; Ar-H); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25°C): δ = 7.8, 23.3, 24.4, 24.8, 33.8, 63.9, 86.0, 128.2, 128.8, 129.4, 129.6, 129.7, 132.7, 135.5, 137.3, 170.1, 191.9 ppm; IR (neat): $\tilde{\nu}$ = 2977, 2933, 1729, 1682, 1370, 1266, 1156, 1129, 1107, 963, 842, 748, 691 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{21}H_{24}O_3S$: 356.1441; found 356.1441 $[M]^+$.

Ethyl 2-methyl-3-(2-naphthyl)-3-oxo-2-(phenylsulfanyl)propanoate (3j): The *ee* was determined by HPLC using a Daicel Chiralcel AS column (hexane/*i*PrOH 99:1); flow rate 0.6 mL min^{-1}; τ_{major} = 19 min; τ_{minor} = 17 min); $[\alpha]_D^{RT}$ = +176 (*c* = 0.56 in CH_2Cl_2, 68% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 0.99 (t, *J*(H,H) = 7.2 Hz, 3H; CH_3), 1.75 (s, 3H; CH_3), 4.13 (dq, *J*(H,H) = 7.2, 1.1 Hz, 2H; C*H*H), 7.20–7.41 (m, 5H; Ar-H), 7.58 (m, 2H), 7.88 (d, *J*(H,H) = 8.5 Hz, 2H; Ar-H), 7.97 (d, *J*(H,H) = 8.2 Hz, 1H; Ar-H), 8.08 (dd, *J*(H,H) = 8.7, 1.7 Hz, 1H; Ar-H), 8.67 ppm (m, 1H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25°C): δ = 13.7, 23.4, 62.4, 63.4, 125.1, 126.7, 127.7, 128.1, 128.6, 128.9, 129.1, 129.8, 129.9, 131.0, 132.3, 132.3, 135.3, 137.4, 171.3, 191.6 ppm; IR (neat): $\tilde{\nu}$ = 3059, 2982, 2935, 1732, 1679, 1626, 1473, 1440, 1372, 1240, 1190, 1099, 1018, 938, 866, 742, 692 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{22}H_{20}O_3S$: 364.1128; found 364.1133 $[M]^+$.

1-Ethyl-1-methylpropyl 2-methyl-3-oxobutanoate (2k): ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 0.83 (t, *J*(H,H) = 7.5 Hz, 6H; $CHMe_2$), 1.28 (d, *J*(H,H) = 7.2 Hz, 3H; CH_3), 1.37 (s, 3H; CH_3), 1.80 (m, 4H; 2×CH_2), 2.22 (s, 3H; CH_3), 3.42 ppm (q, *J*(H,H) = 7 Hz, 1H; CH); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25°C): δ = 7.9, 12.8, 22.6, 28.6, 30.3, 30.4, 54.7, 87.1, 169.5, 204.0 ppm; IR (neat): $\tilde{\nu}$ = 2978, 1715, 1508, 1267, 1134, 849 cm^{-1}.

1,1-Dimethylbutyl 2-methyl-3-oxobutanoate (2l): ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 0.90 (t, *J*(H,H) = 7.5 Hz, 3H; CH_3), 1.24–1.36 (m, 5H; CH_2, CH_3), 1.43 (s, 6H; 2×Me), 1.65–1.75 (m, 2H; CH_2), 2.21 (s, 3H; CH_3), 3.39 ppm (q, *J*(H,H) = 7 Hz, 1H; CH); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25°C): δ = 12.7, 14.4, 17.1, 25.7, 25.8, 28.4, 43.2, 54.7, 84.1, 169.6, 204.0 ppm; IR (neat): $\tilde{\nu}$ = 2964, 1716, 1508, 1267, 1147, 846 cm^{-1}.

1,1,2-Trimethylpropyl 2-methyl-3-oxobutanoate (2m): ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 0.89 (d, *J*(H,H) = 6.8 Hz, 6H; $CHMe_2$), 1.30 (d, *J*(H,H) = 7 Hz, 3H; CH_3), 1.43 (s, 6H; 2×CH_3), 2.15 (m, 1H; CH), 2.23 (s, 3H; CH_3), 3.42 ppm (q, *J*(H,H) = 7 Hz, 1H; CH); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25°C): δ = 12.7, 17.2, 22.5, 22.7, 28.5, 36.5, 54.8, 87.0, 169.6, 203.9 ppm; IR (neat): $\tilde{\nu}$ = 2981, 1715, 1136 cm^{-1}.

