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Synthesis of 1-aryl-1,3-diyne and 2-aryl-1,1-dialkynylethene from the Sonogashira reactions of 2-aryl-1,1-dibromoethene

Hee Bong Lee, Dal Ho Huh, Joon Seok Oh, Gwan-Hong Min, Byung Hyun Kim, Dong Hwal Lee, Jae Kwang Hwang and Young Gyu Kim*

School of Chemical Engineering, College of Engineering, Seoul National University, Seoul 151-744, South Korea

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Abstract—Both 1-aryl-1,3-diyne and 2-aryl-1,1-dialkynylethene were produced from the Sonogashira reactions of 2-aryl-1,1-dibromoethene with 1-alkyne. The ratio of the products varied according to the reaction conditions. The coupling reactions in benzene afforded the 2-aryl-1,1-dialkynylethene as a major product and no 1-aryl-1,3-diyne was isolated. The 1-aryl-1,3-diyne could be obtained in DMF in acceptable yields. When amines were used as a reaction solvent, the coupling reaction gave the 2-aryl-1,1-dialkynylethene (20%) and the conjugated enyne (68%) in diisopropylamine, whereas only the 1-aryl-1,3-diyne was isolated in piperidine in 56% yield.

1. Introduction

As part of a research program directed toward the synthesis of hyperbranched polymers with electroluminescent properties, a novel AB_2 type monomer **1** with a carboxylic acid end group (R=H) was designed to overcome the low yield and the low molecular weight of the polymer product **2** as reported in the previous study (Fig. 1).[1] It would be much easier to determine the degree of branching of **2** just by titration of the acidic groups.

However, an unexpected 1,3-diyne **4** was obtained as a minor product after purification[2] when the cross-coupling reaction of dibromide **3** with 10-undecynoate was carried out to give the desired monomer, 2-aryl-1,1-dialkynylethene **1,** under the typical Sonogashira reaction conditions

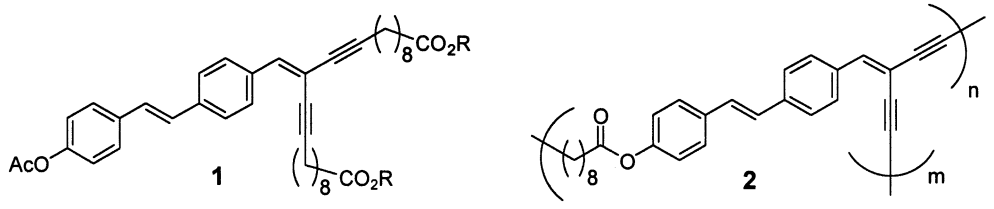
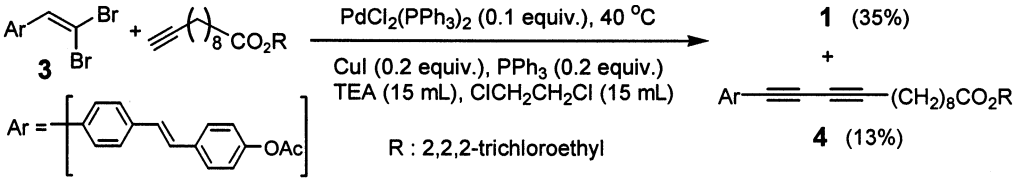


Figure 1. Structures of monomer **1** and polymer **2**.



Scheme 1. Results from the initial Sonogashira reaction.

Keywords: coupling reactions; diyne; enyne; palladium and compounds.
* Corresponding author. Tel.: +82-2-880-8347, Fax: +82-2-885-6989; e-mail: ygkim@plaza.snu.ac.kr

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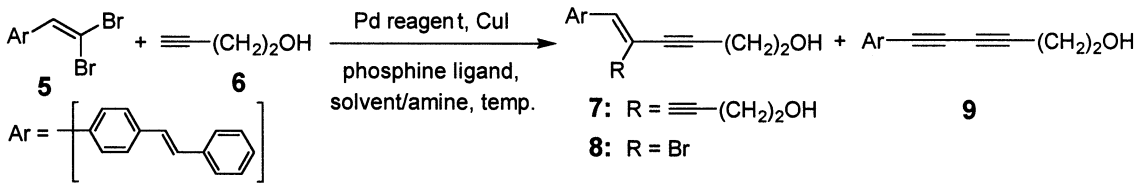


Scheme 2. The model Sonogashira reactions in the present study. See Experimental and the corresponding Tables for the detailed reaction conditions.

Table 1. Effect of the solvents on the Sonogashira reactions.

entry	time (h)	solvent	**5**	yield (%)		
			(% recovery)	**7**	**8**	**9**
1	5	$PhCH_3$	–	37	50	–
2	2	benzene	–	60	15	–
3[a]	0.7	benzene	–	75	–	–
4	20	$ClCH_2CH_2Cl$	18	42	10	–
5	4	THF	–	40	27	–
6	5	EtOAc	–	28	43	–
7	20	acetone	60	10	–	–
8	10	CH_3CN	22	48	18	9
9	13	DMF	45	–	–	32
10[b]	3.5	DMF	–	–	–	58
11[c]	2	DMF	–	–	–	43
12	20	DMSO	11	8	–	62
13	20	NMP	62	6	–	15
14[b]	6	butanol	–	32	–	28

Reaction conditions: **5** (0.5 mmol), **6** (2.2 equiv.), $PdCl_2(PPh_3)_2$ (10 mol%), PPh_3 (20 mol%), CuI (20 mol%), TEA (4 equiv.), solvent (20 mL) at room temperature.
[a] 4.4 equiv. of alkyne **6** was used in 5 mL of benzene.
[b] Reacted at 70°C.
[c] Reacted at 100°C.

