Tetrahedron 66 (2010) 5218–5228

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Diastereoselective synthesis of propargylic fluorides and its application in preparation of monofluorinated sugar

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ARTICLE INFO

Article history:
Received 2 March 2010
Received in revised form 19 April 2010
Accepted 20 April 2010
Available online 24 April 2010

Keywords:
Propargylic fluorides
DAST
Dicobalt octacarbonyl
Alkyne-cobalt carbonyl complex
Monofluorinated sugar

ABSTRACT

An effective method to diastereoselectively synthesize enantioenriched propargylic fluorides was developed via S_N1 type reaction of DAST participated dehydroxy-fluorination of diastereomeric propargylic alcohol cobalt–carbonyl complexes. A serious of propargylic fluorides can be prepared by this approach in good yields with moderate to high diastereoselectivities. To demonstrate the application of this approach in synthesis, monofluorinated sugar **12**, an important and versatile building block, was prepared in an efficient manner.

1. Introduction

Although fluorinated compounds rarely exist in nature, they have attracted considerable attention in life sciences. Because incorporation of fluorine atom(s) into an organic molecule usually leads to profound changes in its physical, chemical, and biological properties.[1] This is probably due to the unique properties of the fluorine atom and/or the carbon–fluorine bond.[2] Therefore, substitution of a hydrogen atom or a hydroxyl group in parent compounds with the fluorine atom is now a common strategy in the course of developing new drug candidates.[1d,3] Among the fluorinated compounds, propargylic fluorides constitute a distinct class of fluorinated compounds that can be used not only as the key building blocks to access many organofluorinated molecules by simple functional group manipulations,[4] but also as the important biological probes and inhibitors in life sciences.[5] Indeed, many biologically active molecules, such as insecticides, herbicides, fluorinated Vitamin D, and prostanoid analogs, contain propargylic fluorides motif.[5] However, the synthetic methods for this class of fluorinated compounds, especially asymmetrically synthetic methods are still limited. The most commonly used method to asymmetrically synthesize propargylic fluorides thus far is dehydroxy-fluorination of enantioenriched propargylic alcohols with ((diethylamino)sulfur trifluoride) (DAST) reported by Gree's group.[6] Recently, an alternative approach to the synthesis of enantioenriched proparylic fluorides via S_E2' fluorination of chiral allenylsilanes with Selectfluor was developed by Gouverneur's group.[7] Very recently, a high enantioselective synthesis of chiral terminal propargylic fluorides was reported by Jørgensen's group.[8] Although these attractive approaches have been developed, new methods to facilitate the access of enantioenriched proparylic fluorides remain highly desirable. Herein, we disclosed an effective method for diastereoselective synthesis of enantioenriched propargylic fluorides from diastereomeric propargylic alcohols via an S_N1 reaction in high yields with moderate to high diastereoselectivities (Scheme 1, Eq. 1) and its application in the synthesis of a monofluorinated sugar.

2. Results and discussion

Our experiments were based on the fact that treatment of compounds **1a**–**b** or **2a** with DAST only provided 7% to 34% yields of the corresponding diastereomeric porpargylic fluorides (Scheme 1), and that cobalt-carbonyl moiety in alkyne-cobalt carbonyl complex (Nicholas reaction[9]) could significantly stabilize the α carbocation. Thus, we envisioned that the stable chiral carbocation intermediates induced by alkyne-cobalt carbonyl complex and the chiral 1,3-dioxolane moiety of diastereomeric mixture of propargylic alcohol **3** and **4**, in which the reaction center is in racemic form, might provide a good platform to access enantioenriched propargylic fluorides in good yields. To the best of our knowledge, the facial diastereoselectivity of intermolecular S_N1

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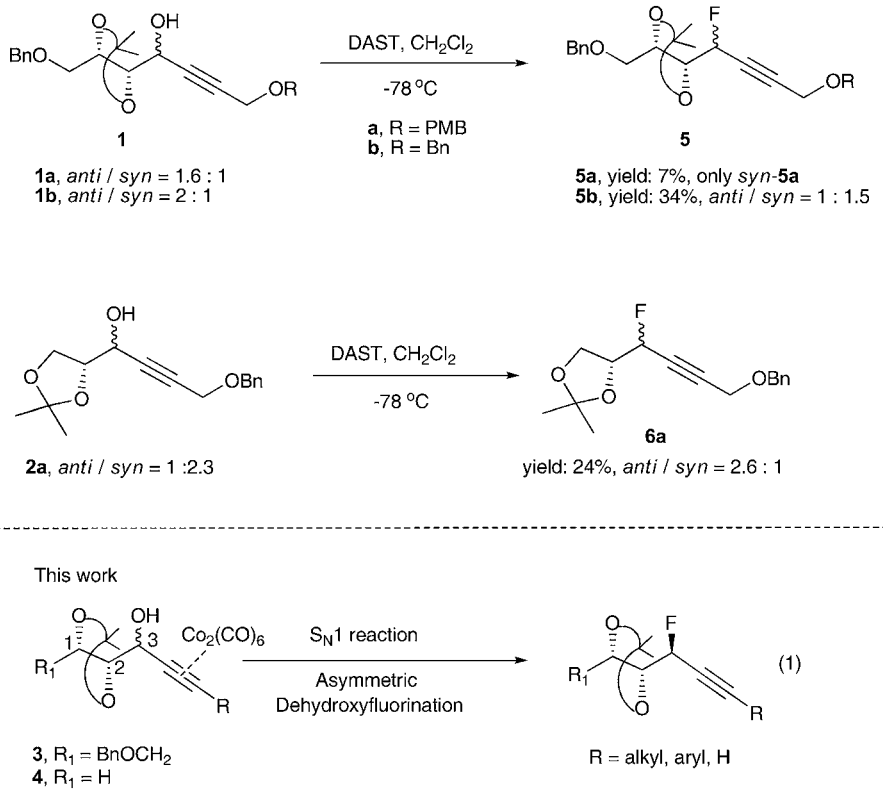
0040-4020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2010.04.078

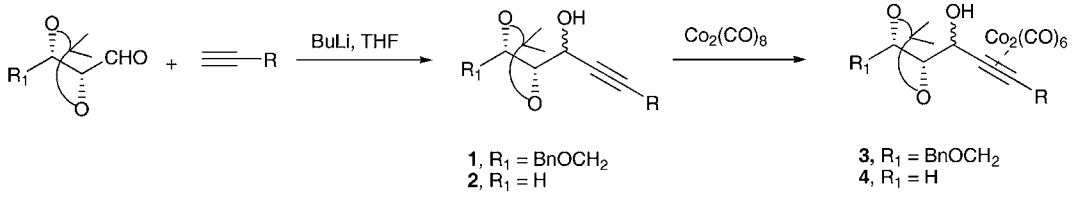


Scheme 1. Dehydroxy-fluorination of diastereomeric propargylic alcohols **1** and **2**.

reactions on putative chiral carbocation intermediates has not been extensively studied.[10] Furthermore, the reaction can be easily scaled up because propargylic alcohols **1** and **2** could be easily obtained by addition of various of alkynes to readily available 4-*O*-benzyl-2,3-*O*-isopropylidene-L-threose[11] and 1-(*R*)-glyceraldehyde acetonide,[12] respectively. In addition, the resulting enantioenriched propargylic fluorides **5** and **6** are versatile building blocks for many unnatural monofluorinated sugars.[13]

Initially, a mixture of alkyne complexes **3a** that was easily prepared in high yield by treatment of propargylic alcohols **1a** with $Co_2(CO)_8$ (Scheme 2) was chosen as model substrates for this study. A survey of a series of reaction conditions showed that treatment of **3a** (*anti*/*syn*=2:1) in CH_2Cl_2 (0.15 M) with 1.2 equiv of DAST at −78 °C to room temperature afforded **7a** in high yield, and *anti*-**7a** was observed as the major product (*anti*/*syn*=5:1) (Table 1, entry 1). Interestingly, when a higher optically enriched *anti*-**3a** (*anti*/*syn*=6.5:1) was employed as the substrate, better diastereoselectivity (*anti*/*syn*=8:1) was provided (Table 1, entry 2). It was noteworthy that a gram-scale reaction of *anti*-**3a** (*anti*/*syn*=6.5:1, 1.3 g) provided **7a** with even higher diastereoselectivity (*anti*/*syn*=9:1) (Table 1, entry 3). Further investigation of other substrates showed that the alkyne complexes **3b** and **3c** also afforded propargylic fluorides in good yields with moderate diastereoselectivities (Table 1, entries 4 and 5). Simple treatment of **7** with cerium (IV) diammonium nitrate (CAN) to remove cobalt-carbonyl moiety afforded final product **5** in good yields (72–90%, two steps from **3**) without erosion of dr value (Table 1). It should be mentioned that the epimers *anti*-**7** and *syn*-**7** can be separated by flash silica gel chromatography,[14] and the subsequent treatment of *anti*-**7** or *syn*-**7** with CAN can provide optically pure *anti*-**5** or *syn*-**5** easily.

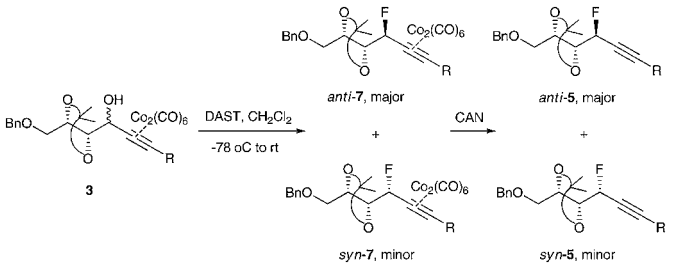
Encouraged by these results, we then investigated the reaction to an expanded broad of substrates. Substrate **4a** (*anti*/*syn*=1:3), in which the substituent benzyloxymethylene ($BnOCH_2$) group at position C1 was omited with respect to **3b**, was first tested and a high diastereoselectivity (*anti*/*syn*=13:1) was achieved (Table 2, entry 1). More results were summarized in Table 2. High yields and



Scheme 2. Preparation of propargylic alcohol cobalt–carbonyl complexes **3** and **4**.

diastereoselectivities (*anti*/*syn*) ranging from 5.1:1 to 17:1 (determined by ^{19}F NMR) were observed for all substrates **4**. For all the aliphatic alkynes, the diastereoselectivities depend on the steric features of the substituents. The less hindered alkyl substituted alkyne complexes provided good to high dr values (Table 2, entries 1–6), while bulky substrates afforded moderate diastereoselectivities (Table 2, entries 7–9). Interestingly, the reaction of compound **4c** also provided higher selectivity (*anti*/*syn*=7.6:1) than its corresponding analogs **3a** (*anti*/*syn*=5:1). In the case of **4f**, the cyclopropyl substituted alkyne complex, the dr values were ranged

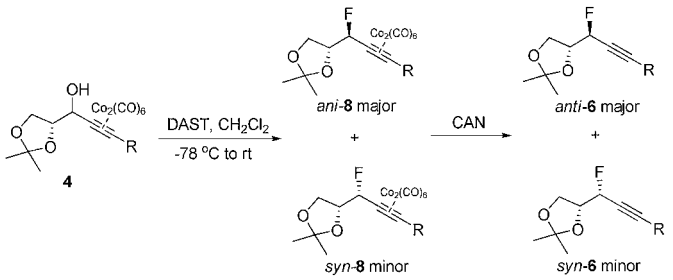
Table 1
Diastereoselective dehydroxy-fluorination of propargylic alcohol cobalt carbonyl complexes **3** with DAST[a]

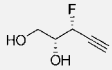
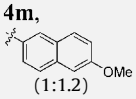


Entry	**3**, R (*anti*/*syn*)	**7** (*anti*/*syn*)[b]	**7** yield (%)[c]	**5** yield (%)[d]
1	**3a**, CH_2OPMB (2:1)	5:1	91	90
2	**3a** (6.5:1)	8:1	(82)	81
3[e]	**3a** (6.5:1)	9:1	(73)	72
4	**3b**, CH_2OBn (1.5:1)	5.4:1	82	81 (*anti*-**5b**, 95 *syn*-**5b**, 98)[f]
5	**3c**, ▷ (1.8:1)	5.4:1	87	84 (*anti*-**5c**, 92 *syn*-**5c**, 87)[f]

[a] Unless otherwise noted, the reaction was carried out by using **3** (0.3 mmol, 1 equiv) and DAST (1.2 equiv) in a 0.15 M CH_2Cl_2 solution at −78 °C to rt.
[b] Determined by ^{19}F NMR before column chromatography.
[c] NMR yield determined by ^{19}F NMR using benzotrifluoride (BTF) as an internal standard, yield in parentheses was isolated yield.
[d] Overall yield, two steps from **3**.
[e] The reaction was carried out on a 1.3 g of scale at −90 °C to −78 °C to rt.
[f] isolated yield from the reaction of *anti*-**7** or *syn*-**7**, respectively.

