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Brief Communication

A Chiral Thiourea as Template for Enantioselective Intramolecular [2+2] Photocycloaddition Reactions

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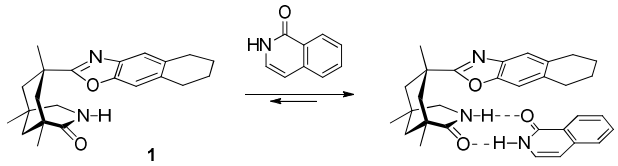
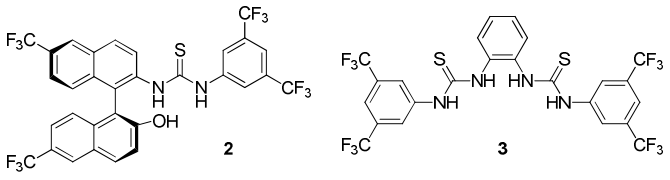
Upon absorption of a photon, substrates of a photochemical reaction undergo rapid bond formation requiring little if any further activation. UV/Vis irradiation initiates the reaction but does not induce a significant asymmetric induction, even if used in circularly polarized form.[1] If photochemical reactions are to be performed enantioselectively, stoichiometric templates have been shown to be powerful tools.[2] Among several templates[3] which operate via hydrogen bonding,[4] lactam **1**[5] has turned out to be very useful for several transformations, including [2+2] photocycloaddition reactions.[6] The combination of an adjacent hydrogen bond donor (NH) and a hydrogen bond acceptor (CO) enables an unambiguous directionality of the binding event (Scheme 1).

SCHEME 1. High Directionality in the Binding of Lactam **1** to a Photochemical Substrate, e.g. 1(2*H*)-Isoquinolone



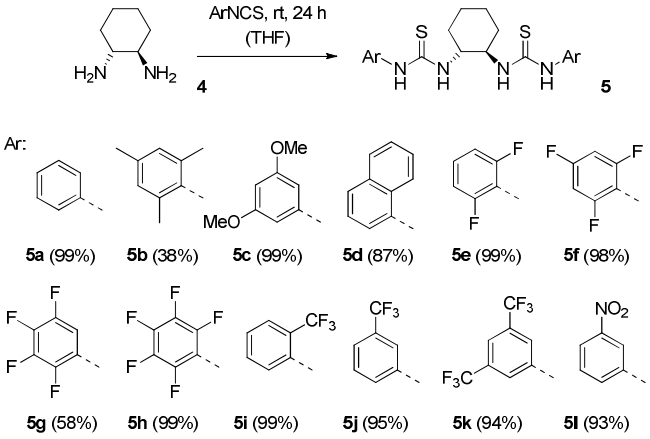
Although chiral thioureas have found widespread use as organocatalysts in thermal reactions[7] applications in photocycloaddition chemistry are rare. The two hydrogen bond donors (NH) at the thiourea core offer limited directionality and are in thermal reactions often combined with a third site for reagent activation, e.g. in Takemoto's catalyst.[8] Thiourea **2** (Figure 1) as developed by the Sivaguru group exhibits an additional hydroxy group at the naphthalene and was used as a catalyst for enantioselective [2+2] photocycloaddition reaction of coumarins.[9,10] Bisthiourea **3** was shown by the Beeler group to bind a cinnamate at each of the two thiourea binding sites and thus increased the regioselectivity of the cinnamate [2+2] photodimerization.[11]

FIGURE 1. Structure of Thioureas **2** and **3** Employed as Catalysts or Templates in [2+2] Photocycloaddition Reactions



Although it was shown already in the seminal study by Schreiner and Wittkopp on thiourea catalysis that binding to a dicarbonyl compound is not necessarily symmetrical[12] we are not aware of a thiourea, which was used as a chiral template in [2+2] photocycloaddition reactions of 1,3-dicarbonyl compounds.[13] In this communication, we present a preliminary study on the intramolecular [2+2] photocycloaddition of 2,3-dihydropyridone-5-carboxylates.[14]

SCHEME 2. Synthesis of Bisthioureas **5** from (1*R*,2*R*)-Diaminocyclohexane (**4**)

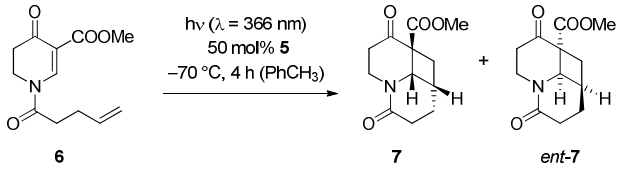


The study commenced with the synthesis of various chiral bisthioureas derived from commercially available (1*R*,2*R*)-diaminocyclohexane (**4**) (Scheme 2). Simple addition of the

respective aryl isothiocyanate (two equiv.) delivered the desired products **5** in high yields, some of which (**5a**,[15a] **5d**,[15b] **5k**,[15c]) have been previously reported.

It was speculated that dihydropyridone substrate **6** (Table 1) would bind to either thiourea unit of the bisthiourea or potentially that two molecules would bind to both thiourea units simultaneously. In any case, only 50 mol% of the template should be sufficient to achieve a significant asymmetric induction. In an initial screening performed at room temperature, bisthioureas were indeed found to be superior to any other class of thioureas (see Supporting Information for further details). In further experiments, the intramolecular [2+2] photocycloaddition to products **7** and *ent*-**7** was performed at λ = 366 nm in toluene at –70 °C and at a concentration of c = 20 mM (Table 1). Gratifyingly, we found that bisthiourea **5k**[16] resulted in a significant enantiomeric excess in favor of one enantiomeric product. Other bisthioureas **5e-5j**, **5l**, which carry an electron deficient aryl group resulted also in a notable enantioselectivity but were inferior to template **5k**.

TABLE 1. Evaluation of Bisthioureas **5** as Chiral Complexing Agents in the Intramolecular [2+2] Photocycloaddition of Dihydropyridone **6**



bisthiourea	**5a**	**5b**	**5c**	**5d**	**5e**	**5f**	**5g**	**5h**	**5i**	**5j**	**5k**	**5l**[a]
yield [%]	99	82	75	54	65	71	87	88	69	60	76	41
ee [%]	<1	<1	<1	2	8	9	18	10	12	14	56	<1

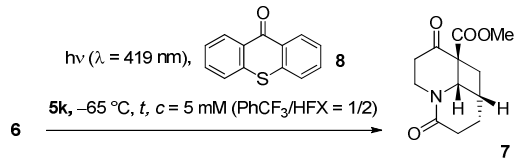
[a] Thiourea **5l** was not fully soluble in toluene solution. The reaction mixture remained heterogenous.

It was confirmed that toluene was the best solvent for direct irradiation by performing the reactions also in other solvents (see SI). In addition, it could be shown that neither a decrease nor

a significant increase in template concentration led to an improved enantioselectivity. With 10 mol% **5k**, the reaction proceeded in 74% yield but the *ee* dropped to 4%. With 2.3 equiv. (230 mol%) of **5k**, the reaction slowed and a yield of 71% was recorded after an irradiation time of 18 hours (23% *ee*). Although an increase in substrate concentration helped to improve the enantioselecitivity (64% *ee* at c = 100 mM), the improvement was again at the expense of an extended reaction time and a decreased overall yield (see SI).

