Organic LETTERS

Letter

pubs.acs.org/OrgLett

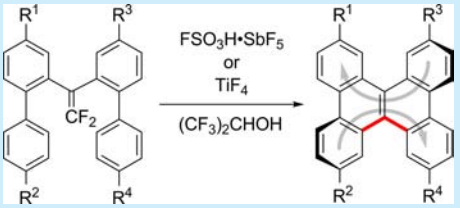
Method for the Synthesis of Dibenzo[*g*,*p*]Chrysenes: Domino Friedel–Crafts-Type Cyclization of Difluoroethenes Bearing Two Biaryl Groups

Naoto Suzuki, Takeshi Fujita, and Junji Ichikawa*

Division of Chemistry, Faculty of Pure and Applied Sciences, University of Tsukuba, Tsukuba, Ibaraki 305-8571, Japan

Supporting Information

ABSTRACT: Dibenzo[*g*,*p*]chrysenes were readily synthesized via the superacid- or TiF_4-mediated domino Friedel–Crafts-type cyclization of 1,1-difluoroethenes bearing two biaryl groups, which were easily prepared via the Suzuki–Miyaura coupling of 1,1-difluoro-2,2-diiodoethene or 1-(biphenyl-2-yl)-1-bromo-2,2-difluoroethene. Using this approach, the activation of both vinylic and aromatic C–F bonds was successfully achieved to make new C–C bonds.

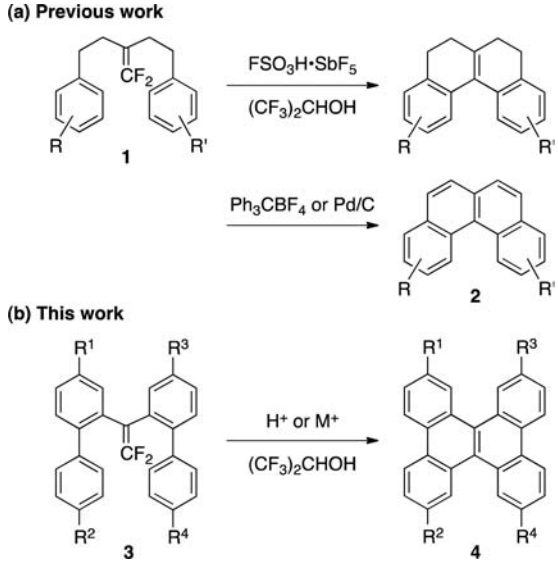


Dibenzo[*g*,*p*]chrysenes constitute a unique class of polycyclic aromatic hydrocarbons (PAHs) because of their characteristic double helical structure.[1] Their twisted π-systems are expected to be suitable for organic semiconductors directed toward electronic devices, such as thin-film transistors and organic light-emitting diodes;[2] thus, they have attracted much interest. So far, dibenzo[*g*,*p*]chrysenes have mainly been synthesized via the following processes: (i) intramolecular oxidative carbon–carbon bond formation of 9,10-diarylphenanthrenes,[3] 1,2-bis(biaryl-2-yl)ethynes,[4] or 9-(biaryl-2-yl)-phenanthrenes;[5] (ii) intramolecular Pd-catalyzed dehydrohalogenation of 9-(biaryl-2-yl)-10-iodophenanthrenes[6] or (*E*)-1,2-diaryl-1,2-bis(2-bromoaryl)ethenes;[7] and (iii) intermolecular metal-catalyzed cross-coupling between 9,10-diborylphenanthrenes and 2,2′-dibromobiaryls[8] or between phenanthrenes and dibenzosiloles.[9] Most of these methods were limited in substrate scope; for example, phenanthrene frameworks were required.

We have already developed facile methods for PAH synthesis via Friedel–Crafts-type cyclizations of fluorinated cationic species.[10] In our previous report, 1,1-difluoroethenes **1**, bearing two 2-arylethyl groups, afforded tetracyclic compounds in high yields by treatment with magic acid ($FSO_3H{\cdot}SbF_5$) in 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP), through the cleavage of two vinylic C–F bonds (Scheme 1a).[10a,c] The cyclized products successfully underwent subsequent oxidation by trityl tetrafluoroborate or palladium on carbon to yield helicenes **2**. Herein, we demonstrate the synthesis of dibenzo[*g*,*p*]chrysenes **4** via the domino Friedel–Crafts-type cyclization of 1,1-difluoroethenes **3** bearing two biaryl groups, mediated by magic acid or titanium(IV) fluoride (Scheme 1b). In this approach, the activation of both vinylic and aromatic C–F bonds was successfully effected to achieve direct construction of two aromatic rings without any oxidation process.[11]

