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PAPER

Diastereoselective three-component reactions of aryldiazoacetates with alcohols/water and alkynals: application to substituted enelactones†

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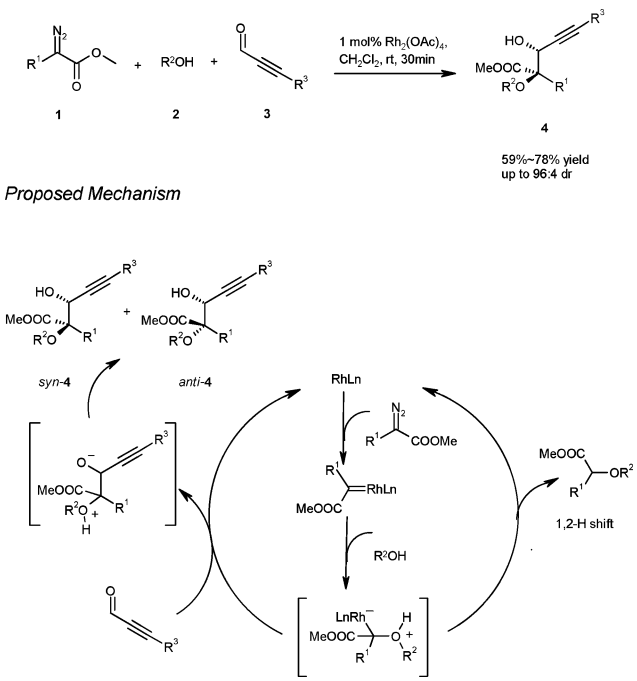
Dirhodium acetate catalyzed three-component reactions of aryl diazoacetates, alcohols or water, and 2-alkynals are reported to afford β-alkynyl α,β-dihydroxyl acid esters in good yield with high diastereoselectivity. Synthetic utility of the reaction was demonstrated in the conversion of the versatile alkynyl functionality to other synthetically useful compounds, including efficient synthesis of 2-aryl-2,3-dihydroxyl enelactones.

Introduction

Multicomponent reactions [1] (MCRs) provide simple, efficient and convergent approaches to construct complex molecules in an atom-economical fashion. This strategy offers significant advantages over classical step-by-step approaches, as it allows the formation of multiple bonds and stereogenic centres in a single synthetic operation from simple precursors.

Our group has previously reported three-component reactions of diazo compounds, aldehydes, and alcohols or water to yield dihydroxy acid frameworks with quaternary stereogenic center(s).[2] However, the efficient synthetic method was mostly limited to aryl aldehydes, and therefore, the synthetic utility was quite limited. To overcome this limitation, one of our challenges is to identify a system in which extended scope of functionality can be incorporated into the products. Herein, we report that 2-alkynal is a good substrate to trap the oxonium ylide derived from diazo compounds and alcohols or water. The three-component reaction yields β-alkynyl α,β-dihydroxy acid esters in good yield with high diastereoselectivity (Scheme 1). The introduced alkynyl group can be easily hydrogenated to alkyl group or converted to other useful molecules.



Scheme 1 Reactions of diazoacetates, alcohols or water, and 2-alkynals catalyzed by dirhodium acetate.

Results and discussion

Initially, the rhodium acetate catalyzed three-component reaction of methyl phenyldiazoacetate **1a** with benzyl alcohol **2a** and propynal **3a** was investigated. The reaction was carried out in CH_2Cl_2 at room temperature in the presence of 1 mol% catalyst. We were delighted to find that the desired product **4a** was isolated in 73% yield with 96 : 4 dr favouring *syn* isomer. The relative stereochemistry of **4a** was established through single-crystal X-ray analysis (Fig. 1).

To demonstrate the generality of this reaction, the substrate scope was explored and the results are summarized in Table 1. Various 2-alkynals with different substituents on the terminal carbon were employed, and it was found that all the substrates gave good yield and similarly high level control of diastereoselectivity (Table 1, entries 1–4). The reaction was extended to other aryldiazoacetates. In general, the reaction was tolerated to the

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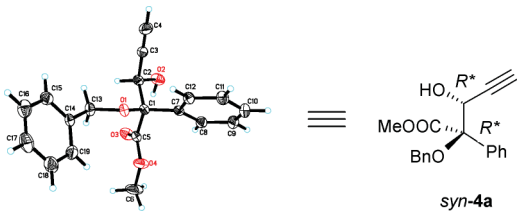
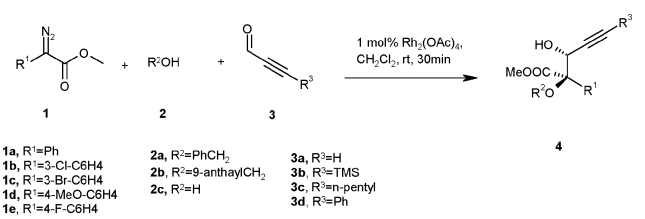


Fig. 1 X-ray single crystal structure of *syn*-**4a**.

