JOC*Article*

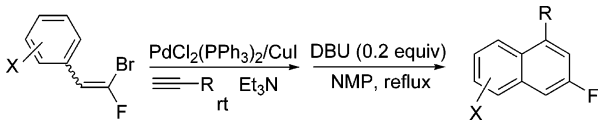
A Simple, Two-Step, Site-Specific Preparation of Fluorinated Naphthalene and Phenanthrene Derivatives from Fluorobromo-Substituted Alkenes

Yi Wang, Jianjun Xu, and Donald J. Burton*

Department of Chemistry, University of Iowa, Iowa City, Iowa 52242

donald-burton@uiowa.edu

Received June 23, 2006



A facile two-step procedure for the site-specific preparation of fluorinated naphthalene and phenanthrene derivatives is described. The Sonogashira reaction of bromofluoro-substituted alkenes with terminal alkynes, followed by base-catalyzed cyclization in refluxing *N*-methyl-2-pyrrolidinone (NMP), affords the corresponding fluorinated naphthalene and phenanthrene derivatives in good yields.

Introduction

Organic compounds in which hydrogen atoms are strategically replaced by fluorine have attracted increased interest for applications in the areas of polymer chemistry, medicinal chemistry, and agricultural chemistry.[1] It is proposed that fluorine modifies the biological activity by altering the physicochemical properties of these compounds.[2] Recently, the fluorination of aromatic compounds, especially the site-specific fluorination of naphthalenes, has been of interest to us because of the growing demand of this class of compounds as pharmaceutical and agricultural agents and the lack of efficient synthetic methodologies to these compounds.[3]

The thermal decomposition of aryl diazonium tetrafluoroborate salts (the Balz−Schiemann reaction) is the most traditional method for incorporation of fluorine onto the aromatic ring.[4] This method has been utilized in the preparation of 2-fluoronaphthalenes.[5] However, the following drawbacks prevent it from being widely employed in the synthesis of fluoroaromatics: hazardous starting materials; intolerance of certain functional groups ortho to the diazonium functional group; and tarry byproducts from the extensive side reactions of the intermediate aryl cation.[6] It has been reported that $Pb(OAc)_4$ and $BF_3{\cdot}Et_2O$ can transform aryl silanes into aryl fluoride, either by two steps or in an one-pot reaction.[6,7] Similarly, aryl boronic acids react with diethanolamine and cesium fluoroxysulfate ($CsSO_4F$) to form aryl fluorides.[8] Other electrophilic fluorinating reagents, such as N-Fluoro compounds, have been utilized to prepare fluoroaromatics directly from arenes.[9] For example, commercially available SelectFluor has been used to prepare monofluoronaphthalenes from naphthalene.[9] However, there is poor regioselectivity, and the resultant mixture of 1- and 2-fluoronaphthalenes is difficult to separate. The addition reaction of fluorinated carbene, :CFX (X = F, Cl, Br), to indene, followed by base-induced rearrangement, can also lead to 2-fluoronaphthalene.[10] However, this reaction is not practical for synthetic purposes due to the difficulty obtaining functional starting materials. Schlosser and co-workers recently reported

(1) (a) *Organofluorine Chemistry: Principle and Commercial Applications*; Banks, R. E., Smart, B. E., Tatlow, J. C., Eds.; Plenum Press: New York, 1994. (b) *Organofluorine Chemicals and Their Industrial Applications*; Banks, R. E., Ed.; Ellis Harwood Ltd.: Chichester, UK, 1979.

(2) (a) *Fluorine in Bioorganic Chemistry*; Welch, J. T., Eswarakrishman, S., Eds.; Wiley: New York, 1991. (b) *Fluoroorganic Chemistry: Synthetic Challenges and Biomedical Rewards*; Resnati, G., Soloshnok, A., Eds.; Tetrahedron Symposia in print No. 58, Tetrahedron, 1996; Vol. 52, pp 1−8. (c) *Biomedical Aspects of Fluorine Chemistry*; Filler, R., Kobayashi, Y., Eds.; Kodasha/Elsevier: New York, 1982. (d) Welch, J. T. *Tetrahedron* **1987**, *43*, 3123−3197. (e) McCarthy, J. R.; Huber, E. W.; Le, T.-B.; Laskovics, F. M.; Matthews, D. P. *Tetrahedron* **1996**, *52*, 45−58.

(3) (a) Meio, G. D.; Morgan, J.; Pinhey, J. T. *Tetrahedron* **1993**, *49*, 8129−8138. (b) Diorazio, L. J.; Widdowson, D. A.; Clough, J. M. *Tetrahedron* **1992**, *48*, 8073−8088. (c) Tagat, J. R.; McCombie, S. W.; Nazareno, D.; Boyle, C. D.; Kozlowski, J. A.; Chackalamannil, S.; Josien, H.; Wang, Y.; Zhou, G. *J. Org. Chem.* **2002**, *67*, 1171−1177.

(4) (a) Balz, G.; Schiemann, G. *Chem. Ber.* **1927**, *60*, 1186−1190. (b) Roe, A. *Org. React.* **1949**, *5*, 193−228.