(Scheme 1).[3] Because few studies have been reported on the formation of 1,3-diynes from the Sonogashira reactions of 1,1-dihaloalkenes,[4] we have systematically investigated the Sonogashira cross-coupling reaction conditions of 2-aryl-1,1-dibromoethene with 1-alkyne,[5,6] and report the results as follows.

2. Results and Discussion

2-((*E*)-4-Stilbenyl)-1,1-dibromoethene (**5**), similar in structure to **3,** and commercially available 3-butyn-1-ol (**6**) were chosen as model substrates to reduce complex side reactions and for simple workup. Dibromide **5** was efficiently prepared from the Heck reaction of 4-bromobenzaldehyde with styrene followed by the Wittig-type dibromoolefination reaction[7] as described in the previous report (see Experimental).[1] The standard Pd-catalyzed cross-coupling reaction between **5** and **6** is shown in Scheme 2 and the detailed reaction conditions are shown in the corresponding table.

First, various solvents with different polarity were examined under the reaction conditions as shown in Table 1. The results indicate that the polarity of the solvents has a significant effect on the reaction products. The reaction in the solvents of low polarity afforded the monosubstituted conjugated enyne **8** as well as the desired disubstituted 2-aryl-1,1-dialkynylethene **7**. However, 1-aryl-1,3-diyne **9** was isolated as a major product in highly polar solvents such as DMF or DMSO. The yield of **9** was improved to 58% by reacting at 70°C (entry 10). No reaction occurred in HMPA (not shown). The similar dependence of the products on the polarity of solvents was also described in the Stille reactions of the 1,1-dibromo-1-alkenes with organostannanes.[6a]

The coupling reactions in the present study gave invariably the conjugated diyne byproduct, 3,5-octadiyne-1,8-diol, obtained from the homocoupling of **6** in about 10–15% yield of the amount of **6** used, whose yields are not included in Table 1 and the following Tables 2–6.

The ratio of the (*E*)- and (*Z*)-isomers of **8** was between about 1:2 and 1:4 in other solvents than benzene and toluene, where the (*Z*)-isomer of **8** was exclusively obtained. The stereochemistry of the (*Z*)-isomer was determined by the

Table 2. Effect of the amine solvents on the Sonogashira reactions.

entry	amine	**6**	time	**5**	yield (%)		
	(5 mL)	(equiv.)	(h)	(% recovery)	**7**	**8**	**9**
1	piperidine	2.2	24	–	–	–	56
2	pyrrolidine	2.2	7	48	–	–	20
3	pyrrolidine	2.2	24	–	–	–	10
4	morpholine	2.2	20	77	–	–	12
5	diisopropylamine	2.2	8	5	20	68	–
6	diisopropylamine	4.4	8	–	65	5	–
7[a]	diisopropylamine	5.5	8	–	61	–	–
8	diethylamine	2.2	20	59	–	15	15
9	isopropylamine	2.2	12	55	–	–	37
10	*t*-butylamine	2.2	7	–	32	7	36
11[b]	butylamine	2.2	20	–	–	–	40

Reaction conditions: **5** (0.5 mmol), **6**, $PdCl_2(PPh_3)_2$ (10 mol%), PPh_3 (20 mol%), CuI (20 mol%), amine (5 mL) at room temperature.
[a] $Pd_2(dba)_3$ (10 mol%) was used.
[b] 5 mL of DMF was added because no conversion to the expected products was observed even after 20 h in butylamine only.

Table 3. Effect of the palladium reagents on the Sonogashira reactions.

entry	Pd reagents (10 mol%)	time (h)	**6** (equiv.)	solvent	**5** (% recovery)	yield (%)		
						7	**8**	**9**
1	$PdCl_2(PPh_3)_2$	2	3.3	benzene	–	70	–	–
2	$Pd_2(dba)_3$	2.5	3.3	benzene	–	56	–	–
3	$Pd(OAc)_2$	3	3.3	benzene	–	61	5	–
4	$PdCl_2(PhCN)_2$	3	3.3	benzene	–	54	7	–
5	$PdCl_2$	6	3.3	benzene	–	50	8	–
6	$Pd(PPh_3)_4$	22	3.3	benzene	–	59	16	–
7	$PdCl_2(PPh_3)_2$	10	2.2	DMF	45	–	–	32
8	$Pd_2(dba)_3$	4	2.2	DMF	10	5	–	50
9	$Pd(OAc)_2$	20	2.2	DMF	–	7	–	40
10[a]	$PdCl_2(PhCN)_2$	10	2.2	DMF	72	–	–	23
11	$PdCl_2$	24	2.2	DMF	31	–	–	45
12	$Pd(PPh_3)_4$	20	2.2	DMF	78	–	–	10

Reaction conditions: **5** (0.5 mmol), **6**, Pd reagent (10 mol%), PPh_3 (20 mol%), CuI (20 mol%), TEA (4 equiv.), solvent (20 mL) at room temperature.
[a] 5 mol% of $PdCl_2(PhCN)_2$ was used.

