AN EFFICIENT SYNTHESIS OF OPTICALLY ACTIVE 4-BENZYLOXY-3-HYDROXY-1-BUTYNE AND ITS CROSS-COUPLING REACTION

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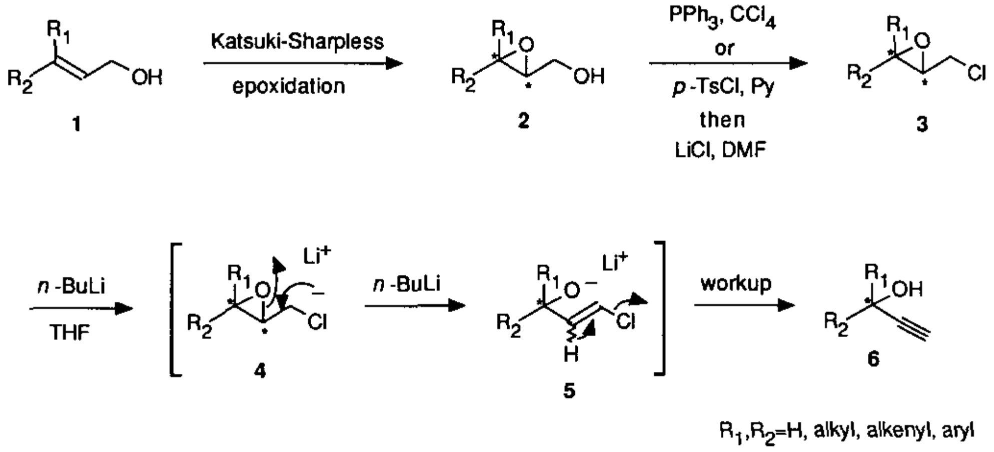
Abstract —— An efficient procedure for the synthesis of optically active 4-benzyloxy-3-hydroxy-1-butyne (**12**: R=H) has been established starting with optically active tartrate ester. Cross-coupling reaction of the resulted acetylene (**12**: R=H) with some aromatic halides (**13a~h**) and transformation of the arylacetylenes (**14a~h**), thus obtained, into the allylic amine derivatives (**17a~h**) have also been examined *via* the allylic alcohol intermediates (**15a~h**) by sequential stereoselective reduction and [3,3] sigmatropic rearrangement.

Recently, we have developed[1] an efficient general method for the preparation of chiral 3-hydroxyacetylene functionalities (**6**) starting from terminal allylic alcohols (1) by the Katsuki-Sharpless epoxidation, followed by the *n*-butyllithium-promoted double elimination reaction of the chloroepoxy intermediates (3) in tetrahydrofuran (THF) (**Scheme 1**). This procedure using chiral tartrate ester as chiral inducer, however, seemed to be less efficient for the preparation of optically pure 4-benzyloxy-3-hydroxy-1-butyne[2] (**12**: R=H), because its methoxy analogue (**12**:

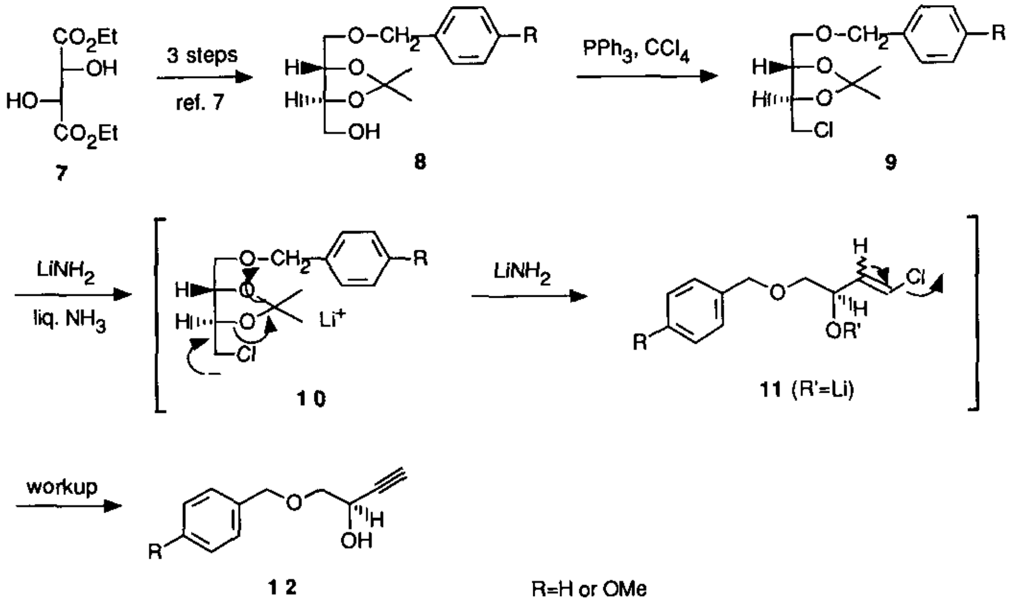


Scheme 1

R=OMe) could have been directly obtained from chiral tartrate ester (**7**) preserving one of its chiral centers *via* **8** and **9** by the lithium amide promoted double elimination reaction in liquid ammonia[3] (**Scheme 2**). In connection to our synthesis of the mycinolide antibiotics[2d] as well as other synthetic projects,[2] we report herewith an efficient synthesis of 4-benzyloxy-3-hydroxy-1-butyne (**12**: R=H) by employing the *n*-butyllithium-promoted double elimination procedure[1] which does not require generation of lithium amide in liquid ammonia.

We next examined the cross-coupling reaction[2a] between the resulted chiral terminal acetylene (**12**: R=H) and some aromatic halides (**13a~h**) under sonication conditions[2a,4] to obtain the corresponding arylacetylene derivatives (**14a~h**). Using these coupling products we further examined the synthesis of optically active allylic amine derivatives (**17a~h**) by sequential stereoselective reduction followed by [3,3] sigmatropic rearrangement[5,6] *via* the allylic alcohols (**15a~h**) and the imidate intermediates (**16a~h**) thereof.

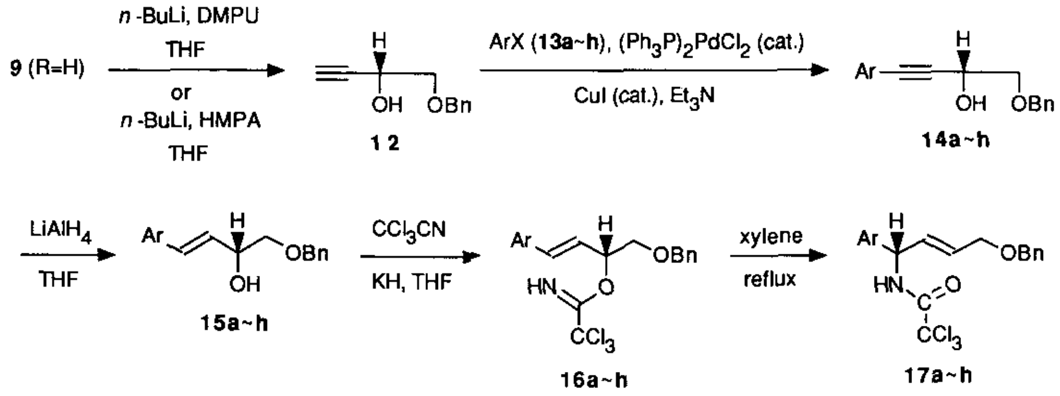
We first treated the chloride (**9**: R=H), obtained from diethyl L-tartrate (**7**) *via* the threitol derivative[7] (**8**: R=H), with an excess of *n*-butyllithium (3~7 equiv.) in THF at −50 ~ −10 °C which could have smoothly converted the chloroepoxides (**3**) into the 3-hydroxyacetylenes[1] (**6**). Contrary to our expectation, the reaction, however, did not



Scheme 2

complete under these conditions which gave rise to a mixture of the acetylene (**12**: R=H) and its precursor vinyl chloride (**11**: R=R'=H). Since exclusive formation of the acetylene (**12**: R=H) could not be realized with more excessive use of *n*-butyllithium even at higher temperature, we added *N*,*N*'-dimethylpropyleneurea (DMPU) as co-solvent which dramatically accelerated the double elimination reaction to afford the desired acetylene (**12**: R=H) as a sole product. The same effect was also observed with the addition of hexamethylphosphoric triamide (HMPA) as co-solvent.[8] The yield of (**12**: R=H) was reached to 96~97% when the chloride (**9**) was exposed to eight equivalents of *n*-butyllithium in THF in the presence of eight equivalents of DMPU or HMPA.

