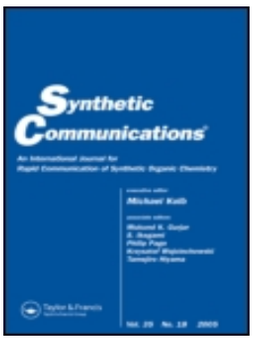


Taylor & Francis
Taylor & Francis Group

Synthetic Communications

An International Journal for Rapid Communication of Synthetic Organic Chemistry

ISSN: 0039-7911 (Print) 1532-2432 (Online) Journal homepage: http://www.tandfonline.com/loi/lsyc20

A NEW METHOD FOR THE PREPARATION OF 2,3-DIARYL-1,1-DIFLUORO-1,3-BUTADIENES

In Howa Jeong , Young Sam Park , Min Wook Chung & Bum Tae Kim

To cite this article: In Howa Jeong , Young Sam Park , Min Wook Chung & Bum Tae Kim (2001) A NEW METHOD FOR THE PREPARATION OF 2,3-DIARYL-1,1-DIFLUORO-1,3-BUTADIENES, Synthetic Communications, 31:15, 2261-2270, DOI: 10.1081/SCC-100104825

To link to this article: http://dx.doi.org/10.1081/SCC-100104825

Published online: 09 Nov 2006.

SYNTHETIC COMMUNICATIONS, 31(15), 2261–2270 (2001)

A NEW METHOD FOR THE PREPARATION OF 2,3-DIARYL-1,1-DIFLUORO-1,3-BUTADIENES

In Howa Jeong,[1,*] Young Sam Park,[1] Min Wook Chung,[1] and Bum Tae Kim[2]

[1]Department of Chemistry, Yonsei University, Wonju 220-710, S. Korea
[2]Korea Research Institute of Chemical Technology, Daejeon 305-606, S. Korea

ABSTRACT

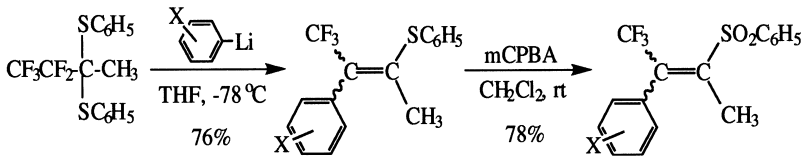
Reactions of 1-trifluoromethyl-1,2-diarylvinyl sulfones **3** with aryllithium afforded aryl substituted adduct **4**. Bromination of **4** with NBS, followed by debromofluorination with Mg, provided 2,3-diaryl-1,1-difluoro-1,3-butadienes (**6**) in good yields.

1,3-Butadienes are important compounds in organic synthesis. For example, Diels-Alder reactions of these compounds with dienophiles are widely used for the preparation of various six-membered rings.[1,2] The electrocyclic reaction of 1,3-butadienes under the photochemical condition is a useful synthetic method for the preparation of cyclobutene ring systems.[3] Although various synthetic methods for the preparation of nonfluorinated 1,3-butadienes and their application have been well established,[4–7] the

* Corresponding author.

methods for the synthesis of fluorinated 1,3-butadienes, especially 1,1-difluoro-1,3-butadienes, have been quite limited in previous literatures.[8–12] The reaction of commercially available 4-bromo-1,1,2-trifluoro-1-butene with potassium hydroxide in the presence of phase-transfer catalyst afforded 1,1,2-trifluoro-1,3-butadiene.[8] The versatile transformations of this compound are very useful synthetic tools to give a variety of functionalized monofluoroalkene compounds.[8,13] 4-Phenyl-1,1-difluoro-1,3-butadiene was obtained in low yield from the reaction of 3,3-difluoroallyltriphenylphosphonium bromide with benzaldehyde in the presence of potassium carbonate.[9] 4-Phenyl-1,1-difluoro-1,3-butadience can be also prepared from the reaction of 1,3-dibromo-1,1-difluoro-compounds, which were synthesized by adding dibromodifluoromethane to olefins, with DBU.[10] Reaction of 4-phenyl-1,1-difluoro-1,3-butadiene with 4-phenyl-1,2,4-triazoline-3,5-dione provided cycloadduct.[10] 1,1-Difluoro-2-triphenylsiloxy-1,3-butadiene was also prepared from the reaction of trifluoroacetyltriphenylsilane with vinylmagnesium bromide.[11] This compound also undergoes Diels-Alder reaction with various dienophiles.[12] However, several previous methods for the synthesis of 1,1-difluoro-1,3-butadienes can not be applied to prepare 2,3-diaryl-1,1-difluoro-1,3-butadienes. In this communication we will describe a new method for the preparation of 2,3-diaryl-1,1-difluoro-1,3-butadienes.