In parallel to the optimization experiments, we found that the intramolecular [2+2] photocycloaddition of substrate **6** could be performed with visible light, if thioxanthone (**8**) was employed as a triplet sensitizer.[17] A 1:2 (v/v) mixture of these solvents had earlier been found to be suitable for low temperature irradiation experiments due its low melting point. Remarkably, the enantioselectivity of the [2+2] photocycloaddition improved significantly under sensitized conditions (Table 2). With 50 mol% thioxanthone the reaction remained incomplete after four hours (entry 1) but the enantioselectivity was promising (76% *ee*). Upon prolonged irradiation, there was no change in enantioselectivity and the reaction went to completion (entry 2) delivering 94% of product. A simultaneous decrease of the loading in template and sensitizer, did not alter the yield but the enantioselectivity decreased as it had done in the direct irradiation experiments (entry 3). Indeed, with 10 mol% of template **5k** a maximum of 20% of substrate can be bound and can thus react enantioselectively. If the template amount was increased to 50 mol%, the enantioselectivity increased as expected while the reaction rate and the yield remained satisfactorily high (entry 4).

TABLE 2. Sensitization of the Enantioselective Intramolecular [2+2] Photocycloaddition **6** → **7**

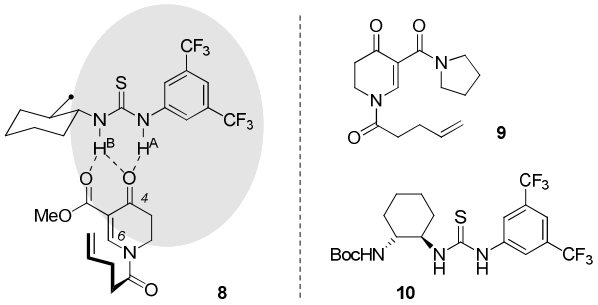


entry	**5k** [mol%]	**8** [mol%]	*t* [h][a]	yield[b] [%]	*ee*[c] [%]
1	50	50	4	51	76
2	50	50	16	94	76
3	10	10	16	93	18
4	50	10	16	91	75

[a] Irradiation time at the indicated conditions. [b] Yield of isolated product after purification by chromatography. [c] The enantiomeric excess was determined by chiral HPLC or GLC analysis.

Structure **7** was assigned to the major photocycloaddition enantiomer based on comparison of the chiroptical data of its decarboxylation product with those of a known photocycloaddition product (see SI for further details).[18] The intramolecular approach of the tethered olefin on carbon atom C6 of the dihydropyridone must thus have occurred from the *si* face. This preference is suggested if coordination of the substrate to the thiourea occurs as shown in Figure 2 for complex **8** and if the other thiourea moiety (in grey) shields the *re* face. Support of a non-symmetric binding was found when determining the chemical shift changes upon mixing substrate **6** and thiourea **5k** in benzene-d_6. The ^{13}C-NMR chemical shift of carbonyl carbon atom C4 is most extensive while there is very little changes observed for the other two carbonyl groups (see SI for further details). If instead of the methyl carboxylate **6**, the respective ethyl carboxylate was employed, there was little change in the reaction outcome (73% yield, 72% *ee*). However, substrate **9** with a second basic carbonyl oxygen atom gave no enantioselectivity.

FIGURE 2. Structure **8** of the putative complex between substrate(s) **6** and bisthiourea **5k**, structure of photocycloaddition precursor **9**, and structure of monothiourea **10**



The second thiourea unit in **5k** can be replaced by a *tert*-butoxycarbonyl (Boc) protecting group. Thiourea **10**[19] was tested only under conditions of direct irradiation under which it delivered the same major product enantiomer as template **5k** (see SI) supporting the hypothesis of an association mode as given for **8**. An intriguing conclusion can be drawn from the increased enantioselectivity observed in the sensitized reactions (Table 2) as compared to the direct irradiation reaction (Table 1). It is conceivable that the increase is due to the thioxanthone acting simultaneously as a sensitizer and a steric shield. This hypothesis is currently further studied in our laboratories and results will be reported in due course.

EXPERIMENTAL SECTION

General Methods:

All reactions sensitive to air or moisture were carried out in flame-dried glassware under a positive pressure of argon using standard *Schlenk* techniques. Dry tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), and diethylether (Et_2O) were obtained from a solvent purification system. Other dry solvents were obtained in the highest purity available and used without further purification. Technical solvents used for aqueous workup and for column chromatography [*n*-pentane (pentane), ethyl acetate (EtOAc), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2), methanol (MeOH)] were distilled prior to use. Photochemical experiments were performed in *Duran* tubes (diameter: 1.2 cm, volume 10 mL or 20 mL each; diameter 2.0 cm, volume 60 mL) in a photochemical reactor equipped with 16 fluorescence lamps: (λ = 366 nm, λ = 419 nm).[20] Prior to irradiation, the mixture was deoxygenated by purging with argon in an ultrasonicating bath for 15 minutes. Flash chromatography was performed on silica gel 60 (230-240 mesh) with the eluent mixtures given in the corresponding procedures. Thin-layer chromatography (TLC) was performed on silica-coated glass plates (silica gel 60 F 254). Compounds were detected by UV (λ = 254 nm, 366 nm) and CAM (cerium ammonium molybdate) solution. All solvents for chromatography were distilled prior to use. Analytical HPLC was performed using a chiral stationary phase (flow rate: 1.0 mL/min, column type and eluent is given for the corresponding compounds) and UV detection (λ = 210 nm or 254 nm) at 20 °C. IR spectra were recorded by the attenuated total reflection (ATR) technique. ^{1}H-NMR and ^{13}C-NMR spectra were recorded at 300 K. Chemical shifts are reported as parts per million (ppm) relative to residual $CHCl_3$ (δ_H = 7.26 ppm and δ_C = 77.0 ppm) or DMSO-d_5 (δ_H = 2.50 ppm and δ_C = 39.5 ppm). All coupling constants (*J*) are reported in Hertz (Hz). Apparent multiplets that occur as a result of accidental equality of coupling constants those of magnetically non-equivalent protons are

marked as virtual (*virt.*). The relative configuration of chiral products and the multiplicity of the ^{13}C-NMR signals were determined by two-dimensional NMR experiments (COSY, NOESY, HSQC, HMBC). Mass spectra were measured with a mass selective quadrupole detector (EI, 70 eV) or with an ion trap mass spectrometer (ESI). HRMS data were determined at a double-focussing magnetic sector instrument (EI, 70 eV) or at a linear ion trap with a Fourier transform ion cyclotron resonance detector (ESI).

General Procedure for the Synthesis of Thioureas 5. To a solution of (1*R*,2*R*)-diaminocyclohexane (1.0 eq) in THF (50 mM) was added the corresponding isothiocyanate (2.1 eq) at room temperature. The mixture was stirred at room temperature for 18 hours. After evaporation of the sovent the crude mixture was purified by column chromatography. Specific conditions and yields are given for each thiourea below.