metal–halogen exchange of the (*Z*)-isomer of **8** at −78°C affording olefin **10** in 89% yield (Scheme 3). The coupling constants of the exchanged proton in **10**, 16.3 and 2.1 Hz, indicate the typical (*E*)-olefinic and propargylic coupling, respectively. The configurational stability of the alkenyllithium intermediate has been demonstrated in the literature.[8]

Next, the impact of amine bases was investigated as reported by Alami and coworkers[9] and the results are listed in Table 2. The amines were used here as a reaction solvent. The nature of amines is critical to determine the reaction products. 1,3-Diyne **9** was isolated as the only product in cyclic secondary amines, isopropyl amine, and butylamine (entries 1–4, 9 and 11). The highest yield (56%) was realized with piperidine whereas the more yield of the 1,3-diyne (72%) was resulted from the initial Sonogashira reaction of **3** and TBS-protected 10-undecyn-1-ol under the similar reaction conditions. However, the reactions in $(i\text{-Pr})_2NH$ produced both **7** and **8**, but we could not isolate **9**. The yield of **7** was increased to 65% using excess of **6** (entry 6). The enyne products, **7** and **8**, were produced

Table 4. Effect of the phosphine ligands on the Sonogashira reactions.

entry	ligands	time (h)	**6** (equiv.)	solvent	**5** (% recovery)	yield (%)		
						7	**8**	**9**
1	PPh_3	2	3.3	benzene	–	70	–	–
2	TFP	2.5	3.3	benzene	–	82	6	–
3	P(*o*-Tol)$_3$	2	3.3	benzene	9	40	13	–
4	dppb	20	3.3	benzene	92	–	5	–
5	P(*p*-MeOPh)$_3$	2.5	3.3	benzene	29	31	12	–
6	PPh_3	4	2.2	DMF	10	5	–	50
7	TFP	2	2.2	DMF	–	5	–	45
8[a]	TFP	4	2.2	DMF	–	30	8	41
9	P(*o*-Tol)$_3$	6	2.2	DMF	–	–	–	52
10	dppb	24	2.2	DMF	54	–	–	15
11	P(*p*-MeOPh)$_3$	6	2.2	DMF	–	10	–	40

Reaction conditions: **5** (0.5 mmol), **6**, $PdCl_2(PPh_3)_2$ in PhH or $Pd_2(dba)_3$ in DMF (10 mol%), phosphine ligand (20 mol%), CuI (20 mol%), TEA (4 equiv.), solvent (20 mL) at room temperature.
[a] 2 mol% of $Pd_2(dba)_3$ was used.

Table 5. Effect of the amount of the Pd catalysts on the Sonogashira reactions.

entry	Pd reagents (mol%)	**6** (equiv.)	time (h)	solvent	**5** (% recovery)	yield (%)		
						7	**8**	**9**
1	$PdCl_2(PPh_3)_2$ (10)	3.3	2	benzene	–	82	6	–
2	$PdCl_2(PPh_3)_2$ (2)	3.3	5	benzene	6	61	25	–
3	$PdCl_2(PPh_3)_2$ (1)	3.3	5	benzene	–	63	25	–
4	$Pd_2(dba)_3$ (10)	2.2	4	DMF	10	5	–	50
5	$Pd_2(dba)_3$ (2)	2.2	17	DMF	58	–	–	16
6	$Pd_2(dba)_3$ (1)	2.2	17	DMF	73	–	–	6

Reaction conditions: **5** (0.5 mmol), **6**, Pd reagent, PPh_3 (20 mol%), CuI (20 mol%), TEA (4 equiv.), solvent (20 mL) at room temperature.

Table 6. Effect of the reaction concentration on the Sonogashira reactions.

entry	conc. (mM)	ligand	**6** (equiv.)	time (h)	solvent	**5** (% recovery)	yield (%)		
							7	**8**	**9**
1	25	TFP	3.3	2	benzene	–	82	6	–
2	50	TFP	3.3	1.5	benzene	–	79	5	–
3	100	TFP	3.3	1.5	benzene	–	80	6	–
4	200	TFP	3.3	1	benzene	–	82	5	–
5	25	PPh_3	2.2	4	DMF	10	5	–	50
6[a]	25	PPh_3	2.2	20	DMF	31	3	–	37
7	50	PPh_3	2.2	2.5	DMF	–	21	–	46
8	100	PPh_3	2.2	1.5	DMF	–	32	–	33
9	200	PPh_3	2.2	1.0	DMF	–	32	–	20
10[a]	200	PPh_3	2.2	3.0	DMF	–	20	–	44

Reaction conditions: **5** (0.5 mmol), **6**, $PdCl_2(PPh_3)_2$ in PhH or $Pd_2(dba)_3$ in DMF (10 mol%), PPh_3 (20 mol%), CuI (20 mol%), TEA (4 equiv.), solvent (20–2.5 mL) at room temperature.
[a] Piperidine was used instead of TEA.

preferentially in the bulky amines whereas the 1,3-diyne product **9** was more favored in the amines of relatively small size.

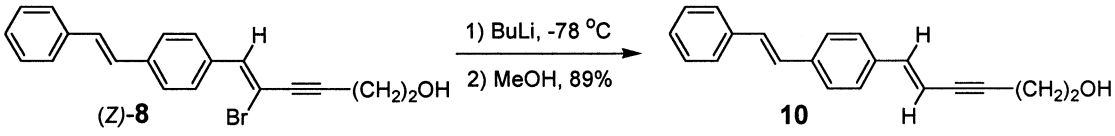
Six palladium catalysts were then tested in either benzene or DMF to optimize the conditions for either **7** or **9**, respectively. The results are summarized in Table 3. In benzene, most of the Pd reagents catalyzed effectively the coupling reactions to give **7** as a major product. However, $Pd_2(dba)_3$ was the most efficient catalyst in DMF in terms of the yield and reaction rate for **9** (entry 8).

