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Integrated Chemical Process. Construction of Highly Substituted Allylic Moieties from Allylic Sulfones in One-Pot

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Abstract: According to "integrated chemical process", a novel one-pot process for construction of highly substituted allylic moieties has been achieved. A series of alkylation of allylic sulfones and palladium-catalyzed reductive desulfonylation by use of $LiBHEt_3$ is integrated. The double alkylation furnishes more substituted olefins. Use of arylzinc compounds in place of the hydride enables electrophilic alkylation/nucleophilic arylation in one-pot. The integrated process provides higher overall yields than the corresponding stepwise process. © 1999 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

Integration of multifold reactions into one-pot is feasible if all reactions could be conducted under the identical reaction conditions. According to this concept designated as "integrated chemical process", we developed an extremely concise route for polyenes[1] and acetylenes[2] by virtue of the double elimination of β-substituted sulfones. In this process, all reactions are set to proceed under basic conditions. In this context, the well-established olefin synthesis through alkylation of allylic sulfones followed by reductive desulfonylation[3] is expected to undergo the analogous integration. Since the normal carbanion technology is invoked for the alkylation, the consolidation is achievable if desulfonylation could proceed under the same conditions as employed for the alkylation. Among various desulfonylation methods so far advanced, palladium-catalyzed $LiBHEt_3$ reduction[4] seems most promising because of its compatibility with basic conditions. Moreover, employment of suitable organometallic reagents in place of $LiBHEt_3$ allows both carbon-carbon bond formation and desulfonylation to be consolidated so that the process could enjoy further compaction. We disclose herein that this can be realized by use of arylzinc reagents.

The integrated chemical process usually gives rise to not only the simplification of the experimental manipulations but also, and more importantly, the increase of overall yield compared to that by the stepwise method due to avoidance of the material loss that is encountered during isolation and purification of the intermediates in the stepwise process.[1,2] There appeared a considerable number of literatures[5] which dealt with accommodation of multifold steps in one-pot but the improvement of yield has not been assessed in detail, to the best of our knowledge, except in one case. Organ et. al reported such examples in the tandem Lewis acid-catalyzed Diels-Alder and allyl silane-aldehyde reactions.[6] Thus, another purpose of this paper, in addition to

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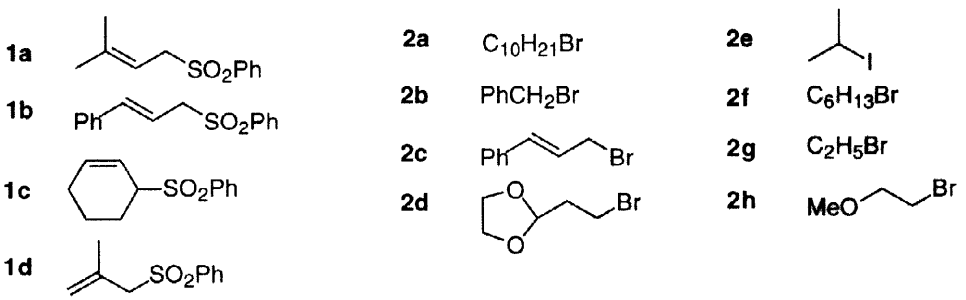
providing a convenient access to highly substituted allylic compounds, is to exemplify the advantage of the integrated chemical process in terms of the overall yield in comparison with the corresponding stepwise process.[7]

RESULTS AND DISCUSSION

Scheme 1 outlines the integration of the alkylation of sulfones followed by reductive desulfonylation to arrive at olefins. Allylic sulfones **1** were treated with BuLi and subsequently alkyl halides **2** (step i). To this reaction mixture were added $Pd(OAc)_2$, phosphine and $LiBHEt_3$ (step ii). The results are summarized in Table 1. As a consequence of screening of phosphines (entries 1-3), 1,3-bis(diphenylphosphino)propane (dppp) was the ligand of our choice since it gave rise to higher yields than 1,4-bis(diphenylphosphino)butane (dppb) and Bu_3P, yet a better outcome emerged with Bu_3P in one exceptional case (entries 8). A variety of allylic sulfones **1** and alkyl halides **2** whose structures are shown below were employable and, in general, reasonable yields of the desired olefins were obtained. The alkyl group was incorporated exclusively at the α-position to furnish a single isomer except **1c**. With this substrate, the hydride attack did not take place regioselectively affording olefin **4** as major products (entries 11 and 12). For comparison, we also performed the stepwise approach where the alkylated sulfones were isolated and, after purification, subjected to desulfonylation under the reaction conditions same as the integrated process. Yields of the respective steps as well as overall yields are shown in the parentheses in the table. It should be noted that at least three trials were run for each reaction to assure the yield and the averaged values given are accurate within the range of ± 5 % deviation. Remarkably, the integrated process always afforded higher yields than the stepwise process except two cases (entries 2 and 3).



Scheme 1

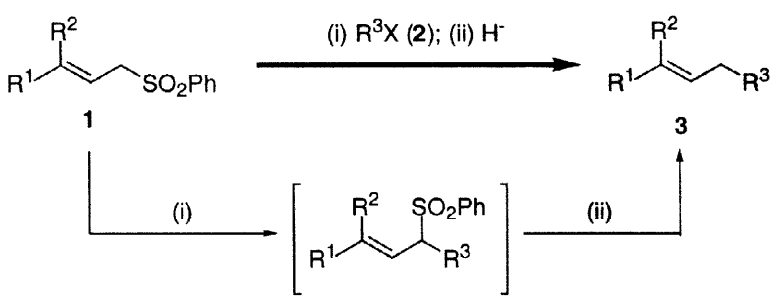
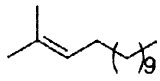
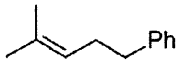
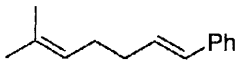
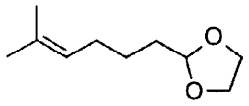
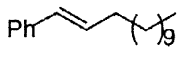
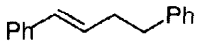
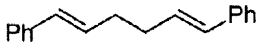
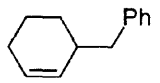
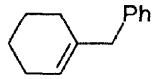
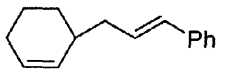
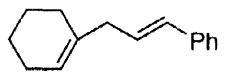


