sup

DATASET · AUGUST 2014

READS
13

3 AUTHORS:

Atanu Bhaumik
IIT Kharagpur
6 PUBLICATIONS **4** CITATIONS
SEE PROFILE

Supravat Samanta
Central Salt and Marine Chemicals Research I…
11 PUBLICATIONS **15** CITATIONS
SEE PROFILE

Tanmaya Pathak
IIT Kharagpur
113 PUBLICATIONS **878** CITATIONS
SEE PROFILE

JOC The Journal of Organic Chemistry

Article

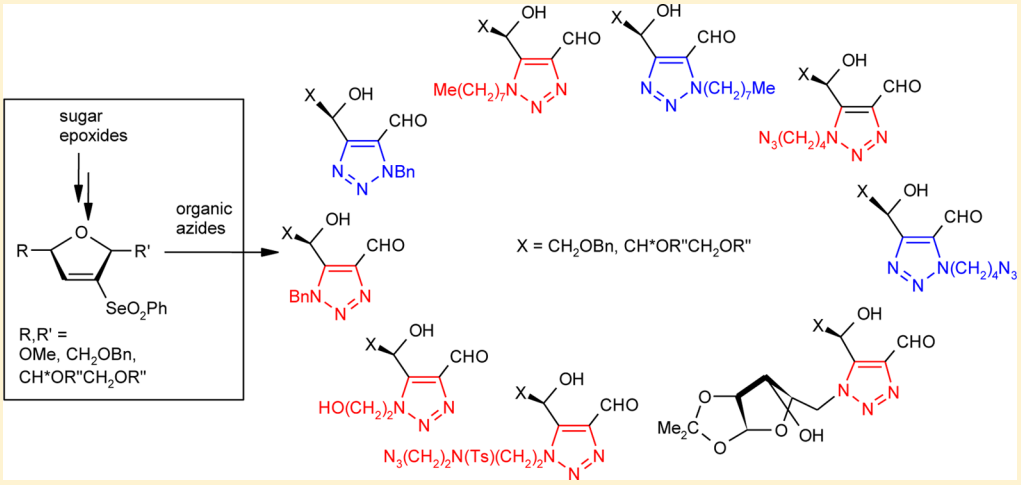
pubs.acs.org/joc

Enantiopure 1,4,5-Trisubstituted 1,2,3-Triazoles from Carbohydrates: Applications of Organoselenium Chemistry

Atanu Bhaumik, Supravat Samanta, and Tanmaya Pathak*

Department of Chemistry, Indian Institute of Technology Kharagpur, Kharagpur 721302, India

Supporting Information



ABSTRACT: A wide range of stable vinyl selenone-modified furanosides has been synthesized for the first time. These 2π-partners undergo 1,3-dipolar cycloaddition reactions with a wide range of organic azides to afford enantiopure trisubstituted triazoles. Furanosyl rings opened up during triazole synthesis to generate polyfunctionalized molecules, ready to undergo further transformations. This strategy is one of the most convenient methods for the synthesis of enantiopure 1,4,5-trisubstituted 1,2,3-triazoles where the chiral components are attached to C-4 or C-5 position of triazole ring. These triazoles are formed in a regioselective manner, and several pairs of regioisomeric triazoles have also been synthesized. The approach affords densely functionalized triazoles, which are amenable to further modifications because of the presence of aldehyde and hydroxyl groups. This powerful and practical route adds to the arsenals of chemists and biologists interested in the synthesis and applications of triazoles.

INTRODUCTION

Long before the discovery of CuAAC[1] or RuAAC[2] strategies for the synthesis of disubstituted triazoles, numerous 1,2,3-triazoles in general[3] and more than 7000 1,4-disubstituted 1-*H*-1,2,3-triazoles[4] were known in medicinal chemistry. These molecules were also known for their stability to acid and basic hydrolysis, reductive and oxidative conditions, high dipole moment, possibility of participating actively in hydrogen bond formation as well as in dipole−dipole and π stacking interactions.[4c] However, the CuAAC strategy or "click" reaction has triggered explosive new developments in the area of 1,2,3-triazoles.[1−5] Increasing attention has recently been directed toward 1,2,3-triazole rings as ligation tools,[4] and significant progress occurred in applying triazole building blocks as either bioactive components in biology[5] or specially functionalized new chemical entities in material chemistry.[6] With the ever increasing demands for new triazoles, a significant number of groups are now involved worldwide in discovering new synthetic strategies.

It is obvious that the use of enantiopure organic azides in 1,3-dipolar cycloaddition reactions would produce chiral triazoles. For example diazides derived from D-mannitol or sugar azides on reactions with different disubstituted acetylenes afforded differently substituted chiral 1,2,3-triazoles.[7] Enantiopure azidoacids or azidoamides in a similar fashion afforded chiral 1,2,3-triazoles.[8] Planar chiral triazole-based phosphanes derived from [2.2]paracyclophanes are efficient ligands for the palladium-catalyzed Suzuki−Miyaura coupling reactions.[9] Chiral 1,2,3-triazolium derivatives, on the other hand, acted as cationic organic catalysts in the asymmetric alkylation of oxindoles (Figure 1).[10] We have recently established that vinyl sulfones in general[11] and terminal ones derived from carbohydrates[11b] are efficient substrates for combining with organic azides via 1,3-dipolar cycloaddition reaction in a

Received: May 1, 2014
Published: July 10, 2014

dx.doi.org/10.1021/jo5009564 | J. Org. Chem. 2014, 79, 6895−6904

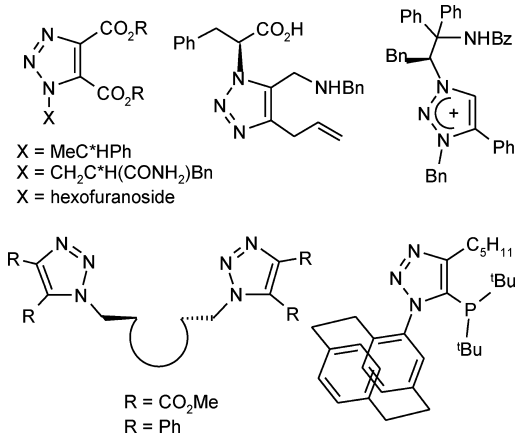
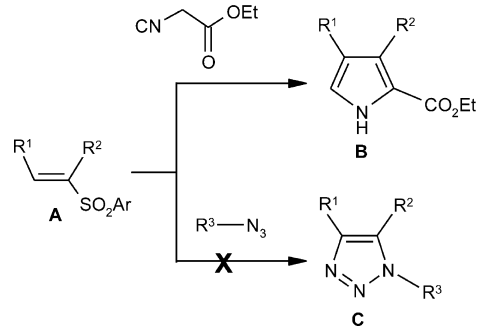


Figure 1. Trisubstituted chiral 1,2,3-triazoles.

regioselective fashion to afford 1,5-disubstituted-1,2,3-triazoles in good to excellent yields.

We also reported that endocyclic vinyl sulfones derived from furanosides and pyranosides **A** reacted with ethylisocyanoacetate to afford enantiopure pyrrole analogues **B** (Scheme 1).[12]

Scheme 1. Vinyl Sulfone as 2π Partner in Cycloaddition Reactions



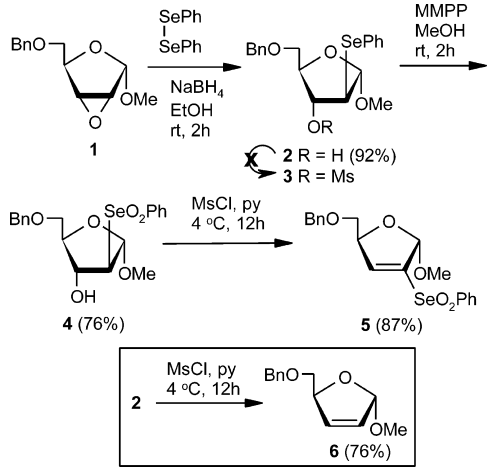
The latter strategy was quite effective in producing a wide range of new enantiopure pyrroles. However, our attempts to extend the strategy of combining organic azides with endocyclic vinyl sulfones derived from furanosides and pyranosides **A** for the generation of enantiopure triazoles **C** failed probably because of the less reactive nature of organic azides in comparison to that of ethylisocyanoacetate (Scheme 1).

Although enantiopure triazoles are easily synthesized by using chiral azides,[7−10,13] the more difficult task of introducing chiral substituents at C-4 and/or C-5 of 1,4,5-trisubstituted 1,2,3-triazoles (1,4,5-TTs) may be achieved by using carbohydrates known as "chiral pool" as was the case with pyrrole synthesis.[12] Since it was not possible to activate azides further, we planned to use a different 2π partner for the cycloaddition reaction. Vinyl selenones have been effectively used in the past as one of the components of cycloaddition reactions.[14c] We therefore intended to employ endocyclic vinyl selenones derived from carbohydrates as the 2π component in the cycloaddition reaction. However, as far as our knowledge goes in the literature the reaction between any vinyl selenone and an organic azide, expected to produce triazoles, has never been attempted. The only report on the reactions between vinyl selenone-modified uridine and sodium azide afforded 1-(2′,3′dideoxy-2′,3′-(2*H*-1,2,3-triazolo)-β-D-glycero-pent-2′-eno-furanosyl)uracil in 64% yield.[14c] Therefore, the regioselectivity of the reaction remained unknown. Although selenoxides and selenones are widely used in synthetic chemistry,[15] vinyl selenones have been used to a limited extent in simpler systems.[16] Selenosugars have also been used as synthetic intermediates. However, virtually all these reports deal with the leaving ability of selenones (and selenoxides) for the generation of olefins.[17] Moreover vinyl selenones derived from carbohydrates have never been reported, although vinyl selenone-modified nucleosides as mentioned above have been efficiently used for accessing a plethora of modified nucleosides.[14] Interestingly, the stability of carbohydrate selenones or selenoxides is notoriously unpredictable. For example, the oxidation of methyl (*R*)-4,6-*O*-benzylidene-3-*Se*-phenyl-3-seleno-α-D-altropyranoside with 2 equiv of H_2O_2 reportedly produced a "selenoxide", which was relatively stable but not isolated; the crude was directly heated to afford the 3-deoxy-hexopyranosid-2-ulose.[18] In another report[19] 9 equiv of H_2O_2 were used for the conversion of sugar selenide to the corresponding "selenoxide", but the elemental analysis or HRMS of the oxidized product was not reported.

RESULTS AND DISCUSSION

Interestingly the stability of β-sulfonyloxyselenides derived from carbohydrates were attributable to steric effect and the deactivating effect exerted by the anomeric center.[19] This information prompted us to initiate a study for using vinyl selenone-modified carbohydrates where the rich chemistry of vinyl selenone and the in-built chirality of a carbohydrate molecule would lead to the formation of enantiopure intermediates. Thus, the known methyl-2,3-anhydro-5-*O*-benzyl-α-D-ribofuranoside **1**[20a,c] (Scheme 2) was reacted with

Scheme 2. Synthesis of Methyl α-D-2-Selenonyl Pent-2-enofuranoside

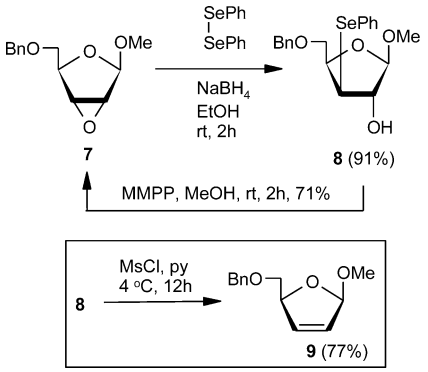


sodium phenyl selenide generated from diphenyl diselenide and sodium borohydride[21] to afford the corresponding β-hydroxy selenide derivative **2** in excellent yield. The β-hydroxy selenide **2** was oxidized by magnesium monoperoxyphthalate hexahydrate (MMPP) in methanol to produce β-hydroxy selenone **4**. Mesylation of the selenone **4** followed by the concomitant elimination of methanesulfonic acid afforded methyl-5-*O*-benzyl-2,3-dideoxy-2-phenylselenonyl-α-D-erythro-pent-2-enofuranoside **5**. Attempted mesylation of **2** did not produce **3** and the olefin **6**[22a] was obtained instead (Scheme 2). Compound **5** was found to be stable and may be stored for a long period

dx.doi.org/10.1021/jo5009564 | J. Org. Chem. 2014, 79, 6895−6904

below 30 °C. The successful synthesis of **5** prompted us to expand the strategy for the preparation of other sugar based vinyl selenone-modified carbohydrates. Interestingly attempted synthesis of the regioisomer of **5** was unsuccessful. Although epoxide **7**[20a,b] was successfully opened by phenylselenide, the product **8** under the oxidation conditions reverted back to the starting material **7**. On the other hand attempted mesylation of **8** produced the olefin **9**[22] (Scheme 3).

