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# Synthesis of Tricyclic Fused 3-Aminopyridines through Intramolecular $Co^{I}$-Catalyzed [2+2+2] Cycloaddition between Ynamides, Nitriles, and Alkynes

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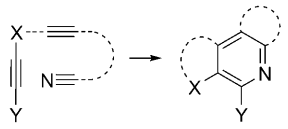
**Abstract:** The first [2+2+2] cocyclizations between ynamides, nitriles, and alkynes are reported. They open a new access to unprecedented nitrogen-containing heterocycles of type 2-trimethylsilyl-3-aminopyridines. Such frameworks, which can be found in various compounds of biological interest, are very difficult to prepare by conventional methods. However, using [CpCo-$(C_2H_4)_2$] (Cp = cyclopentadienyl) as catalyst, the intramolecular cyclizations could be achieved in up to 100% yield. The presence of the trimethylsilyl group allowed a rare type of Hiyama cross-coupling: one of the silylated pyridines could be coupled with *p*-iodoanisole to give a new type of biaryl system.

**Keywords:** alkynes · cobalt · cycloaddition · Hiyama cross-coupling · pyridine

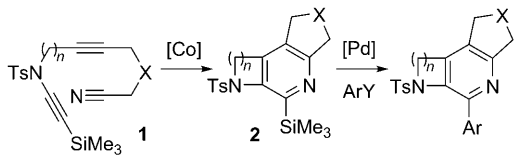
## Introduction

Pyridines are ubiquitous subunits of natural products and pharmaceuticals.[1] Thus, the construction of complex polycyclic pyridines remains an important synthetic goal for creating new and potentially useful systems with biological applications. Among the possible methods to achieve this, the transition-metal-catalyzed [2+2+2] cycloaddition reaction between two alkynes and one nitrile is probably one of the most elegant, as it allows the formation of the two C–C and the C–N bonds of the pyridine ring in a single operational step.[2,3] In principle, this atom-and-step economy procedure, which is tolerant to a wide range of functional groups, should enable the direct formation of polycyclic functionalized pyridines, or at least inherently functionalizable ones owing to the presence of heteroatoms. The incorporation of an heteroatom at C2 has been achieved frequently by [2+2+2] cycloaddition reactions with silicon (Scheme 1, Y = Si),[4] and rarely with phosphorus (Y = P).[5] On the other hand, very few examples of pyridines heterosubstituted at C2 and/or C3 can be found, and they are strictly restricted to silicon (X = Si or X = Y = Si).[6]




Scheme 1. Prototypical [2+2+2] cycloaddition leading to heterosubstituted pyridines.

We reasoned that 2-trimethylsilyl-3-aminopyridines (X = N, Y = Si) could be possibly assembled by carrying out unprecedented [2+2+2] cocyclizations between an ynamide, an alkyne, and a nitrile (Scheme 2).[7] In an intramolecular fashion, this strategy would provide an entry into new polycyclic systems displaying frameworks that can be found in various compounds of biological interest.[1] We report herein our efforts to prepare polyunsaturated precursors of type **1** and their subsequent cobalt-catalyzed cyclizations[8] to give tricyclic fused 2-trimethylsilyl-3-aminopyridines **2**. We also show how we could take advantage of the presence of the




Scheme 2. Synthetic strategy for the formation of tricyclic fused 2-trimethylsilyl-3-aminopyridines and subsequent cross-coupling.

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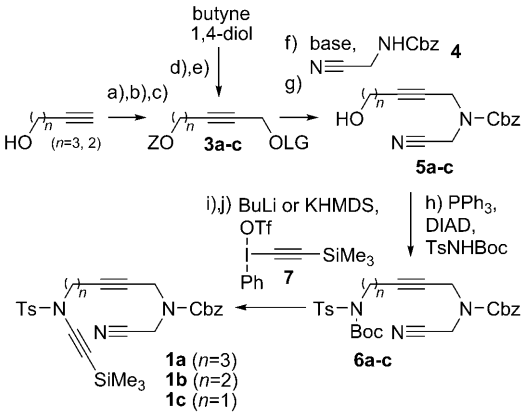
trimethylsilyl group to achieve an easier-than-expected Hiyama cross-coupling.

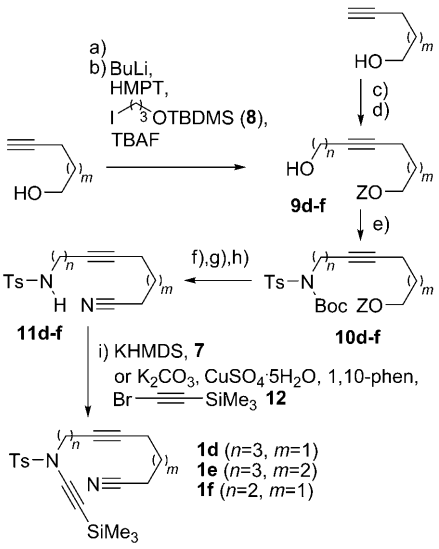
## Results and Discussion

The synthesis of precursors **1** was achieved in seven or eight steps (Schemes 3–5). We chose to introduce the fragile ynamide fragment at the last moment in each case. Compounds **1a–c** exhibit two aliphatic nitrogen tethers with orthogonal protecting groups for subsequent selective deprotection and potential functionalization (Scheme 3, tosyl and carbobenzyloxy). 3-Butynol and 4-pentynol were protected as tetrahydropyranyl (THP) ethers (a, Z = THP), alkylated at the alkyne through deprotonation with BuLi and subsequent addition of *p*-formaldehyde (b), and activated as mesylate (c, leaving group (LG) = Ms, **3a**) or tosylate (LG = Ts, **3b**). On the other hand, 2-butyne-1,4-diol was monoprotected as a silylated ether (d, Z = *tert*-butyldimethylsilyl (TBDMS)) and subsequently tosylated (e, LG = Ts, **3c**). Ynenitriles of type **5** were formed next by substitution of the propargylic mesylates or tosylates by the amine **4**[9] deprotonated by NaH (f). After removal of the protecting group Z (g), the third nitrogen atom was introduced by Mitsunobu reactions with TsNHBoc (Boc = *tert*-butyl oxycarbonyl) (h).[10] Lastly, the Boc group was removed (i)[11] and alkynylation was achieved using Witulski's procedure[12] with the iodonium salt **7** (j).[13] Overall, these steps proceeded with good to excellent yields, except for the formation of the ynamides (31–45%), which is always a delicate matter requiring specific precautions.

Compounds **1d–h**, which exhibit only one nitrogen tether, could also be constructed relatively rapidly from ynols in a similar fashion (Schemes 4 and 5). The starting material was first protected at the oxygen (Scheme 4, a or c, Z = THP, ethoxyethyl (EE), or Ts) and the alkyne was alkylated using the iodide **8** (b), or ethylene oxide (d), to give **9d–f**. These alcohols were submitted to Mitsunobu reaction conditions using TsNHBoc (e). The protecting group Z was removed (f), and the resulting alcohols were mesylated (g). Cyanation with NaCN or KCN was performed next (h). Of particular note is the efficient deprotection of the Boc group of intermediates **10d–f** upon treatment with NaCN in DMF to form **11d–f** in very good overall yields over the three steps f–h. This deprotection[14] was also observed with KCN in dimethyl sulfoxide (DMSO), albeit in lower yield. The formation of ynamides **1d–f** could be achieved under both Witulki's and Hsung's[15] conditions using **7** or **12**,[16] respectively, in low to moderate yields. However, both types of reaction al-




Scheme 3. Synthesis of the precursors **1a–c** from **3a** ($n=3$, Z = THP, LG = Ms), **3b** ($n=2$, Z = THP, LG = Ts), and **3c** ($n=1$, Z = TBDMS, LG = Ts). Reagents and conditions: a) PTSA·$H_2O$ (1 mol%), dihydropyran (DHP) (1.1 equiv), $CH_2Cl_2$, 0°C→RT, 24 h; b) BuLi (1.3 equiv), *p*-formaldehyde (6 equiv), THF, −78°C→RT, overnight, 81% ($n=3$) and 87% ($n=2$), over two steps; c) **3a**: MsCl (1.5 equiv), $Et_3N$ (1.4 equiv), $CH_2Cl_2$, 0°C→RT, overnight, 81%; **3b**: TsCl (3.15 equiv), KOH (3.06 equiv), $Et_2O$, overnight, 85%; d) NaH (1.0 equiv), *tert*-butyldimethylsilyl chloride (TBDMSCl) (1.0 equiv), THF, RT, 4 h, 54%; **3c**: e) TsCl (1.2 equiv), KOH (10 equiv), $Et_2O$, RT, 1 h, 68%; f) $n=3$: KHMDS (1.1 equiv), TBAI (0.1 equiv), **4** (1.1 equiv), THF, RT, 2 h; $n=2$ and $n=1$: NaH (1.1 equiv), **4** (1.1 equiv), DMF, RT, overnight; g) PTSA·$H_2O$ (4 mol%), MeOH, 20 h, 91% (**5a**) and 85% (**5b**), over two steps, or TBAF (1.3 equiv), THF, RT, 12 h, 68% (**5c**), over two steps; h) $PPh_3$ (1.1 equiv), DIAD (1.0 equiv), TsNHBoc (1.0 equiv), THF, 0°C→RT, 3.5 h, 92% (**6a**), 88% (**6b**), and 82% (**6c**); i) PhOH (70 equiv), TMSCl (23 equiv), $CH_2Cl_2$, RT, 2 h, 92% ($n=3$) and 38% ($n=2$), or TFA (3 equiv), $CH_2Cl_2$, MW, 100°C, 20 min, 69% ($n=1$); j) BuLi (1.01 equiv), THF, −78°C→RT, 15 min; **7** (1.2 equiv), toluene, 70°C, 2 h, 31% (**1a**) and 45% (**1b**), or KHMDS (1.0 equiv), **7** (1.2 equiv), toluene, 40°C, 34% (**1c**).

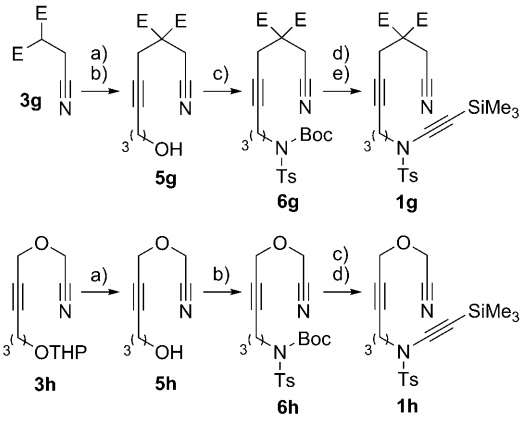



Scheme 4. Synthesis of the precursors **1d–f** from **9d** ($n=3$, $m=1$, Z = THP), **9e** ($n=3$, $m=2$, Z = EE), and **9f** ($n=2$, $m=1$, Z = Ts). Reagents and conditions: a) Standard protection with $m=1$ (Z = THP)[17] and $m=2$ (Z = EE);[18] b) see ref. [19], 51% (**9d**) and 98% (**9e**); c) pyridine (5 equiv), TsCl (2.5 equiv), $CH_2Cl_2$, 0°C→RT, 18 h, 79%; d) BuLi (1.2 equiv), ethylene oxide (3 equiv), $BF_3$·$OEt_2$ (1.2 equiv), THF, −78°C, 2 h, 46% (**9f**); e) $PPh_3$ (1.1 equiv), DIAD (1.0 equiv), TsNHBoc (1.0 equiv), THF, 0°C→RT, 3.5 h, 68% (**10d**), 76% (**10e**), and 53% (**10f**); f) for **10d–e**: PTSA·$H_2O$ (0.01 equiv), MeOH, RT, overnight; g) for **10d–e**: MsCl (1.5 equiv), $Et_3N$ (1.4 equiv), $CH_2Cl_2$, 0°C→RT, overnight; h) for **10d–e**: NaCN (6 equiv), DMF, 80°C, 24 h, 81% (**11d**) and 69% (**11e**) over three steps, or for **10f**: KCN (2 equiv), DMSO, 90°C, overnight, 45% (**11f**); i) KHMDS (1.1 equiv), **7** (1.25 equiv), toluene, 80°C, 24 h, 45% (**1d**) and 30% (**1e**), or $K_2CO_3$ (2 equiv), 1,10-phenanthroline (0.2 equiv), $CuSO_4$·$5H_2O$ (0.1 equiv), **12** (1.0 equiv), toluene, 60°C, 36 h, 19% (**1f**).

lowed the recovery of the unreacted starting material, which could be submitted again to another coupling to eventually yield the precursors for the cyclizations in reasonable amounts.

We used a similar approach to synthesize precursors **1g** and **1h** (Scheme 5, see Experimental Section for details).



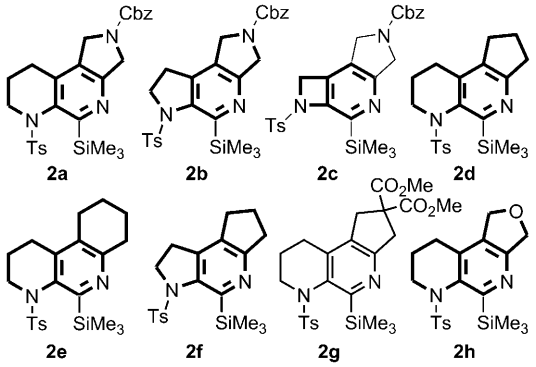

Scheme 5. Synthesis of the precursors **1g** and **1h** (E = $CO_2Me$).