1,1'-[(1*R*,2*R*)-Cyclohexane-1,2-diyl]bis(3-mesitylthiourea) (5b). (1*R*,2*R*)-Diaminocyclohexane (50.0 mg, 0.44 mmol, 1.0 eq) was dissolved in THF and 2-isothiocyanato-1,3,5-trimethylbenzene (163 mg, 0.92 mmol, 2.1 eq) was added. The crude material was purified by column chromatography (pentane:EtOAc = 4:1). The product (77.5 mg, 0.17 mmol, 38%) was isolated as a white solid. m.p.: 197-201 °C. TLC (pentane:EtOAc = 4:1): R_f = 0.17 [UV, $KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3174, 2924, 2854, 1529, 1489, 1230, 850. ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) = 1.20-1.38 (m, 6H), 1.68 (d, ^3J = 8.7 Hz, 2H), 2.15 (s, 6H), 2.22 (s, 2H), 2.30 (s, 12H), 4.21 (s, 2H), 6.00 (s, 2H), 6.79-7.16 (m, 4H), ^{13}C{^{1}H}-NMR ($CDCl_3$ 91 MHz): δ (ppm) = 18.0 (q), 18.6 (q), 21.1 (q), 24.7 (t), 32.6 (t), 58.7 (d), 129.6 (s), 130.0 (s), 136.5 (s), 137.6 (d), 138.9 (s), 180.6 (s). $[\alpha]_D^{20}$ = +141.4 (*c* = 0.3, $CHCl_3$). MS (EI, 70 EV): *m*/*z* (%) = 468 (1), 177 (100)

[$(C_{10}H_{11}NS)^+$], 144 (39), 119 (16) [$(C_9H_{11})^+$], 91 (14), 49 (8). HRMS (EI): Calculated for $C_{26}H_{36}N_4S_2$ [M^+] = 468.2381. Found = 468.2354.

1,1'-[(1*R*,2*R*)-Cyclohexane-1,2-diyl]bis[3-(3,5-dimethoxyphenyl)thiourea] (5c). (1*R*,2*R*)-Diaminocyclohexane (50.0 mg, 0.44 mmol, 1.0 eq) was dissolved in THF and 1-isothiocyanato-3,5-dimethoxybenzene (180 mg, 0.92 mmol, 2.1 eq) was added. The crude material was purified by column chromatography (pentane:EtOAc = 4:1). The product (218 mg, 0.43 mmol, 99 %) was isolated as a white solid. m.p.: 149-152 °C. TLC (pentane:EtOAc = 4:1): R_f = 0.36 [UV, $KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3213, 2935, 2854, 1598, 1510, 1451, 1329, 1257, 1202, 1153, 1122, 1038, 836. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.23-1.34 (m, 4H), 1.74 (d, ^3J = 7.5 Hz, 2H), 2.15 (d, ^3J = 10.3 Hz, 2H), 3.79 (s, 12H), 4.39-4.43 (m, 2H), 6.36 (*virt*. t, $^4J \cong {}^4J \cong$ 2.2 Hz, 2H), 6.41 (d, ^4J = 2.2 Hz, 4H), 6.65 (d, ^3J = 7.0 Hz, 2H), 7.62 (s, 2H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 101 MHz): δ (ppm) = 24.6 (t), 32.3 (t), 55.8 (q), 59.3 (d), 99.5 (s), 103.5 (d), 137.6 (s), 161.9 (d), 180.2 (s). $[\alpha]_D^{20}$ = + 4.1 (*c* = 1.0, $CHCl_3$). MS (EI, 70 EV): *m/z* (%) =322 (8), 207 (26), 195 (54) [$(C_9H_9NO_2S)^+$], 189 (27), 153 (17), 97 (22), 71 (45), 57 (86), 43 (100). HRMS (EI): Calculated for $C_{24}H_{32}N_4O_4S_2$ [M^+] = 504.1865. Found = 504.1861.

1,1'-[(1*R*,2*R*)-Cyclohexane-1,2-diyl]bis[3-(2,6-difluorophenyl)thiourea] (5e). (1*R*,2*R*)-Diaminocyclohexane (50.0 mg, 0.44 mmol, 1.0 eq) was dissolved in THF and 1,3-difluoro-2-isothiocyanatobenzene (157 mg, 0.92 mmol, 2.1 eq) was added. The crude material was purified by column chromatography (pentane: EtOAc = 4:1). The product (199 mg, 0.44 mmol, 99%) was isolated as a white solid. m.p.: 133-137 °C. TLC (pentane:EtOAc = 4:1): R_f = 0.10 [UV, $KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3206, 3040, 2937, 2857, 1598, 1527, 1509, 1470, 1449, 1296, 1240, 1186, 1123, 1002, 776. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.24-1.32 (m, 4H), 1.75 (d, ^3J = 7.4 Hz,

2H), 2.27-2.31 (m, 2H), 4.27 (brs, 2H), 6.93-6.97 (m, 6H), 7.23-7.27 (m, 2H), 7.40 (brs, 2H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 101 MHz): δ (ppm) = 24.7 (t), 32.0 (t), 59.8 (d), 112.5 (dd, $^{2}J_{CF}$ = 22.3 Hz), 113.8 (t, $^{2}J_{CF}$ = 16.4 Hz), 129.2 (dt, $^{3}J_{CF}$ = 9.4 Hz), 158.4 (d, $^{1}J_{CF}$ = 253 Hz), 181.5 (s). $[\alpha]_D^{20}$ = +113.8 (c = 1.0, $CHCl_3$). MS (EI, 70 EV): m/z (%) = 171 (45) [$(C_7H_4F_2NS)^+$], 129 (12), 97 (12), 70 (16), 61 (27), 43 (100). HRMS (EI): Calculated for $C_{20}H_{20}F_4N_4S_2$ [M^+] = 456.1066. Found = 456.1050.

1,1'-[(1*R*,2*R*)-Cyclohexane-1,2-diyl]bis[3-(2,4,6-trifluorophenyl)thiourea] (5f). (1*R*,2*R*)-Diaminocyclohexane (50.0 mg, 0.44 mmol, 1.0 eq) was dissolved in THF and 1,3,5-trifluoro-2-isothiocyanatobenzene (174 mg, 0.92 mmol, 2.1 eq) was added. The crude material was purified by column chromatography (pentane:EtOAc = 4:1). The product (210 mg, 0.43 mmol, 98%) was isolated as a white solid. m.p.: 162-165 °C. TLC (pentane:EtOAc = 4:1): R_f = 0.25 [UV, $KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3209, 3035, 2944, 2864, 1602, 1512, 1449, 1341, 1240, 1175, 1123, 1040, 998, 842. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 1.22-1.23 (m, 4H), 1.65-1.67 (m, 2H), 2.14-2.16 (m, 2H), 4.14 (brs, 2H), 7.20 (t, ^{3}J = 8.8 Hz, 4H), 7.97 (brs, 2H), 8.99 (brs, 2H). $^{13}C\{^{1}H\}$-NMR (DMSO-d_6, 101 MHz): δ (ppm) = 24.3 (t), 31.4 (t), 57.8 (d), 100.8 (dt, $^{3}J_{CF}$ = 26.1 Hz), 112 (s), 159.0 (ddd, $^{1}J_{CF}$ = 250 Hz, $^{3}J_{CF}$ = 15.9 Hz, 7.0 Hz), 160.4 (d, $^{1}J_{CF}$ = 246 Hz), 182.0 (s). $[\alpha]_D^{20}$ = +105.0 (c = 0.5, $CHCl_3$). MS (EI, 70 EV): m/z (%) = 269 (100), 226 (38), 189 (40) [$(C_7H_2F_3NS)^+$], 172 (25), 147 (22), 81 (29), 56 (30). HRMS (EI): Calculated for $C_{20}H_{18}F_6N_4S_2$ [M^+] = 492.0877. Found = 492.0854.