It is noteworthy that the original chiral integrity of tartrate ester (**7**) was virtually preserved under these conditions which could be ascertained (≥98% ee) by ^{1}H nmr (500 MHz) examination of its *R*- and *S*-α-methoxy-α-trifluoromethylphenylacetates (MTPA esters).[9]



Scheme 3

Table 1: Yields and specific rotations of the products (**14**, **15**, and **17**)

Entry	**13**	**14**: %: $[\alpha]_D{}^a$ (c)	**15**: %: $[\alpha]_D{}^a$ (c)	**17**: %: $[\alpha]_D{}^a$ (c)
1	**13a**: C_6H_5I	**14a**: 90.0: +1.46° (0.68)	**15a**: 81.3: −1.55° (1.10)	**17a**: 49.5: −18.5° (6.96)
2	**13b**: 4-MeC_6H_4I	**14b**: 93.0: +4.00° (1.00)	**15b**: 92.7: −1.94° (1.03)	**17b**: 0^b
3	**13c**: 2-F-C_6H_4I	**14c**: 76.2: +5.28° (1.34)	**15c**: 80.2: +3.40° (1.32)	**17c**: 18.1: −12.7° (1.62)
4	**13d**: 3-F-C_6H_4I	**14d**: 77.5: +32.8° (1.28)	**15d**: 83.1: +4.18° (1.30)	**17d**: 15.5: −21.6° (1.37)
5	**13e**: 4-F-C_6H_4I	**14e**: 77.1: +3.78° (1.30)	**15e**: 78.6: +1.04° (1.15)	**17e**: 31.1: −16.7° (3.08)
6	**13f**: 4-$MeOC_6H_4I$	**14f**: 69.5: +9.28° (1.22)	**15f**: 72.8: −5.09° (1.02)	**17f**: 0^b
7	**13g**: 2-I-thiophene	**14g**: 67.2: +5.46° (1.15)	**15g**: 89.6: −2.14° (1.12)	**17g**: 9.9: +14.6° (0.83)
8	**13h**: 2-Br-pyridine	**14h**: 83.2: +3.10° (1.26)	**15h**: 67.9: +1.05° (1.24)	**17h**: 0^b

(a) Measured in $CHCl_3$ at 25±5 °C. (b) Stable imidate (**16**) was not formed.

Cross-coupling reaction of the acetylene (**12**: R=H) with eight aromatic halides (**13a**~**h**) proceeded without difficulty in triethylamine in the presence of bis(triphenylphosphine)palladium(II) chloride and copper(I) iodide under sonication conditions[2a,4] to afford the corresponding arylacetylenes (**14a**~**h**), respectively, in satisfactory yields. Refluxing the arylacetylenes (**14a**~**h**) with lithium aluminum hydride in THF[2a] gave the corresponding allylic alcohols (**15a**~**h**) having *E*-configuration, selectively, in good yields.

Transformation[5] of allylic alcohols (**15a**~**h**) into the corresponding allylic amine derivatives (**17a**~**h**) *via* the imidate intermediates (**16a**~**h**), however, brought about limited success mostly due to difficulty in the formation of the imidates (**16**) though the subsequent [3,3] sigmatropic reaction seemed to proceed smoothly (**Scheme 3**: **Table 1**).

