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FULL PAPER

Palladium-catalyzed highly selective intramolecular bromoamination of alkenes: Efficient synthesis of substituted pyrrolidines

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A new method has been developed for the preparation of substituted pyrrolidines by the palladium-catalyzed intramolecular bromoamination of substituted aminoalkenes. The catalytic system and reaction conditions used for this transformation have been fully optimized. Notably, this reaction exhibits excellent selectivity, affording the pyrrolidine products as single 5-exo-bromoalkylpyrrolidines in excellent yields. Furthermore, this reaction occurs at room temperature under mild conditions, reaching completion within 1 h.

KEYWORDS

bromoamination, palladium catalysis, substituted pyrrolidines

1 | INTRODUCTION

The aminohalogenation of alkenes is a direct method for obtaining compounds containing both halogen and amino functional groups.[1] In particular, vicinal amines have drawn substantial attention due to their promising application as chemotherapy agents in antitumor therapy.[2] The halogen atom in an aminohalogenation product has a high reactivity, which can be replaced by other functional groups to generate many other drug intermediates and participate in a variety of other types of reactions.[3] Several studies have been reported during the past two decades concerning the intermolecular haloamination of alkenes.[4] However, reports concerning the intramolecular haloamination of aminoalkenes, which is a powerful tool for the construction of nitrogen-containing heterocycles carrying a halogen atom vicinal to the nitrogen, are relatively scarce.[5] The substrates required for intramolecular haloamination reactions usually need to be designed and synthesized to obtain useful azacycles. Metal catalysis can potentially provide excellent regioselectivity, as well as providing a platform for the development of asymmetric transformations. For these reasons, there has been considerable interest in the development of metal-catalyzed intramolecular haloamination reactions using Fe,[6] Cu,[7] Ag[8] and Pd catalysts.[9]

Among the various methods reported for the intramolecular haloamination of aminoalkenes, palladium-catalyzed haloamination has attracted particular attention. In 2004, Chemler and co-workers[9a] reported the first intramolecular aminohalogenation reaction of sulfonamidoalkenes using a $Pd(TFA)_2$ catalyst in the presence of a copper halide additive, which served as a stoichiometric oxidant and a source of halide, and gave the desired products in high yields but only moderate regioselectivity. In the same year, Lu and co-workers[9b] reported that alkenes bearing a pendant acylsulfonamide moiety could be cyclized in the presence of a $Pd(OAc)_2$ catalyst with the same halogen source as used by Chemler and co-workers. In 2008, Michael *et al.*[9c] reported the development of an exo-selective intramolecular reaction for the aminochlorination of unsaturated amides and carbamates using $[PdCl_2(CH_3CN)_2]$ as a catalyst in the presence of *N*-chlorosuccinimide as oxidant and halogen source. In 2009, Liu and co-workers[9d] reported the endo-selective Pd-catalyzed intramolecular cyclization/aminofluorination of γ-pentenylsulfonamides for the synthesis of piperidines in the presence of $PhI(OPiv)_2$ and AgF. Liu and co-workers[9e] subsequently reported an endo-selective Pd-catalyzed aminofluorination for the synthesis of fluoro-substituted pyrrolidines from β-alkenylstyrenes.

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However, this reaction exhibited poor substrate scope, as well as poor levels of *cis*/*trans* diastereoselectivity. Despite these efforts in this area, the development of highly regio- and stereoselective methods for the intramolecular aminohalogenation of aminoalkenes still represents a considerable challenge in organic chemistry.

2 | RESULTS AND DISCUSSION

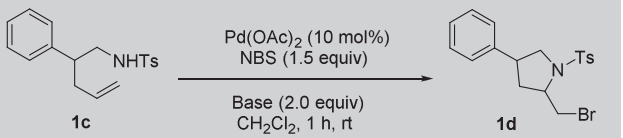
Bromoamination has attracted considerable interest following the discovery of bromine-containing compounds in the biosynthesis of halogenated marine natural products[10] and medicinal plants.[11] We conducted a series of preliminary experiments involving the bromoamination of 4-methyl-*N*-(2-phenylpent-4-en-1-yl)benzenesulfonamide (**1c**) with Pd $(OAc)_2$ and *N*-bromosuccinimide (NBS) in the presence of bases (Table 1).

Initially, the reaction was conducted without palladium and any additive. It was found that the bromoamination of **1c** could occur but with low conversion (Table 1, entry 1). Then 2 eq. of K_2CO_3 was added into the reaction, and the yield was improved obviously (entry 2). However, when the substrate was replaced by another olefin, 4-methyl-*N*-(5-methyl-2-phenylhex-4-en-1-yl)benzenesulfonamide, which has two methyl substituent groups on terminal double bond, a mixture of products was observed and the bromoamination yield was only 15% (entry 3). Then, $Pd(OAc)_2$ was introduced into this reaction, and full conversion was observed within 1 h and the isolated yield was improved to 93% (entry 4). Then other bases were investigated. The addition of KOH and KF gave similar results, but NaOH gave lower yields (entries 5–7). Organic bases such as pyridine, 2,2′-bipyridine and pyrrolidine also gave lower yields(entries 8–10).

The effects of various Pd sources and solvents on the bromoamination reaction were further investigated. As evident from Table 2, $Pd(OAc)_2$ and $Pd(TFA)_2$ both performed well as catalysts for this reaction and provided high yields of the corresponding N-heterocyclic compound **1d** (Table 2, entries 1 and 2). In contrast, $[PdCl_2(MeCN)_2]$ and $PdCl_2$ gave only moderate yields of the desired product (Table 2, entries 3 and 4). Pleasingly, $Pd(PPh_3)_2Cl_2$ gave a much higher yield than any other catalyst, giving the 5-exo-bromoalkylpyrrolidine as the sole product with an isolated yield of 98% (Table 2, entry 5). We also investigated the addition of a Pd(0) complex (Table 2, entry 6) to the reaction mixture, under the assumption that it would be oxidized to a Pd (II) species under the reaction conditions using oxygen as an oxidant. However, this reaction gave a poor yield of the desired product. $PdBF_4(MeCN)_4$ failed to catalyze the bromoamination of **1c** (Table 2, entry 7). Several solvents were also screened for this reaction, including xylene, ether, acetonitrile, $CHCl_3$ and tetrahydrofuran (THF) (Table 2, entries 8–12), but all of these solvents gave inferior results compared with CH_2Cl_2. Based on these results, the optimum conditions were determined to be 10% $Pd(PPh_3)_2Cl_2$, K_2CO_3 (2 eq.), NBS (1.5 eq.) and CH_2Cl_2.