Table 2
Diastereoselective dehydroxy-fluorination of propargylic alcohol cobalt–carbonyl complexes 4 with DAST[a]



Entry	**4**, R (*anti*/*syn*)	**8** (*anti*/*syn*)[b]	**8** yield (%)[c]	**6** yield (%)[d] (*anti*/*syn*)[e]
1	**4a**, CH_2OBn (1:2.3)	13:1	100	88 (14:1) (*anti*-**6a**, 86 *syn*-**6a**, 82)[f]
2	**4b**, $(CH_2)_2OBn$ (1:1.5)	8.1:1	99	87 (9:1)
3	**4c**, CH_2OPMB (1:1)	7.6:1	(91)	*anti*-**6c**, 80[f]; *syn*-**6c**, 75[f]
4	**4d**, $(CH_2)_2OPMB$ (1:2.3)	8.2:1	100	87 (8.2:1)
5	**4e**, $(CH_2)_7CH_3$ (1:1.2)	8.4:1	100	95 (9:1)
6	**4f**, ▷ (1:1.5)	8.3:1 to 17:1	87	84 (8.3:1 to 17:1)
7	**4g**, CH_2OTrt (1:1.3)	5.5:1	100	87, (*anti*-**6g**, 96)[f]
8	**4h**, *t*-Bu (1:1)	5.4:1	100	83, (5:1)
9	**4i**, Cyl (1:1)	6:1	96	94, (6:1)
10	**4j**, TMS (1:1.6)	—	Trace	—
11	**4k**, H (1:1.6)	7:1	89	 **9** **9** 84 (8:1)
12	**4l**, Ph (1:1.4)	6.4:1	94	90 (*syn*-**6l**, 98; *anti*-**6l**, 94)[f]
13	**4m**,  (1:1.2)	5.1:1	98	83 (*anti*-**6m**, 82)[f]

[a] Reactions were carried out by using **4** (0.3 mmol, 1 equiv) and DAST (1.2 equiv) in a 0.15 M CH_2Cl_2 solution at −78 °C to rt.
[b] Determined by ^{19}F NMR before column chromatography.
[c] NMR yield determined by ^{19}F NMR using benzotrifluoride (BTF) as an internal standard, yield in parentheses was isolated yield.
[d] Overall yield, two steps from **4**.
[e] Determined by ^{19}F NMR after column chromatography.
[f] isolated yield from the reaction of *anti*-**8** or *syn*-**8**, respectively.

from 8.3:1 to 17:1 (*anti*/*syn*) (Table 2, entry 6). Under the similar conditions, compound **4j** bearing a TMS failed to provide the product (Table 2, entry 10), while the terminal alkyne complexes **4k** furnished the propargylic fluorides in good yield with dr 7:1 (*anti*/*syn*) (Table 2, entry 11). For the aryl substituted alkyne complexes **4l** and **4m**, the diastereoselectivties (*anti*/*syn*) ranged from 5.1:1 to 6.4:1 (Table 2, entries 12 and 13). Similarly, the enantioenriched fluorinated complexes **8** can be separated by flash silica gel chromatography, which was treated by CAN to provide propargylic fluorides **6** smoothly without erosion of the dr values. Due to the low boil point of compound **6k**, it was deprotected directly by treatment with HCl to afford diol **9** in good yield (Table 2, entry 11).

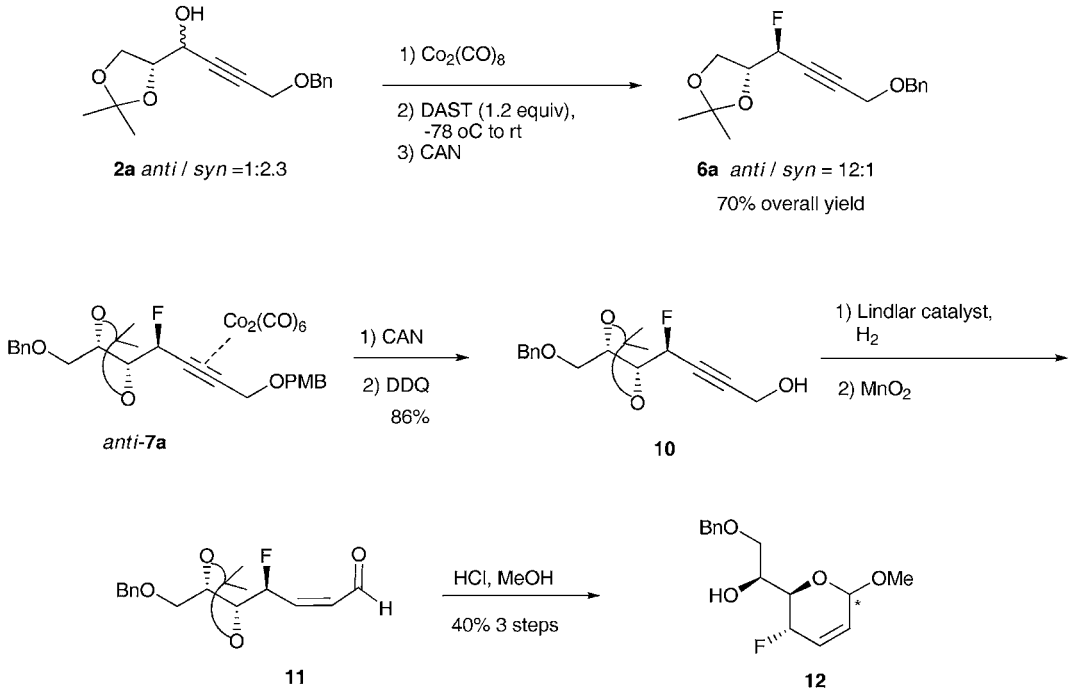
Notably, the enantioenriched propargylic fluorides can be easily accessed by one pot reaction (Scheme 3). Treatment of the mixture of **2a** with $Co_2(CO)_8$ at room temperature, followed by the reaction with DAST at −78 °C to rt, and subsequently with CAN afforded the final product **6a** in good yield (70% overall yield) with high diastereoselectivity (*anti*/*syn*=12:1). Transformation of *anti*-**7a** also proved to be an efficient approach to access monofluorinated sugar **12** that can be used as an important and versatile building block to prepare many other unnatural sugars for chemical biology study, such as antibiotic.[13d] As depicted in Scheme 3, **10** was obtained in 86% yield by deprotection of cobalt-carbonyl moiety of *anti*-**7a** with CAN, followed by treatment of the resulting propargylic fluorides with DDQ. Alcohol **10** was selectively reduced with H_2 in the presence of Lindlar catalyst. The resulting *Z*-alkene was subsequently oxidized with MnO_2 to afford aldehyde **11**, which was then treated with HCl in MeOH to provide monofluorinated sugar **12** in 40% overall yield (three steps).

The absolute configurations of the propargylic fluorides were established through the S_N2 dehydroxy-fluorination of **1** and **2** with DAST. As depicted in Scheme 4, four representative substrates *anti*/*syn*-**1** and *anti*/*syn*-**2**, whose configurations can be assigned according to the literature,[11,15] were chosen for this study.

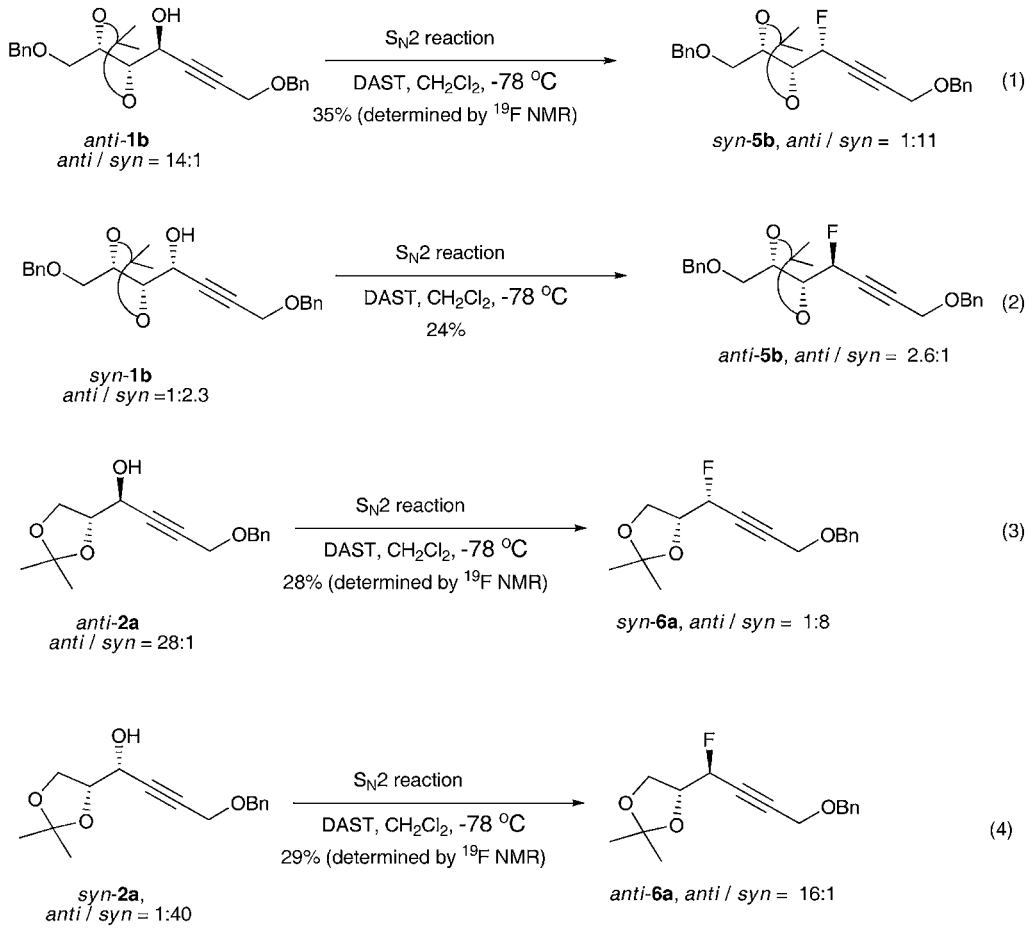
When *anti*-**1b** (*anti*/*syn*=14:1)/*syn*-**1b** (*syn*/*anti*=2.3:1) or *anti*-**2a** (*anti*/*syn*=28:1)/*syn*-**2a** (*anti*/*syn*=1:40) were treated with DAST, the corresponding *syn*-**5b**/*anti*-**5b** or *syn*-**6a**/*anti*-**6a** were provided, respectively. ^{19}F NMR shows that the chemical shifts of *anti*-**5b** (−184.8 ppm) and *anti*-**6a** (−186.5 ppm) are at higher field than their diastereoisomers *syn*-**5b** (−181.2 ppm) and *syn*-**6a** (−181.6 ppm). For all of the major fluorinated products of **5** or **6** prepared by our method, the chemical shifts of ^{19}F NMR signals are at higher field than their corresponding minor ones (see Supplementary data Table SI). Thus, the major products were assigned to be *anti*-**5** or *anti*-**6**. This configuration assignment was further confirmed by the X-ray crystallographic analysis of optically pure *anti*-**5d**[16] and *anti*-**6m**[16] (Fig. 1), in which *anti*-**5d** was prepared from **10** through Mitsunobu reaction.