Scheme 3. Attempted Synthesis of Methyl β-D-3-Selenonyl Pent-2-enofuranoside



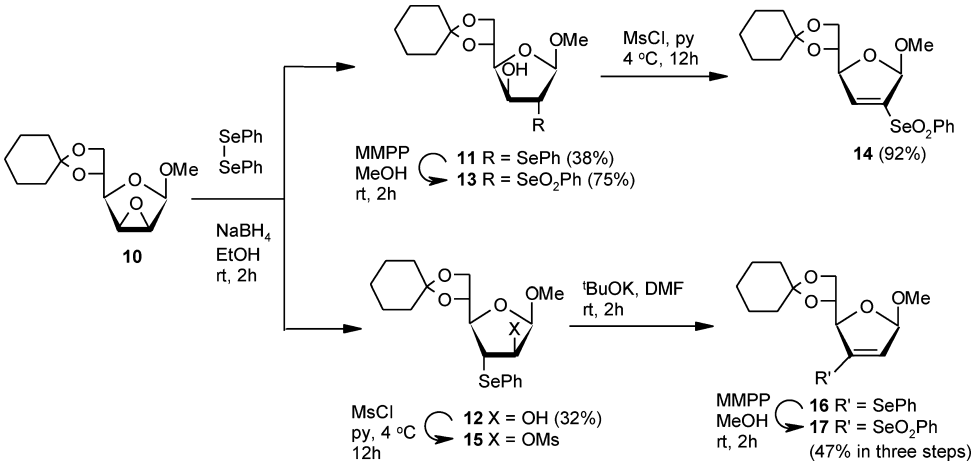
In order to synthesize the corresponding enohexofuranosides, methyl-2,3-anhydro-5,6-*O*-cyclohexylidene-β-D-mannofuranoside **10**[23] was treated with sodium phenyl selenide to afford a mixture of β-hydroxy selenides **11** and **12**, which were separated by simple column chromatography. The major isomer **11** was subjected to the MMPP mediated oxidation in MeOH to produce the selenone derivative **13**, which on mesylation and consecutive elimination afforded methyl-5,6-*O*-cyclohexylidene-2,3-dideoxy-2-phenylselenonyl-β-D-erythro-hex-2-enofuranoside **14** (Scheme 4). Attempted oxidation of **12** produced an inseparable mixture of compounds. Therefore, **12** was mesylated to afford the mesyl derivative **15**. Since **15** degraded slowly at room temperature, the crude compound **15** was immediately treated with potassium *tert*-butoxide in DMF at room temperature to produce vinyl selenide **16**. The latter compound on treatment with MMPP in methanol afforded 3-selenonyl hex-2-enofuranoside **17** in 47% overall yield starting from compound **12** (Scheme 4).

In a similar way methyl-2,3-anhydro-5,6-*O*-cyclohexylidene-α-D-mannofuranoside **18**[23] was reacted with phenyl selenide to afford β-hydroxy selenide **19** as stated above. Attempted oxidation of **19** with MMPP in methanol at room temperature produced the starting epoxide **18**. The free hydroxyl group of compound **19** was mesylated to afford the mesyl derivative **20**, which degraded slowly at room temperature. Therefore, the crude mesyl derivative **20** was directly treated with potassium *tert*-butoxide in DMF at room temperature to produce vinyl selenide **21**, and the latter was subjected to MMPP mediated oxidation in methanol to produce the 3-selenonyl hex-2-enofuranoside **22** in 48% overall yield starting from compound **19** (Scheme 5).

It is evident from Schemes 2−5 that some of the selenosugars are stable to synthetic manipulations, whereas few of them are unstable. A closer look at the structural features of these compounds reveals a pattern, which is in line with the observations mentioned above.[19] For example, the presence of anomeric methoxy group in the vicinity of C-2 of **4** inhibited the intramolecular attack of 3-OH at C-2 carbon (Scheme 2), whereas in case of selenone generated from **8**, the unhindered attack of 2-OH at C-3 afforded the starting epoxide **7**. Mesylation of **8** destabilizes the selenide further triggering elimination of both the functional groups at C-2 and C-3 (Scheme 3). Once again, the anomeric β-methoxy group imparted stability to selenone **13** by protecting the C-2 carbon from the attack of C-3 OH (Scheme 4). On the other hand, selenones derived from **12** (Scheme 4) and **19** (Scheme 5) were unstable probably because C-3 positions of these compounds were easily accessible to intramolecular nucleophilic attack by the C-2 hydroxyl group.

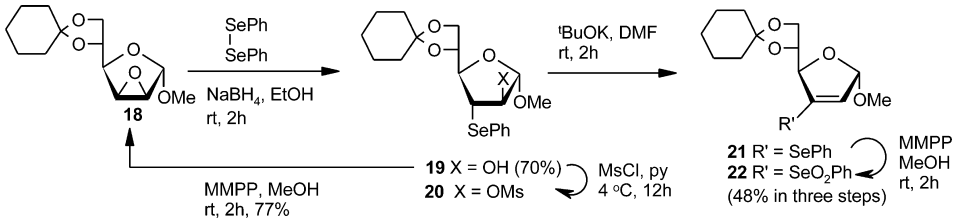
Since the regiochemistry of triazole formation would inevitably depend on the orientation of the vinyl selenone group in the furanoside skeletons, it was imperative to establish the regiochemistry of epoxide opening by phenyl selenide. The regioselectivity of epoxide opening for **1** was unambiguously established with the help of crystal structure of compound **4** (Figure S1, Supporting Information). The β-D-riboepoxide **7** is known[24a] to afford 3-xylo analogues like **8**. It is well documented[24b] that the coupling constant ($J_{1,2}$) values of authentic methyl β-D-xylofuranosides range between 0.0 to 2.0 Hz, which indicated apparently trans relationship between H-1 and H-2, whereas the coupling constant ($J_{1,2}$) values for authentic methyl β-D-arabinofuranosides range between 3.0 to

Scheme 4. Synthesis of Methyl β-D-2-Selenonyl Hex-2-enofuranoside and Methyl β-D-3-Selenonyl Hex-2-enofuranoside



dx.doi.org/10.1021/jo5009564 | J. Org. Chem. 2014, 79, 6895−6904

Scheme 5. Synthesis of Methyl α-D-3-Selenonyl Hex-2-enofuranoside



5.0 Hz, indicating a cis arrangement of H-1 and H-2. In case of compound **11** ($J_{1,2}$ = 0.0 Hz) H-1 and H-2 are trans to each other whereas for **12** ($J_{1,2}$ = 4.4 Hz) H-1 and H-2 are in a cis relationship. The additional support for the structures of the regioisomer **12** and its downstream product **17** was obtained through an indirect route as both the vinyl selenones **17** (**10** → **12** → **15** → **16** → **17**; Scheme 4) and **22** (**18** → **19** → **20** → **21** → **22**; Scheme 5) afforded identical triazoles (Scheme 8; see later). Since **18**, structurally related to α-D-lyxoepoxide[24a] can exclusively afford C-3 substituted product **19** (Scheme 5), it is obvious that **12** is also a C-3 selenofuranoside. Therefore, **11** is a C-2 seleno derivative as depicted in Scheme 4.

In the ^{1}H NMR of **5**, the vinylic proton was masked by aromatic protons. For compound **14**, the vinylic proton appeared as a sharp singlet at δ 7.38 ppm and that for compound **17** the same proton appeared as a doublet (J = 1.6 Hz) at δ 6.94 ppm. The ^{13}C NMR signals at δ 145.7 and 148.7 ppm are assigned to the vinylic carbons of compound **14** and **17** respectively. Compound **22** has a characteristic sharp singlet at δ 6.91 ppm (^{1}H NMR), corresponding to vinylic proton and signal at δ 140.0 ppm (^{13}C NMR) indicate the vinylic carbon.

For the synthesis of triazoles a wide variety of organic azides **a**–**f** (Figure 2) were selected. Thus, 5-*O*-benzyl-2-selenonyl

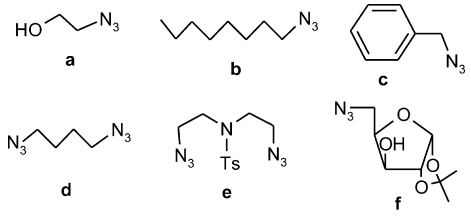
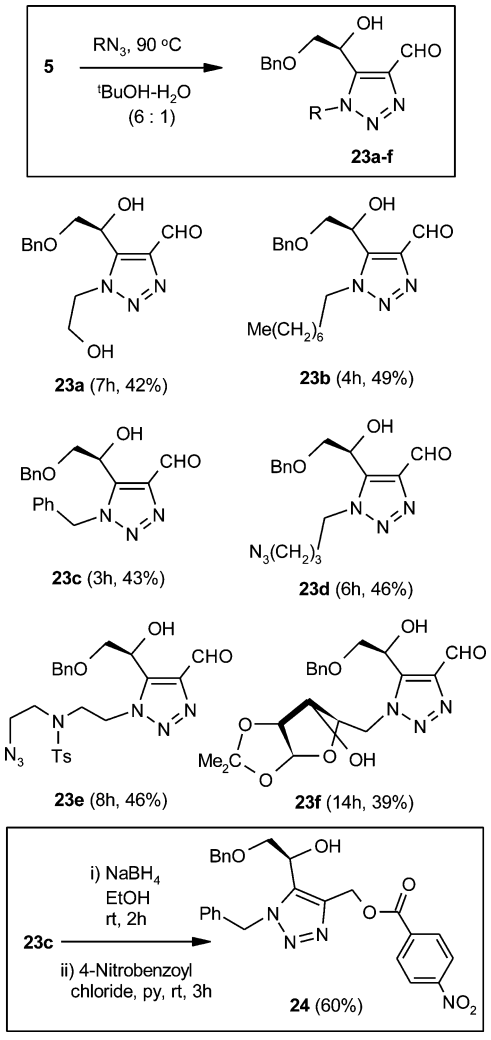


Figure 2. Organic azides used for synthesis of 1,4,5-trisubstituted-1,2,3-triazoles.

pent-2-enofuranoside **5** on reactions with 1.5 equiv of azides **a**, **b**,[25c] **c**,[25c] **d**,[25a] **e**[25b] or **f**[25d] (Figure 2) in *tert*-butanol-water solvent at 90 °C, afforded 1,4,5-trisubstituted-1,2,3-triazoles **23a**–**f** respectively as single products (Scheme 6). Each of the triazoles **23a**–**e** contains one chiral center, one −CHO group and a secondary alcohol group leading to the formation of enantiomers **23a**–**e**. In order to establish the regioselectivity of the triazole formation, compound **23c** was reduced with $NaBH_4$ to the corresponding alcohol, which on esterification with 4-nitrobenzoyl chloride afforded the crystalline ester derivative **24** (Scheme 6). 2-Selenonyl hex-2-enofuranoside **14** on treatment with organic azides **a**–**f** under similar conditions afforded trisubstituted chiral triazole derivatives **25a**–**f** respectively (Scheme 7). The β-anomeric 3-selenonyl hex-2-enofuranoside **17** also reacted with organic azides **b**, **c** and **d** in a similar fashion to afford 1,4,5-trisubstituted chiral 1,2,3-triazoles **26b**–**d** respectively (Scheme 8). The α-anomeric 3-selenonyl hex-2-enofuranoside **22** also reacted with azides **b**–**d**

