Asymmetric Synthesis of Monoprotected Double Allylic Alcohols

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Abstract: The enantioselective synthesis of mono-TBS protected, double allylic alcohols **5** (ee = 90–94%) employing the SAMP/RAMP-hydrazone methodology is reported. Acetonide protected, α-substituted ketodiols **2** were synthesized from SAMP-hydrazone **1** which were converted to exocyclic olefins **3** by a racemization-free Wittig reaction. Acidic acetal cleavage to **4** followed by selective TBS protection furnished title compounds **5** in very good overall yields and enantiomeric excesses.

Key words: asymmetric synthesis, hydrazones, Wittig reaction, allylic alcohols, protecting groups

The double allylic alcohol moiety is a crucial structural feature of many natural products found, for example, in metabolites of marine sponges and microorganisms with ionophoric activity.[1,2] Moreover, due to their triple functionality there is a great potential for derivatisation and use as a versatile building block in asymmetric and natural product synthesis.[3–13] However, to the best of our knowledge only two asymmetric approaches to this type of substrates with high enantiomeric excesses have been reported. One is an olefination, epoxidation and rearrangement pathway.[3,4,9] The other is the Baylis–Hillman[14] reaction using either chiral auxiliaries[15] or chiral catalysts.[16] Both of them proceed with relatively low yields and slow reaction rates or have restriction regarding the choice of substrates.

Herein, we present a straight forward five step synthesis of monoprotected, double allylic alcohols **A** (Figure) with very good enantiomeric excesses, which allow an enantioselective approach to these versatile building blocks for asymmetric synthesis.

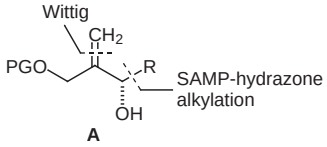
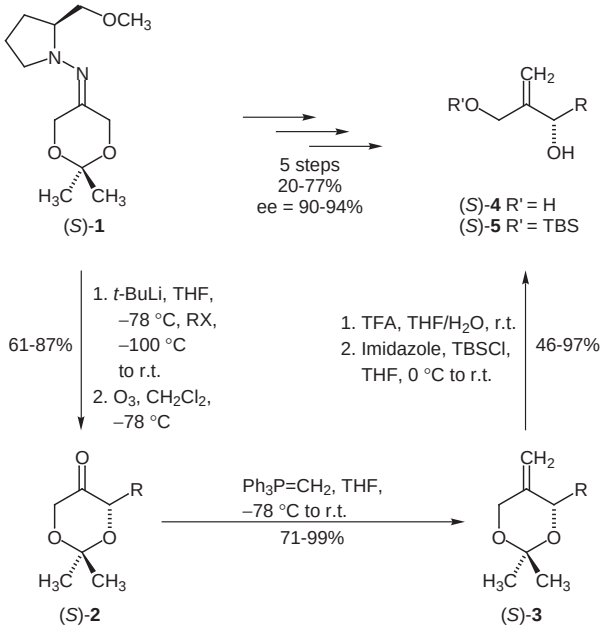


Figure The general structure of the monoprotected double allylic alcohols **A**.

These highly flexible key intermediates should not only be accessible in both enantiomeric forms and high enantiomeric excesses, but also for a wide range of substituents R, for example nonfunctionalized and functionalized alkyl substituents,[17] as well as Michael[18] and aldol adducts.[19] Differentiation between the primary and secondary hydroxy group can be achieved, which leads to the synthesis of derivatives under preservation of the stereocenter. Finally, there is the feasibility to form a new stereogenic center at the prochiral olefinic position through substrate-directed stereoselective reactions,[20] such as, for example, hydrogenation, epoxidation, cyclopropanation or Diels–Alder reactions.

In order to synthesize title double allylic alcohols of type **A**, SAMP-hydrazone (*S*)-**1**, which was readily prepared on a multigram scale by condensation of (*S*)-1-amino-2-methoxymethylpyrrolidine (SAMP) and 2,2-dimethyl-1,3-dioxan-5one,[17] was converted into the acetal protected ketodiols (*S*)-**2** by stereoselective αalkylation following the SAMP/RAMP-hydrazone protocol.[21] Then, *exo*methylene derivatives (*S*)-**3** were synthesized utilizing a racemizationfree Wittig reaction.[22] Subsequent acidic acetal cleavage to (*S*)-**4** followed by *tert*-butyldimethylsilyl (TBS) protection of the primary hydroxy group afforded the title compounds (*S*)-**5** (Scheme).



Scheme

In this manner, a variety of α-substituted ketones (*S*)-**2** were prepared by a two step synthesis[23] starting from SAMP-hydrazone (*S*)-**1** in good overall yields (61–87%) and very good enantiomeric excesses (ee = 90–94%). Al-

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iphatic and sterically hindered, as well as benzylic halides were used as electrophiles for the stereoselective α-alkylation. Oxidative auxiliary cleavage was accomplished utilizing ozone at low temperature (Table 1).

Table 1 Asymmetric Synthesis of 4-Subtituted 2,2-Dimethyl-1,3-dioxan-5-ones (*S*)-**2a–e**

(*S*)-**2**	R	X	Yield[a] (%)	ee[b] (%)	$[\alpha]_D$[c]
(*S*)-**2a**	$(CH_2)_2Ph$	I	87	94	–189.0
(*S*)-**2b**	Bn	Br	84	90	–231.9
(*S*)-**2c**	4-*t*-$BuC_6H_4CH_2$	Br	67	92	–193.7
(*S*)-**2d**	*i*-Pr	I	68	92	–284.4
(*S*)-**2e**	*n*-Bu	I	74[d]; 82[e]	92	–241.2

[a] Overall yield starting from (*S*)-**1**.
[b] Determined by GC on chiral stationary phase by comparison with racemic samples.
[c] All optical rotations were measured in Uvasol grade $CHCl_3$ at $c = 1.00 \pm 0.06$ and $T = 26 \pm 2$ °C.
[d] Yield of α-substituted SAMP-hydrazone.
[e] Yield of dioxanone (*S*)-**2e** after auxiliary cleavage.