1,1,1-Trifluoro-2-aryl-3-phenylsulfonyl-2-butenes (**3**)(E:Z = 45:55) can be easily prepared from the oxidation of 1,1,1-trifluoro-2-aryl-3-phenylthio-2-butenes (**2**), which were synthesized from the reaction of 3,3-bis(phenylthio)-1,1,1,2,2-pentafluorobutane (**1**)[14] with 2.5 equiv. of substituted phenyllithium compounds.



1 **2** **3**

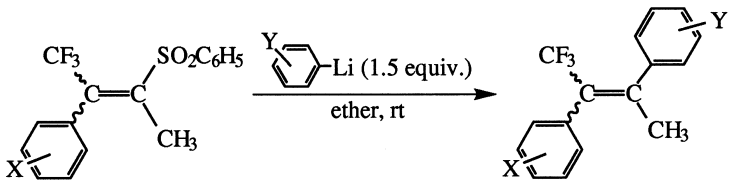
The reaction pathway for the formation of **2** seems likely that the initial reaction of **1** with phenyllithium compounds *via* attack of sulfur atom provides the carbanions bearing a pentafluoroethyl group, which quickly undergoes β-defluorination to give the β-fluoro-β-trifluoromethylvinyl sulfides. These compounds are so reactive that they quickly undergo addition-elimination reaction with phenyllithium compounds presented in solution as soon

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

as they were formed. The treatment of **3** with another 1.5 equiv. of substituted phenyllithium compounds resulted in the formation of *E* and *Z* isomeric mixture (*E*:*Z* = 35:65) of 2,3-diaryl-1,1,1-trifluoro-2-butenes (**4**) in good yields. Assignment of isomers for **4** was based on the chemical shift of CH_3 in each isomer. We observed that the chemical shift ($\delta = 1.84$ ppm) of CH_3 which is arranged to the same side of CF_3 group is lower than the chemical shift ($\delta = 2.35$ ppm) of CH_3 which is arranged to the opposite side of CF_3 group.[15] The results for the formation of **4** are summarized in Table 1.

Allylic bromination of **4** was carried out with N-bromosuccinimide (NBS). Several solvents such as CCl_4, CH_2Cl_2, CH_3CN and benzene were examined in this reaction. The optimized condition was established by refluxing of **4** with NBS (3–5 equiv.) in CH_3CN for 12–24 h. Therefore, the reaction of **4a** with NBS (3 equiv.) in CH_3CN at reflux temperature for 24 h afforded allylic bromide **5a** (*E*:*Z* = 60:40) in 78% yield. The similar treatment of **4d** and **4e** with NBS resulted in the fomation of allylic bromides **5d** and **5e** in 71% and 73% yields, respectively. When **4b** was reacted with NBS (4 equiv.) in CH_3CN for 12 h, however, allylic bromide **5b** was obtained in only 40% yield. The major side product was benzylic

Table 1. Preparation of 2,3-Diaryl-1,1,1-trifluoro-2-butenes (**4**)

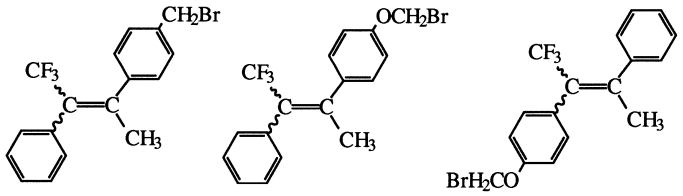


3 **4**

Compound No.	X	Y	**4**, Yield(%)[a,b]
4a	H	H	80
4b	H	CH_3	71
4c	H	OCH_3	68
4d	H	Cl	65
4e	Cl	H	82
4f	CH_3	H	76
4g	CH_3	CH_3	81
4h	CH_3O	H	77
4i	CH_3O	CH_3	82
4j	CH_3O	OCH_3	83