Cyclization precursors, symmetrically or unsymmetrically substituted 1,1-bis(biaryl-2-yl)-2,2-difluoroethenes **3**, were readily prepared from 1,1,1-trifluoro-2-iodoethane (**5**) or 1,1-difluoroethylene (**6**), respectively, which are commercially available starting materials (Scheme 2). The double Suzuki–Miyaura coupling between potassium (biaryl-2-yl)-trifluoroborates and 1,1-difluoro-2,2-diiodoethene (**7**),[12] obtained by successive treatment of **5** with LDA and I_2, gave symmetrical 1,1-bis(biaryl-2-yl)-2,2-difluoroethenes **3a–d** (Scheme 2i). In contrast, unsymmetrical 1,1-bis(biaryl-2-yl)-2,2-difluoroethenes **3e–m** were prepared via the Suzuki–Miyaura coupling between (biaryl-2-yl)trifluoroborates and 1-(biphenyl-2-yl)-1-bromo-2,2-difluoroethene (**8**), which was obtained via the Negishi coupling of the 2,2-difluorovinylzinc–

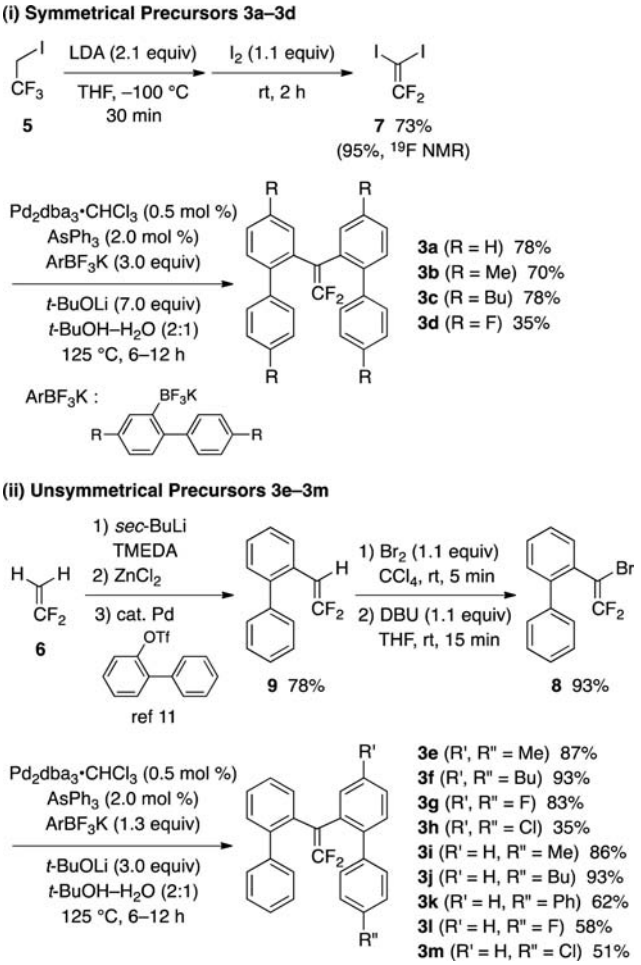
Scheme 1. Domino Friedel–Crafts-Type Cyclization of 1,1-Difluoro-1-ethenes



Received: August 22, 2015
Published: September 29, 2015

DOI: 10.1021/acs.orglett.5b02426
Org. Lett. 2015, 17, 4984–4987

Scheme 2. Preparation of Cyclization Precursors 3

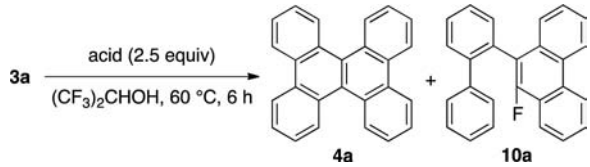


TMEDA complex derived from **6**[13] and subsequent bromination of the intermediary difluoroalkene[14] **9** (Scheme 2ii). With the availability of these two protocols, i and ii, a variety of difluoroethenes **3** were synthesized.