Table 1. One-Pot Alkylation/Desulfonylation (Scheme 1).[a)]

entry	1	2	reactn conditns of step (ii)[b)]	3		yield / %[c)]
1	**1a**	**2a**	dppp (0.1 equiv); 0 °C, 2 h		**3aa**	85 (81 x 79 =64)
2		**2a**	dppb (0.1 equiv); 0 °C, 2 h; r.t., 5 h	**3aa**		78 (81 x 97 = 79)
3		**2a**	Bu_3P (0.4 equiv); 0 °C, 2 h; r.t. 20 h	**3aa**		57 (81 x 84 = 84)
4		**2b**	dppp (0.1 equiv); 0 °C, 2 h		**3ab**	79 (91 x 57 = 52)
5		**2c**	dppp (0.1 equiv); 0 °C, 2 h		**3ac**	81 (93 x 54 = 50)
6		**2d**	dppp (0.1 equiv); 0 °C, 2 h		**3ad**	76
7	**1b**	**2a**	dppp (0.1 equiv); 0 °C, 2.5 h		**3ba**	66 (74 x 66 = 49)
8			Bu_3P (0.4 equiv); 0 °C, 2 h	**3ba**		83 (74 x 77 = 57)
9		**2b**	dppp (0.1 equiv); 0 °C, 4 h		**3bb**	66 (89 x 66 = 59)
10		**2c**	dppp (0.1 equiv); 0 °C, 2 h		**3bc**	46 (70 x 46 = 32)
11	**1c**	**2b**	dppp (0.1 equiv); 0 °C, 2 h; r.t., 20 h		**3cb**	85[d)]
					**4cb**	
12		**2c**	dppp (0.1 equiv); 0 °C, 2 h; r.t., 5 h		**3cc**	93[e)]
					**4cc**	

[a)]Reaction conditions for (i): **1** (1.05 equiv), BuLi (1.05 equiv), **2** (1.0 equiv), THF, -78 °C ~ rt, 2 h. [b)] $Pd(OAc)_2$ (0.1 equiv.); $LiBHEt_3$ (2 equiv.). [c)] Isolated yield. The overall yield in stepwise reaction [(%yield in (i)) x (%yield in (ii))] is given in parentheses. [d)] **3cb**:**4cb** = 18:82. [e)] **3cc**:**4cc** = 39:61.

Another characteristic feature of the allylic sulfone carbanion chemistry is the ease with which two alkyl groups can be incorporated. Thus, integration of the consecutive alkylations and desulfonylation should

provide convenient access to tri- and tetrasubstituted allylic moieties (Scheme 2). Prior to setting out the integration, we screened hydride reagents for the palladium-catalyzed desulfonylation (step iii) using a simple dialkylation product (Table 2). $LiBHEt_3$ has proved to be better than $LiBH[CH(CH_3)CH(CH_3)_2]_3$. Moreover, the poorer result with $Mo(CO)_6$/pyridine catalyst[8] led us to choose the $LiBHEt_3/Pd(OAc)_2$/phosphine system for the present purpose.

Scheme 2

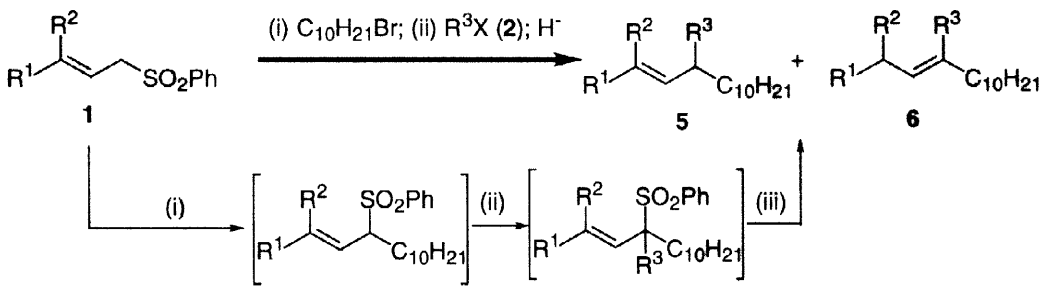
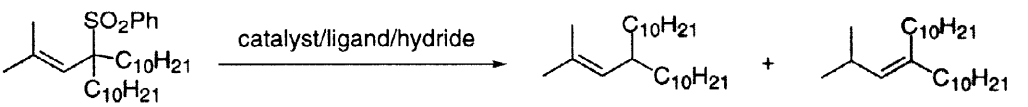


Table 2. Desulfonylation of Dialkylation Product.



entry	catalyst[a]	ligand	hydride[b]	reaction conditions	yield/%[c]
1	$Pd(OAc)_2$	dppp (0.1 equiv.)	$LiBHEt_3$	0 °C, 3 h	79
2	$Pd(OAc)_2$	Bu_3P (0.2 equiv.)	$LiBHEt_3$	0 °C, 2 h; r.t. 2 h	94
3	$Pd(OAc)_2$	dppp (0.1 equiv.)	$LiBH[CH(CH_3)CH(CH_3)_2]_3$	0 °C, 2 h; r.t., 6 h	N.R.
4	$Pd(OAc)_2$	Bu_3P (0.4 equiv.)	$LiBH[CH(CH_3)CH(CH_3)_2]_3$	0 °C, 2 h; r.t., 6 h	78
5	$Mo(CO)_6$	pyridine (0.2 equiv.)	$LiBHEt_3$	0 °C, 3 h; reflux 24 h	38

[a] 0.1 equiv. [b] 2.0 equiv. [c] A mixture of regioisomers (ca. 40:60).

