Notes

Nickel-Catalyzed Cross-Coupling Reaction of Niobium(III)−Alkyne Complexes with Aryl Iodides

Yasushi Obora, Masahiro Kimura, Toshiyuki Ohtake, Makoto Tokunaga, and Yasushi Tsuji*

Catalysis Research Center and Division of Chemistry, Graduate School of Science, Hokkaido University, and CREST, Japan Science and Technology Agency (JST), Sapporo 001-0021, Japan

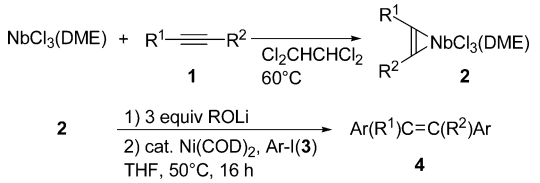
Received January 22, 2006

Summary: Nickel−catalyzed cross-coupling reactions of Nb(III)−alkyne complexes with aryl iodides are reported, in which addition of lithium alkoxide is indispensable and diarylated coupling products are afforded as products.

Alkyne complexes of low-valent early transition metals are useful synthetic reagents, and reactions with various electrophiles have been investigated.[1−3] In particular, Ti(II)−alkyne complexes[1] have been intensively studied. However, these complexes must be generated in situ from Ti(IV) with a reducing reagent. Moreover, the resulting Ti(II)−alkyne complexes are thermally unstable and cannot be utilized in further synthetic reactions which are carried out above −30 °C. Recently, we[4] and Eisch[5] independently found that thermally stable (up to 50 °C) Ti(II)−alkyne complexes can be generated from Ti(O-*i*-Pr)$_4$, alkynes, and *n*-BuLi in THF, and we reported the first Ni(0)-catalyzed cross-coupling reaction of the Ti(II)−alkyne complexes with aryl iodides.[4] Unfortunately, the reaction gave a mixture of mono- and diarylated coupling products.[4]

In contrast, the low-valent Nb(III) complex $NbCl_3$(DME)[6] is stable and is now commercially available. While only a limited number of synthetic applications of the Nb(III) reagents have been explored,[7] we recently reported the $NbCl_3$(DME)-mediated synthesis of 1,1,2-trisubstituted 1*H*-indenes from aliphatic ketones and aryl-substituted alkynes.[8] On the other hand, the transition-metal-catalyzed cross-coupling reactions of organic halides with various organometallic reagents such as Mg, B, Sn, and Si compounds represent one of the most powerful methods for C−C bond formation.[9] In the meantime, thermally stable $NbCl_3$−alkyne complexes are easily prepared from $NbCl_3$(DME) and alkynes,[10] but so far they have not been fully utilized in organic synthesis.[11] In this study, we have found that $NbCl_3$−alkyne complexes are not reactive but could be successfully activated with a lithium alkoxide in Ni(0)-catalyzed cross-coupling reactions with aryl iodides to afford diarylated olefins as products (Scheme 1). Thus, the present reaction provides the unprecedented synthetic usage of organoniobium reagents in catalytic cross-coupling reactions of alkynes via facile Nb(III) complexation. Furthermore, the present transformation also allows access to tetrasubstituted alkenes having different substituents on R^1 and R^2 (in compound **4**, Scheme 1). These compounds could not be obtained from conventional McMurry type reductive coupling of ketones.[12]

Scheme 1. Ni(0)-Catalyzed Cross-Coupling Reactions of Nb(III)−Alkyne Complexes with Aryl Iodides



The cross-coupling reaction was performed as shown in Scheme 1. First, the $NbCl_3$(DME)−alkyne complex **2**[10] was prepared from the alkyne **1** and $NbCl_3$(DME). Then 3 equiv of lithium alkoxide was added to **2** in THF, and the resulting Nb(III) complex was subjected to a cross-coupling reaction with aryl iodides (**3**) in the presence of 20 mol % of Ni(COD)$_2$ at 50 °C. The effect of various reaction conditions was examined with 1-phenyl-1-propyne (**1a**) and iodobenzene as substrates. When 3 equiv of *i*-PrOLi was added to the reaction mixture, the cross-coupling reaction proceeded smoothly to afford the diarylated product 1,1,2-triphenyl-1-propene (**4a**) in 83% yield (entry 1 in Table 1). In contrast, no cross-coupling reaction took place in the absence of the lithium alkoxide (entry 2). In the reaction,

* To whom correspondence should be addressed. E-mail: tsuji@cat.hokudai.ac.jp.