The phosphine ligands were also examined with 10 mol% of $PdCl_2(PPh_3)_2$ in benzene or with 10 mol% of $Pd_2(dba)_3$ in DMF at room temperature, respectively (Table 4). Tri-2-furylphosphine (TFP)[10] and PPh_3 enhanced the coupling reactions effectively in both solvents, whereas the dppb and P(*p*-MeOPh)$_3$ ligands were less efficient. The present results are in contrast to those reported by Shen and Wang.[6a] They reported that P(*p*-MeOPh)$_3$ was one of the effective ligands for the formation of the enynes from the Stille coupling reactions of the 1,1-dibromo-1-alkenes.

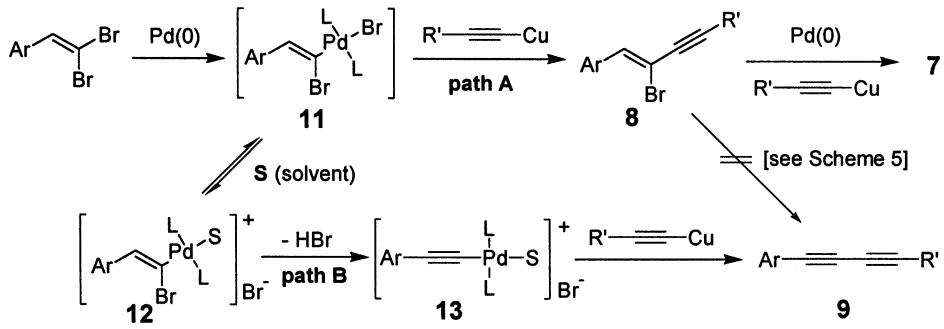
Reduction in the amount of the palladium catalyst decreased the rate and yields of the coupling reactions (Table 5). More significant decrease was observed with the $Pd_2(dba)_3$ catalyst.

Increase of the reaction concentration in benzene accelerated the reaction rate but did not affect the yields of the enyne products much (Table 6, entries 1–4). However, a significant amount of **7** was produced in addition to **9** at the higher concentrations in DMF (entries 7–10). The concentration of the reaction mixture was controlled by reducing the amount of the reaction solvent.

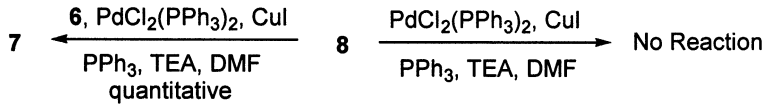
The dependence of the products on the polarity of solvents in the Sonogashira reactions (Table 1) could be explained by the working hypothesis shown in Scheme 4 that is analogous to that proposed by Shen and Wang.[6a] The



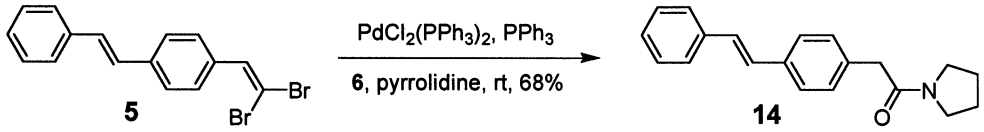
Scheme 3. Determination of stereochemistry for (*Z*)-**8** by metal–halogen exchange.



Scheme 4. Possible reaction pathways for the products in the present study.



Scheme 5. Conversion studies of **8**.



Scheme 6. Formation of the byproduct **14** in pyrrolidine as a reaction solvent.

usual cross-coupling reaction is favored in nonpolar solvents such as benzene or toluene to give **7** or **8** after the oxidative addition of Pd(0) (path A). The highly polar and good coordinating solvents such as DMF or DMSO would favor the solvated ionic complex **12** that is converted into the alkynyl palladium intermediate **13** (path B).

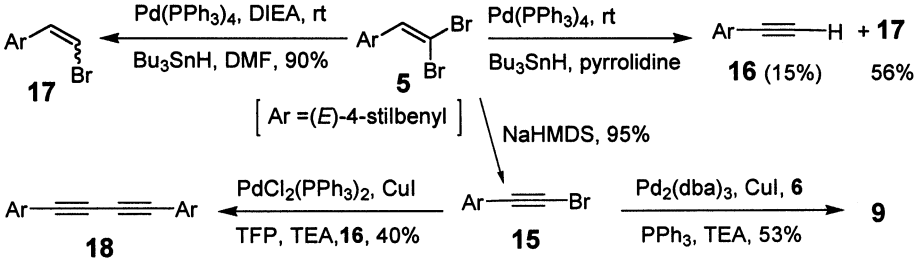
The effect of the amines also supports the possible presence of the intermediate **12** that we could not isolate. Better coordinating amines of small size would favor the preferential formation **12** leading eventually to **9**, whereas poor coordinating amines of large size produced only the enyne products **7** and **8** (entries 5 versus 9, Table 2). The amines of intermediate size gave both products (entries 8 and 10, Table 2). At higher concentration, therefore, both reaction pathways compete even in DMF (entries 7–10, Table 6).

