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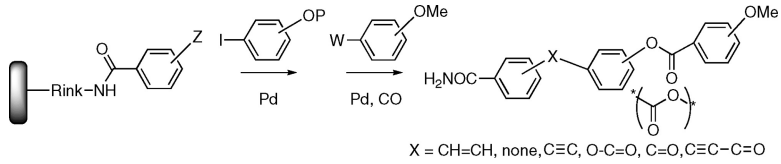

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Sequential Palladium-Catalyzed Coupling Reactions on Solid-Phase

Takayuki Doi,[†] Hitoshi Inoue,[†] Masatoshi Tokita,[‡] Junji Watanabe,[‡] and Takashi Takahashi*,[†]

Department of Applied Chemistry, Tokyo Institute of Technology, and Department of Organic and Polymeric Materials, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro, Tokyo 152-8552, Japan

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Six-types of palladium-catalyzed coupling, Mizoroki-Heck, Migita-Stille, Sonogashira, carbonylative esterification, carbonylative Stille, and carbonylative Sonogashira reactions, were performed on a polymer support. The above coupling reactions of *m*- and *p*-substituted aromatic rings, followed by carbonylative esterification with *m*- and *p*-substituted anisol derivatives were carried out in a combinatorial manner. Acid cleavage from the polymer-support provided the conjugated aromatic ring systems **1** and **2**, which are the core parts of rodlike liquid crystals.

Introduction

Combinatorial synthesis is an effective method for the generation of a diverse library of small molecules, and it has been used not only in the field of drug discovery[1] but also in organic materials,[2] that is, liquid crystals.[3–9] Palladium-catalyzed coupling reactions[10] on a polymer-support are versatile methods for the synthesis of a variety of compounds.[11] We have recently demonstrated that two types of palladium-catalyzed carbonylation,chemoselective esterification and macrolactonization, were sequentially performed in a solid-phase combinatorial synthesis to provide a 122-member macrosphelide library.[12] A palladium-catalyzed coupling reaction has also been used for the synthesis of an organic material library in solution phase[3] and on solid-phase supports.[2,4,5] Here we report six types of palladium-catalyzed coupling reactions and sequential coupling by carbonylative esterification on a polymer support.[13]

Conjugated aromatic ring systems **1** and **2** in Figure 1 are the core of rodlike liquid crystals. Three aromatic rings are conjugated through connecting groups X (double bond, single bond, triple bond, ester, carbonyl, and enonyl) and Y (O–C═O, C═O–O). An electron-withdrawing group is attached as a left-side terminal (T), and an alkoxy chain (OR) is on the right-side tail.[14] A combinatorial synthesis based on the substitution patterns of the benzene rings and various functional groups, X and Y, will give a variety of rodlike liquid-crystal molecules. To efficiently synthesize **1** and **2**, we investigated sequential palladium-catalyzed coupling reactions on a polymer support as follows (Scheme 1): (i) immobilization of substituted benzoic acids **4** onto Rink-amino Synphase Lanterns (**3**);[15] (ii) palladium-catalyzed coupling of **5** with iodobenzene derivatives **6** (P = THP, Tf) by (a) Mizoroki–Heck reaction,[16] (b) Migita–Stille reaction,[17] (c) Sonogashira reaction,[18] (d) carbonylative esterification,[19] (e) carbonylative Migita–Stille reaction,[20,21] and (f) carbonylative Sonogashira reaction;[22] (iii) carbonylative esterification of **7** (P = H) with methoxyphenyl iodide **9** (W = I) and that of **8** (P = Tf) with methoxyphenol **9** (W = OH); and (iv) acid cleavage from the polymer-support would afford amides **1** and **2**.

Results and Discussion

Substituted benzoic acid derivatives, **4**, encoded by colored cogs were quantitatively loaded on Rink-amino Synphase Lanterns, **3** (37.0 μmol/D-series, 1356–13A), using DIC–HOBt in DMF (Scheme 1).[15] We initially optimized the reaction conditions of six types of palladium-catalyzed coupling reactions of the polymer-supported **5**{*1*}, **5**{*3*}, **5**{*5*}, and **5**{*7*} with iodophenyl THP ether *p*-**6**{*1*} or *m*-**6**{*2*} and iodophenyl triflate *p*-**6**{*3*} or *m*-**6**{*4*} in parallel (see Figure 2). The products were analyzed by LC–MS (UV 254 nm) after acid cleavage (50% TFA–CH_2Cl_2) from the polymer support (Table 1).

The Mizoroki–Heck reaction of styrene **5**{*1*} with *para*-substituted phenyl iodide **6**{*1*} efficiently proceeded in the presence of $Pd(dba)_2$ or $Pd(dba)_2$-P(*o*-tol)$_3$ (10 mM) in DMF at 80 °C, leading to stilbene *p*-*p*-**7a**{*1*,*1*} (P = THP) (entries 4 and 5). The use of palladium catalysts, including PPh_3, resulted in low purities (entries 1 and 2) because the phenyl group in PPh_3 was partially introduced to **5**{*1*}.[23] The reaction catalyzed by $Pd(OAc)_2$ induced an over-reaction (entry 3). Next, the reaction of **5**{*1*} with iodophenyl triflate *p*-**6**{*3*} was investigated. Selective activation of aryl iodide in the presence of an aryl triflate moiety is required. It has been reported that Negishi coupling[10] of **6**{*3*} by selective activation of the iodo group in the presence of a triflate moiety was achieved at room temperature using $Pd(dba)_2$ with PPh_3 as an additional ligand.[24] Then, the remaining aryl triflate underwent the second Negishi coupling under heating using $Pd(dba)_2$ with a bidentate ligand, such as 1,1′-bis(diphenylphosphono)ferrocene. In contrast, Mizoroki–Heck reaction of **5**{*1*} with **6**{*3*} was selectively performed

* To whom correspondence should be addressed. Phone: (+81) 3-5734-2120.Fax: +81 3-5734-2884. E-mail: ttak@apc.titech.ac.jp.
[†] Department of Applied Chemistry.
[‡] Department of Organic and Polymeric Materials.