(1) (a) Sato, F.; Urabe, H. In *Titanium and Zirconium in Organic Synthesis*; Marek, I., Ed.; Wiley-VCH: Weinheim, Germany, 2002; p 319. (b) Sato, F.; Urabe, H.; Okamoto, S. *Chem. Rev.* **2000**, *100*, 2835. (c) Kulinkovich, O. G.; de Meijere, A. *Chem. Rev*, **2000**, *100*, 2789. (d) Eisch, J. J.; Gitua, J. N.; Otieno, P. O.; Shi, X. *J. Organomet. Chem.* **2001**, *624*, 229.

(2) (a) Buchwald, S. L.; Nielsen, R. B. *Chem. Rev.* **1988**, *88*, 1047. (b) Broene, R. D.; Buchwald, S. L. *Science* **1993**, *261*, 1696. (c) Negishi, E.; Takahashi, T. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 755. (d) Negishi, E.; Takahashi, T. *Acc. Chem. Res.* **1994**, *27*, 124.

(3) (a) Oshiki, T.; Tanaka, K.; Yamada, J.; Ishiyama, T.; Kataoka, Y.; Mashima, K.; Tani, K.; Takai, K. *Organometallics* **2003**, *22*, 464. (b) Kataoka, Y.; Miyai, J.; Oshima, K.; Takai, K.; Utimoto, K. *J. Org. Chem.* **1992**, *57*, 1973. (c) Takai, K.; Kataoka, Y.; Utimoto, K. *J. Org. Chem.* **1990**, *55*, 1707. (d) Kataoka, Y.; Miyai, J.; Tezuka, M.; Takai, K.; Utimoto, K. *J. Org. Chem.* **1992**, *57*, 6796;

(4) Obora, Y.; Moriya, H.; Tokunaga, M.; Tsuji, Y. *Chem. Commun.* **2003**, 2820.

(5) Eisch, J. J.; Gitua, J. N. *Organometallics* **2003**, *22*, 24.

(6) Roskamp, E. J.; Pedersen, S. F. *J. Am. Chem. Soc.* **1987**, *109*, 6551

(7) (a) Roskamp, E. J.; Dragovich, P. S.; Hartung, J. B.; Pedersen, S. F. *J. Org. Chem.* **1989**, *54*, 4736. (b) Szymononiak, J.; Besançon, J.; Moïse, C. *Tetrahedron* **1992**, *48*, 3867.

(8) Obora, Y.; Kimura, M.; Tokunaga, M.; Tsuji, Y. *Chem. Commun.* **2005**, 901.

(9) *Metal-Catalyzed Cross-Coupling Reactions*; de Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, Germany, 2004; Vols. 1 and 2.

(10) Hartung, J. B.; Pedersen, S. F. *Organometallics* **1990**, *9*, 1414.

(11) Hartung, J. B.; Pedersen, S. F. *J. Am. Chem. Soc.* **1989**, *111*, 5468.

(12) (a) McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513. (b) McMurry, J. E. *Acc. Chem. Res.* **1983**, *16*, 405.

10.1021/om060065w CCC: $33.50
Publication on Web 03/15/2006

Table 1. $Ni(COD)_2$-Catalyzed Cross-Coupling Reactions of Nb(III)−1a with Iodobenzene: Effect of Added ROLi[a]

entry	ROLi	amt of ROLi, equiv	yield of **4a**, %[b]
1	*i*-PrOLi	3	83 (65)
2	none		0
3	*i*-PrOLi	1	13
4	*i*-PrOLi	2	34
5	*i*-PrOLi	4	63[c]
6	*i*-PrOLi	5	51[c]
7	*s*-BuOLi	3	80
8	*c*-C_6H_{11}OLi	3	76
9	$(PhCH_2)_2$CHOLi	3	86
10	EtOLi	3	32
11	*i*-BuOLi	3	33
12	PhOLi	3	0

[a] Reaction conditions: 1-phenyl-1-propyne (**1a**) (1.2 mmol) and $NbCl_3$(DME) (1.4 mmol) in $Cl_2CHCHCl_2$ at 60 °C for 16 h, and then ROLi (1.2−6.0 mmol), iodobenzene (4.8 mmol), and $Ni(COD)_2$ (0.24 mmol) in THF (6 mL) at 50 °C for 16 h. [b] GLC yields. The number in parentheses gives the isolated yield. [c] Monoarylated products (1,1-diphenyl-1-propene and 1,2-diphenyl-1-propene) were obtained in 18% (for entry 5) and 25% yields (for entry 6) as a mixture of stereoisomers.