The cyclizations were carried out with $CpCo(C_2H_4)_2$ (method A), which turns over already at room or lower temperature,[20] or with $CpCo(CO)_2$ (method B), which usually requires heat and visible light to be active (Table 1 and Scheme 6).[2g,21] Gratifyingly, both methods led to successful cycloadditions of precursors **1a–h** with the following details: Compound **2a**, which displays a novel framework of type 2,3,6,7,8,9-hexahydro-1*H*-pyrrolo[3,4-*f*][1,7]naphthyridine (highlighted in Scheme 6), was obtained in high yield with each catalyst (Table 1, entry 1). Tricyclic product **2b** (Table 1, entry 2), which was obtained in 76 and 77% yield, respectively, exhibits the basic skeleton of many derivatives that are, however, all benzocondensed or oxidized as carbonyls at the benzylic positions. Product **2c** (Table 1, entry 3), which was obtained in 50 and 55% yield, respectively, seems to be the first example of a stable 1,2-dihydro-1*H*-azeto[3,4-*c*]pyridine.[22] In this specific case, the formation of the four-membered ring required prolonged heating, even with $[CpCo(C_2H_4)_2]$ as catalyst. Products **2d–f**, which were all formed in excellent yields using method A,[23] are unique examples of 2,3,6,7,8,9-hexahydro-1*H*-cyclopenta[*f*]-[1,7]naphthyridine (**2d**), -cyclopentapyrrolopyridine (**2f**), and octahydro-benzonaphthyridine (**2e**). The presence of ester functionalities was tolerated during the formation of **2g** (Table 1, entry 7, 76% yield). Finally, the cyclization of **1h**, which has an oxygen tether, proved also successful (Table 1, entry 8, 62% yield), although it was necessary in this case to use up to 30 mol% of catalyst. Product **2h** is the first example of 1,3,6,7,8,9-hexahydrofuro[3,4-*f*]-[1,7]naphthyridine.

Table 1. [2+2+2] cycloadditions of the precursors **1a–h**.

| Entry | Substrate | *n* | X | Product | Yield [%][a,b] |
|---|---|---|---|---|---|
| 1 | **1a** | 3 | NCbz | **2a** | 93[d] (91)[e] |
| 2 | **1b** | 2 | NCbz | **2b** | 76[d] (77)[e] |
| 3 | **1c** | 1 | NCbz | **2c** | 50[f] (55)[d] |
| 4 | **1d** | 3 | $CH_2$ | **2d** | 100[c] |
| 5 | **1e** | 3 | $(CH_2)_2$ | **2e** | 100[c] |
| 6 | **1f** | 2 | $CH_2$ | **2f** | 90[c] |
| 7 | **1g** | 3 | $C(CO_2Me)_2$ | **2g** | 76[f] |
| 8 | **1h** | 3 | O | **2h** | 62[g] |

[a] Isolated yields corresponding to method A: $[CpCo(C_2H_4)_2]$, THF, RT, 1 h. [b] In parentheses, isolated yields corresponding to method B: $[CpCo(CO)_2]$, xylenes, reflux, *hv*, 1 h. Catalyst loads to reach full conversion of the substrate: [c] 5 mol%; [d] 10 mol%; [e] 15 mol%; [f] 20 mol%; [g] 30 mol%.



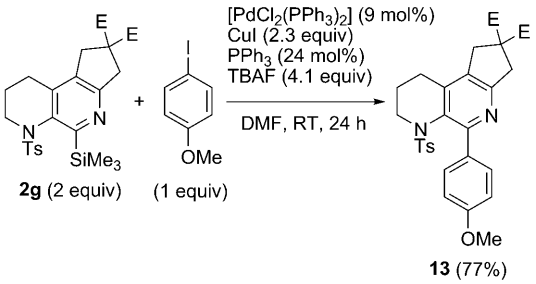

Scheme 6. Tricyclic pyridines prepared by [2+2+2] cycloaddition (the frameworks discussed in the text are highlighted).

An apparently simple and flexible way to functionalize the products would be to deprotect the amino groups and to couple them with other organic moieties. This should be particularly straightforward, even in the case of the bis-amino derivatives **2a–c**, because we took care to introduce orthogonal protecting groups. Another opportunity lies in the silyl group, which, in principle, can be substituted by an aryl or vinyl group under Hiyama cross-coupling conditions.[24] This seems quite challenging because unactivated trialkylsilyl groups are usually poorly reactive, and besides, Hiyama couplings of silylated pyridines are rare.[25] In view of the recent work of Philippe Gros and co-workers, who showed that the incorporation of chloro, fluoro, or methoxy substituents on the pyridine ring of pyridyltrimethylsilanes allows efficient Hiyama cross-couplings,[25a] we reasoned that our products, which bear a nitrogen substituent, could also be valuable partners for such transformations. Gratifyingly, under the same experimental procedure, we were able to substitute the trimethylsilyl group by a *p*-methoxybenzene group in good yield (Scheme 7). The biaryl system **13** was obtained at room temperature in an unoptimized 77% yield.

## Conclusion

We have developed an expedient method for the synthesis of tricyclic fused 2-trimethylsilyl-3-aminopyridines by unprecedented intramolecular [2+2+2] cycloadditions between




Scheme 7. Hiyama cross-coupling between **2g** (E = $CO_2Me$) and *p*-iodoanisole.

ynamides, nitriles, and alkynes. Interestingly, most of these compounds display basic skeletons that are new (or rare) and most probably very difficult to prepare by conventional methods. Although the formation of the ynamides implies the introduction of a trimethylsilyl group, we turned this into an advantage by achieving a Hiyama cross-coupling. This aspect is under active development in our laboratories, in view of preparing compounds of biological interest.

## Experimental Section

**General methods**: Glassware was oven-dried prior to use. Anhydrous THF was obtained by distillation over sodium/benzophenone under nitrogen and used freshly distilled. Toluene and xylenes were distilled from $NaK_{2.8}$ amalgam; $CH_2Cl_2$ from $CaH_2$; DMF from $MgSO_4$. Reagents that are commercially available were used as received. NMR spectra were recorded by using either a Bruker Avance 400 spectrometer fitted with a QNP probe $^{13}C/^{19}F/^{31}P/^{1}H$ or a Bruker ARX 200 spectrometer fitted with a dual $^{13}C/^{1}H$ probe. $^1H$ NMR spectra are referenced at 7.26 ppm and $^{13}C$ NMR spectra are referenced at 77.16 ppm for $CDCl_3$. Chemical shifts are given in ppm. When possible, $^1H$ and $^{13}C$ signals were assigned mostly on the basis of distortion enhancement by polarization transfer (DEPT)- and 2D-NMR (COSY, HMBC) experiments. In the description of the $^{13}C$ NMR spectra, a number at the beginning of the information in parentheses refers to accidentally isochronous carbons. Due to the coexistence of rotamers, some $^1H$ and $^{13}C$ signals are doubled. The two chemical shifts are given, separated by a slash. IR spectra were recorded by using a Tensor 27 (ATR diamond) Bruker spectrometer. IR data is reported as characteristic bands ($cm^{-1}$). Melting points were recorded by using a Stuart Scientific smp3 apparatus and are uncorrected. Purifications were achieved by performing column chromatography (CC) on silica gel (40–63 μm). Microwave reactions were performed by using a Biotage Iniator Microwave Synthetizer 2.0. TLC was performed on silica gel 60 $F_{254}$ from Merck.

**4**: 2-Aminoacetonitrile hydrogenosulfate (41.0 g, 265.94 mmol) was added at 0 °C to a solution of *N*-benzyloxycarboxysuccinimide (60.0 g, 240.75 mmol) in $CH_2Cl_2$ (1.5 L) and $Et_3N$ (56.7 g, 560.33 mmol). After warming for 12 h to Room temperature, the mixture was diluted with $Et_2O$, quenched with 1 N HCl, extracted with $CH_2Cl_2$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford a pale yellow solid (43.2 g, 94 %). $R_f$ = 0.30 (PE/EtOAc 7:3); m.p. 62.3 °C; $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ = 4.07 (d, $J$ = 6.2 Hz, 2H), 5.14 (s, 2H), 5.41 (brs, 1H), 7.35 ppm (s, 5H); $^{13}C$ NMR (50 MHz, $CDCl_3$): $\delta$ = 29.6 ($CH_2$), 67.9 ($CH_2$), 116.3 (C), 128.5 (CH), 128.7 (CH), 128.8 (CH), 135.6 (C), 155.8 ppm (C); IR (neat): $\tilde{\nu}$ = 3324, 1701, 1512, 1244 $cm^{-1}$; HRMS: $m/z$: calcd for $[C_{10}H_{10}N_2O_2Na]^+$: 213.06345; found: 213.06322.

**5a**: Step f: Potassium hexamethyldisilazane (KHMDS) (0.5 M in toluene, 10.5 mL, 5.26 mmol) was added to a solution of **4** (967 mg, 5.08 mmol) and tetrabutylammonium iodide (TBAI) (171 mg, 0.46 mmol) in THF (44 mL) under Ar, followed after 15 min by **3a** (1.28 g, 4.63 mmol). After 1 h, the reaction mixture was quenched with strd aq. $NH_4Cl$, extracted with $Et_2O$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford a brown oil in quantitative yield used without further purification. $R_f$ = 0.57 ($CH_2Cl_2$/$Et_2O$ 96:4); $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 1.56–1.62 (m, 4H), 1.67–1.75 (m, 1H), 1.77–1.85 (m, 3H), 2.34 (tt, $J$ = 7.1, 1.9 Hz, 2H), 3.43–3.53, (m, 2H), 3.78–3.88 (m, 2H), 4.20–4.27 (m, 2H), 4.29–4.39 (m, 2H), 4.57–4.61 (m, 1H), 5.20 (s, 2H), 7.32–7.41 ppm (m, 5H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ = 15.6 ($CH_2$), 19.6 ($CH_2$), 25.4 ($CH_2$), 28.6 ($CH_2$), 30.7 ($CH_2$), 34.0/34.3 ($CH_2$), 37.0/37.2 ($CH_2$), 62.3 ($CH_2$), 65.8 ($CH_2$), 68.5 ($CH_2$), 73.0 (C), 86.2/86.4 (C), 98.8 (CH), 115.4 (C), 128.1 (CH), 128.5 (CH), 128.6 (CH), 135.5 (C), 154.2/154.8 ppm (C); IR (neat): $\tilde{\nu}$ = 3090, 3064, 3033, 2941, 2869, 2284, 2228, 1708, 1031 $cm^{-1}$.

Step g: 4.1 g (11.07 mmol) of the product obtained after step f and *p*-toluene sulfonic acid (PTSA·$H_2O$) (0.29 g, 1.52 mmol) were stirred in MeOH (200 mL) for 20 h. The reaction mixture was quenched with strd aq. $NaHCO_3$, extracted with $Et_2O$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified by CC ($CH_2Cl_2$ to $CH_2Cl_2$/$Et_2O$ 9:1) to afford **5a** as a colorless oil (2.88 g, 91 %). $R_f$ = 0.30 ($CH_2Cl_2$/$Et_2O$ 4:1); $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 1.70 (quint, $J$ = 6.5 Hz, 2H), 2.29 (tt, $J$ = 6.5, 2.1 Hz, 2H), 2.60 (brs, 1H), 3.64 (t, $J$ = 6.5 Hz, 2H), 4.17 (brs, 2H), 4.28 (brs, 2H), 5.16 (s, 2H), 7.30–7.35 ppm (m, 5H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ = 15.1 ($CH_2$), 30.9 ($CH_2$), 34.3/34.6 ($CH_2$), 37.3 ($CH_2$), 61.1 ($CH_2$), 68.5 ($CH_2$), 73.2 (C), 86.2 (C), 115.6 (C), 128.1 (CH), 128.5 (CH), 128.6 (CH), 135.5 (C), 154.3/154.9 ppm (C); IR (neat): $\tilde{\nu}$ = 3400, 3064, 3033, 2947, 2877, 2188, 1703 $cm^{-1}$; HRMS: $m/z$: calcd for $[C_{16}H_{18}N_2O_3Na]^+$: 309.12096; found: 309.12060.

**6a**: Compound **5a** (2.50 g, 8.73 mmol) in THF (40 mL) and $PPh_3$ (2.30 g, 8.75 mmol) were successively added to a solution of TsNHBoc[26] (2.39 g, 8.82 mmol) in THF (35 mL) under Ar at 0 °C, followed by the dropwise addition over 1 h of DIAD (1.78 g, 8.80 mmol) in THF (20 mL) with a syringe pump. After 4 h (TLC monitoring), $SiO_2$ was added and the solvent removed under reduced pressure. Purification by CC (PE/$CH_2Cl_2$ 2:8 to pure $CH_2Cl_2$) afforded **6a** as a pale-yellow oil (2.57 g, 55 %). $R_f$ = 0.50 (PE/$CH_2Cl_2$ 2:8); $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 1.34 (s, 9H), 2.00 (quint, $J$ = 7.1 Hz, 2H), 2.32 (t, $J$ = 7.1 Hz, 2H), 2.45 (s, 3H), 3.93 (t, $J$ = 7.1 Hz, 2H), 4.23–4.29 (m, 2H), 4.29–4.46 (m, 2H), 5.21 (s, 2H), 7.32 (d, $J$ = 8.3 Hz, 2H), 7.35–7.42 (m, 5H), 7.78 ppm (d, $J$ = 8.3 Hz, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ = 16.2 ($CH_2$), 21.6 ($CH_3$), 27.9 ($CH_3$), 28.8 ($CH_2$), 34.0/34.3 ($CH_2$), 36.9/37.1 ($CH_2$), 46.2 ($CH_2$), 68.5 ($CH_2$), 73.6 (C), 84.4 (C), 85.3/85.5 (C), 115.6 (C), 127.8 (CH), 128.2 (CH), 128.5 (CH), 128.6 (CH), 129.3 (CH), 135.5/135.6 (C), 137.3 (C), 144.2 (C), 150.9 (C), 154.2/154.8 ppm (C); IR (neat): $\tilde{\nu}$ = 3065, 3033, 2976, 2933, 2870, 2226, 1713, 1351, 1153 $cm^{-1}$; HRMS: $m/z$: calcd for $[C_{28}H_{33}N_3O_6NaS]^+$: 562.19823; found: 562.19765.