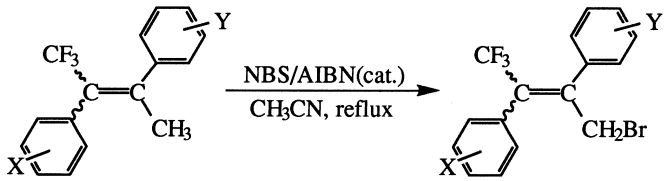
MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

brominated compound **5k**. The similar results were obtained from the reactions of **4f**, **4g** and **4i** with NBS, in which allylic bromides **5f**, **5g** and **5i** were formed in 41%, 57% and 34% yields, respectively. The reactions of **4c** and **4h** with NBS also provided allylic bromides **5c** and **5h** in relatively low yields, in which alkoxy brominated compounds **5l** and **5m** were formed as a major side product, respectively. To make matters worse, the treatment of **4j** with NBS resulted in the formation of a messy reaction mixture. The results for the formation of **5** are summarized in Table 2.



5k **5l** **5m**

Table 2. Preparation of 2,3-Diaryl-4-bromo-1,1,1-trifluoro-2-butenes (**5**)



4 **5**

Compound No.	X	Y	**5**, Yield(%)[a,b]
5a	H	H	78
5b	H	CH_3	40
5c	H	OCH_3	42
5d	H	Cl	71
5e	Cl	H	73
5f	CH_3	H	41
5g	CH_3	CH_3	57
5h	CH_3O	H	40
5i	CH_3O	CH_3	34
5j	CH_3O	OCH_3	–[c]

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

First of all, we examined the debromofluorination of **5** with metals, such as Zn, activated Zn, Zn(Cu) and Mg, to give 1,1-difluorodienes **6**. The use of Zn, activated Zn or Zn(Cu) in this reaction did not afford a desired product **6**, but the reaction of **5a** with Mg (1.5 equiv.) in the presence of catalytic amount of I_2 provided 2,3-diphenyl-1,1-difluoro-1,3-butadiene (**6a**) in 81% yield. Therefore, we decided to use Mg (1.5 equiv.) and I_2 (cat.) in this type of reaction. When **5b–i** was treated with Mg (1.5 equiv.) in the presence of catalytic amount of I_2, 1,1-difluorodiene **6b–i** was synthesized in 42% to 74% yields. The reaction pathway for the formation of **6** seems likely that the initial reaction of **5** with Mg affords oxidative insertion intermediate between vinyl carbon and bromine bond, which quickly undergoes δ-defluorination to give 2,3-diaryl-1,1-difluoro-1,3-butadienes (**6**) *via* six-membered ring transition state [I]. The results of the elimination reaction of **5** with Mg are summarized in Table 3.

In conclusion, the present method provides a new and general procedure for the preparation of various 2,3-diaryl-1,1-difluoro-1,3-butadienes which can not be prepared from the several previous methods. Diels-Alder reactions of **6** with dienophiles are now in progress.

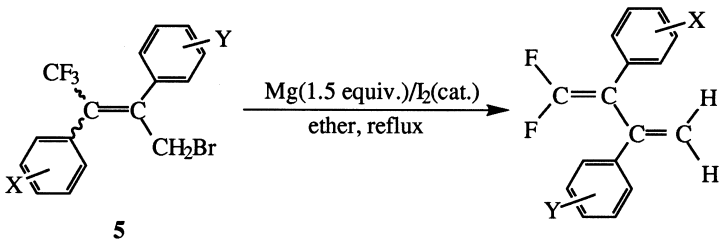
EXPERIMENTAL

Synthesis of 3,3-Bis(phenylthio)-1,1,1,2,2-pentafluorobutane (1)

A 500 mL three-neck round bottom flask equipped with a septum, a solid addition tube filled with $AlCl_3$ (6.09 g, 0.05 mol), a magnetic stir bar and a nitrogen tee connected to a source of argon, was charged with 3,3,4,4,4-pentafluoro-2-butanone (8.1 g, 0.05 mol), thiophenol (11.0 g, 0.1 mol) and 300 mL of dry CH_2Cl_2. The reaction mixture was cooled to $-78^{\circ}C$ and $AlCl_3$ was added in several portions *via* a solid addition tube. After stirring at $-78^{\circ}C$ for 20 h, the reaction mixture was quenched with water at $-78^{\circ}C$. The mixture was poured into 200 mL of H_2O, extracted with CH_2Cl_2 (300 mL × 2). After washing with saturated NaCl water solution, CH_2Cl_2 layer was dried with anhydrous Na_2CO_3. Column chromatography (n-hexane) afforded 15.5 g (85% yield) of 3,3-bis (phenylthio)-1,1,1,2,2-pentafluorobutane (**1**). **1**: oil; ^1H NMR ($CDCl_3$) δ 7.68–7.25 (m, 10H), 1.34 (s, 3H); ^{19}F NMR ($CDCl_3$) δ −109.86 (s, 2F), −75.68 (s, 3F); MS, m/z (relative intensity) 364 (M^+, 3), 255 (100), 215 (33), 177 (10), 165 (9), 134 (10), 109 (61), 77 (13), 65 (10); IR (neat) 3062, 3003, 2944, 1474, 1440, 1315, 1215, 1184, 1148, 1069, 991, 751, 691 cm^{-1}.