1,1'-[(1*R*,2*R*)-Cyclohexane-1,2-diyl]bis[3-(2,3,4,5-tetrafluorophenyl)thiourea] (5g) (1*R*,2*R*)-Diaminocyclohexane (100 mg, 0.88 mmol, 1.0 eq) was dissolved in THF and 1,2,3,4-tetrafluoro-5-isothiocyanatobenzene (383 mg, 1.85 mmol, 2.1 eq) was added. The crude material was

purified by column chromatography (pentane:EtOAc = 4:1). The product (272 mg, 0.52 mmol, 58%) was isolated as a white solid. m.p.: 146-149 °C. TLC (pentane:EtOAc = 4:1): R_f = 0.28 [UV, $KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3220, 3044, 2939, 2860, 1519, 1491, 1333, 1313, 1273, 1257, 1220, 1200, 1060, 969, 951, 849, 711. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.38-1.42 (m, 4H), 1.85-1.87 (m, 2H), 2.27-2.30 (m, 2H), 4.34-4.39 (m, 2H), 7.19 (br s, 2H), 7.23-7.30 (m, 2H), 7.54 (br s, 2H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 126 MHz): δ (ppm) = 24.7 (t), 32.0 (t), 59.9 (d), 110.1 (dd, $^2J_{CF}$ = 21.5 Hz), 120.9 (s), 139.7 (d, $^1J_{CF}$ = 240.3 Hz), 141.7 (d, $^1J_{CF}$ = 239.6 Hz), 143.0 (dd, $^1J_{CF}$ = 246.9 Hz, $^2J_{CF}$ = 9.4 Hz), 146.8 (dd, $^1J_{CF}$ = 248.5 Hz, $^2J_{CF}$ = 10.2 Hz), 181.3 (s). $[\alpha]_D^{20}$ = + 42.9 (c = 1.0, $CHCl_3$). MS (EI, 70 EV): m/z (%) = 206 (6) [$(C_7HF_4NS)^+$] , 94 (100), 66 (26), 57 (20) [$(CNS)^{2+}$] . HRMS (EI): Calculated for $C_{20}H_{16}F_8N_4S_2$ [M^+] = 528.0689. Found = 528.0721.

The isothiocyanate was prepared as follows: Sodiumcarbonate (2.04 g, 24.2 mmol, 4.0 eq) was dissolved in water (8 mL). The mixture was stirred for 10 minutes and dichloromethane (8 mL) was added, followed by 2,3,4,5-tetrafluoroaniline (1.0 g, 6.06 mmol, 1.0 eq). The mixture was cooled to 0 °C and thiophosgene (0.70 mL, 1.04 g, 9.08 mmol, 1.5 eq) was added dropwise via syringe over a period of 20 minutes. The mixture was allowed to warm slowly to room temperature and it was strirred for one hour at room temperature. The mixture was washed with brine (50 mL). The aqueous layer was extracted with dichloromethane (3 × 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude material was purified by chromatography through a short column (pentane:EtOAc = 4:1). 1,2,3,4-Tetrafluoro-5-isothiocyanatobenzene was used in the next step without further purification (vide infra).

1,1'-[(1*R*,2*R*)-Cyclohexane-1,2-diyl]bis[3-(perfluorophenyl)thiourea] (5h) (1*R*,2*R*)-Diaminocyclohexane (50.0 mg, 0.44 mmol, 1.0 eq) was dissolved in THF and 1,2,3,4,5-pentafluoro-6-isothiocyanatobenzene (207 mg, 0.92 mmol, 2.1 eq) was added. The crude material was purified by column chromatography (pentane:EtOAc = 4:1). The product (246 mg, 0.44 mmol, 99%) was isolated as a white solid. m.p.: 207-211 °C. TLC (pentane:EtOAc = 4:1): R_f = 0.41 [UV, $KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3212, 3044, 2941, 2860, 1552, 1518, 1510, 1467, 1341, 1314, 1274, 1227, 987. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.14-1.48 (m, 4H), 1.87 (d, ^3J = 6.4 Hz, 2H), 2.37 (d, ^3J = 9.9 Hz, 2H), 4.22 (brs, 2H), 7.77 (brs, 2H), 7.86 (brs, 2H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 101 MHz): δ (ppm) = 24.7 (t), 31.8 (t), 60.5 (d), 112.3 (dt, $^2J_{CF}$ = 12.9 Hz, $^3J_{CF}$ = 2.1 Hz), 138.1 (d, $^1J_{CF}$ = 254 Hz), 141.2 (d, $^1J_{CF}$ = 256 Hz), 144.2 (ddd, $^1J_{CF}$ = 254 Hz, $^2J_{CF}$ = 10.7 Hz, $^3J_{CF}$ = 2.7 Hz), 182.0 (s). $[\alpha]_D^{20}$ = +106.3 (*c* = 1.0, $CHCl_3$). MS (EI, 70 EV): *m*/*z* (%) = 225 (100) [$(C_7F_5NS)^+$], 193 (26), 183 (42) [$(C_6HF_5N)^+$], 167 (8) [$(C_6F_5)^+$] 117 (23). HRMS (EI): Calculated for $C_{20}H_{14}F_{10}N_4S_2$ [M^+] = 564.0500. Found = 564.0489.

1,1'-[(1*R*,2*R*)-Cyclohexane-1,2-diyl]bis{3-[2-(trifluoromethyl)phenyl]thiourea} (5i) (1*R*,2*R*)-Diaminocyclohexane (50.0 mg, 0.44 mmol, 1.0 eq) was dissolved in THF and 1-isothiocyanato-2-(trifluoromethyl)benzene (187 mg, 0.92 mmol, 2.1 eq) was added. The crude material was purified by column chromatography (pentane: EtOAc = 4:1). The product (214 mg, 0.41 mmol, 94%) was isolated as a white solid. m.p.: 180-182 °C. TLC (pentane:EtOAc = 4:1): R_f = 0.18 [UV, $KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3246, 3176, 3017, 2937, 2860, 1602, 1538, 1522, 1504, 1458, 1322, 1282, 1238, 1173, 1158, 1136, 1123, 1058, 1037, 758. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.15-1.36 (m, 4H), 1.67-1.81 (m, 2H), 2.18 (d, ^3J = 12.7 Hz, 2H), 4.31-4.36 (m, 2H), 6.61 (br s, 2H), 7.41-7.50 (m, 6H), 7.64 (*virt*. t, $^3J \cong {}^3J \cong$ 7.7 Hz, 2H), 7.72 (d, ^3J = 7.8 Hz, 2H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 101 MHz): δ (ppm) = 24.7 (t), 32.0 (t), 59.5 (d), 123.3 (q, $^1J_{CF}$ = 273.4

Hz), 126.8 (q, $^2J_{CF}$ = 30.2 Hz), 127.5 (dq, $^3J_{CF}$ = 5.0 Hz), 128.1 (d), 129.6 (d), 133.7 (d), 133.8 (s), 181.2 (s). $[\alpha]_D^{20}$ = + 71.6 (*c* = 1.0, $CHCl_3$). MS (EI, 70 EV): *m*/*z* (%) = 203 (100) $[(C_8H_4F_3NS)^+]$, 161 (55) $[(C_7H_5F_3N)^+]$, 114 (56), 43 (45). $[(C_6HF_5N)^+]$, 116 (23). HRMS (EI): Calculated for $C_{22}H_{22}F_6N_4S_2$ $[M^+]$ = 520.1190. Found = 520.1177.

