A General and Efficient Method for the Synthesis of Silyl-Protected Arenethiols from Aryl Halides or Triflates

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Abstract: An improved palladium-catalyzed synthesis of silyl-protected arenethiols has been developed. This method is particularly useful because of its experimental simplicity, high generality and high level of functional group toleration. The first synthesis of enantiomerically pure [2.2]paracyclophane-4-thiol was realized employing this method.

Keywords: arenethiols; cross-coupling reaction; [2.2]paracyclophanes; palladium; protecting groups

Introduction

Arenethiols are important intermediates in chemical synthesis. While there are numerous reactions to introduce this functionality[1] starting from aryl halides[2] or phenols,[3] most of these transformations require drastic reaction conditions and tolerate few if any functionalities. Despite the fact that in the last few years the efficiency of palladium-catalyzed cross-coupling reactions for the preparation of aryl ethers and aniline derivatives has improved greatly,[4] analogous methods for the formation of aryl sulfides[5] and especially arenethiols have lagged behind.[6] The first report of a mild palladium-catalyzed synthesis of arenethiols came from Soderquist et al.[7] followed by reports from a Zeneca Pharma group[8] and a Merck group.[9]

The major disadvantage of the former procedures is the synthesis of potassium or sodium triisopropylsilanethiolate (MSTIPS, M = Na or K) from triisopropylsilanethiol (TIPSSH) and sodium or potassium hydride prior to the reaction. These silanethiolates are difficult to utilize, because they are highly sensitive towards moisture. Furthermore we found that potassium hydride inhibits the cross-coupling reaction when not fully removed. We herein report an improved one-pot cross-coupling procedure for the synthesis of triisopropylsilyl-protected arenethiols starting from aryl bromides, aryl iodides, and aryl triflates.

Results and Discussion

4-Bromoanisole and triisopropylsilanethiol were used as the prototypical substrate combination for the optimization of the reaction conditions. Various bases were tested. Separate syntheses of NaSTIPS or KSTIPS from TIPSSH and sodium or potassium hydride and utilization of these substrate bases in the reaction gave good yields in some cases. However, these results were difficult to reproduce because traces of KH or NaH disturbed the reaction up to a total inhibition. Cs_2CO_3 gave superior results in yield, reproducibility, and reagent handling. With limitations, both *t*-BuOK and *t*-BuONa were efficient bases for the reaction. However, we chose Cs_2CO_3 because of the milder reaction conditions and greater range of functional group tolerance. The corresponding alkali metal carbonates gave inferior results up to a total halt of the reaction employing Li_2CO_3 as base. Toluene was the solvent of choice, yielding results superior to DME and THF. $Pd(PPh_3)_4$ was used as catalyst in loadings from 0.5 to 15 mol %, resulting in 5 mol % as being optimal for the reaction. Experiments with a combination of $Pd(OAc)_2$ and PPh_3 instead of $Pd(PPh_3)_4$ gave the same results. Because of the much lower costs, we chose the combination $Pd(OAc)_2$ and PPh_3 instead of $Pd(PPh_3)_4$ in our later experiments. Besides triisopropylsilanethiol, *tert*-butyldimethylsilanethiol (TBDMSSH) and potassium trimethylsilanethiolate[10] (TMSSK) were screened as reagents. While TBDMSSH showed good results, comparable to those of TIPSSH, the utilization of TMSSK resulted in low yields with numerous by-products. Since TIPSSH is commercially available, we preferred it to TBDMSSH.

Thus, the optimized reaction conditions utilized 5 mol % $Pd(OAc)_2$, 22 mol % PPh_3, Cs_2CO_3 (1.3 equivs.) and triisopropylsilanethiol (1.3 equivs.) in dry and degassed toluene at 100 °C under an argon atmosphere.[14] In the first part of this study we applied the reaction conditions to a variety of aryl bromides as shown in Table 1. The results prove that the process is extremely tolerant towards a variety of common functional groups. Aryl bromides containing ether, amino, nitrile, aldehyde or ester groups, or aromatics derived from pyridine, thiophene or [2.2]paracyclophane are all well converted into the corresponding protected thiols. A de-

