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A Highly Efficient Palladium-Catalyzed One-Pot Synthesis of Unsymmetrical Aryl Alkyl Thioethers under Mild Conditions in Water

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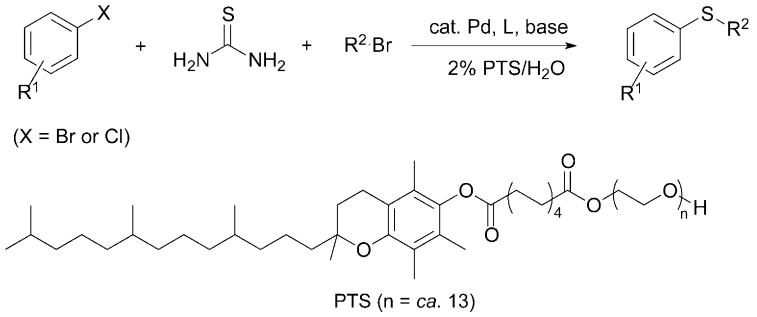
Abstract: A palladium-catalyzed, one-pot synthesis of unsymmetrical aryl alkyl thioethers involving aryl halides (aryl bromides and chlorides), thiourea and alkyl bromides has been realized under mild conditions (room temperature to 50 °C) in water with polyoxyethanyl α-tocopheryl sebacate (PTS) as amphiphile. The PTS/water could be recycled in up to eight runs without an obvious change in its activity.

Keywords: aryl halides; micellar catalysis; polyoxyethanyl α-tocopheryl sebacate (PTS)/water; thiourea; unsymmetrical aryl alkyl thioethers

The formation of C–S bonds represents a key step in the synthesis of many important molecules that are of biological, pharmaceutical, and material interest.[1] Generally, the generation of C–S bonds, especially C_{aryl}–S bonds involved the coupling reaction,[2] the S_NAr reaction[3] and the electrophilic substitution reaction[4] of activated aryl halides with arenethiols. Among them, the transition metal-catalyzed C_{aryl}–S bond formation reactions by direct coupling of aryl halides and arenethiols have received much attention, and various metal catalysts such as Pd,[5] Cu,[6] and Fe[7] etc. have been successfully utilized for the synthesis of aryl sulfides.

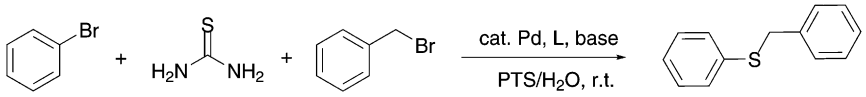
While acknowledging the pioneering work in this field, some drawbacks are still issues to be addressed. For example, the direct use of thiols is environmentally unfriendly due to their foul smell, volatility and toxicity. In addition, most of the reported reactions proceeded in harmful organic solvents and the disposal of these solvents is a major problem. To overcome these problems, different thiol surrogates such as thiourea,[8] potassium thiocyanate,[9] potassium ethyl xanthogenate,[10] potassium thioacetate[11] have been employed to form aryl thiols *in situ*. Moreover, green solvents have also been successfully applied in C_{aryl}–S bond formation reactions. For example, Firouzabadi[8] et al. reported a copper-catalyzed S-arylation of diverse alkyl bromides with aryl halides using thiourea as thiol surrogates in PEG200. Carril[6e] et al. reported a recyclable catalytic system for S-arylation reactions in the presence of water. Although these works provided us with good methods for the preparation of thioethers, the development of an efficient and environmentally benign process with a broad substrate scope especially for aryl chlorides was still in demand.

Recently, reactions in aqueous media or "on water"[12] have gained wide interest since water is inexpensive, non-toxic, and safe with respect to handling. Nevertheless, reactions especially the transition metal-catalyzed coupling reactions "in water" have been extremely limited due to the insolubility of organic substrates. In this context, micellar catalysis is an efficient way to deal with the "bottle-neck". Recently, polyoxyethanyl α-tocopheryl sebacate (PTS, Scheme 1), a non-ionic amphiphile has been introduced by Lipshutz's group and proved to be a versatile "solubilizer" for organic molecules in water. Lipophilic substrates and catalysts can efficiently enter the 25 nm micelles formed by PTS in water leading to cross-coupling reactions such as metathesis reaction,[13] Heck reaction,[13] amination,[14] Suzuki–Miyaura reaction,[15] Fujiwara–Moritani reaction,[16] and Sonogashira reaction[17] etc. at room temperature. Importantly, there is no need for a co-solvent to en-



Scheme 1. One-pot C_{aryl}–S bond formation in PTS/H_2O.