Then, the integrated protocol shown in Scheme 2 was addressed. Sulfone **1a** was treated with BuLi and $C_{10}H_{21}Br$ at -78 °C ~ rt. After consumption of **1a** had been confirmed by TLC monitoring, the second alkylation was performed in a similar way. To this reaction mixture was added $Pd(OAc)_2$, phosphine and $LiBHEt_3$. Usual workup provided the desired dialkylation products. A high level of regioselectivity was attained for both alkylations to give α,α-dialkylation products exclusively. Unfortunately, however, the products were constituted by a mixture of **5** and **6** that emerged as a consequence of non-regioselective hydride attack. The results are summarized in Table 3 along with yields by the corresponding stepwise processes.

Normally, dppp afforded higher yields than the other phosphines except for the reaction between **1a** and **2a**, in which the best yield was obtained with dppb (entry 1). The superiority of the integrated process to the stepwise process in terms of yield is generally seen except one case (entry 3).

Table 3. One-Pot Dialkylation/Desulfonylation (Scheme 2).[a)]

entry	1	R^3X	reactn conditns of desulfonylation	5 + 6 yield / %[b)]	5:6
1	**1a**	**2a**	dppb; 0 °C, 2 h; r.t., 15 h	**5aa** + **6aa** 78 (76 x 87 = 69)	37:63
2	**1a**	**2a**	dppp; 0 °C, 2 h	**5aa** + **6aa** 65 (76 x 79 = 60)	59:41
3	**1a**	**2a**	Bu_3P[c)]; 0 °C, 2 h; r.t., 11 h	**5aa** + **6aa** 51 (76 x 94 = 71)	40:60
4	**1a**	**2c**	dppp; 0 °C, 2 h	**5ac** + **6ac** 77 (83 x 84 = 70)	52:48
5	**1a**	**2e**	dppp; 0 °C, 2 h; r.t. ,15 h	**5ae** + **6ae** 74	74:26

[a)] Reaction conditions: **1** (1.0 equiv.), BuLi (1.0 equiv.), THF, -78 °C, 1 h, $C_{10}H_{21}Br$ (1.0 equiv.), -78 °C~r.t., 2 h; BuLi (1.2 equiv.) , -78 °C, 1 h, R^3X (1.2 equiv.), -78 °C~r.t., 2 h; $Pd(OAc)_2$ (0.1 equiv.); phosphine (0.1 equiv.), $LiBHEt_3$ (2.0 equiv.). [b)] Isolated yield. The overall yield in stepwise reaction [(%yield of dialkylation product) x (%yield of olefin)] is given in parentheses. [c)] 0.4 equiv.

A sequence of nucleophilic alkylation and palladium-catalyzed reductive desulfonylation underlies the above procedures. The π-allylpalladium chemistry enables an alternative means for the direct carbon-carbon bond formation concomitant with desulfonylation of allylic sulfones by use of organometallic electrophiles. We have found that organozinc compounds serve for this purpose[9)] and a protocol for more concise nucleophilic alkylation/electrophilic arylation has been developed (Scheme 3). To the reaction mixture of the mono alkylation products produced by the anionic technology as described above (step i) was added $ZnCl_2$, aryl magnesium bromide, and $Pd(PPh_3)_4$. The results obtained are given in Table 4. The mode of reaction is dependent on the sulfones. Prenyl , cinnamyl and methallyl sulfones, **1a**, **1b**,and **1d**, gave satisfactory yields while only modest yields were obtained with cyclohexenyl sulfone **1c**. The regiochemistry of nucleophilic arylation was not straightforward. Both **1b** and **1c** underwent arylation in a exclusive manner but in the opposite sense (entries 4~9). The γ-selectivity with **1c** can be accounted for in terms of steric hindrance but the analogous explanation

Scheme 3

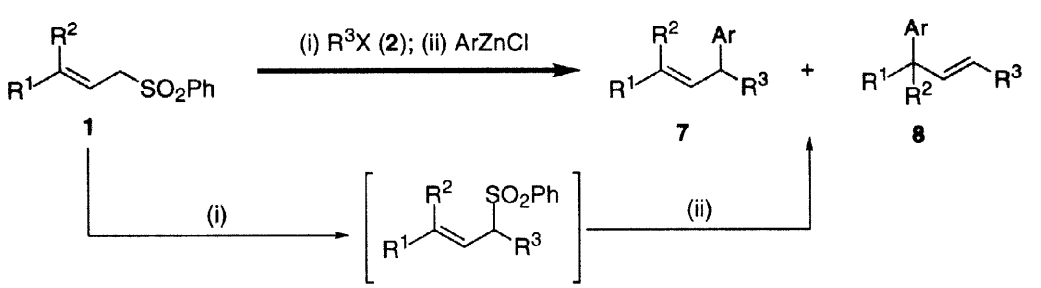
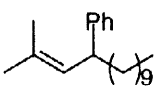
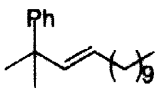
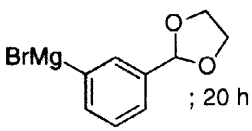
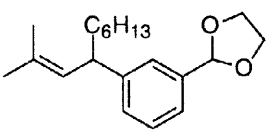
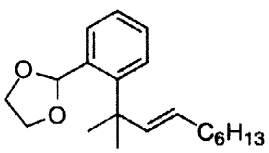
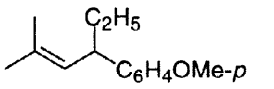
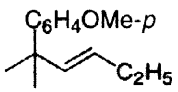
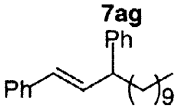
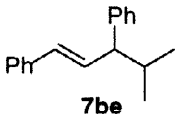
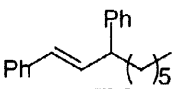
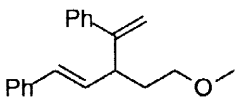
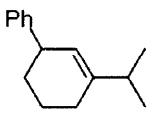
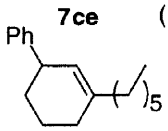
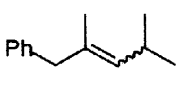
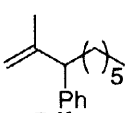
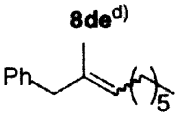