Table 2. $Ni(COD)_2$ Catalyzed Cross-Coupling Reactions of Nb(III)−Alkyne Complexes with Aryl Iodides[a]

	alkyne (**1**)		Ar−I (**3**)		yield of	
entry	R^1	R^2	Ar		**4**, %[b]	E:Z[c]
1	C_6H_5	CH_3	C_6H_5	**4a**	83 (65)	
2	C_6H_5	CH_3	3-CH_3-C_6H_4	**4b**	75 (63)	59:41
3	C_6H_5	CH_3	4-CH_3-C_6H_4	**4c**	71 (62)	59:41
4	C_6H_5	CH_3	4-F-C_6H_4	**4d**	75 (58)	*d*
5	C_6H_5	CH_3	4-CH_3O-C_6H_4	**4e**	67 (46)	55:45
6	C_6H_5	CH_3	4-Cl-C_6H_4	**4f**	50 (35)	53:47
7	C_6H_5	CH_3	4-CH_3OCO-C_6H_4	**4 g**	(53)	55:45
8	C_6H_5	C_6H_5	C_6H_5	**4h**	66	
9	3-CF_3-C_6H_4	CH_3	C_6H_5	**4i**	(72)	51:49
10	4-CH_3-C_6H_4	CH_3	C_6H_5	**4j**	(61)	54:46[e]
11	C_3H_7	CH_3	C_6H_5	**4k**	(55)	64:36[f]
12	C_3H_7	C_3H_7	C_6H_5	**4l**	(51)	65:35[f]

[a] Reaction conditions: alkyne (**1**) (1.2 mmol) and $NbCl_3$(DME) (1.4 mmol) in $Cl_2CHCHCl_2$ at 60 °C for 16 h, and then *i*-PrOLi (3.6 mmol), aryl iodide (**3**) (4.8 mmol), and $Ni(COD)_2$ (0.24 mmol) in THF at 50 °C. [b] GLC yields. The numbers in parentheses show isolated yields. [c] *E*:*Z* or *Z*:*E* ratio unless otherwise noted. [d] Not determined. [e] *E*:*Z* ratio. [f] *Z*:*E* ratio.

addition of 3 equiv of the lithium alkoxide to the Nb(III)−alkyne complex is crucial and showed the highest catalytic activity. Addition of smaller amounts (1 and 2 equiv) of the lithium alkoxide lowered the yields (entries 3 and 4), and larger amounts (4 and 5 equiv) caused formation of the monoarylated products 1,1-diphenyl-1-propene and 1,2-diphenyl-1-propene as byproducts (entries 5 and 6). With regard to the lithium alkoxides (3 equiv), alkoxides derived from secondary alcohols gave high yields (entries 7−9), whereas alkoxides derived from primary alcohols lowered the yields considerably (entries 10 and 11). Lithium phenoxide did not give **4a** at all (entry 12).

As the catalyst precursor, $Ni(COD)_2$ gave the best results. Addition of various phosphines such as PPh_3, 1,2-bis(diphenylphosphino)ethane, and tricyclohexylphosphine to entry 1 (P/Ni = 2) decreased the catalytic activity considerably (yield <50%). Palladium catalysts such as $Pd(DBA)_2$ (DBA = dibenzylideneacetone) and $Pd(PPh_3)_4$ did not afford **4a** at all. Bromobenzene in place of iodobenzene in entry 1 lowered the yield (18%), and no cross-coupling product was obtained at all with chlorobenzene or phenyl trifluoromethanesulfonate.