**1a**: Step i: Compound **6a** (0.118 g, 0.219 mmol) and a solution of trimethylsilyl chloride (TMSCl) (0.550 g, 5.06 mmol) in $CH_2Cl_2$ (1.3 mL) were successively added to a solution of PhOH (1.45 g, 15.44 mmol) in $CH_2Cl_2$ (4 mL) under Ar. After 2 h, the reaction mixture was diluted with $CH_2Cl_2$, quenched with strd aq. $NaHCO_3$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford an oil. Purification of the crude by CC ($CH_2Cl_2$ to $CH_2Cl_2$/$Et_2O$ 1:1) afforded a colorless oil (0.089 g, 92 %). $R_f$ = 0.23 ($CH_2Cl_2$/$Et_2O$ 96:4); $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 1.66 (quint, $J$ = 6.8 Hz, 2H), 2.24 (t, $J$ = 6.8 Hz, 2H), 2.40 (s, 3H), 2.97–3.06 (m, 2H), 4.17 (brs, 2H), 4.28 (brs, 2H), 5.18 (s, 2H), 5.38 (t, $J$ = 6.2 Hz, 1H), 7.28 (d, $J$ = 8.2 Hz, 2H), 7.30–7.37 (m, 5H), 7.75 ppm (d, $J$ = 8.2 Hz, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ = 15.8 ($CH_2$), 21.5 ($CH_3$), 28.1 ($CH_2$), 34.3/34.7 ($CH_2$), 37.3 ($CH_2$), 41.9 ($CH_2$), 68.5 ($CH_2$), 73.9 (C), 85.3 (C), 115.7 (C), 127.1 (CH), 128.2 (CH), 128.5 (CH), 128.6 (CH), 129.8 (CH), 135.5 (C), 136.9 (C), 143.4 (C), 154.3/154.8 ppm (C); IR (neat): $\tilde{\nu}$ = 3274, 3064, 3033, 2946, 2872, 2253, 1704, 1325, 1156 $cm^{-1}$; HRMS: $m/z$: calcd for $[C_{23}H_{25}N_3O_4NaS]^+$: 462.14580; found: 462.14636.

Step j: BuLi (1.9 M in hexanes, 360 μL, 0.682 mmol) was added to a solution of the product obtained after step i (0.297 g, 0.676 mmol) in THF (12 mL) at −78 °C under Ar in a Schlenk tube. After warming to room

temperature, the yellow solution was concentrated under reduced pressure to give a solid directly diluted in toluene (12 mL) and warmed to 70 °C (bath temperature). After 10 min, iodonium salt **7**[27] (0.367 g, 0.815 mmol) was added in portions over 5 min. After 3 h, $SiO_2$ was added, the solvent was removed under reduced pressure, and the crude material purified by CC (pentane/$Et_2O$ 1:1) to afford **1a** as a yellow oil (160 mg, 45 %). $R_f$ = 0.70 (pentane/$Et_2O$ 1:1); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 0.17 (s, 9H), 1.86 (q, $J$ = 6.7 Hz, 2H), 2.31 (t, $J$ = 6.7 Hz, 2H), 2.47 (s, 3H), 3.41 (t, $J$ = 6.7 Hz, 2H), 4.27 (brs, 2H), 4.39 (brs, 2H), 5.22 (s, 2H), 7.32–7.37 (m, 7H), 7.79 ppm (d, $J$ = 8.4 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 0.0 ($CH_3$), 15.6 ($CH_2$), 21.6 ($CH_3$), 26.3 ($CH_2$), 34.0/34.4 ($CH_2$), 37.0 ($CH_2$), 49.8 ($CH_2$), 68.4 ($CH_2$), 73.3 (C), 73.9 (C), 84.9 (C), 94.6 (C), 115.5 (C), 127.7 (CH), 128.1 (CH), 128.4 (CH), 128.5 (CH), 129.6 (CH), 134.0 (C), 135.4 (C), 144.7 (C), 154.2/154.7 ppm (C); IR (neat): $\tilde{\nu}$ = 3065, 3033, 2956, 2157, 1710, 1363, 1168, 840 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{28}H_{33}N_3O_4NaSSi]^+$: 558.18532; found: 558.18530.

**2a**: Method A: Compound **1a** (83 mg, 0.158 mmol) in THF (2 mL) was added to $[CpCo(C_2H_4)_2]$ (1.70 mg, 0.009 mmol) under Ar in a Schlenk tube. After 3 h (TLC monitoring), some $[CpCo(C_2H_4)_2]$ was added (0.60 mg, 0.003 mmol). After a further 2 and then 12 h, the same addition was carried out with 2.0 mg (0.011 mmol) and 1.5 mg (0.008 mmol), respectively, of $[CpCo(C_2H_4)_2]$. $SiO_2$ was added and the solvent was removed under reduced pressure. Two successive CC of the crude material (pentane/$Et_2O$ 3:7) afforded a white solid (77 mg, 93 %). Method B: $[CpCo(CO)_2]$ (38 μL, 0.029 mmol) was added to a refluxing solution of **1a** (336 mg, 0.573 mmol) in degassed xylenes (12.0 mL) and the reaction was irradiated (visible light, halogen lamp, 150 W) for 30 min. $SiO_2$ was added and the solvent was removed under reduced pressure. Two successive CC (PE/$CH_2Cl_2$/$Et_2O$ 5:4:1) of the material gave a white solid (279 mg, 91 %). $R_f$ = 0.31 (PE/$Et_2O$ 3:7); m.p. 133.6 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 0.44/0.45 (2s, 9H), 1.21–1.29 (m, 1H), 1.43–1.54 (m, 1H), 1.69–1.79 (m, 1H), 2.10–2.33 (m, 1H), 2.42/2.43 (2s, 3H), 3.39–3.47 (m, 1H), 4.08–4.16 (m, 1H), 4.50–4.65 (m, 2H), 4.75–4.90 (m, 2H), 5.20–5.35 (m, 2H), 7.21 (d, $J$ = 8.3 Hz, 2H), 7.27–7.45 ppm (m, 7H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 0.0 ($CH_3$), 20.7/20.8 ($CH_2$), 21.3 ($CH_3$), 21.7/21.8 ($CH_2$), 44.8/44.9 ($CH_2$), 48.9/49.2 ($CH_2$), 52.7/53.0 ($CH_2$), 66.8/66.9 ($CH_2$), 126.4/126.6 (C), 127.3/127.4 (CH), 127.8 (CH), 127.9 (CH), 128.2 (CH), 129.4 (CH), 135.9/136.0 (C), 136.2/136.3 (C), 137.3/137.4 (C), 137.6 (C), 143.6/143.7 (C), 154.3/154.8 (C), 155.0/155.2 (C), 168.1/168.2 ppm (C); IR (neat): $\tilde{\nu}$ = 3089, 3064, 3032, 2950, 2896, 1704, 1355, 1161, 840 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{28}H_{34}N_3O_4SSi]^+$: 536.20338; found: 536.20275.

**5b**: Step f: NaH (60 wt % in oil, 118 mg, 0.29 mmol) was added to a solution of **4** (56.1 mg, 0.029 mmol) in DMF (2 mL), followed after 15 min by **3b**[28] (88 mg, 0.26 mmol). After 12 h, the reaction mixture was quenched with strd aq. $NH_4Cl$, extracted with $Et_2O$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford a yellow oil (103 mg) in quantitative yield used without further purification. $R_f$ = 0.03 (PE/$Et_2O$ 7:3); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 1.49–1.85 (m, 6H), 2.50 (tt, $J$ = 6.9, 2.1 Hz, 2H), 3.48–3.57 (m, 2H), 3.78–3.89 (m, 2H), 4.24 (brs, 2H), 4.35 (brs, 2H), 4.61 (brs, 1H), 5.19 (s, 2H), 7.37 ppm (brs, 5H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 19.6 ($CH_2$), 20.3 ($CH_2$), 25.5 ($CH_2$), 30.7 ($CH_2$), 34.1/34.3 ($CH_2$), 37.1 ($CH_2$), 62.5 ($CH_2$), 65.5 ($CH_2$), 68.7 ($CH_2$), 73.9 (C), 84.1 (C), 98.9 (CH), 115.5 (C), 128.3 (CH), 128.6 (CH), 128.7 (CH), 135.6 (C), 154.4/154.9 ppm (C); IR (neat): $\tilde{\nu}$ = 2942, 1709, 1237, 1032 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{20}H_{24}N_2O_4Na]^+$: 379.16283; found: 379.16252.

Step g: The product obtained after step f (0.103 g, 0.289 mmol) and PTSA·$H_2O$ (3.7 mg, 0.019 mmol) were stirred in MeOH (10 mL) for 20 h. The reaction mixture was quenched with strd aq. $NaHCO_3$, extracted with $Et_2O$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified by CC ($CH_2Cl_2$ to $CH_2Cl_2$/$Et_2O$ 9:1) to afford **5b** as a colorless oil (60 mg, 75 %). $R_f$ = 0.23 ($CH_2Cl_2$/$Et_2O$ 7:3); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 2.40 (t, $J$ = 6.2 Hz, 2H), 3.29 (brs, 1H), 3.65 (t, $J$ = 6.2 Hz, 2H), 4.16 (s, 2H), 4.25 (s, 2H), 5.14 (s, 2H), 7.28–7.34 ppm (m, 5H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 23.0 ($CH_2$), 34.4/34.7 ($CH_2$), 37.3/37.5 ($CH_2$), 60.7 ($CH_2$), 68.6 ($CH_2$), 74.7 (C), 83.9 (C), 115.7 (C), 128.2 (CH), 128.5 (CH), 128.7 (CH), 135.4 (C), 154.3/154.8 ppm (C); IR (neat): $\tilde{\nu}$ = 3429, 3033, 2946, 2885, 2227, 1702 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{15}H_{16}N_2O_3Na]^+$: 295.10531; found: 295.10571.

**6b**: Compound **5b** (3.68 g, 13.53 mmol) in THF (40 mL) and $PPh_3$ (3.59 g, 13.68 mmol) were successively added to a solution of TsNHBoc (3.68 g, 13.85 mmol) in THF (80 mL) under Ar at 0 °C, followed by the dropwise addition over 2 h of DIAD (2.79 g, 13.79 mmol) in THF (20 mL) with a syringe pump. After 3 h, $SiO_2$ was added and the solvent removed under reduced pressure. Purification by CC (PE/$CH_2Cl_2$ 2:8 to $CH_2Cl_2$/$Et_2O$ 9:1) afforded a pale-yellow oil (6.23 g, 88 %). $R_f$ = 0.62 ($CH_2Cl_2$/$Et_2O$ 94:6); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 1.34 (s, 9H), 2.45 (s, 3H), 2.70 (brs, 2H), 4.00 (brs, 2H), 4.24–4.27 (m, 2H), 4.35–4.39 (m, 2H), 5.20 (s, 2H), 7.32 (d, $J$ = 8.1 Hz, 2H), 7.35–7.45 (m, 5H), 7.78 ppm (d, $J$ = 8.1 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 20.1 ($CH_2$), 21.6 ($CH_3$), 27.8 ($CH_3$), 34.1/34.4 ($CH_2$), 36.9/37.1 ($CH_2$), 45.2 ($CH_2$), 68.5 ($CH_2$), 75.3 (C), 82.7/82.9 (C), 84.7 (C), 115.5 (C), 127.8 (CH), 128.2 (CH), 128.5 (CH), 128.6 (CH), 129.3 (CH), 135.5 (C), 137.2 (C), 144.4 (C), 150.7 (C), 154.3/154.7 ppm (C); IR (neat): $\tilde{\nu}$ = 2980, 2933, 1714, 1352, 1154 cm$^{-1}$.

**1b**: Step i: A solution of **6b** (6.25 g, 11.850 mmol) in $CH_2Cl_2$ (80 mL) and a solution of TMSCl (34.8 g, 320.3 mmol) in $CH_2Cl_2$ (160 mL) were successively added by using a cannula to a solution of PhOH (93.0 g, 988.2 mmol) in $CH_2Cl_2$ (100 mL) under Ar. After 3 h, the reaction mixture was diluted with $CH_2Cl_2$, quenched with strd aq. $NaHCO_3$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. After two successive CC ($CH_2Cl_2$/PE 9:1 to $CH_2Cl_2$/$Et_2O$ 7:3), the resulting oil was washed with 10 % aq. NaOH to afford a colorless oil (2.52 g, 38 %). $R_f$ = 0.31 ($CH_2Cl_2$/$Et_2O$ 95:5); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 2.35 (brs, 5H), 3.05 (brs, 2H), 4.12 (brs, 2H), 4.24 (brs, 2H), 5.14 (s, 2H), 5.78 (brs, 1H), 7.23–7.33 (m, 7H), 7.74 ppm (d, $J$ = 8.3 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 20.3 ($CH_2$), 21.5 ($CH_3$), 34.6/34.8 ($CH_2$), 37.3/37.4 ($CH_2$), 41.6 ($CH_2$), 68.6 ($CH_2$), 75.3 (C), 82.9 (C), 115.8 (C), 127.0 (CH), 128.2 (CH), 128.5 (CH), 128.7 (CH), 129.8 (CH), 135.4 (C), 137.0 (C), 143.6 (C), 154.3/154.8 ppm (C); IR (neat): $\tilde{\nu}$ = 3272, 3064, 3032, 2948, 2233, 1704, 1326, 1156 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{22}H_{23}N_3O_4NaS]^+$: 448.13015; found: 448.13002.