The enantioenriched *anti*-**1b** was synthesized by following Mukaiyama's procedure[11] (Scheme 5, Eq. 1) and *syn*-**2a** was obtained by the reaction of **2a** with Lipase AK Amano (Scheme 5, Eq. 2). After careful separation by flash silica gel chromatography, the *anti*-**2a**′ can be provided in high dr value, which was subsequently deprotected by K_2CO_3 to afford *anti*-**2a** in 93% yield (Scheme 5, Eq. 3).

Since moderate to high diastereoselectivities of *anti*-propargylic fluorides **5** and **6** were obtained from isomeric mixture of propargylic alcohols **1** and **2**, the possibility of the S_N2 type reaction can be ruled out. This was further confirmed by the reaction of enantioenriched *anti*-**2a** and *syn*-**2a** (Scheme 6). Surprisingly, when



Scheme 3. One pot reaction to prepare *anti*-**6a** from **2a** and transformation of optically pure propargylic fluoride *anti*-**7a** to monofluorinated sugar **12**.



Scheme 4. Dehydroxy-fluorination of enantioenriched *anti*-/*syn*-**1b** and *anti*-/*syn*-**2a** with DAST.

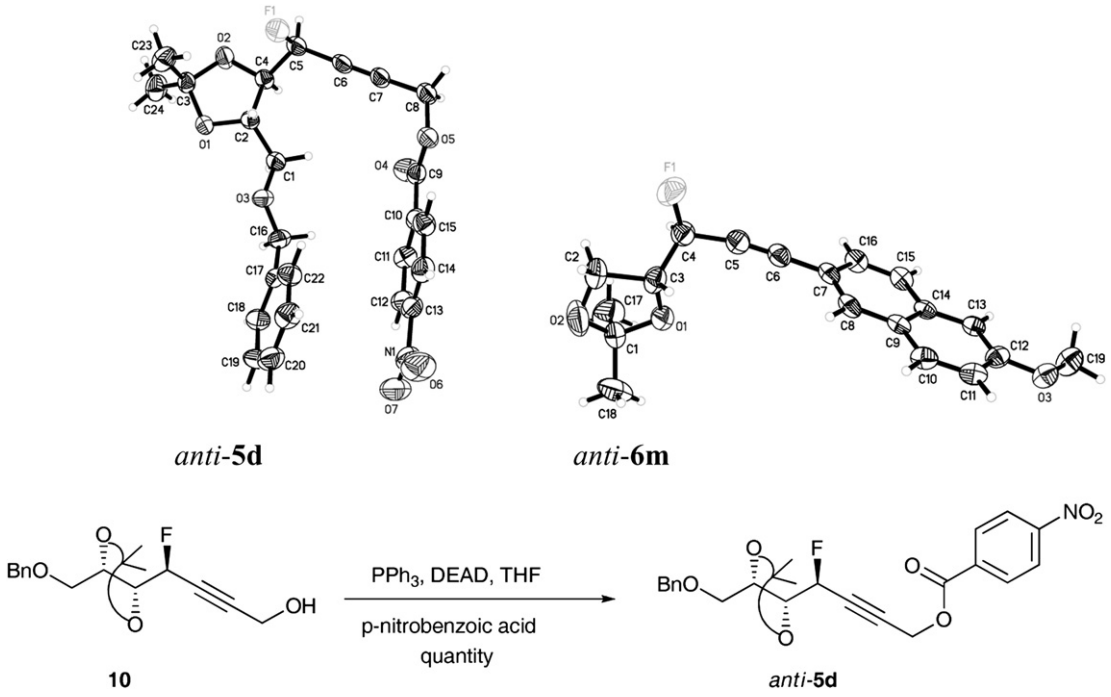
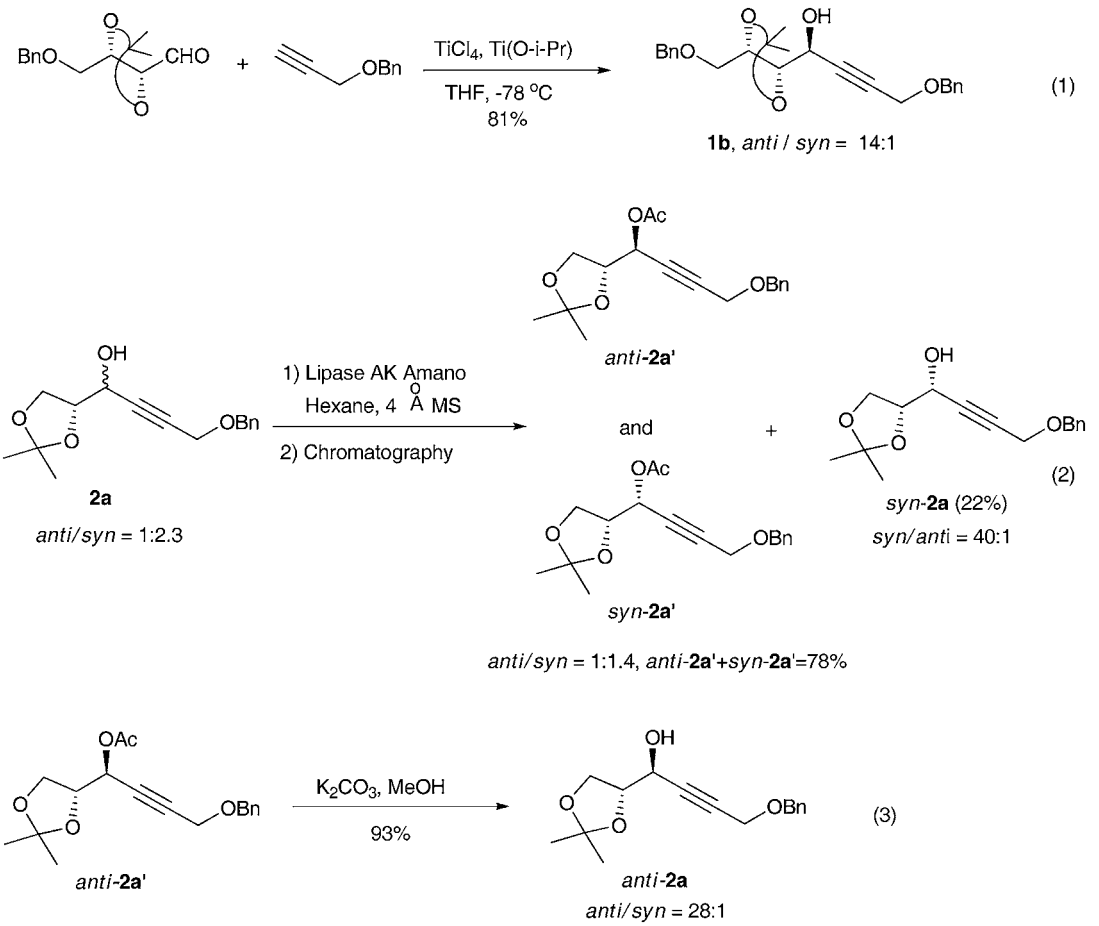
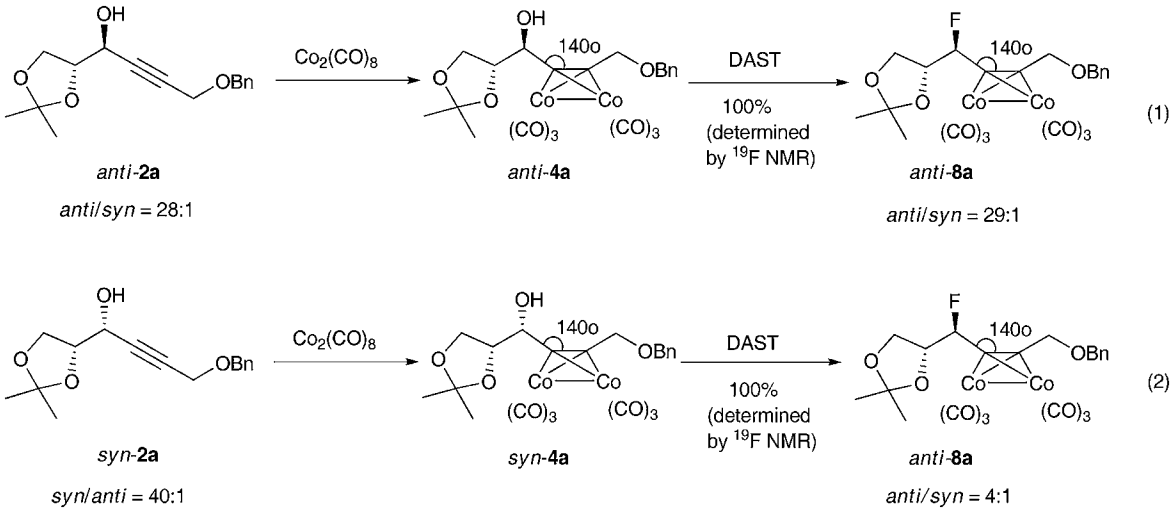


Figure 1. X-ray crystal structure of compound *anti*-**5d** and *anti*-**6m**.

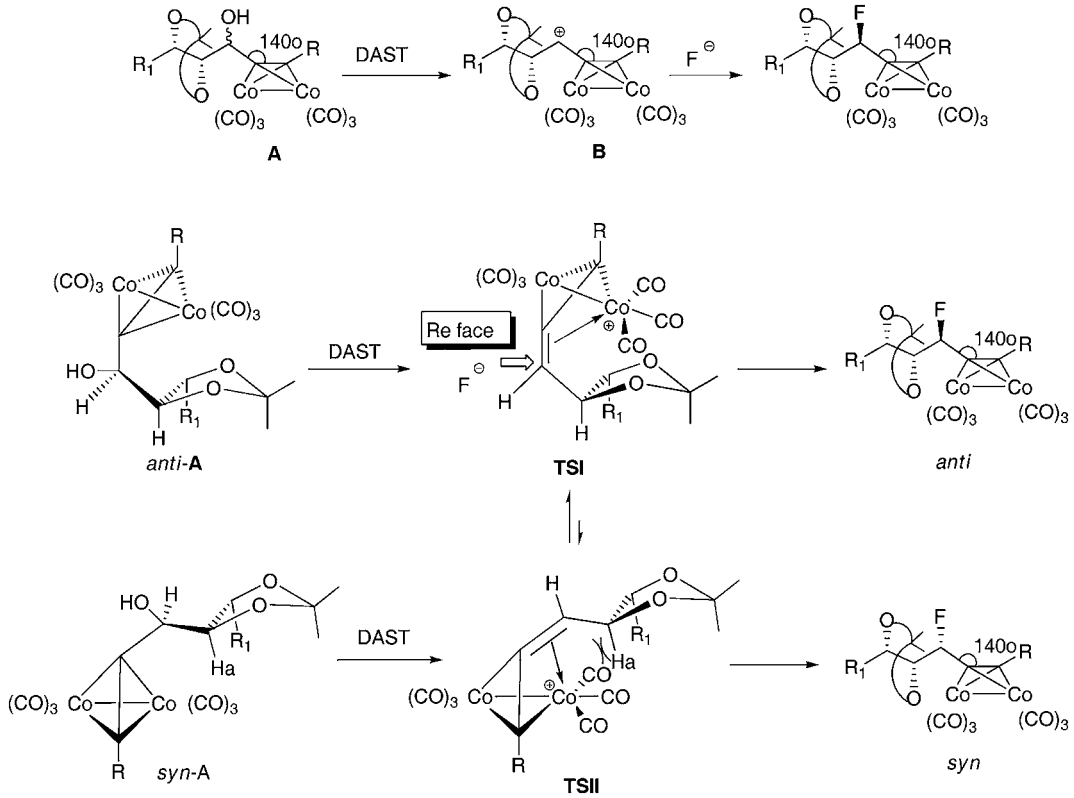


Scheme 5. Preparation of enantioenriched *anti*-**1b** and *anti*-/*syn*-**2a**.