Scheme 6. Synthesis of 1,4,5-Trisubstituted-1,2,3-Triazoles from Methyl α-D-2-Selenonyl Pent-2-enofuranoside

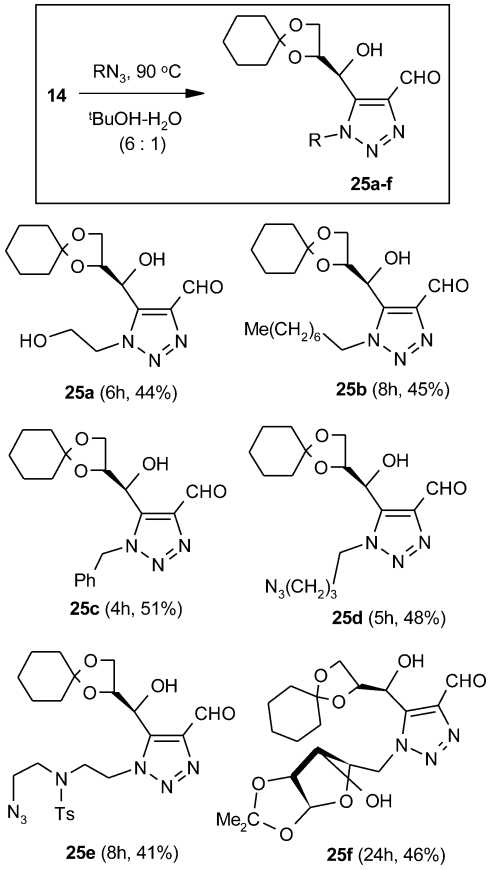


to afford the identical triazoles **26b**–**d** (Scheme 8), indicating that the anomeric configurations do not play any significant role on the regioselectivity of the 1,3-dipolar cycloaddition.

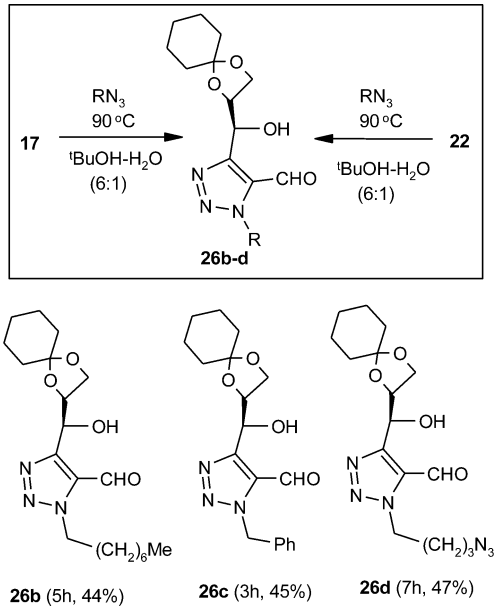
It should be noted that in these reactions, around 65% starting vinyl selenone-modified carbohydrates were consumed and the remaining unreacted portions were recovered in every case. We checked the feasibility of the reaction in water, DMF–water, toluene–water, THF–water and DMSO–water systems. However, the cycloaddition reactions did not proceed in DMF–water, toluene–water, THF–water and the desired triazoles were formed in better yields only in *tert*-butanol-water (6:1) mixture. Approximately one-third of the starting materials remained unreacted even after the addition of excess azides or prolonged reaction time.

dx.doi.org/10.1021/jo5009564 | J. Org. Chem. 2014, 79, 6895–6904

Scheme 7. Synthesis of 1,4,5-Trisubstituted-1,2,3-Triazoles from Methyl β-D-2-Selenonyl Hex-2-enofuranoside



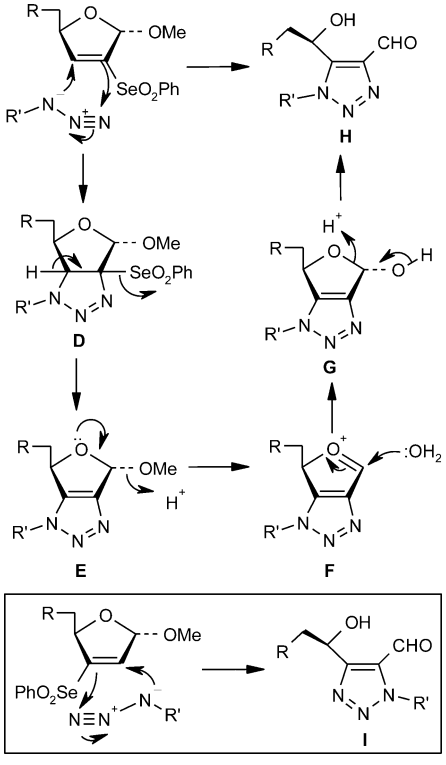
Scheme 8. Synthesis of 1,4,5-Trisubstituted-1,2,3-Triazoles from 3-Selenonyl Hex-2-enofuranosides



For all triazoles sharp singlets between δ 10.04−10.24 ppm (^{1}H NMR) and peaks between δ 181.2−189.1 ppm (^{13}C NMR) indicate the presence of aldehyde group. The single crystal X-ray analysis of compound **24** (Scheme 6; Figure S2, Supporting Information) unambiguously established the regioselective formation of compound **23c**. From the ORTEP diagram of compound **24** and the similar NMR patterns of compound **23a−f** we presumed that all the trisubstituted triazoles **23a−f** synthesized from vinyl selenone **5** have similar configurations. Following an approach[26] described to differentiate between the NMR data of 1,4-disubstituted-1,2,3-triazoles and 1,5-disubstituted-1,2,3-triazoles we concluded that the difference (Δ) between the chemical shift values of C-4/C-5, i.e., (144.8 ppm − 143.0 ppm = 1.8 ppm) of **23c** may be used to identify the regioisomers. In this case it is not necessary to know the exact chemical shifts of C-4/C-5. Thus, all other isomers **23a,b** and **23d−f** described in Scheme 6 afford Δ values ranging between 0.7−1.2 ppm. On the other hand, the difference (Δ) between the chemical shift values of C-4/C-5 for **25a−f** ranges between 0 and 1.1 ppm indicating the similarity between compounds **23** and **25**. However, the differences (Δ) between the chemical shift values of C-4/C-5 for **26b−d** are much larger and ranges between 21.1 and 21.4 ppm, indicating that these compounds are the regioisomers of **25b−d**.

We believed that the cascade of reactions is initiated by the cycloaddition reactions between vinyl selenones and azides as was the case with vinyl sulfones and organic azides.[11] We presumed that the first step is most likely the 1,3 dipolar cycloaddition reaction between a vinyl selenone and an organic azide to form the cyclic intermediate **D** followed by the elimination of phenyl seleninic acid ($PhSeO_2H$) to produce the intermediate **E**. The planarity of the triazole ring attached to the furanoside system created sufficient strain to cleave the hemiacetal bond of the furanoside ring via intermediates **F** and **G** to afford the triazole **H** (Scheme 9). The opening of the sugar ring is similar to the ring rupture in case of pyrrole formation reported earlier.[12] It is probable that phenylseleninic acid catalyzes the cleavage of the acetal bond. It has been

Scheme 9. Plausible Mechanism of the Trisubstituted 1,2,3-Triazole Formation



dx.doi.org/10.1021/jo5009564 | J. Org. Chem. 2014, 79, 6895−6904

established from theoretical calculations[11d] that a particular orientation of the azido group of an organic azide with respect to the vinyl sulfone group dictates the regiochemistry of triazole formation. On the basis of this information, we presume that the regioselectivity of triazole formation is dictated by a severe steric interaction between the R′-group of the organic azides and the PhO_2Se group attached to the sugar ring, which positions two reactive species in such a way that these two groups move away from each other. The regioisomeric triazole **I** is formed from the opposite orientation of the reactants involved as depicted in Scheme 9. Thus, both vinyl selenones **5** and **14** having the PhO_2Se group attached to C-2 afforded triazoles where the −CHO group and the -R′ group are furthest away from each other whereas vinyl selenones **17** and **22** functionalized with PhO_2Se group at C-3 afforded the identical triazoles having the −CHO group and the -R′ group on the same side of the triazole ring. However, further studies are required to establish the exact mechanism of these reactions.

CONCLUSION

We have successfully synthesized a group of stable vinyl selenone-modified carbohydrates from D-xylose and D-glucose. The yields of intermediate steps are good to excellent. We have demonstrated one pot regioselective synthesis of enantiomerically pure 1,4,5-trisubstituted 1,2,3-triazoles having chiral components attached to C-4 or C-5 depending on the structures of the starting vinyl selenones. The reactions are operationally simple and require no catalyst, metal or otherwise. The triazoles are densely functionalized, and depending on the requirements these compounds may be derivatized further because of the presence of at least an aldehyde group and a secondary hydroxyl group. In some cases additional groups like a primary hydroxyl as well as an azido group are also available. This strategy provides an efficient route to the chemists and biologists for accessing a wide variety of trisubstituded 1,2,3-triazoles.

EXPERIMENTAL SECTION

General Methods. Melting points were determined in open-end-capillary tubes and are uncorrected. Carbohydrates and other fine chemicals were obtained from commercial suppliers and used without purification. Solvents were dried and distilled following the standard procedures. TLC was carried out on precoated plates (Merck silica gel 60, f_{254}), and the spots were visualized with UV light or by charring the plates dipped in 5% H_2SO_4−MeOH solution. Column chromatography was performed on silica gel (230−400 mesh). ^1H and ^{13}C NMR for compounds were recorded at 400/200 MHz instrument and 50.3 MHz instrument, respectively, using $CDCl_3$ as the solvent. DEPT experiments were carried out to identify the methylene carbons. High resolution mass spectra were recorded using QTOF mass analyzer. Optical rotations were recorded at 589 nm.

Methyl-5-*O*-benzyl-2-deoxy-2-phenylselanyl-α-D-arabino-furanoside 2. A solution of sodium phenyl selenide in absolute ethanol (10 mL) was prepared from diphenyl diselenide (0.237 g, 0.76 mmol) and $NaBH_4$, (0.051 g, 1.52 mmol). To the solution of selenide was added a solution of oxirane **1** (0.3 g, 1.27 mmol) in absolute ethanol (5 mL), and the mixture was stirred at room temperature. After 2 h ethanol was evaporated under reduced pressure, and the residue was partitioned between satd. aq. solution of NH_4Cl and EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd. Na_2SO_4, filtered, and the filtrate was concentrated under reduced pressure to get a residue. The residue was purified over silica gel to afford compound **2** (0.46 g, 92%). [Eluent: EtOAc:pet ether (1:3)] Colorless gum: $[\alpha]_D^{26}$ +8.1 (*c* 1.31 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 2.59 (d, 1H, *J* = 8.4 Hz), 3.38 (s, 3H), 3.56−3.72 (m, 3H), 4.11−4.12 (m, 1H), 4.15−4.19 (m, 1H), 4.60−4.64 (m, 2H), 5.08 (s, 1H), 7.24−7.36 (m, 8H), 7.53−7.56 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 51.8, 55.3, 70.4 (CH_2), 73.6 (CH_2), 78.1, 84.2, 109.5, 127.8, 127.9, 128.5, 129.0, 129.5, 133.6, 138.0; HRMS [ES^+, $(M + Na)^+$] for $C_{19}H_{22}O_4SeNa$ found 417.0593, calcd 417.0581.