Table 2: Spectral data of the compounds (**14**, **15**, and **17**)

	Ir (film) ν_{max} (cm^{-1})	^{1}H nmr (CDCl$_3$) δ	ms (m/z)	Exact mass *Anal.* Calcd : Found
14a	3400, 2230	2.58 (d, *J*=4.8 Hz, 1H), 3.64 (dd, *J*=10.4, 7.3 Hz, 1H), 3.74 (dd, *J*=10.4, 3.8 Hz, 1H), 4.63 (s, 2H), 4.77 (ddd, *J*=7.3, 4.8, 3.8 Hz, 1H), 7.20-7.45 (m, 10H)	252 (M$^+$), 235, 131 (100%), 91	$C_{17}H_{16}O_2$ (M$^+$) 252.1150 252.1172
14b	3420, 2230	2.32 (s, 3H), 2.62 (d, *J*=4.6 Hz, 1H), 3.63 (dd, *J*=10.0, 7.4 Hz, 1H), 3.73 (dd, *J*=10.0, 3.8 Hz, 1H), 4.63 (s, 2H), 4.76 (ddd, *J*=7.4, 4.6, 3.8 Hz, 1H), 7.07 (d, *J*=8.6 Hz, 2H), 7.22-7.38 (m, 7H)	266 (M$^+$), 249, 145 (100%), 91	$C_{18}H_{18}O_2$ (M$^+$) 266.1306 266.1317
14c	3420, 2240	2.67 (d, *J*=4.6 Hz, 1H), 3.66 (dd, *J*=10.0, 6.9 Hz, 1H), 3.75 (dd, *J*=10.0, 3.9 Hz, 1H), 4.64 (s, 2H), 4.78 (ddd, *J*=6.9, 4.6, 3.9 Hz, 1H), 7.04 (m, 2H), 7.16-7.44 (m, 7H)	270 (M$^+$), 252, 149 (100%), 91	$C_{17}H_{15}O_2F$ (M$^+$) 270.1055 270.1069
14d	3400, 2230	2.62 (br, 1H), 3.64 (dd, *J*=9.9, 7.4 Hz, 1H), 3.73 (dd, *J*=9.9, 3.8 Hz, 1H), 4.63 (s, 2H), 4.75 (m, 1H), 6.94-7.37 (m, 9H)	270 (M$^+$), 252, 149 (100%), 91	$C_{17}H_{15}O_2F$ (M$^+$) 270.1055 270.1080
14e	3410, 2240	2.59 (d, *J*=4.7 Hz, 1H), 3.63 (dd, *J*=9.4, 6.9 Hz, 1H), 3.72 (dd, *J*=9.4, 4.1 Hz, 1H), 4.63 (s, 2H), 4.75 (ddd, *J*=6.9, 4.7, 4.1 Hz, 1H), 6.96 (dd, *J*=8.6, 8.6 Hz, 2H), 7.23-7.43 (m, 7H)	270 (M$^+$), 252, 149 (100%), 91	$C_{17}H_{15}O_2F$ (M$^+$) 270.1055 270.1035
14f	3440, 2230	2.57 (d, *J*=4.6 Hz, 1H), 3.63 (dd, *J*=10.2, 7.3 Hz, 1H), 3.73 (dd, *J*=10.2, 3.7 Hz, 1H), 3.78 (s, 3H), 4.63 (s, 2H), 4.76 (ddd, *J*=7.3, 4.6, 3.7 Hz, 1H), 6.79 (d, *J*=8.7 Hz, 2H), 7.24-7.38 (m, 7H)	282 (M$^+$), 265, 161 (100%), 91	$C_{18}H_{18}O_3$ (M$^+$) 282.1256 282.1268
14g	3420, 2230	2.61 (d, *J*=4.6 Hz, 1H), 3.63 (dd, *J*=9.8, 7.4 Hz, 1H), 3.75 (dd, *J*=9.8, 3.9 Hz, 1H), 4.61 (s, 2H), 4.76 (ddd, *J*=7.4, 4.6, 3.9 Hz, 1H), 6.92 (dd, *J*=6.2, 2.9 Hz, 1H), 7.20 (m, 2H), 7.24-7.36 (m, 5H)	258 (M$^+$), 137 (100%), 91	$C_{15}H_{14}O_2S$ (M$^+$) 258.0714 258.0730
14h	3360, 2230	3.06 (br, 1H), 3.67 (dd, *J*=9.8, 7.4 Hz, 1H), 3.78	253 (M$^+$),	$C_{16}H_{15}NO_2$ (M$^+$)