The racemization-free Wittig olefination[22] converted the chiral key intermediates (*S*)-**2** into *exo*-methylene derivatives (*S*)-**3** in very good yields (71–99%) (Table 2). Methyltriphenylphosphonium bromide was deprotonated using *t*-BuLi at –78 °C in anhydrous THF to furnish the active Wittig species, which converted the ketones (*S*)-**2** into the exocyclic olefins (*S*)-**3**.

Table 2 Asymmetric Synthesis of 5-*exo*-Methylene, 4-Substituted 2,2-Dimethyl-1,3-dioxan-5-ones (*S*)-**3a–e**

(*S*)-**3**	R	Yield[a] (%)	$[\alpha]_D$[b]
(*S*)-**3a**	$(CH_2)_2Ph$	93	–75.1
(*S*)-**3b**	Bn	94	–91.7
(*S*)-**3c**	4-*t*-$BuC_6H_4CH_2$	99	–76.2
(*S*)-**3d**	*i*-Pr	73	–132.5
(*S*)-**3e**	*n*-Bu	71	–97.2

[a] Based on isolated material after flash chromatography.
[b] All optical rotations were measured in Uvasol grade $CHCl_3$ at $c = 1.00 \pm 0.09$ and $T = 26 \pm 3$ °C.

The acetal protecting group was removed by hydrolysis with trifluoroacetic acid (TFA) in a mixture of THF and water at room temperature to afford the double allylic alcohols (*S*)-**4** in excellent yields after aqueous work up (85–99%) (Table 3).[24] No further purification was necessary in order to obtain products in purities which show suitable spectroscopic data and correct elemental analyses.

Table 3 Asymmetric Synthesis of Double Allylic Alcohols (*S*)-**4a–e**

(*S*)-**4**	R	Yield (%)	Mp (°C)	$[\alpha]_D$[a]
(*S*)-**4a**	$(CH_2)_2Ph$	99	-	–36.9
(*S*)-**4b**	Bn	98	50	–28.2
(*S*)-**4c**	4-*t*-$BuC_6H_4CH_2$	97	62–63	–21.6
(*S*)-**4d**	*i*-Pr	86	49–50	–17.0
(*S*)-**4e**	*n*-Bu	85	-	–25.6

[a] All optical rotations were measured in Uvasol grade $CHCl_3$ at $c = 1.00 \pm 0.07$ and $T = 25 \pm 2$ °C.

Finally, protection of the primary hydroxy group of (*S*)-**4** with *tert*-butyldimethylsilyl chloride (TBSCl) in the presence of imidazole in THF at 0 °C gave the title compounds (*S*)-**5** in very good yields after purification by column chromatography (54–99%)[25] (Table 4). Monoprotected alcohols were observed exclusively.

Table 4 Asymmetric Synthesis of Mono-TBS-Protected, Double Allylic Alcohols (*S*)-**5a–e**

(*S*)-**5**	R	Yield[a] (%)	$[\alpha]_D$[b]
(*S*)-**5a**	$(CH_2)_2Ph$	90	–21.0
(*S*)-**5b**	Bn	99	–12.4
(*S*)-**5c**	4-*t*-$BuC_6H_4CH_2$	99	–10.8
(*S*)-**5d**	*i*-Pr	98	–1.0
(*S*)-**5e**	*n*-Bu	54	–10.5

[a] Based on isolated material after flash chromatography.
[b] All optical rotations were measured in Uvasol grade $CHCl_3$ at $c = 1.00 \pm 0.06$ and $T = 26 \pm 3$ °C.

As a representative example, allylic alcohol (*S*)-**5b** was converted into the respective Mosher ester, which indicated that no racemization has occurred during the last three steps.

In summary, we have developed an efficient five step asymmetric synthesis of monoprotected, double allylic alcohols in good overall yields and very good enantiomeric excesses starting from commercially available 2,2-dimethyl-1,3-dioxan-5-one following the SAMP/RAMP-hydrazone protocol as stereoselective key step.

All moisture sensitive reactions were carried out using standard Schlenk techniques. Solvents were dried and purified by conventional methods prior to use. THF was freshly distilled under argon from Na/Pb alloy and benzophenone. Reagents of commercial quality were used from freshly opened containers. Analytical TLC: Silica gel 60 F_{254} plates, Merck, Darmstadt. Preparative column chromatography: Silica gel 60, particle size 0.040–0.063 mm, Merck, Darmstadt. Optical rotation values were measured on a Perkin-Elmer P 241 (589 nm), solvents used were Merck Uvasol quality.

Elemental analyses were obtained from a Heraeus CHNORapid Elementar Vario EL element analyzer. Melting points were measured on a Büchi 510 apparatus and are uncorrected. Mass spectra: Finnigan SSQ7000 or Finnigan MAT 95 (CI 100 eV, EI 70 eV). IR spectra: Perkin-Elmer FT/IR 1760 (measured in $CHCl_3$; all solid samples as KBr). ^{1}H NMR spectra (300 MHz, 400 MHz), ^{13}C NMR (75 MHz, 100 MHz): Varian Gemini 300, Mercury 300, Inova 400 (solvent: $CDCl_3$, TMS as internal standard). Enantiomeric excesses were determined by gas chromatography on chiral stationary phase (Siemens Sichromat; CP Chirasildex CB; 0.25 mm × 25 m).

SAMP hydrazone (*S*)-**1** was prepared by modification[26] of the method of Woodward and Vorbrüggen reported by Hoppe et al.[27] on a 65 mmol scale.