Table 4. One-Pot Electrophilic Alkylation and Desulfonylative Nucleophilic Arylation (Scheme 3).[a]

entry	1	2	ArMgX; reactn time (h)	7	(7:8)	8	yield (7 + 8)/ %[b]
1	**1a**	**2a**	PhMgBr ; 18 h	 **7aa**	(66:34)	 **8aa**	79 (81 x 86 = 70)
2	**1a**	**2f**	 ; 20 h	 **7af**	(59:41)	 **8af**	71
3	**1a**	**2g**	*p*-MeOC$_6$H$_4$MgBr; 20 h	 **7ag**	(63:37)	 **8ag**	88
4	**1b**	**2a**	PhMgBr; 5 h	 **7ba**	(100:0)		74 (76 x 82 = 62)
5	**1b**	**2e**	PhMgBr; 3 h	 **7be**	(100:0)		80 (83 x 80 =66)
6	**1b**	**2f**	PhMgBr; 5 h	 **7bf**	(100:0)		68 (77 x 75 = 58)
7	**1b**	**2h**	PhC(MgBr)=CH$_2$; 5 h	 **7bh**	(100:0)		62 (61 x 84 = 51)
8	**1c**	**2e**[c]	PhMgBr; 3 h	 **7ce**	(100:0)		43 (82 x 46 = 38)
9	**1c**	**2f**	PhMgBr; 3 h	 **7cf**	(100:0)		50 (83 x 54 = 45)
10	**1d**	**2e**[c]	PhMgBr; 4 h		(0:100)	 **8de**[d]	72 (84 x 76 = 64)
11	**1d**	**2f**	PhMgBr; 3 h	 **7df**	(19:81)	 **8df**[e]	88

[a] Reaction conditions: **1** (1.0 mmol), BuLi (1.1 mmol), -78 °C, 1 h; **2** (1.2 mmol), r.t., 1 h; $ZnCl_2$ (3.0 mmol); ArMgBr (3.0 mmol), 0 °C, 30 min; $Pd(PPh_3)_4$ (0.05 mmol), reflux. [b] Isolated yield. The overall yield in stepwise reaction [(%yield of the first alkylation) x (%yield of the second alkylation)] is given in parentheses. [c] BuLi (1.2 mmol); **2e** (1.5 mmol). [d] The *E*:*Z* = 65:35. [e] *E*:*Z* = 62:38.

may not be applicable to **1b** that constantly leads to carbon-carbon bond formation at the α-position irrespective of the sulfone substrates. A mixture of α- and γ-regioisomers constituted the reaction products derived from **1a** and **1d**. In addition, *E,Z*-isomers were formed in γ-arylation products, **8de** and **8df**, from **1d**. In keeping with the previous trends, the integration induced the increase in the overall yield compared to the stepwise route. In entries 8 and 9, the overall yield was primarily governed by the arylation due to its poor yield so that the integration could not give rise to any appreciable advantage over the stepwise process. By contrast, in the other cases where the arylation was relatively clean, circumvention of the intermediate loss is reflected by the improved yields for the integrated process.

In summary, consolidation of the carbanion and π-allylpalladium chemistries has been realized on the basis of "integrated chemical process". This leads to concise synthetic routes for highly substituted allylic moieties as well as increased overall yield. The compounds obtained in this study are not always satisfactory with respect to regiochemistry. These drawbacks, however, are stemmed from the innate character of π-allylpalladium chemistry, not from the integration itself. Thus, improvement of elementary reactions would give rise to cleaner integrated process. It should be pointed out that not only the compaction of chemical processes but also the increase of chemical yield is brought about by merely integrating known reactions. No need for special modifications of the respective reactions testifies the generality of the concept and thus a wide spectrum of applications will be feasible along this line.

EXPERIMENTAL SECTION

General: All reactions were carried out under an atmosphere of nitrogen with freshly distilled solvents under anhydrous conditions, unless otherwise noted. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. BuLi (1.6 M solution in hexanes, Aldrich) was used as received. NMR spectra were recorded at 25 °C on Varian Gemini-300, JEOL Lambda 300 and JEOL Lambda 500 instruments and calibrated with tetramethylsilane (TMS) as an internal reference. Mass spectra were recorded on a Jeol MStation JMS-700 spectrometer. Elemental analyses were performed with the Perkin Elmer PE 2400. Silica gel (Daiso gel IR-60) was used for column chromatography.

One-pot Synthesis of 3aa (Alkylation and Desulfonylation): To a THF solution (5 mL) of **1a** (220 mg, 1.05 mmol) was added BuLi (0.65 mL, 1.0 mmol) at -78 °C and the solution was stirred for 1 h. After addition of **2a** (0.21 mL, 1.0 mmol), the solution was stirred at rt for 2 h and cooled to 0 °C. To the solution was added a THF solution (2 mL) of the palladium catalyst prepared by mixing $Pd(OAc)_2$ (22.5 mg, 0.10 mmol) and dppp (41.2 mg, 0.10 mmol) at rt for 30 min. $LiBHEt_3$ (2.0 mL, 1.0 M THF solution, 2.0 mmol) was added and the mixture was stirred at 0 °C for 2 h. The reaction mixture was combined with water (20 mL) and extracted with EtOAc (20 mL x 3). The organic layer was washed with sat. $NaHCO_3$ solution and brine. Drying (Na_2SO_4) and evaporation left an oil that was purified by column chromatography on silica gel (hexane) to give 2-methyltetradeca-2-ene (**3aa**) (78%).