Under the optimized reaction conditions (entry 1, Table 1), the cross-coupling reactions of the Nb(III)−alkyne complex with aryl iodides (**3**) were carried out in the presence of *i*-PrOLi (Table 2). From **1a**, various aryl iodides gave the corresponding diarylated coupling products **4a**−**g** in good yields (entries 1−7). Furthermore, various alkynes can be utilized as substrates in the present reaction and afforded the diarylated adducts **4h**−**l** in good yields (entries 8−12). In the reaction, the *diarylated* products were obtained almost exclusively and the corresponding *monoarylated* products were afforded in only low yields (<5%), if any. The reactions were not stereoselective, and the products were provided as *E*/*Z* mixtures: ratios of the isomers ranged from 50:50 to 64:36.[13] The present reaction successfully provides cross-coupling products from internal alkynes. A terminal alkyne such as 1-hexyne did not form the $NbCl_3$(DME)−alkyne complex; instead, oligomerization of the alkyne took place.[10]

All trials to isolate reaction products of Nb(III)−alkyne complexes with lithium alkoxides (3 equiv) were unsuccessful. In the $^{13}C\{^1H\}$ NMR spectrum of the reaction mixture of $NbCl_3$−**1a** with *i*-PrOLi (3 equiv) in THF-d_8 (0.5 M) at 20 °C, the methyl and methine ^{13}C resonance of *i*-PrOLi (30.6 and 64.4 ppm) disappeared and two distinct methyl and methine carbon peaks appeared at 26.0 ppm ($\Delta\nu_{1/2}$ = 2.8 Hz) and 74.6 ppm (as a broad peak with $\Delta\nu_{1/2}$ = 19 Hz), respectively. The latter broad methine carbon peak became sharp at 40 °C (74.7 ppm with $\Delta\nu_{1/2}$ = 7.4 Hz) and at −40 °C (73.8 ppm with $\Delta\nu_{1/2}$ = 8.9 Hz) but broader at −10 °C (74.0 ppm with $\Delta\nu_{1/2}$ = 67 Hz). The methyl carbon peak was broader at low temperatures (26.0 ppm with $\Delta\nu_{1/2}$ = 13 Hz at −10 °C and 26.2 ppm with $\Delta\nu_{1/2}$ = 8.0 Hz at −40 °C). With regard to alkyne carbon resonances of the reaction mixture, two sharp peaks appeared at 203.6 and 205.8 ppm at 20 °C and these peaks remained unchanged from −40 to +40 °C: alkyne carbon resonances of the parent $NbCl_3$−**1a** complex appear at 237.5 and 256.2 ppm. Although the role of the alkoxy group in Nb(III)−alkyne complexes is unclear, these results might suggest that *i*-PrO^- substitutes the chloro moieties of the $NbCl_3$−alkyne complex and activates the complex toward the cross-coupling reaction.

In summary, the easily accessible Nb(III)−alkyne complexes can be utilized in nickel-catalyzed cross-coupling reactions with aryl iodides. Addition of lithium alkoxide is indispensable in the reaction, and the diarylated products are obtained in good yields.

Experimental Section

All manipulations were performed under an argon atmosphere using standard Schlenk-type glassware on a dual-manifold Schlenk line. The reagents and the solvents were dried and purified before use by usual procedures.[16] $NbCl_3$(DME) was prepared according to the published method[6] or was purchased from Aldrich. ^1H NMR and $^{13}C\{^1H\}$ NMR spectra were measured with JEOL ECX-400 and JEOL ECX-600 instruments. The mass spectra were measured on Shimadzu QP-5050A (EI) and JEOL JMS-700TZ instruments (HRMS, EI). The GC analysis was carried out on a Shimadzu GC-

(13) For **4j**, the structure of (*E*)-**4j** was unambiguously determined by X-ray crystal structure analysis[14] and the *E*:*Z* ratio has been determined to be 54:46. For **4k**, (*Z*)-**4k** was confirmed by a NOESY spectrum, and the *E*:*Z* ratio of **4l** was determined by ^1H NMR according to the literature.[15]

(14) Crystal data for (*E*)-**4j**: $C_{22}H_{20}$. M_r = 284.40, monoclinic, a = 8.674(9) Å, b = 9.156(9) Å, c = 20.18(3) Å, β = 90.30(4)°, U = 1602.6(35), T = 113 K, space group $P2_1/c$ (No. 14), Z = 4, D_c = 1.179 g cm^{-3}, μ(Mo Kα) = 0.66 cm^{-1}, 12 268 reflections measured, 3676 unique reflections (R_{int} = 0.039), which were used in all calculations. The final R and $R_w(F^2)$ values were 0.048 and 0.127 (all data). See the Supporting Information for details. CCDC 291118.