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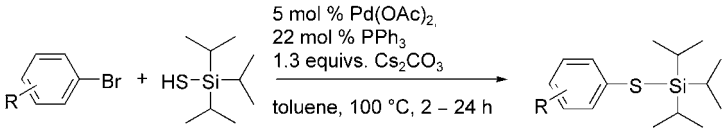
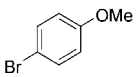
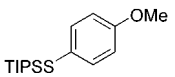
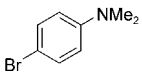
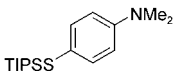
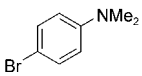
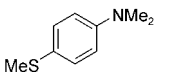
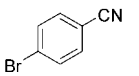
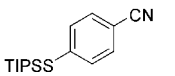
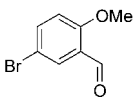
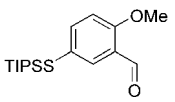
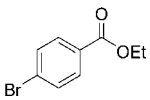
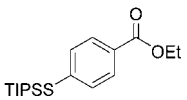
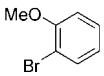
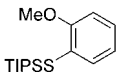
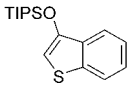
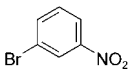
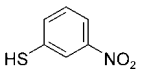
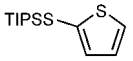
Table 1. Pd-catalyzed carbon-sulfur bond formation of aryl bromides.[a]



0.5 mmol 0.65 mmol

Entry	ArBr	Product	Conversion[b]	Yield[c]
1[d],[9]			quant.	66%
2[11]			98%	86%
3			quant.	65%
4[e],[12]			quant.	91%
5			99%	43%
6			quant.	80%
7[8]			quant.	66%
8			70%	33%
9			99%	71%
10			98%	60%
11[13]			quant.	76%
12			88%	60%

[a] Reaction conditions: ArBr (1.0 equiv.), TIPSSH (1.3 equivs.), Cs_2CO_3 (1.3 equivs.), $Pd(OAc)_2$ (5 mol %), PPh_3 (22 mol %) in toluene at 100 °C under argon. [b] By GC-MS. [c] Isolated yield. [d] The reaction was easily up scaleable, giving still full conversion in a 10-mmol scale. [e] Crude product of the cross-coupling reaction was dissolved in THF with TBAF (2 equivs.) and MeI (2 equivs.) and stirred for 2 h at room temperature.

crease in conversion is observed for 2-bromoanisole (entry 8) as starting material. This decrease in reactivity can only be attributed to a steric hindrance caused by the occupation of the *ortho* position, rather than the electronic characteristics of the starting material. Both electron-rich starting materials, such as (4-bromophenyl)-dimethylamine (entries 3 and 4), 2-bromothiophene (entry 12) and 4-bromo[2.2]paracyclophane (entry 9), as well as electron-deficient starting materials, like 2-bromopyridine (entry 2) and 4-bromobenzoic acid ethyl ester (entry 7), gave excellent conversion under the reaction conditions.

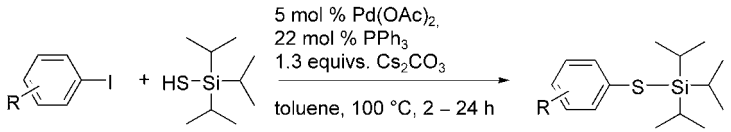
The decrease of the isolated yield compared to the conversion is due to the lability of the sulfur-silicon bond.[15] Under the non-polar chromatography conditions used here, silica gel becomes nucleophilic and therefore cleaves the Si–S bond under formation of an Si–O bond with the silica gel. Electron-deficient products like (2-triisopropylsilanylsulfanyl)-pyridine and triisopropyl-(3-nitrophenylsulfanyl)-silane are completely deprotected to the corresponding 1*H*-pyridine-2-thione (entry 2) and 3-nitrobenzenethiol (entry 11) during flash chromatography. The deprotected products of the other reactions were obtained as by-products over a wide range of fractions, which points towards a slower deprotection along the column. Further evidence that the decrease in the yields is only due to work-up problems is the excellent yield of dimethyl-(4-methylsulfanyl-phenyl)-amine (91%, entry 4), which was synthesized from (4-bromo-phenyl)-dimethylamine according to the general protocol followed by treatment of the crude product with tetrabutylammonium fluoride (TBAF) and MeI in THF. The overall yield of these two subsequent reactions is higher than the yield of the cross-coupling alone (65%, entry 3), which proves the effectiveness of the general protocol.