3aa: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 7.2 Hz, 3H), 1.26 (m, 18H), 1.60 (s, 3H), 1.69 (s, 3H), 1.95 (q, J = 7.4 Hz, 2H), 5.11 (t, J = 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1, 17.6, 22.8, 25.7, 28.1, 29.4, 29.7 (3C), 29.8, 30.0, 32.0, 125.0, 131.0. Anal. calcd for $C_{15}H_{30}$: C, 85.63; H, 14.37%; found: C, 85.76; H, 14.37%.

3ab: ^{1}H NMR ($CDCl_3$) δ 1.56 (s, 3H), 1.68 (s, 3H), 2.29 (q, J = 7.7 Hz, 2H), 2.63 (t, J = 7.5 Hz, 2H), 5.17 (tt, J = 7.1, 1.5 Hz, 1H), 7.13-7.31 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 17.6, 25.7, 30.1, 36.1, 123.7, 125.6, 128.2, 128.4, 132.1, 142.4. Anal. calcd for $C_{12}H_{16}$: C, 89.94; H, 10.06%; found: C, 90.32; H, 10.30%.

3ac: ^{1}H NMR ($CDCl_3$) δ 1.63 (s, 3H), 1.70 (s, 3H), 2.11-2.19 (m, 2H), 2.20-2.28 (m, 2H), 5.17 (tt, J = 6.8, 1.2 Hz, 1H), 6.23 (dt, J = 15.8, 6.5 Hz, 1H), 6.39 (d, J = 15.8 Hz, 1H), 7.17-7.35 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 17.7, 25.7, 27.9, 33.3, 123.8, 125.9, 126.7, 128.4, 129.9, 130.7, 132.0, 137.9. Anal. calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74%; found: C, 89.86; H, 10.08%.

3ad: ^{1}H NMR ($CDCl_3$) δ 1.41-1.50 (m, 2H), 1.60 (s, 3H), 1.63-1.67 (m, 2H), 1.68 (s, 3H), 2.02 (q, J = 7.3 Hz, 2H), 3.81-4.01 (m, 4H), 4.85 (t, J = 4.8 Hz, 1H), 5.11 (tt, J = 7.2, 1.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ

17.6, 24.2, 25.7, 27.7, 33.4, 64.8, 104.6, 124.2, 131.7. Anal. calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66%; found: C, 70.89; H, 10.70%.

3ba: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.6 Hz, 3H), 1.18-1.40 (m, 18H), 1.41-1.49 (m, 2H), 2.20 (q, J = 6.8 Hz, 2H), 6.23 (td, J = 6.7, 15.8 Hz, 1H), 6.37 (d, J = 15.8 Hz, 1H), 7.11-7.20 (m, 1H), 7.25-7.40 (m, 4H). Anal. calcd for $C_{19}H_{30}$: C, 88.30; H, 11.70%; found: C, 88.70; H, 11.85%.

3bb: ^{1}H NMR ($CDCl_3$) δ 2.53 (q, J = 7.8 Hz, 2H), 2.79 (t, J = 7.8 Hz, 2H), 6.26 (dt, J = 15.8, 6.7 Hz, 1H), 6.42 (d, J = 15.8 Hz, 1H), 7.18-7.34 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 34.9, 35.8, 125.9, 126.0, 126.9, 128.3, 128.5 (2C), 129.9, 130.3, 137.7, 141.7. Anal. calcd for $C_{16}H_{16}$: C, 91.37; H, 8.63%; found: C, 91.45; H, 8.23%.

3bc: ^{1}H NMR ($CDCl_3$) δ 2.40 (d, J = 6.5 Hz, 4H), 6.27 (dt, J = 15.8, 6.5 Hz, 2H), 6.44 (d, J = 15.8 Hz, 2H), 7.18-7.36 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 32.9, 126.0, 126.9, 128.5, 129.9, 130.3, 137.7. Anal. calcd for $C_{18}H_{18}$: C, 91.37; H, 8.63%; found: C, 91.76; H, 8.75%.

3cb: ^{1}H NMR ($CDCl_3$) δ 1.20-1.30 (m, 1H), 1.45-1.60 (m, 1H), 1.65-1.75 (m, 2H), 1.95-2.05 (m, 2H), 2.30-2.41 (m, 1H), 2.50-2.65 (m, 2H), 5.55 (d, J = 11.2 Hz, 1H), 5.59-5.70 (m, 1H), 7.10-7.29 (m, 5H).

4cb: ^{1}H NMR ($CDCl_3$) δ 1.45-1.60 (m, 4H), 1.80-1.90 (m, 2H), 1.95-2.05 (m, 2H), 3.22 (s, 2H), 5.42 (brs, 1H), 7.10-7.29 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 22.4, 22.9, 25.3, 28.0, 44.7, 122.9, 125.8, 128.1, 128.9, 137.2, 140.4; HRMS (EI) as a mixture of **3cb** and **4cb** *m/e* calcd for $C_{13}H_{16}$ 172.1252, found 172.1237.

3cc: ^{1}H NMR ($CDCl_3$) δ 1.24-1.35 (m, 1H), 1.48-1.66 (m, 1H), 1.68-1.88 (m, 2H), 1.92-2.08 (m, 2H), 2.13-2.29 (m, 3H), 5.60-5.73 (m, 2H), 6.23 (dt, J = 15.8, 6.9, Hz, 1H), 6.40 (d, J = 15.8 Hz, 1H), 7.15-7.39 (m, 5H).