Using 1,1-bis(biphenyl-2-yl)-2,2-difluoroethene (**3a**) as a model compound, we sought suitable conditions for the domino Friedel–Crafts-type cyclization with a series of Brønsted and Lewis acids (Table 1). The reactions of **3a** with acids were performed in HFIP, which possesses a substantial cation stabilization effect.[10,15,16] When *p*-toluenesulfonic acid (TsOH) was employed, no cyclization products were observed (entry 1). However, on treatment with 2.5 equiv of trifluoromethanesulfonic acid (TfOH), the desired domino cyclization product, dibenzo[*g*,*p*]chrysene (**4a**), was obtained in 59% yield (entry 2). The use of magic acid improved the yield of **4a** to 95% (entry 3). In contrast, among the Lewis acids examined (BF_3·OEt_2, Me_3SiOTf, ZrF_4, $TiCl_4$, TiF_4; entries 4–8), TiF_4 in HFIP specifically promoted the cyclization of **3a** to afford **4a** in 93% yield (entry 8), while reaction in CH_2Cl_2 instead of HFIP selectively gave the monocyclization product, fluorophenanthrene **10a**, in 85% yield (entry 9). These results indicated that the stabilizing effect of HFIP on carbocations might be highly important for the second cyclization.[10,15,16]

Cyclization of other difluoroethenes **3** with magic acid or TiF_4 (method A or B) was examined for the synthesis of substituted dibenzo[*g*,*p*]chrysenes **4** (Table 2). Both symmetrically substituted difluoroethenes **3b–d** and unsymmetrically substituted ones **3e–m** successfully underwent a domino Friedel–Crafts-type cyclization with the appropriate choice of acid promotors. Use of TiF_4 (method B) was preferable for cyclization of alkyl- and aryl-substituted (more reactive) substrates **3b**, **3c**, **3e**, **3f**, **3i**, **3j**, and **3k**, which led to the effective formation of the corresponding dibenzo[*g*,*p*]chrysenes **4b**, **4c**, **4e**, **4f**, **4i**, **4j**, and **4k**. Rapid completion of the reactions with magic acid (method A) was observed for cyclization of the halogen-substituted (less reactive) precursors **3d**, **3g**, **3h**, **3l**, and

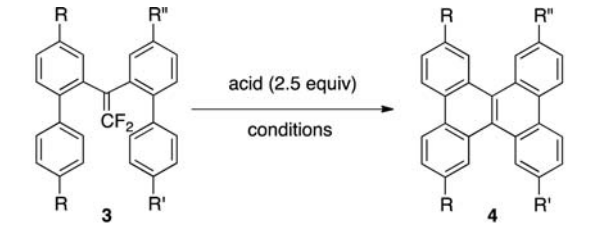
Table 1. Screening of Acids for the Domino Friedel–Crafts-Type Cyclization of Difluoroethene 3a



entry	acid	**4a** (%)[a]	**10a** (%)[a]
1	TsOH	ND[b]	ND[b]
2	TfOH	59	ND[b]
3[c]	FSO_3H·SbF_5	95	ND[b]
4	BF_3·OEt_2	trace	ND[b]
5	Me_3SiOTf	trace	ND[b]
6	ZrF_4	ND[b]	ND[b]
7	$TiCl_4$	ND[b]	ND[b]
8	TiF_4	93	ND[b]
9[d]	TiF_4	ND[b]	85

[a]^{1}H NMR yield using CH_2Br_2 as an internal standard. [b]ND = Not detected. [c]$(CF_3)_2CHOH$–CH_2Cl_2 (10:1), 0 °C, 10 min. [d]CH_2Cl_2, 40 °C, 6 h.

Table 2. Synthesis of Substituted Dibenzo[*g*,*p*]chrysenes 4



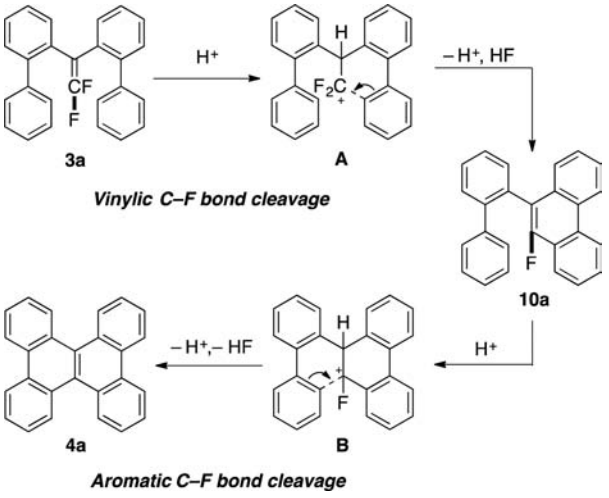
entry	**3**	method	**4** (%)
1	**3a**: R = H	A	**4a** 95
2	**3a**: R = H	B	**4a** 93
3	**3b**: R = Me	B	**4b** 93
4	**3c**: R = Bu	B	**4c** 99
5	**3d**: R = F	A	**4d** 80
6	**3e**: R = Me	B	**4e** 90
7	**3f**: R = Bu	B	**4f** 94
8	**3g**: R = F	A	**4g** 81
9	**3h**: R = Cl	A	**4h** 49
10	**3i**: R = Me	B	**4i** 82
11	**3j**: R = Bu	B	**4j** 98
12	**3k**: R = Ph	B	**4k** 72
13	**3l**: R = F	A	**4l** 80
14	**3m**: R = Cl	A	**4m** 54