Scheme 6. Diastereoselective dehydroxy-fluorination of propargylic alcohols *anti*-**2a** and *syn*-**2a** with DAST.

enantioenriched cobalt–carbonyl complexes *anti*-**4a** derived from *anti*-**2a** (*anti*/*syn*=28:1) was treated with DAST at −78 °C, a high diastereoselectivity (*anti*/*syn*=29:1) of *anti*-**8a** was obtained (Scheme 6, Eq. 1). However, under the same conditions, the *syn*-**4a** (*anti*/*syn*=1:40) only provided moderate dr value (*anti*/*syn*=4:1) (Scheme 6, Eq. 2), suggesting that different cation transition states are involved in the reaction, and the chiral 1,3-dioxolane moiety of **3** and **4** is a critical factor for the diastereoselectivities. The origins of diastereoselectivities for **5** and **6** may be explained in Scheme 7. When the cobalt–carbonyl complexes **A** were treated with DAST, a cationic intermediate **B** was generated. It has been demonstrated that the positive charge of this kind of cation may localize on carbon (carbocation) or cobalt (cobalt cation), in which the latter is assumed to be the better representative of the charge distribution in these complexes.[17] Thus, the cobalt cation intermediates **TSI** and **TSII** were employed to explain the diastereoselectivities. When *anti*-**A** was treated with DAST at −78 °C, the intermediate **TSI** was generated. Because of the steric repulsion between cobalt–carbonyl complex and $BnOCH_2$ and/or H_a, **TSI** is a favored transition state. As a result, the addition of fluoride anion to **TSI** should be from less hindered *Re* face to generate *anti* product. When **TSII** was produced from *syn*-**A**, the diastereoselectivity of the fluorination depends on the isomerization rate between **TSI** and **TSII**. Since the fluorination reaction was carried out at low temperature, the isomerization of **TSII** to **TSI** was slow, and both additions of fluoride anion to **TSI** from less hindered *Re* face and **TSII** from less hindered



Scheme 7. Mechanistic proposal on stereocontrol.

Si face occurred, respectively. As a result, a moderate *anti* diastereoselectivity was observed. Therefore, for the fluorination of isomeric mixture of propargylic alcohols cobalt–carbonyl complexes **7** and **8**, the comprehensive results are *anti* as major products.

3. Conclusion

In summary, an effective method to diastereoselectively synthesize propargylic fluorides via S_N1 type of dehydroxy-fluorination of propargylic alcohols cobalt–carbonyl complexes with DAST was developed. It was demonstrated that the dicobalt octacarbonyl facilitated asymmetric S_N1 type dehydroxy-fluorination between the chiral cation intermediates and fluoride anion. The reaction scope can be extended to a series of aliphatic and aromatic alkynes, which provided an alternative approach to access propargylic fluorides. In view of the biological application, the resulting enantioenriched propargylic fluoride was further transformed into monofluorinated sugar **12** in an efficient manner. Further applications of propargylic fluorides **5** and **6** in the synthesis of bioactive molecules are under active investigation in our laboratory.

4. Experimental section

4.1. General procedure for the synthesis of propargylic alcohol cobalt–carbonyl complexes 3 and 4

Dicobalt octacarbonyl (670 mg, 1.6 mmol, 1.2 equiv) was added portionwise to a solution of propargylic alcohols **1** or **2** (1.6 mmol, 1.0 equiv) in THF (8 mL). The reaction mixture was stirred at room temperature for 12 h and then concentrated. The residue was purified by column chromatography (petroleum ether/ethyl acetate=8:1) to give **3** or **4** as a red oil.

4.2. General procedure for the synthesis of enantioenriched propargylic fluorides cobalt–carbonyl complexes *anti*-7 and *anti*-8

To a solution of **3** or **4** (0.3 mmol, 1 equiv) in dry CH_2Cl_2 (2 mL) was added dropwise DAST (50 μL, 0.36 mmol) at −78 °C under N_2. After stirring for 6 h at −78 °C, the reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was diluted with ethyl acetate, washed with H_2O, brine, dried over Na_2SO_4, and concentrated to give enantioenriched *anti*-**7** or *anti*-**8**. If necessary, **7** or **8** could be further purified by flash silica gel chromatography.

4.3. General procedure for the synthesis of enantioenriched propargylic fluorides *anti*-5 and *anti*-6

To a solution of **7** or **8** (0.3 mmol) in acetone (2 mL) was added ceric ammonium nitrate (CAN) (660 mg, 1.2 mmol, 4 equiv) in portions. After stirring for 15 min at room temperature, the reaction was concentrated. The residue was purified by silica gel chromatography using petroleum ether/ethyl acetate as eluent to give **5** or **6**.

*4.3.1. (4R,5S)-4-((S)-4-(Benzyloxy)-1-fluorobut-2-ynyl)-5-(benzyloxymethyl)-2,2-dimethyl-1,3-dioxolane (anti-**5b**).* $[\alpha]_D^{20}$ −5.16 (*c* 1.2, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.33–7.26 (m, 10H), 5.21 (ddd, *J*=48.0, 3.3, 1.5 Hz, 1H), 4.59 (s, 2H), 4.56 (s, 2H), 4.35–4.29 (m, 1H), 4.15 (d, *J*=6.9 Hz, 2H), 4.10 (dd, *J*=7.8, 3.3 Hz, 1H), 3.71 (dd, *J*=10.5, 3.6 Hz, 1H), 3.65 (dd, *J*=10.8, 6.0 Hz, 1H), 1.46 (s, 3H), 1.45 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −184.8 (ddt, *J*=48.0, 17.8, 6.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 137.7, 136.9, 128.4, 128.3, 128.0, 127.9, 127.9, 127.8, 127.6, 127.5, 110.6, 86.7 (d, *J*=10.4 Hz), 81.5 (d, *J*=176.2 Hz), 79.5 (d, *J*=26.0 Hz), 78.6 (d, *J*=23.0 Hz), 76.2 (d, *J*=3.7 Hz), 73.4, 71.7, 70.5, 56.9 (d, *J*=3.0 Hz), 27.2, 26.5. IR (thin film): ν_{max} 3032, 2988, 2935, 2868, 1726, 1455 cm^{-1}. MS (EI): *m*/*z* (%) 383 (M^+−Me), 249, 91(100), 77, 65, 43. HRMS: calculated for $C_{23}H_{24}O_4F$ (M^+−Me): 383.1659; found: 383.1622.

*4.3.2. (4R,5S)-4-((R)-4-(Benzyloxy)-1-fluorobut-2-ynyl)-5-(benzyloxymethyl)-2,2-dimethyl-1,3-dioxolane (syn-**5b**).* ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.27–7.17 (m, 10H), 5.21 (dd, *J*=47.7, 5.4 Hz, 1H), 4.51 (s, 2H), 4.48 (s, 2H), 4.18–4.14 (m, 1H), 4.07–4.00 (m, 3H), 3.64 (dd, *J*=10.8, 3.9 Hz, 1H), 3.56 (dd, *J*=10.5, 6.0 Hz, 1H), 1.40 (s, 3H), 1.38 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ ppm −181.2 (ddt, *J*=47.7, 13.5, 5.9 Hz). IR (thin film): ν_{max} 2989, 2934, 2864, 1728, 1641, 1455 cm^{-1}. MS (EI): *m*/*z* (%) 383 (M^+−Me), 307, 249, 91 (100), 77, 65, 43.

*4.3.3. (4S,5R)-4-(Benzyloxymethyl)-5-((S)-3-cyclopropyl-1-fluoroprop-2-ynyl)-2,2-dimethyl-1,3-dioxolane (anti-**5c**).* $[\alpha]_D^{20}$ −8.72 (*c* 1.1, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.36–7.26 (m, 5H), 5.19 (dt, *J*=48.9, 1.8 Hz, 1H), 4.62 (s, 2H), 4.34–4.28 (m, 1H), 4.05 (ddd, *J*=17.4, 7.5, 3.0 Hz, 1H), 3.73 (dd, *J*=10.5, 3.9 Hz, 1H), 3.64 (dd, *J*=10.5, 6.0 Hz, 1H), 1.46 (s, 3H), 1.44 (s, 3H), 1.24–1.18 (m, 1H), 0.82–0.65 (m, 4H). ^{19}F NMR (282 MHz, $CDCl_3$): δ ppm −183.0 (ddd, *J*=49.1, 18.3, 3.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 137.9, 128.4, 127.64, 127.60, 110.5, 94.8, 81.7 (d, *J*=174.7 Hz), 78.9 (d, *J*=23.1 Hz), 76.0 (d, *J*=3.7 Hz), 73.5, 70.8, 68.5 (d, *J*=25.3 Hz), 27.3, 26.5 (d, *J*=2.2 Hz), 8.4, 8.35, −0.69, −0.73. IR (thin film): ν_{max} 2990, 2935, 2867, 2241, 1497, 1455 cm^{-1}. MS (EI): *m*/*z* (%) 303 (M^+−Me), 221, 197, 91 (100), 43. HRMS: calculated for $C_{19}H_{23}O_3F$: 318.1631; found: 318.1622.

*4.3.4. (4S,5R)-4-(Benzyloxymethyl)-5-((R)-3-cyclopropyl-1-fluoroprop-2-ynyl)-2,2-dimethyl-1,3-dioxolane (syn-**5c**).* ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.37–7.29 (m, 5H), 5.10 (ddd, *J*=48.9, 6.3, 1.8 Hz, 1H), 4.63 (d, *J*=1.8 Hz, 2H), 4.23–4.17 (m, 1H), 4.09–4.00 (m, 1H), 3.75 (dd, *J*=10.5, 2.7 Hz, 1H), 3.62 (dd, *J*=10.5, 6.0 Hz, 1H). ^{19}F NMR (282 MHz, $CDCl_3$): δ ppm −176.8 (ddd, *J*=53.1, 12.4, 4.2 Hz). IR (thin film): ν_{max} 2989, 2926, 2241, 1455 cm^{-1}. MS (EI): *m*/*z* (%) 303 (M^+−Me), 221, 197, 91(100), 43.

*4.3.5. (4R)-4-(4-(Benzyloxy)-1-fluorobut-2-ynyl)-2,2-dimethyl-1,3-dioxolane (**6a**).* ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.34–7.29 (m, 5H), 5.11 (dd, *J*=48.0, 5.1 Hz, 1H), 4.58 (s, 2H), 4.32–4.24 (m, 3H), 4.14–4.05 (m, 2H), 1.45 (s, 3H), 1.37 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −180.7 (ddt, *J*=47.9, 12.1, 4.8 Hz, 0.07F), −186.1 (ddt, *J*=49.3, 16.4, 6.2 Hz, 0.93F). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ ppm 137.0, 128.4, 128.0, 127.9, 110.5, 85.9 (d, *J*=10.4 Hz), 81.5 (d, *J*=175.6 Hz), 80.2 (d, *J*=25.2 Hz), 76.6 (d, *J*=25.1 Hz), 71.6, 65.0 (d, *J*=3.3 Hz), 57.0 (d, *J*=2.7 Hz), 26.2, 25.1.