1,1'-[(1*R*,2*R*)-Cyclohexane-1,2-diyl]bis{3-[3-(trifluoromethyl)phenyl]thiourea} (5j) (1*R*,2*R*)-Diaminocyclohexane (50.0 mg, 0.44 mmol, 1.0 eq) was dissolved in THF and 1-isothiocyanato-3-(trifluoromethyl)benzene (187 mg, 0.92 mmol, 2.1 eq) was added. The crude material was purified by column chromatography (pentane:EtOAc = 4:1). The product (217 mg, 0.42 mmol, 95%) was isolated as a white solid. m.p.: 154-156 °C. TLC (pentane:EtOAc = 4:1): R_f = 0.23 [UV, $KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3296, 3246, 3147, 3063, 2956, 2031, 1552, 1457, 1327, 1270, 1167, 792, 693. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.21-1.31 (m, 4H), 1.73 (br s, 2H), 2.13-2.14 (m, 2H), 4.33-4.37 (m, 2H), 6.88 (br s, 2H), 7.40-7.52 (m, 8H), 8.31 (s, 2H). $^{13}C\{^1H\}$-NMR ($CDCl_3$, 101 MHz): *δ* (ppm) = 24.6 (t), 32.0 (t), 59.2 (d), 121.6 (dq, $^3J_{CF}$ = 4.0 Hz), 123.4 (dq, $^3J_{CF}$ = 3.7 Hz), 123.6 (q, $^1J_{CF}$ = 272.6 Hz), 128.1 (d), 130.5 (d), 132.2 (q, $^2J_{CF}$ = 32.8 Hz), 137.3 (s), 180.3 (s). $[\alpha]_D^{20}$ = +11.0 (*c* = 0.5, $CHCl_3$). MS (EI, 70 EV): *m*/*z* (%) = 203 (100) $[(C_8H_4F_3NS)^+]$, 145 (48) $[(C_7H_4F_3)^+]$, 95 (26), 75 (17) $[(CH_3N_2S)^+]$, 57 (25). HRMS (EI): Calculated for $C_{22}H_{22}F_6N_4S_2$ $[M^+]$ = 520.1190. Found = 520.1198.

1,1'-[(1*R*,2*R*)-Cyclohexane-1,2-diyl]bis[3-(3-nitrophenyl)thiourea] (5l) (1*R*,2*R*)-Diaminocyclohexane (50.0 mg, 0.44 mmol, 1.0 eq) was dissolved in THF and 1-isothiocyanato-3-nitrobenzene (166 mg, 0.92 mmol, 2.1 eq) was added. The crude material was purified by column chromatography (pentane:EtOAc = 4:1). The product (193 mg, 0.41 mmol, 93%) was isolated as a yellowish solid. m.p.: 206-208 °C. TLC (pentane:EtOAc = 4:1): R_f = 0.45 [UV,

$KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3266, 3098, 2948, 2860, 1522, 1346, 1266, 1212, 730. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 1.28-1.35 (m, 4H), 1.70-1.72 (m, 2H), 2.17-2.20 (m, 2H), 4.33 (br s, 2H), 7.53 (*virt*. t, $^3J \cong {}^3J \cong 8.2$ Hz, 2H), 7.77 (d, $^3J = 7.77$ Hz, 2H), 7.89 (dd, $^3J = 7.9$ Hz, $^4J = 2.2$ Hz, 2H), 8.04-8.05 (m, 2H), 8.57 (br s, 2H), 9.99 (br s, 2H). $^{13}C\{^1H\}$-NMR (DMSO-d_6, 101 MHz): δ (ppm) = 24.2 (t), 31.3 (t), 56.6 (d), 116.5 (d), 118.0 (d), 128.3 (d), 129.7 (d), 140.8 (s), 147.5 (s), 180.0 (s). $[\alpha]_D^{20} = +3.1$ ($c = 0.3$, $CHCl_3$). MS (ESI): *m*/*z* (%) = 475.1 (100) [M+H$^+$],. HRMS (ESI): Calculated for $C_{20}H_{23}N_6O_4S_2$ [M+H$^+$] = 475.1217. Found = 475.1216.

Methyl 4-oxo-1-(pent-4-enoyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (6). To a solution of pent-4-enoic acid (0.56 mL, 5.50 mmol, 1.1 eq) in dichloromethane (10 mL) oxalylic chloride (0.47 mL, 5.50 mmol, 1.1 eq) and a few drops of DMF were added at room temperature. The mixture was stirred at room temperature for two hours. In a second flask 3-(methoxycarbonyl)-4-oxopiperidin-1-ium chloride (0.97 g, 5.00 mmol, 1.0 eq) was dissolved in dichloromethane (10 mL). Triethylamine (2.77 mL, 20.0 mmol, 4.0 eq) and two grains of DMAP were added. The mixture was cooled to 0 °C and the in situ formed pent-4-enoyl chloride was subsequently added slowly over the course of 10 minutes. The resulting mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched with aqueous HCl (1 M) (10 mL). The organic layer was separated and the aqueous layer was extracted three times with EtOAc (3 × 60 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 and filtered. After evaporation the crude material was filtered through a short silica column. The crude material was taken into the next step without further purification. A fraction of the crude product (510 mg, 2.12 mmol, 1.00 eq) was suspended in dry 1,4-dioxane (16 mL). To this mixture 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (550 mg, 2.44 mmol, 1.15 eq) was added at room temperature. The mixture was stirred at room temperature for five hours. Subsequently, the

reaction was quenched by addition of an aqueous saturated $NaHCO_3$-solution (10 mL). The mixture was extracted three times with CH_2Cl_2 (3 × 30 mL) The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 and filtered. After evaporation the crude material was purified by column chromatography (pentane:EtOAc = 1:1). The product (292 mg, 1.23 mmol, 58 % over 2 steps) was isolated as a yellowish solid. m.p.: 88-90 °C. TLC (EtOAc): R_f= 0.55 [UV, $KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3073, 2952, 2913, 1715, 1574, 1128, 918. ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm) = 2.49 (dtt, ^3J = 7.6 Hz, 6.6 Hz, ^4J = 1.2 Hz, 2H), 2.63 (t, ^3J = 7.6 Hz, 2H), 2.78 (t, ^3J = 7.5 Hz, 2H), 3.83 (s, 3H), 4.08 (t, ^3J = 7.5 Hz, 2H), 5.07 (*virt*. dq, ^3J = 10.3 Hz, $^2J \cong {}^4J \cong$ 1.3 Hz, 1H), 5.12 (*virt*. dq, ^3J = 17.0 Hz, $^2J \cong {}^4J \cong$ 1.6 Hz, 1H), 5.85 (ddt, ^3J = 17.0 Hz, 10.3 Hz, 6.6 Hz, 1H), 8.72 (s, 1H). $^{13}C\{^1H\}$ NMR (90 MHz, $CDCl_3$): δ (ppm) = 28.5 (t), 32.8 (t), 36.2 (t), 41.6 (t), 52.3 (q), 108.8 (s), 116.7 (t), 135.9 (d), 149.9 (d), 164.7 (s), 171. (s), 188.3 (s). MS (EI, 70 EV): *m*/*z* (%) = 153 (40) [$(C_7H_7NO_3)^+$], 121 (34), 84 (30) [$(C_5H_7O)^+$], 55 (40), 43 (100). HRMS (EI): Calculated for $C_{12}H_{15}NO_4$ [M^+] = 237.1001. Found = 237.0998.