4cc: ^{1}H NMR ($CDCl_3$) δ 1.48-1.66 (m, 4H), 1.92-2.08 (m, 4H), 2.82 (d, J = 6.9 Hz, 2H), 5.49 (brs, 1H), 6.21 (dt, J = 15.8, 6.9 Hz, 1H), 6.39 (d, J = 15.8 Hz, 1H), 7.15-7.39 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 21.4, 22.4, 22.9, 25.2, 25.3, 28.4, 28.9, 35.5, 39.8, 41.6, 122.1, 125.9, 126.0, 126.7, 126.8, 127.4, 128.4 (2C), 128.8, 129.2, 130.8, 131.1, 131.3, 136.4, 137.7, 137.8. Anal. calcd for $C_{15}H_{18}$ (as a mixture of **3cc** and **4cc**): C, 90.85; H, 9.15%; found: C, 91.01; H, 9.34%.

One-pot Synthesis of 5aa and 6aa (Double Alkylation and Desulfonylation): To a THF solution (4 mL) of **1a** (210 mg, 1.0 mmol) was added BuLi (0.63 mL, 1.0 mmol) at -78 °C and the solution was stirred for 1 h. After addition of **2a** (0.21 mL, 1.0 mmol), the solution was stirred at rt for 2 h and cooled at -78 °C. The solution was treated again with BuLi (0.75 mL, 1.2 mmol) and **2a** (0.25 mL, 1.2 mmol) in the same manner as described above. To the solution was added a THF solution (2 mL) of the palladium catalyst prepared by mixing $Pd(OAc)_2$ (22.5 mg, 0.10 mmol) and dppp (41.2 mg, 0.10 mmol) at rt for 30 min. $LiBHEt_3$ (2.0 mL, 1M THF solution, 2.0 mmol) was added and the mixture was stirred at 0 °C for 2 h and at rt for 15 h. The reaction mixture was combined with water (20 mL) and extracted with EtOAc (20 mL x 3). The organic layer was washed with sat. $NaHCO_3$ solution and brine. Drying (Na_2SO_4) and evaporation left an oil that was purified by column chromatography on silica gel (hexane) to give a mixture of 4-decyl-2-methyltetradeca-2-ene (**5aa**) and 4-decyl-2-methyltetradeca-3-ene (**6aa**) (78% based on **1a**; ratio of the regioisomers was 37:63 by GLC).

5aa: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.6 Hz, 6H), 1.20-1.40 (m, 36H), 1.58 (s, 3H), 1.69 (s, 3H), 2.10-2.20 (m, 1H), 4.78 (d, J = 9.3 Hz, 1H).

6aa: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.6 Hz, 6H), 0.91 (d, J = 6.6 Hz, 6H), 1.20-1.40 (m, 32H), 1.92 (t, J = 7.5 Hz, 2H), 1.97 (t, J = 7.5 Hz, 2H), 2.45-2.55 (m, 1H), 4.90 (d, J = 9.3 Hz, 1H); HRMS (EI) (as a mixture of **5aa** and **6aa**) *m/e* calcd for $C_{25}H_{50}$ 350.3912, found 350.3928.

5ac: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3H), 1.20-1.50 (m, 18H), 2.05-2.15 (m, 1H), 2.18-2.23 (m, 1H), 2.28-2.34 (m, 1H), 4.90 (d, J = 9.4 Hz, 1H), 6.17 (dt, J = 15.7, 6.7 Hz, 1H), 6.34 (d, J = 15.7 Hz, 1H), 7.15-7.22 (m, 1H), 7.25 -7.37 (m, 4H).

6ac: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3H), 0.96 (0.94) (d, J = 6.6 Hz, 6H), 1.20-1.50 (m, 16H), 1.97 (t, J = 7.3 Hz, 2H), 2.54-2.64 (m, 1H), 2.91 (2.84) (d, J = 6.6 Hz, 2H), 5.05 (5.01) (d, J = 9.4 Hz, 1H), 6.14 (dt, J = 15.7, 6.7 Hz, 1H), 6.38 (d, J = 15.7 Hz, 1H), 7.15-7.22 (m, 1H), 7.25-7.37 (m, 4H); HRMS (EI) (as a mixture of **5ac** and **6ac**) *m/e* calcd for $C_{24}H_{38}$ 326.2973, found 326.2977.

5ae: ^{1}H NMR ($CDCl_3$) δ 0.89 (d, J = 7.0 Hz, 6H), 0.90 (t, J = 6.9 Hz, 3H), 1.10-1.50 (m, 18H), 1.50-1.58 (m, 1H), 1.60 (s, 3H), 1.73 (s, 3H), 1.86-1.92 (m, 1H), 4.87 (d, J = 10.0 Hz, 1H).

6ae: ^{1}H NMR ($CDCl_3$) δ 0.90 (t, J = 6.9 Hz, 3H), 0.94 (0.82) (d, J = 6.8 Hz, 6H), 0.99 (0.86) (d, J = 6.8 Hz, 6H), 1.10-1.50 (m, 16H), 2.00 (t, J = 6.7 Hz, 2H), 2.12-2.25 (2.78-2.90) (m, 1H), 2.44-2.58 (2.59-

2.69) (m, 1H), 4.91 (d, J = 9.6 Hz, 1H); HRMS (EI) (as a mixture of **5ae** and **6ae**) *m/e* calcd for $C_{18}H_{36}$ 252.2817, found 252.2862.