4-Substituted Dioxanones (*S*)-2; General Procedure

SAMP-hydrazone (*S*)-**1** (10 mmol) was dissolved in anhyd THF (40 mL). *t*-BuLi (11 mmol, 15% in *n*-pentane) was added dropwise by syringe at –78 °C. After stirring for 2 h at this temperature, the mixture was cooled to –100 °C and the electrophile (11 mmol), dissolved in anhyd THF (2 mL), was added slowly. After further stirring for 2 h at –100 °C, the mixture was allowed to warm to r.t. over 15 h. The mixture was quenched with pH 7 buffer solution (2 mL) and diluted with Et_2O (80 mL). The organic layer was washed with pH 7 buffer solution (10 mL) and brine (2 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The obtained monoalkylated SAMP-hydrazone was dissolved in CH_2Cl_2 (50 mL) and flushed with ozone (60 L h^{-1}) at –78 °C for 15 min. The reaction mixture was allowed to warm to r.t. and flushed with argon. After removal of the solvent under reduced pressure, the crude product was purified by flash chromatography (silica gel,; *n*-pentane–Et_2O, 20:1 to 30:1) to afford the 4-substituted dioxanones (*S*)-**2** as colorless oils (Table 5).

Table 5 Spectroscopic Data of 4-Substituted Dioxanones (*S*)-**2a**–**e**[a]

(*S*)-**2**	IR ($CHCl_3$) (cm^{-1})	^{1}H NMR ($CDCl_3$, TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$, TMS), δ	MS (70 eV) *m*/*z* (%)
(*S*)-**2a**	3473, 3086, 3063, 3028, 2989, 2936, 2865, 2633, 2157, 1951, 1875, 1801, 1746, 1604, 1585, 1497, 1455, 1432, 1379, 1323, 1250, 1225, 1173, 1105, 1071, 1036, 991, 974, 918, 867, 853, 774, 750, 701, 623, 605, 582, 538, 517, 490	1.42 (s, 3 H, CH_3), 1.45 (s, 3 H, CH_3), 1.86 (m, 1 H, CHC*H*H), 2.20 (m, 1 H, CHCH*H*), 2.68 (m, 1 H, PhC*H*H), 2.80 (m, 1 H, PhCH*H*), 3.95 (d, *J* = 17.0, 1 H, OC*H*H), 4.15 (ddd, *J* = 1.5, 3.6, 9.1, 1 H, C*H*), 4.24 (dd, *J* = 1.5, 16.9, 1 H, OCH*H*), 7.16–7.29 (m, 5 H, Ph*H*)	24.1, 24.4 (2 C, CH_3), 30.4, 31.2 (2 C, CH_2), 66.7 (OCH_2), 73.8 (CH), 101.1 (CCH_3), 126.3 (*p*CH), 128.3, 128.6 (4 C, OCH, *m*CH), 141.2 (CPh), 209.8 (C=O)	236 (15), 235 (M^+ + 1, 100), 218 (7), 217 (64), 178 (11), 177 (93), 176 (14), 159 (36), 134 (11), 133 (11), 131 (5), 130 (6)[b]
(*S*)-**2b**	3841, 3752, 3676, 3454, 3090, 3061, 3028, 2989, 2937, 2879, 2345, 2142, 1944, 1873, 1854, 1803, 1747, 1655, 1605, 1582, 1562, 1499, 1454, 1423, 1383, 1332, 1254, 1223, 1173, 1151, 1103, 1083, 1065, 1029, 991, 962, 911, 893, 841, 822, 786, 757, 721, 696, 614, 577, 537, 500, 475, 455	1.35 (s, 3 H, CH_3), 1.43 (s, 3 H, CH_3), 2.79 (dd, *J* = 9.1, 14.8, 1 H, PhC*H*H), 3.24 (dd, *J* = 3.3, 14.8, 1 H, PhCH*H*), 4.01 (d, *J* = 17.0, 1 H, OC*H*H), 4.26 (dd, *J* = 1.5, 17.2, 1 H, OCH*H*), 4.46 (ddd, *J* = 1.4, 3.3, 9.1, 1 H, CH), 7.20–7.31 (m, 5 H, PhH)	23.9, 24.3 (2 C, CH_3), 34.8 (PhCH_2), 66.9 (OCH_2), 75.9 (CH), 101.2 (CCH_3), 123.6 (*p*CH), 128.4, 129.4 (4C, OCH, *m*CH), 137.9 (CPh), 209.0 (C=O)	220 (M^+, 14), 162 (51), 131 (12), 129 (35), 120 (38), 119 (10), 104 (14), 103 (12), 92 (68), 91 (69), 72 (100), 65 (10), 59 (31)
(*S*)-**2c**	3477, 3093, 3056, 3027, 2963, 2905, 2870, 1906, 1749, 1608, 1573, 1516, 1463, 1425, 1375, 1325, 1269, 1252, 1222, 1174, 1099, 1068, 1021, 988, 962, 924, 901, 831, 817, 756, 707, 663, 601, 569, 543, 503, 473	1.31 (s, 9 H, PhCCH_3), 1.38 (s, 3 H, OCCH_3), 1.43 (s, 3 H, OCCH_3), 2.77 (dd, *J* = 8.9, 15.0, 1 H, PhC*H*H), 3.22 (dd, *J* = 3.0, 15.1, 1 H, PhCH*H*), 4.00 (d, *J* = 17.0, 1 H, OC*H*H), 4.26 (dd, *J* = 1.5, 17.2, 1 H, OCH*H*), 4.47 (m, 1H, CH), 7.18–7.33 (m, 4 H, PhH)	24.0, 24.3 (2 C, OCCH_3), 31.8 (3 C, PhCCH_3), 34.3 (PhCH_2), 34.8 (PhCCH_3), 66.9 (OCH_2), 75.9 (CH), 101.2 (OCCH_3), 125.4, 129.0 (4 C, OCPh, *m*CPh), 134.8, 149.3 (2 C, *p*CPh, CPh), 209.1 (C=O)	276 (M^+, 31), 218 (12), 178 (20), 161 (31), 148 (12), 147 (100), 129 (20), 72 (19)
(*S*)-**2d**	3472, 3387, 2970, 2939, 2878, 2638, 1804, 1749, 1464, 1427, 1375, 1326, 1286, 1251, 1226, 1165, 1132, 1103, 1089, 1074, 1029, 975, 962, 925, 873, 852, 769, 706, 663, 619, 555, 537, 510, 467	0.90 (d, *J* = 6.9, 3 H, CHCH_3), 1.03 (d, *J* = 6.9, 3 H, CHCH_3), 1.44 (s, 6 H, CCH_3), 2.24 (septd, *J* = 4.1, 6.9, 1 H, C*H*CH_3), 3.95 (d, *J* = 16.8, 1 H, OC*H*H), 4.03 (dd, *J* = 1.4, 4.1, 1 H, OCH), 4.19 (dd, *J* = 1.5, 16.9, 1 H, OCH*H*)	16.5, 19.0 (2 C, CHCH_3), 23.3, 24.1 (2 C, CCH_3), 28.0 ($CHCH_3$), 67.2 (OCH_2), 78.7 (OCH), 100.5 (CCH_3), 209.7 (C=O)	172 (M^+, 3), 114 (14), 100 (16), 73 (10), 72 (100), 69 (11), 59 (42)
(*S*)-**2e**	3477, 2988, 2958, 2935, 2872, 2593, 2339, 1803, 1748, 1631, 1462, 1428, 1380, 1326, 1272, 1224, 1180, 1164, 1121, 1095, 1067, 1019, 994, 975, 951, 916, 860, 788, 756, 728, 665, 605, 544, 518, 471	0.91 (t, *J* = 7.1, 3 H, CH_2CH_3), 1.44 (s, 3 H, CCH_3), 1.46 (s, 3 H, CCH_3), 1.28–1.44 (m, 4 H, CH_3CH_2, $CH_3CH_2CH_2$), 1.48–1.59 (m, 1 H, CHC*H*H), 1.83–1.92 (m, 1 H, CHCH*H*), 3.98 (d, *J* = 17.0, OC*H*H), 4.21 (ddd, *J* = 1.5, 3.8, 8.4, 1 H, CH), 4.25 (dd, *J* = 1.5, 16.9, 1 H, OCH*H*)	14.1 (CH_2CH_3), 22.7 (CH_2CH_3), 23.7, 24.2 (2 C, CCH_3), 27.4, 28.3 (2 C, $CH_3CH_2CH_2$, $CHCH_2$), 66.8 (OCH_2), 76.9 (CH), 100.9 (CCH_3), 210.0 (C=O)	186 (M^+, 2), 128 (11), 100 (20), 86 (10), 85 (11), 72 (100), 59 (32), 58 (12), 57 (11), 55 (13)