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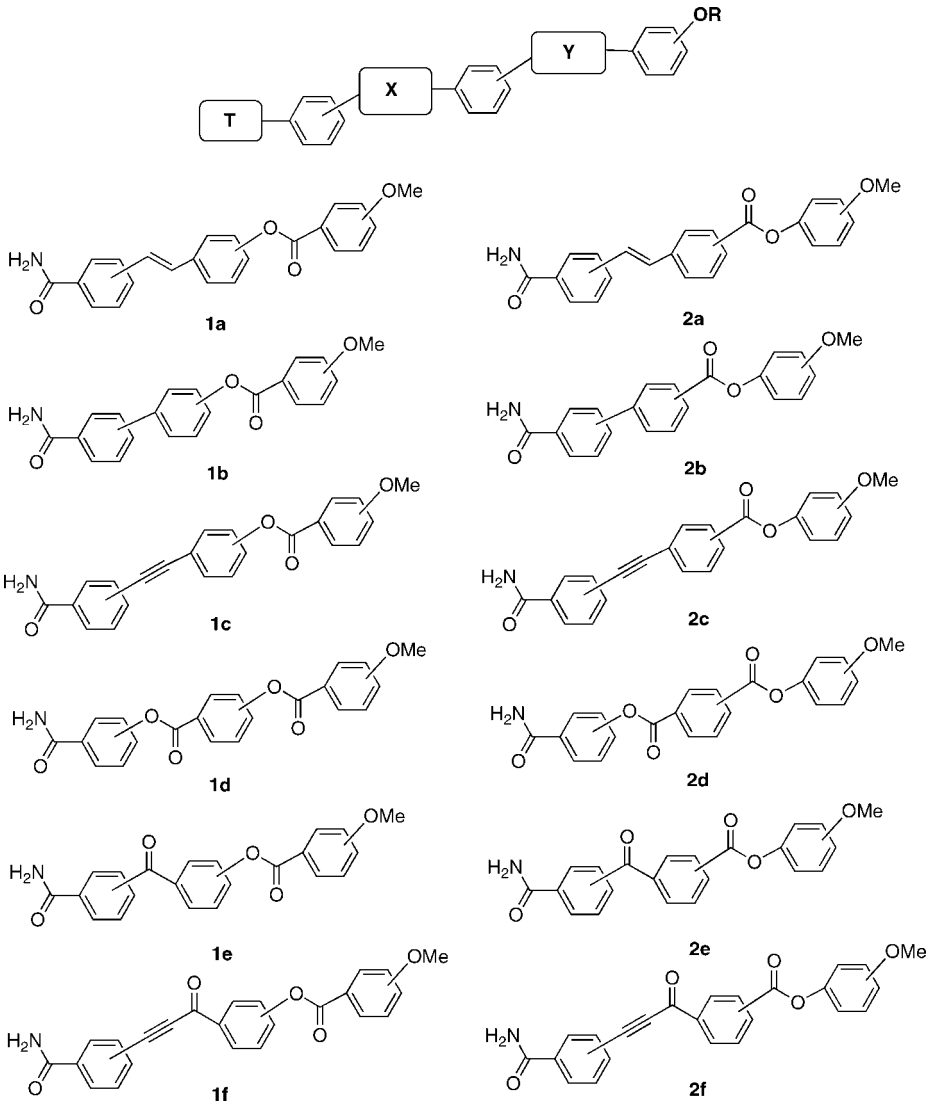


Figure 1. Various conjugated arene systems **1** and **2**.

at 80 °C in the presence of $Pd(dba)_2$ without additional phosphine ligand to afford *p-p*-**8a**{*1*,*3*} (P = Tf) (entry 4). The use of phosphine ligands was not effective and resulted in low conversions (entries 1, 2, and 5).

Migita–Stille coupling of phenylstannane **5**{*3*} with **6**{*1*} using $Pd(dba)_2$–$AsPh_3$ (80 °C) provided the biphenyl product *p-p*-**7b**{*3*,*1*} in 88% purity (entry 10). When PPh_3 was used as a ligand, the phenyl group in PPh_3 was coupled as was observed in the Mizoroki–Heck reaction described above (entries 6 and 7).[23] The product, 4,4′-biphenyldicarboxamide, produced by homo coupling on the polymer support was also observed (4–10%) in all reaction conditions. The reaction with iodophenyl triflate **6**{*3*} was efficiently catalyzed by $Pd(OAc)_2$, $Pd(dba)_2$, or $Pd(dba)_2$–$AsPh_3$ (entries 8, 9, and 10) to provide *p-p*-**8b**{*3*,*3*}. Interestingly, the use of $Pd(PPh_3)_4$ resulted in low conversion (entry 6), as shown in the Mizoroki–Heck reaction (entry 1).

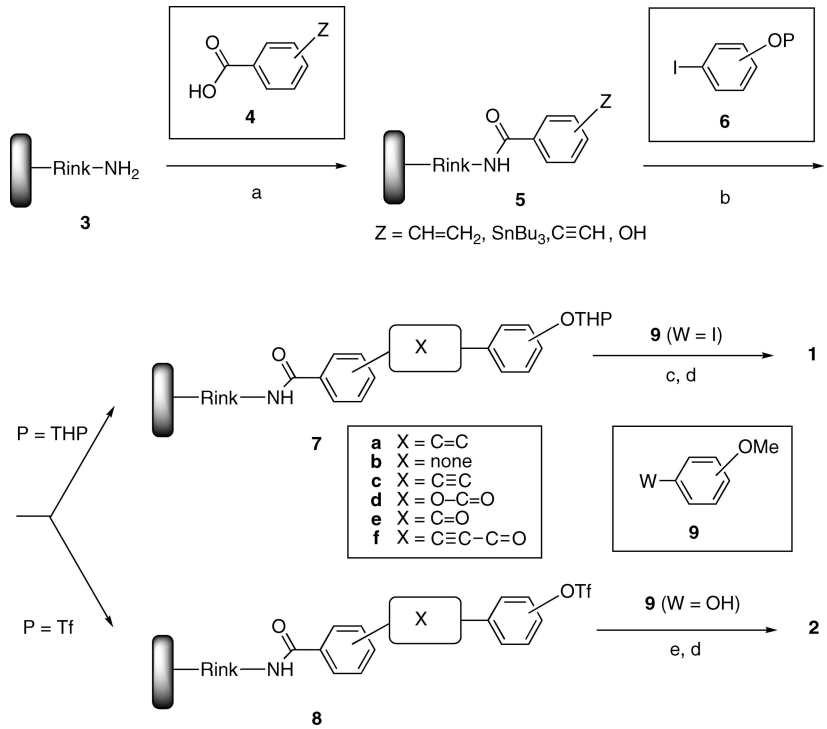
Sonogashira coupling of phenylacetylene **5**{*5*} with *meta*-substituted phenyl iodide **6**{*2*} was performed using $Pd(PPh_3)_4$ or $PdCl_2(PPh_3)_2$ at room temperature in the presence of CuI to afford diphenylacetylene *p-m*-**7c**{*5*,*2*} (entries 11 and 12). In the absence of CuI, a complex mixture was obtained (entries 13, 14, and 15). $Pd(PPh_3)_4$ also effectively catalyzed Sonogashira coupling of **5**{*5*} with *meta*-substituted iodophenyl triflate **6**{*4*} at room temperature to provide *p-m*-**8c**{*5*,*4*} in 96% purity (entry 11).