(5) Nakata, N. *Chem. Ber.* **1931**, *64*, 2059−2069.

(6) Meio, G. D.; Pinhey, J. T. *J. Chem. Soc., Chem. Commun.* **1990**, *15*, 1065−1066.

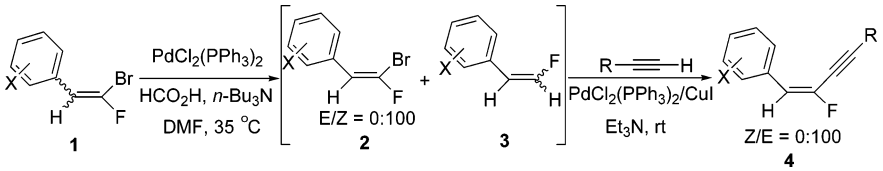
(7) Meio, G. D.; Morgan, J.; Pinhey, J. T. *Tetrahedron* **1993**, *49*, 8129−8138.

(8) Diorazio, L. J.; Widdowson, D. A.; Clough, J. M. *Tetrahedron* **1992**, *48*, 8073−8088.

(9) (a) Shamma, T.; Buchholz, H.; Prakash, G. K. S.; Olah, G. A. *Isr. J. Chem.* **1999**, *39*, 207−210. For reviews of SelectFluor, see: (b) Banks, R. E. *J. Fluorine Chem.* **1998**, *87*, 1−17. (c) Lal, G. S.; Pez, G. P.; Syvret, R. G. *Chem. Rev.* **1996**, *96*, 1737−1755.

10.1021/jo061305k CCC: $33.50
Published on Web 08/23/2006

TABLE 1. Preparation of 4 by the Coupling Reaction between 2 and Terminal Alkynes



entry	X	R	time (h)	product	isolated yield (%)
1	*o*-Cl	*n*-C_5H_{11}	36	**4a**	92
2	*o*-Cl	*n*-$C_{10}H_{21}$	48	**4b**	72
3	*p*-MeO	*n*-C_5H_{11}	21	**4c**	(82)[a]
4	*p*-MeO	Ph	45	**4d**	(78)[a]
5	*o*-(CH=CH)$_2$-*m*	*n*-C_4H_9	63	**4e**	(89)[a]
6	*o*-(CH=CH)$_2$-*m*	Ph	42	**4f**	68

[a] The enyne was not separable from the reduction products; the number in the parentheses is the conversion, which was calculated based on the amount of **2** in the starting mixture of **2** and **3**.

a synthetic route to fluoronaphthalenes via fluoroarynes. However, a regioisomeric mixture was found in their cases.[11] Herein, we wish to report our approach to 3-fluoro-1-substituted naphthalenes via the cyclization of (*E*)-monofluoroenynes. A portion of this research has been reported in a previous communication.[12]

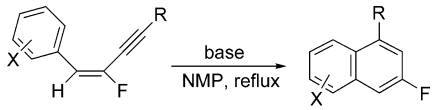
Results and Discussion

Recently, we reported a novel base-catalyzed cyclization of (*E*)-monofluoroenynes.[12] The preparation of (*E*)-monofluoroenynes is illustrated in Table 1. The kinetic reduction of mixtures of 1-bromo-1-fluoroalkenes (*E*/*Z* ≈ 1:1) afforded a mixture of 100% (*Z*)-1-bromo-1-fluoroalkenes and the corresponding reduction products[13] (not separable in most cases), which underwent Sonogashira reaction[14] with terminal alkynes to afford the (*E*)-monofluoroenynes **4**. It was difficult to separate **4** from the reduction products **3** in some cases; therefore, the mixture of **3** and **4** was utilized at this stage (Table 1, entries 3−5).

The mixture of the (*E*)-monofluoroenynes (with the corresponding reduction products, if not separable) and 1,4-diazabicyclo[2,2,2]octane (DABCO) or 1,8-diazabicyclo[5,4,0]-undec-7-ene (DBU) in refluxing *N*-methyl-2-pyrrolidinone (NMP) gave the corresponding cyclized products in good yields (entries 1, 2, 4, and 5). However, when R is Ph or *t*-Bu (entries 6 and 7), no reaction was detected in either case. These results are summarized in Table 2.

The use of NMP as the solvent was important in these reactions. Most reactions could be completed within 10 h in NMP, compared to 87 h in DMF, presumably due to the difference of their boiling points. Excess amount of DABCO (6 equiv) was used as the base, due to sublimation at the reflux temperature of NMP. A catalytic amount (20 mol %) of alternative bases, DBU and *n*-Bu_3N, was investigated, respectively, with **4a** in NMP at reflux temperature. The reaction was smooth and completed within 7 h when DBU was utilized (entry 2), and the desired product was successfully isolated in 80% yield. However, when *n*-Bu_3N was employed as the base (entry 3), the reaction was very slow. After 7 h, only 1/6 of the starting **4a** was consumed, and considerable amount of unidentified side products was detected by ^{19}F NMR analysis of the reaction mixture. Therefore, a catalytic amount of an alternative base (20 mol % DBU) was effective for the cyclization.