With the optimum conditions in hand, we then synthesized a series of substituted aminoalkene substrates, which included eight unknown compounds (**4c**, **5c**, **6c**, **7c**, **8c**, **10c**, **11c**, **12c**), and their structures were confirmed using infrared (IR), ^{1}H NMR, ^{13}C NMR and high-resolution (HR)-MS spectra. These substrates, with varying nature of

TABLE 1 Effect of bases on yield[a]



1c 1d

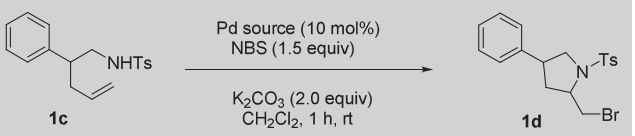
Entry	Pd (%)	Base	Time (h)	Yield (%)[b]
1	None	none	12	10
2	None	K_2CO_3	2	50
3[c]	None	K_2CO_3	2	15 (mixed products)
4	$Pd(OAc)_2$	K_2CO_3	1	93
5	$Pd(OAc)_2$	KOH	1	90
6	$Pd(OAc)_2$	KF	1	90
7	$Pd(OAc)_2$	NaOH	1	80
8	$Pd(OAc)_2$	Pyridine	1	86
9	$Pd(OAc)_2$	2,2′-Bipyridine	1	80
10	$Pd(OAc)_2$	Pyrrolidine	1	75

[a]Reaction conditions: alkene (0.05 mmol), 10 mol% catalyst, NBS (1.5 eq.) and base (2 eq.) in 1.5 ml of CH_2Cl_2.

[b]Isolated yield after chromatographic separation.

[c]With a different substrate bearing two methyl substituent groups on terminal double bond.

TABLE 2 Bromoamination of protected alkenes[a]



1c 1d

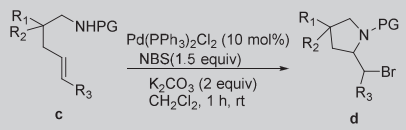
Entry	Pd source	Solvent	*T* (°C)	Yield (%)[b]
1	$Pd(OAc)_2$	CH_2Cl_2	r.t.	93
2	$Pd(TFA)_2$	CH_2Cl_2	r.t.	90
3	$PdCl_2(MeCN)_2$	CH_2Cl_2	r.t.	71
4	$PdCl_2$	CH_2Cl_2	r.t.	86
5	$Pd(PPh_3)_2Cl_2$	CH_2Cl_2	r.t.	98
6	$Pd_2(dba)_3$	CH_2Cl_2	r.t.	15
7	$PdBF_4(MeCN)_4$	CH_2Cl_2	r.t.	NR[c]
8	$Pd(PPh_3)_2Cl_2$	$CHCl_3$	r.t.	91
9	$Pd(PPh_3)_2Cl_2$	Et_2O	r.t.	82
10	$Pd(PPh_3)_2Cl_2$	THF	r.t.	81
11	$Pd(PPh_3)_2Cl_2$	MeCN	r.t.	79
12	$Pd(PPh_3)_2Cl_2$	Xylene	r.t.	82

[a]Reaction conditions: alkene (0.05 mmol), 10 mol% catalyst, NBS (1.5 eq.) and K_2CO_3 (2 eq.) in 1.5 ml of CH_2Cl_2.

[b]Isolated yield after chromatographic separation.

[c]No reaction.

TABLE 3 Scope of bromoamination reactions of alkenes[a]



Entry	Substrate	R	PG	Yield (%)[b]
1	**1c**	R_1 = Ph R_2 = H R_3 = H	Ts	98
2	**2c**	R_1 = *p*-ClPh R_2 = H R_3 = H	Ts	94
3	**3c**	R_1 = Bn R_2 = H R_3 = H	Ts	97
4	**4c**	R_1 = $BnCH_2$ R_2 = H R_3 = H	Ts	95
5	**5c**	R_1 = $BnCH_2$ R_2 = H R_3 = Ph	Ts	86
6	**6c**	R_1 = Bn R_2 = H R_3 = CH_3	Ts	80
7	**7c**	R_1 = $BnCH_2$ R_2 = H R_3 = CH_3	Ts	80
8	**8c**	R_1 = 2-thienyl R_2 = H R_3 = H	Ts	93
9	**9c**	R_1 = Ph R_2 = allyl R_3 = H	Ts	96
10	**10c**	R_1 = 2-thienyl R_2 = allyl R_3 = H	Ts	92
11	**11c**	R_1 = Bn R_2 = 2-butenyl R_3 = CH_3	Ts	90
12	**12c**	R_1 = Ph R_2 = allyl R_3 = H	Boc	NR[c]

[a]Reaction conditions: alkene (0.5 mmol), 10 mol% $Pd(PPh_3)_2Cl_2$, NBS (1.5 eq.) and K_2CO_3 (2 eq.) in 10.0 ml of CH_2Cl_2. The relative configurations of the products were determined by X-ray and NOE experiments.

[b]Isolated yield after chromatographic separation.

[c]No reaction.

substituents at the R_1, R_2 and R_3 positions, as well as the protecting group on the nitrogen atom, were evaluated under the optimized bromoamination conditions (Table 3). The results revealed that the majority of the tested substrates gave the desired products in excellent yields, also tolerating the unactivated alkenes bearing thiophene ring (Table 3, entries 1–11). Notably, all the desired products were formed as single 5-exo-diastereomers under the optimized conditions, which shows the excellent regioselectivities of the palladium catalysis. However, we also found that this methodology only worked well for substrates bearing an *N*-Ts substituent, while the corresponding *N*-Boc-containing substrates failed to give the desired cyclization products (Table 3, entry 12). With the mild conditions, fast reaction speed, high yields and high regioselectivities, this result therefore provides a good supplement for the literature of Pd-catalyzed intramolecular chloroamination of unactivated alkenes.[9c]

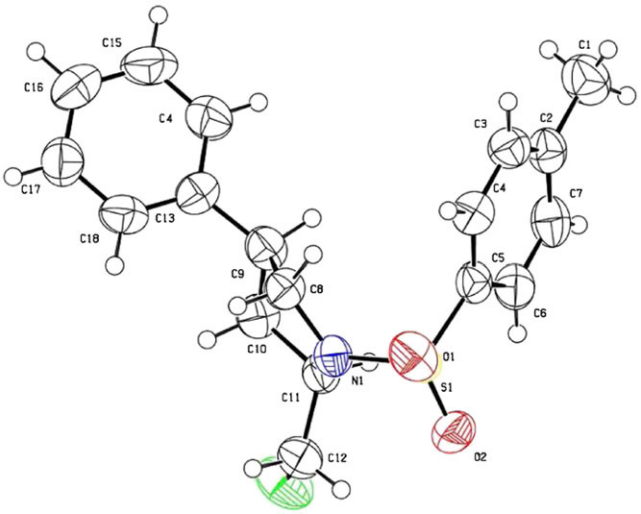


FIGURE 1 ORTEP drawing of compound **1d**

In order to confirm the relative configuration of the products, which were observed in high diastereoselectivity and regioselectivity using our catalyst system, X-ray crystallography of a single crystal of compound **1d** was conducted. As shown in the ORTEP drawing of compound **1d** (Figure 1), the five-membered nitrogen heterocyclic product has envelope conformation, C3-phenyl ring and C5-bromomethyl group is in *cis*-position, which are away from the aromatic ring of *p*-toluenesulfonyl. This configuration may reduce the steric interaction. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC 1443994).