Table 1. Effect of reaction parameters on the preparation of phenyl benzyl thioether.[a]



Entry	Pd source	Ligand	Base	Additive	Conversion [%][b]
1	$PdCl_2(CH_3CN)_2$	–	K_2CO_3	PTS	<5
2	$Pd(OAc)_2$	–	K_2CO_3	PTS	<5
3	$Pd_2(dba)_3$	–	K_2CO_3	PTS	29
4	$Pd(OAc)_2$	1,10-Phen (**1**)	K_2CO_3	PTS	21
5	$Pd(OAc)_2$	PPh_3	K_2CO_3	PTS	40
6	$Pd(OAc)_2$	A-^{ta}Phos (**2**)	K_2CO_3	PTS	86
7	$Pd(OAc)_2$	Xphos (**3**)	K_2CO_3	PTS	97, 82[c], 95[d]
8	$Pd(OAc)_2$	DPEPhos (**4**)	K_2CO_3	PTS	91
9	$Pd(OAc)_2$	Xphos (**3**)	KOH	PTS	90
10	$Pd(OAc)_2$	Xphos (**3**)	KO-*t*-Bu	PTS	95
11	$Pd(OAc)_2$	Xphos (**3**)	K_3PO_4	PTS	70
12	$Pd(OAc)_2$	Xphos (**3**)	Et_3N	PTS	63
13	$Pd(OAc)_2$	Xphos (**3**)	K_2CO_3	PEG-600	46
14	$Pd(OAc)_2$	Xphos (**3**)	K_2CO_3	Trixon X-100	81
15	$Pd(OAc)_2$	Xphos (**3**)	K_2CO_3	SDS	40
16	$Pd(OAc)_2$	Xphos (**3**)	K_2CO_3	TBAB	28
17	$Pd(OAc)_2$	Xphos (**3**)	K_2CO_3	–	11[e]

[a] *Reaction conditions:* bromobenzene (1 mmol), benzyl bromide (1.1 mmol), thiourea (1.2 mmol), base (3 mmol), Pd precatalyst (0.5 mol%), ligand (1 mol%), 2% additive/H_2O (2 mL), room temperature, 4 h.
[b] Conversion based on GC/MS.
[c] 1% PTS/H_2O.
[d] 3% PTS/H_2O.
[e] Reaction "on water" for 12 h.

hance the solubility of water-insoluble substrates in these reactions.

To the best of our knowledge, the transition metal-catalyzed C_{aryl}–S bond formation reactions, especially those utilizing inactivated aryl halides in water are rare. Hence, in continuation of our interest in green approaches for C_{aryl}–S bond formation, we herein report a Pd-catalyzed, one-pot synthesis of unsymmetrical aryl alkyl thioethers by coupling of aryl bromides or chlorides, thiourea and alkyl bromides under very mild conditions in water (Scheme 1).

An initial investigation focused on the reaction of thiourea, benzyl bromide with bromobenzene in 2 wt% PTS/H_2O at room temperature (Table 1).

The palladium precatalysts and ligands (Figure 1) play important roles in the reaction. Among several Pd precatalysts and ligands screened, those bearing monodentate and bidentate phosphine ligands showed high activity, and $Pd(OAc)_2$/XPhos turned out to be the best combination (Table 1, entries 5–8). However, extremely low conversion was detected in the absence of any ligands. When a Pd(0) source such as $Pd_2(dba)_3$ was employed, the conversion was increased to 29%. It could be concluded that the highly active Pd(0) catalyst was responsible for the results. In our catalytic system, the active Pd(0) catalyst was readily generated *in situ* by water-promoted activation of $Pd(OAc)_2$ in the presence of phosphine ligands,