DOI: 10.1021/acs.orglett.5b02426
Org. Lett. 2015, 17, 4984–4987

3m, affording the halogen-substituted dibenzo[*g*,*p*]chrysenes **4d**, **4g**, **4h**, **4l**, and **4m**, in good yields.

A plausible reaction mechanism for this cyclization is shown in Scheme 3. First, protonation of the difluoroethene moiety in **3a**

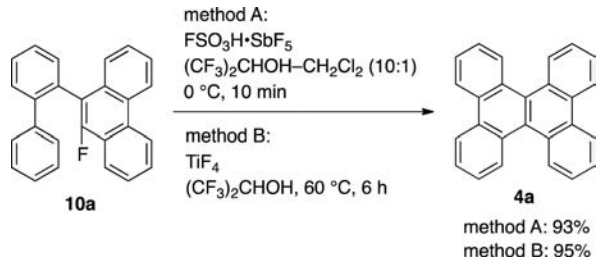
Scheme 3. Proposed Reaction Mechanism



regioselectively generates the cationic intermediate **A**, in which the carbocation is stabilized by the α-fluorine substituents. A Friedel−Crafts-type cyclization followed by the elimination of HF allows C−C bond formation and vinylic C−F bond cleavage to afford 9-(biphenyl-2-yl)-10-fluorophenanthrene **10a**. The second cyclization is induced by the protonation of the phenanthryl moiety in **10a**. Thus, a further Friedel−Crafts-type cyclization proceeds through the fluorine-stabilized arenium ion **B**,[10] resulting in aromatic C−F bond cleavage.[17]

To gain some experimental evidence to support the proposed reaction mechanism, we attempted the acid-mediated cyclization of fluorophenanthrene **10a**, which was prepared via cyclization of **3a** with TiF_4 in CH_2Cl_2 (Table 1, entry 9). Treatment of **10a** with magic acid or TiF_4 in HFIP−CH_2Cl_2 (10:1) or HFIP afforded dibenzo[*g*,*p*]chrysene (**4a**) in excellent yields (Scheme 4). These

Scheme 4. Cyclization of Fluorophenanthrene 10a



results suggested that **10a** was generated in situ as an intermediate by the first cyclization and then underwent the second cyclization, where the aromatic C−F bond cleavage was accomplished. It was noted that cleavage of an aromatic C−F bond, which has been considered to be difficult to activate, was readily achieved under cationic conditions with the aid of a Brønsted or Lewis acid in HFIP.[17]

In conclusion, we have achieved a domino Friedel−Crafts-type cyclization of difluoroethenes, which provides easy access to dibenzo[*g*,*p*]chrysenes. A scalable synthesis of dibenzo[*g*,*p*]-chrysenes is conducted by starting from accessible, storable 1,1,1-trifluoro-2-iodoethane or 1,1-difluoroethene. Dibenzo[*g*,*p*]-chrysenes possess a double helical structure due to the presence of two inherent helicene moieties. Their application to new electronic materials will be stimulated by the approach presented in this study.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02426.

Experimental details, characterization data, and NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: junji@chem.tsukuba.ac.jp.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research is partly supported by MEXT/JSPS KAKENHI (J.I., No. 25288016), the Asahi Glass Foundation (J.I.), and Izumi Science and Technology Foundation (T.F.). We acknowledge the generous gifts of $(CF_3)_2CHOH$ (HFIP) from Central Glass Co., Ltd. and CF_3CH_2I from Tosoh F-Tech, Inc.