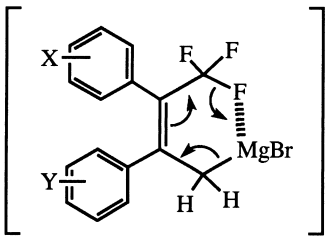
MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

Table 3. Preparation of 2,3-Diaryl-1,1-difluoro-1,3-butadienes (**6**)



5 **6**

Compound No.	X	Y	**6**, Yield(%)[a]
6a	H	H	81
6b	H	CH_3	60
6c	H	OCH_3	65
6d	H	Cl	74
6e	Cl	H	72
6f	CH_3	H	58
6g	CH_3	CH_3	42
6h	CH_3O	H	61
6i	CH_3O	CH_3	45



[I]

Synthesis of 1,1,1-Trifluoro-2-phenyl-3-phenylthio-2-butene (2)

A 250 mL two-neck flask equipped with a septum, a magnetic stir bar and a nitrogen tee connected to a source of argon, was charged with 3,3-bis(phenylthio)-1,1,1,2,2-pentafluorobutane (3.64 g, 0.01 mol) and 50 mL of dry THF. The reaction mixture was cooled to $-78^{\circ}C$ and phenyllithium (1.8 M solution, 11.2 mL) was added dropwise at $-78^{\circ}C$, followed by slow warming to ambient temperature. The reaction mixture was quenched with water (50 mL) and extracted with ether (50 mL × 2). After the ether layer was

dried with anhydrous $MgSO_4$, column chromatography (n-hexane) afforded 2.23 g (76% yield) of (*E*) and (*Z*) isomeric mixture (*E*:*Z* = 45:55) of 1,1,1-trifluoro-2-phenyl-3-phenylthio-2-butene (**2**). **2**: oil; ^{1}H NMR ($CDCl_3$) δ 7.54–7.14 (m, 10H), 2.09 (q, $J = 2.4$ Hz, 3H, *Z* isomer), 1.67 (q, $J = 2.0$ Hz, 3H, *E* isomer); ^{19}F NMR ($CDCl_3$) δ −56.05 (s, 3F, *Z* isomer), −56.58 (s, 3F, *E* isomer); MS, m/z (relative intensity) 294 (M^+, 100), 279 (10), 225 (17), 165 (25), 115 (45), 77 (31), 59 (43); IR (neat) 3062, 3026, 2927, 1607, 1475, 1441, 1310, 1214, 1170, 1115, 1016, 758, 707 cm^{-1}.

Synthesis of 1,1,1-Trifluoro-2-phenyl-3-phenylsulfonyl-2-butene (3)

To a mixture of 1,1,1-trifluoro-2-phenyl-3-phenylthio-2-butene (2.0 g, 6.8 mmol) and 30 mL of CH_2Cl_2 was added *m*-chloroperbenzoic acid (50% technical grade, 27.2 mmol) at 0°C and then the mixture was stirred at ambient temperature for 12 h. After quenching the reaction mixture with saturated $NaHCO_3$ solution and 10% $NaHSO_3$, the mixture was extracted with CH_2Cl_2 (20 mL × 2) and then dried over anhydrous Na_2CO_3. After evaporation of solvent, the crude product was recrystallized (n-hexane: methylene chloride = 1:1) to provide 1.73 g (78% yield) of (*E*) and (*Z*) isomeric mixture (*E*:*Z* = 45:55) of 1,1,1-trifluoro-2-phenyl-3-phenylsulfonyl-2-butene (**3**). **3**: mp 112–114°C; ^{1}H NMR ($CDCl_3$) δ 7.98–6.89 (m, 10H), 2.44 (q, $J = 2.3$ Hz, 3H, *Z* isomer), 1.81 (q, $J = 1.6$ Hz, 3H, *E* isomer); ^{19}F NMR ($CDCl_3$) δ −54.04 (s, 3F, *E* isomer), −59.45 (s, 3F, *Z* isomer); MS, m/z (relative intensity) 326 (M^+, 24), 307 (9), 201 (100), 165 (75), 145 (35), 125 (60), 115 (90), 77 (62), 51 (42); IR (KBr) 3067, 2963, 1799, 1548, 1447, 1335, 1161, 1011, 764 cm^{-1}.