[a] Satisfactory elemental analyses obtained: C, H ±0.4.
[b] CI (isobutane).

exo-Methylene Derivatives (*S*)-3; General Procedure

t-BuLi (26.4 mmol, 15% in *n*-pentane) was added dropwise to a stirred suspension of methyltriphenylphosphonium bromide (26.4 mmol) in anhyd THF (125 mL) at –78 °C and the stirring was continued for 15 min. The mixture was allowed to warm to r.t. over 30 min and cooled again to –78 °C. A solution of the ketone (*S*)-**2** (4.4 mmol) in anhyd THF (8 mL) was added and the reaction mixture was allowed to warm to r.t. over 15 h. The mixture was quenched with H_2O (10 mL) and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude products were purified by flash chromatography (silica gel, *n*-pentane–Et_2O, 25:1 to 60:1) to afford the alkenes (*S*)-**3** as colorless oils (Table 6).

Diols (*S*)-4; General Procedure

exo-Methylene derivative (*S*)-**3** (8.1 mmol) was dissolved in THF (50 mL) and H_2O (28 mL) at r.t. Trifluoroacetic acid (1.31 mL) was added and the mixture was stirred at r.t. until the reaction was complete (TLC control). The reaction was quenched with aq 25% NH_3 (10 mL) and H_2O (30 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), dried ($MgSO_4$) and concentrated in vacuo. No further purification was necessary as the crude diols (*S*)-**4** already showed suitable spectroscopic data and correct elemental analyses (Table 7).

Monoprotected, Double Allylic Alcohols (*S*)-5; General Procedure

Imidazole (1.3 mmol) and diol (*S*)-**4** (0.54 mmol) were dissolved in THF (5 mL) and cooled to 0 °C. *tert*-Butyldimethylsilyl chloride (TBSCl, 0.62 mmol; 50% in toluene) was added slowly. The cool-

Table 6 Spectroscopic Data of *exo*-Methylene Derivatives (*S*)-**3a**–**e**[a]