		(dd, *J*=9.8, 3.8 Hz, 1H), 4.58 (d, *J*=12.0 Hz, 1H), 4.64 (d, *J*=12.0 Hz, 1H), 4.79 (dd, *J*=7.4, 3.8 Hz, 1H), 7.15-7.44 (m, 7H), 7.60 (ddd, *J*=7.8, 7.8, 1.4 Hz, 1H), 8.52 (br s, 1H)	235, 132, 91 (100%)	253.1103	253.1094
15a	3430	2.55 (d, *J*=3.2 Hz, 1H), 3.44 (dd, *J*=9.6, 8.0 Hz, 1H), 3.61 (dd, *J*=9.6, 3.4 Hz, 1H), 4.51 (m, 1H), 4.59 (s, 2H), 6.15 (dd, *J*=16.2, 6.5 Hz, 1H), 6.68 (dd, *J*=16.2, 1.3 Hz, 1H), 7.16-7.40 (m, 10H)	254 (M$^+$), 236, 133 (100%), 91	$C_{17}H_{18}O_2$ (M$^+$) 254.1307	 254.1319
15b	3420	2.35 (s, 3H), 2.58 (d, *J*=3.2 Hz, 1H), 3.47 (dd, *J*=10.0, 7.9 Hz, 1H), 3.62 (dd, *J*=10.0, 3.4 Hz, 1H), 4.52 (m, 1H), 4.60 (s, 2H), 6.13 (dd, *J*=16.3, 6.3 Hz, 1H), 6.66 (d, *J*=16.3 Hz, 1H), 7.11 (d, *J*=9.1 Hz, 2H), 7.27 (d, *J*=9.1 Hz, 2H), 7.30-7.40 (m, 5H)	268 (M$^+$), 250, 147 (100%), 91	$C_{18}H_{20}O_2$ (M$^+$) 268.1463	 268.1439
15c	3450	2.40 (br, 1H), 3.44 (dd, *J*=9.7, 7.9 Hz, 1H), 3.61 (dd, *J*=9.7, 3.4 Hz, 1H), 4.52 (m, 1H), 4.58 (s, 2H), 6.25 (dd, *J*=16.2, 6.1 Hz, 1H), 6.82 (d, *J*=16.2 Hz, 1H), 6.92-7.44 (m, 9H)	272 (M$^+$), 237, 151 (100%), 91	$C_{17}H_{17}O_2F$ (M$^+$) 272.1212	 272.1218
15d	3420	2.50 (br, 1H), 3.43 (dd, *J*=9.7, 7.9 Hz, 1H), 3.60 (dd, *J*=9.7, 7.9 Hz, 1H), 4.50 (m, 1H), 4.58 (s, 2H), 6.15 (dd, *J*=16.4, 5.9 Hz, 1H), 6.64 (d, *J*=16.4 Hz, 1H), 6.90 (m, 1H), 7.08 (m, 1H), 7.23 (m, 1H), 7.27-7.40 (m, 6H)	272 (M$^+$), 255, 151 (100%), 91	$C_{17}H_{17}O_2F$ (M$^+$) 272.1212	 272.1186
15e	3430	2.56 (d, *J*=3.3 Hz, 1H), 3.44 (dd, *J*=9.8, 7.8 Hz, 1H), 3.61 (dd, *J*=9.8, 3.4 Hz, 1H), 4.50 (m, 1H), 4.58 (s, 2H), 6.06 (dd, *J*=16.2, 6.1 Hz, 1H), 6.64 (d, *J*=16.2 Hz, 1H), 6.97 (dd, *J*=8.9, 8.9 Hz, 2H), 7.24-7.39 (m, 7H)	272 (M$^+$), 198, 151, 91 (100%)	$C_{17}H_{17}O_2F$ (M$^+$) 272.1212	 272.1209
15f	3460	2.55 (d, *J*=2.9 Hz, 1H), 3.45 (dd, *J*=9.8, 8.6 Hz, 1H), 3.61 (dd, *J*=9.8, 3.4 Hz, 1H), 3.79 (s, 3H), 4.49 (m, 1H), 4.59 (s, 2H), 6.02 (dd, *J*=16.3, 6.3 Hz, 1H), 6.62 (d, *J*=16.3 Hz, 1H), 6.68 (d, *J*=8.9 Hz, 2H), 7.30 (d, *J*=8.9 Hz, 2H), 7.28-7.38 (m, 5H)	284 (M$^+$), 253, 163 (100%), 91	$C_{18}H_{20}O_3$ (M$^+$) 284.1412	 284.1395
15g	3440	2.22 (br, 1H), 3.40 (dd, *J*=9.7, 8.2 Hz, 1H), 3.58 (dd, *J*=9.7, 3.4 Hz, 1H), 4.45 (m, 1H), 4.57 (s, 2H), 5.98 (dd, *J*=16.0, 5.9 Hz, 1H), 6.79 (d, *J*=16.0 Hz, 1H), 6.92 (d, *J*=3.7 Hz, 2H), 7.12 (dd, *J*=3.7, 3.7 Hz, 1H), 7.26-7.38 (m, 5H)	260 (M$^+$), 229, 139, 91 (100%)	$C_{15}H_{15}O_2S$ (M$^+$) 260.0871	 260.0896