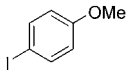
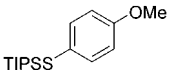
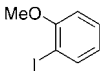
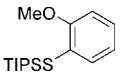
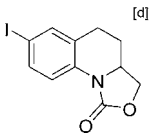
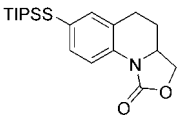
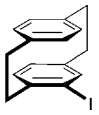
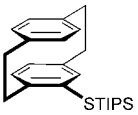
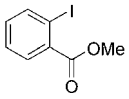
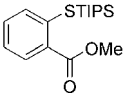
The reaction with 2-bromoacetophenone gave an unexpected result, leading directly to (benzo[*b*]thiophen-3-yloxy)-triisopropylsilane (entry 10). This provides an easy and elegant route for the synthesis of benzo[*b*]thiophen-3-ones.[16] The method reported herein should enable us to synthesize benzo[*b*]thiophen-3-ones containing base-labile and electrophilic groups like esters, aldehydes and nitriles. Further investigations of this reaction are in progress.

After having studied the cross-coupling reaction with aryl bromides, we applied the general protocol to aryl iodides. Like aryl bromides, aryl iodides are also excellent substrates for the C–S bond formation, even exceeding the results of aryl bromides (Table 2).

We chose 4-iodoanisole as substrate to optimize the reaction conditions (entry 1). 2-Iodoanisole was tested (entry 2) because the results with 2-bromoanisole were quite disappointing leading to only 70% conversion and 33% yield (entry 7, Table 1). 2-Iodoanisole (entry 2, Table 2) greatly surpassed this result, giving full conversion and a satisfying yield of 62%, hinting that iodides

Table 2. Pd-catalyzed carbon-sulfur bond formation of aryl iodides.[a]



Entry	ArI	Product	Conversion[b]	Yield[c]
1			quant.	86%
2			quant.	62%
3	 [d]		95%	69%
4			quant.	90%
5[d]			quant.	97%

[a] Reaction conditions: ArI (1.0 equiv.), TIPSSH (1.3 equivs.), Cs_2CO_3 (1.3 equivs.), $Pd(OAc)_2$ (5 mol %), PPh_3 (22 mol %) in toluene at 100 °C under argon.
[b] By GC-MS.
[c] Isolated yield.
[d] Synthesized according to ref.[17]

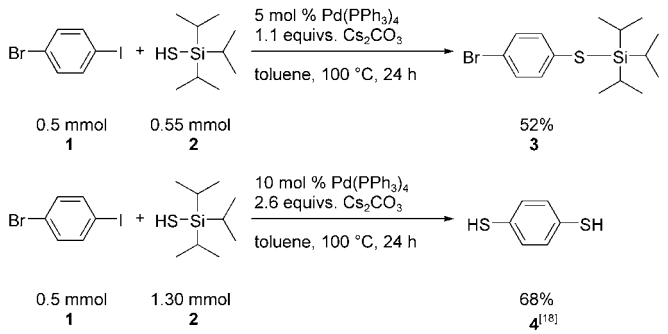
are better substrates than bromides. Even when applied to more complex substrates like the tricyclic carbamate (entry 3)[17] or 4-iodo[2.2]paracyclophane (entry 4), we achieved full conversion and good to excellent yields (69–90%). 2-Iodobenzoic acid methyl ester was tested as an electron-deficient substrate with steric hindrance and a possibly labile ester group. To our delight we achieved full conversion and an excellent yield (97%), which further underpins that both electron-deficient as well as electron-rich aryl halides are excellent substrates for the reaction.

Following these results, we compared aryl bromides and iodides under the same conditions. We chose 4-bromoanisole and 4-iodoanisole as a testing system for the temperature and catalyst loading dependence and for the kinetics of the reaction. While 4-iodoanisole still showed full conversion at 70 °C and a reaction time of 16 h, 4-bromoanisole only gave 77% conversion under these conditions. The differences were eminent concerning the reaction speed. While 4-iodoanisole showed full conversion after only 2 h at 100 °C, 4-bromoanisole still was not fully converted after 8 h. However, it is important to note that catalyst loading showed non-uniform results. While 4-bromoanisole still showed full conversion at a catalyst loading of 2 mol % compared to only 90% for 4-iodoanisole, the results for 0.5 mol % catalyst were reversed, showing 59% conversion for bromoanisole and 70% for iodoanisole.

With these results we compared the reactivity of bromide to iodide in the same molecule (Scheme 1). Analysis by GC-MS showed that we were able to selectively form a carbon-sulfur bond from the iodide, leaving the bromide untouched. With excess of TIPSSH, base and catalyst, a disubstitution of bromide and iodide was achieved.

Finally, we applied the general protocol to aryl triflates. They, too, were excellent substrates for the palladium catalyzed cross-coupling reaction (Table 3).