Alternative pathway to give **9** directly from **8** by dehydrobromination was tested by treating **8** without **6** under otherwise the same reaction conditions (Scheme 5). No expected reaction occurred and most of the starting material was recovered. The similar result has been also reported.[6a] Addition of **6** to the above reaction, however, produced **7** in quantitative yield. The poor yield with pyrrolidine (entry 3, Table 2) seems in part due to the byproduct **14** that contains the pyrrolidine unit (Scheme 6). We could obtain **14** in 68% yield without using CuI. We are currently investigating the mechanism and utility of this side reaction, and will report the results in due course.

In an effort to support that the alkynyl palladium species **13** is a plausible reaction intermediate, we have synthesized **9** independently from the coupling reaction between alkynyl bromide **15**, derived from **5**, and alkyne **6** in the presence of $Pd_2(dba)_3$ (Scheme 7). We could also produce a terminal alkyne **16** by reduction with Bu_3SnH using pyrrolidine as a reaction solvent, albeit in poor yield. The major product in the above reduction reaction, however, was a stereoisomeric mixture of vinyl bromide **17** (56%, (*Z*):(*E*)=~4.5:1). An authentic sample of alkyne **16** was obtained independently in high yield (90%) by treating **5** with BuLi as reported in the literature (see Experimental).[11] The similar reduction reaction with Bu_3SnH in DMF produced, instead, only **17** in high yield ((*Z*):(*E*)=~13:1), which seems complementary to the results reported by Uenishi and coworkers.[12] Although they had the exclusive (*Z*)-selectivity in several common organic solvents, the low stereoselectivity ((*Z*):(*E*)=~2:1) was observed in polar solvents such as EtOH or AcOH with no co-solvent. The conjugated diyne **18** was also prepared by coupling of **15** with **16** in order to show whether **18** is produced as a byproduct in the above cross-coupling reaction studies or not. No significant amount of **18** was observed in the cross-coupling reactions reported. A blank test with **5** under the similar conditions [10% $Pd_2(dba)_3$, 20% CuI, 20% PPh_3, TEA (4 equiv.), DMF, rt, 24 h] resulted in only a trace of **18** (<2%) and most of **5** was recovered.

3. Conclusions

We have established that the Sonogashira reactions of 2-aryl-1,1-dibromoethene **5** with 1-alkyne **6** produce the different products depending on the reaction conditions. Both the solvent polarity and the nature of amines used as a reaction solvent have a significant impact on the product ratio. The alkynyl palladium species **13** seemed to be a possible reaction intermediate for the formation of 1-aryl-1,3-diyne **9**. The result of dependence on the reaction conditions of widely used Sonogashira cross-coupling reactions should be useful for the preparation of these important classes of compounds such as 2-aryl-1,1-dialkynylethenes[13]



Scheme 7. Correlation studies.

and 1-aryl-1,3-diynes.[14] Particularly, the mild reaction conditions like ambient temperature could tolerate a wide range of functional groups present in the starting materials. In addition, 2-aryl-1,1-dibromoethene can be considered as a synthetic equivalent to 2-aryl-1-bromoacetylene under the reaction conditions employed.

4. Experimental

4.1. General Methods

Materials were obtained from commercial suppliers and were used without further purification. For anhydrous solvents, CH_2Cl_2 was distilled from calcium hydride. Diethyl ether, THF, benzene, and toluene were distilled from sodium/benzophenone. All glassware, syringes, needles, and magnetic bars used in the moisture-sensitive reactions were oven-dried at 120°C for at least 4 h and stored in dessicator until use. Upon workup, solvent was removed with a rotary evaporator and then with a high vacuum pump. Reactions were monitored by TLC. Commercially available TLC plates (Silica gel 60 F_{254}, Merck) were visualized under UV light (254 or 365 nm) followed by molybdophosphoric acid staining. Dry-column flash chromatography was done on silica gel 60G (particle size 5-40 μm, Merck). IR spectra were recorded with a JASCO model FT-IR 200. ^{1}H NMR and ^{13}C NMR spectra were measured in $CDCl_3$ at 300 MHz and 75 MHz (JEOL JNM-LA 300), respectively. Multiplicity was denoted by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Coupling constants (*J*) were in hertz (Hz).

4.2. 2-((*E*)-4-Stilbenyl)-1,1-dibromoethene (5)