Carbonylative esterification of phenol **5**{*7*} with phenyl iodide **6**{*1*} was achieved in our standard conditions reported previously[19] ($Pd(PPh_3)_4$/CO (15 atm)/NEt_3/DMAP/80 °C) to give phenyl benzoate *p-p*-**7d**{*7*,*1*} in 94% purity (entry 16). The reaction of **5**{*7*} with iodophenyl triflate **6**{*3*} also gave *p-p*-**8d**{*7*,*3*} in 75% purity under the same reaction conditions (entries 16).

Carbonylative Stille couplings of both **5**{*3*} with **6**{*1*} and **5**{*3*} with **6**{*3*} proceeded efficiently in the presence of $Pd(dba)_2$–$AsPh_3$ at 80 °C under CO (15 atm), leading to diphenyl ketones *p-p*-**7e**{*3*,*1*} and *p-p*-**8e**{*3*,*3*}, respectively (entry 21). None of the biphenyl product was observed.

Carbonylative Sonogashira coupling of **5**{*5*} with *meta*-substituted phenyl iodide **6**{*2*} was effectively catalyzed by $Pd(PPh_3)_4$ at room temperature under CO (15 atm) in the presence of CuI to provide *p-m*-**7f**{*5*,*2*} (entry 22). In the

Scheme 1. Various Palladium-Catalyzed Coupling Reactions on Polymer-Support[a]



[a] Reaction conditions: (a) benzoic acids (0.2 M), DIC-HOBt (0.2 M), DMF, 12 h; (b) see Table 1; (c) AcOH/THF/H_2O = 3/3/1, 80 °C, 10 h; $Pd(PPh_3)_4$ (0.01 M), DMF, **9** (W = I) (0.5 M), CO (15 atm), NEt_3 (0.5 M), DMAP (0.1 M). 80 °C, 48 h; (d) 50% TFA–CH_2Cl_2, RT, 30 min; (e) $Pd(dba)_2$-dppp (0.01 M), DMF, **9** (W = OH) (0.5 M), CO (15 atm), NEt_3 (0.5 M), DMAP (0.1 M), 80 °C, 48 h.

Table 1. Optimization of Reaction Conditions of Palladium-Catalyzed Coupling Reaction of **5** with **6** on Polymer Support[a]