■ REFERENCES

(1) For selected papers on construction of double helical structures, see: (a) Shiraishi, K.; Rajca, A.; Pink, M.; Rajca, S. *J. Am. Chem. Soc.* **2005**, *127*, 9312−9313. (b) Wang, Z.; Shi, J.; Wang, J.; Li, C.; Tian, X.; Cheng, Y.; Wang, H. *Org. Lett.* **2010**, *12*, 456−459. (c) Nakanishi, W.; Matsuno, T.; Ichikawa, J.; Isobe, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 6048−6051. (d) Eversloh, C. L.; Liu, Z.; Müller, B.; Stangl, M.; Li, C.; Müllen, K. *Org. Lett.* **2011**, *13*, 5528−5531. (e) Hatakeyama, T.; Hashimoto, S.; Seki, S.; Nakamura, M. *J. Am. Chem. Soc.* **2011**, *133*, 18614−18617. (f) Luo, J.; Xu, X.; Mao, R.; Miao, Q. *J. Am. Chem. Soc.* **2012**, *134*, 13796−13803. (g) Xiao, S.; Kang, S. J.; Wu, Y.; Ahn, S.; Kim, J. B.; Loo, Y.-L.; Siegrist, T.; Steigerwald, M. L.; Li, H.; Nuckolls, C. *Chem. Sci.* **2013**, *4*, 2018−2023. (h) Nakamura, K.; Furumi, S.; Takeuchi, M.; Shibuya, T.; Tanaka, K. *J. Am. Chem. Soc.* **2014**, *136*, 5555−5558. (i) Hashimoto, S.; Nakatsuka, S.; Nakamura, M.; Hatakeyama, T. *Angew. Chem., Int. Ed.* **2014**, *53*, 14074−14076. (j) Kashihara, H.; Asada, T.; Kamikawa, K. *Chem. - Eur. J.* **2015**, *21*, 6523−6527. (k) Sakamaki, D.; Kumano, D.; Yashima, E.; Seki, S. *Angew. Chem., Int. Ed.* **2015**, *54*, 5404−5407.

(2) (a) Mori, T.; Fujita, K.; Kimura, M. *J. Photopolym. Sci. Technol.* **2010**, *23*, 317−322. (b) Chaudhuri, R.; Hsu, M.-Y.; Li, C.-W.; Wang, C.-I.; Chen, C.-J.; Lai, C.-K.; Chen, L.-Y.; Liu, S.-H.; Wu, C.-C.; Liu, R.-S. *Org. Lett.* **2008**, *10*, 3053−3056.

(3) (a) Mukherjee, A.; Pati, K.; Liu, R.-S. *J. Org. Chem.* **2009**, *74*, 6311−6314. (b) Navale, T. S.; Thakur, K.; Rathore, R. *Org. Lett.* **2011**, *13*, 1634−1637.

(4) (a) Yamaguchi, S.; Swager, T. M. *J. Am. Chem. Soc.* **2001**, *123*, 12087−12088. (b) Mukherjee, A.; Pati, K.; Liu, R.-S. *J. Org. Chem.* **2009**, *74*, 6311−6314.

(5) Mochida, K.; Kawasumi, K.; Segawa, Y.; Itami, K. *J. Am. Chem. Soc.* **2011**, *133*, 10716−10719.

(6) Li, C.-W.; Wang, C.-I.; Liao, H.-Y.; Chaudhuri, R.; Liu, R.-S. *J. Org. Chem.* **2007**, *72*, 9203−9207.

(7) Ueda, Y.; Tsuji, H.; Tanaka, H.; Nakamura, E. *Chem. - Asian J.* **2014**, *9*, 1623−1628.

(8) Shimizu, M.; Nagao, I.; Tomioka, Y.; Kadowaki, T.; Hiyama, T. *Tetrahedron* **2011**, *67*, 8014−8026.

(9) Ozaki, K.; Kawasumi, K.; Shibata, M.; Ito, H.; Itami, K. *Nat. Commun.* **2015**, *6*, 6251.

DOI: 10.1021/acs.orglett.5b02426
Org. Lett. 2015, 17, 4984−4987

(10) (a) Ichikawa, J.; Yokota, M.; Kudo, T.; Umezaki, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 4870−4873. (b) Isobe, H.; Hitosugi, S.; Matsuno, T.; Iwamoto, T.; Ichikawa, J. *Org. Lett.* **2009**, *11*, 4026−4028. (c) Fuchibe, K.; Jyono, H.; Fujiwara, M.; Kudo, T.; Yokota, M.; Ichikawa, J. *Chem. - Eur. J.* **2011**, *17*, 12175−12185. (d) Fuchibe, K.; Mayumi, Y.; Zhao, N.; Watanabe, S.; Yokota, M.; Ichikawa, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 7825−7828. (e) Fuchibe, K.; Mayumi, Y.; Yokota, M.; Aihara, H.; Ichikawa, J. *Bull. Chem. Soc. Jpn.* **2014**, *87*, 942−949. (f) Fuchibe, K.; Morikawa, T.; Shigeno, K.; Fujita, T.; Ichikawa, J. *Org. Lett.* **2015**, *17*, 1126−1129. (g) Fuchibe, K.; Morikawa, T.; Ueda, R.; Okauchi, T.; Ichikawa, J. *J. Fluorine Chem.* **2015**, DOI: 10.1016/j.jfluchem.2015.06.008.