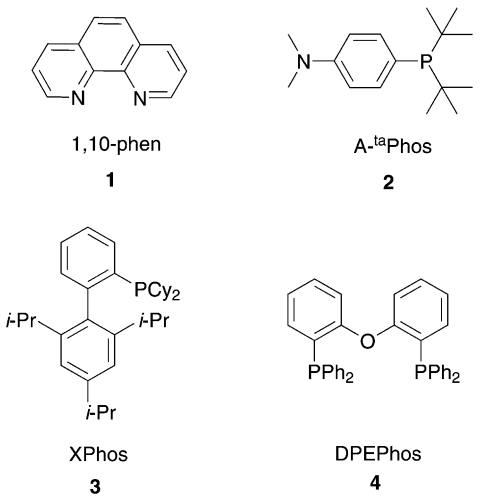


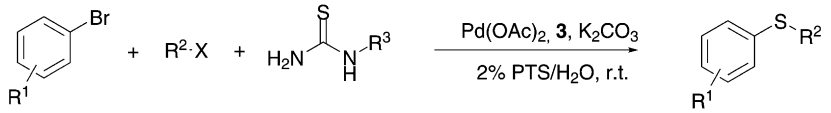
Figure 1. Ligands examined in this study.

which is consistent with observations by Buchwald's group.[18]

The base effect on the reaction was evaluated next. K_2CO_3, KOH and KO-*t*-Bu were all effective and up to 97% conversion was achieved when K_2CO_3 was utilized. Both K_3PO_4 and Et_3N were less effective, affording a moderate conversion. Different surfactants were also investigated on the model reaction. As can be seen from Table 1, other surfactants including PEG-600, Trixon X-100, SDS and TBAB, however, were not as effective. In addition, the corresponding reaction "on water" gave the lowest level of conversion (Table 1, entry 17). It was worth noting that the 1–2% PTS in water was sufficient. A higher loading (3%) offered no advantage, and conversions were somewhat lower under identical conditions (Table 1, entry 7).

Under the optimized conditions, a series of unsymmetrical aryl alkyl thioethers could be successfully synthesized from substituted bromobenzenes, thioureas and alkyl halides at room temperature (Table 2). Firstly, the substituted thioureas were checked and all of them showed good activity, providing the corresponding products in good to excellent yields. Among them, thiourea appeared to be the best choice due to its commercial availability and economic affordability. The substituents on the aryl bromides, however, could affect the reaction in terms of both reaction time and conversion. The aryl bromides bearing electron-donating groups such as OMe at the *para* position were less effective; while electron-withdrawing groups, for example, NO_2, could effectively promote the reaction in a very short time with nearly quantitative conversion (Table 2, entry 7). Various alkyl halides, in addition, could participate in the reactions. As seen from the results presented in Table 2, primary halides (iodides, bromides, chlorides) were easily converted to the corresponding thioethers in good to excellent yields, although a slightly lower yield was observed when an alkyl chloride was employed (Table 2, entries 8–10). Considering the cost and activity, alkyl bromides were chosen as the best substrates. We have also investigated the applicability of our method using secondary and tertiary bromides (Table 2, entries 11 and 12). Under the optimized conditions, cyclohexyl bromide reacted with bromobenzene and thiourea smoothly, affording the product **5f** in 88% yield in

Table 2. One-pot synthesis of unsymmetrical aryl alkyl thioethers from aryl bromides.[a]



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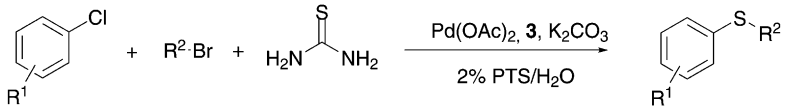
Entry	R^1	R^2-X	R^3	Product	Time [h]	Yield [%][b]
1	H	$PhCH_2Br$	H	**5a**	4	97
2	H	$PhCH_2Br$	Me	**5a**	4	90
3	H	$PhCH_2Br$	Et	**5a**	4	88
4	H	$PhCH_2Br$	Bn	**5a**	4	85
5	4-CH_3	$PhCH_2Br$	H	**5b**	4	92
6	4-OCH_3	$PhCH_2Br$	H	**5c**	6	87
7	4-NO_2	$PhCH_2Br$	H	**5d**	2	99
8	H	*n*-C_4H_9I	H	**5e**	6	91
9	H	*n*-C_4H_9Br	H	**5e**	6	90
10	H	*n*-C_4H_9Cl	H	**5e**	6	83
11	H	cyclohexyl bromide	H	**5f**	6	88
12	H	*tert*-butyl bromide	H	**5g**	12	76

[a] *Reaction conditions:* aryl bromide (1 mmol), alkyl halide (1.1 mmol), substituted thiourea (1.2 mmol), K_2CO_3 (3 mmol), $Pd(OAc)_2$ (0.5 mol%), XPhos **3** (1 mol%), 2% PTS/H_2O (2 mL), room temperature.