TABLE 2. Cyclization of (*E*)-Monofluoroenynes 4



entry	X	R	base	time (h)	product	yield (%)[a]
1	*o*-Cl	*n*-C_5H_{11}	DABCO	6	**5a**	93
2	*o*-Cl	*n*-C_5H_{11}	DBU	7	**5a**	80
3	*o*-Cl	*n*-C_5H_{11}	*n*-Bu_3N	7	**5a**	~8[c]
4	o-Cl	*n*-$C_{10}H_{21}$	DABCO	6	**5b**	94
5	*p*-MeO	*n*-C_5H_{11}	DABCO	11	**5c**	86
6	*p*-MeO	Ph	DABCO	43	N.R.[b]	0
7	*p*-MeO	*t*-Bu	DABCO	5	N.R.[b]	0

[a] Isolated yield of **5**. All products gave satisfactory ^{19}F, ^{1}H, ^{13}C NMR, GC-MS, and HRMS data. [b] No reaction. [c] Determined by ^{19}F NMR.

Since only (*E*)-enynes undergo cyclization to give the cyclized product, to simplify the synthetic route, we investigated the possibility of utilizing the mixture of (*Z*)- and (*E*)-enynes as the precursors for cyclization. First, *E*/*Z* mixtures of **7** (*E*/*Z* ≈ 1:1) were prepared in moderate to good yields from the reaction of **6**, $CFBr_3$, and Ph_3P in refluxing THF.[14] These results are summarized in Table 3.

Subsequent Sonogashira reaction of the *E*/*Z* mixtures of **7a−c** with terminal alkynes in Et_3N at room temperature afforded the corresponding enynes, which were used directly in the next step without purification. Cyclization of the enynes under normal reaction conditions (0.2 equiv of DBU in refluxing NMP) occurred smoothly (less than 7.5 h), and the cyclized compounds **8** were readily isolated in good yields. The yields in the two steps were based on the amount of (*Z*)-**7** in the *E*/*Z* mixtures. Through this improved route, the kinetic reduction step was not required. Thus, this modification provided a more efficient, two-step synthetic route to this class of compounds. These results are summarized in Table 4.

(10) (a) Dolbier, W. R.; Keaffaber, J. J.; Burkholder, C. R.; Koroniak, H.; Pradhan, J. *Tetrahedron* **1992**, *48*, 9649−9660. (b) Nefedov, O. M.; Volchkov, N. V. *J. Fluorine Chem.* **1991**, *54*, 86−86. (c) Parham, W. E.; Twelves, R. R. *J. Org. Chem.* **1957**, *22*, 730−734. (d) Volchkov, N. V.; Zabolotskikh, A. V.; Ignatenko, A. V.; Nefedov, O. M. *Bull. Acad. Sci. SSSR, Div. Chem. Sci. (Engl. Transl.)* **1990**, *39*, 1458−1461.

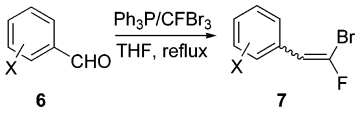
(11) Masson, E.; Schlosser, M. *Eur. J. Org. Chem.* **2005**, 4401−4405.

(12) Xu, J.; Wang, Y.; Burton, D. J. *Org. Lett.* **2006**, *8*, 2555−2558.

(13) Xu, J.; Burton, D. J. *Org. Lett.* **2002**, *4*, 831−833.

(14) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467−4470.

TABLE 3. Preparation of 1-Bromo-1-fluoroalkenes

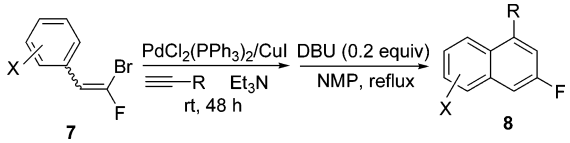


6 7

entry	X	time (h)	ratio of *Z*/*E*[a]	product	isolated yield[b] (%)
1	4-F	6.5	49:51	**7a**	38
2	4-CF_3	6	47:53	**7b**	81
3	3,5-difluoro	6.5	44:56	**7c**	65

[a] The ratio was determined by ^{19}F NMR. [b] Based on the aldehydes.