To a solution of 4-bromobenzaldehyde (3.70 g, 20.0 mmol), $Pd(OAc)_2$ (0.225 g, 1.00 mmol), and P(*o*-Tol)$_3$ (0.609 g, 2.00 mmol) in DMF (120 mL) at room temperature were added styrene (2.80 mL, 24.0 mmol) and triethylamine (8.40 mL, 60.0 mmol) under N_2 atmosphere and the resulting mixture was heated for 30 h at 100°C in an oil bath. After the reaction mixture was cooled to room temperature, water (240 mL) was added and the resulting mixture was extracted with chloroform (3×120 mL). The combined organic layers were washed with water (3×200 mL) and brine (3×30 mL), dried with anhydrous $MgSO_4$, and concentrated under reduced pressure after filtration. The crude product was chromatographed ($CHCl_3$) to give 3.98 g (quantitative) of (*E*)-4-stilbenecarboxaldehyde with a small amount of impurity. Without further purification, this mixture was added to a solution of CBr_4 (9.95 g, 30.0 mmol) and PPh_3 (15.7 g, 60.0 mmol) in CH_2Cl_2 (120 mL) at 0°C under N_2 atmosphere. After stirring for 2 h at 0°C, the reaction mixture was concentrated and the residue was washed with methanol (3×100 mL). The crude product was recrystallized from ethyl acetate (100 mL) to give 5.53 g (76% from 4-bromobenzaldehyde) of pure **5** as a pale yellowish crystal: R_f=0.6 ($CHCl_3$:hexane=1:2); mp 139-140°C; IR (KBr) 3022, 972, 879, 817, 756, 693, 542 cm^{-1}; ^{1}H NMR δ 7.48-7.58 (m, 7H), 7.26-7.40 (m, 3H), 7.17 (d, 1H, *J*=16.4), 7.08 (d, 1H, *J*=16.4); ^{13}C NMR δ 137.7, 137.2, 136.6, 134.4, 129.8, 128.8, 128.7, 128.0, 127.9, 126.6, 126.5, 89.3; MS (EI) *m/z* (%): 366 (M^++4, 49), 364 (M^++2, 100), 362 (M^+, 51), 284 (4), 202 (91), 101 (47); HRMS (EI) calcd for $C_{16}H_{12}Br_2$ 363.9285 (M^++2), found 363.9290.

4.3. Procedure for the standard Sonogashira reactions

To a solution of dibromide **5** (184 mg, 0.500 mmol), palladium reagent (0.0500 mmol), phosphine ligand (0.100 mmol), and CuI (19.5 mg, 0.100 mmol) in solvent (20 mL) at room temperature were added amine reagent (2.00 mmol) and 3-butyn-1-ol (**6**) (78.0 mg, 1.10 mmol) under N_2 atmosphere. After the time indicated in Tables 1–6, saturated aq. NH_4Cl (20 mL) was added to the reaction mixture and the resulting mixture was extracted with chloroform (3×10 mL). The combined organic layers were washed with water (3×20 mL) and brine (3×5 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography to give recovered dibromide **5**, 2-aryl-1,1-dialkynylethene **7**, conjugated enyne **8**, and 1-aryl-1,3-diyne **9** as a yellowish solid. The isolated yields are shown in the Tables. The inseparable products **8** and **9** were isolated as a mixture and the ratio of **8** to **9** was based on the ^{1}H NMR integration of the isolated mixture. The conjugated diyne byproduct, 3,5-octadiyne-1,8-diol, obtained from the homocoupling of **6** was always obtained in about 10-15% yield of the amount of **6** used and their yields are not included in Tables 1–6.

4.3.1. 5-((*E*)-4-Styrenylbenzylidene)nona-3,6-diyne-1,9-diol (7). The analytical sample was recrystallized from chloroform to yield pure **7** as a golden solid: R_f=0.3 (EtOAc: hexane=2:1); mp 149-150°C; IR (KBr) 3343, 3025, 2946, 2214, 1056, 971, 895, 817, 754, 691, 540 cm^{-1}; ^{1}H NMR δ 7.82 (d, 2H, *J*=8.2), 7.48-7.53 (m, 4H), 7.37 (t, 2H, *J*=7.4), 7.25-7.29 (m, 1H), 7.16 (d, 1H, *J*=16.3), 7.08 (d, 1H, *J*=16.3), 6.96 (s, 1H), 3.85 (q, 2H, *J*=6.2), 3.80 (q, 2H, *J*=6.2), 2.75 (t, 2H, *J*=6.2), 2.66 (t, 2H, *J*=6.2), 1.87 (t, 2H, *J*=6.2); ^{13}C NMR δ 142.2, 137.9, 137.1, 134.9, 129.5, 129.0, 128.7, 128.0, 127.8, 126.6, 126.4, 102.6, 92.8, 85.5, 82.7, 80.3, 61.0, 60.9, 24.3, 23.9; MS (EI) *m/z* (%): 342 (M^+, 100), 311 (6), 265 (21), 252 (17); HRMS (EI) calcd for $C_{24}H_{22}O_2$ 342.1620, found 342.1624.

4.3.2. (*Z*)-5-Bromo-6-((*E*)-4-stilbenyl)hex-5-en-3-yn-1-ol ((*Z*)-8). The analytical sample was recrystallized from hexane and ethyl acetate to yield pure (*Z*)-**8** as a tarnished yellow solid: R_f=0.6 (EtOAc:hexane=2:1); mp 145-147°C (dec.); IR (KBr) 3376, 3024, 2944, 2215, 1049, 970, 964, 880, 814, 751, 691, 539 cm^{-1}; ^{1}H NMR δ 7.69 (d, 2H, *J*=8.3), 7.50-7.54 (m, 4H), 7.26-7.40 (m, 3H), 7.19 (s, 1H), 7.17 (d, 1H, *J*=16.3), 7.08 (d, 1H, *J*=16.3), 3.82 (q, 2H, *J*=6.2), 2.74 (t, 2H, *J*=6.2), 1.77 (t, 1H, *J*=6.2); ^{13}C NMR δ 137.8, 137.1, 135.7, 134.0, 129.7, 129.6, 128.7, 128.0, 127.9, 126.6, 126.3, 99.9, 89.4, 82.8, 60.9, 23.9; MS (EI) *m/z* (%): 354 (M^++2, 99), 352 (M^+, 100), 272 (14), 241 (65); HRMS (EI) calcd for $C_{20}H_{17}OBr$ 352.0463 (M^+), found 352.0449.