[b] Isolated yield.

Table 3. One-pot synthesis of unsymmetrical aryl alkyl thioethers from aryl chlorides.[a]



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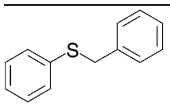
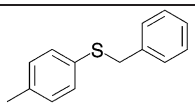


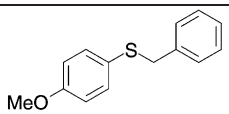
6a

96%, 50 °C, 12 h



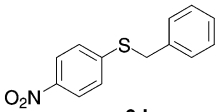
6b

92%, 50 °C, 16 h



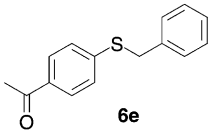
6c

87%, 50 °C, 16 h



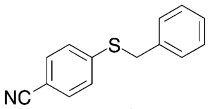
6d

97%, r.t., 12 h



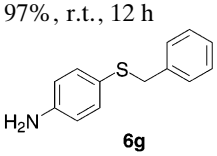
6e

90%, r.t., 12 h



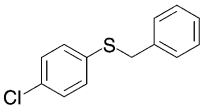
6f

91%, r.t., 12 h



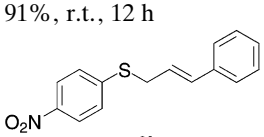
6g

46%, 50 °C, 12 h



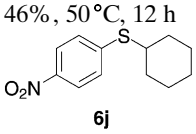
6h

83%, r.t., 12 h



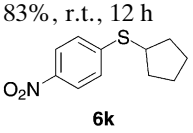
6i

93%, r.t., 12 h



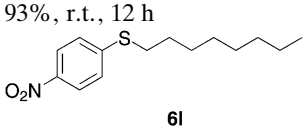
6j

91%, r.t., 12 h



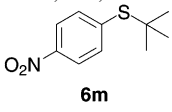
6k

92%, r.t., 12 h



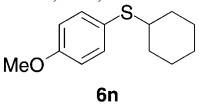
6l

88%, r.t., 12 h



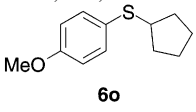
6m

71%, r.t., 16 h



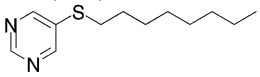
6n

90%, 50 °C, 16 h



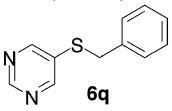
6o

87%, 50 °C, 16 h



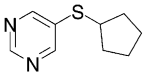
6p

91%, r.t., 12 h



6q

95%, r.t., 12 h



6r

89%, r.t., 12 h

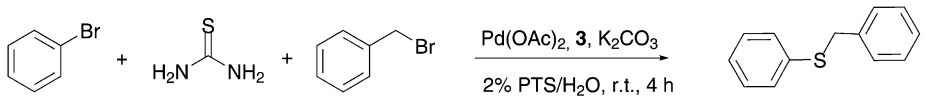
[a] *Reaction conditions:* aryl chloride (1 mmol), alkyl bromide (1.1 mmol), thiourea (1.2 mmol), K_2CO_3 (3 mmol), $Pd(OAc)_2$ (0.5 mol%), XPhos **3** (1 mol%), 2% PTS/H_2O (2 mL).

6 h. However, *tert*-butyl bromide reacted sluggishly and a 76% yield was obtained by prolonging the reaction time.

The transition metal-catalyzed coupling reactions using aryl chlorides in water under mild conditions, in particular at room temperature, are still a challenging task in this field. To probe the scope of our catalytic system, we further extended this protocol to aryl chlorides.