Step j: BuLi (1.9 M in hexanes, 330 μL, 0.633 mmol) was added to a solution of the product obtained after step i (0.270 g, 0.634 mmol) in THF (12 mL) at −78 °C under Ar in a Schlenk tube. After warming to room temperature the yellow solution was concentrated under reduced pressure to give a solid that was directly diluted with toluene (12 mL) and warmed to 70 °C (bath temperature). After 10 min, iodonium salt **7** (0.346 g, 0.768 mmol) was added in portions over 5 min. After 2 h, $SiO_2$ was added, the solvent was removed under reduced pressure and the crude material purified by CC (pentane/$Et_2O$ 1:1) to afford **1b** as a yellow oil (103 mg, 31 %). $R_f$ = 0.70 (pentane/$Et_2O$ 1:1); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 0.18 (s, 9H), 2.47 (s, 3H), 2.57 (t, $J$ = 7.3 Hz, 2H), 3.47 (t, $J$ = 7.3 Hz, 2H), 4.21/4.24 (2s, 2H), 4.33/4.37 (2s, 2H), 5.22 (s, 2H), 7.30–7.40 (m, 7H), 7.79 ppm (d, $J$ = 8.4 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 0.1 ($CH_3$), 18.6 ($CH_2$), 21.7 ($CH_3$), 34.2/34.5 ($CH_2$), 36.9/37.1 ($CH_2$), 49.8 ($CH_2$), 68.6 ($CH_2$), 73.9 (C), 75.3 (C), 82.0/82.1 (C), 94.2 (C), 115.5 (C), 127.7 (CH), 128.2 (CH), 128.5 (CH), 128.7 (CH), 129.7 (CH), 134.3 (C), 135.5 (C), 144.9 (C), 154.3/154.7 ppm (C); IR (neat): $\tilde{\nu}$ = 3066, 3034, 2958, 2899, 2157, 1712, 1366, 1169, 843 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{27}H_{31}N_3O_4NaSSi]^+$: 544.16967; found: 544.16975.

**2b**: Method A: Compound **1b** (94 mg, 0.180 mmol) in THF (1 mL) was added to $[CpCo(C_2H_4)_2]$ (1.70 mg, 0.009 mmol) under Ar in a Schlenk tube. After 15 h (TLC monitoring), some $[CpCo(C_2H_4)_2]$ was added (1.70 mg, 0.009 mmol). After a further 3 h, $SiO_2$ was added and the solvent was removed under reduced pressure. CC of the crude material (pentane/$Et_2O$ 3:7) afforded a white solid that was purified again by CC (same eluent) to afford a white solid (70 mg, 76 %). Method B: $[CpCo(CO)_2]$ (18 μL, 0.014 mmol) was added to a refluxing solution of **1b** (145 mg, 0.278 mmol) in degassed xylenes (5.6 mL) and the reaction irradiated (visible light, halogen lamp, 150 W) for 30 min. Some $[CpCo(CO)_2]$ (18 μL, 0.014 mmol) was then added and the reaction was irradiated while refluxing for 30 min. This operation was performed once more and then $SiO_2$ was added and the solvent removed under reduced

pressure. Two successive CC (PE/$CH_2Cl_2$/$Et_2O$ 5:3:2) of the material gave a white solid (117 mg, 77%). $R_f$=0.23 (PE/$Et_2O$ 7:3); m.p. 143.3°C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.25 (s, 9H), 1.70–1.80 (m, 2H), 2.20 (s, 3H), 3.74–3.78 (m, 2H), 4.27/4.30 (2s, 2H), 4.61 (m, 2H), 5.00/5.04 (2s, 2H), 6.96 (d, $J$=8.3 Hz, 2H), 7.05–7.25 ppm (m, 7H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=0.0 ($CH_3$), 21.7 ($CH_3$), 26.5 ($CH_2$), 49.5/49.7 ($CH_2$), 51.4 ($CH_2$), 52.8/53.1 ($CH_2$), 67.3/67.4 ($CH_2$), 125.4 (C), 125.6 (C), 127.9 (CH), 128.2 (CH), 128.3 (CH), 128.6 (CH), 129.7 (CH), 133.7/133.9 (C), 136.6 (C), 138.9/139.1 (C), 144.6/144.9 (C), 154.7/155.2 (C), 155.9/156.2 (C), 161.0/161.1 ppm (C); IR (neat): $\tilde{\nu}$=3064, 3032, 2952, 2899, 2869, 1704, 1354, 1164 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{27}H_{32}N_3O_4SSi]$: 522.18773; found:522.18715.

**5c**: Step f: NaH (60 wt% in oil, 32.1 mg, 0.802 mmol) was added to a solution of **4** (156.5 mg, 0.823 mmol) in DMF (3 mL), followed after 15 min by **3c**[29] (294 mg, 0.829 mmol). After a further 12 h, the reaction mixture was quenched with strd aq. $NH_4Cl$, extracted with $Et_2O$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified by CC (PE/EtOAc 9:1) to afford a yellow oil (221 mg, 74%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$=0.15 (s, 6H), 0.95 (s, 9H), 4.20–4.40 (m, 6H), 5.20 (s, 2H), 7.35–7.45 ppm (m, 5H); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta$=−7.4 ($CH_3$), 13.8 (C), 20.7 ($CH_3$), 35.8 ($CH_2$), 36.1 ($CH_2$), 53.0 ($CH_2$), 69.9 ($CH_2$), 79.5 (C), 82.3 (C), 114.9 (C), 127.3 (CH), 127.4 (CH), 128.7 (CH), 136.3 (C), 156.8 ppm (C); IR (neat): $\tilde{\nu}$=2929, 2857, 1712, 1237, 834 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{20}H_{28}N_2O_3NaSi]^+$: 395.17614; found: 395.17609.

Step g: The product obtained after step f (0.212 g, 0.564 mmol) and tetrabutyl ammonium fluoride (TBAF) (1M in THF, 0.75 mL, 0.75 mmol) were stirred in THF (10 mL) for 12 h. The reaction mixture was quenched with water, extracted with $Et_2O$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified by CC ($CH_2Cl_2$ to $CH_2Cl_2$/$Et_2O$ 4:1) to afford a yellow oil (134 mg, 92%). $R_f$=0.34 ($CH_2Cl_2$/$Et_2O$ 4:1); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=3.02 (brs, 1H), 4.21–4.23 (m, 4H), 4.27 (brs, 2H), 5.16 (s, 2H), 7.31–7.35 ppm (m, 5H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=34.5/34.8 ($CH_2$), 37.2/37.3 ($CH_2$), 50.8 ($CH_2$), 68.7 ($CH_2$), 78.4 (C), 84.6 (C), 115.6 (C), 128.3 (CH), 128.6 (CH), 128.7 (CH), 135.4 (C), 154.4/154.8 ppm (C); IR (neat): $\tilde{\nu}$=3064, 3032, 2924, 2865, 2252, 1701, 1497, 1450, 1014 cm$^{-1}$.

**6c**: Compound **5c** (1.36 g, 5.27 mmol) in THF (20 mL) and $PPh_3$ (1.66 g, 6.32 mmol) were successively added to a solution of TsNHBoc (1.74 g, 6.41 mmol) in THF (30 mL) under Ar at 0°C, followed by the dropwise addition over 3 h of DIAD (1.28 g, 6.32 mmol) in THF (7 mL) with a syringe pump. After 7 h, $SiO_2$ was added and the solvent removed under reduced pressure. Purification by two successive CC (PE/$CH_2Cl_2$ 2:8 to pure $CH_2Cl_2$) afforded a colorless oil (2.35 g, 82%). $R_f$=0.28 ($CH_2Cl_2$); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=1.35 (s, 9H), 2.45 (s, 3H), 4.33 (brs, 4H), 4.66 (t, $J$=1.6 Hz, 2H), 5.22 (s, 2H), 7.25–7.35 (m, 7H), 7.86 ppm (d, $J$=7.3 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=21.7 ($CH_3$), 27.8 ($CH_3$), 33.8/34.1 ($CH_2$), 35.8 ($CH_2$), 36.5/36.7 ($CH_2$), 68.7 ($CH_2$), 77.2 (C), 81.5/81.8 (C), 85.2 (C), 115.1 (C), 128.0 (CH), 128.2 (CH), 128.6 (CH), 128.7 (CH), 129.3 (CH), 135.3 (C), 136.6 (C), 144.7 (C), 150.2 (C), 154.6 ppm (C); IR (neat): $\tilde{\nu}$=3066, 3033, 2982, 2935, 1716, 1356, 1147 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{26}H_{29}N_3O_6NaS]^+$: 534.16693; found: 534.16646.

**1c**: Step i: A solution of **6c** (2.35 g, 4.59 mmol) in $CH_2Cl_2$ (20 mL) and freshly distilled TFA (1.06 mL, 13.8 mmol) was microwaved at 100°C for 20 min. The reaction mixture was then quenched with strd aq. $NaHCO_3$, extracted with $CH_2Cl_2$, washed with brine, dried over $MgSO_4$, filtered, concentrated under reduced pressure and purified by CC ($CH_2Cl_2$ to $CH_2Cl_2$/$Et_2O$ 95:5) to afford a yellow oil (1.31 g, 69%). $R_f$=0.47 ($CH_2Cl_2$/$Et_2O$ 9:1); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=2.38 (s, 3H), 3.79/3.80 (2s, 2H), 3.99 (brs, 2H), 4.11 (brs, 2H), 5.15 (s, 2H), 5.54 (brs, 1H), 7.25–7.36 (m, 7H), 7.75 ppm (d, $J$=8.0 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=21.5 ($CH_3$), 32.9 ($CH_2$), 34.2/34.5 ($CH_2$), 36.8 ($CH_2$), 68.7 ($CH_2$), 77.7 (C), 80.5 (C), 115.5 (C), 127.4 (CH), 128.2 (CH), 128.6 (CH), 128.7 (CH), 129.7 (CH), 135.3 (C), 136.6 (C), 143.9 (C), 154.1/154.6 ppm (C); IR (neat): $\tilde{\nu}$=3263, 3090, 3064, 2982, 2957, 2926, 2871, 2253, 1705, 1328, 1156 cm$^{-1}$.

Step j: KHMDS (227 mg, 1.080 mmol) was added under vigorous stirring to a solution of the product obtained after step i (0.444 g, 1.080 mmol) in toluene (20 mL) under Ar in a Schlenk tube. After 5 min, iodonium salt **7** (0.585 g, 1.300 mmol) was added and the reaction warmed to 40°C (bath temperature) for 1 h. $SiO_2$ was added and the solvent was removed under reduced pressure. CC of the crude material ($CH_2Cl_2$ to $CH_2Cl_2$/$Et_2O$ 9:1) afforded **1c** as a yellow oil (186 mg, 34%). $R_f$=0.55 ($CH_2Cl_2$); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.18 (s, 9H), 2.46 (s, 3H), 4.14 (brs, 4H), 4.26 (t, $J$=1.9 Hz, 2H), 5.20 (s, 2H), 7.30–7.45 (m, 7H), 7.81 ppm (d, $J$=7.8 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=0.0 ($CH_3$), 21.7 ($CH_3$), 33.7/33.8 ($CH_2$), 36.2/36.4 ($CH_2$), 41.7 ($CH_2$), 68.7 ($CH_2$), 74.2 (C), 78.4/78.5 (C), 79.1/79.3 (C), 94.2 (C), 114.9 (C), 128.2 (CH), 128.6 (CH), 128.7 (CH), 129.5 (CH), 133.9 (C), 135.2 (C), 145.3 (C), 154.0/154.3 ppm (C), one $CH_{arom}$ hidden; IR (neat): $\tilde{\nu}$=3034, 2958, 2169, 1712, 1367, 1169, 841 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{26}H_{29}N_3O_4NaSSi]^+$: 530.15402; found: 530.15363.