					P = THP				P = Tf			
entry	**5**	Z in **5**	catalyst	conditions[b]	**6**	**7**	conversion (%)	purity (%)	**6**	**8**	conversion (%)	purity (%)
1	**5**{*1*}	CH=CH_2	$Pd(PPh_3)_4$	a	**6**{*1*}	*p-p*-**7a**{*1,1*}	62	27	**6**{*3*}	*p-p*-**8a**{*1,3*}	<5	5
2	**5**{*1*}	CH=CH_2	$PdCl_2(PPh_3)_2$	a	**6**{*1*}	*p-p*-**7a**{*1,1*}	96	50	**6**{*3*}	*p-p*-**8a**{*1,3*}	<5	<5
3	**5**{*1*}	CH=CH_2	$Pd(OAc)_2$	a	**6**{*1*}	*p-p*-**7a**{*1,1*}	>99	80	**6**{*3*}	*p-p*-**8a**{*1,3*}	80	64
4	**5**{*1*}	CH=CH_2	$Pd(dba)_2$	a	**6**{*1*}	*p-p*-**7a**{*1,1*}	97	82	**6**{*3*}	*p-p*-**8a**{*1,3*}	86	75
5	**5**{*1*}	CH=CH_2	$Pd(dba)_2$-2P(*o*-tol)$_3$	a	**6**{*1*}	*p-p*-**7a**{*1,1*}	91	87	**6**{*3*}	*p-p*-**8a**{*1,3*}	45	40
6	**5**{*3*}	$SnBu_3$	$Pd(PPh_3)_4$	b	**6**{*1*}	*p-p*-**7b**{*3,1*}	91	<5	**6**{*3*}	*p-p*-**8b**{*3,3*}	13	10
7	**5**{*3*}	$SnBu_3$	$PdCl_2(PPh_3)_2$	b	**6**{*1*}	*p-p*-**7b**{*3,1*}	95	<5	**6**{*3*}	*p-p*-**8b**{*3,3*}	97	77
8	**5**{*3*}	$SnBu_3$	$Pd(OAc)_2$	b	**6**{*1*}	*p-p*-**7b**{*3,1*}	88	76	**6**{*3*}	*p-p*-**8b**{*3,3*}	>99	93
9	**5**{*3*}	$SnBu_3$	$Pd(dba)_2$	b	**6**{*1*}	*p-p*-**7b**{*3,1*}	78	64	**6**{*3*}	*p-p*-**8b**{*3,3*}	>99	92
10	**5**{*3*}	$SnBu_3$	$Pd(dba)_2$-2$AsPh_3$	b	**6**{*1*}	*p-p*-**7b**{*3,1*}	96	88	**6**{*3*}	*p-p*-**8b**{*3,3*}	>99	88
11	**5**{*5*}	CCH	$Pd(PPh_3)_4$	c	**6**{*2*}	*p-m*-**7c**{*5,2*}	>99	90	**6**{*4*}	*p-m*-**8c**{*5,4*}	>99	96
12	**5**{*5*}	CCH	$PdCl_2(PPh_3)_2$	c	**6**{*2*}	*p-m*-**7c**{*5,2*}	>99	89	**6**{*4*}	*p-m*-**8c**{*5,4*}	>99	90
13	**5**{*5*}	CCH	$Pd(OAc)_2$	a	**6**{*2*}	*p-m*-**7c**{*5,2*}	>99	<5	**6**{*4*}	*p-m*-**8c**{*5,4*}	>99	77b
14	**5**{*5*}	CCH	$Pd(dba)_2$	a	**6**{*2*}	*p-m*-**7c**{*5,2*}	>99	<5	**6**{*4*}	*p-m*-**8c**{*5,4*}	>99	87b
15	**5**{*5*}	CCH	$Pd(dba)_2$-2P(*o*-tol)$_3$	a	**6**{*2*}	*p-m*-**7c**{*5,2*}	>99	<5	**6**{*4*}	*p-m*-**8c**{*5,4*}	>99	83b
16	**5**{*7*}	OH	$Pd(PPh_3)_4$	d	**6**{*1*}	*p-p*-**7d**{*7,1*}	94	94	**6**{*3*}	*p-p*-**8d**{*7,3*}	95	75
17	**5**{*3*}	$SnBu_3$	$Pd(PPh_3)_4$	e	**6**{*1*}	*p-p*-**7e**{*3,1*}	41	30	**6**{*3*}	*p-p*-**8e**{*3,3*}	13	11
18	**5**{*3*}	$SnBu_3$	$PdCl_2(PPh_3)_2$	e	**6**{*1*}	*p-p*-**7e**{*3,1*}	86	82	**6**{*3*}	*p-p*-**8e**{*3,3*}	46	41
19	**5**{*3*}	$SnBu_3$	$Pd(OAc)_2$	e	**6**{*1*}	*p-p*-**7e**{*3,1*}	98	93	**6**{*3*}	*p-p*-**8e**{*3,3*}	>99	93
20	**5**{*3*}	$SnBu_3$	$Pd(dba)_2$	e	**6**{*1*}	*p-p*-**7e**{*3,1*}	96	90	**6**{*3*}	*p-p*-**8e**{*3,3*}	>99	95
21	**5**{*3*}	$SnBu_3$	$Pd(dba)_2$–2$AsPh_3$	e	**6**{*1*}	*p-p*-**7e**{*3,1*}	98	95	**6**{*3*}	*p-p*-**8e**{*3,3*}	>99	98
22	**5**{*5*}	CCH	$Pd(PPh_3)_4$	f	**6**{*2*}	*p-m*-**7f**{*5,2*}	98	95	**6**{*4*}	*p-m*-**8f**{*5,4*}	>99	58
23	**5**{*5*}	CCH	$PdCl_2(PPh_3)_2$	f	**6**{*2*}	*p-m*-**7f**{*5,2*}	95	81	**6**{*4*}	*p-m*-**8f**{*5,4*}	>99	72
24	**5**{*5*}	CCH	$PdCl_2(PPh_3)_2$	g	**6**{*2*}	*p-m*-**7f**{*5,2*}	>99	95	**6**{*4*}	*p-m*-**8f**{*5,4*}	>99	42
25	**5**{*5*}	CCH	$Pd(dba)_2$-2P(*o*-tol)$_3$	h	**6**{*2*}	*p-m*-**7f**{*5,2*}	>99	83	**6**{*4*}	*p-m*-**8f**{*5,4*}		

[a] Conversion and purity were determined by reversed-phase HPLC with peak areas of UV (254 nm) after cleavage from the polymer support with 50% TFA–CH_2Cl_2. The THP group was cleaved under the conditions listed. [b] Reaction conditions: palladium catalyst (0.01 M), DMF (a) **6** (0.2 M), NEt_3 (0.2 M), 80 °C, 24 h; (b) **6** (0.2 M), 80 °C, 24 h; (c) **6** (0.2 M), CuI (0.03 M), NEt_3 (0.2 M), RT, 24 h; (d) **6** (0.5 M), CO (15 atm), NEt_3 (0.5 M), DMAP (0.1 M), 80 °C, 24 h; (e) **6** (0.2 M), CO (15 atm), 80 °C, 24 h; (f) **6** (0.2 M), CO (15 atm), CuI (0.03 M), NEt_3 (0.2 M), RT, 24 h; (g) **6** (0.2 M), CO (15 atm), CuI (0.03 M), NEt_3 (0.2 M), 80 °C, 24 h; (h) **6** (0.2 M), CO (15 atm), NEt_3 (0.2 M), 80 °C, 24 h.

absence of CuI, the reaction also proceeded at 80 °C using $Pd(dba)_2$-P(*o*-tol)$_3$ (entry 25). In the reaction with iodophenyl triflate **6**{*4*}, $PdCl_2(PPh_3)_2$ is more effective than $Pd(PPh_3)_4$ at room temperature, and *p-m*-**8f**{*5,4*} was obtained in 72% purity (entry 23). At 80 °C, however, Sonogashira coupling product *p-m*-**8c**{*5,4*} was partially formed without carbonyl insertion. Therefore, the purity of the desired product *p-m*-**8f**{*5,4*} was only 42% (entry 24).[25]