Again, we chose 4-trifluoromethanesulfonic acid 4-methoxyphenyl ester as substrate to optimize the reaction conditions (entry 1). With both electron-deficient (entry 2) and electron-rich 4-substituted aryl triflates

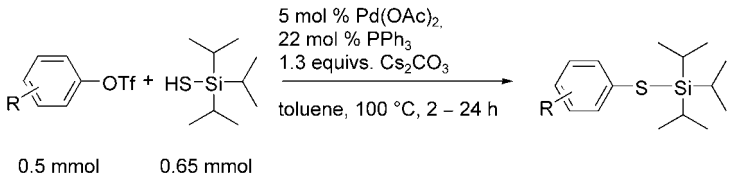


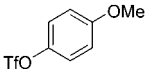
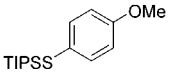
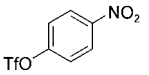
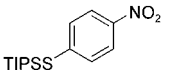
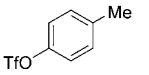
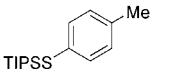
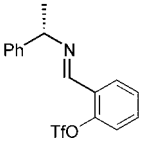
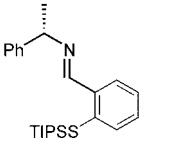
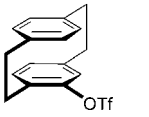
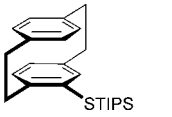
Scheme 1. Chemoselectivity of aryl bromides and iodides.

(entry 3) we achieved high conversion and good yields (81–90%). (*S*)-Trifluoromethanesulfonic acid 2-(isopropyliminomethyl)-phenyl ester (entry 4) was chosen as a substrate, because the resulting arenethiol, is a potential catalyst ligand for the 1,4-addition to α,β-unsaturated ketones, showing structural similarities to the systems of van Koten[18] and Pfaltz.[19] Trifluoromethanesulfonic acid (4-[2.2]paracyclophane) ester was especially interesting as a starting material (entry 5), because we were able to synthesize both enantiomers in high enantiomeric purity.

For the synthesis of enantiomerically pure trifluoromethanesulfonic acid (4-[2.2]paracyclophane) ester we started from racemic 4-acetoxy-[2.2]paracyclophane[20] and applied the literature known enzymatic resolution with *Candida cylindracea* lipase (CCL).[21] (S_p)-4-Hydroxy-[2.2]paracyclophane was obtained in 40% yield and 90% ee. The remaining (R_p)-acetoxy[2.2]paracyclophane was obtained in 42% yield with an enantiomeric excess of >99%. Hydrolysis to the phenol proceeded in quantitative yield and without any racemization. The resulting enantiomerically pure phenols were then converted to the corresponding triflates in excellent yields (97%) by treatment with sodium hydride followed by the addition of triflate anhydride. Cross-coupling of the triflate employing the general protocol gave enantiomerically pure (*R*)-4-triisopropylsilanylsulfuryl[2.2]paracyclophane in good yields (59%). Deprotection with TBAF in THF to yield (*R*)-[2.2]paracyclophane-4-thiol proceeded quantitatively. This represents the

Table 3. Pd-catalyzed carbon-sulfur bond formation of aryl triflates.[a]



Entry	ArOTf	Product	Conversion[b]	Yield[c]
1			75%	57%
2			quant.	90%[d]
3			96%	81%
4			94%	79%
5			82%	59% for (*R*), 62% for (*rac*)

[a] Reaction conditions: ArOTf (1.0 equiv.), TIPSSH (1.3 equivs.), Cs_2CO_3 (1.3 equivs.), $Pd(OAc)_2$ (5 mol %), PPh_3 (22 mol %) in toluene at 100 °C under argon.
[b] By GC-MS.
[c] Isolated yield.
[d] Yield of protected (56%) and unprotected (34%) thiol combined.

first synthesis of enantiomerically pure [2.2]paracyclophane-4-thiol which, up until now, could only be synthesized as a racemate.[22]

Conclusion

In summary, we have developed a general and efficient palladium-catalyzed carbon-sulfur bond formation protocol for aryl bromides, iodides, and triflates. This method is particularly noteworthy given its experimental simplicity, high generality, and high level of functional group toleration. Therefore, it represents a convenient route from phenols to arenethiols *via* the corresponding triflates. Additionally, we herein report the first synthesis of enantiomerically pure [2.2]paracyclophane-4-thiol, providing the starting point for a new generation of sulfur-containing [2.2]paracyclophane ligands which can be used in asymmetric catalysis.[23]