3 | CONCLUSIONS

In summary, an efficient and highly selective palladium-catalyzed intramolecular bromoamination reaction was successfully developed for the synthesis of substituted pyrrolidines from acyclic aminoalkenes under mild conditions. This reaction occurred with excellent regioselectivity to give the 5-exo-bromoalkylpyrrolidines as single products, which provides another good example for the high selectivity of palladium catalysis. Moreover, the palladium-catalyzed process also could provide a platform for the development of an enantioselective version of this reaction, and further work including developing asymmetric catalysis and a study of the mechanism is currently underway in our laboratory.

4 | EXPERIMENTAL

4.1 | General remarks

All available reagents and solvents were used as supplied commercially and all were purchased from Aldrich, Alfa

Aesar and Acros. Analytical TLC was performed on 0.2 mm coated science silica gel (GF-254) plates purchased from Yantai, China. Visualization was accomplished with UV light (254 nm). MS were recorded with a Dionex UltiMate3000 liquid chromatograph–Bruker microTOF-QII mass spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded with Varian Mercury 300 MHz or Varian Unity 400 MHz spectrometers, and $CDCl_3$ was purchased from Aldrich. Flash column chromatography was performed on silica gel 60 (particle size 200–300 mesh ASTM, purchased from Yantai, China) with hexanes–ethyl acetate. The chemical shifts (δ) are reported in ppm from tetramethylsilame (TMS) with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26 ppm). ^{13}C NMR chemical shifts are reported in ppm from TMS with the solvent resonance as internal standard ($CDCl_3$, δ = 77.0 ppm).

4.2 | Preparation of starting materials

All starting materials were synthesized using reported methods.[12] Twelve kinds of compounds were obtained through these methods, including eight unknown compounds (**4c**, **5c**, **6c**, **7c**, **8c**, **10c**, **11c**, **12c**), which were confirmed using IR, ^{1}H NMR, ^{13}C NMR, HR-MS and elemental analysis. The steps are summarized in Scheme 1.

4.3 | Spectra data for new starting materials

4.3.1 | 4-Methyl-*N*-(2-phenethylpent-4-enyl) benzenesulfonamide (4c)

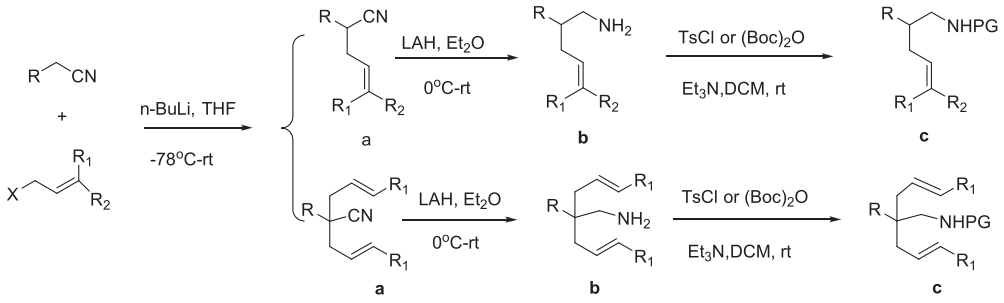
Yellow solid; m.p. 33–34°C. IR (KBr, cm^{-1}): ν 3286, 3052, 3024, 2927, 2858, 1639, 1600, 1496, 1454, 1300, 1161, 1095, 914, 813, 698, 663, 551. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.72 (d, J = 8.0 Hz, 2 H, $C^{19}H$, $C^{23}H$), 7.29 (d, J = 8.0 Hz, 3 H, $C^{2}H$, $C^{20}H$, $C^{23}H$), 7.24 (br.s, 1 H, $C^{1}H$), 7.18 (t, J = 7.4 Hz, 1 H, $C^{3}H$), 7.11 (d, J = 7.2 Hz, 2 H, $C^{4}H$, $C^{6}H$), 5.72–5.62 (m, 1 H, $C^{13}H$), 5.12–4.99 (m, 2 H, $C^{14}H_2$), 4.46 (t, J = 6.2 Hz, 1 H, NH), 4.13 (dd, J = 14.0, J = 6.8 Hz, 1 H, $C^{7}H$), 2.91 (t, J = 5.8 Hz, 2 H, $C^{11}H_2$), 2.55 (t, J = 7.4 Hz, 2 H, $C^{8}H_2$), 2.42 (s, 3 H, $C^{24}H_3$), 2.12–2.07 (m, 1 H, $C^{7}H$), 1.60–1.57 (m, 3 H, $C^{9}H$, $C^{10}H_2$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 150.1 (C^{5}), 143.4 (C^{13}), 141.9 (C^{21}), 139.7 (C^{18}), 136.8 (C^{20}), 135.6 (C^{22}), 129.7 (C^{1}), 128.3 (C^{3}), 128.2 (C^{4}), 127.1 (C^{6}), 125.8 (C^{19}), 117.2 (C^{23}), 111.5 (C^{2}), 45.8 (C^{14}), 37.2 (C^{11}), 35.9 (C^{10}), 32.9 (C^{7}), 32.7 (C^{8}), 27.3 (C^{9}), 21.5 (C^{21}). HR-MS (ESI) calcd for $C_{20}H_{25}NO_2S$ $[M - H]^+$ 342.1524, found 342.1528. Anal. Calcd (%): C, 69.94; H, 7.34; N, 4.08. Found (%): C, 69.87; H, 7.38; N, 4.04.

4.3.2 | 4-Methyl-*N*-(2-phenethyl-5-phenylpent-4-en-1-yl) benzenesulfonamide (5c)

White solid; m.p. 107–108°C. IR (KBr, cm^{-1}): ν 3282, 3024, 2954, 2923, 2854, 1600, 1461, 1377, 1157, 1091, 813, 744, 694, 551. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.72 (d, J = 8.0 Hz, 2 H, $C^{25}H$, $C^{29}H$), 7.31–7.17 (m, 10 H, $C^{11\text{-}15}H_5$, $C^{16\text{-}20}H_5$), 7.12 (d, J = 7.6 Hz, 2 H, $C^{26}H$, $C^{28}H$), 6.34 (d, J = 16.0 Hz, 1 H, $C^{6}H$), 6.06–5.98 (m, 1 H, $C^{5}H$), 4.66 (br.s, 1 H, NH), 2.92 (t, J = 5.8 Hz, 2 H, $C^{8}H_2$), 2.59 (t, J = 7.6 Hz, 2 H, $C^{1}H_2$), 2.37 (s, 3 H, $C^{30}H_3$), 2.30–2.17 (m, 2 H, $C^{3}H_2$), 1.71–1.60 (m, 3 H, $C^{2}H$, $C^{8}H_2$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 143.4 (C^{10}), 141.8 (C^{27}), 137.3 (C^{23}), 136.7 (C^{22}), 132.3 (C^{6}), 129.7 (C^{28}), 128.5 (C^{26}), 128.4 (C^{25}), 128.3 (C^{29}), 127.2 (C^{20}), 127.1 (C^{16}), 126.0 (C^{19}), 125.9 (C^{17}), 45.8 (C^{11}), 37.7 (C^{12}), 34.9 (C^{14}), 33.0 (C^{15}), 32.9 (C^{18}), 31.9 (C^{3}), 29.7 (C^{5}), 29.4 (C^{3}), 24.5 (C^{8}), 22.7 (C^{1}), 21.5 (C^{2}), 19.8 (C^{4}), 14.2 (C^{30}). HR-MS (ESI) calcd for $C_{26}H_{29}NO_2S$ $[M + Na]^+$ 442.1814, found 442.1819. Anal. Calcd (%): C, 74.43; H, 6.97; N, 3.34. Found (%): C, 74.47; H, 7.04; N, 3.19.

