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Pd-catalyzed selective tandem arylation–alkylation of 1,1-dihalo-1-alkenes with aryl- and alkylzinc derivatives to produce α-alkyl-substituted styrene derivatives

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This paper is dedicated to Professor Jean-Pierre Genêt on the occasion of his 60th birthday

Abstract

Trans-selective monoarylation of 1,1-dibromo- and 1,1-dichloro-1-alkenes (**1**) can be achieved in >80% yields and in ≥98–99% stereoselectivity with arylzinc bromides in the presence of a catalytic amount of Cl_2Pd(DPEphos) or Cl_2Pd(dppb), the former permitting cleaner and higher yielding reactions. Although THF is a generally satisfactory solvent, ether and toluene are superior to THF in some cases. The second substitution of (*Z*)-α-bromostyrenes (**3**) with alkylzincs in the presence of 2 mol% of $Pd(^tBu_3P)_2$ proceeds to give the corresponding **2** in >90% yields and in ≥98–99% stereoselectivity. Although somewhat less satisfactory, the use of Cl_2Pd(DPEphos) permits a one-pot tandem arylation–alkylation.

Keywords: Pd-Catalyzed tandem cross-coupling; Arylation–alkylation; 1,1-Dihalo-1-alkenes; α-Alkyl-substituted styrenes; Aryl- and alkylzincs

1. Introduction

We recently reported a highly stereoselective tandem alkynylation–alkylation of 1,1-dihalo-1-alkenes [1] in which the use of $Pd(^tBu_3P)_2$ [2] for the second alkylation step was critically important for observing high product yields (≥90%) and high stereoselectivity (≥98% *E*). On the other hand, more conventional Pd–phosphine complexes including PPh_3, TFP (tris(2-furyl)phosphine), dppp, and dppf led to disappointingly low product yields and formation of the *Z* isomers to significant and varying extents. On the other hand, $Pd(^tBu_3P)_2$ was unsatisfactory for the first alkynylation of 1,1-dihalo-1-alkenes to produce 3-halo-3-en-1-ynes, thereby preventing the development of one-pot tandem alkynylation–alkylation procedures. For selective monoalkynylation, Cl_2Pd(DPEphos) [3] proved to be the most satisfactory ligand among those examined.

We also sought a related efficient and selective route to (*E*)-α,-dialkyl-substituted styrenes **2** via sequential arylation–alkylation of 1,1-dihalo-1-alkenes (**1**) derived from alkyl aldehydes. Selective monoarylation of 1,1-dihalo-1-alkenes has previously been achieved with arylmetals containing Mg [4], Zn [4,5], and Sn [6]. However, while several examples of Pd-catalyzed *trans*-monoarylation of 2-alkyl-1,1-dihalo-1-alkenes have been reported [5,6], none of the products have been alkylated in the second step to produce **2**. Although **2** can be efficiently and selectively prepared from arylacetylenes via alkylmetallation—alkylative cross-coupling [7], incorporation of secondary and tertiary alkyl groups including chiral alkyl groups by this method has been difficult.

2. Pd-Catalyzed *trans*-selective monoarylation of 1,1-dihalo-1-alkenes

In the seminal investigation by Minato et al. [4], *trans*-selective monoarylation of 1,1-dihalo-1-alkenes

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containing Ph, *p*-MeC_6H_4, *p*-ClC_6H_4, 2-thienyl, Me, Cl groups in the C2 position were selectively monoarylated mostly with arylmagnesium halides containing Ph, *p*-$MeOC_6H_4$, and *p*-ClC_6H_4 in the presence of Cl_2Pd(dppb), where dppb is bis(diphenylphosphino)butane in 76–98% yields except in one special case. A single example of the use of PhZnCl was also reported. Subsequently, the use of arylzinc halides containing Ph, *p*- and *m*-ClC_6H_4, *p*-FC_6H_4, 2-thienyl, and 2-furyl was reported to produce the desired monoarylated derivatives mostly in 80–100% yields in the presence of Cl_2Pd(dppb) [5]. Both Mg and Zn as well as Cl_2Pd(dppb) may therefore be judged to be favorable metals and a catalyst, respectively, for achieving the desired transformation. Although arylboron derivatives [8] do not appear to have been employed for *trans*-selective monoarylation of 1,1-dihalo-1-alkenes, arylstannanes containing Ph, 2- and 3-furyl have been used to produce the desired monoarylated compounds in yields ranging from 12 to 97% in the presence of a Pd–TFP complex [6]. Two potentially serious side reactions noted in this study were (i) competitive diarylation and (ii) alkyne formation via dehydrobromination. Although relative merits and demerits among the metals mentioned above may not be generalized in definitive terms, the available data suggest that Mg and Zn tend to be generally more satisfactory than Sn. Concerns over the toxicity associated with Sn along with its comparatively higher costs and the comparatively lower functional group compatibility associated with Mg led us to focus attention on the use of arylzinc derivatives in this study.