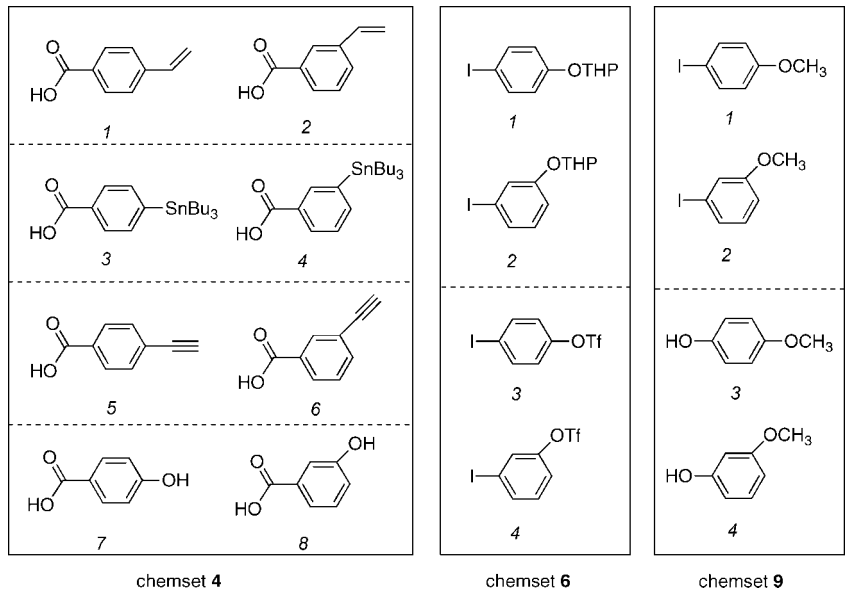


Figure 2. Structures of chemsets **4**, **6**, and **9**.

After the six coupling methods were optimized on solid-phase supports, we next investigated the diversity of these methods for the syntheses of various conjugated aromatic systems. A combinatorial synthesis of **1** and **2** (R = Me), based on the building blocks **4**, **6**, and **9** shown in Figure 2 was carried out by a split-and-mix method using the Synphase Lanterns with colored cogs.[15] Six coupling reactions of the two respective *para*- and *meta*-substituted units, **4**{*1–8*}, with four phenyl iodides, **6**{*1–4*}, were performed under the optimized reaction conditions described above (see Experimental Section). The twenty-four polymer-supported THP ethers, **7a–f** prepared from **6**{*1*} and **6**{*2*} were combined and their THP groups were removed in a single flask (AcOH/THF/H_2O = 3/3/1, 80 °C, 10 h). After the Lanterns were split into two glass tubes, the tubes were placed separately in autoclaves. Carbonylation of the resulting polymer-supported phenols with *p*-iodoanisole **9**{*1*} and *m*-iodoanisole **9**{*2*} was performed in the presence of $Pd(PPh_3)_4$ under 15 atm of CO for 48 h. Acid cleavage from the polymer support, in parallel, provided forty-eight amides **1** (Table 2). In the same way, twenty-four polymer-supported aryl triflates **8a–f** prepared from **6**{*3*} and **6**{*4*} underwent carbonylation with *p*-methoxyphenol **9**{*3*} and *m*-methoxyphenol **9**{*4*} at 80 °C in 48 h in the presence of $Pd(dba)_2$–dppp.[26] Acid cleavage afforded another forty-eight amides **2**. The purities of the products were determined by reversed-phase HPLC (UV at 254 nm) (Table 2). None of diarylynones **1f** and **2f** were obtained in all substitution patterns, although the first coupling reaction was achieved in **7f**{*5,2*} (Table 1). The diarylynone in **7f** would probably react under carbonylation conditions, resulting in a complex mixture. In the synthesis of **2d**, it was found that *trans*-esterification of **2d** with methoxyphenol occurred under the carbonylation conditions resulting in the formation of **5**{*7*} and **5**{*8*} (Z = OH), whereas **1d** remained under the carbonylation conditions. Interestingly, all combinations of *para*- and *meta*- substitution patterns were compatible in the other examples.[27]

Conclusion

In summary, we have demonstrated that palladium-catalyzed coupling reactions on polymer supports afforded various core parts of rodlike liquid crystals. In the synthesis, various functionalized benzene derivatives, **4**, bearing vinyl, tributylstannyl, ethynyl, and hydroxy groups were loaded on a polymer support, and those underwent palladium-catalyzed coupling reactions with aryl iodide derivatives **6**, even though a triflate moiety was attached to the phenyl ring. Sequentially, the carbonylative esterification of the polymer-supported conjugated phenols and aryl triflates was achieved. Although diarylynones **1f** and **2f** were not formed and **2d** underwent transesterification under the reaction conditions, **1a–e**, **2a–c**, and **2e** were synthesized in all *para*- and *meta*-substituted patterns. These solid-phase sequential coupling methods will be applied to the synthesis of rodlike liquid crystals.

Experimental Section

^{1}H spectra were recorded on JEOL Model ECP-400 (400 MHz) spectrometer. Chemical shifts are reported in parts per million (ppm) from tetramethylsilane with the solvent resonance as the internal standard (DMSO-d_6, δ 2.50). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and assignment. ^{13}C NMR spectra were recorded on JEOL Model ECP-400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million with the solvent resonance as an internal standard (DMSO-d_6, δ 39.6). Mass spectra (ESI-TOF) were measured on an Applied BioSystems Mariner TK3500 Biospectrometry Workstation mass spectrometer. Reversed-phase HPLC analysis was performed on Hewlett Packard HP-1100 series system with Waters Symmetry (C18, 5 μm, 4.6 × 50 mm, flow rate 1.0

Table 2. Palladium-Catalyzed Sequential Coupling Reactions of **4**, **6**, And **9** on a Polymer Support[a]