(15) (a) Leimner, J.; Weyerstahl, P. *Chem. Ber.* **1982**, *115*, 3697. (b) Besançon, J.; Szymoniak, J.; Moïse, C. *J. Organomet. Chem.* **1992**, *426*, 325.

(16) Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*, 4th ed.; Butterworth-Heinemann: Oxford, U.K., 1997.

17A instrument equipped with an integrator (C-R6A) with a capillary column (CBP1, Shimadzu, length 25 m × 0.25 mm i.d.) The GC yields of the product **4** were determined relative to the internal standard (tridecane). Column chromatography was carried out with silica gel (Wako, Wakogel C-200). The stereoisomer ratios of **4** were determined by measuring area ratios of the corresponding GC peaks. The structure and stereochemistry of **4a**,[17] **4h**,[18] and **4l**[15] were identified by comparing their spectral data with reported values. Single-crystal X-ray diffraction data of (*E*)-**4j** were collected on a Rigaku Saturn70 CCD diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.710 70 Å) at −160 °C. All calculations were preformed using the CrystalStructure crystallographic package (version 3.7)[19] (see the Supporting Information for details).

Typical Experimental Procedure (Table 1, Entry 1). A mixture of 1-phenyl-1-propyne (**1a**; 139 mg, 1.2 mmol), $NbCl_3$(DME) (405 mg, 1.4 mmol), and 1,2-dichloroethane (3.0 mL) was stirred for 16 h at 60 °C. The resulting solution was evaporated under vacuum (0.1 mmHg) to afford a dark brown oil. The residual oil was dissolved in THF (6.0 mL), and *i*-PrOLi (3.6 mL, 3.6 mmol, 1.0 M solution in hexane) was added dropwise over 5 min. This mixture was stirred for 30 min at room temperature to afford a dark orange solution. To this solution was added iodobenzene (**3a**; 979 mg, 4.8 mmol), and the mixture was heated to 50 °C. Then a THF (6.0 mL) solution of $Ni(COD)_2$ (66 mg, 0.24 mmol) was added dropwise over 10 min and the reaction mixture was stirred for 16 h at 50 °C. After this time, KOH(aq) (10 wt %, 3.0 mL) was added to the reaction mixture and the whole solution was extracted with ether to afford a yellow solution. GLC and GC-MS analysis of the reaction mixture showed that the cross-coupling product **4a**[17] was formed in 83% yield, and it was isolated in 65% yield by column chromatography (silica gel with hexane).

4b. *E*/*Z* mixture (the two isomers in a 59:41 ratio). ^{1}H NMR ($CDCl_3$): δ 2.12−2.17 (m, 9H), 2.24 (s, 3H), 2.25 (s, 3H), 2.37 (s, 3H), 6.70−7.42 (m, 26H). ^{13}C NMR ($CDCl_3$): δ 21.4 (CH_3), 21.5 ($2CH_3$), 21.6 (CH_3), 23.4 (CH_3), 23.5 (CH_3), 124.4 (CH), 125.8 (CH), 126.5 (2CH), 126.6 (2CH), 126.7 (CH), 127.0 (2CH), 127.2 (CH), 127.3 (CH), 127.4 (CH), 127.5 (CH), 127.7 (CH), 127.8 (CH), 128.0 (CH), 128.1 (CH), 128.2 (2CH), 129.9 (CH), 130.0 (CH), 130.1 (2CH), 130.7 (CH), 130.8 (CH), 131.5 (CH), 135.6 (C), 135.7 (C), 136.8 (C), 137.3 (C), 137.4 (C), 137.7 (C), 139.3 (2C), 143.1 (C), 143.3 (C), 143.7 (C), 143.8 (C), 144.1 (2C). HRMS (*m*/*z*): calcd for $C_{23}H_{22}$, 298.1722; found, 298.1712, 298.1723.