Even though the use of arylzinc derivatives in conjunction with Cl_2Pd(dppb) was known to be satisfactory in many cases (vide supra) [4,5], our recent finding that Cl_2Pd(DPEphos) was generally the most satisfactory catalyst and was superior to $Pd(PPh_3)_4$, $Cl_2Pd(TFP)_2$, Cl_2Pd(dppf), and even Cl_2Pd(dppb) in *trans*-selective monoalkynylation [1] prompted us to screen ligands and other parameters for the Pd-catalyzed monoarylation of 1,1-dihalo-1-alkenes. The experimental results summarized in Table 1 indicate the following.

Firstly, Cl_2Pd(DPEphos) and Cl_2Pd(dppb) are indeed the two most satisfactory catalysts among those tested. With the latter, however, diphenylation producing **4a** in 14% yield is a notable side reaction observed with 1,1-dibromo-1-octene (entry 3). Overall, Cl_2Pd(DPEphos) does appear to be superior to Cl_2Pd(dppb), which, in turn, is distinctly superior to Cl_2Pd(dppf), $Pd(PPh_3)_4$, and $Pd(^tBu_3P)_2$. In fact, nearly exclusive diphenylation took place with $Pd(^tBu_3P)_2$ as a catalyst (entry 5).

Secondly, in all favorable cases, *trans*-selectivity is $\geq$ 98%, as has been previously demonstrated for various cases of monosubstitution [1,4–6,8].

Finally, selection of a proper solvent appears to be a delicate and critical issue, since promotion of the desired monosubstitution may also lead to that of the undesirable disubstitution. Indeed, phenylation of 1,1-dichloro-1-octene even with Cl_2Pd(DPEphos) as a catalyst led to the formation of the undesirable diphenylated compound **4a** in 11% yield, when it was run in THF (entry 7). On the other hand, the same reaction run in refluxing ether produced the desired **3a** in 84% isolated yield along with a 4% yield of **4a** (entry 8). It appears advisable to screen representative solvents for optimization of the reaction conditions, even when the optimized reagents and catalyst are used.

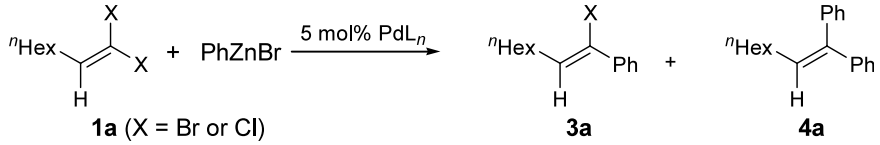
With the experimental findings presented above in mind, the synthetic scope of the Pd-catalyzed *trans*-selective monoarylation of 1,1-dihalo-1-alkenes (**1**) containing ^nHex, ^tBu, Ph, and $Me_3SiC{\equiv}C$ with arylzinc bromides containing Ph, 2-thienyl, and 2-thiazolyl in the presence of Cl_2Pd(DPEphos) was explored, and the experimental results are summarized in Table 2 along with a couple of additional sets of results obtained with those obtained with Cl_2Pd(dppb) as a catalyst and presented in brackets for further comparison with Cl_2Pd(DPEphos) as a catalyst. Uniformly satisfactory results combining (i) 82–94% isolated yields of the desired **3**, (ii) $>98\%$ *trans*-selectivity, (iii) low levels ($\leq 4\%$ except for entry 4) of undesirable diarylation producing **4**, and (iv) low levels ($\leq 6\%$ except for entry 10) of undesirable alkyne formation can be observed. Even so, however, solvent optimization mentioned above is desirable in some cases. Thus, in the reaction of 1,1-dibromo-1-octene with 2-thiazolylzinc bromide, toluene proved to be more satisfactory than either THF or ether (entries 4–6). Comparison of Cl_2Pd(DPEphos) with Cl_2Pd(dppb) in two additional cases further indicates that the former is superior to the latter (entries 11–14).

3. Pd-Catalyzed stereospecific alkylation of (*Z*)-α-halostyrenes with retention of configuration

Our recent studies have indicated that the Pd-catalyzed cross-coupling of stereodefined alkenyl halides can undergo partial or even essentially full stereoinversions under the influence of proximal π-bonds, such as alkynyl [1] and alkenyl [9], thereby mandating modification of the conventional assumption that the Pd-catalyzed cross-coupling of alkenyl halides may be expected to proceed with retention of configuration. It has also been found that, in the Pd-catalyzed alkylation of 2-halo-1-en-3-ynes, undesirable stereoisomerization can be essentially prevented by using $Pd(^tBu_3P)_2$ as a catalyst rather than more conventional $Pd(PPh_3)_4$ and other Pd–phosphine complexes as well as Cl_2Pd(DPEphos) [1].