	1a	purity (%)	RT (min)	**1b**	purity (%)	RT (min)	**1c**	purity (%)	RT (min)
p-p-p	{*1,1,1*}	73	5.02	{*3,1,1*}	73	4.60	{*5,1,1*}	74	5.05
p-p-m	{*1,1,2*}	80	5.05	{*3,1,2*}	66	4.62	{*5,1,2*}	67	5.15
p-p-m	{*1,2,1*}	84	4.99	{*3,2,1*}	80	4.58	{*5,2,1*}	88	5.11
p-m-m	{*1,2,2*}	82	5.05	{*3,2,2*}	83	4.64	{*5,2,2*}	81	5.15
m-p-p	{*2,1,1*}	85	5.05	{*4,1,1*}	69	4.70	{*6,1,1*}	75	5.11
m-p-m	{*2,1,2*}	82	5.11	{*4,1,2*}	71	4.76	{*6,1,2*}	71	5.05
m-m-p	{*2,2,1*}	84	5.08	{*4,2,1*}	82	4.64	{*6,2,1*}	86	4.99
m-m-m	{*2,2,2*}	84	4.99	{*4,2,2*}	79	4.76	{*6,2,2*}	78	5.05
	1d	purity (%)	RT (min)	**1e**	purity (%)	RT (min)	**1f**	purity (%)	RT (min)
p-p-p	{*7,1,1*}	82	4.82	{*3,1,1*}	86	4.52	{*5,1,1*}	<10	
p-p-m	{*7,1,2*}	81	4.84	{*3,1,2*}	81	4.55	{*5,1,2*}	<10	
p-p-m	{*7,2,1*}	66	4.76	{*3,2,1*}	84	4.49	{*5,2,1*}	<10	
p-m-m	{*7,2,2*}	59	4.70	{*3,2,2*}	80	4.55	{*5,2,2*}	<10	
m-p-p	{*8,1,1*}	87	4.82	{*4,1,1*}	86	4.52	{*6,1,1*}	<10	
m-p-m	{*8,1,2*}	88	4.76	{*4,1,2*}	84	4.58	{*6,1,2*}	<10	
m-m-p	{*8,2,1*}	85	4.64	{*4,2,1*}	87	4.52	{*6,2,1*}	<10	
m-m-m	{*8,2,2*}	79	4.76	{*4,2,2*}	88	4.55	{*6,2,2*}	<10	
	2a	purity (%)	RT (min)	**2b**	purity (%)	RT (min)	**2c**	purity (%)	RT (min)
p-p-p	{*1,3,3*}	74	5.95	{*3,3,3*}	84	5.70	{*5,3,3*}	88	6.20
p-p-m	{*1,3,4*}	70	6.02	{*3,3,4*}	79	5.75	{*5,3,4*}	90	6.28
p-p-m	{*1,4,3*}	51	6.11	{*3,4,3*}	80	5.75	{*5,4,3*}	87	6.22
p-m-m	{*1,4,4*}	57	5.99	{*3,4,4*}	81	5.81	{*5,4,4*}	91	6.32
m-p-p	{*2,3,3*}	79	6.05	{*4,3,3*}	83	5.78	{*6,3,3*}	90	6.22
m-p-m	{*2,3,4*}	77	6.05	{*4,3,4*}	83	5.75	{*6,3,4*}	92	6.17
m-m-p	{*2,4,3*}	60	6.11	{*4,4,3*}	81	5.75	{*6,4,3*}	94	6.11
m-m-m	{*2,4,4*}	62	6.17	{*4,4,4*}	78	5.81	{*6,4,4*}	90	6.17
	2d	purity (%)	RT (min)	**2e**	purity (%)	RT (min)	**2f**	purity (%)	RT (min)
p-p-p	{*7,3,3*}	<10		{*3,3,3*}	91	5.62	{*5,3,3*}	<10	
p-p-m	{*7,3,4*}	<10		{*3,3,4*}	92	5.64	{*5,3,4*}	<10	
p-p-m	{*7,4,3*}	<10		{*3,4,3*}	94	5.52	{*5,4,3*}	<10	
p-m-m	{*7,4,4*}	<10		{*3,4,4*}	90	5.48	{*5,4,4*}	<10	
m-p-p	{*8,3,3*}	<10		{*4,3,3*}	96	5.58	{*6,3,3*}	<10	
m-p-m	{*8,3,4*}	<10		{*4,3,4*}	89	5.58	{*6,3,4*}	<10	
m-m-p	{*8,4,3*}	<10		{*4,4,3*}	92	5.67	{*6,4,3*}	<10	
m-m-m	{*8,4,4*}	<10		{*4,4,4*}	93	5.62	{*6,4,4*}	<10	

[a] Purity was determined by reversed-phase HPLC with peak areas detected by UV (254 nm).

mL min^{-1}) and a linear gradient of 10–90% of MeOH in water (0–5 min) and 90% MeOH in water (5–7 min) using 20 mM of ammonium acetate. Peak areas were integrated with UV at 254 nm.

General Procedure for the Preparation of Polymer-Supported Benzoate Derivative 5. Fmoc-protected Rink amide Synphase lanterns (96 lanterns, D series; loading, 37.0 μmol; batch no., 1356-13A) were treated with a solution of 20% piperidine in DMF. After they were left at room temperature for 30 min, the lanterns were washed with DMF (5 min × 3) and dichlolomethane (5 min × 3) and were dried in vacuo to provide Rink-amino lanterns **3**, which were divided into eight fractions and encoded by color cogs.

The above-mentioned lanterns, **3**, were dipped into a mixture of benzoic acid derivative **4** (0.2 M), 1-hydroxybenzotriazole (HOBt) (0.24 M), and diisopropylethylamine (DIEA) (0.20 M) in DMF . After they were agitated at room temperature for 12 h, the lanterns were sequentially washed with DMF (5 min × 3), THF (5 min × 3), [NaOH in MeOH (0.10 M)/THF (5 min × 3) in case of **4**{*7*} and **4**{*8*}], MeOH (5 min × 3), and dichloromethane (5 min × 3) and were dried to provide polymer-supported benzoate **5**.

General Procedure for the Washing after Palladium-Catalyzed Reactions. The lanterns were sequentially washed with DMF (5 min × 3), THF (5 min × 3), and dichloromethane (5 min × 3) and dried in vacuo.

General Procedure for the Acid Cleavage and Product Analysis. The lanterns were treated with 50% TFA in dichloromethane for 30 min. After removal of the solvent, the products were analyzed by LC-MS (UV 254 nm).

General Procedure for the Mizoroki–Heck Reaction of 5{*1–2*} with 6{*1–2*}. The lanterns **5**{*1–2*} were treated with **6**{*1*} or **6**{*2*} (0.2 M), $Pd(dba)_2$ (10 mM), tri-*o*-tolylphosphine (20 mM), and triethylamine (0.20 M) in DMF at 80 °C for 24 h. The lanterns were washed according to the general method.

General Procedure for the Mizoroki–Heck Reaction of 5{*1–2*} with 6{*3–4*}. The lanterns **5**{*1–2*} were treated with **6**{*3*} or **6**{*4*} (0.2 M), $Pd(dba)_2$ (10 mM), and triethylamine (0.20 M) in DMF at 80 °C for 24 h. The lanterns were washed according to the general method.