(*S*)-**3**	IR ($CHCl_3$) (cm^{-1})	^{1}H NMR ($CDCl_3$, TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$, TMS) δ	MS (70 eV) *m*/*z* (%)
(*S*)-**3a**	3520, 3384, 3084, 3063, 3026, 2989, 2938, 2854, 2587, 2310, 1946, 1874, 1805, 1657, 1604, 1584, 1546, 1496, 1454, 1414, 1379, 1348, 1261, 1224, 1198, 1158, 1104, 1087, 1064, 1032, 979, 958, 897, 854, 808, 778, 750, 700, 580, 517, 468	1.42 (s, 3 H, CCH_3), 1.44 (s, 3 H, CCH_3), 1.87–1.98 (m, 1 H, OC-C*H*H), 2.00–2.10 (m, 1 H, OCCH*H*), 2.63–2.72 (m, 1 H, PhC*H*H), 2.86 (m, 1 H, PhCH*H*), 4.24 (t, *J* = 1.1, 2 H, OCH_2), 4.28 (d, *J* = 8.1, 1 H, CH), 4.82 (dt, *J* = 1.1, 5.2, 2 H, CCH_2), 7.15–7.31 (m, 5 H, PhH)	22.1 (C*C*H$_3$), 27.6 (C*C*H$_3$), 31.4, 34.2 (2 C, OC*C*H$_2$, Ph*C*H$_2$), 64.5 (OCH_2), 69.5 (CH), 99.9 (*C*CH$_3$), 106.6 (C*C*H$_2$), 126.1 (*p*CPh), 128.6, 128.9 (4 C, OCPh, *m*CPh), 142.3 (CPh), 146.3 (*C*CH$_2$)	233 (M^+ + 1, 22), 175 (19), 158 (14), 157 (100)[b]
(*S*)-**3b**	3377, 3085, 3064, 3028, 2989, 2938, 2854, 2606, 1946, 1804, 1657, 1605, 1497, 1454, 1416, 1378, 1349, 1253, 1226, 1200, 1159, 1081, 1053, 1027, 965, 898, 825, 751, 699, 590, 564, 520, 502, 460	1.29 (s, 3 H, CCH_3), 1.31 (s, 3 H, CCH_3), 2.83 (dd, *J* = 8.5, 14.3, 1 H, PhC*H*H), 3.01 (dd, *J* = 4.3, 14.4, 1 H, PhCH*H*), 4.19 (d, *J* = 0.8, 2 H, OCH_2), 4.54 (m, 1 H, CH), 4.82 (m, 2 H, CCH_2), 7.11–7.24 (m, 5 H, PhH)	22.4 (C*C*H$_3$), 27.6 (C*C*H$_3$), 39.2 (Ph*C*H$_2$), 64.6 (OCH_2), 71.8 (CH), 100.0 (*C*CH$_3$), 107.3 (C*C*H$_2$), 126.3 (*p*CPh), 128.3, 129.5 (4C, OCPh, *m*CPh), 138.7 (CPh), 146.0 (*C*CH$_2$)	220 (14), 219 (M^+ + 1, 100), 162 (11), 161 (91), 143 (64), 127 (14)[b]
(*S*)-**3c**	3887, 3521, 3371, 3083, 3056, 2962, 2867, 2714, 2593, 2385, 1902, 1790, 1658, 1610, 1515, 1462, 1413, 1377, 1268, 1253, 1226, 1200, 1158, 1096, 1061, 1028, 966, 899, 832, 750, 717, 655, 569, 519, 479	1.31 (s, 9 H, PhCC*H*$_3$), 1.39 (s, 6 H, OCC*H*$_3$), 2.88 (dd, *J* = 8.0, 14.6, 1 H, PhC*H*H), 3.04 (dd, *J* = 4.4, 14.6, 1 H, PhCH*H*), 4.26 (d, *J* = 1.1, 2 H, OCH_2), 4.62 (m, 1 H, CH), 4.88 (m, 2 H, CCH_2), 7.19 (d, *J* = 8.2, 2 H, PhH), 7.20 (d, *J* = 8.2, 2 H, PhH)	22.3 (C*C*H$_3$), 27.5 (C*C*H$_3$), 31.7 (3 C, PhC*C*H$_3$), 34.6 (Ph*C*CH$_3$), 38.6 (OC*C*H$_2$), 64.6 (OCH_2), 71.7 (CH), 99.9 (*C*CH$_3$), 107.4 (C*C*H$_2$), 125.2, 129.1 (4 C, OCPh, *m*CPh), 135.6 (CPh), 146.0 (*C*CH$_2$), 149.1 (CPh)	274 (M^+, 3), 216 (15), 128 (10), 127 (100), 69 (23), 59 (15)
(*S*)-**3d**	3356, 3079, 2988, 2967, 2937, 2902, 2874, 2855, 1785, 1656, 1459, 1414, 1379, 1371, 1340, 1259, 1223, 1201, 1183, 1167, 1130, 1107, 1065, 1014, 947, 930, 873, 831, 767, 718, 655, 608, 519	0.92 (d, *J* = 6.9, 3 H, CHC*H*$_3$), 1.00 (d, *J* = 6.9, 3 H, CHC*H*$_3$), 1.37 (s, 3 H, CCH_3), 1.40 (s, 3 H, CC*H*$_3$), 2.03 (septd, *J* = 3.7, 6.8, 1 H, C*H*CH$_3$), 4.12 (dt, *J* = 1.1, 13.2, 1 H, OC*H*H), 4.16 (m, 1 H, OCH), 4.26 (dq, *J* = 1.6, 13.2, 1 H, OCH*H*), 4.79 (d, *J* = 1.1, 1 H, CC*H*H), 4.89 (q, *J* = 1.6, CCH*H*)	16.1 (CH*C*H$_3$), 19.8 (CH*C*H$_3$), 23.3 (C*C*H$_3$), 27.1 (C*C*H$_3$), 30.7 (*C*HCH$_3$), 64.8 (OCH_2), 75.5 (OCH), 99.7 (*C*CH$_3$), 106.8 (C*C*H$_2$), 146.1 (*C*CH$_2$)	170 (M^+, 0.2), 127 (100), 95 (27), 69 (39), 67 (18), 59 (33), 55 (12)
(*S*)-**3e**	3556, 3082, 2989, 2958, 2859, 2728, 1657, 1459, 1413, 1379, 1348, 1338, 1262, 1227, 1198, 1165, 1119, 1090, 1064, 1050, 1023, 1005, 957, 904, 862, 792, 749, 715, 589, 519, 486, 467	0.92 (t, *J* = 7.1, 3 H, CH$_2$C*H*$_3$), 1.29–1.40 (m, 3 H, CH_2alkyl), 1.38 (d, *J* = 0.6, 3 H, CCH_3), 1.45 (d, *J* = 0.6, 3 H, CCH_3), 1.47–1.63 (m, 2 H, CH_2alkyl, OCC*H*H), 1.70–1.81 (m, 1 H, OCCH*H*), 4.25 (q, *J* = 1.2, 2 H, OCH_2), 4.30 (m, 1 H, CH), 4.82 (qd, *J* = 1.5, 4.6, 2 H, CCH_2)	14.4 (CH$_2$*C*H$_3$), 22.3 (C*C*H$_3$), 23.0 (CH_2alkyl), 27.5 (C*C*H$_3$), 27.7, 32.3 (2 C, CH_2alkyl), 64.5 (OCH_2), 70.7 (CH), 99.8 (*C*CH$_3$), 106.3 (C*C*H$_2$), 146.6 (*C*CH$_2$)	185 (M^+, 74), 127 (100), 109 (10)