*4.3.6. (R)-4-((S)-4-(Benzyloxy)-1-fluorobut-2-ynyl)-2,2-dimethyl-1,3-dioxolane (anti-**6a**).* $[\alpha]_D^{20}$ 10.93 (*c* 1.48, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.35–7.25 (m, 5H), 5.13 (ddd, *J*=48.0, 4.2, 1.5 Hz, 1H), 4.59 (s, 3H), 4.33–4.23 (m, 3H), 4.16–4.09 (m, 2H), 1.46 (s, 3H), 1.38 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ ppm −186.1 (d, *J*=48.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 137.0, 128.4, 128.0, 127.96, 110.6, 85.9 (d, *J*=13.7 Hz), 81.6 (d, *J*=175.6 Hz), 80.2 (d, *J*=33.4 Hz), 76.6 (d, *J*=25.1 Hz), 71.7, 65.0 (d, *J*=4.3 Hz), 57.0 (d, *J*=3.6 Hz), 26.2, 25.2. IR (thin film): ν_{max} 2987, 2936, 1714, 1523, 1455 cm^{-1}. MS (EI): *m*/*z* (%) 278 (M^+), 157, 101 (100). HRMS: calculated for $C_{16}H_{19}O_3F$: 278.1318; found: 278.1311.

*4.3.7. (R)-4-((R)-4-(Benzyloxy)-1-fluorobut-2-ynyl)-2,2-dimethyl-1,3-dioxolane (syn-**6a**).* ^{1}H NMR (300 MHz, $CDCl_3$, 293 K, TMS): 7.36–7.30 (m, 5H), 5.10 (ddt, *J*=48.6, 5.4, 1.5 Hz, 1H), 4.59 (s, 2H), 4.41–4.30 (m, 1H), 4.24 (dd, *J*=6.3, 1.2 Hz, 1H), 4.16–4.10 (m, 1H), 3.94 (dd, *J*=8.7, 6 Hz, 1H), 1.47 (s, 3H), 1.48 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ ppm −180.7 (ddt, *J*=49.6, 12.1, 6.2 Hz).

*4.3.8. (4R)-4-(5-(Benzyloxy)-1-fluoropent-2-ynyl)-2,2-dimethyl-1,3-dioxolane (**6b**).* ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.40–7.25 (m, 5H),

5.16–4.92 (dt, *J*=48.9, 2.1 Hz, 1H), 4.54 (s, 2H), 4.30–4.19 (m, 1H), 4.12–4.03 (m, 2H), 3.59 (t, *J*=6.6 Hz, 2H), 2.57 (m, 2H), 1.44 (s, 3H), 1.37 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −179.2 (dm, *J*=49.6 Hz, 0.08F), −185.7 (ddt, *J*=47.6, 15.5, 6.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ ppm 137.8, 128.3, 127.7, 127.6, 110.4, 87.7 (d, *J*=10.5 Hz), 80.5 (d, *J*=175.8 Hz), 77.0 (d, *J*=24.6 Hz), 75.0 (d, *J*=25.1 Hz), 73.0, 67.7 (d, *J*=2.9 Hz), 65.0 (d, *J*=3.9 Hz), 26.2, 25.3, 20.2. IR (thin film): ν_{max} 3032, 2989, 2930, 2241, 1455 cm^{-1}. MS (EI): *m*/*z* (%) 277 (M^+-H^+), 101, 91 (100). HRMS: calculated for $C_{17}H_{21}O_3F$: 292.1475; found: 292.1476.

*4.3.9. (R)-4-((S)-1-Fluoro-4-(4-methoxybenzyloxy) but-2-ynyl)-2,2-dimethyl-1,3-dioxolane (anti-**6c**).* $[\alpha]_D^{20}$ 10.71 (*c* 1.24, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.29 (d, *J*=8.5 Hz, 2H), 6.90 (d, *J*=8.5 Hz, 2H), 5.14 (dd, *J*=48.3, 4.5 Hz, 1H), 4.54 (s, 1H), 4.31 (ddd, *J*=15.3, 10.5, 5.1 Hz, 1H), 4.22 (dd, *J*=6, 0.6 Hz, 1H), 4.17–4.07 (m, 2H), 3.82 (s, 3H), 1.47 (s, 3H), 1.39 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ ppm −185.8 (ddt, *J*=48.2, 13.8, 5.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.4, 129.7, 129.0, 113.8, 110.5, 86.0 (d, *J*=9.5 Hz), 81.6 (d, *J*=176.5 Hz), 80.1 (d, *J*=25.3 Hz), 76.6 (d, *J*=24.6 Hz), 71.3, 65.0 (d, *J*=4.0 Hz), 56.6, 55.2, 26.21, 25.17. IR (thin film): ν_{max} 2988, 2937, 1612, 1514, 1422, 1250, 1220, 1112, 1074, 846, 819 cm^{-1}. MS (EI): *m*/*z* (%) 308 (M^+), 157, 136, 121 (100), 101. HRMS: calculated for $C_{17}H_{21}O_4F$: 308.1424; found: 308.1429.

*4.3.10. (R)-4-((R)-1-Fluoro-4-(4-methoxybenzyloxy) but-2-ynyl)-2,2-dimethyl-1,3-dioxolane (syn-**6c**).* ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.27 (d, *J*=8.1 Hz, 2H), 6.88 (d, *J*=8.7 Hz, 2H), 5.09 (ddd, *J*=48.6, 6.9, 1.2 Hz, 1H), 4.51 (s, 2H), 4.35 (m, 1H), 4.17 (d, *J*=6.6 Hz, 2H), 4.12 (td, *J*=8.7, 1.5 Hz, 1H), 3.94 (dd, *J*=9.0, 6.0 Hz, 1H), 3.80 (s, 3H), 1.47 (s, 3H), 1.38 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ ppm −180.6 (ddt, *J*=47.6, 11.3, 5.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 159.5, 129.7, 129.0, 113.8, 111.0, 86.3, 83.1 (d, *J*=174.5 Hz), 79.6 (d, *J*=25.4 Hz), 76.7 (d, *J*=23.1 Hz), 71.4, 65.5 (d, *J*=4.6 Hz), 56.6 (d, *J*=2.9 Hz), 55.2, 26.5, 25.2. IR (thin film): ν_{max} 2991, 2936, 1613, 1515 cm^{-1}. MS (EI): *m*/*z* (%) 308 (M^+), 293, 157, 136, 121 (100). HRMS: calculated for $C_{17}H_{21}O_4F$: 308.1424; found: 308.1422.

*4.3.11. (4R)-4-(1-Fluoro-5-(4-methoxybenzyloxy)pent-2-ynyl)-2,2-dimethyl-1,3-dioxolane (**6d**).* ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.24 (d, *J*=8.5 Hz, 2H), 6.86 (d, *J*=8.5 Hz, 2H), 5.06 (dt, *J*=48.9, 2.1 Hz, 1H), 4.45 (s, 1H), 4.25 (m, 1H), 4.12–4.02 (m, 2H), 3.78 (s, 3H), 3.54 (t, *J*=7.2 Hz, 2H), 2.55 (q, *J*=3.9 Hz, 2H), 1.44 (s, 3H), 1.37 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −179.2 (dm, *J*=49.9 Hz, 0.11F), −185.8 (ddt, *J*=50.8, 15.5, 6.5 Hz, 0.89F). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ ppm 159.3, 129.9, 129.3, 113.8, 110.4, 87.8 (d, *J*=10.6 Hz), 81.8 (d, *J*=174.2 Hz), 76.8, 75.0 (d, *J*=25.0 Hz), 72.6, 67.4 (d, *J*=3.0 Hz), 65.0 (d, *J*=4.0 Hz), 55.2, 30.3, 29.7, 26.5, 26.2, 25.3, 20.1. IR (thin film): ν_{max} 2989, 2936, 2866, 2241, 1614, 1587, 1515 cm^{-1}. MS (EI): *m*/*z* (%) 322 (M^+), 307, 221, 189, 121 (100), 101, 43. HRMS: calculated for $C_{18}H_{23}O_4$ F: 322.1580; found: 322.1584.

*4.3.12. (4R)-4-(1-Fluoroundec-2-ynyl)-2,2-dimethyl-1,3-dioxolane (**6e**).* ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 5.32 (dt, *J*=49.5, 2.1 Hz, 0.9H), 4.99 (dt, *J*=49.5 Hz, 0.1H), 4.28–4.17 (m, 1H), 4.11–4.01 (m, 2H), 2.22 (qd, *J*=6.9, 2.1 Hz, 2H), 1.52–1.25 (m, 18H), 0.86 (t, *J*=6.3 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −178.2 (ddt, *J*=49.6, 12.4, 6.5 Hz, 0.1F), −185.4 (ddt, *J*=48.8, 16.6, 7.0 Hz, 0.9F). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ ppm 110.3, 91.0 (d, *J*=5.2 Hz), 81.8 (d, *J*=174.2 Hz), 77.0 (d, *J*=27.8 Hz), 73.8 (d, *J*=12.5 Hz), 64.8 (d, *J*=3.8 Hz), 31.8, 29.1, 29.0, 28.7, 26.1, 25.3, 22.6, 18.7, 14.0. IR (thin film): ν_{max} 2930, 2858, 2238, 1381 cm^{-1}. MS (EI): *m*/*z* (%) 255 (M^+-H^+), 205, 101 (100), 43, 41. HRMS: calculated for $C_{16}H_{27}O_2F$: 270.1995; found: 270.1996.

*4.3.13. (4R)-4-(-3-Cyclopropyl-1-fluoroprop-2-ynyl)-2,2-dimethyl-1,3-dioxolane (**6f**).* ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 5.02 (ddd, *J*=49.5, 3.9, 1.8 Hz, 1H), 4.22 (ddd, *J*=22.5, 10.5, 5.7 Hz, 1H), 4.11–4.02 (m, 2H), 1.44 (s, 3H), 1.37 (s, 3H), 1.28 (m, 1H), 0.85–0.70 (m, 4H). ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −177.5 (dd, *J*=51.4, 14.1 Hz, 0.05F), −184.2 (ddd, *J*=49.9, 16.1, 4.5 Hz, 0.95F). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 110.4, 94.1 (d, *J*=15.0 Hz), 81.9 (d, *J*=174.9 Hz), 77.3, 76.9, 69.0 (d, *J*=25.2 Hz), 64.9 (d, *J*=3.8 Hz), 26.2, 25.3, 8.4, −0.1, −0.6. IR (thin film): ν_{max} 2989, 2929, 2855, 2243 cm^{-1}. MS (EI): *m*/*z* (%) 197 (M^+-H^+), 97 (100), 77, 61, 57, 51, 41. HRMS: calculated for $C_{11}H_{15}O_2F$: 198.1056; found: 198.1053.