Methyl-5-*O*-benzyl-2-deoxy-2-phenylselenonyl-α-D-arabino-furanoside 4. To the solution of compound **2** (0.1 g, 0.25 mmol) in MeOH (10 mL) MMPP (0.370 g, 0.75 mmol) was added, and the reaction mixture was stirred for 2 h at room temperature. After completion of the reaction (TLC) mixture was filtered, and the filtrate was evaporated under reduced pressure to get a residue, which was partitioned between water (50 mL) and EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd. Na_2SO_4, filtered, and the filtrate was concentrated under reduced pressure to get a residue. The residue was purified over silica gel to afford compound **4** (0.082 g, 76%). [Eluent: EtOAc:pet ether (1:1)] White solid: mp 81 °C (from EtOH); $[\alpha]_D^{26}$ +4.7 (*c* 1.30 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 3.33 (s, 3H), 3.57−3.70 (m, 2H), 4.11−4.15 (m, 2H), 4.52 (s, 2H), 4.79−4.82 (m, 1H), 5.33 (d, 1H, *J* = 2.4 Hz), 7.27−7.35 (m, 5H), 7.56−7.60 (m, 2H), 7.66−7.69 (m, 1H), 7.97 (d, 2H, *J* = 7.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 55.9, 68.9 (CH_2), 71.9, 73.8 (CH_2), 81.0, 81.5, 102.0, 127.6, 128.0, 128.6, 130.6, 134.9, 137.9, 140.6; HRMS [ES^+, $(M + Na)^+$] for $C_{19}H_{22}O_6SeNa$ found 449.0501, calcd 449.0479.

Methyl-5-*O*-benzyl-2,3-dideoxy-2-phenylselenonyl-α-D-erythro-pent-2-enofuranoside 5. To a well-stirred solution of **4** (0.04 g, 0.094 mmol) in anhyd. pyridine (5 mL) methanesulfonyl chloride (0.014 mL, 0.188 mmol) was added at 0 °C, and the mixture was left overnight at +4 °C. The reaction mixture was poured into satd. aq. $NaHCO_3$ solution (50 mL), which was then extracted with EtOAc (3 × 15 mL). The combine extracts were dried over anhyd. Na_2SO_4, filtered, and the filtrate was evaporated under reduced pressure. Residual pyridine was coevaporated with toluene. The residue was purified over silica gel to furnish compound **5** (0.033 g, 87%). [Eluent: EtOAc:pet ether (2:3)] Brownish gum: $[\alpha]_D^{26}$ −6.8 (*c* 1.27 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 3.25 (s, 3H), 3.53−3.65 (m, 2H), 4.49 (s, 2H), 5.16 t, 1H, *J* = 4.4 Hz), 6.03 (d, 1H, *J* = 4.4 Hz), 7.27−7.33 (m, 6H), 7.55−7.68 (m, 3H), 7.96 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 54.9, 70.6 (CH_2), 73.7 (CH_2), 84.8, 106.7, 127.1, 127.8, 128.0, 128.5, 130.2, 134.5, 137.5, 141.7, 142.1, 145.4; HRMS [ES^+, $(M + Na)^+$] for $C_{19}H_{20}O_5SeNa$ found 431.0389, calcd 431.0374.

Methyl-5-*O*-benzyl-2,3-dideoxy-α-D-pent-2-enofuranoside 6. To a well-stirred solution of **2** (0.1 g, 0.25 mmol) in anhyd. pyridine (5 mL) methanesulfonyl chloride (0.028 mL, 0.37 mmol) was added at 0 °C, and the mixture was left overnight at +4 °C. The reaction mixture was poured into ice-cold water (50 mL), which was then extracted with EtOAc (3 × 15 mL). The combined organic layer was dried over anhyd. Na_2SO_4, filtered and evaporated under reduced pressure. Residual pyridine was coevaporated with toluene. The residue was purified over silica gel to furnish compound **6** (0.043 g, 76%). [Eluent: EtOAc:pet ether (1:4)] Colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 3.41 (s, 3H), 3.53−3.55 (m, 2H), 4.55−4.63 (m, 2H), 5.06−5.09 (m, 1H), 5.82−5.83 (m, 1H), 5.86−5.88 (m, 1H), 6.20 (dd, 1H, *J* = 1.2 Hz, 6.0 Hz), 7.28−7.35 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 54.4, 72.4 (CH_2), 73.6 (CH_2), 84.6, 109.5, 127.6, 127.9, 128.1, 128.6, 133.4, 138.2; HRMS [ES^+, $(M + H)^+$] for $C_{13}H_{17}O_3$ found 221.1188, calcd 221.1178.

Methyl-5-*O*-benzyl-3-deoxy-3-phenylselanyl-β-D-xylofuranoside 8. Compound **7** (0.3 g, 1.27 mmol) was converted to **8** (0.456 g, 91%) following the procedure described for the preparation of compound **2**. [Eluent: EtOAc:pet ether (1:3)] Colorless oil: $[\alpha]_D^{26}$ +27.5 (*c* 1.00 in $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 2.01 (d, 1H, *J* = 5.0 Hz), 3.38 (s, 3H), 3.58−3.64 (m, 1H), 3.76 (d, 2H, *J* = 5.0 Hz), 4.47 (s, 1H), 4.56 (s, 2H), 4.60−4.66 (m, 1H), 4.81 (d, 1H, *J* = 1.8 Hz), 7.21−7.33 (m, 8H), 7.51−7.56 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 49.5, 55.3, 70.3 (CH_2), 73.5 (CH_2), 78.0, 86.7, 111.6, 127.8, 127.9, 128.4, 128.9, 129.2, 129.4, 133.5, 137.9; HRMS [ES^+, $(M + Na)^+$] for $C_{19}H_{22}O_4SeNa$ found 417.0593, calcd 417.0581.

Attempted Oxidation of Methyl-5-*O*-benzyl-3-deoxy-3-phenylselanyl-β-D-xylofuranoside 8. Compound **8** (0.1 g, 0.25 mmol)

dx.doi.org/10.1021/jo5009564 | J. Org. Chem. 2014, 79, 6895−6904

was converted to compound **7** (0.039 g, 71%) while oxidized following the procedure described for the preparation of compound **4**. [Eluent: EtOAc:pet ether (1:5)] Colorless gum: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.37 (s, 3H), 3.40−3.63 (m, 2H), 3.66 (d, 1H, J = 2.6 Hz), 3.82 (d, 1H, J = 2.6 Hz), 4.32 (q, 1H, J = 6.0 Hz), 4.57 (s, 2H), 4.95 (s, 1H), 7.35−7.50 (m, 5H).

Methyl-5-*O*-benzyl-2,3-dideoxy-β-D-pent-2-enofuranoside 9. Compound **8** (0.1 g, 0.25 mmol) was converted to compound **9** (0.044 g, 77%) while mesylated following the procedure described for the preparation of compound **6**. [Eluent: EtOAc:pet ether (1:5)] Colorless gum: ^{1}H NMR (200 MHz, $CDCl_3$) 3.41 (s, 3H), 3.51−3.61 (m, 2H), 4.53−4.67 (m, 2H), 4.90 (t, 1H, J = 5.6 Hz), 5.73 (s, 1H), 5.87 (d, 1H, J = 6.0 Hz), 6.20 (d, 1H, J = 6.0 Hz), 7.27−7.35 (m, 5H).

Methyl-5,6-*O*-cyclohexylidene-2-deoxy-2-phenylselanyl-β-D-glucofuranoside 11 and Methyl-5,6-*O*-cyclohexylidene-3-deoxy-3-phenylselanyl-β-D-mannofuranoside 12. Compound **10** (0.58 g, 2.26 mmol) was converted to compound **11** (0.356 g, 38%) and **12** (0.302 g, 32%), following the procedure described for the preparation of compound **2**. Compound **11**: [Eluent: EtOAc:pet ether (1:5)] Colorless gum; $[\alpha]_D^{26}$ +22.2 (c 0.92 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33−1.62 (m, 10H), 3.34 (s, 3H), 3.73 (s, 1H), 3.98−4.01 (m, 1H), 4.12−4.16 (m, 1H), 4.29−4.37 (m, 3H), 4.99 (s, 1H), 7.30−7.32 (m, 3H), 7.56 (t, 2H, J = 3.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 24.0 (CH_2), 24.2 (CH_2), 25.2 (CH_2), 34.9 (CH_2), 36.6 (CH_2), 51.1, 55.5, 66.9 (CH_2), 74.0, 76.4, 83.8, 109.2, 110.0, 128.2, 129.6, 134.0; HRMS [ES$^+$, (M + Na)$^+$] for $C_{19}H_{26}O_5SeNa$ found 437.0828, calcd 437.0843. Compound **12**: [Eluent: EtOAc:pet ether (1:3)] Yellowish gum; $[\alpha]_D^{26}$ +47.3 (c 1.22 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37−1.59 (m, 10H), 3.43 (s, 3H), 3.73 (s, 1H), 3.98−4.05 (m, 4H), 4.26−4.39 (m, 2H), 4.77 (d, 1H, J = 4.4 Hz), 7.26−7.33 (m, 3H), 7.55−7.58 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.9 (CH_2), 24.1 (CH_2), 25.2 (CH_2), 34.9 (CH_2), 36.3 (CH_2), 46.4, 55.5, 65.8 (CH_2), 74.2, 77.2, 82.9, 102.0, 110.3, 128.5, 129.3, 129.5, 136.0; HRMS [ES$^+$, (M + Na)$^+$] for $C_{19}H_{26}O_5SeNa$ found 437.0823, calcd 437.0843.

Methyl-5,6-*O*-cyclohexylidene-2-deoxy-2-phenylselenonyl-β-D-glucofuranoside 13. Compound **11** (0.1 g, 0.24 mmol) was converted to compound **13** (0.08 g, 75%) following the procedure described for the preparation of compound **4**. [Eluent: EtOAc:pet ether (3:2)] Colorless gum: $[\alpha]_D^{26}$ +7.7 (c 0.47 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25−1.62 (m, 10H), 3.32 (bs, 1H), 3.38 (s, 3H), 3.96−4.04 (m, 2H), 4.11−4.15 (m, 2H), 4.35−4.40 (m, 1H), 5.00 (t, 1H, J = 1.6 Hz), 5.47 (d, 1H, J = 2.0 Hz), 7.67−7.70 (m, 2H), 7.74−7.78 (m, 1H), 8.00−8.02 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 24.0 (CH_2), 24.2 (CH_2), 25.2 (CH_2), 34.8 (CH_2), 36.6 (CH_2), 56.5, 67.2 (CH_2), 71.6, 73.7, 79.8, 83.1, 103.1, 110.9, 127.5, 130.7, 135.0, 140.8; HRMS [ES$^+$, (M + Na)$^+$] for $C_{19}H_{26}O_7SeNa$ found 469.0728, calcd 469.0741.

Methyl-5,6-*O*-cyclohexylidene-2,3-dideoxy-2-phenylselenonyl-β-D-erythro-hex-2-enofuranosid 14. Compound **13** (0.08 g, 0.18 mmol) was converted to compound **14** (0.070 g, 92%) following the procedure described for the preparation of compound **5**. [Eluent: EtOAc:pet ether (1:1)] Yellowish gum: $[\alpha]_D^{26}$ −149.4 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25−1.70 (m, 10H), 3.33 (s, 3H), 3.91−4.06 (m, 3H), 4.75 (d, 1H, J = 8.0 Hz), 5.98 (s, 1H), 7.38 (s, 1H), 7.62−7.73 (m, 3H), 8.02 (d, 2H, J = 8.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.9 (CH_2), 24.2 (CH_2), 25.2 (CH_2), 34.7 (CH_2), 36.8 (CH_2), 56.0, 66.8 (CH_2), 77.2, 86.6, 107.3, 111.1, 127.3, 130.3, 134.6, 142.4, 145.7; HRMS [ES$^+$, (M + H)$^+$] for $C_{19}H_{25}O_6Se$ found 429.0817, calcd 429.0816.