(11) For recent reviews on C−F bond activation, see: (a) Amii, H.; Uneyama, K. *Chem. Rev.* **2009**, *109*, 2119−2183. (b) Stahl, T.; Klare, H. F. T.; Oestreich, M. *ACS Catal.* **2013**, *3*, 1578−1587. (c) Ahrens, T.; Kohlmann, J.; Ahrens, M.; Braun, T. *Chem. Rev.* **2015**, *115*, 931−972. (d) Unzner, T. A.; Magauer, T. *Tetrahedron Lett.* **2015**, *56*, 877−883.

(12) Fujita, T.; Suzuki, N.; Ichitsuka, T.; Ichikawa, J. *J. Fluorine Chem.* **2013**, *155*, 97−101.

(13) (a) Fujita, T.; Ichitsuka, T.; Fuchibe, K.; Ichikawa, J. *Chem. Lett.* **2011**, *40*, 986−988. (b) Ichitsuka, T.; Takanohashi, T.; Fujita, T.; Ichikawa, J. *J. Fluorine Chem.* **2015**, *170*, 29−37.

(14) Burton, D. J.; Anderson, A. L.; Takei, R.; Koch, H. F.; Shih, T. L. *J. Fluorine Chem.* **1980**, *16*, 229−235.

(15) For selected papers on carbocationic processes in HFIP, see: (a) Ichikawa, J.; Miyazaki, S.; Fujiwara, M.; Minami, T. *J. Org. Chem.* **1995**, *60*, 2320−2321. (b) Ichikawa, J.; Jyono, H.; Kudo, T.; Fujiwara, M.; Yokota, M. *Synthesis* **2005**, 39−46. (c) Ichikawa, J.; Kaneko, M.; Yokota, M.; Itonaga, M.; Yokoyama, T. *Org. Lett.* **2006**, *8*, 3167−3170. (d) Nishiwaki, N.; Kamimura, R.; Shono, K.; Kawakami, T.; Nakayama, K.; Nishino, K.; Nakayama, T.; Takahashi, K.; Nakamura, A.; Hosokawa, T. *Tetrahedron Lett.* **2010**, *51*, 3590−3592. (e) Champagne, P. A.; Benhassine, Y.; Desroches, J.; Paquin, J.-F. *Angew. Chem., Int. Ed.* **2014**, *53*, 13835−13839. (f) Gaster, E.; Vainer, Y.; Regev, A.; Narute, S.; Sudheendran, K.; Werbeloff, A.; Shalit, H.; Pappo, D. *Angew. Chem., Int. Ed.* **2015**, *54*, 4198−4202. (g) Ricardo, C. L.; Mo, X.; McCubbin, J. A.; Hall, D. G. *Chem. - Eur. J.* **2015**, *21*, 4218−4223.

(16) For reviews on fluorinated alcohols, see: (a) Bégué, J.-P.; Bonnet-Delpon, D.; Crousse, B. *Synlett* **2004**, 18−29. (b) Shuklov, I. A.; Dubrovina, N. V.; Börner, A. *Synthesis* **2007**, *2007*, 2925−2943. (c) Dohi, T.; Yamaoka, N.; Kita, Y. *Tetrahedron* **2010**, *66*, 5775−5785. (d) Khaksar, S. *J. Fluorine Chem.* **2015**, *172*, 51−61.

(17) Similarly, Lewis acid mediated defluorinative coupling reactions have been also reported as efficient synthetic methods for PAHs by Siegel and Amsharov. See: (a) Allemann, O.; Duttwyler, S.; Romanato, P.; Baldridge, K. K.; Siegel, J. S. *Science* **2011**, *332*, 574−577. (b) Amsharov, K. Y.; Kabdulov, M. A.; Jansen, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 4594−4597.

DOI: 10.1021/acs.orglett.5b02426
Org. Lett. 2015, 17, 4984−4987