4c. *E*/*Z* mixture (the two isomers in a 59:41 ratio). ^{1}H NMR ($CDCl_3$): δ 2.09 (s, 3H), 2.12 (s, 3H), 2.20 (s, 3H), 2.26 (s, 3H), 2.28 (s, 3H), 2.36 (s, 3H), 6.74−7.36 (m, 26H). ^{13}C NMR ($CDCl_3$): δ 21.2 ($2CH_3$), 21.3 (CH_3), 21.4 (CH_3), 23.4 (CH_3), 23.5 (CH_3), 125.7 (CH), 126.5 (CH), 127.5 (2CH), 128.1 (2CH), 128.3 (2CH), 128.6 (2CH), 128.7 (2CH), 128.9 (2CH), 129.2 (2CH), 129.3 (2CH), 130.0 (2CH), 130.1 (2CH), 130.8 (2CH), 131.0 (2CH), 135.0 (2C), 135.3 (2C), 135.7 (2C), 136.2 (C), 138.8 (C), 140.4 (C), 140.9 (C), 141.1 (C), 141.2 (C), 143.6 (C), 144.1 (C). HRMS (*m*/*z*): calcd for $C_{23}H_{22}$, 298.1722; found, 298.1711, 298.1720.

4d. *E*/*Z* mixture (the two isomers appeared as a single peak in the capillary GC measurement). ^{1}H NMR ($CDCl_3$): δ 2.13 (s, 6H), 6.71−7.39 (m, 26H). ^{13}C NMR ($CDCl_3$): δ 23.4 ($2CH_3$), 114.6 (d, $^2J_{C-F}$ = 21 Hz, 2CH), 114.9 (d, $^2J_{C-F}$ = 21 Hz, 2CH), 115.0 (d, $^2J_{C-F}$ = 21 Hz, 2CH), 115.2 (d, $^2J_{C-F}$ = 21 Hz, 2CH), 126.2 (CH), 126.9 (CH), 127.7 (2CH), 128.3 (2CH), 130.0 (2CH), 130.8 (2CH), 130.9 (d, $^3J_{C-F}$ = 9 Hz, 4CH), 131.6 (d, $^3J_{C-F}$ = 9 Hz, 2CH), 132.4 (d, $^3J_{C-F}$ = 9 Hz, 2CH), 135.0 (d, $^4J_{C-F}$ = 4 Hz, C), 138.7 (C), 138.8 (C), 139.0 (d, $^4J_{C-F}$ = 4 Hz, C), 139.3 (d, $^4J_{C-F}$ = 4 Hz, C), 139.8 (d, $^4J_{C-F}$ = 4 Hz, C), 142.8 (2C), 143.2 (2C), 161.2 (d, $^1J_{C-F}$ = 247 Hz, C), 161.4 (d, $^1J_{C-F}$ = 247 Hz, 2C), 161.7 (d, $^1J_{C-F}$ = 247 Hz, C). HRMS (*m*/*z*): calcd for $C_{21}H_{16}F_2$, 306.1220; found, 306.1226.

4e. *E*/*Z* mixture (the two isomers in a 55:45 ratio). ^{1}H NMR ($CDCl_3$): δ 2.08 (s, 3H), 2.12 (s, 3H), 3.70 (s, 3H), 3.74 (s, 3H), 3.76 (s, 3H), 3.82 (s, 3H), 6.55−7.35 (m, 26H). ^{13}C NMR ($CDCl_3$): δ 23.4 (CH_3), 23.5 (CH_3), 55.1 (CH_3), 55.2 ($2CH_3$), 55.3 (CH_3), 112.9 (2CH), 113.3 (2CH), 113.4 (2CH), 113.5 (2CH), 125.7 (CH), 126.5 (CH), 127.5 (2CH), 128.1 (2CH), 130.1 (2CH), 130.5 (4CH), 131.0 (2CH), 131.3 (2CH), 132.1 (2CH), 134.2 (C), 134.7 (C), 135.9 (C), 136.3 (C), 136.5 (2C), 138.2 (C), 138.4 (C), 143.8 (C), 144.2 (C), 157.5 (C), 157.9 (2C), 158.2 (C). HRMS (*m*/*z*): calcd for $C_{23}H_{22}O_2$, 330.1620; found, 330.1616, 330.1624.