4.3.3 | *N*-(2-Benzylhex-4-en-1-yl)-4-methylbenzenesulfonamide(6c)

White solid; m.p. 47–48°C. IR (KBr, cm^{-1}): ν 3282, 3058, 3028, 2958, 2923, 2854, 1600, 1496, 1323, 1261, 1157, 1091, 1029, 802, 744, 659, 551. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.67 (d, J = 8.0 Hz, 2 H, $C^{19}H$, $C^{23}H$), 7.26 (dd, J = 18.0, J = 8.0 Hz, 4 H, $C^{2}H$, $C^{3}H$, $C^{5}H$, $C^{6}H$), 7.20 (d, J = 7.2 Hz, 1 H, $C^{1}H$), 7.05 (d, J = 7.2 Hz, 2 H, $C^{20}H$, $C^{22}H$), 5.44–5.36 (m,



SCHEME 1 Substrate synthesis

1 H, $C^{11}H$), 5.31–5.21 (m, 1 H, $C^{12}H$), 4.37–4.34 (m, 1 H, NH), 2.89–2.78 (m, 2 H, $C^{9}H_2$), 2.58–2.47 (m, 2 H, $C^{7}H_2$), 2.43 (s, 3 H, $C^{24}H_3$), 2.01–1.88 (m, 2 H, $C^{10}H_2$), 1.85–1.76 (m, 1 H, $C^{8}H$), 1.62 (d, J = 6.0 Hz, 3 H, $C^{14}H_3$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 143.3 (C^4), 139.7 (C^{24}), 136.8 (C^{18}), 129.6 (C^{20}), 129.0 (C^{22}), 128.3 (C^{11}), 127.9 (C^3), 127.8 (C^5), 127.4 (C^{19}), 127.1 (C^{23}), 126.1 (C^2), 46.2 (C^6), 45.7 (C^1), 40.5 (C^{12}), 40.0 (C^9), 38.0 (C^7), 34.5 (C^8), 28.9 (C^{10}), 21.5 (C^{24}), 17.9 (C^{14}). HR-MS (ESI) calcd for $C_{20}H_{25}NO_2S$ $[M - H]^+$ 342.1524, found: 342.1528. Anal. Calcd (%): C, 69.94; H, 7.34; N, 4.08. Found (%): C, 70.03; H, 7.10; N, 4.12.

4.3.4 | 4-Methyl-*N*-(2-phenethylhex-4-en-1-yl) benzenesulfonamide (7c)

White solid; m.p. 49–50°C. IR (KBr, cm^{-1}): ν 3282, 3052, 3024, 2923, 2854, 1598, 1454, 1323, 1161, 1091, 968, 813, 740, 663, 551. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.72 (d, J = 8.0 Hz, 2 H, $C^{20}H$, $C^{24}H$), 7.29 (d, J = 8.0 Hz, 3 H, $C^{21}H$, $C^{23}H$, C^1H), 7.24 (s, 1 H, C^2H), 7.17 (t, J = 7.4 Hz, 1 H, C^6H), 7.10 (d, J = 7.6 Hz, 2 H, C^3H, C^4H), 5.44–5.35 (m, 1 H, $C^{11}H$), 5.29–5.21 (m, 1 H, $C^{12}H$), 4.42 (t, J = 6.4 Hz, 1 H, NH), 2.91–2.87 (m, 2 H, $C^{13}H_2$), 2.54 (t, J = 7.0 Hz, 2 H, C^7H_2), 2.42 (s, 3 H, $C^{25}H_3$), 2.02–1.93 (m, 1 H, C^9H), 1.61 (d, J = 6.4 Hz, 3 H, $C^{15}H_3$), 1.58–1.53 (m, 4 H, C^8H_2, $C^{10}H_2$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 143.3 (C^5), 142.0 (C^{23}), 136.8 (C^{19}), 129.6 (C^{11}), 128.3 (C^{21}), 128.2 (C^{23}), 127.8 (C^{24}), 127.6 (C^{20}), 127.0 (C^1), 125.8 (C^3), 46.2 (C^4), 45.8 (C^6), 37.7 (C^2), 37.4 (C^{12}), 34.5 (C^{13}), 32.9 (C^7), 32.8 (C^8), 28.9 (C^{10}), 21.5 (C^9), 17.9 (C^{25}), 12.9 (C^{15}). HR-MS (ESI) calcd for $C_{21}H_{27}NO_2S$ $[M - H]^+$ 356.1678, found 356.1684. Anal. Calcd (%): C, 70.55; H, 7.61; N, 3.92. Found (%): C, 70.51; H, 7.65; N, 4.01.

4.3.5 | 4-Methyl-*N*-(2-(thiophen-2-yl)pent-4-en-1-yl) benzenesulfonamide(8c)

Yellow solid; m.p. 40–41°C. IR (KBr, cm^{-1}): ν 3282, 3024, 2954, 2923, 2854, 1600, 1461, 1377, 1157, 1091, 813, 744, 694, 551. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.67 (d, J = 8.0 Hz, 2 H, $C^{16}H$, $C^{20}H$), 7.30 (d, J = 8.0 Hz, 2 H, $C^{17}H$, $C^{19}H$), 7.18 (d, J = 5.2 Hz, 2 H, C^2H, C^3H), 6.93 (t, J = 4.2 Hz, 1 H, C^4H), 6.76 (d, J = 2.8 Hz, 1 H, C^6H), 5.70–5.60 (m, 1 H, C^9H), 5.04–4.99 (m, 2 H, $C^{10}H_2$), 4.34 (br.s, 1 H, NH), 3.14–3.07 (m, 1 H, C^7H), 2.99–2.93 (m, 1 H, C^7H), 2.44 (s, 3 H, $C^{21}H_3$), 2.37 (t, J = 7.0 Hz, 2 H, C^8H_2). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 144.5 (C^1), 143.4 (C^{18}), 136.8 (C^{15}), 134.8 (C^9), 129.7 (C^{17}), 127.0 (C^{19}), 126.9 (C^{20}), 125.1 (C^{16}), 124.2 (C^2), 117.5 (C^3), 48.4 (C^4), 40.9 (C^{11}), 38.8 (C^7), 30.6 (C^6), 29.7 (C^8), 21.5 (C^{21}). HR-MS (ESI) calcd for $C_{16}H_{19}NO_2S_2$ $[M + Na]^+$ 344.0746, found 344.0755. Anal. Calcd (%): C, 59.78; H, 5.96; N, 4.36. Found (%): C, 60.01; H, 5.98; N, 4.35.