General Procedure for the Migita–Stille Reaction of 5{*3–4*} with 6{*1–2*}. The lanterns **5**{*3–4*} were treated with **6**{*1*} or **6**{*2*} (0.2 M), $Pd(dba)_2$ (10 mM), and triphenylarsine (20 mM) in DMF at 80 °C for 24 h. The lanterns were washed according to the general method.

General Procedure for the Migita–Stille Reaction of 5{*3–4*} with 6{*3–4*}. The lanterns **5**{*3–4*} were treated with **6**{*3*} or **6**{*4*} (0.2 M) and $Pd(dba)_2$ (10 mM) in DMF at 80 °C for 24 h. The lanterns were washed according to the general method.

General Procedure for the Sonogashira Reaction of 5{*5–6*} with 6{*1–4*}. The lanterns **5**{*5–6*} were treated with **6**{*1*}, **6**{*2*}, **6**{*3*}, or **6**{*4*} (0.2 M), $Pd(PPh_3)_4$ (10 mM), CuI (30 mM), and triethylamine (0.2 M) in DMF at room temperature for 24 h. The lanterns were washed according to the general method.

General Procedure for Carbonylative Esterification of 5{*7–8*} with 6{*1–4*}. The lanterns **5**{*7–8*} were treated with **6**{*1*}, **6**{*2*}, **6**{*3*}, or **6**{*4*} (0.5 M), $Pd(PPh_3)_4$ (10 mM), 4-(dimethylamino)pyridine (DMAP) (0.1 M), and triethylamine (0.5 M) in DMF at 80 °C under CO (15 atm) for 24 h. The lanterns were washed according to the general method.

General Procedure for Carbonylative Migita–Stille Reaction of 5{*3–4*} with 6{*1–4*}. The lanterns **5**{*3–4*} were treated with **6**{*1*}, **6**{*2*}, **6**{*3*}, or **6**{*4*} (0.2 M), $Pd(dba)_2$ (10 mM), and triphenylarsine (20 mM) in DMF at 80 °C under CO (15 atm) for 24 h. The lanterns were washed according to the general method.

General Procedure for Carbonylative Sonogashira Reaction of 5{*5–6*} with 6{*1–2*}. The lanterns **5**{*5–6*} were treated with **6**{*1*} or **6**{*2*} (0.2 M), $Pd(PPh_3)_4$ (10 mM), CuI (30 mM), and triethylamine (0.2 M) in DMF at room temperature under CO (15 atm) for 24 h. The lanterns were washed according to the general method.

General Procedure for Carbonylative Sonogashira Reaction of 5{*5–6*} with 6{*3–4*}. The lanterns **5**{*5–6*} were treated with **6**{*3*} or **6**{*4*} (0.2 M), $PdCl_2(PPh_3)_2$ (10 mM), CuI (30 mM), and triethylamine (0.2 M) in DMF at room temperature under CO (15 atm) for 24 h. The lanterns were washed according to the general method.

General Procedure for Carbonylative Esterification of 7 with Iodoanisole 9{*1–2*}. The lanterns **7** were treated with acetic acid, water, and THF (3/1/3) at 80 °C for 10 h. The lanterns were washed with THF (5 min × 3) and dichloromethane (5 min × 3) and dried in vacuo. Then polymer-supported phenols were treated with **9**{*1*} or **9**{*2*} (0.5 M), $Pd(PPh_3)_4$ (10 mM), 4-(dimethylamino)pyridine (DMAP) (0.1 M), and triethylamine (0.5 M) in DMF at 80 °C under CO (15 atm) for 48 h. The lanterns were washed according to the general method.

General Procedure for Carbonylative Esterification of 8 with Methoxyphenol 9{*3–4*}. The polymer-supported triflates **8** were treated with **9**{*3*} or **9**{*4*} (0.5 M), $Pd(dba)_2$ (10 mM), 1,3-bis(diphenylphosphino)propane (10 mM), 4-(dimethylamino)pyridine (DMAP) (0.1 M), and triethylamine (0.5 M) in DMF at 80 °C under CO (15 atm) for 48 h. The lanterns were washed according to the general method.

Selected Spectral Data. 1a{*2,1,1*}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.86 (s, 3H, OCH_3), 7.11 (d, 2H, J = 8.7 Hz, aromatic), 7.27 (d, 2H, J = 8.7 Hz, aromatic), 7.29 (d, 1H, J = 16.4 Hz, alkene), 7.37 (d, 1H, J = 16.4 Hz, alkene), 7.45 (t, 1H, J = 7.7 Hz, aromatic), 7.69 (d, 2H, J = 8.7 Hz, aromatic), 7.71 (d, 1H, J = 7.7 Hz, aromatic), 7.75 (d, 1H, J = 7.7 Hz, aromatic), 8.03 (brs, 2H, NH), 8.08 (d, 2H, J = 8.7 Hz, aromatic), 8.13 (s, 1H, aromatic). ^{13}C NMR (100 MHz, DMSO-d_6): δ 56.2, 114.8, 121.5, 122.9, 125.8, 127.2, 128.1, 128.6, 128.9, 129.2, 129.9, 132.6, 135.2, 135.3, 137.6, 150.8, 164.3, 164.7, 168.3; MS(ESI-TOF): *m*/*z* 374.2 $[M + H]^+$.

1b{*3,1,2*}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.85 (s, 3H, OCH_3), 7.32 (d, 1H, J = 7.2 Hz, aromatic), 7.40 (d, 2H, J = 7.7 Hz, aromatic), 7.53 (t, 1H, J = 7.2 Hz, aromatic), 7.62 (s, 1H, aromatic), 7.74 (d, 1H, J = 7.2 Hz, aromatic), 7.78 (d, 2H, J = 8.2 Hz, aromatic), 7.81 (d, 2H, J = 7.7 Hz, aromatic), 7.97 (d, 2H, J = 8.2 Hz, aromatic), 8.03 (brs, 2H, NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 56.0, 114.9, 120.7, 122.7, 123.0, 127.0, 127.2, 128.6, 128.7, 130.8, 133.7, 137.6, 142.4, 151.1, 160.0, 165.0, 168.0. MS(ESI-TOF): *m*/*z* 348.1 $[M + H]^+$.