Methyl-5,6-*O*-cyclohexylidene-2,3-dideoxy-3-phenylselenonyl-β-D-erythro-hex-2-enofuranoside 17. To a well-stirred solution of **12** (0.209 g, 0.5 mmol) in anhyd. pyridine (10 mL) methanesulfonyl chloride (0.076 mL, 1.00 mmol) was added at 0 °C, and the reaction mixture was left overnight at +4 °C. Ice cold water (50 mL) was added to the reaction mixture, and the mixture was extracted with EtOAc (3 × 20 mL). The combined extract was evaporated, and the residual pyridine was coevaporated with toluene to obtain compound **15** quantitatively. To a solution of crude **15** in dry DMF (8 mL), potassium *tert*-butoxide (0.11 g, 1.00 mmol) was added at 0 °C, and the stirring was continued at room temperature for 2 h. The solution was partitioned between satd. aq. NH_4Cl and EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd. Na_2SO_4, filtered, and the filtrate was evaporated under reduced pressure to give compound **16**. To a solution of **16** in MeOH (10 mL) MMPP (0.74 g, 1.50 mmol) was added. The reaction mixture was stirred for 2 h at room temperature and filtered. The filtrate was evaporated under reduced pressure, and the residue was partitioned between satd. aq. $NaHCO_3$ (60 mL) and EtOAc (3 × 10 mL). Organic layers were pooled together, dried over anhyd. Na_2SO_4, filtered, and the filtrate was evaporated to dryness under reduced pressure to get a gummy residue. The resulting residue was purified over silica gel to yield compound **17**. (0.102 g, 47% in three steps). [Eluent: EtOAc:pet ether (1:2)] Colorless gum: $[\alpha]_D^{26}$ −99.7 (c 0.92 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25−1.64 (m, 10H), 3.45 (s, 3H), 3.87−3.91 (m, 1H), 3.96−3.99 (m, 1H), 4.05−4.10 (m, 1H), 5.01−5.03 (m, 1H), 5.73 (d, 1H, J = 0.8 Hz), 6.94 (d, 1H, J = 1.6 Hz), 7.62−7.72 (m, 3H), 7.99−8.01 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.7 (CH_2), 24.0 (CH_2), 25.2 (CH_2), 34.6 (CH_2), 36.1 (CH_2), 56.5, 65.5 (CH_2), 77.1, 84.1, 107.4, 111.2, 127.1, 127.2, 130.2, 130.3, 134.6, 139.8, 142.2, 148.7; HRMS [ES$^+$, (M + Na)$^+$] for $C_{19}H_{24}O_6SeNa$ found 451.0640, calcd 451.0636.

Methyl-5,6-*O*-cyclohexylidene-3-deoxy-3-phenylselanyl-α-D-mannofuranoside 19. Compound **18** (0.58 g, 2.26 mmol) was converted to compound **19** (0.66 g, 70%) following the procedure described for the preparation of compound **2**. [Eluent: EtOAc:pet ether (1:5)] Yellowish gum: $[\alpha]_D^{26}$ −35.2 (c 0.66 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38−1.64 (m, 10H), 3.34−3.39 (m, 5H), 3.47 (bs, 1H), 3.94−3.98 (m, 1H), 4.31 (bs, 1H), 4.35−4.39 (m, 2H), 4.92 (s, 1H), 7.29−7.30 (m, 3H), 7.59−7.61 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.7 (CH_2), 24.0 (CH_2), 25.2 (CH_2), 34.1 (CH_2), 35.6 (CH_2), 44.8, 55.0, 65.2 (CH_2), 75.5, 81.0, 87.2, 109.7, 111.0, 128.0, 129.6, 130.6, 133.9; HRMS [ES$^+$, (M + Na)$^+$] for $C_{19}H_{26}O_5SeNa$ found 437.0828, calcd 437.0843.

Methyl-5,6-*O*-cyclohexylidene-2,3-dideoxy-3-phenylselenonyl-α-D-erythro-hex-2-enofuranoside 22. Compound **19** (0.2 g, 0.48 mmol) was converted into compound **22** (0.099 g, 48% in three steps) following the procedure described under the preparation of compound **17**. [Eluent: EtOAc:pet ether (1:2)] Colorless gum: $[\alpha]_D^{26}$ −77.7 (c 1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23−1.62 (m, 10H), 3.38 (s, 3H), 3.83−3.88 (m, 1H), 3.94−3.97 (m, 1H), 4.07−4.11 (m, 1H), 5.12−5.14 (m, 1H), 5.86 (d, 1H, J = 4.4 Hz), 6.91 (s, 1H), 7.53−7.55 (m, 2H), 7.61−7.70 (m, 1H), 7.99 (d, 2H, J = 7.2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.8 (CH_2), 24.0 (CH_2), 25.2 (CH_2), 34.7 (CH_2), 36.0 (CH_2), 55.1, 65.4 (CH_2), 76.2, 84.5, 107.2, 111.4, 127.3, 130.4, 134.7, 140.0, 142.1, 148.7; HRMS [ES$^+$, (M + Na)$^+$] for $C_{19}H_{24}O_6SeNa$ found 451.0646, calcd 451.0636.

Attempted Oxidation of Methyl-5,6-*O*-cyclohexylidene-3-deoxy-3-phenylselanyl-α-D-mannofuranoside 19. Compound **19** (0.1 g, 0.24 mmol) was converted to compound **18** (0.048 g, 77%) while oxidized following the procedure described for the preparation of compound **4**. [Eluent: EtOAc:pet ether (1:5)] Colorless gum: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22−1.64 (m, 10H), 3.39 (s, 3H), 3.67 (d, 1H, J = 2.8 Hz), 3.83−3.88 (m, 2H), 3.93−3.96 (m, 1H), 4.08−4.16 (m, 2H), 4.90 (s, 1H).

General Procedure for the Synthesis of 1,4,5-Trisubstituted-1,2,3-Triazoles 23a−f, 25a−f, 26b−d. A mixture of vinyl selenone (1 mmol), and organic azide (1.5 mmol) in *tert*-butanol-water (6 mL + 1 mL)/mmol of vinyl selenone was heated at 90 °C. Heating was continued until the reaction reached a saturation point (TLC) and then cooled to room temperature. Volatile matters were evaporated under a vacuum, and the residue was partitioned between EtOAc and satd. aq. $NaHCO_3$ solution. Then organic part was separated, dried over anhyd. Na_2SO_4, filtered, and the filtrate was evaporated to dryness under reduced pressure. The residue was purified by silica column chromatography to afford the corresponding 1,4,5-trisubstituted 1,2,3-triazoles.

(*S*)-5-(2-*O*-Benzyl-1-hydroxyethyl)-1-(2-hydroxyethyl)-1*H*-1,2,3-triazole-4-carboxaldehyde 23a. Following the general procedure compound **5** (0.1 g, 0.24 mmol) was converted to

dx.doi.org/10.1021/jo5009564 | J. Org. Chem. 2014, 79, 6895−6904

compound **23a** (0.03 g, 42%; 66% based on 0.036 g recovered starting material). [Eluent: EtOAc:pet ether (3:2)] Colorless oil: $[\alpha]_D^{26}$ −12.4 (*c* 1.10 in $CHCl_3$); IR 1635 cm^{-1} (CHO); ^1H NMR (400 MHz, $CDCl_3$) δ 3.60−3.67 (m, 1H), 3.81−3.85 (m, 1H), 3.96−4.05 (m, 2H), 4.38−4.61 (m, 4H), 5.29−5.32 (m, 1H), 7.09−7.11 (m, 2H), 7.28−7.35 (m, 3H), 10.04 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 52.3 (CH_2), 61.2 (CH_2), 65.0, 72.4 (CH_2), 73.8 (CH_2), 128.0, 128.4, 128.7, 137.0, 143.7, 144.0, 187.8; HRMS [ES^+, $(M + H)^+$] for $C_{14}H_{18}N_3O_4$ found 292.1299, calcd 292.1297.

(*S*)-5-(2-*O*-Benzyl-1-hydroxyethyl)-1-octyl-1*H*-1,2,3-triazole-4-carboxaldehyde 23b. Following the general procedure compound **5** (0.1 g, 0.24 mmol) was converted to compound **23b** (0.043 g, 49%; 72% based on 0.032 g recovered starting material). [Eluent: EtOAc:pet ether (1:4)] Colorless oil: $[\alpha]_D^{26}$ +19.6 (*c* 1.13 in $CHCl_3$); IR 1636 cm^{-1} (CHO); ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, *J* = 6.6 Hz), 1.26−1.31 (m, 10H), 1.86−1.94 (m, 2H), 3.55 (t, 1H, *J* = 7.8 Hz), 3.81−3.83 (m, 1H), 4.30−4.48 (m, 4H), 5.12 (bs, 2H), 7.11−7.13 (m, 2H), 7.28−7.36 (m, 3H), 10.06 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.2, 22.7 (CH_2), 26.7 (CH_2), 29.1 (CH_2), 29.2 (CH_2), 30.0 (CH_2), 31.8 (CH_2), 49.8 (CH_2), 65.0, 72.7 (CH_2), 73.6 (CH_2), 127.9, 128.2, 128.6, 137.2, 143.0, 144.2, 188.2; HRMS [ES^+, $(M + H)^+$] for $C_{20}H_{30}N_3O_3$ found 360.2272, calcd 360.2287.

(*S*)-1-Benzyl-5-(2-*O*-benzyl-1-hydroxyethyl)-1*H*-1,2,3-triazole-4-carboxaldehyde 23c. Following the general procedure compound **5** (0.1 g, 0.24 mmol) was converted to compound **23c** (0.034 g, 43%; 67% based on 0.038 g recovered starting material). [Eluent: EtOAc:pet ether (1:3)] Colorless oil: $[\alpha]_D^{26}$ +23.5 (*c* 0.93 in $CHCl_3$); IR 1639 cm^{-1} (CHO); ^1H NMR (400 MHz, $CDCl_3$) δ 3.38−3.61 (m, 2H), 4.33−4.41 (m, 2H), 4.91 (d, 1H, *J* = 10.4 Hz), 5.09−5.19 (m, 1H), 5.63 (q, 2H, *J* = 15.6 Hz), 7.11−7.33 (m, 10H), 10.08 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 53.4 (CH_2), 65.1, 72.6 (CH_2), 73.6 (CH_2), 127.8, 127.9, 128.2, 128.7, 129.0, 129.3, 134.1, 137.3, 143.0, 144.8, 188.1; HRMS [ES^+, $(M + H)^+$] for $C_{19}H_{20}N_3O_3$ found 338.1532, calcd 338.1505.

(*S*)-1-(4-Azidobutyl)-5-(2-*O*-benzyl-1-hydroxyethyl)-1*H*-1,2,3-triazole-4-carboxaldehyde 23d. Following the general procedure compound **5** (0.1 g, 0.24 mmol) was converted to compound **23d** (0.038 g, 46%; 69% based on 0.035 g recovered starting material). [Eluent: EtOAc:pet ether (1:2)] Colorless oil: $[\alpha]_D^{26}$ −18.8 (*c* 1.05 in $CHCl_3$); IR 1642 cm^{-1} (CHO), 2098 cm^{-1} (N_3); ^1H NMR (400 MHz, $CDCl_3$) δ 1.53−1.60 (m, 2H), 1.92−2.04 (m, 2H), 3.20−3.26 (m, 2H), 3.51−3.58 (m, 1H), 3.81−3.85 (m, 1H), 4.35−4.47 (m, 4H), 4.95 (bs, 1H), 5.12 (d, 1H, *J* = 4.8 Hz), 7.10−7.12 (m, 2H), 7.29−7.35 (m, 3H), 10.07 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.8 (CH_2), 26.9 (CH_2), 48.9 (CH_2), 50.5 (CH_2), 64.7, 72.4 (CH_2), 73.5 (CH_2), 127.8, 128.1, 128.5, 136.9, 142.9, 144.0, 188.0; HRMS [ES^+, $(M + H)^+$] for $C_{16}H_{21}N_6O_3$ found 345.1680, calcd 345.1675.