As the results shown in Table 3 indicate, the reaction of α-halostyrenes with alkylzinc derivatives containing

Table 1
Reaction of 1,1-dichloro-1-octene or 1,1-dibromo-1-octene with PhZnBr in the presence of a Pd–phosphine catalyst



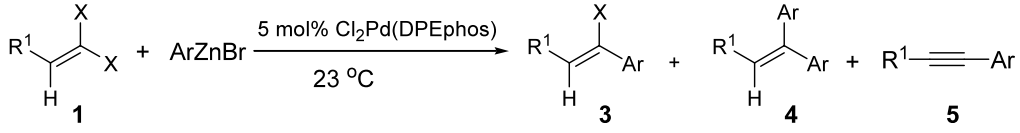
1a (X = Br or Cl) **3a** **4a**

Entry	X	PdL_n	Solvent	Temperature (°C)	Time (h)	Yield or recovery (%) [a]		
						1a	**3a** [b]	**4a**
1	Br	$Pd(PPh_3)_4$	THF	23	3	< 1	61	38
2	Br	Cl_2Pd(DPEphos)	THF	23	1	< 1	99(94)	< 1
3	Br	Cl_2Pd(dppb)	THF	23	3	< 1	81	14
4	Br	Cl_2Pd(dppf)	THF	23	3	< 1	53	< 1
5	Br	$Pd(^tBu_3)_2$	THF	23	1	46	< 1	52
6	Cl	$Pd(PPh_3)_4$	THF	50	3	93	6 [c]	< 1
7	Cl	Cl_2Pd(DPEphos)	THF	50	6	19	69	11
8	Cl	Cl_2Pd(DPEphos)	ether	reflux	1	2	96(84)	4
9	Cl	Cl_2Pd(dppb)	ether	reflux	2	5	88	2

[a] By GLC. The numbers in parentheses are isolated yields. The yield of **4a** is based on **1a**.
[b] The *Z*/*E* ratios were ≥98/2 to 99/1 except in entry 6.
[c] 3% each of the *Z* and *E* isomers.

Me, Et, and ^{n}Bu in the presence of 2–5 mol% of $Pd(^tBu_3P)_2$ cleanly produced the desired α,-disubstituted (*E*)-styrene derivatives in uniformly high yields (> 90% isolated) and in ≥98–99% stereoselectivity. Despite the highly satisfactory results shown in Table 3, however, some limitations were also noted. Unlike its bromo analogue, the reaction of (*Z*)-α-chloro–hexylstyrene with either Me_2Zn or Et_2Zn in the presence of 5 mol%

Table 2
Reaction of 1,1-dibromo- and 1,1-dichloro-1-alkenes with arylzinc bromides in the presence of Cl_2Pd(DPEphos)

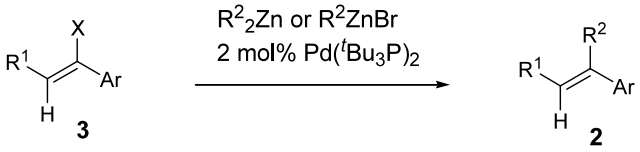


1 **3** **4** **5**

Entry	R^1	X	Ar	Solvent	Time (h)	**1**	**3** [a]	**4**	**5**
1 [b]	^{n}Hex	Br	Ph	THF	1	< 1	94(99)	< 1	< 1
2 [c]	^{n}Hex	Cl	Ph	ether [d]	1	2	84(96)	4	< 1
3	^{n}Hex	Br	2-thienyl	THF	1	< 1	85(88)	11	< 1
4	^{n}Hex	Br	2-thiazolyl	toluene	24	5	84(87)	< 1	6
[5	^{n}Hex	Br	2-thiazolyl	THF	12	< 1	73(78)	2	18]
[6	^{n}Hex	Br	2-thiazolyl	ether	24	23	[e] (63)	< 1	11]
7	(*S*)-Et(Me)CH	Br	Ph	THF	1	< 1	86(95)	2	< 1
8	(*S*)-Et(Me)CH	Cl	Ph	ether	1	9	83(89)	< 1	< 1
9	(*S*)-Et(Me)CH	Br	2-thienyl	THF	1	< 1	91(97)	< 1	< 1
10	(*S*)-Et(Me)CH	Br	2-thiazolyl	toluene	24	< 1	82(87)	< 1	14
11	Ph	Cl	Ph	THF	6	9	82(88)	2	2
[12 [f]	Ph	Cl	Ph	THF	6	28	[e] (73)	2	2]
13	Me_3Si–	Cl	Ph	THF	24	6	90(91)	< 1	5
[14 [f]	Me_3Si–	Cl	Ph	THF [g]	12	14	[e] (75)	5	6]

[a] Isolated yields with GLC yields in parentheses.
[b] Same as entry 2 in Table 1.
[c] Same as entry 8 in Table 1.
[d] Refluxed.
[e] Not isolated.
[f] Cl_2Pd(dppb) used as a catalyst.
[g] Run at 50 °C.