15h	3400	2.60 (br, 1H), 3.45 (dd, *J*=9.5, 7.9 Hz, 1H), 3.68 (dd, *J*=9.5, 3.4 Hz, 1H), 4.60 (s, 2H), 4.60 (m, 1H), 6.64 (dd, *J*=15.9, 3.4 Hz, 1H), 6.84 (d, *J*=15.9 Hz, 1H), 7.05-7.42 (m, 7H), 7.63 (ddd, *J*=7.7, 7.7, 1.7 Hz, 1H), 8.54 (br d, *J*=4.6 Hz, 1H)	255 (M^+), 136 (100%), 91	$C_{16}H_{17}NO_2$ (M^+) 255.1259 255.1239
17a	3430, 3330, 1700	4.07 (dd, *J*=5.4, 1.1 Hz, 2H), 5.56 (dd, *J*=7.1, 5.7 Hz, 1H), 5.79 (ddt, *J*=15.9, 5.4, 1.1 Hz, 1H), 5.95 (ddt, *J*=15.9, 5.7, 1.1 Hz, 1H), 6.88 (d, *J*=7.1 Hz, 1H), 7.20-7.44 (m, 10H)	363, 361 (M^+-HCl), 130, 91 (100%)	$C_{19}H_{17}NO_2{}^{35}Cl^{37}Cl$ (M^+-HCl) 363.0607 363.0580 $C_{19}H_{17}NO_2{}^{35}Cl_2$ (M^+-HCl) 361.0637 361.0628
17c	3430, 3330, 1705	4.03 (d, *J*=5.0 Hz, 2H), 4.49 (s, 2H), 5.68 (m, 1H), 5.74 (dt, *J*=15.6, 5.0 Hz, 1H), 5.96 (dd, *J*=15.6, 5.7 Hz, 1H), 7.04-7.66 (m, 9H)	310, 308 (M^+-C_7H_7O), 148, 91 (100%)	$C_{12}H_{10}NO_2F^{35}Cl_2{}^{37}Cl$ (M^+-C_7H_7O) 309.9782 309.9771 $C_{12}H_{10}NO_2F^{35}Cl_3$ (M^+-C_7H_7O) 307.9812 307.9819
17d	3430, 3330, 1705	4.07 (d, *J*=4.6 Hz, 2H), 4.52 (s, 2H), 5.54 (dd, *J*=7.4, 5.3 Hz, 1H), 5.80 (dt, *J*=15.7, 4.6 Hz, 1H), 5.94 (dd, *J*=15.7, 5.3 Hz, 1H), 6.89 (d, *J*=7.4 Hz, 1H), 6.94-7.13(m, 3H)	310, 308 (M^+-C_7H_7O), 148, 91 (100%)	$C_{12}H_{10}NO_2F^{35}Cl_2{}^{37}Cl$ (M^+-C_7H_7O) 309.9782 309.9764 $C_{12}H_{10}NO_2F^{35}Cl_3$ (M^+-C_7H_7) 307.9812 307.9786
17e	3420, 3330, 1710	4.07 (dd, *J*=4.6, 0.6 Hz, 2H), 4.52 (s, 2H), 5.53 (dd, *J*=7.0, 5.7 Hz, 1H), 5.78 (dt, *J*=15.5, 4.6 Hz, 1H), 5.94 (ddt, *J*=15.5, 5.7, 0.6 Hz, 1H), 6.86 (d, *J*=7.0 Hz, 1H), 7.04 (dd, *J*=8.9, 8.9 Hz, 2H), 7.20-7.38 (m, 7H)	309, 307 (M^+-C_7H_8O), 148, 91 (100%)	$C_{12}H_9NO_2F^{35}Cl_3$ (M^+-C_7H_8O) 306.9734 306.9762
17g	3410, 3320, 1705, 1670	4.09 (d, *J*=4.6 Hz, 2H), 4.47 (s, 2H), 5.81 (m, 1H), 5.90 (dt, *J*=15.2, 4.6 Hz, 1H), 6.02 (dd, *J*=15.2, 5.1 Hz, 1H), 6.92 (m, 1H), 7.00 (m, 2H), 7.20-7.44 (m, 6H)	297, 295 (M^+-C_7H_7O), 178, 91 (100%)	$C_{10}H_{18}NOS^{35}Cl_3$ (M^+-C_7H_7O) 294.9392 294.9429