(*S*)-1-(*N*-(2-Azidoethyl)-*N*-ethyl-4-methyl-benzenesulfonamide)-5-(2-*O*-benzyl-1-hydroxyethyl)-1*H*-1,2,3-triazole-4-carboxaldehyde 23e. Following the general procedure compound **5** (0.1 g, 0.24 mmol) was converted to compound **23e** (0.058 g, 46%; 77% based on 0.04 g recovered starting material). [Eluent: EtOAc:pet ether (1:4)] Colorless oil: $[\alpha]_D^{26}$ −23.3 (*c* 1.05 in $CHCl_3$); IR 1638 cm^{-1} (CHO), 2104 cm^{-1} (N_3); ^1H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 3.10−3.22 (m, 2H), 3.56−3.44 (m, 2H), 3.57−3.64 (m, 3H), 3.82−3.85 (m, 1H), 3.81−3.84 (m, 1H), 4.44 (q, 2H, *J* = 12.0 Hz), 4.64−4.79 (m, 3H), 5.32 (d, 1H, *J* = 5.2 Hz), 7.09−7.11 (m, 2H), 7.24−7.35 (m, 5H), 7.67 (d, 2H, *J* = 8.4 Hz), 10.06 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.7, 49.1 (CH_2), 49.6 (CH_2), 50.9 (CH_2), 65.1, 72.6 (CH_2), 73.7 (CH_2), 127.5, 128.0, 128.2, 128.7, 130.2, 135.3, 137.2, 143.3, 144.0, 144.5, 187.7; HRMS [ES^+, $(M + H)^+$] for $C_{23}H_{28}N_7O_5S$ found 514.1854, calcd 514.1873.

(*S*)-5-(2-*O*-Benzyl-1-hydroxyethyl)-1-(((3*aS*,5*R*,6*R*,6*aS*)-6-hydroxy-2,2-dimethyl-dihydro-5*H*-furo[2,3-*d*][1,3]dioxol-5-yl)-methyl)-1*H*-1,2,3-triazole-4-carboxaldehyde 23f. Following the general procedure compound **5** (0.1 g, 0.24 mmol) was converted to compound **23f** (0.040 g, 39%; 65% based on 0.041 g recovered starting material). [Eluent: EtOAc:pet ether (2:3)] Colorless oil: $[\alpha]_D^{26}$ −45.2 (*c* 1.40 in $CHCl_3$); IR 1635 cm^{-1} (CHO); ^1H NMR (400 MHz, $CDCl_3$) δ 1.28 (s, 3H), 1.43 (s, 3H), 3.59−3.63 (m, 1H), 3.73−3.77 (m, 1H), 4.14 (d, 1H, *J* = 2.0 Hz), 4.65−4.71 (m, 6H), 5.33 (d, 1H, *J* = 4.8 Hz), 5.91 (d, 1H, *J* = 3.6 Hz), 7.12−7.14 (m, 2H), 7.26−7.32 (m, 3H), 10.05 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 26.3, 27.0, 47.4 (CH_2), 65.3, 72.1 (CH_2), 73.6 (CH_2), 74.3, 79.1, 85.4, 105.2, 112.4, 128.0, 128.3, 128.7, 137.2, 143.3, 144.0, 187.6; HRMS [ES^+, $(M + H)^+$] for $C_{20}H_{26}N_3O_7$ found 420.1784, calcd 420.1771.

(*S*)(1-Benzyl-5-(2-*O*-benzyl-1-hydroxyethyl)-1*H*-1,2,3-triazole-4-yl)methyl 4-nitrobenzoate 24. $NaBH_4$ (0.012 g, 0.3 mmol) was added to a solution of compound **23c** (0.035 g, 0.1 mmol) in ethanol (6 mL), and the mixture was stirred at room temperature for 2 h. Volatile matters were evaporated under a vacuum, and the residue was partitioned between EtOAc and satd. aq. NH_4Cl solution. Organic layers were pooled together, dried over anhyd. Na_2SO_4, filtered, and the filtrate was evaporated to dryness. The residue thus obtained was dissolved in pyridine (5 mL), and 4-nitrobenzoyl chloride (0.055 g, 0.3 mmol) was added to the solution at room temparature. After 3 h (TLC), the mixture was partitioned between EtOAc (2 × 10 mL) and satd. aq. $NaHCO_3$ solution. Organic layers were pooled together, dried over anhyd. Na_2SO_4, filtered, and the filtrate was evaporated to dryness to give a residue. The residue thus obtained was purified over silica gel coloumn to afford compound **24** (0.03 g, 60% in two steps). [Eluent: EtOAc:pet ether (1:3)] White solid: mp 118 °C (from EtOH); $[\alpha]_D^{26}$ +32.7 (*c* 1.00 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 3.30−3.42 (m, 2H), 4.37 (q, 2H, *J* = 12.0 Hz), 5.20−5.23 (m, 1H), 5.55 (s, 2H), 5.67 (q, 2H, *J* = 15.2 Hz), 7.16−7.22 (m, 4H), 7.27−7.34 (m, 6H), 8.21 (q, 4H, *J* = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.0 (CH_2), 58.6 (CH_2), 64.8, 72.1 (CH_2), 73.4 (CH_2), 123.5, 127.4, 127.6, 128.1, 128.5, 128.5, 129.0, 130.9, 134.6, 134.9, 135.0, 136.9, 140.2, 150.5, 164.7; HRMS [ES^+, $(M + H)^+$] for $C_{26}H_{25}N_4O_6$ found 489.1752, calcd 489.1774.

(*S*)-5-(2,3-*O*-Cyclohexylidene-1-hydroxypropyl)-1-(2-hydroxyethyl)-1*H*-1,2,3-triazole-4-carboxaldehyde 25a. Following the general procedure compound **14** (0.1 g, 0.23 mmol) was converted to compound **25a** (0.032 g, 44%; 65% based on 0.032 g recovered starting material). [Eluent: EtOAc:pet ether (1:3)] Colorless oil: $[\alpha]_D^{26}$ −38.7 (*c* 1.50 in $CHCl_3$); IR 1635 cm^{-1} (CHO); ^1H NMR (400 MHz, $CDCl_3$) δ 1.29−1.64 (m, 10H), 3.37−3.49 (m, 1H), 4.07−4.24 (m, 5H), 4.52−4.65 (m, 2H), 4.86 (s, 1H), 5.20 (d, 1H, *J* = 8.0 Hz), 10.11 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.6 (CH_2), 24.1 (CH_2), 25.1 (CH_2), 34.0 (CH_2), 36.3 (CH_2), 52.0 (CH_2), 61.1 (CH_2), 67.4 (CH_2), 67.8, 77.5, 111.3, 144.2, 188.6; HRMS [ES^+, $(M + H)^+$] for $C_{14}H_{22}N_3O_5$ found 312.1538, calcd 312.1559.

(*S*)-5-(2,3-*O*-Cyclohexylidene-1-hydroxypropyl)-1-octyl-1*H*-1,2,3-triazole-4-carboxaldehyde 25b. Following the general procedure compound **14** (0.1 g, 0.23 mmol) was converted to compound **25b** (0.039 g, 45%; 65% based on 0.029 g recovered starting material). [Eluent: EtOAc:pet ether (1:3)] Brownish oil: $[\alpha]_D^{26}$ −22.3 (*c* 1.05 in $CHCl_3$); IR 1636 cm^{-1} (CHO); ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, 3H, *J* = 6.6 Hz), 1.24−1.67 (m, 20H), 1.96−2.00 (m, 2H), 4.09−4.42 (m, 5H), 4.56 (bs, 1H), 5.30 (bs, 1H), 10.11 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.2, 22.8 (CH_2), 23.6 (CH_2), 24.2 (CH_2), 25.2 (CH_2), 26.8 (CH_2), 29.2 (CH_2), 29.9 (CH_2), 31.9 (CH_2), 33.9 (CH_2), 36.5 (CH_2), 49.7 (CH_2), 67.5 (CH_2), 68.0, 77.5, 111.2, 143.5, 144.5, 189.1; HRMS [ES^+, $(M + H)^+$] for $C_{20}H_{34}N_3O_4$ found 380.2525, calcd 380.2549.

(*S*)-1-Benzyl-5-(2,3-*O*-cyclohexylidene-1-hydroxypropyl)-1*H*-1,2,3-triazole-4-carboxaldehyde 25c. Following the general procedure compound **14** (0.1 g, 0.23 mmol) was converted to compound **25c** (0.042 g, 51%; 71% based on 0.029 g recovered starting material). [Eluent: EtOAc:pet ether (1:3)] Colorless oil: $[\alpha]_D^{26}$ +29.8 (c 1.00 in $CHCl_3$); IR 1641 cm^{-1} (CHO); ^1H NMR (400 MHz, $CDCl_3$) δ 1.28−1.73 (m, 10H), 4.07−4.24 (m, 3H), 4.59 (s, 1H), 5.28 (bs, 1H), 5.70 (q, 2H, *J* = 15.4 Hz), 7.19−7.39 (m, 5H), 10.13 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.7 (CH_2), 24.2 (CH_2), 25.1 (CH_2), 34.0 (CH_2), 36.5 (CH_2), 53.2 (CH_2), 67.5 (CH_2), 67.9, 77.7, 111.3, 127.5, 129.0, 129.4, 133.7, 143.8, 144.9, 189.0; HRMS [ES^+, $(M + Na)^+$] for $C_{19}H_{23}N_3O_4Na$ found 380.1607, calcd 380.1586.

dx.doi.org/10.1021/jo5009564 | *J. Org. Chem.* 2014, 79, 6895−6904

(*S*)-1-(4-Azidobutyl)-5-(2,3-*O*-cyclohexylidene-1-hydroxypropyl)-1*H*-1,2,3-triazole-4-carboxaldehyde 25d. Following the general procedure compound **14** (0.1 g, 0.23 mmol) was converted to compound **25d** (0.041 g, 48%; 72% based on 0.031 g recovered starting material). [Eluent: EtOAc:pet ether (1:4)] Colorless oil: $[\alpha]_D^{26}$ −16.7 (*c* 1.00 in $CHCl_3$); IR 1655 cm^{-1} (CHO), 2093 cm^{-1} (N_3); ^1H NMR (400 MHz, $CDCl_3$) δ 1.25−1.71 (m, 12H), 2.06−2.16 (m, 2H), 3.36−3.39 (m, 2H), 4.09−4.26 (m, 3H), 4.36−4.61 (m, 3H), 5.27 (d, 1H, *J* = 12.0 Hz), 10.12 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.7 (CH_2), 24.2 (CH_2), 25.1 (CH_2), 26.3 (CH_2), 27.1 (CH_2), 33.9 (CH_2), 36.5 (CH_2), 49.1 (CH_2), 51.0 (CH_2), 67.5 (CH_2), 68.0, 77.5, 111.3, 143.5, 144.6, 189.0; HRMS [ES^+, $(M + H)^+$] for $C_{16}H_{25}N_6O_4$ found 365.1933, calcd 365.1937.