**2c**: Method A: Compound **1c** (30 mg, 0.059 mmol) in xylenes (0.8 mL) was added to $[CpCo(C_2H_4)_2]$ (1.90 mg, 0.014 mmol) under Ar in a Schlenk tube. After 3 h (TLC monitoring), $[CpCo(C_2H_4)_2]$ was added (0.60 mg, 0.003 mmol). After a further 3 h, the reaction mixture was poured onto silica and eluted (PE/$Et_2O$ 3:7) to afford a white solid (17 mg, 50%). Method B: $[CpCo(CO)_2]$ (17 μL, 0.014 mmol) was added to a refluxing solution of **1c** (139 mg, 0.274 mmol) in degassed xylenes (5.5 mL), and the reaction irradiated (visible light, halogen lamp, 150 W) for 30 min. Some $[CpCo(CO)_2]$ (18 μL, 0.014 mmol) was then added and the reaction irradiated while refluxing for 30 min, after which $SiO_2$ was added and the solvent removed under reduced pressure. Two successive CC (PE/$CH_2Cl_2$/$Et_2O$ 5:3:2) of the crude material gave a white solid (76 mg, 55%). $R_f$=0.25 (PE/$CH_2Cl_2$/$Et_2O$ 5:3:2); m.p. 79.3°C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.50/0.51 (2s, 9H), 2.39/2.40 (2s, 3H), 4.57 (s, 2H), 4.66/4.70 (m, 4H), 5.18/5.21 (2s, 2H), 7.22/7.25 (2d, $J$=8.1 Hz, 2H), 7.30–7.43 (m, 5H), 7.60/7.63 ppm (2d, $J$=8.1 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=0.0 ($CH_3$), 22.8 ($CH_3$), 49.7/50.0 ($CH_2$), 53.7/54.0 ($CH_2$), 62.0/62.1 ($CH_2$), 68.4 ($CH_2$), 124.4/124.6 (C), 129.1 (CH), 129.2 (CH), 129.3 (CH), 129.7 (CH), 131.0 (CH), 132.7 (C), 134.2/134.4 (C), 137.6 (C), 146.1 (C), 153.3 (C), 155.3 (C), 155.7/156.0 (C), 156.1/156.4 ppm (C); IR (neat): $\tilde{\nu}$=2923, 2871, 1706, 1358, 1167, 845 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{26}H_{30}O_4N_3SSi]^+$: 508.17208; found: 508.17135.

**10d**: $PPh_3$ (0.559 g, 2.28 mmol) and TsNHBoc (0.585 g, 2.28 mmol) were successively added to a solution of **9d**[30] (0.487 g, 2.28 mmol) in THF (11 mL) under Ar at 0°C, followed by the dropwise addition over 1 h of DIAD (0.45 mL, 2.28 mmol) with a syringe pump. After 3 h, $SiO_2$ was added and the solvent removed under reduced pressure. Purification by CC (cyclohexane/EtOAc 85:5) afforded a colorless oil (0.72 g, 68%). $R_f$=0.65 (cyclohexane/EtOAc 3:2); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=1.33 (s, 9H), 1.49–1.56 (m, 4H), 1.76–1.81 (m, 4H), 1.93 (quint, $J$=7.0 Hz, 2H), 2.20–2.28 (m, 4H), 2.44 (s, 3H), 3.47–3.52 (m, 2H), 3.78–3.90 (m, 4H), 4.60 (brs, 1H), 7.30 (d, $J$=8.0 Hz, 2H), 7.78 ppm (d, $J$=8.0 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=15.6 ($CH_2$), 16.3 ($CH_2$), 19.5 ($CH_2$), 21.5 ($CH_3$), 25.4 ($CH_2$), 27.8 ($CH_3$), 29.1 ($CH_2$), 29.4 ($CH_2$), 30.6 ($CH_2$), 46.4 ($CH_2$), 62.1 ($CH_2$), 66.0 ($CH_2$), 79.0 (C), 80.4 (C), 84.3 (C), 98.8 (CH), 127.9 (CH), 129.4 (CH), 137.5 (C), 144.2 (C), 151.0 ppm (C); IR (neat): $\tilde{\nu}$=2938, 1724, 1353, 1154 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{25}H_{39}NO_6NaS]^+$: 504.2396; found: 504.2409.

**11d**: Step f: Compound **10d** (0.716 g, 1.53 mmol) and PTSA·$H_2O$ (3.0 mg, 0.016 mmol) were stirred in MeOH (3 mL) for 12 h. The reaction mixture was quenched with strd aq. $NaHCO_3$, extracted with $CH_2Cl_2$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford a colorless oil (0.42 g, 70%). $^1$H NMR (200 MHz, $CDCl_3$): $\delta$=1.32 (s, 9H), 1.73 (quint, $J$=6.3 Hz, 2H), 1.89–1.96 (m, 2H), 2.20–2.31 (m, 4H), 2.43 (s, 3H), 3.77 (t, $J$=6.0 Hz, 2H), 3.90 (t, $J$=7.4 Hz, 2H), 7.29 (d, $J$=8.3 Hz, 2H), 7.76 ppm (d, $J$=8.3 Hz, 2H), OH unobserved; $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta$=15.4 ($CH_2$), 16.4 ($CH_2$), 21.8 ($CH_3$), 28.0 ($CH_3$), 29.5 ($CH_2$), 31.4 ($CH_2$), 46.5 ($CH_2$), 61.8 ($CH_2$), 79.6 (C), 80.3 (C), 84.4 (C), 127.9 (CH), 129.4 (CH), 137.3 (C), 144.3 (C), 151.0 ppm (C); IR (neat): $\tilde{\nu}$=3440, 2934, 1726, 1351, 1351, 1154, 1153 cm$^{-1}$.

Step g: MsCl (0.170 mL, 2.199 mmol) was added dropwise to a solution of the product obtained after step f (0.420 g, 1.099 mmol) and $Et_3N$ (0.306 mL, 2.199 mmol) in $CH_2Cl_2$ (6 mL) at 0 °C. 12 h after warming to room temperature, the reaction mixture was quenched with strd aq. $NaHCO_3$, extracted with $CH_2Cl_2$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford, after purification by CC (PE/EtOAc 3:2), a colorless oil (0.492 g, 94%). $^1$H NMR (400 MHz, $CDCl_3$): $\delta=1.32$ (s, 9H), 1.91–1.95 (m, 4H), 2.24 (tt, $J=7.0$, 2.3 Hz, 2H), 2.33 (tt, $J=6.7$, 2.4 Hz, 2H), 2.44 (s, 3H), 3.02 (s, 3H), 3.90 (t, $J=7.6$ Hz, 2H), 4.37 (t, $J=6.1$ Hz, 2H), 7.30 (d, $J=8.0$ Hz, 2H), 7.76 ppm (d, $J=8.0$ Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta=15.1$ ($CH_2$), 16.4 ($CH_2$), 21.8 ($CH_3$), 28.0 ($CH_3$), 28.4 ($CH_2$), 29.4 ($CH_2$), 37.3 ($CH_3$), 46.5 ($CH_2$), 68.9 ($CH_2$), 78.7 (C), 80.4 (C), 84.4 (C), 127.9 (CH), 129.4 (CH), 137.5 (C), 144.3 (C), 151.0 ppm (C); IR (neat): $\tilde{\nu}=2936$, 1724, 1349, 1153 cm$^{-1}$.

Step h: NaCN (0.287 g, 5.870 mmol) was added to the product obtained after step g (0.447 g, 0.978 mmol) in DMF (10 mL). The mixture was warmed to 80 °C for 24 h, diluted with $Et_2O$ and washed with water, brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude material by CC (PE/EtOAc 9:1) afforded **11d** as a yellow oil (0.283 g, 80%). $R_f=0.35$ (PE/EtOAc 9:1); $^1$H NMR (400 MHz, $CDCl_3$): $\delta=1.63$ (q, $J=7.0$ Hz, 2H), 1.77 (q, $J=7.0$ Hz, 2H), 2.18 (tt, $J=7.0$, 2.3 Hz, 2H), 2.27 (tt, $J=7.0$, 2.3 Hz, 2H), 2.41 (s, 3H), 2.43 (t, $J=7.0$ Hz, 2H), 3.01 (q, $J=6.4$ Hz, 2H), 4.93 (t, $J=6.4$ Hz, 1H), 7.30 (d, $J=8.0$ Hz, 2H), 7.73 ppm (d, $J=8.0$ Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta=16.0$ ($CH_2$), 16.2 ($CH_2$), 17.9 ($CH_2$), 21.6 ($CH_3$), 24.7 ($CH_2$), 28.5 ($CH_2$), 42.3 ($CH_2$), 78.6 (C), 80.7 (C), 119.5 (C), 127.2 (CH), 129.8 (CH), 137.0 (C), 143.5 ppm (C); IR (neat): $\tilde{\nu}=3268$, 2933, 1662, 1323, 1155 cm$^{-1}$.

**1d**: KHMDS (0.5 M in toluene, 720 μL, 362 mmol) was added under vigorous stirring to a solution of **11d** (0.100 g, 0.323 mmol) in toluene under Ar in a Schlenk tube. After 10 min, iodonium salt **7** (0.185 g, 0.411 mmol) was added and the reaction mixture heated at 80 °C (bath temperature) for 24 h. $SiO_2$ was added and the solvent was removed under reduced pressure. CC of the crude material (PE/EtOAc 8:2) afforded a yellow oil (60 mg, 45%). $R_f=0.60$ (PE/EtOAc 3:2); $^1$H NMR (200 MHz, $CDCl_3$): $\delta=0.15$ (s, 9H), 1.76–1.87 (m, 4H), 2.18–2.37 (m, 4H), 2.45 (s, 3H), 2.48–2.57 (m, 2H), 3.39 (t, $J=7.0$ Hz, 2H), 7.34 (d, $J=8.0$ Hz, 2H), 7.78 ppm (d, $J=8.0$ Hz, 2H); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta=0.2$ ($CH_3$), 15.9 ($CH_2$), 16.2 ($CH_2$), 18.0 ($CH_2$), 21.8 ($CH_3$), 24.9 ($CH_2$), 27.1 ($CH_2$), 50.3 ($CH_2$), 73.5 (C), 77.7 (C), 78.5 (C), 80.6 (C), 127.9 (CH), 129.7 (CH), 134.5 (C), 144.8 ppm (C), C≡N unobserved; IR (neat): $\tilde{\nu}=2982$, 2361, 1726, 1350, 1148 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{21}H_{28}N_2O_2NaSSi]^+$: 423.15330; found: 423.15384.

**2d**: Method A: Compound **1d** (30 mg, 0.075 mmol) was added to a solution of $[CpCo(C_2H_4)_2]$ (0.72 mg, 0.004 mmol) in THF (2 mL) under Ar in a Schlenk tube. After 1 h (TLC monitoring), $SiO_2$ was added and the solvent was removed under reduced pressure. CC of the crude material (PE/EtOAc 4:1) afforded a white solid (30 mg, 100%). $R_f=0.40$ (PE/EtOAc 8:2); $^1$H NMR (400 MHz, $CDCl_3$): $\delta=0.44$ (s, 9H), 1.14–1.22 (m, 1H), 1.40–1.50 (m, 1H), 1.68–1.77 (m, 1H), 2.10–2.25 (m, 3H), 2.42 (s, 3H), 2.69 (t, $J=7.5$ Hz, 2H), 3.06–3.11 (m, 2H), 3.37–3.44 (m, 1H), 4.06–4.13 (m, 1H), 7.18 (d, $J=8.0$ Hz, 2H), 7.20 ppm (d, $J=8.0$ Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta=0.5$ ($CH_3$), 21.5 ($CH_2$), 21.7 ($CH_2$), 22.3 ($CH_2$), 23.1 ($CH_2$), 28.6 ($CH_3$), 34.5 ($CH_2$), 45.4 ($CH_2$), 127.8 (CH), 129.6 (CH), 133.4 (C), 136.7 (C), 136.8 (C), 139.0 (C), 143.7 (C), 163.5 (C), 165.5 ppm (C); IR (neat): $\tilde{\nu}=2954$, 2360, 1160, 838 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{21}H_{29}N_2O_2SSi]^+$: 401.17135; found: 401.17156.

**9e**: $^1$H NMR (200 MHz, $CDCl_3$): $\delta=1.19$ (t, $J=7.0$ Hz, 3H), 1.31 (d, $J=5.0$ Hz, 3H), 1.54–1.59 (m, 2H), 1.63–1.70 (m, 2H), 1.72 (quint, $J=7.0$ Hz, 2H, and OH), 2.16 (tt, $J=7.0$, 2.5 Hz, 2H), 2.26 (tt, $J=7.0$, 2.5 Hz, 2H), 3.40–3.48 (m, 2H), 3.53–3.63 (m, 2H), 3.74 (t, $J=6.0$ Hz, 2H), 4.66 ppm (q, $J=5.0$ Hz, H); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta=15.4$ ($CH_3$), 15.5 ($CH_2$), 18.7 ($CH_2$), 20.0 ($CH_3$), 25.9 ($CH_2$), 29.2 ($CH_2$), 31.7 ($CH_2$), 60.8 ($CH_2$), 62.1 ($CH_2$), 64.8 ($CH_2$), 79.8 (C), 80.8 (C), 99.7 ppm (CH); IR (neat): $\tilde{\nu}=3380$, 2930, 2350 cm$^{-1}$.

**10e**: $PPh_3$ (0.557 g, 2.13 mmol) and TsNHBoc (0.576 g, 2.13 mmol) were successively added to a solution of **9e** (0.485 g, 2.13 mmol) in THF (10 mL) under Ar at 0 °C, followed by the dropwise addition over 1 h of DIAD (0.52 mL, 2.13 mmol) with a syringe pump. After 2 h, $SiO_2$ was added and the solvent removed under reduced pressure. Purification by CC (PE/EtOAc 9:1) afforded a colorless oil (0.77 g, 76%). $R_f=0.62$ (PE/EtOAc 9:1); $^1$H NMR (200 MHz, $CDCl_3$): $\delta=1.18$ (t, $J=7.0$ Hz, 3H), 1.29 (d, $J=5.0$ Hz, 3H), 1.33 (s, 9H), 1.51–1.75 (m, 4H), 1.91 (t, $J=7.5$ Hz, 2H), 2.15–2.24 (m, 4H), 2.43 (s, 3H), 3.41–3.70 (m, 4H), 3.87 (t, $J=7.5$ Hz, 2H), 4.66 (q, $J=5.0$ Hz, 1H), 7.28 (d, $J=8.0$ Hz, 2H), 7.77 ppm (d, $J=8.0$ Hz, 2H); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta=14.3$ ($CH_2$), 15.5 ($CH_2$), 16.5 ($CH_2$), 20.0 ($CH_3$), 21.8 ($CH_3$), 25.9 ($CH_3$), 28.0 ($CH_2$), 29.2 ($CH_3$), 29.6 ($CH_2$), 46.6 ($CH_2$), 60.9 ($CH_2$), 64.8 ($CH_2$), 78.0 (C), 80.7 (C), 84.6 (C), 99.6 (CH), 128.0 (CH), 129.4 (CH), 137.4 (C), 144.2 (C), 151.0 ppm (C); IR (neat): $\tilde{\nu}=2978$, 1726, 1354, 1154 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{25}H_{39}NO_6NaS]^+$: 504.2396; found: 504.2409.