TABLE 4. Simplified Procedure for the Synthesis of Substituted 3-Fluoronaphthalenes



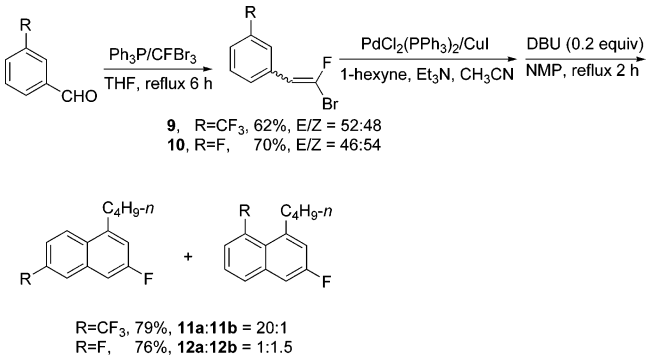
7 8

entry	X	R	time (h)	product	isolated yield[a] (%)
1	4-F	*n*-C_4H_9	5	**8a**	77
2	4-F	*n*-C_5H_{11}	7.5	**8b**	77
3	4-CF_3	*n*-C_4H_9	3	**8c**	89
4	4-CF_3	*n*-C_5H_{11}	2	**8d**	82
5	4-CF_3	*n*-$C_{10}H_{21}$	2	**8e**	74
6	4-CF_3	$PhCH_2CH_2$	3	**8f**	69
7	3,5-difluoro	*n*-C_4H_9	2	**8g**	55
8	3,5-difluoro	*n*-C_5H_{11}	3	**8h**	66

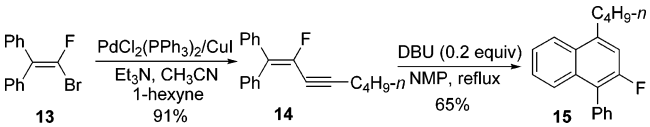
[a] Two steps, based on the (*Z*)-1-bromo-1-fluoroalkenes.

After we demonstrated the success of cyclization of the *o*-substituted and *p*-substituted 1-aryl-2-fluoroenynes in the presence of base (DBU or DABCO) in NMP, we were prompted to investigate the reactivity of the *meta*-substituted 1-aryl-2-fluoroenyne under similar reaction conditions since the enyne may give two possible products from two possible cyclization directions. Reaction of 3-trifluoromethylbenzaldehyde or 3-fluorobenzaldehyde, Ph_3P, and $CFBr_3$ in THF gave the 1-bromo-1-fluoroethene **9** or **10** in good yield, respectively. Subsequent Sonogashira reaction of **9** or **10** with 1-hexyne in MeCN (using Et_3N as base) gave the corresponding enyne, which was used directly for cyclization without characterization. To our surprise, a mixture of **11a** and **11b**, where **11a** was predominant, was obtained after DBU-catalyzed cyclization when the substrate was CF_3-substituted enyne (ratio of **11a**:**11b** was 20:1, determined by ^{19}F NMR spectrum). In the ^1H NMR spectrum of the mixture, a singlet peak at 8.07 ppm (in the major product) indicated that **11a** was the dominant product. The yield of the cyclization step was based on (*Z*)-**9** (Scheme 1). This high regioselectivity was presumably due to steric hindrance of the CF_3 group since the steric bulk of CF_3 is comparable to that of *i*-Bu.[16] However, in the case of cyclization of *m*-fluoroaryl-substituted enyne, a mixture of **12a** and **12b** was formed, where **12b** was the major product (**12a**:**12b** = 1:1.5). The assignment of **12b** was based on our observation of a characteristic through-space coupling[17] ($^5J_{HF}$ = 3.6 Hz) between benzylic hydrogens and fluorine (=R) on the other ring. The formation of **12b** as the major product could be attributed to a weak nonconventional hydrogen bonding[17c,18] between benzylic hydrogens and fluorine (=R).

SCHEME 1. Cyclization of *m*-Substituted 1-Aryl-2-fluoroenynes

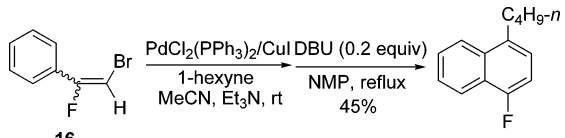


SCHEME 2. Synthesis of 1,4-Disubstituted 2-Fluoronaphthalene



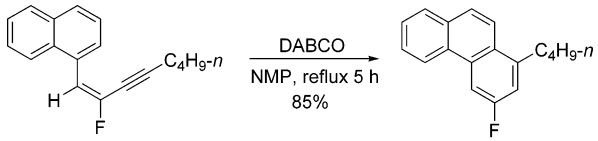
13 14 15

SCHEME 3. Synthesis of 4-Fluoro-1-Substituted Naphthalene



16 *E*/*Z* = 88:12 17

SCHEME 4. Preparation of 5e



4e 5e

Not only trisubstituted fluoroenynes but also tetrasubstituted analogues could be utilized to prepare fluorinated naphthalenes, as demonstrated in Scheme 2. The Sonogashira reaction of 1-bromo-1-fluoro-2,2-diphenylethene **13**, which was prepared by the method of Kvicala et al.,[19] with 1-hexyne afforded the corresponding enyne **14**. Subsequent cyclization of **14** gave the fluorinated naphthalene derivative **15** in the presence of 0.2 equiv of DBU in NMP. Therefore, not only 3-fluoro-1-substituted naphthalenes could be synthesized via this cyclization

(15) Vanderhaar, R. W.; Burton, D. J.; Naae, D. G. *J. Fluorine Chem.* **1971**−**1972**, *1*, 381−383.