Table 3
Reaction of (*Z*)-α-halostyrenes with alkylzinc derivatives in the presence of a catalytic amount of $Pd(^tBu_3P)_2$



Entry	R^1	Ar	X	R^2_2Zn or R^2ZnBr	Temperarure (°C)	Time (h)	Yield [a] of **2** [b] (%)
1	^{n}Hex	Ph	Br	Me_2Zn	23	1	92(96)
2	^{n}Hex	Ph	Br	Et_2Zn	23	3	95(99)
3	^{n}Hex	Ph	Br	^{n}BuZnBr	23	2	95(99)
4	^{n}Hex	2-thienyl	Br	Me_2Zn	23	1	96(99)
5	^{n}Hex	2-thiazolyl	Br	Me_2Zn	23	1	91(98)
6	(*S*)-Et(Me)CH	Ph	Br	Me_2Zn	23	1	95(97)
7	(*S*)-Et(Me)CH	Ph	Br	Et_2Zn	23	3	94(99)
8	(*S*)-Et(Me)CH	2-thienyl	Br	Me_2Zn	23	1	92(98)
9	(*S*)-Et(Me)CH	2-thiazolyl	Br	Me_2Zn	23	1	92(97)
10	Ph	Ph	CI	Me_2Zn	50	3	91(99)
11	Me_3Si–	Ph	Cl	Me_2Zn	40	12	93(96)

[a] Isolated yields with GLC in parentheses.
[b] All products were ≥98–99% *E*.

of $Pd(^tBu_3P)_2$ in THF did not proceed to a detectable extent even at 50 °C. In sharp contrast, the corresponding reaction with MeMgBr at 50 °C gave the desired product in nearly quantitative yield. So, despite generally unfavorable chemoselectivity profiles that the Grignard reagents display, their distinctively higher reactivity observed in this case makes it worthwhile to consider Mg as a potentially useful metal countercation in certain cases of Pd-catalyzed cross-coupling. On the other hand, the reaction of (*Z*)-1-bromo-1-phenyl-1-octene with Me_4Sn in the presence of 5 mol% of $Pd(^tBu_3P)_2$ in THF at 23 °C did not produce the desired product **2a** within several hours. Upon refluxing the reaction mixture, **2a** was formed in 23% GLC yield along with no less than six by-products, the total amount of which was estimated to be more than the amount of **2a**. However, the reaction did proceed much more readily and cleanly in DMF. After 24 h at 23 °C, **2a** was formed in 84% GLC yield along with a 5% yield of its *Z* isomer. The use of 5 mol% of $Pd_2(dba)_3$ and 30 mol% of TFP in conjunction with Me_4Sn and DMF, as previously reported for the only previously known case of Pd-catalyzed methylation of (*Z*)-α-bromostyrenes [6], led to the formation of **2a** in 69% yield and in 95% stereoselectivity. Although only a very limited amount of experimental data is available for comparison, the Pd-catalyzed alkylation with alkylstannanes does appear to be slower than those with Zn or Mg. Moreover, both product yields and stereoselectivity appear to be comparatively lower.

In our previous investigation [1], it was not feasible to develop a procedure for one-pot tandem alkynylation–alkylation of 1,1-dihalo-1-alkenes. In this study, however, the presence of an aryl group in place of an alkynyl group in conjugation with a bromoalkenyl group might be expected to significantly alter the reaction course, especially stereochemistry. With this in mind, the reaction of **1a** first with 1.2 molar equivalents of PhZnBr and then with 1.5 molar equivalents of Me_2Zn in the presence of 5 mol% of Cl_2Pd(DPEphos) was carried out in one reaction vessel. The desired product **3a** and its *Z* isomer were formed in 83 and 3% GLC yields, respectively. Whereas there was no indication for the formation of the *Z* isomer in the alkylation catalyzed by $Pd(^tBu_3P)_2$, the presence of the *Z* isomer in this reaction was readily seen in both GLC and NMR analyses. In cases where removal of the *Z* isomer is facile and practical, however, the one-pot procedure might prove to be more desirable in an overall sense than the two-pot procedure reported herein. Efforts are currently being made to develop such a one-pot procedure and carefully compare both options.

4. Experimental

4.1. General method

All experiments were conducted under dry argon atmosphere. THF, diethyl ether, and benzene were dried and distilled by the standard methods. Flash chromatographic separations were carried out on 230–400 mesh silica gel 60. Gas chromatography was performed on a HP 6890 Gas Chromatograph using an HP-5 capillary column (30 m × 0.32 mm, 0.5 μm film) with appropriate hydrocarbons as internal standards. ^{1}H- and ^{13}C-NMR

spectra were recorded in $CDCl_3$ on a Varian Inova-300 spectrometer. IR spectra were recorded on a Perkin–Elmer Spectrum 2000 FT-IR spectrometer. LRMS and HRMS were obtained on Hewlett Packed 5995 GC-MS and Kratos MS-50 mass spectrometers, respectively. Optical rotations were measured on an Autopol III automatic polarimeter.

4.2. Starting materials and reagents

$ZnBr_2$ was dried under vacuum prior to use. Dimethylzinc, diethylzinc, phenyllithium, 2-thiazolylzinc bromide, 2-thienylzinc bromide and $Pd(dppf)Cl_2$ were purchased and used as received. 1,1-Dihalo-1-alkenes were prepared from their corresponding aldehydes by the method of Corey and Fuchs [10]. $Pd(PPh_3)_4$ [11], $Pd(DPEphos)Cl_2$ [12], and $Pd(^tBu_3P)_2$ [2d] were prepared according to the literature procedures.