EXPERIMENTAL SECTION

Optical rotations were measured with a JASCO-DIP-370 digital polarimeter. Ir spectra were measured with a JASCO-IR-700 spectrophotometer. ^1H Nmr spectra were recorded on JEOL-JNM-FX90A (90 MHz) and JEOL-JNM-GX500 (500 MHz) spectrometers. Mass spectra were measured with a JEOL JMS-DX303 instrument. Reactions were carried out under argon.

(2*S*,3*S*)-1-Benzyloxy-4-chloro-2,3-(*O*-isopropylidene)butane-2,3-diol (9: R=H) —— A mixture of the alcohol[7] (**8**: R=H) (3.20 g, 12.7 mmol), prepared from diethyl L-tartrate (**7**), and triphenylphosphine (4.98 g, 19.0 mmol) was refluxed for 30 h. After cooling the mixture was filtered through Celite pad and evaporated under reduced pressure. The residue was purified on a silica gel column (100 g) using Et_2O-hexane (1:4 v/v) as eluent to give the chloride (**9**: R=H) (3.35 g, 98%) as a colorless oil; $[\alpha]_D^{28}$ +2.09° (*c* 1.05, $CHCl_3$). Ir (film) ν_{max}: 1380, 1370, 840, 740, 700 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 1.44 (s, 6H), 3.48-3.84 (m, 4H), 3.92-4.24 (m, 2H), 4.59 (s, 2H), 7.33 (s, 5H); ms (m/z): 272, 270 (M^+), 91 (100%). Exact mass Calcd for $C_{14}H_{19}O_3{}^{37}Cl$: 272.0993 and for $C_{14}H_{19}O_3{}^{35}Cl$: 270.1023. Found: 272.1026 and 270.1016. *Anal.* Calcd for $C_{14}H_{19}O_3Cl$: C 62.10, H 7.07, Cl 13.09. Found: C 62.37, H 7.30, Cl 13.23.

(*R*)-4-Benzyloxy-3-hydroxy-1-butyne (12: R=H) —— (a) To a stirred solution of *n*-butyllithium (15% v/v in hexane, 62.0 ml, 99.2 mmol) in THF (100 ml) containing dimethylpropyleneurea (DMPU) (12.0 ml, 99.2 mmol) was added dropwise the chloride (**9**: R=H) (3.35 g, 12.4 mmol) in THF (20 ml) at –30 °C and the stirring was continued for 2 weeks at room temperature. The mixture was treated with saturated aqueous $NaHCO_3$ and extracted with ether. The extract was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified on a silica gel column (300 g) using AcOEt-hexane (1:4 v/v) as eluent to give the acetylene (**12**: R=H) (2.10 g, 96%) as a colorless oil.