*4.3.14. (R)-4-((S)-1-Fluoro-4-(trityloxy)but-2-ynyl)-2,2-dimethyl-1,3-dioxolane (anti-**6g**).* $[\alpha]_D^{20}$ 9.2, (*c* 1.2, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.46–7.21 (m, 15H), 5.09 (dt, *J*=48.6, 2.1 Hz, 1H), 4.22 (ddd, *J*=17.1, 6.3, 4.5 Hz, 1H), 4.11–4.04 (m, 2H), 3.85 (d, *J*=3.3 Hz, 2H), 1.45 (s, 3H), 1.37 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ ppm −187.4 (ddt, *J*=49.1, 16.1, 7.9 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ ppm 146.8, 143.2, 128.5, 127.95, 127.90, 127.89, 127.2, 110.6, 87.6, 86.8 (d, *J*=10.0 Hz), 82.0, 81.6 (d, *J*=176.4 Hz), 76.6 (d, *J*=8.4 Hz), 64.9 (d, *J*=3.8 Hz), 52.9 (d, *J*=2.3 Hz), 29.7. 26.2. 25.3. IR (thin film): ν_{max} 3060, 2988, 2927, 1491, 1449 cm^{-1}. MS (EI): *m*/*z* (%) 430 (M^+), 415, 353, 243 (100), 183, 165, 105, 77, 43. HRMS: calculated for $C_{28}H_{27}O_3F$: 430.1944; found: 430.1939.

*4.3.15. (4R)-4-(1-Fluoro-4,4-dimethylpent-2-ynyl)-2,2-dimethyl-1,3-dioxolane (**6h**).* ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 5.05 (dd, *J*=49.5, 3.0 Hz, 0.85H), 4.96 (dd, *J*=49.5, 7.5 Hz, 0.15H), 4.19 (m, 1H), 4.00 (dt, *J*=16.8, 8.7 Hz, 2H), 1.38 (s, 3H), 1.31 (s, 3H), 1.16 (s, 9H). ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −177.6 (dd, *J*=49.7, 8.8 Hz, 0.17F), −185.9 (dd, *J*=48.9, 19.2 Hz, 0.83F). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ ppm 110.8, 110.4, 99.0 (d, *J*=10.4 Hz), 81.7 (d, *J*=174.2 Hz), 77.3, 72.2 (d, *J*=25.7 Hz), 65.7, 64.7 (d, *J*=4.4 Hz), 30.9, 30.3, 29.7, 27.4, 26.6, 25.4, 25.3. IR (thin film): ν_{max} 2990, 2935, 2242, 1383 cm^{-1}. MS (EI): *m*/*z* (%) 183, 141, 101 (100), 91, 77, 73, 43, 41. HRMS: calculated for $C_{12}H_{19}O_2F$: 214.1369; found: 214.1373.

*4.3.16. (4R)-4-(3-Cyclohexyl-1-fluoroprop-2-ynyl)-2,2-dimethyl-1,3-dioxolane (**6i**).* ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 5.10 (dm, *J*=49.2 Hz, 0.86H), 5.02 (dm, *J*=49.5 Hz, 0.14H), 4.30–4.18 (m, 1H), 4.11–4.01 (m, 2H), 2.42 (m, 1H), 1.79–1.26 (m, 16H). ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −177.7 (dt, *J*=50.5, 9.9 Hz, 0.16F), −185.6 (ddd, *J*=49.7, 16.9, 5.3 Hz, 0.84F). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ ppm 110.6, 110.4, 95.0 (d, *J*=10.4 Hz), 81.8 (d, *J*=173.4 Hz), 77.3, 73.7 (d, *J*=24.6 Hz), 65.7 (d, *J*=3.8 Hz), 64.8 (d, *J*=4.0 Hz), 32.1 (d, *J*=2.0 Hz), 28.9 (d, *J*=3.4 Hz), 26.6, 26.1, 25.7, 25.4, 25.3, 24.6. IR (thin film): ν_{max} 2989, 2934, 2857, 2235, 1451 cm^{-1}. MS (EI): *m*/*z* (%) 225 (M^+–Me), 183, 101 (100), 91, 73, 43. HRMS: calculated for $C_{14}H_{21}O_2F$: 240.1526; found: 240.1529.

*4.3.17. (2R)-3-Fluoropent-4-yne-1,2-diol (**9**).* To a solution of **8k** (0.3 mmol) in acetone (2 mL), was added CAN (660 mg, 1.2 mmol) in portions. After stirring for 30 min at room temperature, the reaction mixture was diluted with ethyl ether, washed with water, brine, dried over Na_2SO_4, filtered, and concentrated at 0 °C. The residue was dissolved in methanol (2 mL) and H_2O (0.2 mL), THF (0.3 mL), concentrated HCl (eight drops) was added. After stirring for 2 days at room temperature, the reaction mixture was diluted with ethyl acetate, washed with water, brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel chromatography (petroleum ether/ethyl acetate=1:1) to give product **9** (*anti*/*syn*=8:1) (28 mg, 80% overall yield) as a light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 5.17 (ddd, *J*=47.7, 4.8, 2.1 Hz, 0.89H), 5.13 (ddd, *J*=48.9, 6.6, 1.2 Hz, 0.11H), 4.00–3.75 (m, 3H), 2.79 (dd, *J*=6.3, 1.8 Hz, 1H), 2.53 (br, 2H). ^{19}F NMR (282 MHz, $CDCl_3$): δ ppm −187.8 (ddd, *J*=46.8, 13.3, 4.5 Hz, 0.89F), −189.1 (ddd, *J*=49.1, 14.1, 5.1 Hz, 0.11F). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 82.7 (d, *J*=172.6 Hz), 78.8 (d, *J*=10.8 Hz), 72.7, 72.5, 61.8 (d, *J*=4.6 Hz). IR (thin film): ν_{max} 3298, 2924, 2852, 2127, 1463 cm^{-1}. MS (EI): *m*/*z* (%)

118 (M^+) 68, 61(100), 57, 43, 40. HRMS: calculated for $C_5H_7O_2F$: 118.0430; found: 118.0428.

*4.3.18. (R)-4-((S)-1-Fluoro-3-phenylprop-2-ynyl)-2,2-dimethyl-1,3-dioxolane (anti-**6l**).* $[\alpha]_D^{20}$ 17.78 (*c* 1.6, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ ppm 7.48–7.25 (m, 5H), 5.32 (dd, *J*=49.2, 4.8 Hz, 1H), 4.40 (m, 1H), 4.21–4.12 (m, 2H), 1.49 (s, 3H), 1.40 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −184.8 (dd, *J*=49.1, 16.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 131.9, 129.1, 128.3, 121.3 (d, *J*=3.7 Hz), 110.6, 89.4 (d, *J*=10.4 Hz), 83.0 (d, *J*=1.3 Hz), 82.7 (d, *J*=51.7 Hz), 82.2, 82.1 (d, *J*=176.4 Hz), 76.8 (d, *J*=24.6 Hz), 65.0 (d, *J*=3.9 Hz), 26.2, 25.3. IR (thin film): ν_{max} 2988, 2936, 2229, 1491 cm^{-1}. MS (EI): *m*/*z* (%) 234 (M^+), 219, 177, 159, 133, 101 (100), 43. HRMS: calculated for $C_{14}H_{15}O_2F$: 234.1056; found: 234.1055.

*4.3.19. (R)-4-((R)-1-Fluoro-3-phenylprop-2-ynyl)-2,2-dimethyl-1,3-dioxolane (syn-**6l**).* $[\alpha]_D^{20}$ 40.44 (*c* 1.2, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ ppm 7.47–7.31 (m, 5H), 5.28 (dd, *J*=48.9, 7.2 Hz, 1H), 4.45 (m, 1H), 4.19 (t, *J*=9 Hz, 1H), 4.04 (dd, *J*=9 Hz, *J*=6 Hz, 1H), 1.50 (s, 3H), 1.41 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ ppm −178.7 (dd, *J*=49.1, 10.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 131.9, 131.9, 129.3, 128.4, 121.2 (d, *J*=3.7 Hz), 111.0, 89.6 (d, *J*=10.4 Hz), 83.7 (d, *J*=174.2 Hz), 81.9 (d, *J*=24.6 Hz), 76.9 (d, *J*=24.2 Hz), 65.7 (d, *J*=3.7 Hz), 26.6, 25.3.

*4.3.20. (4R)-4-(1-Fluoro-3-(6-methoxynaphthalen-2-yl)prop-2-ynyl)-2,2-dimethyl-1,3-dioxolane (**6m**).* ^1H NMR (300 MHz, $CDCl_3$): δ ppm 7.90 (s, 1H), 7.67–7.63 (m, 2H), 7.44 (d, *J*=8.1 Hz, 1H), 7.14 (d, *J*=9.0 Hz, 1H), 7.06 (s, 1H), 5.36 (dd, *J*=49.2, 4.5 Hz, 1H), 4.45–4.37 (m, 1H), 4.19 (d, *J*=6.0 Hz, 2H), 3.88 (s, 3H), 1.50 (s, 3H), 1.41 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ ppm −179.1 (dd, *J*=48.0, 10.2 Hz, 0.16F), −185.2 (dd, *J*=50.3, 16.7 Hz, 0.84F). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ ppm 158.6, 134.5, 132.1, 129.3, 128.8, 128.7, 128.1, 126.8, 119.6, 116.1, 116.0, 110.6, 105.6, 90.0 (d, *J*=10.5 Hz), 82.2 (d, *J*=175.5 Hz), 81.9 (d, *J*=24.7 Hz), 77.0 (d, *J*=24.7 Hz), 65.0 (d, *J*=3.8 Hz), 55.3, 26.3, 25.4. IR (thin film): ν_{max} 2986, 2226, 1624, 1600, 1486 cm^{-1}. MS (EI): *m*/*z* (%) 314 (M^+), 101 (100). HRMS: calculated for $C_{19}H_{19}O_3F$: 314.1318; found: 314.1320.

*4.3.21. (R)-4-((S)-1-Fluoro-3-(6-methoxynaphthalen-2-yl)prop-2-ynyl)-2,2-dimethyl-1,3-dioxolane (anti-**6m**).* Mp 88 °C; $[\alpha]_D^{20}$ 9.8 (*c* 0.15, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ ppm 7.92 (s, 1H), 7.68 (dd, *J*=9.0 Hz, 2H), 7.45 (d, *J*=8.1 Hz, 1H), 7.16 (dd, *J*=8.7, 2.1 Hz, 1H), 7.10 (s, 1H), 5.36 (dd, *J*=49.2, *J*=4.5 Hz, 1H), 4.43 (ddd, *J*=15.9, 10.5, 5.4 Hz, 1H), 4.19 (m, 2H), 3.91 (s, 3H), 1.51 (s, 3H), 1.41 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ ppm 185.1 (dd, *J*=49.4, 17.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 158.6, 134.6, 132.1 (d, *J*=3.8 Hz), 129.4, 128.8 (d, *J*=3.0 Hz), 128.2, 126.9, 119.6, 116.1 (d, *J*=3.8 Hz), 110.6, 105.8, 90.1 (d, *J*=10.6 Hz), 82.2 (d, *J*=174.4 Hz), 82.0 (d, *J*=25.1 Hz), 77.0 (d, *J*=25.1 Hz), 65.1 (d, *J*=3.7 Hz), 55.3, 26.3, 25.4. IR (thin film): ν_{max} 2986, 2226, 1624, 1600, 1486 cm^{-1}. MS (EI): *m*/*z* (%) 314 (M^+), 101 (100). HRMS: calculated for $C_{19}H_{19}O_3F$: 314.1318; found: 314.1321.

4.4. One pot reaction to prepare *anti*-6a from propargylic alcohol 2a

To a solution of **2a** (*anti*/*syn*=1:2.3, 83 mg, 0.3 mmol) in CH_2Cl_2 (2 mL) was added $Co_2(CO)_8$ (114 mg, 0.33 mmol). After stirring at room temperature for 12 h, the reaction mixture was cooled to −78 °C and DAST (50 μL, 0.36 mmol) was added. The resulting mixture was stirred at −78 °C for 9 h and warmed up to room temperature naturally. Stirring continued for 12 h at room temperature and then acetone (2 mL) was added, followed by addition of CAN (660 mg, 1.2 mmol) in portions. After stirring for 30 min at room temperature, the reaction mixture was diluted with ethyl acetate, washed with water, brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel chromatography (petroleum ether/ethyl acetate=20:1) to give product *anti*-**6a** (*anti*/*syn*=12:1) (58 mg, 70% overall yield) as a light yellow oil.