4.3.6 | *N*-(2-Allyl-2-(thiophen-2-yl)pent-4-en-1-yl)-4-methylbenzenesulfonamide (10c)

White solid; m.p. 104–105°C. IR (KBr, cm^{-1}): ν 3290, 3074, 2954, 2923, 2873, 1635, 1596, 1323, 1161, 1080, 1002, 918, 813, 702, 667, 551. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.65 (d, J = 8.4 Hz, 2 H, $C^{17}H$, $C^{21}H$), 7.30 (d, J = 8.0 Hz, 2 H, $C^{18}H$, $C^{20}H$), 7.21 (d, J = 6.0 Hz, 2 H, C^2H, C^3H), 6.95–6.93 (m, 1 H, C^4H), 6.79 (d, J = 4.4 Hz, 1 H, C^7H), 5.67–5.57 (m, 2 H, C^9H, $C^{12}H$), 5.08 (d, J = 4.0 Hz, 2 H, $C^{10}H$, $C^{15}H$), 5.05 (br.s, 2 H, $C^{10}H$, $C^{15}H$), 4.13 (t, J = 6.6 Hz, 1 H, NH), 3.04 (d, J = 6.8 Hz, 2 H, $C^{11}H_2$), 2.53–2.48 (m, 1 H, C^7H), 2.44 (s, 3 H, $C^{24}H_3$), 2.41 (t, J = 7.0 Hz, 2 H, C^8H_2). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 148.4 (C^1), 143.4 (C^{16}), 136.3 (C^{12},C^9), 132.5 (C^{20}), 129.7 (C^{18}), 127.0 (C^{21}), 126.8 (C^{17}), 124.6 (C^2), 124.4 (C^3), 119.1 (C^4), 50.9 (C^{15}, C^{10}), 43.9 (C^7), 40.7 (C^8, C^{11}), 29.7 (C^6), 21.5 (C^{24}). HR-MS (ESI) calcd for $C_{19}H_{23}NO_2S_2$ $[M + Na]^+$ 384.1063, found 384.1068. Anal. Calcd (%): C, 63.13; H, 6.41; N, 3.87. Found (%): C, 63.17; H, 6.37; N, 3.91.

4.3.7 | *N*-(2-Benzyl-2-(2-buten-1-yl)hex-4-en-1-yl)-4-methylbenzenesulfonamide (11c)

Pale yellow solid; m.p. 142–143°C. IR (KBr, cm^{-1}): ν 3286, 3028, 2923, 2854, 1600, 1496, 1454, 1415, 1326, 1164, 1080, 972, 910, 813, 732, 702, 667, 551. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.68 (d, J = 8.0 Hz, 2 H, $C^{27}H$, $C^{23}H$), 7.30 (d, J = 8.4 Hz, 2 H, $C^{24}H$, $C^{26}H$), 7.22–7.19 (m, 3 H, $C^{15}H$, $C^{16}H$, $C^{17}H$), 7.11–7.07 (m, 2 H, $C^{14}H$, $C^{18}H$), 5.50–5.34 (m, 4 H, C^8H, C^5H, C^3H, C^7H), 4.40 (t, J = 7.6 Hz, 1 H, NH), 2.64 (d, J = 6.8 Hz, 2 H, C^6H_2), 2.56 (d, J = 12.8 Hz, 2 H, $C^{12}H_2$), 2.43 (s, 3 H, $C^{28}H_3$), 1.89 (d, J = 6.0 Hz, 3 H, $C^{11}H_3$), 1.64 (d, J = 5.2 Hz, 4 H, C^4H_2, C^2H_2), 1.55 (d, J = 6.4 Hz, 3 H, $C^{10}H_3$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 143.3 (C^{25}), 137.5 (C^{13}), 137.4 (C^{22}), 136.4 (C^{24}), 130.4 (C^{26}), 129.6 (C^{23}), 129.0 (C^{27}), 128.1 (C^3), 127.1 (C^5), 126.9 (C^{15}), 126.3 (C^{17}), 125.9 (C^{14}), 125.1 (C^{18}), 48.7 (C^{16}), 48.6 (C^7), 41.2 (C^8), 41.1 (C^6), 40.7 (C^{12}), 40.5 (C^2), 38.0 (C^4), 31.9 (C^1), 21.5 (C^{28}), 18.1 (C^{10}), 13.2 (C^{11}). HR-MS (ESI) calcd for $C_{24}H_{31}NO_2S$ $[M + H]^+$ 398.2154, found 398.2125. Anal. Calcd (%): C, 72.51; H, 7.86; N, 3.52. Found (%): C, 72.60; H, 8.01; N, 3.53.

4.3.8 | *Tert*-butyl-(2-allyl-2-phenylpent-4-en-1-yl)carbamate (12c)

Colorless solid; m.p. 105–106°C. IR (KBr, cm^{-1}): ν 3448, 2977, 2927, 2360, 2333, 1745, 1701, 1508, 1454, 1365, 1238, 1168, 914, 702. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.37–7.35 (m, 4 H, C^2H, C^3H, C^5H, C^6H), 7.23 (t, J = 6.6 Hz, 1 H, C^1H), 5.69–5.59 (m, 2 H, $C^{11}H$, C^9H), 5.08 (s, 1 H, $C^{14}H$), 5.05–5.03 (m, 3 H, $C^{14}H$, $C^{13}H_2$), 4.29 (br.s, 1 H, NH), 3.46 (d, J = 5.6 Hz, 2 H, $C^{12}H_2$), 2.51–2.41 (m, 4 H, $C^{18}H_2$, $C^{10}H_2$), 1.39 (s, 9 H, C^5H_3,

C^6H_3, C^7H_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 155.7 (C^1), 145.7 (C^4), 143.5 (C^{11}, C^9), 133.9 (C^2), 128.4 (C^6), 126.7 (C^1), 126.3 (C^3), 118.2 (C^5), 79.1 (C^{13}, C^{14}), 60.4 (C^4), 47.0 (C^{12}), 44.5 (C^8, C^{10}), 40.2 (C^7), 28.3 (C^5, C^6, C^7). HR-MS (ESI) calcd for $C_{19}H_{27}NO_2$ $[M + Na]^+$ 324.1939, found: 324.1918. Anal. Calcd (%): C, 75.71; H, 9.03; N, 4.65. Found (%): C, 75.67; H, 8.96; N, 4.63.

4.4 | General procedure for bromoamination

Bis(triphenylphosphine)palladium(II) dichloride (17.96 mg, 0.08 mmol), **c** (0.8 mmol) and K_2CO_3 (2 eq.) were dissolved in CH_2Cl_2 (15 ml) and allowed to stir for 5 min. NBS (266.97 mg, 1.5 mmol) was then added at room temperature. The reactions were stirred for 1 h. Then the reaction mixture was extracted with water (10 ml), and the combined organic phases dried over Mg_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane–EtOAc, 160:1) to afford the desired product **d** (Scheme 2). Notably, all the products are unknown compounds except **1d**, and their structures were confirmed using IR, ^1H NMR, ^{13}C NMR, HR-MS and elemental analysis.