Ethyl-4-oxo-1-(pent-4-enoyl)-1,4,5,6-tetrahydropyridine-3-carboxylate. In analogy to the procedure for the preparation of methyl ester **6** the corresponding ethyl ester was synthesized from 3-(ethoxycarbonyl)-4-oxopiperidin-1-ium chloride (765 mg, 3.68 mmol). The desired product (483 mg, 1.84 mmol, 50%) was isolated over two steps as a yellowish solid. m.p.: 58-60 °C. TLC (pentane:EtOAc = 1:1): R_f= 0.20 [UV, $KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3524, 3077, 2979, 2930, 1739, 1691, 1577, 1308, 1220, 1132, 909. ^{1}H-NMR (360 MHz, $CDCl_3$): δ (ppm) = 1.34 (t, ^3J = 7.1 Hz, 3H), 2.33-2.55 (m, 2H), 2.61 (t, ^3J = 7.4 Hz, 2H), 2.77 (t, ^3J = 7.3 Hz, 2H), 4.07 (t, ^3J = 7.3 Hz, 2H), 4.28 (q, ^3J = 7.1 Hz, 2H), 5.06 (*virt*. dq, ^3J = 10.3 Hz, $^4J \cong {}^2J \cong$ 1.2 Hz, 1H), 5.12 (*virt*. dq, ^3J = 17.1 Hz, $^4J \cong {}^2J \cong$ 1.6 Hz, 1H), 5.83 (ddt, ^3J = 17.1 Hz, 10.3 Hz, 6.6 Hz, 1H), 8.70 (s, 1H), $^{13}C\{^1H\}$-NMR (90 MHz, $CDCl_3$): δ (ppm) = 14.4 (q), 28.5 (t), 32.8 (t), 36.3 (t),

41.6 (t), 61.1 (t), 109.1 (s), 116.6 (t), 135.9 (d), 149.5 (d), 164.0 (s), 171.4 (s), 188.4 (s). MS (EI, 70 EV): *m*/*z* (%) = 251 (4) [M^+], 166 (15) [$(C_8H_8NO_3)^+$], 124 (21) [$(C_6H_6NO_2)^+$], 83 (21) [$(C_5H_7O)^+$], 55 (100), 43 (65). HRMS (EI): Calculated for $C_{13}H_{17}NO_4$ [M^+] = 251.1158. Found = 251.1149.

General procedure for racemic photoreactions. The solution of the corresponding substrate (*c* = 20 mM) was purged with argon in an ultrasonicating bath for 10 minutes. The mixture was irradiated at room temperature at λ = 366 nm until the reaction was complete. The solvent was removed under reduced pressure and the crude material was purified by column chromatography using an appropriate solvent system, as described in the individual procedure.

General procedure for enantioselective photoreactions at λ = 366 nm. A solution of the corresponding substrate and thiourea (50 mol%) in toluene (*c* = 20 mM) was purged with argon in an ultrasonicating bath for 10 minutes. The mixture was irradiated at −70 °C at λ = 366 nm for four hours. The solvent was removed under reduced pressure and the crude material was purified by column chromatography using an appropriate system, as described in the individual procedure.

General procedure for sensitized enantioselective photoreactions at λ = 419 nm. A solution of the corresponding substrate, thiourea (50 mol%) and thioxanthone (10 mol%) in a mixture of trifluorotoluene and hexafluoroxylene (1:2, *c* = 5 mM) was purged with argon in an ultrasonicating bath for 10 minutes. The mixture was irradiated at −65 °C at λ = 419 nm for 16 hours. The solvent was removed under reduced pressure and the crude material was purified by column chromatography using an appropriate system, as described in the individual procedure.

Methyl (4´*S*,7a*S*,8a*S*)-3,7-dioxohexahydro-1*H*,5*H*-cyclobutanequinolizine-7a(4´*H*)-carboxylate (7) A solution of ester **6** (11.5 mg, 0.05 mmol, 1.0 eq) was irradiated in the corresponding solvent (see Tables 1 and 2). After irradiation the solvent was removed under reduced pressure and the crude material was purified by column chromatography (EtOAc). Yields for the individual reactions are given in Tables 1 and 2. In the racemic reaction, which was performed in toluene, the product *rac*-**7** (11.4 mg, 0.05 mmol, 99%) was isolated as a colorless oil. TLC (EtOAc): R_f = 0.34 [$KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2953, 2361, 1733, 1709, 1643, 1433, 1355, 1244, 1160, 1088, 945. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.49-1.63 (m, 1H), 2.05-2.21 (m, 2H), 2.33 (dd, ^2J = 12.7 Hz, ^3J = 7.2 Hz, 1H), 2.37-2.45 (m, 1H), 2.57-2.76 (m, 2H), 2.79-2.93 (m 1H), 2.98 (ddd, ^2J = 12.7 Hz, ^3J = 9.0 Hz, ^4J = 1.9 Hz, 1H), 3.10 (ddd, ^2J = 13.5 Hz, ^3J = 10.3 Hz, 6.7 Hz, 1H), 3.79 (s, 3H), 4.44 (*virt*. dq, $^3J \cong$ 8.1 Hz, $^4J \cong$ 1.8 Hz, 1H), 4.79 (ddd, ^2J = 13.5 Hz, ^3J = 6.8 Hz, 2.7 Hz, 1H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 26.8 (t), 28.9 (d), 31.3 (t), 33.3 (t), 38.3 (t), 38.3 (t), 53.4 (q), 54.6 (s), 58.7 (d), 170.0 (s), 170.6 (s), 204.8 (s). $[\alpha]_D^{20}$ = –36.5 (*c* = 0.8, $CHCl_3$) [75% *ee*]. MS (EI, 70 EV): *m*/*z* (%) = 237 (20) [M^+], 164 (27), 140 (45), 110 (62), 98 (83), 96 (100), 82 (54), 55 (35). HRMS (EI): Calculated for $C_{12}H_{15}NO_4$ [M^+] = 237.1001. Found = 237.0994. Chiral HPLC (AD-H, 250 × 4.6 mm, *n*-hexane/*i*-PrOH = 90:10, 1 mL/min, λ = 210 nm, 254 nm): t_R [racemate] = 16.9 min, 22.1 min; t_R [**7**] = 18.1 min, 23.1 min. Chiral GLC: t_{R1} = 556 min, t_{R2} = 558 min [60 °C (1 min), 150 °C (0.16 °C/min), 150 °C (10 min), 220 °C (10 °C/min), 220 °C (5 min)].