One-pot Synthesis of 7aa and 8aa (Alkylation and Desulfonylation-Arylation): To a THF solution (3 mL) of **1a** (210 mg, 1.0 mmol) was added BuLi (0.69 mL, 1.1 mmol) at -78 °C and the solution was stirred for 1 h. After addition of **2a** (0.25 mL, 1.2 mmol), the solution was stirred at rt for 1 h. To the mixture were added $ZnCl_2$ (409 mg, 3.0 mmol) and an ether solution (3.3 mL) of PhMgBr at 0 °C, which had been prepared from bromobenzene (3.2 mL, 30 mmol) and magnesium turning (875 mg, 36 mmol) in ether (30 mL). After addition of $Pd(PPh_3)_4$ (58 mg, 0.05 mmol), the mixture was heated under reflux for 3 h. The reaction mixture was combined with water (20 mL) and extracted with EtOAc (20 mL x 3). The organic layer was washed with sat. $NaHCO_3$ solution and brine. Drying (Na_2SO_4) and evaporation left an oil that was purified by column chromatography on silica gel (hexane) to give a mixture of 4-phenyl-2-methyltetradeca-2-ene (**7aa**) and 2-methyl-2-phenyltetradeca-3-ene (**8aa**) (79%; ratio of the regioisomers was 66:34 by NMR).

7aa: ^{1}H NMR ($CDCl_3$) δ 0.87 (t, J = 6.7 Hz, 3H), 1.15-1.41 (m, 18H), 1.65 (s, 3H), 1.70 (s, 3H), 3.42 (td, J = 7.8, 9.6 Hz, 1H), 5.26 (d, J = 9.6 Hz, 1H), 7.08-7.43 (m, 5H).

8aa: ^{1}H NMR ($CDCl_3$) δ 0.87 (t, J = 6.7 Hz, 3H), 1.15-1.41 (m, 16H), 1.37 (s, 6H), 2.03 (q, J = 7.1 Hz, 2H), 5.42 (dt, J = 15.1, 7.1 Hz, 1H), 5.61 (d, J = 15.1 Hz, 1H), 7.08-7.43 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.1, 18.1, 22.7, 25.9, 27.6, 29.0, 29.2, 29.4, 29.5, 29.6, 29.7, 32.0, 32.7, 37.4, 40.2, 44.4, 125.6, 125.7, 126.1, 126.6, 127.3, 128.0, 128.3, 129.2, 131.0, 139.9, 146.5, 149.5. Anal. calcd for $C_{21}H_{34}$ (as a mixture of **7aa** and **8aa**): C, 88.04; H, 11.96%; found: C, 88.31; H, 12.18%.

7af: ^{1}H NMR ($CDCl_3$) δ 0.86 (t, J = 6.9 Hz, 3H), 1.07-1.48 (m, 10H), 1.64 (s, 3H), 1.69 (s, 3H), 3.45 (q, J = 7.6 Hz, 1H), 3.93-4.24 (m, 4H), 5.24 (d, J = 7.6 Hz, 1H), 5.79 (s, 1H), 7.12-7.49 (m, 4H).

8af: ^{1}H NMR ($CDCl_3$) δ 0.86 (t, J = 6.9 Hz, 3H), 1.07-1.48 (m, 8H), 1.38 (s, 6H), 2.03 (q, J = 7.7 Hz, 2H), 3.93-4.24 (m, 4H), 5.42 (dt, J = 15.1, 7.7 Hz, 1H), 5.60 (d, J = 15.1 Hz, 1H), 5.79 (s, 1H), 7.12-7.49 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 14.0, 18.1, 22.6, 25.8, 27.5, 28.8, 28.9, 29.3, 29.5, 31.7, 31.8, 32.6, 37.3, 40.3, 44.3, 65.2, 103.8, 104.0, 123.6, 123.7, 124.1, 125.3, 126.7, 127.2, 128.0, 128.1, 128.3, 128.9, 131.1, 137.3, 137.6, 139.7, 146.6, 149.6. Anal. calcd for $C_{20}H_{30}O_2$ (as a mixture of **7af** and **8af**): C, 79.42; H, 10.00%; found: C, 79.57; H, 10.28%.

7ag: ^{1}H NMR ($CDCl_3$) δ 0.83 (t, J = 7.4 Hz, 3H), 1.48-1.69 (m, 2H), 1.65 (s, 3H), 1.70 (s, 3H), 3.30 (q, J = 7.6 Hz, 1H), 3.78 (s, 3H), 5.23 (d, J = 7.6 Hz, 1H), 6.77-7.34 (m, 4H).

8ag: ^{1}H NMR ($CDCl_3$) δ 0.99 (t, J = 7.4 Hz, 3H), 1.35 (s, 6H), 1.96-2.12 (m, 2H), 3.79 (s, 3H), 5.43 (dt, J = 15.2, 7.7 Hz, 1H), 5.59 (d, J = 15.2 Hz, 1H), 6.72-7.34 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 12.1, 14.0, 18.0, 25.6, 25.8, 29.1, 30.2, 39.4, 45.1, 55.1, 113.2, 113.6, 127.1, 127.8, 128.1, 129.1, 130.9, 138.3, 139.2, 141.5, 157.4, 157.5. Anal. calcd for $C_{14}H_{20}O$ (as a mixture of **7ag** and **8ag**): C, 82.30; H, 9.87%; found: C, 82.38; H, 10.02%.

7ba: ^{1}H NMR ($CDCl_3$) δ 0.87 (t, J = 6.7 Hz, 3H), 1.15-1.36 (m, 16H), 1.79 (q, J = 7.3 Hz, 2H), 3.39 (q, J = 7.3 Hz, 1H), 6.32 (dd, J = 15.8, 7.3 Hz, 1H), 6.40 (d, J = 15.8 Hz, 1H), 7.15-7.63 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.7, 27.6, 29.3, 29.5, 29.6 (2C), 29.7, 31.9, 35.9, 49.2, 126.1, 126.9, 127.1, 127.2, 127.6, 128.4, 128.7, 129.2, 134.5, 144.7. Anal. calcd for $C_{25}H_{34}$: C, 89.76; H, 10.24%; found: C, 89.71; H, 10.33%.