1-Ethyl-1-methylpropyl 2-methyl-3-oxo-2-(phenylsulfanyl)butanoate (3k): The *ee* was determined by HPLC using a Daicel Chiralcel OJ column (hexane/*i*PrOH 99:1); flow rate 0.6 mL min^{-1}; τ_{major} = 28 min; τ_{minor} = 22 min); $[\alpha]_D^{RT}$ = −49.5 (*c* = 0.52 in CH_2Cl_2, 91% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 0.88 (t, *J*(H,H) = 7.5 Hz, 6H; 2×CH_2CH_3), 1.45 (brs, 6H; 2×CH_3), 1.69–1.99 (m, 4H; 2×CH_2CH_3), 2.41 (s, 3H; CH_3), 7.26–7.45 ppm (m, 5H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25°C): δ = 8.0, 20.8, 22.4, 26.1, 30.3, 30.4, 66.5, 89.1, 128.9, 129.7, 129.7, 136.7, 168.7, 199.3 ppm; IR (neat): $\tilde{\nu}$ = 2977, 1712, 1254, 1120, 852, 748, 693 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{17}H_{24}O_3S$: 308.1441; found 308.1439 $[M]^+$.

1,1-Dimethylbutyl 2-methyl-3-oxo-2-(phenylsulfanyl)butanoate (3l): The *ee* was determined by HPLC using a Daicel Chiralcel AD-H column (hexane/*i*PrOH 99:1); flow rate 0.3 mL min^{-1}; τ_{major} = 22 min; τ_{minor} = 24 min); $[\alpha]_D^{RT}$ = −62.0 (*c* = 0.735 in CH_2Cl_2, 92.5% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ = 0.92 (t, *J*(H,H) = 7.5 Hz, 3H; CH_3), 1.25–1.41 (m, 2H; CH_2), 1.45 (s, 3H; CH_3), 1.47 (s, 3H; CH_3), 1.48 (s, 3H; CH_3), 1.72 (m, 2H; CH_2), 2.39 (s, 3H; CH_3), 7.27–7.44 ppm (m, 5H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25°C): δ = 14.3, 17.1, 20.6, 25.5, 25.5,

26.0, 43.3, 66.5, 85.9, 128.9, 129.6, 129.7, 136.8, 168.8, 199.3 ppm; IR (neat): $\tilde{\nu}$ = 2962, 2935, 2874, 1712, 1370, 1260, 1230, 1158, 1123, 749, 693 cm^{-1}; HRMS: *m/z*: calcd for $C_{17}H_{24}O_3S$: 308.1441; found 308.1441 $[M]^+$.

1,1,2-Trimethylpropyl 2-methyl-3-oxo-2-(phenylsulfanyl)butanoate (3m): The *ee* was determined by HPLC using a Daicel Chiralcel AD-H column (hexane/*i*PrOH 99:1); flow rate 0.3 mL min^{-1}; τ_{major} = 25 min; τ_{minor} = 23 min); $[\alpha]_D^{RT}$ = −60.8 (*c* = 0.56 in CH_2Cl_2, 97% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 0.91 (m, 6H; CHMe_2), 1.44–1.50 (m, 9H; 3×CH_3), 2.11 (m, 1H; CH), 2.40 (s, 3H; CH_3), 7.27–7.44 ppm (m, 5H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 17.2, 17.3, 20.6, 22.3, 22.5, 26.0, 37.0, 66.6, 88.8, 128.9, 129.6, 129.7, 136.8, 168.7, 199.3 ppm; IR (neat): $\tilde{\nu}$ = 2980, 1712, 1254, 1122, 748, 693 cm^{-1}; HRMS: *m/z*: calcd for $C_{17}H_{24}O_3S$: 308.1441; found 308.1441 $[M]^+$.

Ethyl 2-(benzylsulfanyl)-2-methyl-3-oxobutanoate (3n): The *ee* was determined by HPLC using a Daicel Chiralcel AD-H column (hexane/*i*PrOH 99:1); flow rate 0.4 mL min^{-1}; τ_{major} = 32 min; τ_{minor} = 30 min); $[\alpha]_D^{RT}$ = −15.5 (*c* = 0.46 in CH_2Cl_2, 56% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.31 (t, *J*(H,H) = 7.3 Hz, 3H; CH_3), 1.71 (s, 3H; CH_3), 2.32 (s, 3H; CH_3), 3.93 (s, 2H; SCH_2), 4.28 (q, *J*(H,H) = 7.3 Hz, 2H; CH_2), 7.20–7.40 ppm (m, 5H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 14.0, 20.1, 26.1, 44.0, 62.5, 66.5, 127.7, 128.7, 129.3, 136.2, 169.7, 199.6 ppm; IR (neat): $\tilde{\nu}$ = 2982, 1713, 1454, 1249, 1110, 1016, 699 cm^{-1}; HRMS: *m/z*: calcd for: 265.0893; found 265.0891 $[M-H]^+$.