Ethyl (4a*S*,7a*S*,8a*S*)-3,7-dioxohexahydro-1*H*,5*H*-cyclobutanequinolizine-7a(4a*H*)-carboxylate According to the general procedure for racemic photoreactions, a solution of the ethyl ester (25.1 mg, 0.10 mmol, 1.0 eq) in toluene was irradiated. After complete conversion the

solvent was removed under reduced pressure and the crude material was purified by column chromatography (EtOAc). The product (19.6 mg, 0.08 mmol, 78%) was isolated as a colorless oil.

According to the general procedure for sensitized enantioselective photoreactions at λ = 419 nm, a solution of ethylester (12.7 mg, 0.05 mmol, 1.0 eq), thiourea **5k** (50 mol%) and thioxanthone (**8**) (10 mol%) in a mixture of trifluorotoluene and hexafluoroxylene was irradiated. After 16 hours the solvent was removed under reduced pressure and the crude material was purified by column chromatography (EtOAc). The product (9.30 mg, 0.04 mmol, 73%) was isolated as a colorless oil (72% *ee*). TLC (EtOAc): R_f = 0.39 [$KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2948, 2871, 1737, 1707, 1656, 1462, 1425, 1241, 1203, 1160, 1089. ^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.29 (t, ^3J = 7.1 Hz, 3H), 1.51-1.61 (m, 1H), 2.04-2.20 (m, 2H), 2.31 (dd, ^2J = 12.7 Hz, ^3J = 6.5 Hz, 1H), 2.37-2.44 (m, 1H), 2.59-2.74 (m, 2H), 2.80-2.90 (m, 1H), 2.98 (ddd, ^2J = 12.7 Hz, ^3J = 9.0 Hz, ^4J = 1.8 Hz, 1H), 3.11 (ddd, ^2J = 13.5 Hz, ^3J = 10.7 Hz, 6.2 Hz, 1H), 4.25 (qd, ^3J = 7.1 Hz, ^2J = 1.7 Hz, 2H), 4.43 (d, ^3J = 8.9 Hz, 1H), 4.79 (ddd, ^2J = 13.5 Hz, ^3J = 7.1 Hz, 2.3 Hz, 1H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 91 MHz): δ (ppm) = 14.2 (q), 26.9 (t), 28.9 (d), 31.4 (t), 33.1 (t), 38.3 (t), 38.3 (t), 54.7 (s), 58.8 (d), 62.6 (t), 169.5 (s), 170.6 (s), 204.9 (s). $[\alpha]_D^{20}$ = –29.1 (*c* = 0.8, $CHCl_3$) [70% *ee*]. MS (EI, 70 EV): *m*/*z* (%) = 251 (11) [M^+], 206 (16) [$(C_{11}H_{12}NO_3)^+$], 167 (27), 164 (76), 149 (100) [$(C_8H_7NO_2)^+$] , 139 (17), 124 (25), 121 (30), 109 (81) [$(C_6H_7NO)^+$], 96 (94) [$(C_6H_8O)^+$], 82 (51), 69 (25), 55 (55), 41 (27). HRMS (EI): Calculated for $C_{13}H_{17}NO_4$ [M^+] = 251.1158. Found = 251.1154. Chiral HPLC (AD-H, 250 × 4.6 mm, *n*-heptane/*i*-PrOH = 90:10, 1mL/min, λ = 210 nm, 254 nm): t_R [racemate] = 13.7 min, 16.4 min; t_R [enantioenriched product] = 14.0 min, 16.4 min.

1-(Pent-4-enoyl)-5-(pyrrolidine-1-carbonyl)-2,3-dihydropyridin-4(1*H*)-one (9)

Borontrichloride (11.4 mL, 1M, 11.4 mmol, 1.1 eq) was added to a solution of pyrrolidine (6.00 mL, 5.21 g, 73.3 mmol, 7.1 eq) in dichloromethane (15 mL). The mixture was stirred at 0 °C for one hour. Meanwhile methyl 4-oxo-1-(pent-4-enoyl)-piperidine-3-carboxylate (2.47 g, 10.3 mmol, 1.0 eq), as described in the procedure for ester **6**, was dissolved in dichloromethane (10 mL) and the solution was added to the mixture slowly at 0 °C by syringe. After two hours the mixture was acidified with concentrated HCl to pH = 1 and saturated with NaCl. The mixture was extracted twice with dichloromethane (2 × 100 mL), dried over Na_2SO_4, filtered and evaporated. After a short filtration over SiO_2 (EtOAc) the crude material was used without further purification. The crude material (1.95 g, 7.01 mmol, 1.0 eq) was dissolved in THF (10 mL) and added slowly to a mixture of NaH (364 mg, 60%, 9.11 mmol, 1.3 eq) in THF (40 mL) at 0 °C. After 45 minutes of stirring at 0 °C the mixture was cooled to −78 °C and a solution of phenylselenyl bromide (1.98 g, 8.41 mmol, 1.2 eq) in THF (10 mL) was added slowly. The mixture was stirred at −78 °C for one hour and subsequently warmed to room temperature. After two hours at room temperature, a saturated aqueous solution of $NaHCO_3$ (100 mL) was added. The mixture was extracted with EtOAC (100 mL) and three times with dichloromethane (3 × 100 mL). The combined organic layers were dried over Na_2SO_4, filtered and evaporated. The residue was dissolved in dichloromethane (30 mL) and cooled to 0 °C. Water (8 mL) and aqueous hydrogenperoxide (36%, 30 mL) were added. The mixture was stirred at 0 °C for one hour. A saturated aqueous solution of $NaHCO_3$ (70 mL) was added and the mixture was extracted four times with dichloromethane (4 × 100 mL). The combined organic layers were dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure. The crude material was recrystallized from cyclohexane:EtOAc (30 mL:6 mL). The product (471 mg, 1.70 mmol, 17%) was isolated as a yellowish solid. m.p.: 97-100 °C. TLC (CH_2Cl_2:MeOH = 95:5): R_f = 0.45 [UV,

$KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3208, 2967, 2872, 1667, 1598, 1509, 1448, 1294, 1187, 1160, 1122, 1038, 999, 906, 837. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.81-1.94 (m, 4H), 2.45 (dtt, ^3J = 8.2 Hz, 6.8 Hz, ^4J = 1.4 Hz, 2H), 2.58 (t, ^3J = 8.2 Hz, 2H), 2.70 (t, ^3J = 7.4 Hz, 2H), 3.35 (t, ^3J = 6.6 Hz, 2H), 3.53 (t, ^3J = 6.6 Hz, 2H), 4.07 (t, ^3J = 7.4 Hz, 2H), 5.03 (*virt*. dq ^3J = 10.2 Hz, $^4J \cong {}^2J \cong$ 1.3 Hz, 1H), 5.08 (*virt*. dq, ^3J = 17.1 Hz, $^4J \cong {}^2J \cong$ 1.6 Hz, 1H), 5.82 (ddt, ^3J = 17.1 Hz, 10.2 Hz, 6.8 Hz, 1H), 8.15 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ (ppm) =24.5 (t), 26.2 (t), 28.5 (t), 32.7 (t), 35.7 (t), 46.4(t), 48.3 (t), 115.6 (s), 116.4 (d), 136.1 (d), 164.2 (s) 171.3 (s), 188.7 (s). MS (EI, 70 EV): *m*/*z* (%) = 255 (4), 168 (6), 149 (5), 98 (55) [$(C_5H_8NO)^+$], 85 (30), 70 (100) [$(C_7H_8N)^+$], 55 (54). HRMS (EI): Calculated for $C_{15}H_{20}N_2O_3$ [M^+] = 276.1474. Found = 276.1465.

