The synthesis of substituted tetrahydrofuran (THF) has been important because they are ubiquitous in many natural products such as annonaceous acetogenins, polyether antibiotics and C-nucleosides.\(^1\)\(^2\) The efficient and stereoselective manner of the preparation of the substituted THF has been a significant challenge for synthetic chemists. There are numerous synthetic methodologies that involve the preparation of the multisubstituted THFs.\(^3\) Among those, the formation of carbon-oxygen or carbon-carbon bonds via intramolecular \(S_n1\), \(S_n2\) or \(S_n2'\) addition reactions is worthy to mention as the effective approaches to these heterocyclic compounds.\(^4\)

An approach that has been envisioned by us is to employ a methodology involving a stereoselective preparation of allenes by the \(S_n2'\) hydride addition to an alkynyloxirane.\(^5\)

The \(S_n\) addition of the hydride to the alkynyloxirane \(A\) afforded the highly stereoselective allenediol \(B\). The stereo-defined allene would be subsequently converted to a \(trans\)-dihydrofuran and the following hydrogenation of the corresponding olefin of the dihydrofuran would offer the trisubstituted THF.

The synthesis was initiated with commercially available enynol \(1.\)\(^6\) The alcohol was protected as a benzyl group. One carbon homoligation of the corresponding lithium acetylide with gaseous formaldehyde at 78 °C first then, warmed to room temperature afforded the propargyl alcohol \(3.\) The epoxidation of the compound \(3\) with \(meta\)-chloroperbenzoic acid gave the alkynyl epoxide \(4.\) The addition of disobutyl aluminium hydride (DABAH) to the alkynyloxirane \(4\) at 0 °C gave the \(cis\)-allenediol \(5\) in 60% yield with the high diastereoselectivity. The \(^1\)H NMR analysis showed exclusively the \(syn\) addition product. The previous example of this type of reaction showed exclusively \(syn\) addition that was contrasted with CuH addition resulting an \(anti\) addition product.\(^7\) Presumably the hydroxy group might assist the aluminium hydride addition resulting the \(syn\) addition product exclusively. Interestingly the addition of DABAH to the alkynyloxirane at -78 °C gave the \(S_n2\) addition adduct \(9\) in 76% yield with a small amount of the allenediol.
EXPERIMENTAL SECTION

General

1H NMR and 13C NMR spectra were recorded using 200 and 300 MHz NMR spectrometers. The chemical shifts are reported in ppm using CDCl3 as solvent and TMS as an internal standard. Infrared spectra were recorded Perkin Elmer Paragon 500 FT-IR spectrometer. Flash chromatography was performed using E. Merck silica gel 60 (200-400 mesh).

(E)-3-Methyl-5-(benzyloxy)-3-penten-1-yne (2)

To a solution of 3.30 g (0.0343 mol) of the trans-alcohol 1 in 10 mL benzene was added 1.50 g (0.0377 mol) of NaH in 60% mineral oil at 0 °C. After the hydrogen evolution stopped 6.20 g (0.036 mol) of benzyl bromide was added. The solution was stirred at 80 °C for 24 hrs. Water was added slowly at 0 °C and then 3% HCl was added. The aqueous layer was separated and extracted with ether three times. The extracts were washed with saturated sodium bicarbonate and subsequently with brine, dried over MgSO4 and concentrated under reduced pressure. The residue was chromatographed on silica gel. Elution with 2% ether in hexanes afforded 4.26 g (67%) of the benzyl ether 2:

IR (film) ν 3300, 2100, 1470, 1600, 1450 cm⁻¹;
1H NMR (200 MHz, CDCl3) δ 7.34 (5H, s, phenyl Hs), 6.10 (1H, t, J=12.0 Hz, vinyl H ), 4.51 (2H, s, benzyl H), 4.10 (2H, d, J=13 Hz, -OCH₂-), 2.84 (1H, s, acetylenic H), 1.08 (3H, s, vinyl CH₃) ppm; MS(EI), m/z (real intensity) 185(27), 149(22), 107(74), 91(100), 77(33), 65(20), 53(12).