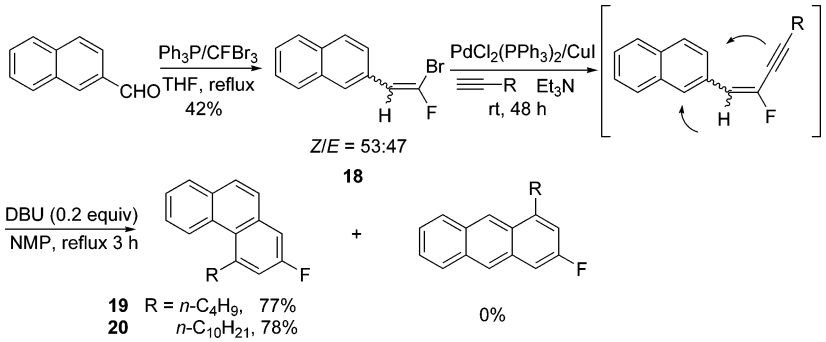
(16) *Organofluorine Compounds: Chemistry and Application*; Hiyama, T., Ed.; Springer: New York, 2000; pp 2−3.

(17) (a) Gribble, G. W.; Keavy, D. J.; Branz, S. E.; Kelly, W. J.; Pals, M. A. *Tetrahedron Lett.* **1988**, *29*, 6227−6230. (b) Gribble, G. W.; Kelly, W. J. *Tetrahedron Lett.* **1985**, *26*, 3779−3782. (c) Adcock, W.; Rizvi, S. Q. A. *Aust. J. Chem.* **1973**, *26*, 2659−2663.

(18) For examples of C−F···H−C hydrogen bonding, see: (a) Mele, A.; Vergani, B.; Viani, F.; Meille, S. V.; Farina, A.; Bravo, P. *Eur. J. Org. Chem.* **1999**, 187−196. (b) Parsch, J.; Engels, W. *J. Am. Chem. Soc.* **2002**, *124*, 5664−5672. For reviews, see: (c) *Organofluorine Chemistry*; Uneyama, K., Ed.; Blackwell: Oxford, UK, 2006; pp 173−185. (d) Howard, J. A. K.; Hoy, V. J.; O'Hagen, D.; Smith, G. T. *Tetrahedron* **1996**, *52*, 12613−12622. (e) Dunitz, J. D.; Taylor, R. *Chem.*−*Eur. J.* **1997**, *3*, 89−98.

(19) Kvicala, J.; Hrabal, R.; Czernek, J.; Bartosova, I.; Paleta, O.; Pelter, A. *J. Fluorine Chem.* **2002**, *113*, 211−218.

SCHEME 5. Synthesis of Fluorinated Phenanthrenes 19 and 20



methodology, but also 1,4-disubstituted-2-fluoronaphthalene could be prepared as well in good yield by this methodology.

In addition, via the base-catalyzed cyclization, 4-fluoro-1-substituted naphthalene derivatives could be prepared, as well, as illustrated in Scheme 3. The starting *E*, *Z* mixture **16** was prepared according to the published procedure by Rolando and co-workers.[20] Reaction of **16** with 1-hexyne under Sonogashira conditions afforded the corresponding enynes, which underwent cyclization to give 4-fluoro-1-substituted **17**. The overall yield (two steps) was based on the amount of the *E* isomer in the starting material.

We also extended this novel base-catalyzed cyclization to the preparation of fluorinated polycyclic aromatic hydrocarbons. Since there is only one direction for **4e** to cyclize, a mixture of **4e** (along with reduction product) and DABCO in NMP afforded the expected fluorinated phenanthrene **5e** in 85% yield (based on **4e**) (Scheme 4).

The structure of **5e** was confirmed by its single X-ray crystallographic structure determination.[21] However, no reaction was observed when **4f** was employed as the substrate.

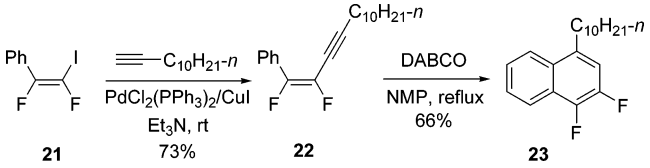
When 2-naphthaldehyde was employed as the substrate, **18** was obtained as an *E*, *Z* mixture. Theoretically, the subsequent cyclization of the enynes, which were prepared by Sonogashira reaction of **18** with terminal alkynes, would give two possible products: the fluorinated phenanthrene and/or the anthracene from two possible cyclization directions, respectively. Surprisingly, the phenanthrene derivative was formed as the sole product (Scheme 5), based on the fact that there are no singlet peaks at lower field from the 9-H and 10-H in the ^{1}H NMR spectrum of either **19** or **20**, a characteristic signal of anthracene.[22]

The phenanthrene structure was confirmed by single X-ray crystallographic structure determination of compound **20**.[21]