**11e**: Step f: Compound **10e** (0.775 g, 1.611 mmol) and PTSA·$H_2O$ (3.0 mg, 0.016 mmol) were stirred in MeOH (4 mL) for 12 h. The reaction mixture was quenched with strd aq. $NaHCO_3$, extracted with $CH_2Cl_2$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford a pale yellow oil (0.60 g, 91%). $R_f=0.23$ (cyclohexane/EtOAc 7:3); $^1$H NMR (200 MHz, $CDCl_3$): $\delta=1.33$ (s, 9H), 1.55–1.60 (m, 3H), 1.68–1.75 (m, 2H), 1.93 (quint, $J=7.0$ Hz, 2H), 2.18–2.26 (m, 4H), 2.43 (s, 3H), 3.66 (t, $J=6.6$ Hz, 2H), 3.91 (t, $J=7.7$ Hz, 2H), 7.29 (d, $J=8.1$, Hz, 2H), 7.76 ppm (d, $J=8.1$ Hz, 2H); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta=16.5$ ($CH_2$), 18.7 ($CH_2$), 21.8 ($CH_3$), 25.3 ($CH_2$), 28.0 ($CH_3$), 29.5 ($CH_2$), 32.0 ($CH_2$), 46.7 ($CH_2$), 62.7 ($CH_2$), 79.2 (C), 80.8 (C), 84.4 (C), 127.9 (CH), 129.4 (CH), 137.5 (C), 144.3 (C), 151.1 ppm (C); IR (neat): $\tilde{\nu}=3389$, 2934, 1724, 1350, 1153 cm$^{-1}$.

Step g: MsCl (0.226 mL, 2.93 mmol) was added dropwise to a solution of the product obtained after step f (0.600 g, 1.47 mmol) and $Et_3N$ (0.409 mL, 2.93 mmol) in $CH_2Cl_2$ (7 mL) at 0 °C. 12 h after warming to room temperature, the reaction mixture was quenched with strd aq. $NaHCO_3$, extracted with $CH_2Cl_2$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford, after purification by CC (cyclohexane/EtOAc 85:15) a colorless oil (0.496 g, 70%). $R_f=0.52$ (cyclohexane/EtOAc 7:3); $^1$H NMR (200 MHz, $CDCl_3$): $\delta=1.32$ (s, 9H), 1.64 (br s, 2H), 1.85–1.92 (m, 4H), 2.23 (t, $J=6.0$ Hz, 4H), 2.44 (s, 3H), 2.99 (s, 3H), 3.89 (t, $J=7.6$ Hz, 2H), 4.26 (t, $J=6.3$ Hz, 2H), 7.30 (d, $J=8.4$ Hz, 2H), 7.76 ppm (d, $J=8.4$ Hz, 2H); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta=16.5$ ($CH_2$), 18.3 ($CH_2$), 21.8 ($CH_3$), 24.9 ($CH_2$), 28.0 ($CH_3$), 28.3 ($CH_2$), 29.5 ($CH_2$), 37.5 ($CH_3$), 46.6 ($CH_2$), 69.9 ($CH_2$), 79.7/79.9 (C), 106.4 (C), 114.1 (C), 127.9 (CH), 129.4 (CH), 137.5 (C), 144.3 (C), 151.0 ppm (C); IR (neat): $\tilde{\nu}=2936$, 1722, 1348, 1153, 671 cm$^{-1}$.

Step h: NaCN (0.289 g, 5.901 mmol) was added to a solution of the product obtained after step g (0.478 g, 0.984 mmol) in DMF (10 mL). The mixture was warmed to 80 °C and stirred for 24 h, diluted with $Et_2O$ and washed with water, brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude material by CC (PE/EtOAc 9:1) afforded **11e** as a yellow oil (0.250 g, 81%). $R_f=0.37$ (PE/EtOAc 9:1); $^1$H NMR (200 MHz, $CDCl_3$): $\delta=1.57$–1.63 (m, 4H), 1.71–1.76 (m, 2H), 2.16–2.19 (m, 4H), 2.37 (t, $J=7.0$ Hz, 2H), 2.42 (s, 3H), 3.05 (q, $J=6.5$ Hz, 2H), 4.70 (t, $J=6.5$ Hz, 1H), 7.32 (d, $J=8.0$ Hz, 2H), 7.73 ppm (d, $J=8.0$ Hz, 2H); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta=16.2$ ($CH_2$), 16.9 ($CH_2$), 18.0 ($CH_2$), 21.7 ($CH_3$), 24.5 ($CH_2$), 27.7 ($CH_2$), 28.6 ($CH_2$), 42.5 ($CH_2$), 79.7 (C), 80.2 (C), 119.7 (C), 127.2 (CH), 129.8 (CH), 137.0 (C), 143.5 ppm (C); IR (neat): $\tilde{\nu}=3270$, 2931, 1323, 1155 cm$^{-1}$.

**1e**: KHMDS (0.5 M in toluene, 720 μL, 0.354 mmol) was added under vigorous stirring to a solution of **11e** (0.100 g, 0.314 mmol) in toluene under Ar in a Schlenk tube. After 10 min, iodonium salt **7** (0.185 g, 0.411 mmol) was added and the reaction mixture heated at 80 °C (bath temperature) for 24 h. After TLC monitoring, $SiO_2$ was added, the solvent was removed under reduced pressure and CC of the material (PE/EtOAc 8:2) afforded a yellow oil (45 mg, 30%). $R_f=0.27$ (PE/EtOAc 8:2); $^1$H NMR (200 MHz, $CDCl_3$): $\delta=0.15$ (s, 9H), 1.60–1.66 (m, 2H), 1.75–1.80 (m, 4H), 2.10–2.25 (m, 4H), 2.34 (t, $J=7.0$ Hz, 2H), 2.45 (s, 3H), 3.45 (t, $J=6.5$ Hz, 2H), 7.31 (d, $J=8.0$ Hz, 2H), 7.76 ppm (d, $J=8.0$ Hz, 2H); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta=0.2$ ($CH_3$), 15.9 ($CH_2$), 16.9 ($CH_2$), 18.1 ($CH_2$), 21.7 ($CH_3$), 24.6 ($CH_2$), 27.3 ($CH_2$), 27.7 ($CH_2$), 50.3 ($CH_2$), 66.9 (C), 73.7 (C), 79.8 (C), 95.3 (C), 103.9 (C), 127.9 (CH), 129.7 (CH), 134.0

(C), 144.8 ppm (C); IR (neat): $\tilde{\nu}$ = 2955, 2360, 2341, 2160, 1366, 1170, 844 $cm^{-1}$; HRMS: *m/z*: calcd for $[C_{22}H_{30}N_2O_2NaSi]^+$: 437.16895; found: 437.16960.

**2e**: Method A: Compound **1e** (40 mg, 0.096 mmol) was added to a solution of $[CpCo(C_2H_4)_2]$ (0.90 mg, 0.005 mmol) in THF (2 mL) under Ar in a Schlenk tube. After 1 h, $SiO_2$ was added and the solvent removed in vacuo. CC of the material (PE/EtOAc 4:1) afforded a white solid (40 mg, 100%). $R_f$ = 0.30 (PE/EtOAc 8:2); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 0.41 (s, 9H), 1.04–1.12 (m, 1H), 1.32–1.42 (m, 1H), 1.63–1.70 (m, 1H), 1.77–1.85 (m, 4H), 2.22–2.29 (m, 1H), 2.39 (s, 3H), 2.42 (m, 2H), 2.89–3.02 (m, 2H), 3.34–3.41 (m, 1H), 4.00–4.07 (m, 1H), 7.15 (d, $J$ = 8.0 Hz, 2H), 7.28 ppm (d, $J$ = 8.0 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 0.4 ($CH_3$), 21.5 ($CH_2$), 21.9 ($CH_2$), 22.0 ($CH_2$), 23.1 ($CH_2$), 23.3 ($CH_3$), 25.7 ($CH_2$), 33.7 ($CH_2$), 45.5 ($CH_2$), 128.2 (CH), 129.9 (CH), 136.4 (C), 137.0 (C), 137.1 (C), 141.3 (C), 143.9 (C), 155.5 (C), 164.4 ppm (C); IR (neat): $\tilde{\nu}$ = 2937, 2360, 2341, 1397, 1162, 840 $cm^{-1}$; HRMS: *m/z*: calcd for $[C_{22}H_{31}N_2O_2SSi]^+$: 415.18700; found: 415.18722.

**9f**: BuLi (2.5 M in hexanes, 2.1 mL, 5.1 mmol) was added to toluene-4-sulfonic acid pent-4-ynyl ester (1.0 g, 4.2 mmol) in THF (4 mL) at −78 °C, followed after 30 min by ethylene oxide (0.63 mL, 12.6 mmol) and $BF_3{\cdot}OEt_2$ (0.63 mL, 5.1 mmol). After 2 h at −78 °C, the reaction mixture was quenched with strd aq. $NH_4Cl$, extracted with $Et_2O$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by CC (PE/EtOAc 3:2) afforded a colorless oil (0.55 g, 46%). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 1.81 (quint, $J$ = 6.3 Hz, 2H), 1.94 (br s, 1H), 2.24 (tt, $J$ = 6.8, 2.2 Hz, 2H), 2.34 (tt, $J$ = 6.2, 2.2 Hz, 2H), 2.44 (s, 3H), 3.63 (t, $J$ = 6.2 Hz, 2H), 4.14 (t, $J$ = 6.0 Hz, 2H), 7.34 (d, $J$ = 8.1 Hz, 2H), 7.78 ppm (d, $J$ = 8.1 Hz, 2H); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta$ = 15.1 ($CH_2$), 21.7 ($CH_3$), 23.2 ($CH_2$), 28.2 ($CH_2$), 61.4 ($CH_2$), 69.1 ($CH_2$), 78.2 (C), 80.0 (C), 128.0 (CH), 129.9 (CH), 133.2 (C), 144.9 ppm (C); IR (neat): $\tilde{\nu}$ = 3375, 2922, 1353, 1188, 924 $cm^{-1}$; HRMS: *m/z*: calcd for $[C_{14}H_{18}O_4NaS]^+$: 305.0824; found: 305.0817.

**10f**: $PPh_3$ (1.02 g, 3.90 mmol) and TsNHBoc (1.05 g, 3.90 mmol) were successively added to a solution of **9f** (1.10 g, 3.90 mmol) in THF (20 mL) under Ar at 0 °C, followed by the dropwise addition over 1 h of DIAD (0.65 mL, 3.90 mmol) with a syringe pump. After 3 h, $SiO_2$ was added and the solvent removed under reduced pressure. Purification by CC (PE/EtOAc 7:3) afforded a pale-yellow oil (1.1 g, 53%). $R_f$ = 0.56 (PE/EtOAc 3:2); $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ = 1.32 (s, 9H), 1.80 (quint, $J$ = 6.9 Hz, 2H), 2.11 (tt, $J$ = 6.8, 2.3 Hz, 2H), 2.35 (br s, 6H), 2.51 (tt, $J$ = 8.0, 2.0 Hz, 2H), 3.88 (t, $J$ = 7.4 Hz, 2H), 4.97 (quint, $J$ = 6.3 Hz, 2H), 7.29 (d, $J$ = 8.6 Hz, 2H), 7.35 (d, $J$ = 8.6 Hz, 2H), 7.77 (d, $J$ = 8.4 Hz, 2H), 7.79 ppm (d, $J$ = 8.4 Hz, 2H); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta$ = 15.2 ($CH_2$), 20.3 ($CH_2$), 21.8 ($CH_3$), 22.1 ($CH_3$), 28.0 ($CH_3$), 28.2 ($CH_2$), 45.8 ($CH_2$), 69.2 ($CH_2$), 70.2 (C), 80.2 (C), 84.6 (C), 127.9 (CH), 128.1 (CH), 129.4 (CH), 130.0 (CH), 133.2 (C), 137.5 (C), 144.4 (C), 144.9 (C), 150.9 ppm (C); IR (neat): $\tilde{\nu}$ = 2924, 2361, 1727, 1355, 1174, 1156 $cm^{-1}$; HRMS: *m/z*: calcd for $[C_{26}H_{33}O_7NNaS_2]^+$: 558.1596; found: 558.1597.