(*S*)-1-(*N*-(2-Azidoethyl)-*N*-ethyl-4-methyl-benzenesulfonamide)-5-(2,3-*O*-cyclohexylidene-1-hydroxypropyl)-1*H*-1,2,3-triazole-4-carboxaldehyde 25e. Following the general procedure compound **14** (0.1 g, 0.23 mmol) was converted to compound **25e** (0.052 g, 41%; 66% based on 0.036 g recovered starting material). [Eluent: EtOAc:pet ether (1:2)] Colorless oil: $[\alpha]_D^{26}$ +15.5 (*c* 0.53 in $CHCl_3$); IR 1640 cm^{-1} (CHO), 2120 cm^{-1} (N_3); ^1H NMR (400 MHz, $CDCl_3$) δ 1.21−1.68 (m, 10H), 2.43 (s, 3H), 3.22−3.25 (m, 2H), 3.41−3.46 (m, 2H), 3.61−3.71 (m, 2H), 4.10−4.17 (m, 2H), 4.23−4.25 (m, 1H), 4.74−4.86 (m, 3H), 5.12 (d, 1H, *J* = 11.6 Hz), 7.33 (d, 2H, *J* = 8.4 Hz), 7.70 (d, 2H, *J* = 8.0 Hz), 10.13 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.8 (CH_2), 23.8 (CH_2), 24.3 (CH_2), 25.2 (CH_2), 34.3 (CH_2), 36.2 (CH_2), 49.3 (CH_2), 49.8 (CH_2), 51.0 (CH_2), 67.6 (CH_2), 67.9, 77.7, 100.2, 111.4, 127.6, 130.3, 135.3, 144.0, 144.5, 144.6, 188.6; HRMS [ES^+, $(M + Na)^+$] for $C_{23}H_{31}N_7O_6SNa$ found 556.1960, calcd 556.1954.

(*S*)-5-(2,3-*O*-Cyclohexylidene-1-hydroxypropyl)-1-(((3*aS*,5*R*,6*R*,6*aS*)-6-hydroxy-2,2-dimethyl-dihydro-5*H*-furo-[2,3-*d*][1,3]dioxol-5-yl)methyl)-1*H*-1,2,3-triazole-4-carboxaldehyde 25f. Following the general procedure compound **14** (0.1 g, 0.23 mmol) was converted to compound **25f** (0.047 g, 46%; 63% based on 0.03 g recovered starting material). [Eluent: EtOAc:pet ether (1:2)] Colorless oil: $[\alpha]_D^{26}$ +13.3 (*c* 1.00 in $CHCl_3$); IR 1638 cm^{-1} (CHO); ^1H NMR (400 MHz, $CDCl_3$) δ 1.23−1.67 (m, 16H), 3.17 (bs, 1H), 4.10−4.22 (m, 4H), 4.57 (d, 1H, *J* = 3.6 Hz), 4.66 (s, 3H), 4.82−4.85 (m, 1H), 5.23 (d, 1H, *J* = 11.2 Hz), 5.97 (d, 1H, *J* = 3.6 Hz), 10.12 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.5 (CH_2), 23.9 (CH_2), 24.8 (CH_2), 26.0, 26.7, 33.9 (CH_2), 35.9 (CH_2), 46.5 (CH_2), 67.0 (CH_2), 67.6, 73.9, 77.1, 78.6, 85.2, 104.9, 111.2, 112.0, 143.7, 143.8, 188.3; HRMS [ES^+, $(M + H)^+$] for $C_{20}H_{30}N_3O_8$ found 440.2018, calcd 440.2033.

(*S*)-5-(2,3-*O*-Cyclohexylidene-1-hydroxypropyl)-3-octyl-3*H*-1,2,3-triazole-4-carboxaldehyde 26b. Following the general procedure compound **17** (0.1 g, 0.23 mmol) was converted to compound **26b** (0.037 g, 44%; 61% based on 0.031 g recovered starting material). [Eluent: EtOAc:pet ether (1:5)] Colorless oil: $[\alpha]_D^{26}$ −22.3 (*c* 1.05 in $CHCl_3$); IR 1675 cm^{-1} (CHO); ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, 3H, *J* = 6.8 Hz), 1.21−1.87 (m, 22H), 3.18 (d, 1H, *J* = 3.2 Hz), 3.92−3.96 (m, 1H), 4.07−4.10 (m, 1H), 4.54−4.58 (m, 1H), 4.65−4.69 (m, 2H), 5.22 (d, 1H, *J* = 4.8 Hz), 10.24 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.3, 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 26.6 (CH_2), 29.2 (CH_2), 29.3 (CH_2), 30.2 (CH_2), 31.9 (CH_2), 34.4 (CH_2), 36.3 (CH_2), 51.5 (CH_2), 65.3 (CH_2), 68.5, 77.5, 110.8, 131.1, 152.3, 181.2; HRMS [ES^+, $(M + H)^+$] for $C_{20}H_{34}N_3O_4$ found 380.2563, calcd 380.2549.

(*S*)-3-Benzyl-5-(2,3-*O*-cyclohexylidene-1-hydroxypropyl)-3*H*-1,2,3-triazole-4-carboxaldehyde 26c. Following the general procedure compound **17** (0.1 g, 0.23 mmol) was converted to compound **26c** (0.038 g, 45%; 68% based on 0.033 g recovered starting material). [Eluent: EtOAc:pet ether (1:4)] Colorless oil: $[\alpha]_D^{26}$ +47.5 (*c* 1.20 in $CHCl_3$); IR 1681 cm^{-1} (CHO); ^1H NMR (400 MHz, $CDCl_3$) δ 1.15−1.59 (m, 10H), 3.87−3.91 (m, 1H), 4.06 (t, 1H, *J* = 7.6 Hz), 4.55 (d, 1H, *J* = 5.6 Hz), 5.20 (d, 1H, *J* = 4.4 Hz), 5.86 (s, 2H), 7.30 (s, 5H), 10.17 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.8 (CH_2), 24.1 (CH_2), 25.2 (CH_2), 34.4 (CH_2), 36.2 (CH_2), 54.4 (CH_2), 65.2 (CH_2), 68.6, 77.2, 110.8, 128.4, 128.8, 129.0, 131.1, 134.6, 152.5, 181.2; HRMS [ES^+, $(M + Na)^+$] for $C_{19}H_{23}N_3O_4Na$ found 380.1563, calcd 380.1586.

(*S*)-3-(4-Azidobutyl)-5-(2,3-*O*-cyclohexylidene-1-hydroxypropyl)-3*H*-1,2,3-triazole-4-carboxaldehyde 26d. Following the general procedure compound **17** (0.1 g, 0.23 mmol) was converted to compound **26d** (0.04 g, 47%; 66% based on 0.031 g recovered starting material). [Eluent: EtOAc:pet ether (1:3)] Colorless oil: $[\alpha]_D^{26}$ +42.2 (*c* 1.50 in $CHCl_3$); IR 1660 cm^{-1} (CHO), 2102 cm^{-1} (N_3); ^1H NMR (400 MHz, $CDCl_3$) δ 1.15−1.64 (m, 12H), 1.94−2.01 (m, 2H), 3.33 (t, 2H, *J* = 6.6 Hz), 3.91−3.95 (m, 1H), 4.06−4.10 (m, 1H), 4.55−4.59 (m, 1H), 4.72 (t, 2H, *J* = 7.0 Hz), 5.23 (d, 1H, *J* = 4.8 Hz), 10.24 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.8 (CH_2), 24.1 (CH_2), 25.2 (CH_2), 25.9 (CH_2), 27.3 (CH_2), 34.4 (CH_2), 36.3 (CH_2), 50.7 (CH_2), 50.9 (CH_2), 65.2 (CH_2), 68.5, 77.5, 110.8, 131.2, 152.5, 181.4; HRMS [ES^+, $(M + H)^+$] for $C_{16}H_{25}N_6O_4$ found 365.1939, calcd 365.1937.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Full spectroscopic data of all new compounds and crystal data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: tpathak@chem.iitkgp.ernet.in.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

A.B. thanks the Council of Scientific and Industrial Research (CSIR), New Delhi, India for a fellowship. Financial support by the Council of Scientific and Industrial Research (CSIR), New Delhi, India is gratefully acknowledged. The Department of Science and Technology, New Delhi, India is also thanked for the creation of 400 MHz facility under IRPHA program and DST-FIST for single crystal X-ray facility.

■ DEDICATION

Dedicated to Prof. Jyoti Chattopadhyaya on the occasion of his 65th birthday.

■ REFERENCES

(1) (a) Tornøe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057−3062. (b) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596−2599.

(2) For metal-catalyzed 1,5-disubstituted-1,2,3-triazole synthesis, see: (a) Zhang, L.; Chen, X.; Xue, P.; Sun, H. H. Y.; Williams, I. D.; Sharpless, K. B.; Fokin, V. V.; Jia, G. *J. Am. Chem. Soc.* **2005**, *127*, 15998−15999. (b) Rasmuseen, L. K.; Boren, B. C.; Fokin, V. V. *Org. Lett.* **2007**, *9*, 5337−5339. (c) Boren, B. C.; Narayan, S.; Rasmuseen, L. K.; Zhang, L.; Zhao, H.; Lin, Z.; Jia, G.; Fokin, V. V. *J. Am. Chem. Soc.* **2008**, *130*, 8923−8930. (d) Kwok, S. W.; Fotsing, J. R.; Fraser, R. J.; Rodionov, V. O.; Fokin, V. V. *Org. Lett.* **2010**, *12*, 4217−4219.

(3) (a) Rolf, H.; Guenter, S.; Leander, M. *Chem. Ber.* **1967**, *100*, 2494−2507. (b) Rolf, H. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984. (c) Tome, A. C. *Sci. Synth.* **2004**, *13*, 415−601.

(4) For recent reviews on 1,2,3-triazoles by CuAAC route, see: (a) Bock, V. D.; Hiemstra, H.; Maarseveen, J. H.V. *Eur. J. Org. Chem.* **2006**, 51−68. (b) Santoyo-Gonzalez, F.; Hernandez-Mateo, F. *Top. Heterocycl. Chem.* **2007**, *7*, 133−177. (c) Tron, G. C.; Pirali, T.; Billington, R. A.; Canonico, P. L.; Sorba, G.; Genazzani, A. A. *Med. Res. Rev.* **2008**, *28*, 278−308. (d) Meldal, M.; Tornøe, C. W. *Chem. Rev.* **2008**, *108*, 2952−3015. (e) Kappe, C. O.; Van der Eycken, E. *Chem. Soc. Rev.* **2010**, *39*, 1280−1290. (f) Hein, J. E.; Fokin, V. V. *Chem. Soc. Rev.* **2010**, *39*, 1302−1315. (g) Holub, J. M.; Kirshenbaum, K. *Chem. Soc. Rev.* **2010**, *39*, 1325−1337. (h) Dondoni, A. *Org. Biomol. Chem.* **2010**, *8*, 3366−3385. (i) Pedersen, D. S.; Abell, A. *Eur. J. Org. Chem.*

2011, 2399−2411. (j) Kushwaha, D.; Dwivedi, P.; Kuanar, S. K.; Tiwari, V. K. *Curr. Org. Syn.* **2013**, *10*, 90−135.

(5) For recent reviews on the applications of CuAAC reactions in biology, see: (a) Gramlich, P. M. E.; Wirges, C. T.; Manetto, A.; Carell, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 8350−8358. (b) Moorhouse, A. D.; Moses, J. E. *ChemMedChem* **2008**, *3*, 715−723. (c) Lutz, J.-F.; Zarafshani, Z. *Adv. Drug Delivery Rev.* **2008**, *60*, 958−970. (d) Holub, J. M.; Kirshenbaum, K. *Chem. Soc. Rev.* **2010**, *39*, 1325−1337. (e) El-Sagheer, A. H.; Brown, T. *Chem. Soc. Rev.* **2010**, *39*, 1388−1405. (f) Aragao-Leoneti, V.; Campo, V. L.; Gomes, A. S.; Field, R. A.; Carvalho, I. *Tetrahedron* **2010**, *66*, 9475−9492. (g) Dehn, S.; Chapman, R.; Jolliffe, K. A.; Perrier, S. *Polym. Rev.* **2011**, *51*, 214−234. (h) Lallana, E.; Riguera, R.; Fernandez-Megia, E. *Angew. Chem., Int. Ed.* **2011**, *50*, 8794−8804. (i) El-Sagheer, A. H.; Brown, T. *Acc. Chem. Res.* **2012**, *45*, 1258−1267. (j) Zheng, T.; Rouhanifard, S. H.; Jalloh, A. S.; Wu, P. *Top. Heterocycl. Chem.* **2012**, *28*, 163−183. (k) Beal, D. M.; Jones, L. H. *Angew. Chem., Int. Ed.* **2012**, *51*, 6320−6326. (l) Fabritz, S.; Hoerner, S.; Avrutina, O.; Kolmar, H. *Org. Biomol. Chem.* **2013**, *11*, 2224−2236.