4.3.3. 6-((*E*)-4-Stilbenyl)hexa-3,5-diyn-1-ol (9). The analytical sample was recrystallized from hexane and ethyl acetate to yield pure **9** as a tarnished yellow solid: R_f=0.6

(EtOAc:hexane=2:1); mp 137-139°C (dec.); IR (KBr) 3348, 3024, 2948, 2241, 1039, 971, 824, 752, 691, 545 cm^{-1}; ^1H NMR δ 7.46-7.53 (m, 6H), 7.26-7.40 (m, 3H), 7.14 (d, 1H, J=16.3), 7.06 (d, 1H, J=16.3), 3.81 (q, 2H, J=6.2), 2.66 (t, 2H, J=6.2), 1.76 (t, 1H, J=6.2); ^{13}C NMR δ 138.1, 136.9, 132.9, 130.1, 128.7, 128.0, 127.7, 126.6, 126.4, 120.6, 81.5, 75.6, 74.8, 67.0, 60.8, 24.0; MS (EI) m/z (%): 272 (M^+, 100), 241 (76); HRMS (EI) calcd for $C_{20}H_{16}O$ 272.1202, found 272.1201.

4.4. (*E*)-6-((*E*)-4-Stilbenyl)hex-5-en-3-yn-1-ol (10)

To a solution of the (*Z*)-isomer of **8** (100 mg, 0.280 mmol) in THF (10 mL) at −78°C was added slowly 0.9 mL of BuLi (1.6 M solution in hexane, 1.44 mmol) under N_2 atmosphere. After stirring for 10 min at −78°C, addition of excess methanol (5 mL) was followed by addition of water (20 mL). The resulting mixture was extracted with chloroform (3×20 mL). The combined organic layers were washed with water (3×20 mL) and brine (3×5 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography to give 72.0 mg (89%) of enyne **10** as a yellowish solid. The analytical sample was recrystallized from hexane and chloroform to yield pure **10**: R_f=0.57 (EtOAc:hexane=2:1); mp 168°C (dec.); IR (KBr) 3413, 3031, 2927, 1045, 968, 821, 694, 532 cm^{-1}; ^1H NMR δ 7.46-7.53 (m, 4H), 7.34-7.39 (m, 4H), 7.24-7.29 (m, 1H), 7.13 (d, 1H, J=16.5), 7.07 (d, 1H, J=16.5), 6.91 (d, 1H, J=16.3), 6.16 (dt, 1H, J=16.3, 2.1), 3.79 (t, 2H, J=6.1), 2.67 (dt, 2H, J=6.1 and 2.1), 1.87 (br, 1H); ^{13}C NMR δ 140.5, 137.6, 137.1, 135.6, 129.0, 128.7, 128.0, 127.8, 126.8, 126.6, 126.5, 107.9, 89.1, 81.8, 61.2, 24.1; MS (EI) m/z (%): 274 (M^+, 100), 241 (16), 228 (38); HRMS (EI) calcd for $C_{20}H_{18}O$ 274.1358, found 274.1366.

4.5. Pyrrolidine ((*E*)-4-styrenyl)phenylacetamide (14)

To a solution of dibromide **5** (184 mg, 0.500 mmol), $PdCl_2(PPh_3)_2$ (35.1 mg, 0.0500 mmol) and PPh_3 (26.1 mg, 0.100 mmol) in pyrrolidine (5 mL) at room temperature was added **6** (78.0 mg, 1.10 mmol) under N_2 atmosphere. After stirring for 20 h, 1 N HCl (20 mL) was added to the reaction mixture and the resulting mixture was extracted with chloroform (3×10 mL). The combined organic layers were washed with water (3×20 mL) and brine (3×5 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography to give 100 mg (68%) of acetamide **14** as a pale yellow solid: R_f=0.15 (EtOAc:hexane=2:1); mp 147–148°C; IR (KBr) 3026, 2966, 1641, 1426, 962, 792, 697, 534 cm^{-1}; ^1H NMR δ 7.46–7.53 (m, 4H), 7.23–7.38 (m, 5H), 7.09 (s, 2H), 3.66 (s, 2H), 3.50 (t, 2H, J=6.8), 3.43 (t, 2H, J=6.7), 1.80–1.97 (m, 4H); ^{13}C NMR δ 169.3, 137.3, 135.8, 134.3, 129.2, 128.6, 128.4, 128.2, 127.5, 126.6, 126.4, 46.8, 45.9, 42.0, 26.1, 24.3; MS (EI) m/z (%): 291 (M^+, 79), 193 (26), 98 (100); HRMS (EI) calcd for $C_{20}H_{21}ON$ 291.1623, found 291.1615.

4.6. 1-Bromo-2-((*E*)-4-stilbenyl)ethyne (15)

To a solution of dibromide **5** (110 mg, 0.300 mmol) in dry THF (5 mL) at −78°C was added 0.36 mL of NaHMDS (1.0 M solution in THF, 0.360 mmol) under N_2 atmosphere. After stirring for 2 h at −78°C, saturated aq. NH_4Cl (20 mL) was added and the resulting mixture was extracted with chloroform (3×20 mL). The combined organic layers were washed with water (3×20 mL) and brine (3×5 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography to give 82.0 mg (95%) of alkynyl bromide **15** as a yellowish solid. The analytical sample was recrystallized from hexane to yield pure **15**: R_f=0.6 ($CHCl_3$:hexane=1:2); mp 120°C; IR (KBr) 3026, 2193, 971, 823, 754, 690, 544 cm^{-1}; ^1H NMR δ 7.26-7.53 (m, 9H), 7.14 (d, 1H, J=16.3), 7.06 (d, 1H, J=16.3); ^{13}C NMR δ 137.7, 136.9, 132.3, 129.9, 128.7, 127.9, 127.7, 126.6, 126.3, 121.6, 80.2, 50.5; MS (EI) m/z (%): 284 (M^++2, 58), 282 (M^+, 59), 202 (100), 101 (23); HRMS (EI) calcd for $C_{16}H_{11}Br$ 282.0044, found 282.0053.