Synthesis of 1,1,1-Trifluoro-2,3-diphenyl-2-butene (4a)

To a mixture of 1,1,1-trifluoro-2-phenyl-3-phenylsulfonyl-2-butene (0.652 g, 2.0 mmol) and 5 mL of ether was added phenyllithium (1.8 M solution, 7.0 mmol) at room temperature and then the mixture was stirred at room temperature for 1 h. After quenching the reaction mixture with saturated NaCl solution, the mixture was extracted with ether (10 mL × 2) and then dried over anhydrous $MgSO_4$. After evaporation of solvent, the crude product was chromatographed (n-hexane) to provide 0.419 g (80% yield) of (*E*) and (*Z*) isomeric mixture (*E*:*Z* = 35:65) of 1,1,1-trifluoro-2,3-diphenyl-2-butene (**4a**). **4a**: oil; ^{1}H NMR ($CDCl_3$) δ 7.51–6.88 (m, 10H), 2.35 (q, $J = 2.8$ Hz, 3H, *Z* isomer), 1.84 (q, $J = 2.2$ Hz, 3H, *E* isomer); ^{19}F NMR ($CDCl_3$) δ −56.28 (s, 3F, *E* isomer), −56.68 (s, 3F, *Z* isomer); MS,

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

m/z (relative intensity) 262 (M^+, 96), 193 (53), 184 (98), 178 (28), 115 (34), 103 (100), 91 (17), 77 (48), 51 (12); IR (neat) 3060, 3027, 2957, 2925, 2854, 1638, 1492, 1443, 1331, 1264, 1208, 1162, 1116, 1029, 761, 699 cm^{-1}.

Synthesis of 4-Bromo-1,1,1-trifluoro-2,3-diphenyl-2-butene (5a)

A mixture of 1,1,1-trifluoro-2,3-diphenyl-2-butene (0.393 g, 1.5 mmol), N-bromosuccinimide (0.68 g, 4.5 mmol), AIBN (cat.) and 5 mL of CH_3CN was heated to reflux for 24 h. After cooling to room temperature and then evaporating solvent, the crude mixture was chromatographed on SiO_2 to give 0.40 g (78% yield) of (*E*) and (*Z*) isomeric mixture (*E*:*Z* = 60:40) of 4-bromo-1,1,1-trifluoro-2,3-diphenyl-2-butene (**5a**). **5a**: oil; ^1H NMR ($CDCl_3$) δ 7.58–7.05 (m, 10H), 4.51 (s, 2H, *E* isomer), 3.91 (s, 2H, *Z* isomer); ^{19}F NMR ($CDCl_3$) δ −57.03 (s, 3F, *Z* isomer), −57.45 (s, 3F, *E* isomer); MS, m/z (relative intensity) 342 (M^+, Br-81, 16), 340 (M^+, Br-79, 16), 261 (48), 221 (22), 191 (34), 183 (100), 133 (15), 115 (8), 77 (8), 51 (8); IR (neat) 3059, 3025, 2927, 1491, 1444, 1329, 1269, 1206, 1168, 1117, 898, 762, 698 cm^{-1}.

Synthesis of 1,1-Difluoro-2,3-diphenyl-1,3-butadiene (6a)