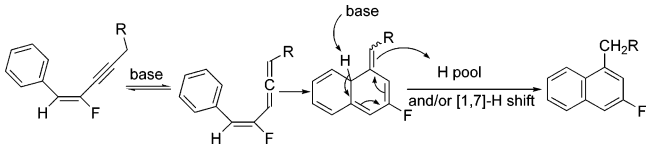
The exclusive formation of the fluorinated phenanthrenes could be rationalized by reported computational studies which have shown that the total molecular energy of phenanthrene is lower than that of anthracene, and these molecular energies were calculated by an ab initio molecular orbital method.[23]

After the successful cyclization of monofluoroenynes, we extended the reaction to difluoroenynes. Difluoroenyne **22** was prepared from (*E*)-1,2-difluoro-1-iodo-2-phenylethene **21**, which was synthesized by the method reported from this lab,[24] via a Sonogashira reaction with 1-decyne. Cyclization under similar reaction conditions afforded the difluorinated naphthalene **23** (Scheme 6).

SCHEME 6. Synthesis of 1,2-Difluoronaphthalene



SCHEME 7. Mechanism for the Formation of Naphthalenes



Since the *t*-Bu- or Ph-substituted enyne did not produce the desired cyclized product, it suggested that the mechanism might involve an allene as an intermediate. On the basis of these experiments and the deuterium experiment reported in the previous communication, the following mechanism was proposed (Scheme 7).[12] First, the base catalyzes the isomerization of the enyne to the allene,[25] which undergoes a 6π cycloaddition to form a two-ring system. The final product could be formed either from abstraction of H on C-9 by base followed by acquisition of H from the proton pool (either from base·H$^+$ or trace amount of moisture in the system) or from a [1,7]-H shift without assistance of the base.[26] This proposed mechanism not only explains the failure of the *t*-Bu or Ph derivatives due to the absence of propargyl hydrogen(s) in the enyne but is also consistent with the results of the deuterium analogue reported in the previous communication.[12]

Conclusion

A simple and site-specific preparation of 1-fluorosubstituted, 2-fluorosubstituted, 1,2-difluorosubstituted naphthalenes, as well

(20) Eddarir, S.; Francesch, C.; Mestdagh, H.; Rolando, C. *Bull. Soc. Chim. Fr.* **1997**, *134*, 741−755.

(21) CCDC 609268 (**5e**) and CCDC 608645 (**20**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK.; fax: +44 1223 336033. Also see the Supporting Information.

(22) *Spectrometric Identification of Organic Compounds*, 5th ed.; Silverstein, R. M., Bassler, G. C., Morrill, T. C., Eds.; John Wiley & Sons: New York, 1991; p 219.

(23) (a) Gong, X.; Xiao, H. *J. Phy. Org. Chem*. **1999**, *12*, 441−446. (b) Zakrzewski, V. G.; Dolgounitcheva, O.; Ortiz, J. V. *J. Chem. Phys.* **1996**, *105*, 8748−8753.

(24) Davis, C. R.; Burton, D. J. *J. Org. Chem.* **1997**, *62*, 9217−9222.

(25) *Allenes in Organic Synthesis*; Schuster, H. F., Coppola, G. M., Eds.; Wiley: New York, 1984.

(26) Nicolaou, K. C.; Vassilikogiannakis, G.; Simonsen, K. B.; Baran, P. S.; Zhong, Y.; Vidali, V. P.; Pitsinos, E. N.; Couladouros, E. A. *J. Am. Chem. Soc.* **2000**, *122*, 3071−3079.

as fluorinated phenanthrenes from bromofluoro-substituted alkenes has been developed. This procedure is one of the most direct methods to incorporate fluorine into naphthalenes and phenanthrenes. Our work continues to explore the overall scope of this novel base-catalyzed cyclization.

Experimental Section

The preparation of **4a**, **4b**, **4c**, **5a**, **5b**, **5c**, **7b**, **8c**, **8f**, **22**, and **23** has been reported in the previous communication.[12]

General Procedure for the Preparation of (*E*)-Monofluoroenynes 4: An oven-dried 50 mL round-bottom flask equipped with a stirring bar was charged with 0.028 g (0.04 mmol) of $PdCl_2(PPh_3)_2$ and 5 mL of Et_3N. A mixture of (*Z*)-1-bromo-1-fluoroalkene **2** and the corresponding reduced products **3** (containing 1 mmol of **2**) was added. The mixture was stirred for 10 min, and the terminal acetylene (1.5 mmol) was added. Finally, CuI (2 mg, 0.01 mmol) was added, and the reaction mixture was stirred at room temperature. When the reaction was completed, the mixture was directly added to a silica gel column and the desired (*E*)-monofluoroenyne **4** was obtained.