4f. *E*/*Z* mixture (the two isomers in a 53:47 ratio). ^{1}H NMR ($CDCl_3$): δ 2.10 (s, 3H), 2.11 (s, 3H), 6.79−7.64 (m, 26H). ^{13}C NMR ($CDCl_3$): δ 23.2 (CH_3), 23.3 (CH_3), 126.4 (CH), 127.1 (CH), 127.8 (2CH), 127.9 (2CH), 128.2 (2CH), 128.4 (4CH), 128.5 (2CH), 130.0 (2CH), 130.7 (4CH), 130.8 (2CH), 131.4 (2CH), 132.0 (C), 132.18 (C), 132.26 (2CH), 132.3 (C), 132.7 (C), 135.1 (C), 135.3 (C), 138.9 (C), 139.0 (C), 141.3 (C), 141.7 (C), 142.1 (C), 142.2 (C), 142.4 (C), 142.8 (C). HRMS (*m*/*z*): calcd for $C_{21}H_{16}Cl_2$, 338.0629; found, 338.0621, 338.0613.

4g. *E*/*Z* mixture (the two isomers in a 55:45 ratio). ^{1}H NMR ($CDCl_3$): δ 2.13 (s, 3H), 2.16 (s, 3H), 3.81 (s, 3H), 3.85 (s, 6H), 3.91 (s, 3H), 6.83−8.05 (m, 26H). ^{13}C NMR ($CDCl_3$): δ 23.1 (CH_3), 23.2 (CH_3), 52.0 (CH_3), 52.1 ($2CH_3$), 52.2 (CH_3), 126.6 (CH), 127.3 (CH), 127.86 (4CH), 127.90 (C), 128.2 (C), 128.3 (C), 128.4 (2CH), 128.7 (C), 129.0 (2CH), 129.4 (4CH), 129.5 (2CH), 129.7 (2CH), 130.0 (2CH), 130.1 (2CH), 130.8 (2CH), 130.9 (2CH), 135.9 (C), 136.6 (C), 139.9 (2C), 141.9 (C), 142.3 (C), 147.6 (C), 147.9 (C), 148.6 (C), 148.7 (C), 166.9 (2C), 167.0 (2C). HRMS (*m*/*z*): calcd for $C_{25}H_{22}O_4$, 386.1518; found, 386.1526, 386.1528.

4i. *E*/*Z* mixture (the two isomers in a 51:49 ratio). ^{1}H NMR ($CDCl_3$): δ 2.18 (s, 3H), 2.22 (s, 3H), 6.92−7.62 (m, 28H). ^{13}C NMR ($CDCl_3$): δ 23.4 (CH_3), 23.6 (CH_3), 122.6 (q, $^3J_{C-F}$ = 4 Hz, 2CH), 123.6 (q, $^3J_{C-F}$ = 4 Hz, 2CH), 124.2 (q, $^1J_{C-F}$ = 270 Hz, CF_3), 124.4 (q, $^1J_{C-F}$ = 270 Hz, CF_3), 126.3 (CH), 126.6 (CH), 126.8 (CH), 127.1 (CH), 127.8 (2CH), 127.9 (CH), 128.1 (2CH), 128.2 (2CH), 128.5 (2CH), 128.8 (CH), 128.8−131.2 (2C), 129.2 (2CH), 129.3 (2CH), 130.1 (2CH), 130.9 (2CH), 133.6 (CH), 134.2 (CH), 137.2 (C), 137.8 (C), 138.1 (C), 138.2 (C), 142.4 (C), 142.7 (C), 143.5 (C), 143.6 (C), 143.9 (C), 144.4 (C). HRMS (*m*/*z*): calcd for $C_{22}H_{17}F_3$, 338.1282; found, 338.1283, 338.1273.

4j. *E*/*Z* mixture (the two isomers in a 54:46 ratio). ^{1}H NMR ($CDCl_3$): δ 2.11 (s, 3H), 2.14 (s, 3H), 2.19 (s, 3H), 2.36 (s, 3H), 6.7−7.4 (m, 28H). ^{13}C NMR ($CDCl_3$): δ 21.2 (CH_3), 21.3 (CH_3), 23.4 (CH_3), 23.5 (CH_3), 125.8 (CH), 126.2 (2CH), 126.6 (CH), 127.4 (2CH), 127.8 (2CH), 127.9 (2CH), 128.1 (2CH), 128.2 (2CH), 128.9 (2CH), 129.3 (2CH), 129.4 (2CH), 130.0 (2CH), 130.1 (2CH), 130.8 (2CH), 130.9 (2CH), 135.2 (C), 135.4 (C), 135.5 (C), 136.3 (C), 139.2 (C), 139.3 (C), 140.2 (C), 140.7 (C), 143.4 (C), 143.9 (C), 144.2 (C), 144.3 (C). HRMS (*m*/*z*): calcd for $C_{22}H_{20}$, 284.1565; found, 284.1573 (for *Z* isomer), 284.1554 (for *E* isomer). The stereostructure (*E*)-**4j** was determined by an X-ray crystal structure analysis (see the Supporting Information).