4.2.1. Synthesis of phenylzinc bromide

Phenyllithium (0.67 ml, 1.8 M in cyclohexane, 1.2 mmol) was added to a solution of dried $ZnBr_2$ (270 mg, 1.2 mmol) in THF (or diethyl ether) (5 ml) at 0 °C. The mixture was stirred at 23 °C for 30 min. The phenylzinc reagent was used directly in the arylation.

4.2.2. Synthesis of butylzinc bromide

Butyl-lithium (0.80 ml, 2.5 M in hexane, 2.0 mmol) was added to a solution of dried $ZnBr_2$ (450 mg, 2.0 mmol) in THF (5 ml) at 0 °C. The mixture was stirred at 23 °C for 30 min. The butylzinc reagent was used directly in the alkylation.

4.3. General procedure for the preparation of (*Z*)-α-bromo- or chlorostyrenes

A solution of a starting 1,1-dibromo- or 1,1-dichloro-1-alkene (1.0 mmol), an arylzinc bromide (1.2 mmol), and a palladium catalyst were stirred in the solvent at the corresponding temperature for the time indicated in Tables 1 and 2. The reaction mixture was quenched with aqueous NH_4Cl, extracted with ether, washed with brine, dried over Na_2SO_4, and evaporated under vacuum. The crude products were subjected to column chromatography (silica gel 230–400 mesh, hexanes) to give the corresponding products.

4.3.1. (1*Z*)-1-Bromo-1-phenyl-1-octene

Yield, 94%. Stereoisomeric purity, ≥98%. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.96 (t, $J = 6.4$ Hz, 3H), 1.35–1.6 (m, 8H) 2.35–2.5 (m, 2H), 6.25 (t, $J = 6.9$ Hz, 1H), 7.3–7.4 (m, 3H), 7.55–7.6 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.08, 22.61, 28.40, 28.99, 31.68, 32.53, 125.24, 127.48 (2C), 128.14 (3C), 131.88, 140.08. IR (neat) 3059, 2856, 1596, 1444, 1122 cm^{-1}. MS (CI) *m/z* (%) 267 (20) [$M^+ + 1$]. HRMS Calc. for $C_{14}H_{19}Br$ 266.0670, Found 266.0676.

4.3.2. (1*Z*)-1-Chloro-1-phenyl-1-octene [13]

Yield, 84%. Stereoisomeric purity, ≥98%. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.97 (t, $J = 6.2$ Hz, 3H), 1.35–1.6 (m, 8H) 2.4–2.5 (m, 2H), 6.19 (t, $J = 7.0$ Hz, 1H), 7.3–7.45 (m, 3H), 7.6–7.65 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.07, 22.63, 28.58, 29.03, 29.62, 31.70, 126.32 (2C), 128.08, 128.11, 128.20 (2C), 132.65, 138.42.

4.3.3. (1*Z*)-1-Bromo-1-(2'-thienyl)-1-octene

Yield, 85%. Stereoisomeric purity, ≥98%. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.89 (t, $J = 6.5$ Hz, 3H), 1.25–1.55 (m, 8H) 2.25–2.4 (m, 2H), 6.27 (t, $J = 9.0$ Hz, 1H), 6.9–7.0 (m, 1H), 7.15–7.25 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.07, 22.59, 28.37, 28.96, 31.65, 32.16, 117.02, 124.92, 126.42, 126.90, 130.48, 143.27. IR (neat) 3107, 3076, 2855, 1594, 1465, 1229 cm^{-1}. MS (CI) *m/z* (%) 273 (34) [$M^+ + 1$]. HRMS Calc. for $C_{12}H_{17}BrS$ 272.0234, Found 272.0232.

4.3.4. (1*Z*)-1-Bromo-1-(2-thiazolyl)-1-octene

Yield, 84%. Stereoisomeric purity, ≥98%. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.89 (t, $J = 6.2$ Hz, 3H), 1.25–1.6 (m, 8H) 2.3–2.45 (m, 2H), 7.08 (t, $J = 7.2$ Hz, 1H), 7.28 (d, $J = 3.1$ Hz, 1H), 7.80 (d, $J = 3.1$ Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 13.89, 22.38, 27.87, 28.79, 31.42, 31.84, 116.24, 119.53, 134.92, 143.38, 167.41. IR (neat) 3067, 2857, 1595, 1479, 1218, 1123 cm^{-1}. MS (CI) *m/z* (%) 267 (100) [$M^+ + 1$]. HRMS Calc. for $C_{11}H_{16}BrNS$ 273.0187, Found 273.0187.