1c{*5,1,1*}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.86 (s, 3H, OCH_3), 7.12 (d, 2H, J = 8.7 Hz, aromatic), 7.34 (d, 2H, J = 8.7 Hz, aromatic), 7.63 (d, 2H, J = 8.2 Hz, aromatic), 7.66 (d, 2H, J = 8.7 Hz, aromatic), 7.91 (d, 2H, J = 8.2 Hz, aromatic), 8.05 (s, 2H, NH), 8.08 (d, 2H, J = 8.7 Hz, aromatic). ^{13}C NMR (100 MHz, DMSO-d_6): δ 56.2, 89.4, 91.1, 114.9, 120.0, 121.2, 123.2, 125.5, 128.4, 131.8, 132.6, 133.3, 134.7, 151.6, 164.4, 164.5, 167.6. MS(ESI-TOF): *m*/*z* 372.1 $[M + H]^+$.

1d{*7,1,1*}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.87 (s, 3H, OCH_3), 7.13 (d, 2H, J = 8.7 Hz, aromatic), 7.38 (d, 2H, J = 8.7 Hz, aromatic), 7.52 (d, 2H, J = 8.7 Hz, aromatic), 7.96 (d, 2H, J = 8.7 Hz, aromatic), 8.03 (brs, 2H, NH), 8.11 (d, 2H, J = 8.7 Hz, aromatic), 8.22 (d, 2H, J = 8.7 Hz, aromatic). ^{13}C NMR (100 MHz, DMSO-d_6): δ 56.2, 114.9, 121.0, 122.3, 123.3, 126.8, 129.6, 132.1, 132.6, 132.8, 153.3, 155.7, 164.2, 164.3, 164.5, 167.6. MS(ESI-TOF): *m*/*z* 392.1 $[M + H]^+$.

1e{*3,1,1*}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.87 (s, 3H, OCH_3), 7.12 (d, 2H, J = 8.7 Hz, aromatic), 7.47 (d, 2H, J = 8.7 Hz, aromatic), 7.79 (d, 2H, J = 8.2 Hz, aromatic), 7.85 (d, 2H, J = 8.7 Hz, aromatic), 8.02 (d, 2H, J = 8.2 Hz, aromatic), 8.10 (d, 2H, J = 8.7 Hz, aromatic), 8.16 (brs, 2H, NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 56.2, 114.9, 121.1, 122.9, 128.2, 129.9, 132.0, 132.7, 134.7, 138.2, 139.7, 154.8, 164.3, 164.5, 167.7, 195.0. MS(ESI-TOF): *m*/*z* 376.1 $[M + H]^+$.

2a{*2,3,3*}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.77 (s, 3H, OCH_3), 6.99 (d, 2H, J = 8.7 Hz, aromatic), 7.19 (d, 2H, J = 8.7 Hz, aromatic), 7.41–7.48 (m, 2H, aromatic and alkene), 7.52 (d, 1H, J = 16.4 Hz, alkene), 7.77 (d, 1H, J = 8.2 Hz, aromatic), 7.80 (d, 1H, J = 8.2 Hz, aromatic), 7.82 (d, 2H, J = 8.7 Hz, aromatic), 8.03 (brs, 2H, NH), 8.11 (d, 2H, J = 8.7 Hz, aromatic), 8.18 (s, 1H, aromatic). ^{13}C NMR (100 MHz, DMSO-d_6) δ 56.0, 115.0, 123.2, 123.4, 126.3, 127.4, 128.3, 128.6, 129.3, 130.3, 130.8, 131.6, 135.4, 137.1, 142.8, 144.5, 157.5, 165.2, 168.2. MS(ESI-TOF): *m*/*z* 374.1 $[M + H]^+$.

2c{*6,3,3*}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.76 (s, 3H, OCH_3), 6.99 (d, 2H, J = 8.7 Hz, aromatic), 7.21 (d, 2H, J = 8.7 Hz, aromatic), 7.54 (t, 1H, J = 8.2 Hz, aromatic), 7.74 (d, 1H, J = 8.2 Hz, aromatic), 7.77 (d, 2H, J = 8.2 Hz, aromatic), 7.93 (d, 1H, J = 8.2 Hz, aromatic), 8.11 (brs, 3H, NH, aromatic), 8.14 (d, 2H, J = 8.2 Hz, aromatic). ^{13}C NMR (100 MHz, DMSO-d_6): δ 56.0, 89.4, 92.6, 115.0,

122.2, 123.2, 127.9, 129.0, 129.5, 130.6, 131.1, 132.4, 134.6, 135.4, 144.4, 157.6, 164.8, 167.4. MS(ESI-TOF): *m*/*z* 372.1 $[M + H]^+$.

2e{*3*,*3*,*3*}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.77 (s, 3H, OCH_3), 7.00 (d, 2H, $J = 9.2$ Hz, aromatic), 7.23 (d, 2H, $J = 9.2$ Hz, aromatic), 7.82 (d, 2H, $J = 8.2$ Hz, aromatic), 7.91 (d, 2H, $J = 8.2$ Hz, aromatic), 8.03 (d, 2H, $J = 8.2$ Hz, aromatic), 8.18 (brs, 2H, NH), 8.26 (d, 2H, $J = 8.2$ Hz, aromatic). ^{13}C NMR (100 MHz, DMSO-d_6): δ 56.0, 115.1, 123.2, 128.3, 130.2, 130.5, 132.9, 138.6, 139.0, 141.6, 144.4, 157.7, 164.8, 167.6, 195.5. MS(ESI-TOF): *m*/*z* 376.1 $[M + H]^+$.

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(25) Carbonylative Heck reaction of **5**{*1*} with **6**{*1*} did not proceed under 15 atm of CO.
(26) Addition of the bidentate ligand, dppe or dppf, to $Pd(dba)_2$ was effective for the carbonylation of **7e** (P = Tf) but not for the carbonylation of **7a** (P = Tf) (<20% conversion).
(27) All products were determined by LC/MS.^{1}H and^{13}C NMR spectra for seven compounds selected were good agreement with their structures.

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