Experimental Section

General Remarks

All catalysis reactions were performed in 10-mL vials under an argon atmosphere. Substrates were purchased from commercial sources and were used without further purification. Enantiomeric excesses were determined by GC on a chiral stationary phase (CP-Chirasil-Dex). GC-MS was measured on a HP 5890 Series II GC with an HP 5972 MS. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC300 (250 MHz/67 MHz), Bruker AM400 (400 MHz/100 MHz) or Bruker DRX500 (500 MHz/125 MHz), using $CDCl_3$ as the solvent and shift reference ($CHCl_3$ 7.26 ppm/77.00 ppm). The mass spectra were recorded on a Finnigan MAT 90. Elemental analyses were measured on a Heraeus CHN-O-Rapid. The IR spectra were recorded on a Bruker IFS 88. Optical rotations were determined on a Perkin Elmer 241 polarimeter (Na, 589 nm). Solvents were purified according to standard procedures.

(*R*)-Trifluoromethanesulfonic Acid (4-[2.2]Paracyclophane) Ester (Table 3, entry 4, starting material)

A 50-mL Schlenk-flask was flame-dried under a stream of argon and allowed to cool to room temperature. It was charged with enantiomerically pure (*R*)-4-hydroxy-[2.2]paracyclophane (50 mg, 0.223 mmol) and dry toluene (30 ml). Mineral oil-free NaH (24 mg, 1.00 mmol) was added carefully under a stream of argon. The reaction mixture was cooled to 0 °C and trifluoromethanesulfonic acid (189 mg, 0.669 mmol) was added slowly. The mixture was stirred for another 10 min at 0 °C and was then warmed to room temperature and stirred for 24 h. Saturated aqueous NH_4Cl and diethyl ether were added and the mixture was transferred into a separatory funnel and the organic layer was washed with brine. The collected organic layers were dried with Na_2SO_4, filtered, and concentrated under vacuum. The crude product was purified by flash chromatography (cyclohexane) to afford as a colourless oil (*R*)-trifluoromethanesulfonic acid (4-[2.2]paracyclophane) ester; yield: 74 mg (97%).

The racemate was prepared accordingly. $R_f = 0.10$ (cyclohexane); $[\alpha]_{589}^{293}$: +18.07° (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 6.93$ (dd, $J = 7.9$ Hz, 1.6 Hz, 1H), 6.65–6.55 (m, 3H), 6.53–6.51 (m, 1H), 6.50 (dd, $J = 4.1$ Hz, 1.9 Hz, 1H), 6.48 (d, $J = 1.9$ Hz, 1H), 3.44 (ddd, $J = 13.7$ Hz, 9.7 Hz, 3.6 Hz, 1H), 3.25–2.97 (m, 6H); 2.83 (ddd, $J = 13.8$ Hz, 9.7 Hz, 6.4 Hz, 1 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) $\delta = 148.0$, 142.9, 139.3139.1, 136.0, 133.5, 132.5, 132.3, 131.9, 129.4, 127.7, 118.5 (q, $J = 320.8$ Hz, 1C), 35.1, 34.6, 34.0, 31.5; ^{19}F NMR (376.5 MHz, $CDCl_3$) $\delta = -74.9$ (s, 3F); FT-IR (neat): $\nu =$ 3016, 2929, 2859, 1605, 1415, 1210, 975, 885 cm^{-1}; MS: *m/z* (rel. int. %) = 356 (13), 223 (17), 104 (100); HR-MS: *m/z* calculated for $C_{17}H_{15}SO_3F_3$: 356.0694; found: 356.0692.

General Procedure for the Cross-Coupling Reaction

A sealable tube was charged with $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), PPh_3 (29 mg, 0.11 mmol) Cs_2CO_3 (212 mg, 0.65 mmol) and aryl halide or aryl triflate (0.50 mmol) and was sealed afterwards. The sealed tube was evacuated and refilled with argon. This procedure was repeated three times. Dry toluene (5 mL) and triisopropylsilanethiol (124 mg, 0.65 mmol) were added subsequently *via* syringe. The solution turned deep red and was warmed to 100 °C for 16 h. After cooling to room temperature, 5 mL of aqueous NH_4Cl were added. The reaction contents were transferred to a separatory funnel and extracted twice with diethyl ether. The collected organic layers were dried with Na_2SO_4, filtered, and concentrated under vacuum. The crude product was purified by flash chromatography (cyclohexane/ethylene glycol dimethyl ether, 20:1) to yield triisopropylsilyl arenethiol. Deprotection to the corresponding arenethiols was achieved by stirring in THF with TBAF at room temperature for 2 hours.