Intramolecular [2+2] photocycloaddition of 9: **(4a*SR*,7a*SR*,8a*SR*)-8a-(Pyrrolidine-1-carbonyl)octahydro-1*H*,5*H*-cyclobutanequinolizine-1,5-dione.** According to the general procedure for racemic photoreactions, a solution of amide **9** (27.5 mg, 0.10 mmol, 1.0 eq) in acetonitrile was irradiated. After complete conversion the solvent was removed under reduced pressure and the crude material was purified by column chromatography (CH_2Cl_2:MeOH = 95:5). The product (23.4 mg, 0.08 mmol, 85%) was isolated as a colorless oil.

According to the general procedure for sensitized enantioselective photoreactions at λ = 419 nm, a solution of amide **9** (13.8 mg, 0.05 mmol, 1.0 eq), thiourea **5k** (50 mol%) and thioxanthone (**8**) (10 mol%) in a mixture of trifluorotoluene and hexafluoroxylene was irradiated. After 16 hours the solvent was removed under reduced pressure and the crude material was purified by column chromatography (CH_2Cl_2:MeOH = 95:5). The product (12.8 mg, 0.05 mmol, 93%) was isolated as a colorless oil in racemic form. TLC (CH_2Cl_2:MeOH = 95:5): R_f = 0.19 [UV, $KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3185, 3025, 2945, 1633, 1514, 1415, 1323, 1247, 1120, 1036, 998. ^{1}H-NMR

(300 MHz, $CDCl_3$): δ (ppm) = 1.40-1.54 (m, 1H), 1.76-1.88 (m, 4H), 2.95-2.17 (m, 2H), 2.33 (dt, ^2J = 15.4 Hz, ^3J = 3.1 Hz, 1H), 2.48-2.74 (m, 5H), 3.09-3.17 (m, 1H), 3.34-3.57 (m, 4H), 4.64 (ddd, ^2J = 13.3 Hz, ^3J = 9.0 Hz, 1.7 Hz, 1H), 4.95 (d, ^3J = 8.2 Hz, 1H). $^{13}C\{^1H\}$-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 23.7 (t), 26.4 (t), 27.4 (t), 28.7 (d), 31.7 (t), 32.0 (t), 38.4 (t), 38.6 (t), 46.2 (t), 47.3 (s), 58.1 (t), 58.7 (d), 165.6 (s), 170.6 (s), 205.3 (s). MS (EI, 70 EV): *m*/*z* (%) = 108 (15) [$(C_6H_6NO)^{2+}$], 92 (57), 91 (100), 79 (17), 77 (13), 51 (7). HRMS (EI): Calculated for $C_{15}H_{20}N_2O_3$ [M^+] = 276.1474. Found = 276.1464. Chiral HPLC (AD-H, 250 × 4.6 mm, *n*-heptane/*i*-PrOH = 80:20, 1 mL/min, λ = 210 nm, 254 nm): t_R [racemate] = 12.0 min, 13.4 min..

Decarboxylation of Photoproduct 7. Photoproduct **7** (6.00 mg, 25.3 µmol, 1.0eq) was dissolved in THF/water (1.0 mL/ 0.5 mL) and lithium hydroxide monohydrate (1.60 mg, 37.9 µmol, 1.5 eq) was added. The mixture was stirred at room temperature for two hours. Subsequently the mixture was acidified with HCl (2M) and extracted three times with dichloromethane (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude material was purified by column chromatography (EtOAc) to give the product (4.0 mg, 21.8 µmol, 86%) as a colorless oil. $[\alpha]_D^{20}$ = –49.8 (*c* = 0.4 CH_2Cl_2).
The enantiomer of this compound is known and shows a positive specific rotation. The analytical data were in accordance with the reported values.[18a]

***tert*-Butyl [(1*R*,2*R*)-2-{3-[3,5-bis(trifluoromethyl)phenyl]thioureido}cyclohexyl]carbamate (10)** (1*R*,2*R*)-Diaminocyclohexane (150 mg, 1.31 mmol, 1.0 eq) was dissolved in 1,4-dioxane (9 mL). In an additional flask di-*tert*-butyldicarbonate (315 mg, 1.44 mmol, 1.1 eq) was dissolved in 1,4-dioxane (15 mL). This mixture was added slowly to the stirring mixture by syringe. The reaction was stirred over night at room temperature and the solvent was evaporated under

reduced pressure. The crude material was dissolved in THF (25 mL) and 1-isothiocyanato-3,5-bis(trifluoromethyl)benzene (390 mg, 0.26 mL, 1.44 mmol, 1.1 eq) was added at room temperature. The mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure. The crude material was purified by column chromatography (pentane: EtOAc = 4:1). Product **10**[19] (467 mg 0.91 mmol, 73%) was isolated as a white solid. m.p.: 96-99 °C. TLC (pentane:EtOAc = 4:1): R_f = 0.43 [UV, $KMnO_4$]. IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3292, 2979, 2937, 2860, 1671, 1527, 1384, 1275, 1170, 1130, 681. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.07-1.21 (m, 2H), 1.42 (s, 12 H), 1.69-1.72 (m, 1H), 2.00 (d, ^3J = 12 Hz, 1H), 2.21-2.24 (m, 1H), 3.24-3.27 (m, 1H), 4.40 (br s, 1H), 4.92 (d, ^3J = 6.8 Hz, 1H), 7.07 (br s, 1H), 7.68 (s, 1H), 7.83 (s, 2H), 8.09 (br s, 1H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 101 MHz): δ (ppm) = 25.0 (t), 28.5 (q), 33.1 (t), 55.3 (d), 79.5 (d), 119.6 (d), 120.6 (q, $^1J_{CF}$ = 200.7 Hz), 124.3 (d), 132.8 (q, $^2J_{CF}$ = 33.5 Hz), 139.1 (s), 156.7 (s), 181.0 (s). $[\alpha]_D^{20}$ = +20.6 (c = 1.0, $CHCl_3$). MS (EI, 70 EV): m/z (%) = 271 (4) [$(C_9H_3F_6NS)^+$], 202 (6), 197 (16) [$(C_{11}H_{19}NO_2)^+$], 141 (62), 97 (100), 57 (93). HRMS (EI): Calculated for $C_{20}H_{25}F_6N_3O_2S_2$ [M^+] = 485.1566. Found = 485.1556.

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SUPPORTING INFORMATION

^{1}H- and ^{13}C-NMR spectra of all compounds reported in the Experimental Section, HPLC and GLC traces of representative products. This information is available free of charge via the Internet at http://pubs.acs.org.

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