(*E*)-2-Fluoro-1-(4-methoxyphenyl)-4-phenylbut-1-en-3-yne (4d) (not separated from the corresponding reduced products): Similarly, a mixture of $PdCl_2(PPh_3)_2$ (0.028 g, 0.04 mmol), Et_3N (5 mL), phenylacetylene (0.153 g, 1.5 mmol), and CuI (2 mg, 0.01 mmol) was reacted with 474 mg of a mixture of (*Z*)-1-bromo-1-fluoro-2-(4-methoxyphenyl)ethene **2** and the corresponding reduced products **3** (containing 1 mmol of **2**) at room temperature for 45 h. After silica gel column chromatography (ethyl acetate:hexanes = 5:95, $R_f = 0.31$), 0.49 g of a mixture of **4d** and the reduced products **3** was obtained as a colorless oil (could not be completely separated); yield 78%. The weight percentage of **4d** is 40%. ^{19}F NMR ($CDCl_3$) of **4d**: δ −106.0 (m, 1 F); (*Z*)-reduced product: δ −125.4 (dd, $^2J_{FH} = 82.7$ Hz, $^3J_{FH(trans)} = 45.9$ Hz) ppm; (*E*)-reduced product: δ −132.7 (dm, $J = 84.2$ Hz) ppm. ^{1}H NMR ($CDCl_3$) of **4d**: δ 7.64 (d, $J = 8.9$ Hz, 2 H), 7.45 (d, $J = 8.8$ Hz, 2 H), 7.33−7.41 (m, 3 H), 6.90 (dm, $J = 9.4$ Hz, 2 H) or 6.87 (dm, $J = 8.9$ Hz, 2 H), 6.61 (d, $^3J_{HF(cis)} = 16.9$ Hz, 1 H) ppm; (*Z*)-reduced product: δ 7.51−7.55 (m), 7.33−7.41 (m), 6.59 (dd, $^2J_{HF} = 83.1$ Hz, $^3J_{HH(cis)} = 5.3$ Hz), 5.54 (dd, $^3J_{HF(trans)} = 45.3$ Hz, $^3J_{HH(cis)} = 5.4$ Hz) ppm; (*E*)-reduced product: δ 6.34 (dd, $^3J_{HF(cis)} = 19.6$ Hz, $^3J_{HH} = 11.3$ Hz) ppm. ^{13}C NMR ($CDCl_3$) of the **4d** and the reduced products: δ 159.5, 158.9, 158.7, 148.6 (d, $J = 256.8$ Hz), 146.6 (d, $^1J_{CF} = 267.5$), 139.6 (d, $J = 228.0$ Hz), 132.2, 131.3, 129.9 (d, $J = 7.3$ Hz), 129.2, 129.0, 128.3, 128.2, 127.0, 125.0, 124.6 (d, $J = 12.3$ Hz), 124.2 (d, $J = 5.0$ Hz), 121.5, 121.1, 117.2 (d, $J = 33.2$ Hz), 113.9, 113.7 (d, $J = 9.3$ Hz), 113.1 (d, $J = 15.8$ Hz), 110.1, 97.3, 81.6 (d, $J = 12.4$ Hz), 54.5, 54.4 ppm. GC-MS *m*/*z* (relative intensity) of **4d**: 254 ($M^+ + 2$, 1), 253 (22), 252 (M^+, 100), 237 (27), 236 (13), 220 (19), 219 (46), 209 (73), 207 (53), 189 (32), 183 (26), 181 (9), 163 (7), 157 (5), 126 (10), 110 (7), 104 (10), 91 (9), 81 (6); *m*/*z* (relative intensity) of the reduced products: 154 (1), 153 ($M^+ + 1$, 11), 152 (M^+, 100), 138 (5), 137 (71), 120 (3), 110 (5), 109 (82), 107 (10), 101 (9), 89 (8), 83 (44), 81 (7), 75 (8), 63 (12), 57 (13).

General Procedure for the Preparation of Substituted 3-Fluoronaphthalenes and Derivatives 5: An oven-dried 50 mL round-bottom flask equipped with a stirring bar, and a cold water condenser was charged with DABCO (0.34 g, 3.0 mmol) and NMP (4 mL). (*E*)-Monofluoroenyne **4** (0.5 mmol) or a mixture of (*E*)-monofluoroenyne **4** and the reduced products **3** (containing 0.5 mmol of **4**) was added. The mixture was refluxed for 6 h. When the reaction was completed, the reaction mixture was directly poured onto a silica gel column and pure product was obtained.