4.3.5. (1*Z*, 3*S*)-1-Bromo-3-methyl-1-phenyl-1-pentene

Yield, 86%. Stereoisomeric purity, ≥98%. $[\alpha]_D^{23}$ + 32.7 (*c* 4.6, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.94 (t, $J = 7.3$ Hz, 3H), 1.07 (d, $J = 6.7$ Hz, 3H), 1.4–1.5 (m, 2H), 2.65–2.8 (m, 1H), 5.96 (d, $J = 9.0$ Hz, 1H), 7.25–7.35 (m, 3H), 7.45–7.55 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 11.80, 19.32, 29.51, 38.82, 124.06, 127.58 (2C), 128.14 (2C), 128.18, 137.52, 140.17. IR (neat) 3082, 3032, 2961, 2872, 1596, 1490, 1455, 1120 cm^{-1}.

4.3.6. (1*Z*, 3*S*)-1-Chloro-3-methyl-1-phenyl-1-pentene

Yield, 83%. Stereoisomeric purity, ≥98%. $[\alpha]_D^{23}$ + 39.5 (*c* 3.9, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.98 (t, $J = 7.3$ Hz, 3H), 1.11 (d, $J = 6.7$ Hz, 3H), 1.2–1.4 (m, 2H), 2.75–2.9 (m, 1H), 5.95 (d, $J = 9.0$ Hz, 1H), 7.25–7.4 (m, 3H), 7.5–7.65 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 11.82, 19.56, 29.70, 36.01, 126.40 (2C), 128.14, 128.19 (2C), 131.69, 133.81, 138.45. IR (neat) 3065, 2873, 1596, 1491, 1456, 1121 cm^{-1}. MS (CI) *m/z* (%) 194 (45) [M^+]. HRMS Calc. for $C_{12}H_{15}Cl$ 194.0862, Found 194.0856.

4.3.7. (1Z, 3S)-1-Bromo-3-methyl-1-(2'-thienyl)-1-pentene

Yield, 86%. Stereoisomeric purity, ≥98%. $[\alpha]_D^{23}$ + 39.2 (*c* 5.3, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.92 (t, $J = 6.3$ Hz, 3H), 1.05 (d, $J = 6.7$ Hz, 3H), 1.35–1.5 (m, 2H), 2.6–2.75 (m, 1H), 6.04 (d, $J = 9.0$ Hz, 1H), 6.9–7.0 (m, 1H), 7.1–7.25 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.20, 19.73, 29.88, 38.96, 116.30, 125.29, 126.92, 127.27, 136.26, 143.67. MS (CI) *m/z* (%) 245 (22) $[M^+ + 1]$. HRMS Calc. for $C_{10}H_{13}Br$ 243.9921, Found 243.9922.

4.3.8. (1Z, 3S)-1-Bromo-3-methyl-1-(2'-thiazolyl)-1-penene

Yield, 82%. Stereoisomeric purity, ≥98%. $[\alpha]_D^{23}$ + 32.5 (*c* 3.5, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.94 (t, $J = 7.5$ Hz, 3H), 1.10 (d, $J = 6.7$ Hz, 3H), 1.45–1.55 (m, 2H), 2.65–2.8 (m, 1H), 6.88 (d, $J = 9.3$ Hz, 1H), 7.30 (d, $J = 3.2$ Hz, 1H), 7.82 (d, $J = 3.2$ Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 11.75, 18.97, 29.18, 38.46, 115.17, 119.72, 140.21, 143.67, 167.73. IR (neat) 3060, 2926, 1595, 1480, 1456, 1130 cm^{-1}. MS (CI) *m/z* (%) 247 (100) $[M^+ + 1]$. HRMS Calc. for $C_9H_{12}BrNS$ 244.9824, Found 244.9826.

4.3.9. (1Z)-1-Chloro-1,2-diphenylethene

Yield, 82%. Stereoisomeric purity, ≥98%. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.08 (s, 1H), 7.25–7.45 (m, 6H), 7.7–7.8 (m, 4H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 126.06, 126.68 (2C), 127.96, 128.24 (2C), 128.36 (2C), 128.70 (2C), 129.43, 132.04, 135.23, 139.22.

4.3.10. (1Z)-1-Chloro-4-trimethylsilyl-1-buten-3-yne

Yield, 90%. Stereoisomeric purity, ≥98%. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.28 (s, 9H), 6.25 (s, 1H), 7.35–7.4 (m, 3H), 7.55–7.65 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ −0.15, 100.88, 104.04, 107.01, 126.26 (2C), 128.47 (2C), 129.65, 136.45, 143.49. IR (neat) 3062, 3031, 2960, 2129, 1595, 1490, 1446, 1250, 1087 cm^{-1}. MS (CI) *m/z* (%) 235 (100) $[M^+ + 1]$. HRMS Calc. for $C_{13}H_{15}BrSi$ 234.0632, Found 234.0626.