[a] Satisfactory elemental analyses obtained for: C, H ±0.4.
[b] CI (isobutane).

Table 7 Spectroscopic Data of Double Allylic Alcohols (*S*)-**4a**–**e**[a]

(*S*)-**4**	IR ($CHCl_3$) (cm^{-1})	^1H NMR ($CDCl_3$, TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$, TMS), δ	MS (70 eV) *m*/*z* (%)
(*S*)-**4a**	3941, 3782, 3352, 3085, 3062, 3026, 2999, 2930, 2864, 1948, 1874, 1809, 1655, 1603, 1534, 1496, 1454, 1310, 1205, 1145, 1112, 1032, 914, 845, 803, 749, 700, 620, 588, 532, 496	1.75–1.93 (m, 2 H, $OCCH_2$), 2.55 (ddd, *J* = 6.7, 9.3, 13.9, 1 H PhC*H*H), 2.66 (ddd, *J* = 6.1, 9.6, 13.9, 1 H, PhCH*H*), 3.01 (br s, 2 H, OH), 4.05 (d, *J* = 13.2, 1 H, HOC*H*H), 4.14 (dd, *J* = 5.9, 7.6, 1 H, CH), 4.19 (d, *J* = 13.2, 1 H, HOCH*H*), 5.03 (d, *J* = 13.4, 2 H, CCH_2), 7.08–7.23 (m, 5 H, PhH)	32.4, 37.5 (2 C, Ph*C*H_2, HOC*C*H_2), 64.1 (HOCH_2), 74.1 (CH), 113.1 (C*C*H_2), 126.2 (*p*CPh), 128.7 (4 C, OCPh, *m*CPh), 141.9 (CPh), 149.6 (*C*CH_2)	193 (M^+ + 1, 37), 175 (19), 158 (13), 157 (100)[b]
(*S*)-**4b**	3934, 3815, 3719, 3359, 3086, 3062, 3028, 3000, 2921, 2871, 2632, 1950, 1881, 1812, 1757, 1655, 1603, 1545, 1496, 1454, 1309, 1238, 1181, 1154, 1111, 1030, 915, 852, 747, 701, 619, 583, 542	2.53 (br s, 2 H, OH), 2.79 (dd, *J* = 8.8, 13.7, 1 H, PhC*H*H), 2.87 (dd, *J* = 4.9, 13.7, 1 H, PhCH*H*), 4.07 (d, *J* = 13.2, 1 H, HOC*H*H), 4.20 (d, *J* = 13.2, 1 H, HOCH*H*), 4.37 (dd, *J* = 4.9, 8.8, 1 H, CH), 5.04 (d, *J* = 12.4, 2 H, CCH_2), 7.12–7.26 (m, 5 H, PhH)	43.2 (Ph*C*H_2), 64.4 (HOCH_2), 75.2 (CH), 113.1 (C*C*H_2), 126.9 (*p*CPh), 128.8, 129.6 (4 C, OCPh, *m*CPh), 138.2 (CPh), 149.3 (*C*CH_2)	178 (M^+, 1), 92 (100), 91 (59), 87 (47), 69 (23), 65 (10)
(*S*)-**4c**	3904, 3856, 3840, 3822, 3803, 3752, 3677, 3656, 3631, 3274, 3061, 3023, 2998, 2960, 2931, 2860, 2739, 2678, 2588, 2453, 2372, 2345, 2312, 2050, 1904, 1846, 1793, 1656, 1561, 1513, 1460, 1411, 1361, 1330, 1270, 1228, 1203, 1158, 1117, 1067, 1046, 1023, 980, 920, 852, 838, 800, 751, 730, 687, 574, 529, 489, 457	1.25 (s, 9 H, CCH_3), 2.08 (br s, 2 H, OH), 2.77 (dd, *J* = 9.1, 13.7, 1 H, PhC*H*H), 2.88 (dd, *J* = 4.3, 13.6, 1 H, PhCH*H*), 4.14 (d, *J* = 12.9, 1 H, HOC*H*H), 4.27 (d, *J* = 13.2, 1 H, HOCH*H*), 4.41 (dd, *J* = 4.3, 9.2, 1 H, CH), 5.09 (d, *J* = 4.4, 2 H, CCH_2), 7.11 (d, *J* = 8.5, 2 H, PhH), 7.28 (d, *J* = 8.2, 2 H, PhH)	31.7 (3 C, C*C*H_3), 34.8 (*C*CH_3), 42.8 (Ph*C*H_2), 64.6 (HOCH_2), 75.3 (CH), 113.0 (C*C*H_2), 125.8, 129.2 (4 C, OCPh, *m*CPh), 134.9 (CPh), 149.4, 149.8 (2 C, CPh, *C*CH_2)	234 (M^+, 1), 148 (57), 147 (64), 134 (10), 133 (100), 132 (21), 117 (22), 105 (13), 92 (11), 91 (12), 87 (28), 57 (12)
(*S*)-**4d**	3947, 3906, 3885, 3840, 3801, 3782,,3753, 3736, 3676, 3631, 3401, 3089, 2959, 2925, 2897, 2870, 2676, 2588, 2529, 2466, 2425, 2372, 2343, 2296, 2228, 2185, 2112, 2040, 1978, 1812, 1658, 1562, 1545, 1498, 1467, 1384, 1344, 1319, 1297, 1249, 1167, 1114, 1059, 1028, 991, 957, 904, 868, 807, 742, 671, 633, 555, 503	0.79 (d, *J* = 6.6, 3 H, CHCH_3), 0.93 (d, *J* = 6.6, 3 H, CHCH_3), 1.78 (octet, *J* = 6.7, 1 H, C*H*CH_3), 2.33 (br s, 2 H, OH), 3.80 (d, *J* = 7.7, 1 H, HOC*H*), 4.06 (d, *J* = 13.2, 1 H, HOC*H*H), 4.23 (d, *J* = 13.2, 1 H, HOCH*H*), 5.01 (d, *J* = 0.6, 1 H, CC*H*H), 5.11 (d, *J* = 1.4, 1 H, CCH*H*)	18.5 (CH*C*H_3), 19.8 (CH*C*H_3), 32.2 (*C*HCH_3), 64.4 (HOCH_2), 81.1 (HOCH), 113.9 (C*C*H_2), 148.9 (*C*CH_2)	131 (M^+ + 1, 13), 113 (100)[b]
(*S*)-**4e**	see Ref.[28]	0.84 (t, *J* = 7.0, 3 H, CH_3), 1.13–1.34 (m, 4 H, CH_2alkyl), 1.46–1.58 (m, 2 H, CH_2alkyl), 3.47 (br s, 1 H, OH), 3.62 (br s, 1 H, OH), 4.03 (d, *J* = 13.5, 1 H, HOC*H*H), 4.11 (t, *J* = 6.7, 1 H, CH), 4.18 (d, *J* = 13.5, 1 H, HOCH*H*), 5.00 (s, 1 H, CC*H*H), 5.04 (d, *J* = 0.6, 1 H, CCH*H*)	14.3 (CH_3), 22.8, 28.1, 35.4 (3 C, CH_2alkyl), 63.6 (HOCH_2), 64.6 (CH), 112.6 (C*C*H_2), 149.9 (*C*CH_2)	145 (M^+ + 1, 13), 127 (100), 109 (15)[b]