1-Butyl-3-fluorophenanthrene (5e): Similarly, 187 mg of a mixture of (*E*)-1-(2-fluorooct-1-en-3-ynyl)naphthalene **4e** and the corresponding reduced products (containing 0.7 mmol of **4e**) and DABCO (0.48 g, 4.2 mmol) in 3 mL of NMP was refluxed for 5 h. Silica gel column chromatography (hexanes only, $R_f = 0.42$) gave 0.15 g of white solid, 85% yield, mp 57−58 °C. ^{19}F NMR ($CDCl_3$): δ −114.9 (t, $J = 10.2$ Hz, 1 F) ppm. ^{1}H NMR ($CDCl_3$): δ 8.55 (dm, $J = 7.1$ Hz, 1 H), 8.18 (dd, $J = 11.0$, 2.5 Hz, 1 H), 7.94 (d, $J = 9.2$ Hz, 1 H), 7.89 (dm, $J = 7.0$ Hz, 1 H), 7.72 (d, $J = 9.2$ Hz, 1 H), 7.64 (td, $J = 6.7$, 1.7 Hz, 1 H), 7.60 (td, $J = 7.0$, 1.5 Hz, 1 H), 7.21 (dd, $J = 9.2$, 2.4 Hz, 1 H), 3.11 (t, $J = 7.8$ Hz, 2 H), 1.76 (tt, $J = 7.8$, 7.5 Hz, 2 H), 1.48 (sextet, $J = 7.4$ Hz, 2 H), 0.99 (t, $J = 7.3$ Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ 161.1 (d, $^1J_{CF} = 244.8$ Hz), 142.7 (d, $J = 7.7$ Hz), 132.3 (d, $J = 8.4$ Hz), 131.9, 130.2 (d, $J = 5.4$ Hz), 128.4, 127.0, 126.9, 126.5, 125.7 (d, $J = 3.0$ Hz), 123.1, 122.2, 115.8 (d, $J = 24.4$ Hz), 105.6 (d, $J = 22.1$ Hz), 33.1, 33.0, 22.7, 14.0 ppm. GC-MS *m*/*z* (relative intensity): 254 ($M^+ + 2$, 1), 253 ($M^+ + 1$, 15), 252 (M^+, 75), 221 (7), 220 (9), 210 (61), 209 (100), 207 (26), 196 (5), 189 (10), 183 (22), 110 (4), 92 (4). HRMS calcd 252.1314 for $C_{18}H_{17}F$, found 252.1314.

Simple Two-Step Procedure for the Preparation of 8: A 10 mL round-bottom flask equipped with a stirring bar was charged with $PdCl_2(PPh_3)_2$ (40 mg, 0.057 mmol) and 3 mL of Et_3N. A mixture of (*Z*)- and (*E*)-1-bromo-1-fluoroalkene (1.0 mmol) was added. The mixture was stirred for 10 min, and the terminal alkyne (1.2 mmol) was added. Then CuI (10 mg, 0.050 mmol) was added, and the reaction mixture was stirred at room temperature for 48 h. When the reaction was completed, the mixture was directly poured onto a silica gel column and the mixture of monofluoroenynes (*Z* and *E*) was obtained, and it was used directly in the next step.

An oven dried 10 mL round-bottom flask equipped with a stirring bar and a cold water condenser was charged with DBU (0.03 mL, 0.2 mmol) and the mixture of monofluoroenynes (1 mmol) in NMP (4 mL). Then the mixture was refluxed for about 6 h. When the reaction was completed, the mixture was cooled to room temperature and poured onto a silica gel column, and the pure product was obtained.

1-Butyl-3,7-difluoronaphthalene (8a): Colorless oil. ^{19}F NMR ($CDCl_3$): δ −115.9 (m, 1 F), −117.2 (m, 1 F) ppm. ^{1}H NMR ($CDCl_3$): δ 7.76 (dd, $J = 9.0$, 5.8 Hz, 1 H), 7.61 (dd, $J = 11.1$, 2.5 Hz, 1 H), 7.32−7.25 (m, 2 H), 7.15 (dd, $J = 9.6$, 2.5 Hz, 1 H), 2.99 (t, $J = 7.8$ Hz, 2 H), 1.76−1.69 (m, 2 H), 1.54−1.42 (m, 2 H), 0.98 (t, $J = 7.5$ Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ 160.1 (dd, $J = 242.7$, 2.8 Hz), 159.7 (dd, $J = 243.0$, 2.8 Hz), 141.7 (dd, $J = 8.2$, 5.8 Hz), 131.5 (dd, $J = 9.4$, 1.0 Hz), 130.2 (dd, $J = 8.9$, 5.6 Hz), 129.8 (dd, $J = 8.3$, 1.0 Hz), 116.9 (d, $J = 6.6$ Hz), 116.7 (d, $J = 6.9$ Hz), 109.0 (dd, $J = 20.3$, 1.0 Hz), 107.8 (dd, $J = 21.4$, 1.1 Hz), 32.6 (d, $J = 1.5$ Hz), 32.3, 22.8, 13.9 ppm. HRMS calcd 220.1064 for $C_{14}H_{14}F_2$, found 220.1061.

Acknowledgment. Financial support from the National Science Foundation is acknowledged. We are indebted to Dr. Dale Swenson for the determination of the X-ray structures.

Supporting Information Available: Experimental procedure for the synthesis of **4e**,**f**, **7a**, **7c**, **8b**, **8d**,**e**, **8g**,**h**, **9**−**12**, **14**, **15**, **17**−**20** and their characterization by ^{1}H, ^{19}F, and ^{13}C NMR and HRMS; copies of ^{1}H, ^{19}F, and ^{13}C NMR of compounds **4d**−**f**, **5e**, **7c**, **8a**,**b**, **8d**,**e**, **8g**,**h**, **9**−**12**, **14**, **15**, **17**, **19**, and **20**; ORTEP plots of **5e** and **20**; complete X-ray crystallographic data of compounds **5e** and **20** (CIFs). This material is available free of charge via the Internet at http://pubs.acs.org.

JO061305K