2-Methyl-3-oxo-*N*-(1(*S*)-phenylethyl)pentanamide (4b): $[\alpha]_D^{RT}$ = −33.6 (*c* = 0.50 in CH_2Cl_2, 0% *de*); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.04 (t, *J*(H,H) = 7.5 Hz, 3H; CH_3), 1.41 (d, *J*(H,H) = 7.5 Hz, 3H; CH_3), 1.48 (d, *J*(H,H) = 7.5 Hz, 3H; CH_3), 2.57 (q, *J*(H,H) = 7.5 Hz, 2H; CH_2), 3.42 (q, *J*(H,H) = 7.5 Hz, 1H; CH), 5.08 (m, 1H; CH), 6.54 (m, 1H; NH), 7.24–7.37 ppm (m, 5H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C), 2 diastereoisomers: δ = 7.5, 7.5, 15.3, 15.3, 21.9, 21.9, 34.8, 34.8, 48.9, 49.0, 54.1, 54.1, 125.9, 126.0, 127.3, 127.4, 128.7, 143.0, 143.0, 168.5, 168.6, 210.6, 210.7 ppm; IR (KBr): $\tilde{\nu}$ = 3296, 2979, 2937, 1727, 1637, 1544, 1447, 1135, 1020, 970, 753, 700 cm^{-1}; elemental analysis calcd (%) for $C_{14}H_{19}NO_2$ (233.3): C 72.07, H 8.21, N 6.00; found C 71.93, H 8.66, N 5.97.

2-Methyl-3-oxo-*N*-phenyl-2-(phenylsulfanyl)pentanamide (5a): The *ee* was determined by HPLC using a Daicel Chiralcel OJ column (hexane/*i*PrOH 99:1); flow rate 0.9 mL min^{-1}; τ_{major} = 89 min; τ_{minor} = 59 min); $[\alpha]_D^{RT}$ = −20.0 (*c* = 0.54 in CH_2Cl_2, 36% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.13 (t, *J*(H,H) = 7.2 Hz, 3H; CH_3), 1.70 (s, 3H; CH_3), 2.69 (dq, *J*(H,H) = 18.1, 7.2 Hz, 1H; CH*H*), 2.89 (dq, *J*(H,H) = 18.1, 7.2 Hz, 1H; C*H*H), 7.13 (t, *J*(H,H) = 7.5 Hz, 1H; Ar−H), 7.25–7.51 (m, 9H), 9.05 ppm (br s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 8.4, 20.6, 31.8, 64.9, 119.9, 124.7, 129.0, 129.2, 130.1, 136.3, 137.3, 167.0, 206.1 ppm; IR (KBr): $\tilde{\nu}$ = 3251, 2975, 2937, 1710, 1656, 1597, 1541, 1500, 1489, 1444, 1316, 1250, 1157, 1096, 1084, 1028, 966, 925, 901, 756, 692 cm^{-1}; HRMS: *m/z*: calcd for $C_{18}H_{19}NO_2S$: 313.1132; found 313.1133 $[M]^+$.

2(*R*,*S*)-Methyl-3-oxo-*N*-(1(*S*)-phenylethyl)-2(*R*,*S*)-(phenylsulfanyl)pentanamide (5b): The dr was determined by HPLC using a Daicel Chiralcel OD-H column (hexane/*i*PrOH 99:1); flow rate 0.5 mL min^{-1}; τ_1 = 46 min; τ_2 = 49.5 min); $[\alpha]_D^{RT}$ = −48.6 (*c* = 0.505 in CH_2Cl_2, 0% *de*); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C), 2 diastereoisomers: δ = 1.04 (t, *J*-(H,H) = 7.5 Hz, 3H; CH_3), 1.12 (t, *J*(H,H) = 7.5 Hz, 3H; CH_3), 1.45 (d, *J*(H,H) = 7 Hz, 3H; CH_3), 1.49–1.56 (m, 6H, 2×CH_3), 1.58 (s, 3H, CH_3), 2.44–2.79 (m, 4H, 2×CH_2), 5.08 (m, 2H, 2×CH), 7.15–7.43 ppm (m, 20H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C), 2 diastereoisomers: δ = 8.3, 8.5, 20.9, 21.6, 21.8, 31.5, 31.5, 49.6, 49.6, 64.9, 65.2, 125.9, 126.3, 127.4, 127.6, 128.7, 128.8, 129.0, 129.1, 129.2, 129.5, 129.6, 129.7, 135.9, 136.0, 142.5, 142.8, 168.0, 168.2, 205.6, 205.6 ppm; IR (KBr): $\tilde{\nu}$ = 3360, 2971, 2930, 1708, 1670, 1521, 1454, 1438, 1240, 1168, 1086, 1025, 970, 772, 751, 705, 692, 604 cm^{-1}; elemental analysis calcd (%) for $C_{20}H_{23}NO_2S$ (341.5): C 70.35, H 6.79, N 4.10; found C 70.24, H 6.87, N 4.13.