As depicted in Table 3, the electronic property of different substituents on the aryl chlorides affected the reaction significantly. Those aryl chlorides bearing electron-withdrawing groups such as NO_2, $COCH_3$, CN at the *para* position worked very well in this system at room temperature within 12 h, affording products in excellent yields. Those aryl chlorides bearing electron-donating groups such as CH_3, OCH_3, NH_2 were less effective. Generally, a slightly elevated temperature and prolonged reaction time were required. It was worth noting that only 46% yield of product **6g** was obtained under the optimized conditions and by-products were observed. Next, a series of alkyl bromides including allyl bromide, cyclohexyl bromide, *n*-octyl bromide and *tert*-butyl bromide was evaluated using 4-nitrochlorobenzene as substrate (see products **6i**–**6o**) and it can be seen that all the reactions proceeded smoothly to provide the corresponding products in good to excellent yields. While the electron-rich aryl chlorides, for example, 4-chloroanisole furnished the corresponding products **6n** and **6o** in high yields, albeit at a slightly elevated temperature and prolonged reaction time. Heterocycles such as 5-chloropyrimidine also showed high activity to give **6p**, **6q** and **6r** in 91%, 95% and 89% yields, respectively.

Table 4. Recycling of PTS/H_2O.



Cycle:	1	2	3	4	5	6	7	8
Yield:	97%	98%	98%	98%	98%	97%	96%	96%

Another advantage of this protocol is the recyclability of the aqueous phase due to the preferred solubility of PTS in water, as opposed to common organic solvents (e.g., hydrocarbons, Et_2O, and EtOAc). The coupling reaction of bromobenzene, benzyl bromide and thiourea was conducted under the optimized conditions for 4 h, followed by extraction with minimal amounts of EtOAc several times. After that, new starting materials, Xphos and K_2CO_3 were added to the micellar palladium catalyst solution. As illustrated in Table 4, almost the same conversion could be realized even after 8 runs.

A plausible mechanism is also presented (Scheme 2). In this reaction, two points should be mentioned. Firstly, the highly active Pd(0) catalyst was generated by reduction of $Pd(OAc)_2$ using X-Phos ligand. The presence of water enormously promoted the reduction process.[19] Secondly, the thiolate ion was believed to be generated by hydrolysis of *S*-alkylisothiouronium salt (**7**), which was generated *in situ* from thiourea and alkyl bromide.[8,20] The thiolate ion and aryl halide then underwent the classic palladium-catalyzed oxidative addition and elimination reaction in the presence of Pd(0) to produce the aryl alkyl thioethers with urea as by-product.

In summary, a highly efficient protocol for the Pd-catalyzed, one-pot synthesis of unsymmetrical aryl alkyl thioethers in water has been developed. The micellar environment is mainly responsible for the high reaction efficiency. The combination of $Pd(OAc)_2$ and X-Phos shows extremely high catalytic activity for the reaction, giving a series of thioethers in good to excellent yields. Various functional groups are tolerated and the aryl halides can react smoothly at room temperature, although slightly elevated temperature and prolonged reaction time are necessary for electron-rich aryl chlorides. The mild conditions, environmentally benign thiol surrogates, water as solvent and recyclability of PTS/H_2O make it more advantageous than the methods previously reported. Studies on new applications of PTS/H_2O in organic chemistry are currently underway in our laboratory.

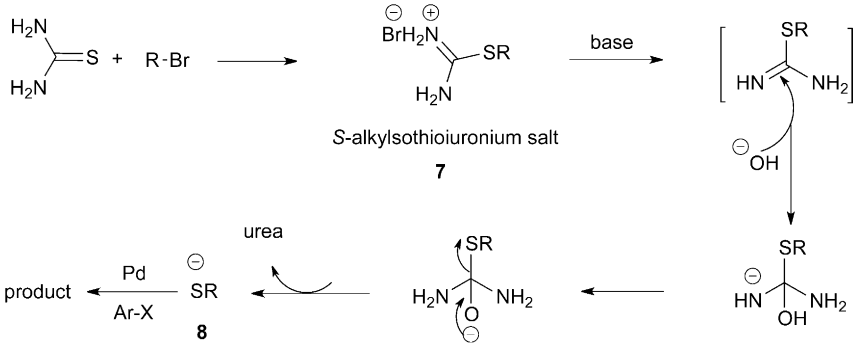
Experimental Section

General Remarks

$Pd(OAc)_2$, ligands and PTS (15 wt% in H_2O) were obtained from Aldrich. Water (HPLC grade) was purchased from Acros and degassed by sparging with argon prior to use. The solution of 15 wt% PTS (1 mL) was diluted with degassed water (6.5 mL) to give the 2 wt% aqueous PTS solution (7.5 mL). Other commercially available reagents were used without further purification. ^1H and ^{13}C NMR spectra were recorded ion a 300 MHz spectrometer in $CDCl_3$ using TMS as internal standard. Chemical shifts are reported in ppm (δ), and coupling constants (J), in Hz. GC/MS analyses were performed on a Saturn 2000GC/MS instrument. All the products are known compounds and were identified by comparing of their physical and spectra data with those reported in the literature.