Dimethyl-(4-triisopropylsilanylsulfanyl-phenyl)-amine (Table 1, entry 3): yield: 65%; $R_f = 0.11$ (cyclohexane/ethylene glycol dimethyl ether, 100:1); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.32$ (d, $J = 8.2$ Hz, 2H), 6.59 (d, $J = 8.2$ Hz, 2H), 2.92 (s, 6H), 1.22 (sept, $J = 7.5$ Hz, 3H), 1.08 (d, $J = 7.5$ Hz, 18H); ^{13}C NMR: $\delta = 149.5$, 136.2, 115.8, 112.9, 40.5, 18.5, 12.9; FT-IR (neat): $\nu = 2944$, 2866, 1596, 1503, 1352, 1193, 882, 812 cm^{-1}; MS: *m/z* (rel. int. %) = 309 (100), 266 (95), 224 (19), 148 (23), 105 (19); HR-MS: *m/z* calculated for $C_{17}H_{31}NSSi$: 309.1947; found: 309.1945.

4-Triisopropylsilanylsulfanyl-benzonitrile (Table 1, entry 5): yield: 43%; $R_f = 0.27$ (cyclohexane/ethylene glycol dimethyl ether, 50:1); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 7.57$ (d, $J = 8.5$ Hz, 1H), 7.48 (d, $J = 8.5$ Hz, 1H), 1.4–1.2 (m, 3 H), 1.08 (d, $J = 6.7$ Hz, 18H); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta =$ 140.1, 135.5, 131.9, 118.7, 110.1, 18.4, 13.2; FT-IR (neat): $\nu =$ 3065, 2948, 2228, 1591, 1485, 1086, 1018, 884, 676 cm^{-1}; MS: *m/z* (rel. int. %) = 291 (28), 248 (100), 220 (19), 206 (27), 178 (44), 135 (29); HR-MS: *m/z* calculated for $C_{16}H_{25}NSSi$: 291.1477; found: 291.1473.

2-Methoxy-5-triisopropylsilanylsulfanyl-benzaldehyde (Table 1, entry 6): yield: 80%; $R_f = 0.45$ (cyclohexane/ethylene glycol dimethyl ether, 20/1); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta =$ 10.38 (s, 1H), 7.91 (d, $J = 2.3$ Hz, 1H), 7.63 (dd, $J = 8.6$ Hz, 2.3 Hz, 1H), 6.86 (d, $J = 8.6$ Hz, 1H), 3.90 (s, 3H), 1.30–1.11 (m, 3H), 1.06 (d, $J = 6.4$ Hz, 18H); ^{13}C NMR (62.5 MHz,

$CDCl_3$): δ = 189.0, 160.8, 142.5, 135.0, 124.8, 123.0, 112.1, 55.7, 18.4, 12.9; FT-IR (neat): ν = 2945, 2867, 1678, 1588, 1480, 1244, 1021, 883, 826, 644 cm^{-1}; MS: *m/z* (rel. int. %) = 324 (54), 281 (100), 239 (27), 181 (23), 167 (20); HR-MS: *m/z* calculated for $C_{17}H_{28}SO_2Si$: 324.1579; found: 324.1581; anal. calcd. C 62.91, H 8.70; found: C 62.86, H 8.25.

Triisopropyl-(2-methoxyphenylsulfanyl)-silane (Table 1, entry 8 and Table 2 entry 2): yield: 62%; R_f = 0.51 (cyclohexane/ethylene glycol dimethyl ether, 20/1); ^1H NMR (250 MHz, $CDCl_3$): δ = 7.35 (dd, *J* = 7.9 Hz, 1.5 Hz, 1H), 7.06 (ddd, *J* = 7.8 Hz, 7.8 Hz, 1.5 Hz, 1H), 6.79–6.69 (m, 2H), 3.78 (s, 3H), 1.3–1.1 (m, 3H), 0.93 (d, *J* = 7.0 Hz, 18H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 137.5, 133.8, 133.5, 128.4, 120.5, 110.7, 55.4, 18.3, 13.3; FT-IR (neat): ν = 3060, 2945, 2866, 1581, 1478, 1246, 1066, 1028, 882, 750, 673 cm^{-1}; MS: *m/z* (rel. int. %) = 296 (2), 262 (11), 253 (51), 238 (20), 183 (50), 167 (58), 77 (60), 43 (100); HR-MS: *m/z* calculated for $C_{16}H_{28}SOSi$: 296.1630; found: 296.1634.