***tert*-Butyl ethyl methyl(phenylsulfanyl)malonate (5c)**: The *ee* was determined by HPLC using a Daicel Chiralcel AD-H column (hexane/*i*PrOH 99:1); flow rate 0.6 mL min^{-1}; τ_{major} = 10.9 min; τ_{minor} = 9.9 min); $[\alpha]_D^{RT}$ = +6.7 (*c* = 0.55 in CH_2Cl_2, 64% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 1.26 (t, *J*(H,H) = 7 Hz, 3H; CH_3), 1.44 (s, 9H; CMe_3), 1.58 (s, 3H; CH_3), 4.20 (m, 2H; CH_2), 7.27–7.39 (m, 3H; Ar-H), 7.55 ppm (m, 2H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 14.0, 22.3, 27.7, 60.5, 61.9, 82.8, 128.7, 129.6, 130.2, 137.1, 168.1, 169.5 ppm; IR (neat): $\tilde{\nu}$ = 2981, 2936, 1729, 1370, 1259, 1164, 1110, 1024, 846, 752, 692 cm^{-1}; HRMS: *m/z*: calcd for $C_{16}H_{22}O_4S$: 310.1234; found 310.1231 $[M]^+$.

α-Acetyl-α-phenylsulfanyl-γ-butyrolactone (7a): The *ee* was determined by HPLC using a Daicel Chiralcel OD-H column (hexane/*i*PrOH 99:1); flow rate 0.6 mL min^{-1}; τ_{major} = 50.4 min; τ_{minor} = 56 min); $[\alpha]_D^{RT}$ = −38.6 (*c* = 0.56 in CH_2Cl_2, 20% *ee*); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 2.22 (m, 1H; C*H*H), 2.60 (s, 3H; CH_3), 2.89 (m, 1H; CH*H*), 4.26 (m, 2H; CH_2), 7.30–7.50 ppm (m, 5H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 26.0, 31.2, 63.7, 65.8, 129.0, 129.5, 130.3, 135.6, 171.4, 199.0 ppm; IR (neat): $\tilde{\nu}$ = 1770, 1704, 1158, 1023, 751, 690 cm^{-1}; HRMS: *m/z*: calcd for $C_{12}H_{12}O_3S$: 236.0502; found 236.0504 $[M]^+$.

α-Phenylsulfanyl-γ-butyrolactone (7c):[35] The *ee* was determined by HPLC using a Daicel Chiralcel OD-H column (hexane/*i*PrOH 99:1); flow rate 0.6 mL min^{-1}; τ_1 = 101 min; τ_2 = 110 min, racemate); ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 2.29 (m, 1H; C*H*H), 2.66 (m, 1H; CH*H*), 3.86 (dd, *J*(H,H) = 7.2 Hz, 1H; SCH), 4.21 (m, 2H; CH_2), 7.35 (m, 3H; Ar-H), 7.55 ppm (m, 2H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 29.9, 44.3, 66.4, 128.7, 129.2, 131.7, 133.5, 174.9 ppm; IR (neat): $\tilde{\nu}$ = 2918, 1765, 1479, 1439, 1371, 1153, 1023, 743, 690 cm^{-1}; HRMS: *m/z*: calcd for $C_{10}H_{10}O_2S$: 194.0397; found 194.0397 $[M]^+$.

***tert*-Butyl 1-(2,4-dinitrophenylsulfanyl-2-oxocyclopentanecarboxylate (10)**:[16] The *ee* was determined by HPLC using a Daicel Chiralcel AD column (hexane/*i*PrOH 90:10); flow rate 1 mL min^{-1}; τ_{major} = 12.1 min; τ_{minor} = 9.2 min); $[\alpha]_D^{RT}$ = −147 (*c* = 0.5 in $CHCl_3$, 39% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.43 (s, 9H; CMe_3), 2.12–2.22 (m, 2H; CH_2), 2.32–2.42 (m, 1H; C*H*H), 2.50–2.62 (m, 1H; CH*H*), 2.63–2.76 (m, 2H; CH_2), 8.13 (d, *J*(H,H) = 9 Hz, 1H; Ar-H), 8.30 (d, *J*(H,H) = 9 Hz, 1H; Ar-H), 8.97 ppm (s, 1H; Ar-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 19.4, 27.7, 37.1, 37.3, 63.9, 84.6, 121.0, 126.3, 131.5, 142.3, 145.0, 167.3, 207.7 ppm; LRMS: *m/z*: calcd for $C_{16}H_{18}N_2O_3S$: 405; found 404.9 $[M+Na]^+$.

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