4.5 | Spectral data for bromoamination products

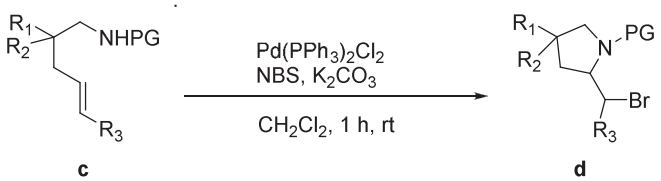
2d. White solid; yield 94%; m.p. 114–115°C. ^1H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.79 (d, J = 8.0 Hz, 2 H, $C^{19}H$, $C^{23}H$), 7.37 (d, J = 8.0 Hz, 2 H, $C^{20}H$, $C^{22}H$), 7.27–7.25 (m, 2 H, C^2H, C^6H), 7.04 (d, J = 4.4 Hz, 2 H, C^3H, C^5H), 4.05–3.98 (m, 1 H, C^9H), 3.88–3.83 (m, 2 H, $C^{12}H_2$), 3.63–3.58 (m, 1 H, $C^{11}H$), 3.34 (t, J = 11.2 Hz, 1 H, $C^{11}H$), 2.73–2.62 (m, 1 H, C^7H), 2.51–2.45 (m, 1 H, C^8H), 2.46 (s, 3 H, $C^{24}H_3$), 2.02–1.94 (m, 1 H, C^8H). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 144.1 (C^{18}), 137.3 (C^{21}), 134.8 (C^4), 133.0 (C^1), 130.0 (C^3), 128.8 (C^5), 128.4 (C^{20}), 127.6 (C^{22}), 127.5 (C^2), 60.3 (C^6), 55.5 (C^{19}), 42.5 (C^{23}), 40.7 (C^9), 39.0 (C^{11}), 37.4 (C^{12}), 36.3 (C^7), 35.6 (C^8), 21.6 (C^{24}). HR-MS (ESI) calcd for $C_{18}H_{19}BrClNO_2S$ $[M + Na]^+$ 451.9850, found: 449.9906. Anal. Calcd (%): C, 50.42; H, 4.47; N, 3.27. Found (%): C, 50.64; H, 4.61; N, 3.03.

3d. White solid; yield 97%; m.p. 104–105°C. ^1H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.62 (q, J_1 = 23.6, J_2 = 8.4 Hz, 2 H, $C^{19}H$, $C^{23}H$), 7.26 (q, J_1 = 16.4, J_2 = 8.4 Hz, 2 H, $C^{20}H$, $C^{22}H$), 7.21–7.17 (m, 2 H, C^4H, C^6H), 7.13 (t, J = 7.2 Hz, 1 H, C^2H), 6.95 (q, J_1 = 14.8, J_2 = 7.2 Hz, 2 H, C^1H, C^3H), 3.78–3.70 (m, 2 H, $C^{14}H_2$), 3.48–3.43 (m, 2 H, $C^{12}H_2$), 2.97 (t, J = 11.0 Hz, 1 H, $C^{10}H$), 2.55–2.42 (m, 2 H, C^7H_2), 2,38 (s, 3 H, $C^{24}H_3$), 2.14–2.07 (m, 1 H, C^8H), 1.71 (s, 1H, C^9H), 1.40 (s, 1H, C^9H). ^{13}C NMR (400 MHz, $CDCl_3$, δ, ppm): 142.8 (C^{18}), 138.4 (C^5), 133.6 (C^{21}), 128.8 (C^{20}), 127.5 (C^{22}), 127.3 (C^1), 126.6 (C^3), 126.4 (C^{19}), 125.4 (C^{23}), 59.5 (C^4), 54.0 (C^6), 38.9 (C^2), 37.4 (C^{10}), 37.3 (C^{12}), 37.1 (C^7), 37.0 (C^{14}), 36.5 (C^8), 28.7 (C^9), 20.6 (C^{24}). HR-MS (ESI) calcd for $C_{19}H_{22}BrNO_2S$ $[M + Na]^+$ 430.0432, found 430.0452. Anal. Calcd (%): C, 55.88; H, 5.43; N, 3.43. Found (%): C, 56.01; H, 5.38; N, 3.28.

4d. Pale yellow oil; yield 95%. ^1H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.63 (q, J_1 = 16.4, J_2 = 8.4 Hz, 2 H, $C^{20}H$, $C^{24}H$), 7.19 (q, J_1 = 17.6, J_2 = 8.4 Hz, 4 H, $C^{21}H$, $C^{23}H$, $C^{12}H$, $C^{16}H$), 7.12 (d, J = 6.8 Hz, 1 H, $C^{14}H$), 6.99 (d, J = 7.2 Hz, 2 H, $C^{13}H$, $C^{15}H$), 3.78–3.68 (m, 2 H, C^8H_2), 3.55 (q, J_1 = 11.6, J_2 = 6.0 Hz, 1 H, C^3H), 3.42 (t, J = 9.0 Hz, 1 H, C^5H), 2.90 (t, J = 10.6 Hz, 1 H, C^5H), 2.47–2.40 (m, 2 H, C^6H_2), 2.36(s, 3 H, $C^{25}H_3$), 2.15 (t, J = 6.4 Hz, 1 H, C^1H), 1.57–1.49 (m, 2 H, C^6H), 1.43–1.37 (m, 2 H, C^7H). ^{13}C NMR (400 MHz, $CDCl_3$, δ, ppm): 143.8 (C^{19}), 141.2 (C^{11}), 134.6 (C^{22}), 129.9 (C^{21}), 128.4 (C^{23}), 128.2 (C^{20}), 127.4 (C^{24}), 126.1 (C^{13}), 60.5 (C^{15}), 55.2 (C^{12}), 38.4 (C^{16}), 37.6 (C^{14}), 37.5 (C^3), 36.2 (C^5), 36.0 (C^7), 35.9 (C^6), 34.2 (C^8), 33.7 (C^1), 29.7 (C^2), 21.6 (C^{25}). HR-MS (ESI) calcd for $C_{20}H_{24}BrNO_2S$ $[M + Na]^+$ 444.0597, found: 444.0609. Anal. Calcd (%): C, 56.87; H, 5.73; N, 3.32. Found (%): C, 56.76; H, 6.03; N, 3.61.

5d. Colorless oil; yield 86%. IR (KBr, cm^{-1}): ν 3028, 2923, 2858, 1596, 1496, 1454, 1338, 1157, 1091, 813, 729. ^1H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.35–7.33 (m, 2 H, $C^{26}H$, $C^{30}H$), 7.29–7.26 (m, 2 H, $C^{27}H$, $C^{29}H$), 7.22–7.17 (m, 5 H, $C^{18}H$, $C^{19}H$, $C^{20}H$, $C^{21}H$, $C^{22}H$), 7.16–7.13 (m, 3 H, $C^{14}H$, $C^{15}H$, $C^{16}H$), 7.09–7.07 (m, 2 H, $C^{13}H$, $C^{17}H$), 4.58–4.56 (m, 1 H, C^8H), 4.41–4.36 (m, 2 H, C^5H_2), 3.97 (dd, J = 12.8 Hz, J = 17.2 Hz, 1 H, C^3H), 2.99–2.94 (m, 1 H, C^7H), 2.66–2.57 (m, 2 H, C^5H_2), 2.46–2.40 (m, 1 H, C^7H), 2.33 (s, 3 H, $C^{31}H_3$), 1.92–1.89 (s, 1 H, C^1H), 1.77–1.72 (m, 4H, C^6H2, C^2H_2). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 142.9 (C^{25}), 141.4 (C^{12}), 137.6 (C^{11}), 136.3 (C^{28}), 129.0 (C^{27}), 128.6 (C^{29}), 128.3 (C^{30}), 128.2 (C^{26}), 127.9 (C^{14}), 127.9 (C^{16}), 127.8 (C^{19}), 127.3 (C^{21}), 125.9 (C^{13}), 67.0 (C^{17}), 51.5 (C^{18}), 49.3 (C^{22}), 38.9 (C^{15}), 35.4 (C^{20}), 35.1 (C^3), 34.7 (C^5), 34 (C^8), 32.8 (C^7), 31.5 (C^6), 29.6 (C^1), 22.6 (C^2), 21.4 (C^{31}). HR-MS (ESI) calcd for $C_{26}H_{28}BrNO_2S$ $[M + K]^+$ 536.1689, found 536.0661. Anal. Calcd (%): C, 62.65; H, 5.66; N, 2.81. Found (%): C, 63.01; H, 5.96; N, 2.6%.