**11f**: NaCN (0.312 g, 4.80 mmol) was added to a solution of **10f** (0.847 g, 2.40 mmol) in DMSO (4 mL). The mixture was warmed to 80 °C for 12 h, cooled to room temperature, diluted with $Et_2O$, washed with water, brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude material by CC (PE/EtOAc 3:2) afforded a yellow oil (0.310 g, 45%). $R_f$ = 0.31 (PE/EtOAc 3:2); $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ = 1.80 (q, $J$ = 6.0 Hz, 2H), 2.25–2.37 (m, 4H), 2.43 (s, 3H), 2.46 (t, $J$ = 6.0 Hz, 2H), 3.05 (q, $J$ = 7.0 Hz, 2H), 4.81 (t, $J$ = 6.0 Hz, 1H), 7.33 (d, $J$ = 8.0 Hz, 2H), 7.74 ppm (d, $J$ = 8.0 Hz, 2H); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta$ = 16.3 ($CH_2$), 18.0 ($CH_2$), 20.2 ($CH_2$), 21.7 ($CH_3$), 24.5 ($CH_2$), 42.1 ($CH_2$), 78.3 (C), 80.0 (C), 119.4 (C), 127.2 (CH), 129.9 (CH), 137.0 (C), 143.7 ppm (C); IR (neat): $\tilde{\nu}$ = 3271, 2923, 1323, 1155 $cm^{-1}$; HRMS: *m/z*: calcd for $[C_{15}H_{18}N_2O_2NaS]^+$: 313.0987; found: 313.0971.

**1f**: Potassium carbonate (0.288 g, 2.088 mmol), 1,10-phenanthroline (0.038 g, 0.209 mmol), $CuSO_4{\cdot}5H_2O$ (0.026 g, 0.104 mmol) and 2-bromoethynyltrimethylsilane (0.203 g, 1.149 mmol) were successively added in a sealed tube to a solution of **11f** (0.303 g, 1.044 mmol) in toluene (1.0 mL). The mixture was then heated for 36 h at 60 °C (bath temperature). After filtration over a short pad of Celite and removal of the solvent under reduced pressure, a CC of the crude material (PE/EtOAc 9:1) afforded a yellow oil (70 mg, 19%). $R_f$ = 0.97 (PE/EtOAc 4:1); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 0.15 (s, 9H), 1.81 (q, $J$ = 7.0 Hz, 2H), 2.31 (tt, $J$ = 7.2, 2.3 Hz, 2H), 2.44 (s, 3H), 2.45–2.51 (m, 4H), 3.42 (t, $J$ = 7.0 Hz, 2H), 7.33 (d, $J$ = 8.0 Hz, 2H), 7.74 ppm (d, $J$ = 8.0 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 0.2 ($CH_3$), 16.2 ($CH_2$), 18.0 ($CH_2$), 18.7 ($CH_2$), 21.8 ($CH_3$), 24.7 ($CH_2$), 50.4 ($CH_2$), 73.8 (C), 77.9 (C), 79.9 (C), 94.5 (C), 119.5 (C), 127.9 (CH), 129.8 (CH), 134.5 (C), 144.9 ppm (C); IR (neat): $\tilde{\nu}$ = 2958, 2361, 2158, 1368, 1170, 844 $cm^{-1}$.

**2f**: Method A: Compound **1f** (30 mg, 0.078 mmol) was added to a solution of $[CpCo(C_2H_4)_2]$ (0.70 mg, 0.004 mmol) in THF (2 mL) under Ar in a Schlenk tube. After 1 h (TLC monitoring), $SiO_2$ was added and the solvent was removed under reduced pressure. CC of the crude material (PE/EtOAc 4:1) afforded a white solid (30 mg, 90%). $R_f$ = 0.90 (PE/EtOAc 4:1); m.p. 158.3 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 0.44 (s, 9H), 1.92 (t, $J$ = 7.5 Hz, 2H), 2.09 (q, $J$ = 7.5 Hz, 2H), 2.38 (s, 3H), 2.60 (t, $J$ = 7.5 Hz, 2H), 3.02 (t, $J$ = 7.5 Hz, 2H), 3.89 (t, $J$ = 7.5 Hz, 2H), 7.33 (d, $J$ = 8.0 Hz, 2H), 7.74 ppm (d, $J$ = 8.0 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 0.1 ($CH_3$), 21.7 ($CH_3$), 23.5 ($CH_2$), 26.7 ($CH_2$), 29.1 ($CH_2$), 34.3 ($CH_2$), 51.4 ($CH_2$), 128.0 (CH), 129.5 (CH), 132.1 (C), 134.2 (C), 140.0 (C), 143.8 (C), 144.2 (C), 158.1 (C), 164.2 ppm (C); IR (neat): $\tilde{\nu}$ = 2954, 1382, 1164 $cm^{-1}$; HRMS: *m/z*: calcd for $[C_{20}H_{27}N_2O_2SSi]^+$: 387.15570; found: 387.15529.

**3g**: A mixture of chloroacetonitrile (3.2 mL, 50.0 mmol) and malonic acid dimethyl ester (6.61 g, 50.0 mmol) in THF (50 mL) was added dropwise to a suspension of NaH (60 wt% in oil, 2.01 g, 50.0 mmol) in THF (50 mL) at 0 °C. 2 h after warming to room temperature, the mixture was diluted with $Et_2O$, quenched with strd aq. $NH_4Cl$, extracted with $CH_2Cl_2$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified by distillation under reduced pressure (110 °C, $8.10^{-2}$ Torr) to afford a colorless oil (3.63 g, 42%). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 2.92 (d, $J$ = 6.9 Hz, 2H), 3.74 (t, $J$ = 7.2 Hz, 1H), 3.81 ppm (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 17.1 ($CH_2$), 47.9 (CH), 53.6 ($CH_3$), 116.7 (C), 166.9 ppm (C); IR (neat): $\tilde{\nu}$ = 2959, 2922, 2196, 1736, 1217 $cm^{-1}$; HRMS: *m/z*: calcd for $[C_7H_9NO_4Na]^+$: 194.04238; found: 194.04200.

**5g**: Step a: A mixture of **3g** (3.57 g, 20.86 mmol) and toluene-4-sulfonic acid 6-(tetrahydro-pyran-2-yloxy)-hex-2-ynyl ester (8.0 g, 22.70 mmol) in THF (30 mL) was added dropwise to a suspension of NaH (60 wt% in oil, 0.875 g, 21.87 mmol) in THF (30 mL) at 0 °C. 2 h after warming to room temperature, the mixture was diluted with $Et_2O$, quenched with strd aq. $NH_4Cl$, extracted with $Et_2O$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified by CC (PE/EtOAc 9:1) to afford a colorless oil (2.91 g, 39%). $R_f$ = 0.05 (PE/EtOAc 9:1); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 1.51–1.79 (m, 8H), 2.23 (tt, $J$ = 7.0, 2.4 Hz, 2H), 2.94 (s, 2H), 3.10 (s, 2H), 3.37–3.51 (m, 2H), 3.72–3.85 (m, 8H), 4.55 ppm (br s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 15.3 ($CH_2$), 19.4 ($CH_2$), 21.6 ($CH_2$), 23.8 ($CH_2$), 25.3 ($CH_2$), 28.7 ($CH_2$), 30.5 ($CH_2$), 53.4 ($CH_3$), 55.0 (C), 61.9 ($CH_2$), 65.5 ($CH_2$), 72.7 (C), 84.5 (C), 98.6 (CH), 115.9 (C), 167.8 ppm (C); IR (neat): $\tilde{\nu}$ = 2946, 2249, 1739, 1436, 1203, 1032 $cm^{-1}$; HRMS: *m/z*: calcd for $[C_{18}H_{25}NO_6Na]^+$: 374.15741; found: 374.15709.

Step b: The product obtained after step a (1.51 g, 4.30 mmol) and $PTSA{\cdot}H_2O$ (0.030 g, 0.16 mmol) were stirred in MeOH (110 mL) for 5 h. The reaction mixture was quenched with water, extracted with $Et_2O$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford **5g** as a colorless oil (0.93 g, 81%). $R_f$ = 0.08 (PE/$Et_2O$ 1:1); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 1.69 (m, 3H), 2.25 (tt, $J$ = 6.9, 2.4 Hz, 2H), 2.96 (t, $J$ = 2.3 Hz, 2H), 3.11 (s, 2H), 3.68 (t, $J$ = 6.1 Hz, 2H), 3.79 ppm (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 15.3 ($CH_2$), 22.0 ($CH_2$), 24.1 ($CH_2$), 31.4 ($CH_2$), 53.8 ($CH_3$), 55.3 (C), 61.5 ($CH_2$), 73.3 (C), 84.8 (C), 116.2 (C), 168.1 ppm (C); IR (neat): $\tilde{\nu}$ = 3402, 2955, 1736, 1436, 1210, 1057 $cm^{-1}$; HRMS: *m/z*: calcd for $[C_{13}H_{17}NO_5Na]^+$: 290.09989; found: 290.09958.

**6g**: Compound **5g** (0.905 g, 3.38 mmol) in THF (4 mL) and $PPh_3$ (0.933 g, 3.56 mmol) were successively added to a solution of TsNHBoc (0.922 g, 3.40 mmol) in THF (30 mL) under Ar at 0 °C, followed by the dropwise addition over 3 h of DIAD (0.70 mL, 3.55 mmol) in THF

(6 mL) with a syringe pump. After 2 h, $SiO_2$ was added and the solvent removed under reduced pressure. Purification by CC ($PE/CH_2Cl_2$ 2:8 to $CH_2Cl_2/Et_2O$ 95:5) afforded a colorless oil containing **6g** admixed with TsNHBoc which was removed by washing with 1 M aq. NaOH to give a colorless oil (0.736 g, 42%). $R_f$=0.41 ($CH_2Cl_2$); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=1.28 (s, 9H), 1.86 (q, $J$=7.0 Hz, 2H), 2.19 (t, $J$=6.8 Hz, 2H), 2.38 (s, 3H), 2.93 (s, 2H), 3.14 (s, 2H), 3.75 (s, 6H), 3.82 (t, $J$=7.4 Hz, 2H), 7.26 (d, $J$=8.2 Hz, 2H), 7.73 ppm (d, $J$=8.2 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=16.0 ($CH_2$), 21.4 ($CH_3$), 21.7 ($CH_2$), 23.9 ($CH_2$), 27.7 ($CH_3$), 28.9 ($CH_2$), 46.1 ($CH_2$), 53.5 ($CH_3$), 55.1 (C), 73.4 (C), 83.7 (C), 84.1 (C), 116.1 (C), 127.6 (CH), 129.2 (CH), 137.2 (C), 144.1 (C), 150.7 (C), 167.9 ppm (C); IR (neat): $\tilde{\nu}$=2958, 1742, 1356, 1288, 1157 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{25}H_{32}N_2O_8NaS]^+$: 543.17716; found: 543.17646.

**1g**: Step d: A solution of **6g** (0.695 g, 1.33 mmol) in $CH_2Cl_2$ (5 mL) and freshly distilled TFA (100 µL, 1.35 mmol) was microwaved at 110 °C for 2 h. The reaction mixture was quenched with water, extracted with $CH_2Cl_2$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford, after purification by CC ($CH_2Cl_2$ to $CH_2Cl_2/Et_2O$ 95:5), a colorless oil (0.447 g, 80%). $R_f$=0.20 ($CH_2Cl_2/Et_2O$ 95:5); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=1.59 (q, $J$=6.8 Hz, 2H), 2.15 (tt, $J$=6.8, 2.2 Hz, 2H), 2.40 (s, 3H), 2.90 (t, $J$=2.2 Hz, 2H), 2.95 (q, $J$=6.7 Hz, 2H), 3.06 (s, 2H), 3.76 (s, 6H), 5.18 (t, $J$=6.2 Hz, 1H), 7.29 (d, $J$=8.3 Hz, 2H), 7.73 ppm (d, $J$=8.3 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=15.7 ($CH_2$), 21.4 ($CH_3$), 21.8 ($CH_2$), 23.9 ($CH_2$), 28.4 ($CH_2$), 41.9 ($CH_2$), 53.6 ($CH_3$), 55.1 (C), 73.6 (C), 83.8 (C), 116.2 (C), 127.0 (CH), 129.7 (CH), 136.9 (C), 143.4 (C), 168.0 ppm (C); IR (neat): $\tilde{\nu}$= 3284, 1737, 1435, 1156 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{20}H_{24}N_2O_6NaS]^+$: 443.12473; found: 443.12431.

Step e: BuLi (2.4 M in hexanes, 370 µL, 0.910 mmol) was added to a solution of the product obtained after step d (0.376 g, 0.894 mmol) in THF (15 mL) at −78 °C under Ar in a Schlenk tube. After warming to room temperature the yellow solution was concentrated under reduced pressure to give a solid directly diluted with toluene (15 mL). Iodonium salt **7** (0.460 g, 1.020 mmol) was added in portions over 5 min. After a further 2 h, $SiO_2$ was added and the solvent removed under reduced pressure. CC of the crude material ($PE/Et_2O$ 3:2) afforded a yellow oil (167 mg, 36%). $R_f$=0.51 ($PE/Et_2O$ 3:2); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.11 (s, 9H), 1.74 (q, $J$=6.8 Hz, 2H), 2.17 (tt, $J$=6.8, 2.2 Hz, 2H), 2.41 (s, 3H), 2.93 (t, $J$=2.6 Hz, 2H), 3.11 (s, 2H), 3.32 (t, $J$=6.8 Hz, 2H), 3.76 (s, 6H), 7.31 (d, $J$=8.2 Hz, 2H), 7.75 ppm (d, $J$=8.2 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=0.0 ($CH_3$), 15.6 ($CH_2$), 21.6 ($CH_3$), 21.8 ($CH_2$), 23.9 ($CH_2$), 26.9 ($CH_2$), 49.9 ($CH_2$), 53.6 ($CH_3$), 55.1 (C), 73.3 (C), 73.7 (C), 83.5 (C), 94.8 (C), 116.1 (C), 127.7 (CH), 129.7 (CH), 134.2 (C), 144.7 (C), 167.9 ppm (C); IR (neat): $\tilde{\nu}$=2956, 2157, 1740, 1168, 841 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{25}H_{32}N_2O_6NaSSi]^+$: 539.16426; found: 539.16333.