4.4. General procedure for the alkylation of (Z)-α-bromo- or chlorostyrenes

A mixture of $Pd(^tBu_3P)_2$ (5.1 mg, 0.01 mmol), a monobromide or a monochloride (0.5 mmol), and an alkylzinc reagent or methylmagnesium bromide (1.0 mmol) in THF (5 ml) was stirred at the temperature indicated in Table 3. The reaction mixture was quenched with aqueous NH_4Cl at 0 °C, extracted with ether, washed with brine, dried over Na_2SO_4, and evaporated under vacuum. The crude product was subjected to column chromatography (silica gel, hexanes) to give the corresponding products.

4.4.1. (2E)-2-Phenyl-2-nonene [14]

Yield, 92%. Stereoisomeric purity, ≥98%. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.95 (t, $J = 6.4$ Hz, 3H), 1.3–1.55 (m, 8H), 2.08 (s, 3H), 2.2–2.3 (m, 2H), 5.84 (t, $J = 6.1$ Hz, 1H), 7.25–7.45 (m, 5H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.10, 15.73, 22.67, 28.80, 29.09, 29.59, 31.82, 125.58 (2C), 126.38, 128.10 (2C), 128.82, 134.44, 144.06.

4.4.2. (3E)-3-Phenyl-3-decene

Yield, 95%. Stereoisomeric purity, ≥98%. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.92 (t, $J = 6.1$ Hz, 3H), 1.00 (t, $J = 7.5$ Hz, 3H), 1.2–1.5 (m, 8H), 2.15–2.25 (m, 2H), 2.45–2.6 (m, 2H), 5.66 (t, $J = 7.3$ Hz, 1H), 7.25–7.4 (m, 5H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 13.59, 14.09, 22.67, 22.88, 28.43, 29.12, 29.90, 31.82, 126.27 (2C), 126.35, 128.11 (2C), 128.52, 141.38, 143.18. IR (neat) 3055, 2927, 2855, 1598, 1490, 1466, 1120 cm^{-1}. MS (CI) *m/z* (%) 217 (100) $[M^+ + 1]$. HRMS Calc. for $C_{16}H_{24}$ 216.1878, Found 216.1883.

4.4.3. (5E)-5-Phenyl-5-dodecene

Yield, 95%. Stereoisomeric purity, ≥98%. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.85-0.95 (m, 6H), 1.3–1.5 (m, 12H), 2.1–2.25 (m, 2H), 2.48 (t, $J = 6.7$ Hz, 2H), 5.63 (t, $J = 7.2$ Hz, 1H), 7.15–7.35 (m, 5H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 13.96, 14.10, 22.69, 22.71, 28.59, 29.14, 29.48, 29.92, 30.96, 31.85, 126.31 (3C), 128.08 (2C), 119.12, 140.06, 143.54.

4.4.4. (2E)-2-(2'-Thienyl)-2-nonene

Yield, 92%. Stereoisomeric purity, ≥98%. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.89 (t, $J = 6.4$ Hz, 3H), 1.25–1.5 (m, 8H), 2.03 (s, 3H), 2.17–2.25 (m, 2H), 5.94 (t, $J = 7.3$ Hz, 1H), 6.9–6.95 (m 2H), 7.0–7.1 (m, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.09, 15.70, 22.64, 28.48, 29.06, 29.49, 31.77, 121.77, 122.64, 127.12, 127.71, 128.61, 148.18. IR (neat) 3072, 2956, 2855, 1591, 1457, 1120 cm^{-1}. MS (CI) *m/z* (%) 209 (100) $[M^+ + 1]$. HRMS Calc. for $C_{13}H_{20}S$ 208.1286, Found 208.1294.

4.4.5. (2E)-2-(2'-Thiazolyl)-2-nonene

Yield, 93%. Stereoisomeric purity, ≥98%. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.89 (t, $J = 7.4$ Hz, 3H), 1.3–1.5 (m, 8H), 2.15 (s, 3H), 2.2–2.3 (m, 2H), 6.46 (t, $J = 7.3$ Hz, 1H), 7.13 (d, J = 3.3 Hz, 1H), 7.71 (d, $J = 3.3$ Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.00, 14.80, 22.54, 28.54, 28.99 (2C), 31.65, 117.11, 129.75, 133.45, 142.61, 171.91.

4.4.6. (2E,4S)-4-Methyl-2-phenyl-2-hexene

Yield, 92%. Stereoisomeric purity, ≥98%. $[\alpha]_D^{23}$ + 50.1 (*c* 2.4, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.98 (t, $J = 7.3$ Hz, 3H), 1.10 (d, $J = 6.7$ Hz, 3H), 1.2–1.6 (m, 2H), 2.11 (d, $J = 1.0$ Hz, 3H), 2.4–2.65 (m, 1H), 5.63 (dd, $J = 8.4$, 1.0 Hz, 1H), 7.25–7.5 (m, 5H). ^{13}C-

NMR (75 MHz, $CDCl_3$) δ 12.02, 15.99, 20.69, 30.51, 34.85, 125.66 (2C), 126.41, 128.09 (2C), 133.36, 135.00, 144.14. IR (neat) 3024, 2960, 1597, 1493, 1455, 1120 cm^{-1}. MS (CI) *m/z* (%) 175 (100) $[M^+ + 1]$. HRMS Calc. for $C_{13}H_{18}$ 174.1409, Found 174.1408.