[a] Satisfactory elemental analyses obtained: C, H ±0.4.
[b] CI (isobutane).

ing bath was removed and the reaction mixture was stirred at r.t. for 5 h. The suspension was filtered through silica gel and Celite, washed with Et_2O and concentrated in vacuo. The crude product was purified by flash chromatography (silica gel; *n*-pentane–Et_2O, 4:1 to 10:1) to yield the mono-TBS-protected, double allylic alcohols (*S*)-**5** as colorless oils (Table 8).

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Table 8 Spectroscopic Data of Mono-TBS-Protected, Double Allylic Alcohols (*S*)-**5a**–**e**[a]

(*S*)-**5**	IR ($CHCl_3$) (cm^{-1})	^1H NMR ($CDCl_3$, TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$, TMS), δ	MS (70 eV) *m*/*z* (%)
(*S*)-**5a**	3891, 3404, 3085, 3063, 3027, 2953, 2930, 2886, 2857, 2740, 2710, 1941, 1805, 1654, 1604, 1496, 1469, 1391, 1362, 1256, 1113, 1069, 1007, 969, 912, 839, 778, 749, 699, 672, 620, 586, 494	0.02 (s, 6 H, $SiCH_3$), 0.84 (s, 9 H, CCH_3), 1.78–1.95 (m, 2 H, $HOCCH_2$), 2.53–2.63 (m, 2 H, PhC*H*H, OH), 2.67–2.76 (m, 1 H, PhCH*H*), 4.09–4.15 (m, 1 H, CH), 4.14 (d, *J* = 13.2, 1 H, TBSOC*H*H), 4.25 (d, *J* = 13.2, 1 H, TBSOCH*H*), 5.01 (s, 1H, CC*H*H), 5.04 (d, *J* = 1.4 Hz, CCH*H*), 7.08–7.24 (m, 5 H, PhH)	–5.0 (2 C, $SiCH_3$), 18.6 (CCH_3), 26.2 (3C, CCH_3), 32.5, 37.8 (2 C, PhCH_2, $HOCCH_2$), 65.0 (TBSOCH_2), 73.8 (CH), 111.7 (CCH_2), 126.0 (*p*CPh), 128.6, 128.7 (4 C, OCPh, *m*CPh), 142.2 (CPh), 149.5 (CCH_2)	308 (26), 307 (M^+ + 1, 100), 290 (10), 289 (38), 157 (41)[b]
(*S*)-**5b**	3417, 3086, 3063, 3029, 2954, 2930, 2887, 2854, 2739, 2710, 1943, 1809, 1655, 1603, 1496, 1469, 1391, 1362, 1256, 1181, 1111, 1078, 1007, 966, 911, 839, 778, 745, 700, 671, 619, 541, 492	0.03 (s, 3 H, $SiCH_3$), 0.04 (s, 3 H, $SiCH_3$), 0.86 (s, 9 H, CCH_3), 2.37 (d, *J* = 4.4, 1 H, OH), 2.81 (dd, *J* = 8.5, 13.7, 1 H, PhC*H*H), 2.90 (dd, *J* = 4.9, 13.7, 1 H, PhCH*H*), 4.18 (d, *J* = 13.2, 1 H, TBSOC*H*H), 4.25 (d, *J* = 13.2, 1 H, TBSOCH*H*), 4.35 (m, 1 H, CH), 5.00 (s, 1 H, CC*H*H), 5.04 (d, *J* = 1.4, 1 H, CCH*H*), 7.13–7.26 (m, 5 H, PhH)	–5.0 (2 C, $SiCH_3$), 18.7 (CCH_3), 26.3 (3C, CCH_3), 43.2 (PhCH_2), 65.0 (TBSOCH_2), 75.0 (CH), 111.7 (CCH_2), 126.6 (*p*CPh), 128.6, 129.6 (4 C, OCPh, *m*CPh), 138.7 (CPh), 149.2 (CCH_2)	294 (21), 293 (M^+ + 1, 100), 276 (18), 275 (82), 143 (19)[b]