4k. *E*/*Z* mixture (the two isomers in a 64:36 ratio). *E* isomer: ^{1}H NMR ($CDCl_3$) δ 0.76 (t, *J* = 7.3 Hz, 3H), 1.25 (sex, *J* = 7.3 Hz, 2H), 1.88 (s, 3H), 2.25 (t, 2H), 6.97−7.43 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 14.0 (CH_3), 21.8 (CH_2), 22.9 (CH_3), 37.2 (CH_2), 126.3 (2CH), 128.2 (2CH), 128.3 (4CH), 129.0 (2CH), 133.5 (C), 138.2 (C), 143.0 (C), 144.7 (C); HRMS (*m*/*z*) calcd for $C_{18}H_{20}$ 236.1565, found 236.1573. *Z* isomer: ^{1}H NMR ($CDCl_3$) δ 0.98 (t, *J* = 7.3 Hz, 3H), 1.44 (sex, *J* = 7.3 Hz, 2H), 2.22 (s, 3H), 2.60 (t, *J* = 7.3 Hz, 2H), 6.97−7.43 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3),

(17) Katritzky, A. R.; Cheng, D.; Henderson, S. A.; Li, J. *J. Org. Chem.* **1998**, *63*, 6704.

(18) (a) Proulx, T. W.; Smith, W. B. *J. Magn. Reson.* **1976**, *23*, 477. (b) Smith, W. B. *Org. Magn. Reson.* **1981**, *15*, 317.

(19) (a) Crystal Structure Analysis Package; Rigaku and Rigaku/MSC, 9009 New Trails Dr., The Woodlands TX 77381, 2000−2004. (b) Watkin, D. J.; Prout, C. K.; Carruthers, J. R.; Betteridge, P. W. Chemical Crystallography Laboratory, Oxford, U.K., 1996.

21.1 (CH_3), 21.4 (CH_2), 37.1 (CH_2), 125.59 (CH), 125.63 (CH), 127.5 (4CH) 129.3 (2CH), 129.8 (2CH), 133.2 (C), 138.4 (C), 143.7 (C), 144.9 (C); HRMS (*m*/*z*) calcd for $C_{18}H_{20}$ 236.1565, found 236.1573. The stereostructure of (*Z*)-**4k** was confirmed by a NOESY spectrum. An NOE correlation between methyl protons (2.22 ppm) and methylene protons of the propyl group (2.60 ppm) was observed.

4l.[15] *E*/*Z* mixture (the two isomers in a 65:35 ratio). *E* isomer: ^{1}H NMR ($CDCl_3$) δ 0.72 (t, $J = 7$ Hz, 6H), 1.20 (sex, $J = 7$ Hz, 4H), 2.14 (t, $J = 7$ Hz, 4H), 6.93−7.40 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 13.9 ($2CH_3$), 21.6 ($2CH_2$), 37.5 ($2CH_2$), 126.2 (CH), 128.0 (2CH), 128.9 (2CH), 138.38 (C), 143.0 (C); HRMS (*m*/*z*) calcd for $C_{20}H_{24}$ 264.1878, found 264.1887. *Z* isomer: ^{1}H NMR ($CDCl_3$) δ 0.93 (t, $J = 7$ Hz, 6H), 1.37 (sex, $J = 7$ Hz, 4H), 2.56 (t, $J = 7$ Hz, 4H), 6.93−7.40 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 14.1 ($2CH_3$), 21.7 ($2CH_2$), 36.4 ($2CH_2$), 125.5 (CH), 127.4 (2CH), 129.9 (2CH), 138.43 (C), 143.6 (C); HRMS (*m*/*z*) calcd for $C_{20}H_{24}$ 264.1878, found 264.1868.

Supporting Information Available: Crystallographic data for (*E*)-**4j** (CIF and PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

OM060065W