(b) To a stirred solution of *n*-butyllithium (1.40 M in hexane, 62.0 ml, 86.8 mmol) in THF (100 ml) containing HMPA (17.2 ml, 98.9 mmol) was added dropwise the chloride (**9**: R=H) (3.35 g, 12.4 mmol) in THF (20 mml) at –30 °C and the stirring was continued for 1 h at the same temperature. The mixture was treated with saturated aqueous NH_4Cl and extracted with ether. The extract was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified on a silica gel column (80 g) using Et_2O-hexane (1:4 v/v) as eluent to give the acetylene (**12**: R=H) (2.11 g, 97%) as a colorless oil; $[\alpha]_D^{29}$ –10.80° (*c* 1.00, $CHCl_3$). Optical purity was determined to be ≥98% ee by measurement of ^1H nmr spectra of *R*- and *S*-MTPA esters. Spectroscopic data (ir, ^1H nmr, ms) were identical with those of an authentic material.[1]

(*R*)-4-Benzyloxy-3-hydroxy-1-phenyl-1-butyne (14a) —— A mixture of the acetylene (**12**: R=H) (352 mg, 2.0 mmol), $(Ph_3P)_2PdCl_2$ (42.1 mg, 60.0 μmol), CuI (7.6 mg, 40.0 μmol) and iodobenzene (**13a**) (816 mg, 4.0 mmol) in triethylamine (10 ml) was sonicated for 2 h at 40 °C. The mixture was diluted with ether and filtered through Celite pad. The filtrate was evaporated and the residue was purified on a silica gel column (25 g) using AcOEt-hexane (1:4 v/v) as eluent to give the phenylacetylene (**14a**) (453 mg, 90%) as a colorless oil. Spectral data are shown in **Table 2**.

Compounds (**14b~h**) were obtained by the same treatments on (**13b~h**) (see, **Tables 1 and 2**).

(*R*)-(*E*)-4-Benzyloxy-3-hydroxy-1-phenyl-1-butene (15a) —— To a stirred solution of the acetylene (**14a**) (373 mg, 1.48 mmol) in THF (10 ml) was added $LiAlH_4$ (85.0 mg, 2.22 mmol) and the mixture was refluxed for 1.5 h. After cooling, the mixture was treated with 30% NH_4OH and was filtered through Celite pad. The filtrate was dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified on a silica gel column (15 g) using AcOEt-hexane (3:7 v/v) as eluent to give the allyl alcohol (**15a**) (306 mg, 81 mmol) as a colorless oil. Spectral data are shown in **Table 2.**

Compounds (**15b~h**) were obtained by the same treatments on (**14b~h**) (see, **Tables 1** and **2**).

4-Benzyloxy-1-trichloroacetylamino-1-phenyl-2-butene (17a) —— To a stirred solution of the allyl alcohol (**14a**) (140 mg, 0.55 mmol) in THF (1.0 ml) was added sequentially KH (35% in oil, 13.0 mg, 0.11 mmol) and CCl_3CN (66.0 μl, 0.66 mmol) at 0 °C. After 3 h, the mixture was diluted with hexane and the insoluble material was removed by filtration using Celite pad. The filtrate was evaporated under reduced pressure and the residue containing crude imidate (**16a**) was dissolved in xylene (3.0 ml) and refluxed for 15 h. After cooling the mixture was evaporated under reduced pressure and the residue was taken up into ether. The ethereal layer was washed with water, brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified on a medium pressure silica gel column using AcOEt-hexane (1:4 v/v) as eluent to give the amide (**17a**) (106 mg, 50%) as a pale yellow oil. Spectral data are shown in **Table 2**.

Compound (**17c~e, g**) were obtained by the same treatments on (**15a~h**) (see, **Tables 1** and **2**).

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