6d. White solid; yield 80%; m.p. 79–80°C. ^1H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.74 (d, J = 8.0 Hz, 1 H, $C^{20}H$), 7.68 (s, 1 H, $C^{24}H$), 7.66 (s, 1 H, $C^{21}H$), 7.33



c d

R_1 = Ph, Bn, $BnCH_2$, *p*-ClPh, 2-thienyl
R_2 = H, Allyl, 2-Butenyl
R_3 = H, CH_3, Ph

SCHEME 2 Procedure for bromoamination

(d, J = 4.0 Hz, 1 H, $C^{23}H$), 7.29 (d, J = 8.8 Hz, 3 H, $C^{13}H$, $C^{14}H$, $C^{15}H$), 7.24 (s, 1 H, $C^{12}H$), 7.02 (d, J = 6.8 Hz, 1 H, $C^{16}H$), 4.80–4.74 (m, 1 H, $C^{7}H$), 3.70–3.65 (m, 1 H, $C^{3}H$), 3.56–3.51 (m, 1 H, $C^{5}H$), 2.98 (t, J = 11.2 Hz, 1 H, $C^{5}H$), 2.58 (t, J = 7.4 Hz, 2 H, $C^{6}H_2$), 2.44 (s, 5 H, $C^{35}H_3$, $C^{6}H_2$), 1.99–1.93 (m, 1 H, $C^{10}H$), 1.85–1.78 (m, 1 H, $C^{10}H$), 1.74–1.70 (m, 1 H, $C^{10}H$), 1.66 (d, J = 7.2 Hz, 1 H, $C^{1}H$). ^{13}C NMR (400 MHz, $CDCl_3$, δ, ppm): 143.6 (C^{19}), 139.6 (C^{11}), 135.8 (C^{22}), 129.8 (C^{21}), 128.5 (C^{23}), 128.3 (C^{20}), 127.7 (C^{24}), 127.3 (C^{13}), 126.4 (C^{15}), 65.0 (C^{12}), 56.2 (C^{16}), 54.5 (C^{14}), 53.9 (C^{3}), 40.2 (C^{5}), 39.1 (C^{7}), 38.9 (C^{6}), 37.9 (C^{1}), 33.7 (C^{2}), 22.7 (C^{10}), 21.6 (C^{25}). HR-MS (ESI) calcd for $C_{20}H_{24}BrNO_2S$ $[M + Na]^+$ 446.0564, found 446.0588. Anal. Calcd (%): C, 56.87; H, 5.73; N, 3.32. Found (%): C, 57.26; H, 5.96; N, 3.16.

7d. White solid; yield 80%; m.p. 81–82°C. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.74 (d, J = 8.4 Hz, 1 H, $C^{21}H$), 7.67 (d, J = 8.4 Hz, 1 H, $C^{25}H$), 7.31 (q, J_1 = 15.6, J_2 = 8.0 Hz, 3 H, $C^{21}H$, $C^{25}H$, $C^{15}H$), 7.24–7.18 (m, 2 H, $C^{13}H$, $C^{17}H$), 7.0 (t, J = 9.0 Hz, 2 H, $C^{14}H$, $C^{16}H$), 4.80–4.61 (m, 1 H, $C^{8}H$), 3.80–3.65 (m, 1 H, $C^{3}H$), 3.56–3.41 (m, 1 H, $C^{5}H$), 3.01–2.91 (m, 1 H, $C^{5}H$), 2.58 (t, J = 7.6 Hz, 2 H, $C^{7}H_2$), 2.44 (s, 5 H, $C^{26}H_3$, $C^{7}H_2$), 2.00–1.93 (m, 1 H, $C^{11}H$), 1.81–1.70 (m, 2 H, $C^{11}H_2$), 1.66 (d, J = 6.8 Hz, 1 H, $C^{1}H$), 1.60–1.56 (m, 2 H, $C^{2}H_2$). ^{13}C NMR (400 MHz, $CDCl_3$, δ, ppm): 143.6 (C^{20}), 139.7 (C^{12}), 135.8 (C^{23}), 129.8 (C^{24}), 128.6 (C^{22}), 128.5 (C^{21}), 128.3 (C^{25}), 127.7 (C^{14}), 127.3 (C^{16}), 126.4 (C^{13}), 64.9 (C^{17}), 56.2 (C^{15}), 54.5 (C^{3}), 40.2 (C^{5}), 39.1 (C^{8}), 38.9 (C^{7}), 33.6 (C^{6}), 29.7 (C^{1}), 23.2 (C^{2}), 22.7 (C^{11}), 21.6 (C^{26}). HR-MS (ESI) calcd for $C_{21}H_{26}BrNO_2S$ $[M + Na]^+$ 460.0758, found: 460.0745. Anal. Calcd (%): C, 57.80; H, 6.01; N, 3.21. Found (%): C, 58.11; H, 6.41; N, 2.99.

8d. White solid; yield 93%; m.p. 71–72°C. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.79–7.77 (m, 2 H, $C^{17}H$, $C^{21}H$), 7.36 (d, J = 7.2 Hz, 2 H, $C^{20}H$, $C^{18}H$), 7.16–7.15 (m, 1 H, $C^{4}H$), 6.93–6.89 (m, 1 H, $C^{2}H$), 6.77–6.73 (m, 1 H, $C^{3}H$), 4.00–3.92 (m, 1H, $C^{8}H$), 3.92–3.81 (m, 2 H, $C^{11}H_2$), 3.58–3.44 (m, 1 H, $C^{10}H$), 3.43–3.38 (m, 1 H, $C^{10}H$), 2.96–2.92 (m, 1 H, $C^{6}H$), 2.57–2.51 (m, 1 H, $C^{7}H$), 2.45 (s, 3 H, $C^{22}H_3$), 2.06–1.97 (m, 1 H, $C^{7}H$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 144.1 (C^{1}), 142.2 (C^{16}), 134.7 (C^{19}), 129.9 (C^{20}), 130.0 (C^{18}), 127.4 (C^{21}), 126.9 (C^{17}), 124.1 (C^{3}), 123.9 (C^{2}), 123.8 (C^{4}), 60.3 (C^{8}), 56.0 (C^{10}), 40.1 (C^{11}), 38.7 (C^{7}), 37.1 (C^{6}), 21.6 (C^{22}). HR-MS (ESI) calcd for: $C_{16}H_{18}BrNO_2S_2$ $[M + H]^+$ 400.0012, found: 400.0041. Anal. Calcd (%): C, 48.00; H, 4.53; N, 3.50. Found (%): C, 48.59; H, 4.91; N, 3.05.