(*S*)-**5c**	3856, 3809, 3415, 3091, 3055, 3024, 2957, 2901, 2858, 2739, 2711, 1903, 1790, 1654, 1515, 1469, 1391, 1363, 1256, 1203, 1110, 1062, 1007, 967, 938, 910, 839, 816, 778, 720, 669, 569	0.03 (s, 6 H, $SiCH_3$), 0.86 (s, 9 H, $SiCCH_3$), 1.24 (s, 9 H, PhCCH_3), 2.30 (d, *J* = 4.4, 1 H, OH), 2.76 (dd, *J* = 8.9, 13.7, 1 H, PhC*H*H), 2.87 (dd, *J* = 4.8, 13.7, 1 H, PhCH*H*), 4.17 (d, *J* = 13.3, 1 H, TBSOC*H*H), 4.24 (d, *J* = 13.3, 1 H, TBSOCH*H*), 4.34 (m, 1 H, C*H*), 5.05 (dt, *J* = 1.3, 4.0, 2 H, CCH_2), 7.10 (d, *J* = 8.1, 2 H, PhH), 7.26 (d, *J* = 8.5, 2 H, PhH)	–4.9 (2 C, $SiCH_3$), 18.7 ($SiCCH_3$), 26.3 (3C, $SiCCH_3$), 31.8 (3C, PhCCH_3), 34.8 (PhCCH_3), 42.8 (PhCH_2), 65.0 (TBSOCH_2), 74.8 (CH), 111.5 (CCH_2), 125.6, 129.2 (4 C, OCPh, *m*CPh), 135.5 (CPh), 149.4, 149.5 (2 C, CPh, CCH_2)	348 (M^+, 1), 202 (13), 201 (90), 143 (56), 133 (12), 129 (24), 105 (13), 75 (34), 73 (26), 71 (15), 57 (100)
(*S*)-**5d**	3438, 3091, 2957, 2931, 2894, 2858, 2740, 2711, 1822, 1654, 1481, 1388, 1363, 1256, 1171, 1093, 1023, 983, 956, 938, 909, 838, 778, 672, 610, 569, 502	0.02 (s, 6 H, $SiCH_3$), 0.79 (d, *J* = 6.6, 3 H, $CHCH_3$), 0.85 (s, 9 H, CCH_3), 0.93 (d, *J* = 6.6, 3 H, $CHCH_3$), 1.74 (octet, *J* = 6.7, 1 H, C*H*CH_3), 2.41 (d, *J* = 5.5, 1 H, OH), 3.71 (dd, *J* = 5.5, 7.4, 1 H, HOC*H*), 4.10 (d, *J* = 13.2, 1 H, TBSOC*H*H), 4.24 (d, *J* = 13.2, 1 H, TBSOCH*H*), 4.97 (s, 1H, CC*H*H), 5.06 (q, *J* = 1.6, 1 H, CCH*H*)	–5.1 (2 C, $SiCH_3$), 18.5 ($CHCH_3$), 18.6 (CCH_3), 19.8 ($CHCH_3$), 26.2 (3 C, CCH_3), 32.3 ($CHCH_3$), 64.8 (TBSOCH_2), 80.8 (HOCH), 112.6 (CCH_2), 148.7 (CCH_2)	246 (19), 245 (M^+ + 1, 100), 228 (15), 227 (81), 187 (10), 95 (41)[b]
(*S*)-**5e**	3857, 3395, 3092, 2957, 2931, 2859, 2739, 2710, 1823, 1654, 1464, 1390, 1362, 1259, 1094, 1006, 939, 909, 838, 777, 730, 670, 616, 546	0.03 (s, 6 H, $SiCH_3$), 0.85 (s, 9 H, CCH_3), 0.85 (t, *J* = 3.3, 3 H, CH_2CH_3), 1.16–1.38 (m, 4 H, CH_2alkyl), 1.49–1.58 (m, 2 H, CH_2alkyl), 2.45 (d, *J* = 4.1, 1 H, OH), 4.08 (m, 1 H, CH), 4.13 (d, *J* = 13.2, 1 H, TBSOC*H*H), 4.24 (d, *J* = 13.2, 1 H, TBSOCH*H*), 4.98 (s, 1 H, CC*H*H), 5.02 (d, *J* = 1.7, 1 H, CCH*H*)	–5.1 (2 C, $SiCH_3$), 14.4 (CH_2CH_3), 18.6 (CCH_3), 23.0 (CH_2alkyl), 26.2 (3 C, CCH_3), 28.3, 35.8 (2 C, CH_2alkyl), 64.8 (TBSOCH_2), 74.6 (CH), 111.4 (CCH_2), 149.8 (CCH_2)	260 (17), 259 (M^+ + 1, 89), 242 (21), 241 (100), 201 (19), 109 (12)[b]

[a] Satisfactory HRMS data or elemental analyses obtained: C, H ±0.4.
[b] CI (isobutane).

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