(Benzo[*b*]thiophen-3-yloxy)-triisopropylsilane (Table 1, entry 10): yield: 60%; R_f = 0.53 (cyclohexane); ^1H NMR (250 MHz, $CDCl_3$): δ = 7.85–7.79 (m, 1H), 7.78–7.71 (m, 1H), 7.43–7.30 (m, 2H), 6.42 (s, 1H), 1.46–1.29 (m, 3H), 1.16 (d, *J* = 7.0 Hz, 18H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ = 146.8, 137.2, 134.1, 124.7, 123.6, 122.9, 121.1, 102.3, 17.9, 12.6; FT-IR (neat): ν = 2945, 2867, 1568, 1524, 1463, 1431, 1357, 1180, 881, 727 cm^{-1}; MS: *m/z* (rel. int. %) = 306 (100), 263 (97), 235 (28), 207 (21); HR-MS: *m/z* calculated for $C_{17}H_{26}OSSi$: 306.1474; found: 306.1476; anal. calcd. C 66.61, H 8.55; found: C 66.74, H 8.30.

Triisopropyl-(thiophen-2-ylsulfanyl)-silane (Table 1, entry 12): yield: 60%; R_f = 0.77 (cyclohexane/ethylene glycol dimethyl ether, 20/1); ^1H NMR (250 MHz, $CDCl_3$): δ = 7.19 (dd, *J* = 5.4 Hz, 1.2 Hz, 1H), 7.04 (dd, *J* = 3.5 Hz, 1.2 Hz), 6.90 (dd, *J* = 5.4 Hz, 3.5 Hz, 1H), 1.3–1.15 (m, 3H), 1.10 (d, *J* =6.9 Hz, 18H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 133.91, 129.25, 127.53, 127.3, 18.36, 12.90; FT-IR (neat): ν = 2945, 2867, 1462, 1406, 1215, 985, 882, 692 cm^{-1}; MS: *m/z* (rel. int. %) = 272 (100), 229 (60), 187 (23), 159 (26), 157 (58), 115 (45); HRMS: *m/z* calculated for $C_{13}H_{24}S_2Si$: 272.1089; found: 272.1093.

7-Triisopropylsilanylsulfanyl-3,3a,4,5-tetrahydro-oxazolo[3,4-*a*]quinolin-1-one (Table 2, entry 3): yield: 69%; R_f = 0.02 (cyclohexane/dichloromethane, 1:1); ^1H NMR (500 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.7 Hz, 1H), 7.33 (dd, *J* = 8.6 Hz, 2.1 Hz, 1H), 7.28 (d, *J* = 2.1 Hz, 1H), 4.59 (dd, *J* = 8.5 Hz, 8.4 Hz, 1H), 4.18 (dddd, *J* = 11.8 Hz, 8.6 Hz, 8.4 Hz, 2.8 Hz, 1H), 4.04 (dd, *J* = 8.6 Hz, 8.5 Hz, 1H), 2.97–2.86 (m, 2H), 2.19 (dddd, *J* = 12.6 Hz, 12.2 Hz, 11.8 Hz, 5.7 Hz, 1H), 1.82 (dddd, *J* = 12.6 Hz, 12.2 Hz, 11.8 Hz, 5.7 Hz, 1H), 1.24 (sept, *J* = 7.5 Hz, 3H), 1.09 (d, *J* = 7.5 Hz, 9H), 1.08 (d, *J* = 7.5 Hz, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 154.2, 135.9, 134.1, 133.7, 125.4, 125.0, 118.2, 67.4, 54.4, 26.4, 26.3, 18.4, 12.9; FT-IR (neat): ν = 2944, 2867, 1740, 1487, 1395, 1323, 1218, 1036, 882, 829, 752, 652 cm^{-1}; MS: *m/z* (rel. int. %) = 377 (84), 334 (100), 290 (52), 262 (58), 220 (84); HR-MS: *m/z* calculated for $C_{20}H_{31}NSiO_2S$: 377.1845; found: 377.1849; anal. calcd. N 3.71, C 63.61, H 8.27; found: N 3.55, C 63.25, H 7.86.

(4-Bromophenylsulfanyl)-triisopropylsilane (3): 52% yield. R_f = 0.82 (cyclohexane/ethylene glycol dimethyl ether, 20:1); ^1H NMR (250 MHz, $CDCl_3$) δ = 7.5–7.3 (m, 4 H), 1.3–1.15 (m, 3 H), 1.07 (d, *J* = 6.7 Hz, 18 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ = 136.9, 132.2, 131.6, 120.9, 18.4, 13.0; FT-IR (neat): ν = 2945, 2866, 1471, 1009, 816, 671 cm^{-1}; MS: *m/z* (rel. int.) = 346 (34), 344 (32), 303 (100), 301 (88), 261 (25), 259 (25), 233 (22), 231 (22); HRMS: *m/z* calculated for $C_{15}H_{25}BrSSi$: 344.0630; found: 344.0627.