(E)-4-Methyl-6-(benzyloxy)-4-hexen-2-yn-1-ol (3)

To a solution of 2.0 g (0.011 mol) of the benzyl ether 2 in 20 mL of THF was added 4.8 mL (0.012 mol) of 2.5 M n-BuLi in hexanes at -78 °C. The solution was stirred for 1 hr and then an excess gaseous formaldehyde was passed into the solution. The solution was stirred for the additional hour. The reaction mixture was warmed to room temperature and quenched with water. The aqueous layer was separated and extracted with ether three times. The extracts were washed with brine, dried over MgSO4 and concentrated under reduced pressure. The residue was chromatographed on silica gel. Elution with...
40% ether in hexanes afforded 1.22 g (52%) of the alcohol 3. IR (film) 3400, 1030, 1600, 1450 cm⁻¹.
1H NMR (200 MHz, CDCl₃) δ 7.33 (5H, m, phenyl Hs), 6.02 (1H, brt, J=12 Hz, vinyl H), 4.50 (2H, s, benzyl CH₂), 3.83 (2H, s, -CH₂OH), 4.09 (3H, d, J=13 Hz, -OCH₂-), 1.78 (3H, s, vinyl CH₂) ppm.

(E)-1-Methyl-4,5-epoxy-6-(benzoxyl)-4-hexen-2-yn-1-ol (4)

To a solution of 2.30 g (0.0106 mol) of the enol 3 in 25 mL of CH₂Cl₂ was added 3.67 g (0.0213 mol) of m-CPBA. The solution was stirred for 3.6 h at room temperature. The solution was quenched with saturated NaHCO₃. The aqueous layer was separated and extracted with ether three times. The extracts were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. The residue was chromatographed on silica gel. Elution with 50% ether in hexanes afforded 1.36 g (56%) of the epoxyd 4. IR (film) 3450, 2250, 1600, 1450 cm⁻¹. 1H NMR (200 MHz, CDCl₃) δ 7.34 (5H, m, phenyl Hs), 4.36 (2H, ABX, J×J=11 Hz, Jₓ=10 Hz, J₆=22 Hz, benzylic CH₃), 4.28 (2H, s, -CH₂OH), 3.50 (2H, m, -OC₃H₅), 3.41 (1H, dd, Jₓ=11, J₆=10 Hz, epoxide H), 1.49 (3H, s, vinyl CH₂) ppm.

rel-(2S,5R)-4-Methyl-6-(benzoxyl)-2,3-hexadien-1,5-diol (5a)

To a solution of 200 mg (0.696 mmol) of the trans-alkynylloxirane 4 in 3 mL of CH₂Cl₂ was added 0.23 mL of 1 M DIBAH in hexanes at 0 °C. The solution was stirred for 1.5 h and extracted with ether three times. The extracts were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. The residue was chromatographed on silica gel. Elution with 75% ether in hexanes afforded 120 mg (60%) of the trans-allenenediol 5a. IR (film) 3400, 1980, 1450 cm⁻¹. 1H NMR (200 MHz, CDCl₃) 7.37 (5H, m, phenyl Hs), 5.54 (1H, brs, vinyl H), 4.60 (2H, s, benzylic Hs), 4.25 (1H, m, methine H), 4.10 (2H, d, J=2.0 Hz, CH₃OH), 3.62 and 3.52 (2H, m, methylene), 3.20 (1H, brs, -OH), 2.91 (1H, brs, -OH), 1.77 (3H, s, vinyl CH₃) ppm.
13C NMR (125 MHz, CDCl₃) 199.70, 173.63, 128.42, 127.84, 102.98, 94.26, 73.45, 72.55, 71.22, 59.96, 15.64 ppm.

rel-(2R,3R,5R)-5-[1-tert-Butyl-dimethyl-silyl-oxymethyl]-3-methylytetrahydrofuran-2-y1-methanol (8)

To a solution of 130 mg (0.037 mmol) of the dihydrofuran in 2 mL of ethyl acetate was added 65 mg of palladium on charcoal. The suspension was stirred for 2 days. The reaction mixture was filtered. The filtrate was concentrated under reduced pressure. The residue was chromatographed on silica gel. Elution with 60% ether in hexanes afforded 81 mg (88%) of the tetrahydrofuran 8. IR (film) 3450, 1480, 1250 cm⁻¹. 1H NMR (300 MHz, CDCl₃) δ 3.98 (1H, m, H-5), 3.69 (1H, dd, J=8.7 Hz and 2.4 Hz, H-1), 3.57 (2H, d, J=4.5 Hz, -CH₂OTBS), 3.50-3.42 (3H, m, -CH₂OH), 2.99 (2H, m, methylene), 0.97 (3H, d, J=6.0 Hz, -C₂H₅), 0.84 (9H, s, Si(CH₃)₃), 0.08 (6H, s, -Si(CH₃)₃) ppm.
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8. The enylol 1 was purchased from Sigma-Aldrich Fine Chemicals.