(6) For recent reviews on the applications of CuAAC reactions in material science, see: (a) Crowley, J. D.; Goldup, S. M.; Lee, A.-L.; Leigh, D. A.; McBurney, R. T. *Chem. Soc. Rev.* **2009**, *38*, 1530−1541. (b) Santoyo-Gonzalez, F.; Hernandez-Mateo, F. *Chem. Soc. Rev.* **2009**, *38*, 3449−3462. (c) Iha, R. K.; Wooley, K. L.; Nystrom, A. M.; Burke, D. J.; Kade, M. J.; Hawker, C. J. *Chem. Rev.* **2009**, *109*, 5620−5686. (d) Haenni, K. D.; Leigh, D. A. *Chem. Soc. Rev.* **2010**, *39*, 1240−1251. (e) Chu, Ch.; Liu, R. *Chem. Soc. Rev.* **2011**, *40*, 2177−2188. (f) Liang, L.; Astruc, D. *Coord. Chem. Rev.* **2011**, *255*, 2933−2945. (g) Juricek, M.; Kouwer, P. H. J.; Rowan, A. E. *Chem. Commun.* **2011**, *47*, 8740−8749. (h) Astruc, D.; Liang, L.; Rapakousiou, A.; Ruiz, J. *Acc. Chem. Res.* **2012**, *45*, 630−640. (i) Wong, C.-H.; Zimmerman, S. C. *Chem. Commun.* **2013**, *49*, 1679−1695. (j) El Brahmi, N.; El Kazzouli, S.; Mignani, S.; Bousmina, M.; Majoral, J. P. *Tetrahedron* **2013**, *69*, 3103−3133. (k) Casarrubios, L.; De la Torre, M. C.; Sierra, M. A. *Chem.—Eur. J.* **2013**, *19*, 3534−3541.

(7) (a) Nazhaoui, M.; Gross, B.; Joly, J.-P. *Tetrahedron Lett.* **1993**, *34*, 1287−1290. (b) Marco-Contelles, J.; Rodríguez-Fernández, M. *J. Org. Chem.* **2001**, *66*, 3717−3725.

(8) (a) Ma, D.-Y.; Wang, D.-X.; Zheng, Q.-Y.; Wang, M.-X. *Tetrahedron: Asymmetry* **2006**, *17*, 2366−2376. (b) Balducci, E.; Bellucci, L.; Petricci, E.; Taddei, M.; Tafi, A. *J. Org. Chem.* **2009**, *74*, 1314−1321.

(9) Glover, J. E.; Martin, D. J.; Plieger, P. G.; Rowlands, G. J. *Eur. J. Org. Chem.* **2013**, 1671−1675.

(10) Ohmatsu, K.; Kiyokawa, M.; Ooi, T. *J. Am. Chem. Soc.* **2011**, *133*, 1307−1309.

(11) (a) Dey, S.; Datta, D.; Pathak, T. *Synlett* **2011**, 2521−2524. (b) Kayet, A.; Pathak, T. *J. Org. Chem.* **2013**, *78*, 9865−9875. (c) Dey, S.; Pathak, T. *RSC Adv.* **2014**, *4*, 9275−9278. (d) Sahu, D.; Dey, S.; Pathak, T.; Ganguly, B. *Org. Lett.* **2014**, *16*, 2100−2103.

(12) Bhattacharya, R.; Atta, A. K.; Dey, D.; Pathak, T. *J. Org. Chem.* **2009**, *74*, 669−674.

(13) (a) Tiecco, M.; Testaferri, L.; Santi, C.; Tomassini, C.; Marini, F.; Bagnoli, L.; Temperini, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3131−3133. (b) Tilliet, M.; Frölander, A.; Levacher, V.; Moberg, C. *Tetrahedron* **2008**, *64*, 10244−10249.

(14) (a) Wu, J.-C.; Chattopadhyaya, J. *Tetrahedron* **1989**, *45*, 4507−4522. (b) Wu, J.-C.; Chattopadhyaya, J. *Tetrahedron* **1990**, *46*, 2587−2592. (c) Tong, W.; Wu, J.-C.; Sandström, A.; Chattopadhyaya, J. *Tetrahedron* **1990**, *46*, 3037−3060. (d) Tong, W.; Xi, Z.; Gioeli, C.; Chattopadhyaya, J. *Tetrahedron* **1991**, *47*, 3431−3450.

(15) (a) Reich, H. J. *Acc. Chem. Res.* **1979**, *12*, 22−30. (b) Reich, H. J.; Wollowitz, S. *Organic Reactions* **1993**, *44*, 1−296. (c) Back, T. G. *Organoselenium Chemistry: A Practical Approach*; Oxford University Press: New York, 1999; pp 1−295. (d) Back, T. G. *Organoselenium Chem.* **1999**, 7−33. (e) Toshimitsu, A.; Uemura, S. *Organoselenium Chem.* **1999**, 241−256. (f) Nishibayashi, Y.; Uemura, S. *Top. Curr. Chem.* **2000**, *208*, 201−235. (g) Procter, D. J. *J. Chem. Soc. Perkin Trans. 1* **2001**, 335−354. (h) Mukherjee, A. J.; Zade, S. S.; Singh, H. B.; Sunoj, R. B. *Chem. Rev.* **2010**, *110*, 4357−4416. (i) Nishibayashi, Y.; Uemura, S. *Organoselenium Chem.* **2012**, 287−320. (j) Marini, F.; Sternativo, S. *Synlett* **2013**, 11−19.

(16) (a) Shimizu, M.; Kuwajima, I. *J. Org. Chem.* **1980**, *45*, 4063−4065. (b) Posner, G. H.; Hulce, M.; Mallamo, J. P. *J. Org. Chem.* **1981**, *46*, 5246−5248. (c) Ando, R.; Sugawara, T.; Kuwazima, I. *J. Chem. Soc., Chem. Commun.* **1983**, 1514−1515. (d) Kuwajima, I.; Ando, R.; Sugawara, T. *Tetrahedron Lett.* **1983**, *24*, 4429−4432. (e) Ando, R.; Sugawara, T.; Shimizu, M.; Kuwazima, I. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2897−2904. (f) Sugawara, T.; Kuwazima, I. *Tetrahedron Lett.* **1985**, *26*, 5571−5574. (g) Tiecco, M.; Chianelli, D.; Testaferri, L.; Tingoli, M.; Bartoli, D. *Tetrahedron* **1986**, *42*, 4889−4896. (h) Marini, F.; Sternativo, S.; Verme, F. D.; Testaferri, L.; Tiecco, M. *Adv. Synth. Catal.* **2009**, *351*, 1801−1806. (i) Bagnoli, L.; Scarponi, C.; Testaferri, L.; Tiecco, M. *Tetrahedron: Asymmetry* **2009**, *20*, 1506−1514. (j) Sternativo, S.; Marini, F.; Verme, F. D.; Calandriello, A.; Testaferri, L.; Tiecco, M. *Tetrahedron* **2010**, *66*, 6851−6857. (k) Bagnoli, L.; Scarponi, C.; Rossi, M. G.; Testaferri, L.; Tiecco, M. *Chem.—Eur. J.* **2011**, *17*, 993−999. (l) Sternativo, S.; Calandriello, A.; Costantino, F.; Testaferri, L.; Tiecco, M.; Marini, F. *Angew. Chem., Int. Ed.* **2011**, *50*, 9382−9385. (m) Sternativo, S.; Walczak, O.; Battistelli, B.; Testaferri, L.; Marini, F. *Tetrahedron* **2012**, *68*, 10536−10541. (n) Buyvk, T.; Wang, Q.; Zhu, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 1−6. (o) Sternativo, S.; Battistelli, B.; Bagnoli, L.; Santi, C.; Testaferri, L.; Marini, F. *Tetrahedron Lett.* **2013**, *54*, 6755−6757.

(17) (a) Kimiaki, F.; Sadamu, Y.; Toshio, M. *J. Chem. Soc., Chem. Commun.* **1980**, 66−68. (b) Nishimura, Y.; Umezawa, H.; Umezawa, S. *Tetrahedron Lett.* **1981**, *22*, 77−80. (c) Morgans, D. J. *Tetrahedron Lett.* **1981**, *22*, 3721−3724. (d) Rollin, P.; Bencomo, V. V.; Sinaÿ, P. *Synthesis* **1984**, 134−135. (e) Lancelin, J. M.; Pougny, J. R.; Sinaÿ, P. *Carbohydr. Res.* **1985**, *136*, 369−374. (f) Bravo, F.; Kassou, M.; Díaz, Y.; Castillón, S. *Carbohydr. Res.* **2001**, *336*, 83−97. (g) Yang, W.-B.; Wu, C.-Y.; Chang, C.-C.; Wang, S.-H.; Teo, C.-F.; Lin, C.-H. *Tetrahedron Lett.* **2001**, *42*, 6907−6910. (h) Yang, W.-B.; Yang, Y.-Y.; Gu, Y.-F.; Wang, S.-H.; Chang, C.-C.; Lin, C.-H. *J. Org. Chem.* **2002**, *67*, 3773−3782. (i) Jürs, S.; Thiem, J. *Synthesis* **2006**, 2117−2120.

(18) Health, C. E.; Gillam, M. C.; Callis, C. S.; Patto, R. R.; Abelt, C. J. *Carbohydr. Res.* **1998**, *307*, 371−373.

(19) Martin, O. R.; Rafka, R. J.; Szarek, W. A. *Carbohydr. Res.* **1989**, *185*, 77−89.

(20) (a) Anderson, C. D.; Goodman, L.; Baker, B. R. *J. Am. Chem. Soc.* **1958**, *80*, 5247−5252. (b) Wright, J. A.; Taylor, N. F. *Carbohydr. Res.* **1968**, *6*, 347−354. (c) Wright, J. A.; Taylor, N. F.; Fox, J. J. *J. Org. Chem.* **1969**, *34*, 2632−2636.

(21) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 2697−2699.

(22) (a) Taniguchi, M.; Koga, K.; Yamada, S. *Tetrahedron* **1974**, *30*, 3547−3552. (b) Clive, D. L. J.; Wickens, P. L.; Sgarbi, P. W. M. *J. Org. Chem.* **1996**, *61*, 7426−7437.

(23) Das, I.; Suresh, G.; Décout, J.-L.; Pathak, T. *Carbohydr. Res.* **2008**, *343*, 1287−1296.

(24) (a) Williams, N. R. *Adv. Carbohydr. Biochem.* **1970**, *25*, 109−179. (b) Sanki, A. K.; Pathak, T. *Tetrahedron* **2003**, *59*, 7203−7214.

(25) (a) Blumenstein, J. J.; Michejda, C. J. *Tetrahedron Lett.* **1991**, *32*, 183−186. (b) Díaz, D. D.; Punna, S.; Holzer, P.; Mcpherson, A. K.; Sharpless, K. B.; Fokin, V. V.; Finn, M. G. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 4392−4403. (c) Rad, M. N. S.; Behrouz, S.; Nezhad, A. K. *Tetrahedron Lett.* **2007**, *48*, 3445−3449. (d) Angelica, M. V.; Patricia, F. C.; Pedro, M.; Fabiano, R. S.; Jairton, D.; Diogo, L. S. *Tetrahedron* **2013**, *69*, 201−206.

(26) Creary, X.; Anderson, A.; Borphy, C.; Crowell, F.; Funk, Z. *J. Org. Chem.* **2012**, *77*, 8756−8761.