4.7. ((*E*)-4-Stilbenyl)ethyne (16) from dibromide 6 using BuLi

To a solution of dibromide **6** (174 mg, 0.476 mmol) in dry THF (10 mL) at room temperature was added 1.20 mL of BuLi (1.6 M solution in hexane, 1.92 mmol) under N_2 atmosphere. After stirring for 1 h, water (20 mL) was added and the resulting mixture was extracted with chloroform (3×20 mL). The combined organic layers were washed with water (3×20 mL) and brine (3×5 mL), dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography to give 88.0 mg (90%) of alkyne **16** as a yellowish solid. The analytical sample was recrystallized from hexane to yield pure **16**: R_f=0.57 ($CHCl_3$: hexane=1:2); mp 121°C; IR (KBr) 3285, 3023, 2105, 970, 824, 691, 548 cm^{-1}; ^1H NMR δ 7.45–7.54 (m, 6H), 7.35–7.40 (m, 2H), 7.24–7.31 (m, 1H), 7.14 (d, 1H, J=16.4), 7.07 (d, 1H, J=16.4), 3.13 (s, 1H); ^{13}C NMR δ 137.7, 136.9, 132.4, 129.8, 128.7, 127.9, 127.7, 126.6, 126.3, 120.9, 83.7, 77.9; MS (EI) m/z (%): 204 (M^+, 100), 189 (18), 101 (9); HRMS (EI) calcd for $C_{16}H_{12}$ 204.0939, found 204.0940.

4.8. 1-Bromo-2-((*E*)-4-stilbenyl)ethene (17)

To a solution of dibromide **5** (174 mg, 0.476 mmol), $Pd(PPh_3)_4$ (28.0 mg, 0.0238 mmol) in DMF (5 mL) at room temperature were added diisopropylethylamine (0.124 mL, 0.720 mmol) and Bu_3SnH (146 mg, 0.500 mmol) under N_2 atmosphere. After 1 h of stirring, water (20 mL) was added and the resulting mixture was extracted with chloroform (3×20 mL). The combined organic layers were washed with water (3×20 mL) and brine (3×5 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography to give 121 mg (90%) of a stereoisomeric mixture, **17** ((*Z*):(*E*)=~13:1), as a yellowish solid. The (*Z*)-isomer of **17**: R_f=0.57 ($CHCl_3$:hexane=1:2); IR (KBr) 3022, 2922, 965, 828, 688, 538 cm^{-1}; ^1H NMR δ 7.72 (d, 2H, J=8.4), 7.51–7.54 (m, 4H), 7.26–7.40 (m, 3H), 7.17 (d, 1H, J=16.4), 7.10 (d, 1H, J=16.4), 7. 07 (d, 1H, J=8.1), 6.43 (d, 1H, J=8.1); ^{13}C NMR δ 137.3, 137.2, 134.1, 131.9, 129.4, 129.3, 128.7, 128.1, 127.8, 126.5, 126.3, 106.2; MS

(EI) *m/z* (%) 286 (M^++2, 99), 284 (M^+, 100), 203 (60), 101 (31).

4.9. 1,4-Bis((*E*)-4-stilbenyl)buta-1,3-diyne (18)

To a solution of alkynyl bromide **15** (70.0 mg, 0.247 mmol), $PdCl_2(PPh_3)_2$ (17.4 mg, 0.025 mmol), TFP (11.5 mg, 0.049 mmol), and CuI (9.4 mg, 0.049 mmol) in benzene (3 mL) at room temperature were added TEA (100.1 mg, 0.989 mmol) and alkyne **16** (50.5 mg, 0.247 mmol) under N_2 atmosphere. After 2 h of stirring, the product was obtained as a floating solid. A solution of saturated aq. NH_4Cl (10 mL) was added to the reaction mixture and the resulting mixture was extracted with chloroform (3×10 mL). The residue was washed with chloroform (3×20 mL). The crude product was recrystallized from benzene (150 mL) to give 40.0 mg (40%) of homodiyne **18** as yellowish needles: R_f=0.31 (EtOAc:hexane=1:2); mp 274-275°C; IR (KBr) 3022, 2141, 1494, 1446, 1408, 970, 821, 754, 669, 542 cm^{-1}; ^1H NMR δ 7.45–7.52 (m, 6H), 7.33–7.38 (m, 2H), 7.25–7.29 (m, 1H), 7.15 (d, 1H, *J*=16.3), 7.10 (d, 1H, *J*=16.3); ^{13}C NMR δ 137.1, 132.9, 130.5, 128.8, 128.1, 128.0, 127.9, 126.5, 120.9, 100.7, 77.2; MS (EI) *m/z* (%) 406 (M^+, 100), 114 (34); HRMS (EI) calcd for $C_{32}H_{22}$ 406.1722, found 406.1729.

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