Typical Procedure for One-Pot synthesis of Aryl Alkyl Thioethers

A three-necked flask was purged with N_2 and then was charged with $Pd(OAc)_2$ (1.1 mg, 0.005 mmol), XPhos (4.8 mg, 0.01 mmol), K_2CO_3 (414.6 mg, 3 mmol), aryl halide (1 mmol), alkyl bromide (1.1 mmol) and thiourea (91 mg,



Scheme 2. Plausible mechanism.

1.2 mmol), followed by addition of degassed PTS solution (2.0 mL, 2 wt%) *via* syringe. The mixture was then stirred at room temperature or 50 °C for a certain time as monitored by GC/MS. After completeion of the reaction, the mixture was cooled to room temperature (if necessary), diluted with brine and extracted with ethyl acetate. The combined organic extract was dried over anhydrous Na_2SO_4, filtered, and concentrated by rotary evaporation to give a crude product. Purification by silica gel chromatography eluting with EtOAc/*n*-hexane afforded the pure thioether.

Recycling Procedure

A three-necked flask was purged with N_2 and then was charged with $Pd(OAc)_2$ (1.1 mg, 0.005 mmol), XPhos (4.8 mg, 0.01 mmol), K_2CO_3 (414.6 mg, 3 mmol), bromobenzene (157.7 mg, 1 mmol), benzyl bromide (188.1 mg, 1.1 mmol) and thiourea (91 mg, 1.2 mmol), followed by addition of degassed PTS solution (2.0 mL, 2 wt%) *via* syringe. The mixture was then stirred at room temperature for 4 h. After completion of the reaction, ethyl acetate (3 mL) was then added to the reaction mixture and stirred for 30 s. The reaction mixture was then allowed to separate and the EtOAc layer was removed by pipet. The aqueous layer was successively washed with EtOAc (3×3 mL). The combined EtOAc extract layers were dried over anhydrous Na_2SO_4, filtered, concentrated by rotary evaporation and the residue was purified by silica gel chromatography eluting with EtOAc/*n*-hexane. For the second run, the fresh starting materials, Xphos and K_2CO_3 were added to the micellar palladium catalyst solution and stirred at room temperature for another 4 h. The work-up was conducted in exactly the same way as described for the first cycle.

Characterization Data of Compounds

5a (6a)[21]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.22–7.12 (m, 10H), 3.49 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.7, 136.9, 129.8, 129.4, 128.8, 127.7, 127.5, 126.6, 43.5.

5b (6b)[22]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30–7.10 (m, 10H), 6.98–6.95 (m, 2H), 4.13 (s, 2H), 2.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.7, 135.4, 131.4, 129.6, 128.5, 127.9, 127.4, 126.0, 125.9, 38.7, 20.0.

5c (6c)[23]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.17–7.08 (m, 7H), 6.70–6.66 (m, 2H), 3.88 (s, 2H), 3.62 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.1, 137.0, 132.9, 127.8, 127.3, 125.9, 125.0, 113.3, 54.2, 40.1.

5d (6d)[8]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02–7.97 (m, 2H), 7.32–7.17 (m, 7H), 4.16 (s,2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.2, 145.1, 135.4, 129.7, 128.8, 128.7,127.8, 126.5, 123.9, 36.9.

5e[24]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30–7.17 (m, 4H), 7.13–7.07 (m, 1H), 2.88 (t, *J* = 7.5 Hz, 2H), 1.62(p, *J*=7.5 Hz, 2H), 1.43 (sex, *J* = 7.5 Hz, 2H), 0.93 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.9, 130.9, 129.1, 128.7, 126.9, 125.5, 33.1, 31.1, 21.9, 13.5.

5f[25]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 12.0 Hz, 2H), 7.30–7.17 (m, 1H), 2.01–1.92 (m, 2H), 1.81–1.74 (m, 2H), 1.65–1.57 (m, 1H), 1.44–1.20 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.1, 131.8, 128.7, 126.5, 46.5, 33.3, 26.0, 25.7.