4.4.7. (3E,5S)-5-Methyl-3-phenyl-3-octene

Yield, 94%. Stereoisomeric purity, $\geq 98\%$. $[\alpha]_D^{23}$ + 61.0 (*c* 2.4, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.85–1.05 (m, 9H), 1.25–1.5 (m, 2H), 2.35–2.55 (m, 3H), 5.37 (d, $J = 9.8$ Hz, 1H), 7.15–7.4 (m, 5H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.13, 13.90, 21.15, 23.06, 30.55, 34.58, 126.38, 126.40 (2C), 128.09 (2C), 134.08, 140.30, 143.23. IR (neat) 3066, 3022, 2963, 2872, 1598, 1492, 1455, 1120 cm^{-1}. MS (CI) *m/z* (%) 189 (100) $[M^+ + 1]$. HRMS Calc. for $C_{14}H_{10}$ 188.1565, Found 188.1572.

4.4.8. (2E,4S)-4-Methyl-2-(2′-thienyl)-2-hexene

Yield, 93%. Stereoisomeric purity, $\geq 98\%$. $[\alpha]_D^{23}$ +7.0 (*c* 4.6, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.88 (t, $J = 7.3$ Hz, 3H), 1.00 (d, $J = 6.6$ Hz, 3H), 1.2–1.5 (m, 2H), 2.03 (d, $J = 1.0$ Hz, 3H), 2.35–2.5 (m, 1H), 5.70 (dd, $J = 7.4$, 1.0 Hz, 1H), 6.9–6.95 (m, 2H), 7.0–7.1 (m, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.00, 15.97, 20.60, 30.36, 34.64, 121.86, 122.62, 127.08, 127.50, 133.73, 148.23. IR (neat) 3055, 2925, 1591, 1456, 1382, 1120 cm^{-1}. MS (CI) *m/z* (%) 181 (100) $[M^+ + 1]$. HRMS Calc. for $C_{11}H_{16}S$ 180.0973, Found 180.0972.

4.4.9. (2E,4S)-4-Methyl-2-(2′-thiazolyl)-2-hexene

Yield, 92%. Stereoisomeric purity, $\geq 98\%$. $[\alpha]_D^{23}$ + 55.6 (*c* 2.4, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.90 (t, $J = 7.3$ Hz, 3H), 1.05 (d, $J = 6.6$ Hz, 3H), 1.25–1.55 (m, 2H), 2.16 (d, $J = 0.9$ Hz, 3H), 2.45–2.6 (m, 1H), 6.26 (dd, $J = 9.8$, 0.9 Hz, 1H), 7.14 (d, $J = 3.3$ Hz, 1H), 7.72 (d, $J = 3.3$ Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 11.92, 15.08, 20.12, 29.98, 34.77, 117.14, 128.62, 139.16, 142.59, 172.01. IR (neat) 3060, 2962, 1594, 1486, 1121 cm^{-1}. MS (CI) *m/z* (%) 182 (100) $[M^+ + 1]$. HRMS Calc. for $C_{10}H_{15}NS$ 181.0925, Found 181.0929.

4.4.10. (1E)-1,2-Diphenyl-1-propene [15]

Yield, 91%. Stereoisomeric purity, $\geq 98\%$. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.27 (s, 3H), 6.83 (s, 1H), 7.25–7.55 (m, 10H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 17.43, 125.97 (2C), 126.43, 127.14, 127.67, 128.14 (2C), 128.29 (2C), 129.18 (2C), 137.38, 138.32, 143.92.

4.4.11. (3E)-4-Phenyl-1-trimethylsilyl-3-penten-1-yne

Yield, 93%. Stereoisomeric purity, $\geq 98\%$. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.27 (s, 9H), 2.35 (d, $J = 0.8$ Hz, 3H), 5.92 (d, $J = 0.8$ Hz, 1H), 7.3–7.5 (m, 5H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 0.06 (3C), 18.66, 100.26, 103.77, 106.58, 125.40 (2C), 128.17, 128.38 (2C), 140.72, 149.73. IR (neat) 3081, 3059, 3025, 2959, 2131, 1598, 1494, 1445, 1250, 1102 cm^{-1}. MS (CI) *m/z* (%) 215 (100) $[M^+ + 1]$. HRMS Calc. for $C_{14}H_{18}Si$ 214.1178, Found 214.1186.

4.5. One-pot procedure for the preparation of (2E)-2-phenyl-2-nonene

A solution of 1,1-dibromo-1-octene (266 mg, 1.0 mmol), phenylzinc bromide (1.2 mmol), and Pd(DPE-phos)Cl_2 (35.7 mg, 0.05 mmol) in 10 ml of THF was stirred at 23 °C. After 1 h, Me_2Zn (0.75 ml, 2 M in toluene, 1.5 mmol) was added, and the mixture was stirred at 55 °C (oil bath) for 10 h. GLC analysis indicated 83% of the title compound along with 3% of its *Z*-isomer.

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