7be: ^{1}H NMR ($CDCl_3$) δ 0.81 (d, J = 6.7 Hz, 3H), 1.06 (d, J = 6.7 Hz, 3H), 1.98-2.11 (m, 1H), 3.00-3.09 (m, 1H), 6.32-6.44 (m, 2H), 7.15-7.38 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 20.9, 21.2, 33.2, 57.6, 126.0, 126.1, 127.0, 127.9, 128.4, 128.5, 130.3, 133.2, 137.6, 144.3. Anal. calcd for $C_{18}H_{20}$: C, 91.47; H, 8.53%; found: C, 91.37; H, 8.37%.

7bf: ^{1}H NMR ($CDCl_3$) δ 0.86 (t, J = 6.8 Hz, 3H), 1.16-1.40 (m, 16H), 1.79 (q, J = 7.5 Hz, 2H), 3.40 (td, J = 7.5, 6.7 Hz, 1H), 6.32 (dd, J = 15.8, 6.7 Hz, 1H), 6.40 (d, J = 15.8 Hz, 1H), 7.15-7.37 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.6, 27.6, 29.3, 31.8, 35.9, 49.2, 126.1, 126.2, 127.0, 127.6, 128.4, 128.5, 129.2, 134.5, 137.6, 144.7. Anal. calcd for $C_{21}H_{26}$: C, 90.59; H, 9.41%; found: C, 90.79; H, 9.71%.

7bh: ^{1}H NMR ($CDCl_3$) δ 1.74-1.89 (m, 1H), 1.93-2.08 (m, 1H), 3.29 (s, 3H), 3.38-3.49 (m, 1H), 3.56 (td, J = 6.2, 8.1 Hz, 1H), 5.17 (s, 1H), 5.33 (s 1H), 6.21 (dd, J = 15.9, 8.1 Hz, 1H), 6.44 (d, J = 15.9 Hz, 1H), 7.18-7.42 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 34.1, 44.2, 58.5, 70.4, 113.1, 126.1, 126.7, 127.1, 127.2, 128.1, 128.2, 128.4, 130.4, 132.6, 137.4, 142.1, 151.4. Anal. calcd for $C_{20}H_{22}O_2$: C, 86.29; H, 7.97%; found: C, 86.15; H, 8.21%.

7ce: ^{1}H NMR ($CDCl_3$) δ 1.05 (d, J = 6.8 Hz, 6H), 1.41-1.67 (m, 2H), 1.70-1.81 (m, 2H), 1.92-2.11 (m, 3H), 2.18-2.33 (m, 1H), 3.34-3.47 (br, 1H), 5.40-5.47 (br, 1H), 7.15-7.36 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 21.5, 21.6, 21.7, 25.9, 32.9, 35.3, 41.9, 121.6, 125.6, 125.8, 127.7, 128.2, 128.3, 144.9, 147.5; HRMS (EI) *m/e* calcd for $C_{15}H_{20}$ 200.1565, found 200.1578.
7cf: ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 6.7 Hz, 3H), 1.24-1.35 (m, 6H), 1.38-1.81 (m, 5H), 1.89-2.10 (m, 5H), 3.31-3.45 (br, 1H), 5.40-5.45 (br, 1H), 7.11-7.36 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.1, 21.7, 22.7, 27.7, 28.2, 29.1, 31.8, 32.8, 38.0, 42.2, 123.9, 125.8, 127.7, 128.2, 139.3, 147.4; HRMS (EI) *m/e* calcd for $C_{18}H_{26}$ 242.2034, found 242.2031.
8de (a 65:35 mixture of *E* and *Z* stereoisomer): *E* isomer: ^{1}H NMR ($CDCl_3$) δ 0.97 (d, J = 6.6 Hz, 6H), 1.53 (d, J = 1.5 Hz, 3H), 2.45-2.59 (m, 1H), 3.25 (s, 2H), 5.09-5.16 (m, 1H), 7.14-7.32 (m, 5H): *Z* isomer: ^{1}H NMR ($CDCl_3$) δ 1.00 (d, J = 6.6 Hz, 6H), 1.58 (d, J = 1.5 Hz, 3H), 2.60-2.72 (m, 1H), 3.38 (s, 2H), 5.09-5.16 (m, 1H), 7.14-7.32 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 15.7, 23.2, 23.2, 23.5, 27.2, 27.3, 38.0, 46.2, 125.8, 125.8, 128.2, 128.3, 128.5, 128.7, 131.1, 131.8, 134.6, 134.7, 140.2, 140.5; HRMS (EI) *m/e* calcd for $C_{13}H_{18}$ 174.1408, found 174.1410.
7df: ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 7.5 Hz, 3H), 1.18-1.40 (m, 10H), 1.61 (s, 3H), 3.19 (t, J = 7.2 Hz, 1H), 4.81 (s, 1H), 4.90 (s, 1H), 7.14-7.31 (m, 5H).
8df (a 62:38 mixture of *E* and *Z* isomer): *E* isomer: ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 7.5 Hz, 3H), 1.18-1.40 (m, 10H), 1.55 (s, 3H), 2.02 (q, J = 7.2 Hz, 2H), 3.28 (s, 3H), 5.21-5.35 (m, 1H), 7.14-7.31 (m, 5H): *Z* isomer: ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 7.5 Hz, 3H), 1.18-1.40 (m, 10H), 1.52 (s, 3H), 2.13 (q, J = 7.2 Hz, 2H), 3.36 (s, 3H), 5.21-5.35 (m, 1H), 7.14-7.31 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.1, 15.7, 20.9, 22.7, 23.3, 27.8, 28.1, 28.2, 29.0, 29.2, 29.4, 29.8, 30.1, 31.8, 33.0, 37.9, 46.3, 52.8, 110.1, 125.8, 125.9, 126.0, 127.0, 127.8, 128.1, 128.3, 128.5, 128.8, 133.5, 134.1, 140.3, 140.5; HRMS (EI) (as a mixture of **7df** and **8df**) *m/e* calcd for $C_{16}H_{24}$ 216.1878, found 216.1885.

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