9d. White solid; yield 96%; m.p. 90–91°C. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.46 (d, J = 8.4 Hz, 2 H, $C^{21}H$, $C^{25}H$), 7.30–7.17 (m, 2 H, $C^{22}H$, $C^{24}H$), 7.10 (d, J = 3.6 Hz, 1 H, $C^{15}H$), 7.08 (s, 2 H, $C^{13}H$, $C^{17}H$), 6.91–6.89 (m, 2 H, $C^{14}H$, $C^{16}H$), 5.50–5.19 (m, 1 H, $C^{8}H$), 4.91–4.85 (m, 2 H, $C^{9}H_2$), 4.02 (q, J_1 = 10.0, J_2 = 3.2 Hz, 1 H, $C^{4}H$), 3.71 (d, J = 10.0 Hz, 2 H, $C^{10}H_2$), 3.52–3.42 (m, 2 H, $C^{6}H_2$), 2.43 (t, J = 7.60 Hz, 1 H, $C^{7}H$), 2.35 (t, J = 6.8 Hz, 2 H, $C^{3}H_2$), 2.29 (s, 3 H, $C^{26}H_3$), 2.17 (q, J_1 = 13.6, J_2 = 6.0 Hz, 1 H, $C^{7}H$). ^{13}C NMR (400 MHz, $CDCl_3$, δ, ppm): 142.6 (C^{1}), 142.4 (C^{20}), 132.3 (C^{8}), 132.1 (C^{23}), 128.8 (C^{22}), 128.6 (C^{24}), 127.4 (C^{21}), 126.4 (C^{25}), 125.3 (C^{14}), 125.1 (C^{16}), 117.6 (C^{15}), 59.1 (C^{13}), 58.9 (C^{17}), 47.1 (C^{9}), 44.6 (C^{4}), 42.7 (C^{6}), 40.0 (C^{7}), 39.3 (C^{3}), 35.8 (C^{5}), 28.7 (C^{10}), 20.5 (C^{26}). HR-MS (ESI) calcd for $C_{21}H_{24}BrNO_2S$ $[M + Na]^+$ 458.0577, found 458.0588. Anal. Calcd (%): C, 58.06; H, 5.57; N, 3.22. Found (%): C, 58.67; H, 5.97; N, 3.09.

10d. Colorless oil; yield 92%. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.78 (d, J = 8.0 Hz, 2 H, $C^{20}H$, $C^{24}H$), 7.36 (d, J = 8.2 Hz, 2 H, $C^{21}H$, $C^{23}H$), 7.19 (d, J = 5.2 Hz, 1 H, $C^{4}H$), 6.93–6.91 (m, 1 H, $C^{2}H$), 6.80 (d, J = 3.6 Hz, 1 H, $C^{3}H$), 5.42–5.32 (m, 1 H, $C^{12}H$), 4.94 (d, J = 10.0 Hz, 1 H, $C^{13}H$), 4.79 (d, J = 16.8 Hz, 1 H, $C^{13}H$), 4.03–3.99 (m, 1 H, $C^{8}H$), 3.79 (dd, J = 9.6, J = 2.8 Hz, 1 H, $C^{14}H$), 3.70 (d, J = 10.4 Hz, 1 H, $C^{14}H$), 3.51–3.48 (m, 1 H, $C^{10}H$), 3.30 (t, J = 5.6 Hz, 1 H, $C^{10}H$), 2.49 (s, 3H, $C^{25}H_3$), 2.46–2.21(m, 2H, $C^{11}H_2$), 2.17–1.98 (m, 2H, $C^{7}H_2$). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 147.6 (C^{1}), 144.0 (C^{26}), 134.7 (C^{12}), 132.9 (C^{22}), 129.8 (C^{21}), 127.5 (C^{23}), 126.7 (C^{20}), 124.0 (C^{24}), 123.9 (C^{2}), 118.7 (C^{3}), 59.7 (C^{4}), 59.5 (C^{13}), 46.7 (C^{8}), 44.3 (C^{10}), 42.6 (C^{11}), 36.4 (C^{7}), 30.5 (C^{5}), 29.7 (C^{14}), 21.6 (C^{25}). HR-MS (ESI) calcd for $C_{19}H_{22}BrNO_2S_2$ $[M + Na]^+$ 462.0167, found: 462.0173. Anal. Calcd (%): C, 51.82; H, 5.03; N, 3.18. Found (%): C, 51.67; H, 4.93; N, 3.09.

11d. Colorless oil; yield 90%. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.82 (d, J = 8.4 Hz, 1 H, $C^{24}H$), 7.73 (d, J = 8.0 Hz, 1 H, $C^{28}H$), 7.35–7.20 (m, 5 H, $C^{25}H$, $C^{27}H$, $C^{17}H$, $C^{18}H$, $C^{19}H$), 7.12–7.07 (m, 2 H, $C^{16}H$, $C^{20}H$), 5.57–5.42 (m, 1 H, $C^{8}H$), 5.34–5.26 (m, 1 H, $C^{9}H$), 4.96–4.84 (m, 1 H, $C^{10}H$), 4.03–3.71 (m, 1 H, $C^{4}H$), 3.32–3.19 (m, 2 H, $C^{6}H_2$), 2.66–2.58 (m, 1 H, $C^{1}H$), 2.40 (s, 3 H, $C^{29}H_3$), 2.32–2.22 (m, 1 H, $C^{1}H$), 2.11–2.04 (m, 1 H, $C^{7}H$), 1.99–1.91 (m, 1 H, $C^{7}H$), 1.87–1.77 (m, 2 H, $C^{3}H_2$), 1.71–1.67 (m, 3 H, $C^{13}H_3$), 1.54 (d, J = 6.8 Hz, 3 H, $C^{14}H_3$). ^{13}C NMR (400 MHz, $CDCl_3$, δ, ppm): 143.4 (C^{23}), 137.8 (C^{26}), 137.1 (C^{15}), 130.6 (C^{8}), 130.0 (C^{25}), 129.7 (C^{27}), 128.2 (C^{24}), 127.2 (C^{28}), 126.5 (C^{17}), 126.0 (C^{19}), 63.6 (C^{16}), 57.7 (C^{20}), 55.8 (C^{18}), 45.4 (C^{20}), 41.7 (C^{4}), 40.5 (C^{6}), 38.5 (C^{1}), 37.3 (C^{7}), 36.7 (C^{10}), 36.1 (C^{2}), 29.7 (C^{3}), 22.3 (C^{13}), 21.6 (C^{29}), 18.2 (C^{14}). HR-MS (ESI) calcd for $C_{24}H_{30}BrNO_2S$ $[M + Na]^+$ 500.1039, found: 500.1058. Anal. Calcd (%): C, 60.50; H, 6.35; N, 2.94. Found (%): C, 60.43; H, 6.19; N, 2.69.

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