*4.4.1. (S)-4-((4R,5S)-5-(Benzyloxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-fluorobut-2-yn-1-ol (**10**).* *anti*-**7a** (2.56 g, 3.3 mmol) was dissolved in acetone (25 mL), and ceric ammonium nitrate (7.2 g, 13.0 mmol) was added in portions. The mixture was stirred at room temperature for 15 min and diluted with ethyl acetate, washed with water, brine, dried over Na_2SO_4, filtered, and concentrated. The resulting residue was dissolved in CH_2Cl_2 (14 mL), DDQ (0.74 g, 3.3 mmol) and H_2O (2 mL) were added. The mixture was stirred at room temperature overnight. The reaction was quenched with water and extracted with ether. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate=10:1) to give alcohol **10** (778 mg, 88% yield) as a yellow oil. $[\alpha]_D^{20}$ −7.48 (*c* 2.2, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ 7.35–7.29 (m, 5H), 5.25 (ddd, *J*=48.6, 3.0, 1.2 Hz, 1H), 4.61 (s, 2H), 4.34–4.29 (m, 1H), 4.17 (dd, *J*=6.6, Hz *J*=1.2 Hz, 2H), 4.10 (ddd, *J*=17.7, 7.8, 3.3 Hz, 1H), 3.69 (dd, *J*=22.8, 10.5 Hz, 1H), 3.68 (dd, *J*=24.9, 10.5 Hz, 1H), 2.29 (s, 1H), 1.46 (s, 3H), 1.44 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ ppm −186.0 (ddt, *J*=48.2, 18.3, 5.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 137.7, 128.4, 127.7, 110.7, 89.1 (d, *J*=9.6 Hz), 81.3 (d, *J*=175.2 Hz), 78.6 (d, *J*=26.0 Hz), 78.5 (d, *J*=22.3 Hz), 76.1 (d, *J*=3.7 Hz), 73.5, 70.4, 50.5, 27.2, 26.4. IR (thin film): ν_{max} 3340, 3034, 2991, 1498, 1455, 1379 cm^{-1}. MS (EI): *m*/*z* (%) 308 (M^+), 293, 221, 187, 91 (100). HRMS: calculated for $C_{17}H_{21}O_4F$: 308.1424; found: 308.1427.

*4.4.2. (S,Z)-4-((4R,5S)-5-(Benzyloxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-fluorobut-2-enal (**11**).* To a solution of **10** (400 mg, 1.28 mmol) in ethyl alcohol (20 mL) was added Lindlar catalyst (88 mg) at room temperature. Then H_2 was introduced into the flask. The reaction was stirred with a H_2-balloon for 4 h. The Lindlar catalyst was filtered through a short Celite pad and the filtrate was concentrated to give *Z*-alcohol. ^1H NMR (300 MHz, $CDCl_3$) δ ppm 7.39–7.26 (m, 5H), 5.97 (m, 1H), 5.67 (m, 1H), 5.36 (dt, *J*=47.1, 6.0 Hz, 1H), 4.60 (s, 1H), 4.19–4.14 (m, 3H), 3.97 (m, 1H), 3.72–3.60 (m, 2H), 2.23 (s, 1H), 1.437 (s, 3H), 1.432 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −184.4 (dt, *J*=46.0 Hz, *J*=12.7 Hz). ^{13}C NMR (100.7 MHz, $CDCl_3$) δ ppm 127.5, 134.9 (d, *J*=10.4 Hz), 128.3, 127.6, 125.9 (d, *J*=22.4 Hz), 110.1, 88.2 (d, *J*=165.8 Hz), 78.1 (d, *J*=26.8 Hz), 77.4 (d, *J*=3.0 Hz), 70.2, 58.4, 26.9, 26.5. IR (thin film): ν_{max} 3400, 2990, 2870, 1455 cm^{-1}. MS (EI): *m*/*z* (%) 310(M^+), 295, 275, 221, 162, 91(100), 59, 43. HRMS: calculated for $C_{17}H_{23}O_4F$: 310.1580; found: 310.1576.

Z-alcohol was used to do the next step without purification. To a solution of crude *Z*-alcohol in CH_2Cl_2 (20 mL) was added MnO_2 (1.2 g, 13.8 mmol) at room temperature. After the reaction mixture was stirred for 12 h, another 13.8 mmol of MnO_2 was added, and the reaction mixture was stirred for 24 h. The MnO_2 was then filtered and the filtrate was concentrated. The resulting residue was purified with silica gel chromatography (petroleum ether/ethyl acetate=20:1) to give aldehyde **11** (300 mg, 75% yield two steps) as a light yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ ppm 9.98 (d, *J*=6.9 Hz, 1H), 7.36–7.27 (m, 5H), 6.52 (ddd, *J*=20.4, 11.7, 7.2 Hz, 1H), 6.11 (dd, *J*=11.4, 6.9 Hz, 1H), 5.73 (dt, *J*=47.7, 6.3 Hz, 1H), 4.59 (s, 2H), 4.21–4.07 (m, 2H), 3.64 (d, *J*=4.5 Hz, 2H), 1.43 (s, 3H), 1.41 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −184.4 (ddd, *J*=47.6, 19.5, 12.7 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ ppm 190.9 (d, *J*=2.8 Hz), 142.1 (d, *J*=21.9 Hz), 137.5, 132.0 (d, *J*=5.5 Hz), 128.4, 127.8, 127.7, 110.6, 89.0 (d, *J*=172.8 Hz), 78.3 (d, *J*=24.7 Hz), 77.4, 73.6, 70.0, 26.9, 26.6. IR (thin film): ν_{max} 2990, 2867, 1686 cm^{-1}. MS (EI): *m*/*z* (%) 293 (M^+−Me), 91(100). HRMS: calculated for $C_{17}H_{21}O_4F$: 308.1424; found: 308.1423.

*4.4.3. (1S)-2-(Benzyloxy)-1-((3S)-3-fluoro-6-methoxy-3,6-dihydro-2H-pyran-2-yl)ethanol (**12**).* To a solution of **13** (61 mg, 0.2 mmol) in MeOH/THF/H_2O (2 mL/0.3 mL/0.2 mL) was added concentrated HCl eight drops. The resulting mixture was stirred at room temperature for 30 h. Ethyl acetate was added, and the mixture was washed with saturated aqueous $NaHCO_3$, brine, dried over Na_2SO_4, filtered, and concentrated. The resulting residue was purified with silica gel chromatography (petroleum ether/ethyl acetate=8:1) to give **12** (28 mg, 53%) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.36–7.26 (m, 5H), 6.06 (t, J=11.7 Hz, 1H), 5.81 (dd, J=10.2, 2.1 Hz, 1H), 5.24 (ddd, J=48.9, 8.7, 0.9 Hz, 1H), 4.91 (s, 1H), 4.59 (s, 2H), 4.14 (m, 1H), 3.92 (td, J=9.0, 1.5 Hz, 1H), 3.73–3.62 (m, 2H), 3.89 (s, 3H), 2.43 (br, 1H). ^{19}F NMR (282 MHz, $CDCl_3$): δ ppm −196.9 (ddd, J=48.0, 11.6, 5.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 137.8, 129.5, 129.3, 128.4, 127.7 (d, J=11.1 Hz), 127.6, 95.4 (d, J=2.3 Hz), 82.4 (d, J=166.8 Hz), 73.4, 71.0, 68.0, 68.0 (d, J=23.7 Hz), 56.2. IR (thin film): ν_{max} 3460, 2980, 1455, 1394 cm^{-1}. MS (EI): m/z (%) 282 (M^+), 91 (100), 43. HRMS: calculated for $C_{15}H_{19}O_4F$: 282.1267; found: 282.1270.

*4.4.4. (S)-4-((4R,5S)-5-(Benzyloxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-fluorobut-2-ynyl 4-nitrobenzoate (anti-**5d**).* To a THF solution (4 mL) of **10** (93 mg, 0.3 mmol), PPh_3 (134 mg, 0.51 mmol) and p-nitrobenzoic acid (96 mg, 0.57 mmol) was added DEAD (90 mg, 0.51 mmol) at 0 °C. After stirring for 30 min at same temperature, the reaction mixture was concentrated. The residue was purified by column chromatography (petroleum ether/ethyl acetate=20:1) to give *anti*-**5d** (137 mg, quantity) as a white solid. Mp 61 °C; $[\alpha]_D^{20}$ −6.94 (c 1.0, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 8.29 (d, J=8.7 Hz, 2H), 8.22 (d, J=8.7 Hz, 2H), 7.38–7.28 (m, 5H), 5.31 (dd, J=47.7, 1.2 Hz, 1H), 4.97 (d, J=6.3 Hz, 2H), 4.60 (s, 1H), 4.34–4.29 (m, 1H), 4.17 (ddd, J=16.5, 8.4, 3.6 Hz, 1H), 3.72–3.69 (m, 2H), 1.47 (s, 3H), 1.45 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ ppm −185.4 (ddt, J=48.6, 16.9, 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 163.8, 150.8, 137.7, 134.5, 131.2, 130.9, 128.4, 127.8, 127.6, 123.6, 110.9, 83.9 (J=9.9 Hz), 81.5 (J=175.2 Hz), 80.6 (J=25.9 Hz), 78.6 (J=23.14 Hz), 76.1 (J=4.4 Hz), 73.54, 70.46, 52.98, 27.25, 26.55. IR (KBr): ν_{max} 3121, 2871, 1726, 1530 cm^{-1}. MS (EI): m/z (%) 457(M^+), 442, 150, 91(100), 43. HRMS: calculated for $C_{24}H_{24}NO_7F$: 457.1537; found: 457.1534.

*4.4.5. (S)-4-Benzyloxy)-1-((4R,5R)-5-(benzyloxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)but-2-yn-1-ol (anti-**1b**).* A solution of n-BuLi (1.6 M in hexanes, 3.0 mL, 4.8 mmol) was slowly added to a solution of alkyne (0.76 mL, 5.2 mmol) in anhydrous THF (40 mL) at −78 °C. After the mixture was stirred at −78 °C for 15 min, a brown solution of Ti(O-i-Pr)$_4$ and $TiCl_4$ (1 M solution in DCM, 2.4 mL, 2.4 mmol) was added dropwise to the reaction mixture and the resulting mixture was stirred at −78 °C for 1.5 h. A solution of aldehyde (1.0 g, 4.0 mmol) in anhydrous THF (30 mL) was then added. The resulting mixture was stirred at −78 °C for 2 h and then slowly warmed to room temperature and stirred overnight. The reaction was quenched by addition of phosphate buffer pH=7 (200 mL) and filtered through a Celite plug. The filtrate was evaporated under reduced pressure to give a mixture of an oil and an aqueous solution. Ether (200 mL) and water (100 mL) were added. The organic phase was separated and washed with brine (100 mL), dried over $MgSO_4$, filtered, and concentrated to give a yellow oil. The crude material was purified by column chromatography (petroleum ether/ethyl acetate=15:1→10:1) to give alcohol *anti*-**1b** (*anti*/*syn*=14:1) as an orange oil (1.28 g, 81%). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS): δ ppm 7.35–7.27 (m, 10H), 4.60–4.55 (m, 5H), 4.28–4.13 (m, 3H), 4.01(d, J=7.5, 4.2 Hz, 1H), 3.69 (d, J=5.1 Hz, 2H), 2.36 (br, 1H), 1.45 (s, 3H), 1.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 137.5, 137.0, 128.22, 128.20, 128.17, 127.8, 127.7, 127.6, 127.49, 127.47, 109.8, 83.7, 82.3, 79.8, 76.5, 73.3, 71.4, 70.6, 62.2, 57.0, 26.8. IR (thin film): ν_{max} 3423, 3032, 2988, 2935, 2868, 1497, 1455, 1250, 1216, 1168, 908, 859, 745, 699 cm^{-1}. MS (EI): m/z (%) 381(M^+−Me), 313, 253, 221, 179, 91(100), 77. HRMS: calculated for $C_{23}H_{25}O_5$: 381.1702 (M−CH_3); found: 381.1704 (M^+−Me).