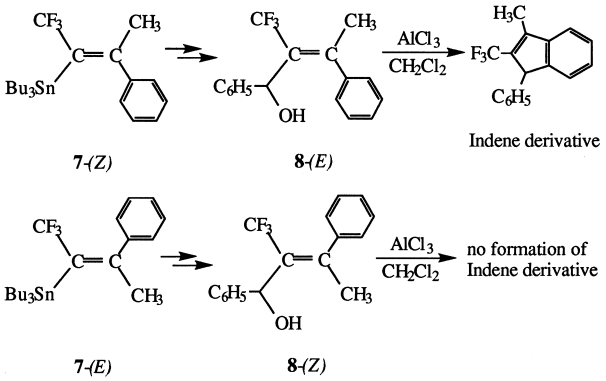
A mixture of 4-bromo-1,1,1-trifluoro-2,3-diphenyl-2-butene (0.408 g, 1.2 mmol), Mg (0.044 g, 1.8 mmol), iodine(cat.) and 5 mL of ether was heated to reflux for 1 h. After cooling to room temperature and quenching the reaction mixture with 10% HCl solution, the mixture was extracted with ether (10 mL × 2) and then dried over anhydrous $MgSO_4$. After evaporation of solvent, the crude product was chromatographed (n-hexane) to provide 0.235 g (81% yield) of 1,1-difluoro-2,3-diphenyl-1,3-butadiene (**6a**). **6a**: oil; ^1H NMR ($CDCl_3$) δ 7.48–7.18 (m, 10H), 5.88 (s, 1H), 5.40 (s, 1H); ^{19}F NMR ($CDCl_3$) δ −84.60 (d, *J* = 29.5 Hz, 1F), −88.34 (d, *J* = 29.6 Hz, 1F); MS, m/z (relative intensity) 242 (M^+, 100), 221 (71), 191 (18), 178 (21), 164 (23), 127 (59), 115 (19), 91 (14), 77 (21), 51 (16); IR (neat) 3058, 3027, 2942, 1707, 1495, 1445, 1264, 1234, 1035, 967, 912, 763, 696 cm^{-1}.

ACKNOWLEDGMENT

This work was supported by Korea Research Foundation Grant (KRF-1999-015-DP0218).

REFERENCES

1. Wasserman, A. "*Diels-Alder Reactions*," Elsevier, New York, 1965.
2. Brieger, G. and Bennett, J.N. Chem. Rev. **1980**, *80*, 63.
3. Goldstein, M.J. and Leight, R.S. J. Am. Chem. Soc. **1977**, *99*, 8112.
4. Ishino, Y.; Nishiguchi, I. and Takihira, F. Tetrahedron Lett. **1980**, *21*, 1527.
5. Kleijn, H.; Westmijze; H.; Meijer, J. and Vermeer, P. Recl. Trav. Chim. Pays-Bas **1980**, *99*, 340.
6. Carpita, A.; Benetti, M. and Rossi, R. Gazz. Chim. Ital. **1982**, *112*, 415.
7. Araki, Y.; Ohmura, M. and Butsugan, Y. Synthesis **1985**, 963.
8. Matsuo, N. and Kende, A.S. J. Org. Chem. **1988**, *53*, 2304.
9. Weiming, Q. and Burton, D.J. J. Fluorine Chem. **1993**, *65*, 143.
10. Elsheimer, S.; Foti, C.J. and Bartberger, M.D. J. Org. Chem. **1996**, *61*, 6252.
11. Jin, F.-Q. and Xu, Y.-Y. J. Fluorine Chem. **1995**, *71*, 1.
12. Jin, F.-Q. and Xu, Y.-Y. J. Chem. Soc. Chem. Commun. **1993**, 815.
13. Matsuo, N. and Kende, A.S. Bull. Chem. Soc. Jpn. **1991**, *64*, 3193.
14. Jeong, I.H.; Min, Y.K.; Kim, Y.S.; Cho, K.Y. and Kim, K.J. Bull. Korean Chem. Soc. **1991**, *12*, 355.
15. Authetic samples of (*E*) and (*Z*)-1,1,1-trifluoro-2,3-diphenyl-2-butenes(**4a**) were prepared from the cross-coupling reaction of separable (*E*) and (*Z*)-2-tributylstannyl-1,1,1-trifluoro-3-phenyl-2-butenes(**7**) with iodobenzene in the presence of $(PPh_3)_4Pd$ (10 mol%) and CuI (10 mol%). (*E*) and (*Z*)-2-tributylstannyl-1,1,1-trifluoro-3-phenyl-2-butenes (**7**) were figured out *via* occurrence of cyclization of (*E*) and (*Z*)-2-trifluoromethyl-1,3-diphenyl-2-buten-1-ols (**8**) which can be prepared from the cross-coupling reaction of each (*E*) and



MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

(*Z*)-2-tributylstannyl-1,1,1-trifluoro-3-phenyl-2-butenes(**7**)withbenzoyl chloride, followed by reduction with $LiAlH_4$.[16] The (*E*) isomer of **8** underwent Friedel-Craft's type of cyclization to give indene derivative in the presence of $AlCl_3$, but the (*Z*) isomer of **8** did not undergo cyclization.

16. Park, Y.S. Thesis, Yonsei University, 2000.

Received in Japan July 18, 2000

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016