(*S*)-Isopropyl-(2-triisopropylsilanylsulfanylbenzylidene)-amine (Table 3, entry 4): yield: 79% yield; > 98% ee; $[\alpha]_{589}^{293}$: −31° (*c* 1.0, $CHCl_3$); R_f = 0.38 (cyclohexane/ethylene glycol dimethyl ether/triethylamine, 60:3:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.00 (dd, *J* = 7.3 Hz, 2.2 Hz, 1H), 7.42 (dd, *J* = 7.2 Hz, 1.8 Hz, 1H) 7.4–7.1 (m, 7 H), 4.55 (q, *J* = 6.6 Hz, 1 H), 1.53 (d, *J* = 6.6 Hz, 3H), 1.2–1.0 (m, 3H), 0.96 (d, *J* = 7.4 Hz, 9H), 0.95 (d, *J* = 7.4 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.5, 136.8, 133.8, 133.6, 130.1, 128.7, 128.5, 128.3, 127,3. 126.7, 126.6, 69.8, 24.7, 18.3, 13.3; FT-IR (neat): ν = 2944, 2866, 1633, 1462, 882, 758, 698, 673 cm^{-1}, MS: *m/z* (rel. int. %) = 397 (1), 354 (4), 250 (12), 105 (49), 43 (100); HRMS: *m/z* calculated for $C_{24}H_{35}NSSi$: 397.2259; found: 397.2255.

(*R*)-(4-Triisopropylsilanylsulfanyl)-[2.2]paracyclophane (Table 3, entry 5): yield: 90%; ee, $[\alpha]_{589}^{293}$: −36° (*c* 1.0, $CHCl_3$); R_f = 0.64 (cyclohexane/ethylene glycol dimethyl ether, 20:1); ^1H NMR (500 MHz, $CDCl_3$): δ = 7.06 (dd, *J* = 7.8 Hz, 1.6 Hz, 1H), 6.55–6.50 (m, 2H), 6.48 (dd, *J* = 8.8 Hz, 1.9 Hz, 1H), 6.45 (dd, *J* = 8.2 Hz, 1.6 Hz, 1H), 6.42 (d, *J* = 1.6 Hz, 1H), 6.41 (d, *J* = 7.8 Hz, 1H), 3.80 (ddd, *J* = 12.9 Hz, 10.4 Hz, 2.5 Hz, 1H), 3.25 (ddd, *J* = 13.1 Hz, 10.3 Hz, 5.9 Hz, 1H), 3.2–3.0 (m, 4H), 2.94–2.85 (m, 1H), 2.78 (ddd, *J* = 13.0 Hz, 10.4 Hz, 5.9 Hz, 1H), 1.20–1.05 (m, 3H), 1.03 (d, *J* = 6.90 Hz, 9H), 0.97 (d, *J* = 7.2 Hz, 9H); ^{13}C NMR (62 MHz, $CDCl_3$): δ = 144.0, 142.2, 139.7, 139.3, 139.0, 134.3, 132.9, 132.6, 132.3, 131.4, 131.4, 129.1, 35.5, 35.4, 34.8, 34.0, 18.3, 18.2, 13.0; FT-IR (neat): ν = 2945, 1892,1586, 1499, 1018, 884, 720 cm^{-1}; MS: *m/z* (rel. int. %) = 396 (3), 288 (14), 286 (14), 262 (24), 104 (100); HR-MS: *m/z* calculated for $C_{25}H_{36}SSi$: 396.2307; found: 396.2303.

(*R*)-[2.2]Paracyclophane-4-thiol (Table 3, entry 4): 59% yield. > 98% ee, $[\alpha]_{589}^{293}$: +7.2° (*c* 1.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ = 7.21 (dd, *J* = 7.9 Hz, 1.8 Hz, 1H), 6.57 (dd, *J* = 7.63 Hz, 1.83 Hz, 1H), 6.5–6.3 (m, 4H), 6.21 (d, *J* = 1.6 Hz, 1H), 3.5–2.7 (m, 8H). This compound yielded spectral data consistent with literature reports for the racemate, see, for example: Hopf et al.[22]

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