*4.4.6. (R)-4-(Benzyloxy)-1-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)but-2-yn-1-ol (syn-**2a**) and (S)-4-(benzyloxy)-1-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)but-2-ynyl acetate (anti-**2a′**).* The alcohol **2a** (1.5 g, 5.4 mmol) was dissolved in hexane (10.5 mL) and 4 Å MS (1.89 g, powdered) was added. Then Lipase AK Amano (950 mg) was added all at once, followed by the addition of vinyl acetate (3.8 mL, 41.3 mmol). The solution was vigorously stirred at rt for 35 h, after which time the mixture was filtered through Celite. The volatiles were evaporated under reduced pressure. The residue was purified by column chromatography (petroleum ether/ethyl acetate=100:1→50:1→20:1→5:1) yielded *anti*-**2a′** and *syn*-**2a′** 1.34 g (78%) as a colorless oil and *syn*-**2a** (*anti*/*syn*=1:40, determined by HPLC) as a colorless oil 333 mg (22%).

syn-**2a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.39–7.26 (m, 5H), 4.58 (s, 2H), 4.49 (m, 0.1H), 4.37 (m, 0.9H), 4.24–4.16 (m, 3H), 4.12–4.04 (m, 1.1H), 3.90 (dd, J=8.7, 5.4 Hz, 0.9H), 2.42, and 2.40 (s, 2H), 1.46 (s, 3H), 1.37 (s, 3H). IR (thin film): ν_{max} 3393, 1722, 1455 cm^{-1}. MS (EI): m/z (%) 275 (M^+−H^+), 261 (M^+−Me), 171, 128, 101(100). HRMS: calculated for $C_{16}H_{20}O_4$: 276.1362; found: 276.1353.

anti-**2a′**: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.35–7.30 (m, 5H), 5.56 (dt, J=4.2, 1.8 Hz, 1H), 4.58 (s, 2H), 4.36–4.30 (m, 1H), 4.21 (d, J=1.8 Hz, 2H), 4.12 (dd, J=8.7, 6.9 Hz, 1H), 3.99 (dd, J=8.4, 6.0 Hz, 1H), 2.13 (s, 3H), 1.45 (s, 3H), 1.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) ppm 169.5, 137.1, 128.4, 128.1, 127.9, 110.5, 82.8, 80.7, 76.3, 71.6, 65.6, 63.7, 57.1, 26.2, 25.2, 20.8. IR (thin film): ν_{max} 2989, 1749, 1373, 1227 cm^{-1}. MS (EI): m/z (%) 303(M^+−Me), 171, 101(100), 91. HRMS: calculated for $C_{18}H_{22}O_5$: 318.1467; found: 318.1472.

*4.4.7. (S)-4-(Benzyloxy)-1-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)but-2-yn-1-ol (anti-**2a**).* To a solution of *anti*-**2a′** (246 mg, 1.0 mmol) in MeOH (3.5 mL) was added K_2CO_3 (161 mg, 1.2 mmol). After stirring for 20 min, the reaction mixture was quenched with saturated NH_4Cl, extracted with ethyl acetate, washed with water, brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography (petroleum ether/ethyl acetate=10:1→6:1) to give alcohol *anti*-**2a** (*anti*/*syn*=28:1, determined by HPLC) as an oil (200 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.39–7.26 (m, 5H), 4.58 (s, 2H), 4.49 (m, 0.9H), 4.37 (m, 0.1H), 4.24–4.16 (m, 3H), 4.12–4.04 (m, 1.9H), 3.90 (dd, J=8.7, 5.4 Hz, 0.1H), 2.42, and 2.40 (s, 2H), 1.46 (s, 3H), 1.37 (s, 3H). IR (thin film): ν_{max} 3393, 1722, 1455 cm^{-1}. MS (EI): m/z (%) 275 (M^+−H^+), 261 (M^+−Me), 171, 128, 101(100). HRMS: calculated for $C_{16}H_{20}O_4$: 276.1362; found: 276.1353.

Acknowledgements

National Natural Science Foundation of China (20852003, 20902100, and 20832008), the Shanghai Rising-Star Program (09QA1406900) and SIOC are greatly acknowledged for funding this work. Professor Feng-Ling Qing was also greatly acknowledged for help.

Supplementary data

Experimental information, characterization data of compounds **1** and **2**, ^{1}H and ^{13}C NMR spectra of **5**, **6**, **10**–**12**. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.04.078. This data include MOL files and InChiKeys of the most important compounds described in this article.

References and notes

1. For recent reviews, see: (a) Smart, B. E. *J. Fluorine Chem.* **2001**, *109*, 3; (b) Maienfisch, P.; Hall, R. G. *Chimia* **2004**, *58*, 93; (c) Special issue on "Fluorine in

the Life Sciences"*ChemBioChem* **2004**, *5*, 557; (d) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320.
2. (a) Kirsch, P. *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*; Wiley-VCH: Weinheim, 2004; (b) Hiyama, T.; Kanie, K.; Kusumoto, T.; Morizawa, Y.; Shimizu, M. *Organofluorine Compounds: Chemistry and Applications*; Springer: Berlin, 2000; (c) Biomedical frontiers of fluorine chemistry In *ACS Symposium Series 639*; Ojima, I., McCarthy, J. R., Welch, J. T., Eds.; American Chemical Society: Washington, DC, 1996; For recent reviews: (d) Ismail, F. M. D. *J. Fluorine Chem.* **2002**, *118*, 27; (e) Nyffeler, P. T.; Durón, S. G.; Burkart, M. D.; Vincent, S. P.; Wong, C.-H. *Angew. Chem., Int. Ed.* **2005**, *44*, 192; (f) Shimizu, M.; Hiyama, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 214; (g) Hamashima, Y.; Sodeoka, M. *Synlett* **2006**, 1467; (h) Pihko, P. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 544; (i) O'Hagan, D. *Chem. Soc. Rev.* **2008**, *37*, 308.
3. For recent reviews, see: (a) Kirk, K. L. *J. Fluorine Chem.* **2006**, *127*, 1013; (b) Bégué, J.-P.; Bonnet-Delpon, D. *J. Fluorine Chem.* **2006**, *127*, 992; (c) Müller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881; (d) Hagmann, W. K. *J. Med. Chem.* **2008**, *51*, 4359; (e) Amii, H.; Uneyama, K. *Chem. Rev.* **2009**, *109*, 2119.
4. (a) Miles, J. A. L.; Percy, J. M. *Sci. Synth.* **2006**, *34*, 277; (b) Gree, D.; Gree, R. *Tetrahedron Lett.* **2007**, *48*, 5435.
5. For recent review, see: Pacheco, M. C.; Purser, S.; Gouverneur, V. *Chem. Rev.* **2008**, *108*, 1943 references therein.
6. (a) Prakesh, M.; Kerouredan, E.; Gree, D.; Gree, R.; DeChancie, J.; Houk, K. N. *J. Fluorine Chem.* **2004**, *125*, 537; (b) Prakesh, M.; Gree, D.; Gree, R. *Acc. Chem. Res.* **2002**, *35*, 175; (c) Prakesh, M.; Gree, D.; Gree, R. *J. Org. Chem.* **2001**, *66*, 3146; (d) Madiot, V.; Lesot, P.; Gree, D.; Courtieu, J.; Gree, R. *Chem. Commun.* **2000**, 169; (e) Madiot, V.; Gree, D.; Gree, R. *Tetrahedron Lett.* **1999**, *40*, 6403; (f) Gree, D.; Madiot, V.; Gree, R. *Tetrahedron Lett.* **1999**, *40*, 6399.
7. (a) Carroll, L.; Pacheco, M. C.; Garcia, L.; Gouverneur, V. *Chem. Commun.* **2006**, 4113; (b) Carroll, L.; McCullough, S.; Rees, T.; Claridge, T. D. W.; Gouverneur, V. *Org. Biomol. Chem.* **2008**, *6*, 1731.
8. Jiang, H.; Falcicchio, A.; Jensen, K. L.; Paixao, M. W.; Bertelsen, S.; Jorgensen, K. A. *J. Am. Chem. Soc.* **2009**, *131*, 7153.
9. (a) Nicholas, K. M. *Acc. Chem. Res.* **1987**, *20*, 207; (b) Teobald, B. J. *Tetrahedron* **2002**, *58*, 4133.
10. For selected reviews see: (a) Muller, T. J. J. *Eur. J. Org. Chem.* **2001**, 2021 For selected recent papers, see: (b) Muhlthau, F.; Schuster, O.; Bach, T. *J. Am. Chem. Soc.* **2005**, *127*, 9348; (c) Muhlthau, F.; Stadler, D.; Goeppert, A.; Olah, G. A.; Prakash, G. K. S.; Bach, T. *J. Am. Chem. Soc.* **2006**, *128*, 9668; (d) Chung, J. Y. L.; Mancheno, D.; Dormer, P. G.; Variankaval, N,; Ball, R. G.; Tsou, N. N. *Org. Lett.* **2008**, *10*, 3037; (e) Stadler, D.; Bach, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 7557; (f) Rubenbauer, P.; Herdtweck, E.; Strassner, T.; Bach T.. *Angew. Chem., Int. Ed.* **2008**, *47*, 10106; (g) Cozzi, P. G.; Benfatti, F.; Zoli, L. *Angew. Chem., Int. Ed.* **2009**, *48*, 1313.
11. Mukaiyama, T.; Suzuki, K.; Yamada, T.; Tabusa, F. *Tetrahedron* **1990**, *46*, 265.
12. Fischer, H. O. L.; Baer, E. *Helv. Chim. Acta* **1934**, *17*, 622.
13. For selected recent papers relating to fluorinated sugars: (a) Hallis, T. M.; Zhao, Z.; Liu, H.-W. *J. Am. Chem. Soc.* **2000**, *122*, 10493; (b) Mikhailopulo, I. A.; Pricota, T. I.; Sivets, G. G.; Altona, C. *J. Org. Chem.* **2003**, *68*, 5897; (c) Boydell, A. J.; Vinader, V.; Linclau, B. *Angew. Chem., Int. Ed.* **2004**, *43*, 5677; (d) Ueda, T.; Feng, F.; Sadamoto, R.; Niikura, K.; Monde, K.; Nishimura, S.-I. *Org. Lett.* **2004**, *6*, 1753.
14. The separation of propargylic fluorides by silica gel chromatography should be very fast, otherwise some product would be decomposed on the column.
15. (a) Mulzer, J.; Greifenberg, S.; Beckstett, A.; Gottwald, M. *Liebigs Ann. Chem.* **1992**, 1131; (b) Dhondi, P. K.; Carberry, P.; Choi, L. B.; Chisholm, J. D. *J. Org. Chem.* **2007**, *72*, 9590.
16. CCDC 740533 and 740534 contain the supplementary crystallographic data for *anti*-**5d** and *anti*-**6m**, respectively. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
17. Schreiber, S. L.; Klimas, M. T.; Sammakia, T. *J. Am. Chem. Soc.* **1987**, *109*, 5749.