5g[26]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53–7.50 (m, 2H), 7.33–7.31 (m, 3H), 1.26 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.4, 132.7, 128.6, 128.4, 45.8, 30.9.

6e[27]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.17 (m, 7H), 6.88–6.79 (m, 2H), 4.02 (s, 2H), 3.81(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.6, 144.6, 136.7, 134.6, 129.2, 129.1, 127.9, 127.3, 37.6, 26.8.

6f[27]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57–7.42 (m, 2H), 7.40–7.22 (m, 7H), 4.21 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.9, 136.1, 132.6, 129.2, 129.1, 128.1, 127.7, 119.2, 109.0, 37.5.

6g[27]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30–7.12 (m, 7H), 6.62–6.54 (m, 2H), 3.98 (s, 2H), 3.71 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.6, 138.9, 135.2, 129.3, 128.7, 127.3, 123.3, 115.8, 42.2.

6h[28]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26–7.21 (m, 5H), 7.20 (s, 4H), 4.07 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.1, 134.7, 132.5, 131.5, 129.0, 128.8, 128.6, 127.3, 39.3.

6i[29]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.05–8.01 (d, *J* = 9.0 Hz, 2H), 7.60–7.22 (m, 7H), 6.58–6.03 (m, 2H), 3.81–3.78 (d, *J* = 6.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.8, 134.0, 132.3, 131.5, 129.1, 128.6, 126.9, 126.3, 123.9, 123.0, 33.9.

6j[8]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.05–7.99 (m, 2H), 7.29–7.23 (m, 2H),3.32–3.24 (m, 1H), 1.99–1.95 (m, 2H), 1.74–1.70 (m, 2H), 1.70–1.27 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.9, 144.0, 126.5, 122.8, 43.7, 31.8, 24.8, 24.5.

6k[8]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06–8.01 (m, 2H), 7.28–7.23 (m,2H), 3.70–3.65(m, 1H), 2.13–2.10 (m, 2H), 1.74–1.58 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.8, 145.8, 125.4, 122.8, 43.3, 32.3, 23.9.

6l[30]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.03–7.96 (m, 2H), 7.23–7.16 (m, 2H), 2.89 (t, *J* = 7.5 Hz, 2H), 1.64–1.58 (m, 2H), 1.35–1.17 (m, 10H), 0.80–0.75 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.2, 144.7, 125.8, 123.8, 31.8, 31.7, 29.1, 29.0, 28.8, 28.4, 22.6, 14.0.

6m[8]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10–8.06 (d, *J* = 10.6 Hz, 2H), 7.60–7.56 (d, *J* = 9.3 Hz, 2H),1.28 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.6, 142.2, 136.8, 123.2, 47.5, 31.0.

6n[31]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.26 (m, 2H), 6.77–6.71 (m, 2H), 3.71 (s, 3H), 2.82 (m, 1H), 1.84–1.18 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.2, 134.5, 123.9, 115.3, 113.2, 54.2,46.8, 32.3, 28.6, 25.0, 24.7.

6o[31]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.26 (m, 2H), 6.79–6.73 (m, 2H), 3.73 (s, 3H), 3.73–3.32 (m, 1H), 1.90–1.86 (m, 2H), 1.70–1.68 (m, 2H), 1.56–1.46 (m, 4H),; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.9, 138.1, 134.1, 116.3, 114.3, 55.2, 47.9, 33.4, 30.5, 24.6.

6p[8]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.03–7.96 (m, 2H), 7.23–7.16 (m, 2H), 2.89 (t, *J* = 7.5 Hz, 2H), 1.64–1.58 (m, 2H), 1.35–1.17 (m, 10H), 0.80–0.75 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.2, 144.7, 125.8, 123.8, 31.8, 31.7, 29.1, 29.0, 28.8, 28.4, 22.6, 14.0.

6q[8]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.9 (s, 1H), 8.49 (s, 2H), 7.29–7.12 (m, 5H), 4.02 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.2, 155.4, 134.9, 127.8, 127.7, 126.7, 37.9.

6r[8]**:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.06 (s, 1H), 8.63 (s, 2H), 3.59–3.48 (m, 1H), 1.75–1.70 (m, 2H), 1.61–1.51 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.2, 155.7, 133.4, 45.7, 33.7, 24.6.

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