**2g**: Method A: Compound **1g** (145 mg, 0.280 mmol) in THF (1 mL) was added to $[CpCo(C_2H_4)_2]$ (5.1 mg, 0.028 mmol) under Ar in a Schlenk tube. After 12 h (TLC monitoring), some $[CpCo(C_2H_4)_2]$ was added (4.6 mg, 0.025 mmol). After a further 2 h, $SiO_2$ was added and the solvent removed under reduced pressure. Two successive CC of the mixture ($PE/Et_2O$ 1:1) afforded a white solid (110 mg, 76%). $R_f$=0.29 ($PE/Et_2O$ 1:1); m.p. 173.3 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.42 (s, 9H), 1.17–1.27 (m, 2H), 1.39–1.50 (m, 1H), 1.65–1.75 (m, 1H), 2.15–2.22 (m, 1H), 2.42 (s, 3H), 3.25/3.29 (2s, 1H), 3.37–3.41 (m, 2H), 3.74/3.76 (2s, 1H), 3.78/3.81 (2s, 6H), 4.05–4.12 (m, 1H), 7.20 (d, $J$=8.0 Hz, 2H), 7.28 ppm (d, $J$=8.0 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=0.4 ($CH_3$), 21.1 ($CH_2$), 21.7 ($CH_3$), 22.2 ($CH_2$), 36.6 ($CH_2$), 42.0 ($CH_2$), 45.1 ($CH_2$), 53.2 ($CH_3$), 58.1 (C), 127.8 (CH), 129.7 (CH), 129.8 (C), 136.4 (C), 137.4 (C), 139.0 (C), 143.8 (C), 158.7 (C), 167.2 (C), 171.9 ppm (C); IR (neat): $\tilde{\nu}$=2953, 1736, 1162, 844 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{25}H_{33}N_2O_6SSi]^+$: 517.18231; found: 517.18160.

**13**: $PPh_3$ (1.2 mg, 0.0046 mmol) and CuI (8.3 mg, 0.0436 mmol) were successively added to a solution of $[PdCl_2(PPh_3)_2]$ (1.2 mg, 0.0017 mmol) in degassed DMF (0.2 mL) under Ar, followed by 4-iodoanisole (4.5 mg, 0.0192 mmol), **2g** (20.0 mg, 0.0387 mmol), and TBAF (1 M in THF, 80 µL, 0.080 mmol). The orange reaction mixture turned brown after 24 h. Removal of DMF under reduced pressure and CC of the crude material ($PE/Et_2O$ 1:1) afforded a solid that was washed with hexane to give a white solid (8.2 mg, 77%). $R_f$=0.23 ($PE/Et_2O$ 1:1); m.p. 208.0 °C (dec.); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=1.25 (brs, 1H), 1.82 (brs, 1H), 2.38 (brs, 5H), 2.58 (brs, 1H), 3.29 (brs, 1H), 3.50 (s, 2H), 3.75 (s, 4H), 3.83 (s, 6H), 4.08 (brs, 1H), 6.80 (d, $J$=7.1 Hz, 2H), 7.06 (d, $J$=7.1 Hz, 2H), 7.13 (d, $J$=7.7 Hz, 2H), 7.46 ppm (d, $J$=7.7 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=21.7 ($CH_3$), 21.8 ($CH_2$), 22.7 ($CH_2$), 36.8 ($CH_2$), 42.1 ($CH_2$), 45.3 ($CH_2$), 53.3/53.4 ($CH_3$), 55.4 ($CH_3$), 58.3 (C), 113.7 (CH), 127.7 (CH), 129.3 (CH), 129.9 (C), 130.3 (CH), 130.7 (C), 132.6 (C), 136.6 (C), 142.6 (C), 143.5 (C), 156.6 (C), 158.5 (C), 159.6 (C), 171.8/172.0 ppm (C); IR (neat): $\tilde{\nu}$=2954, 2360, 1735, 1247 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{29}H_{31}N_2O_7S]^+$: 551.18465; found: 551.18312.

**3h**: NaH (60 wt% in oil, 1.31 g, 33.10 mmol) and bromoacetonitrile (4.76 g, 39.72 mmol) were added to a solution of 6-(tetrahydro-pyran-2-yloxy)-hex-2-yn-1-ol (6.56 g, 33.10 mmol) in DMF (160 mL) at 0 °C. The mixture was warmed to room temperature. After 30 min, the mixture was diluted with $Et_2O$, quenched with strd aq. $NH_4Cl$, extracted with $Et_2O$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified by CC ($PE/Et_2O$ 1:1) to afford a colorless oil (1.17 g, 15%). $R_f$=0.45 ($PE/Et_2O$ 1:1); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=1.49–1.82 (m, 8H), 2.33 (tt, $J$=7.1, 2.1 Hz, 2H), 3.40–3.50 (m, 2H), 3.72–3.86 (m, 2H), 4.26 (s, 2H), 4.32 (s, 2H), 4.55 ppm (brs, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=15.1 ($CH_2$), 19.1 ($CH_2$), 25.0 ($CH_2$), 28.2 ($CH_2$), 30.2 ($CH_2$), 53.4 ($CH_2$), 58.2 ($CH_2$), 61.6 ($CH_2$), 65.2 ($CH_2$), 73.3 ($CH_2$), 88.5 ($CH_2$), 98.2 (CH), 115.4 ppm (C); IR (neat): $\tilde{\nu}$=2941, 2231, 1323, 1031 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{13}H_{19}NO_3Na]^+$: 260.12571; found: 260.12550.

**5h**: Compound **3h** (1.14 g, 4.82 mmol) and PTSA·$H_2O$ (0.036 g, 0.19 mmol) were stirred in MeOH (90 mL) for 5 h. The reaction mixture was quenched with water, extracted with $Et_2O$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford a pale yellow oil (0.533 g, 72%). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=1.65 (q, $J$=6.8 Hz, 2H), 2.25 (tt, $J$=7.1, 2.1 Hz, 2H), 2.96 (brs, 1H), 3.58 (t, $J$=6.1 Hz, 2H), 4.19 (t, $J$=2.2 Hz, 2H), 4.26 ppm (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=14.9 ($CH_2$), 30.8 ($CH_2$), 53.8 ($CH_2$), 58.7 ($CH_2$), 60.7 ($CH_2$), 73.5 (C), 88.9 (C), 115.7 ppm (C); IR (neat): $\tilde{\nu}$=3366, 2927, 2229, 1085 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_8H_{11}NO_2Na]^+$: 176.06820; found: 176.06797.

**6h**: Compound **5h** (0.530 g, 3.46 mmol) in THF (12 mL) and $PPh_3$ (1.00 g, 3.81 mmol) were successively added to a solution of TsNHBoc (0.988 g, 3.64 mmol) in THF (12 mL) under Ar at 0 °C, followed by the dropwise addition over 4 h of DIAD (0.768 g, 3.80 mmol) in THF (6 mL) with a syringe pump. After 12 h, $SiO_2$ was added and the solvent removed under reduced pressure. Purification by CC ($PE/CH_2Cl_2$ 2:8 to $CH_2Cl_2/Et_2O$ 95:5) afforded a colorless oil (0.46 g, 33%). $R_f$=0.35 ($CH_2Cl_2$); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=1.34 (s, 9H), 1.99 (q, $J$=7.2 Hz, 2H), 2.35 (tt, $J$=7.0, 2.2 Hz, 2H), 2.43 (s, 3H), 3.92 (t, $J$=7.3 Hz, 2H), 4.29 (s, 2H), 4.40 (s, 2H), 7.31 (d, $J$=7.9 Hz, 2H), 7.77 ppm (d, $J$=7.9 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=16.2 ($CH_2$), 21.4 ($CH_3$), 27.7 ($CH_3$), 28.7 ($CH_2$), 46.2 ($CH_2$), 53.8 ($CH_2$), 58.5 ($CH_2$), 74.1 (C), 84.2 (C), 88.2 (C), 115.8 (C), 127.6 (CH), 129.2 (CH), 137.2 (C), 144.2 (C), 150.8 ppm (C); IR (neat): $\tilde{\nu}$=2978, 1723, 1349, 1154, 1086 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{20}H_{26}N_2O_5NaS]^+$: 429.14546; found: 429.14492.

**1h**: Step c: A solution of **6h** (0.416 g, 1.02 mmol) in $CH_2Cl_2$ (5 mL) and freshly distilled TFA (76 µL, 1.02 mmol) was microwaved at 110 °C for 2 h. The reaction mixture was quenched with water, extracted with $CH_2Cl_2$, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford, after purification by CC ($CH_2Cl_2$ to $CH_2Cl_2/Et_2O$ 95:5), a yellow oil (0.24 g, 77%). $R_f$=0.55 $CH_2Cl_2/Et_2O$ 95:5); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=1.65 (q, $J$=6.8 Hz, 2H), 2.44 (tt, $J$=6.9, 2.1 Hz, 2H), 2.39 (s, 3H), 2.97 (q, $J$=6.6 Hz, 2H), 4.20 (t, $J$=2.1 Hz, 2H), 4.29 (s, 2H), 5.26 (t, $J$=6.2 Hz, 1H), 7.27 (d, $J$=7.9 Hz, 2H), 7.78 ppm (d, $J$=7.9 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=15.8 ($CH_2$), 21.4 ($CH_3$), 28.0 ($CH_2$), 41.9 ($CH_2$), 54.0 ($CH_2$), 58.7 ($CH_2$), 74.3 (C), 88.1 (C), 115.9 (C), 127.0 (CH), 129.7 (CH), 136.7 (C), 143.4 ppm; IR (neat): $\tilde{\nu}$=3278, 2925, 1322, 1154, 1086 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{15}H_{18}N_2O_3NaS]^+$: 329.09303; found: 329.09276.

Step d: BuLi (2.4 M in hexanes, 150 μL, 0.360 mmol) was added to a solution of the product obtained after step c (0.117 g, 0.382 mmol) in THF (6 mL) at −78 °C under Ar in a Schlenk tube. After warming to room temperature, the yellow solution was concentrated under reduced pressure to give a solid directly diluted with toluene (6 mL). Iodonium salt **7** (0.195 g, 0.433 mmol) was added in portions over 5 min. After a further 2 h, $SiO_2$ was added and the solvent removed under reduced pressure. CC of the crude material (PE/$Et_2O$ 4:1) afforded a yellow oil (17 mg, 11 %). $R_f$ = 0.40 (PE/$Et_2O$ 3:2); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 0.15 (s, 9H), 1.86 (q, $J$ = 6.8 Hz, 2H), 2.33 (tt, $J$ = 6.9, 2.2 Hz, 2H), 2.45 (s, 3H), 3.40 (t, $J$ = 6.8 Hz, 2H), 4.30 (t, $J$ = 2.1 Hz, 2H), 4.38 (s, 2H), 7.34 (d, $J$ = 8.3 Hz, 2H), 7.78 ppm (d, $J$ = 8.3 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 0.2 ($CH_3$), 15.9 ($CH_2$), 21.8 ($CH_3$), 26.7 ($CH_2$), 50.1 ($CH_2$), 54.0 ($CH_2$), 58.7 ($CH_2$), 73.6 (C), 74.5 (C), 88.1 (C), 94.8 (C), 115.8 (C), 127.9 (CH), 129.8 (CH), 134.3 (C), 144.9 ppm (C); IR (neat): $\tilde{\nu}$ = 3069, 2958, 2160, 1364, 1169, 844 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{20}H_{26}N_2O_3NaSSi]^+$: 425.13256; found: 425.13220.

**2h**: Method A: Compound **1h** (40 mg, 0.099 mmol) in THF (0.6 mL) was added to $[CpCo(C_2H_4)_2]$ (1.60 mg, 0.009 mmol) under Ar in a Schlenk tube. After 4 h (TLC monitoring), some $[CpCo(C_2H_4)_2]$ was added (1.1 mg, 0.006 mmol). After a further 12 h, some $[CpCo(C_2H_4)_2]$ (2.70 mg, 0.015 mmol) was added, and after 3 h, $SiO_2$ was added and the solvent removed under reduced pressure. CC of the mixture (PE/$Et_2O$ 1:1) afforded a white solid (25 mg, 62 %). $R_f$ = 0.62 (PE/$Et_2O$ 3:7); m.p. 128.2 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 0.43 (s, 9H), 1.20–1.28 (m, 1H), 1.43–1.50 (m, 1H), 1.69–1.74 (m, 1H), 2.10 (m, 1H), 2.41 (s, 3H), 3.39–3.46 (m, 1H), 4.07–4.15 (m, 1H), 4.91–4.99 (m, 2H), 5.06–5.15 (m, 2H), 7.20 (d, $J$ = 8.1 Hz, 2H), 7.32 ppm (d, $J$ = 8.1 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 0.4 ($CH_3$), 21.2 ($CH_2$), 21.7 ($CH_3$), 22.5 ($CH_2$), 45.4 ($CH_2$), 71.0 ($CH_2$), 73.5 ($CH_2$), 127.8 (CH), 128.8 (C), 129.8 (CH), 136.6 (C), 137.0 (C), 137.8 (C), 144.0 (C), 158.5 (C), 168.2 ppm (C); IR (neat): $\tilde{\nu}$ = 2949, 1353, 1161, 843 cm$^{-1}$; HRMS: $m/z$: calcd for $[C_{20}H_{27}N_2O_3SSi]^+$: 403.15062; found: 403.15024.

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