Table 1 Reactions of diazoacetates, alcohols or water, and 2-alkynals catalyzed by dirhodium acetate[a]



Entry	1	2	3	4	dr[b] (*syn*/*anti*)	Yield[c]
1	**1a**	**2a**	**3a**	**4a**	96/4	73
2	**1a**	**2a**	**3b**	**4b**	96/4	75
3	**1a**	**2a**	**3c**	**4c**	92/8	59[d]
4	**1a**	**2a**	**3d**	**4d**	95/5	78
5	**1b**	**2a**	**3b**	**4f**	95/5	65
6	**1c**	**2a**	**3b**	**4g**	90/10	62
7	**1d**	**2a**	**3b**	**4h**	96/4	76
8	**1e**	**2a**	**3b**	**4i**	95/5	73
9	**1a**	**2c**	**3a**	**4j**	73/27	75
10	**1a**	**2c**	**3b**	**4k**	70/30	71
11	**1a**	**2c**	**3c**	**4l**	59/41	56[d]
12	**1a**	**2b**	**3b**	**4e**	>99/1	75

[a] Reaction conditions: unless otherwise noted, the reaction was carried out in CH_2Cl_2 at rt in the presence of 1 mol% of $Rh_2(OAc)_4$ with **1**:**2**:**3** = 1.2 : 1.2 : 1.0 mmol. [b] Determined by HPLC. [c] Isolated yield. [d] **1a**:**2a**:**3c** = 1.5 : 1.5 : 1.0 mmol.

substituted aryl diazo compounds, as good yield and high dr were obtained with diazo compounds **1b–1e** (Table 1, entries 5–8). Other diazo compounds such as ethyl diazoacetate and diazoacetophenone were used under such conditions, however, resulting in a complex reaction mixture. We were gratified to find that water can be served as a substrate to participate in this three-component reaction to afford free hydroxy product in good yield, though with moderate diastereoselectivity (Table 1, entries 9–11). The stereochemistry of *anti*-**4j** was confirmed by its X-ray single crystal analysis (Fig. 2). The low diastereoselectivity is probably due to the small size of the water molecule. With the use of a more sterically hindered 9-anthracenemethanol, the diastereoselectivity of the reaction was improved to greater than 99 : 1 (Table 1, entry 12).

To demonstrate the synthetic utility of the reaction, *syn*-**4a** was hydrogenated to give the alkyl substituted product **5** in quantitative yield in the presence of 10% Pd/C as a catalyst (Scheme 2). This can be a supplementary approach for the introduction of β-alkyl group in the reaction system.

To further demonstrate the synthetic utility of the reaction, the product *syn*-**4j** was selected to undergo additional transformation (Scheme 3). In presence of CuI and a base, *syn*-**4j** was treated with allyl bromide to give corresponding coupling product **6** in an

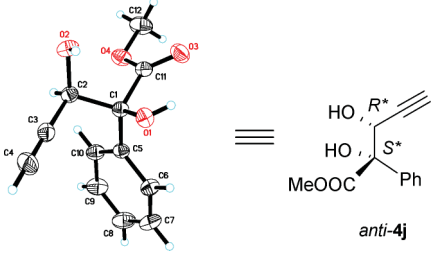
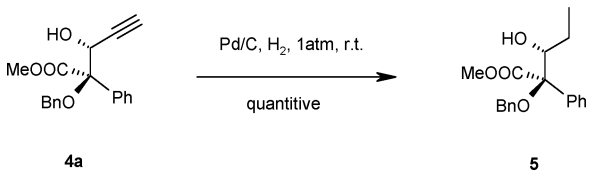
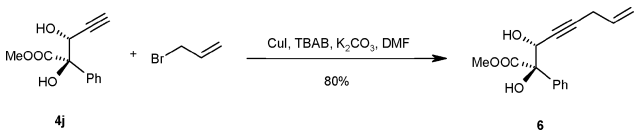


Fig. 2 X-ray single crystal structure of *anti*-**4j**.



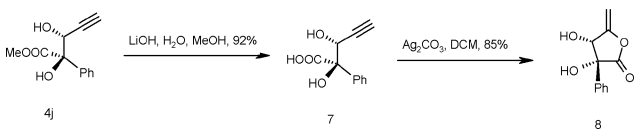
Scheme 2 Hydrogenation of *syn*-**4a**.



Scheme 3 Coupling reaction of *syn*-**4j** with allyl bromide.

80% yield. Compound **6** can be a useful intermediate for further transformation.[3]

Polysubstituted enelactones have been found to be structural motifs presented in biologically active natural products such as cyanobacterin[4] and peumusolide A.[5] Moreover, these derivatives are versatile precursors to enelactams, and also serve as building blocks used in the synthesis of natural products.[6] An application of our method is demonstrated in the efficient synthesis of 2-aryl-2,3-dihydroxy enelactones (Scheme 4). For example, product *syn*-**4j** was hydrolyzed to corresponding alkynyl acid **7** in a 92% yield. Treatment of **7** with Ag_2CO_3 in dichloromethane afforded dihydroxy enelactone **8** in an 85% yield.



Scheme 4 Synthesis of enelactone **8** from *syn*-**4j**.

Conclusion

In conclusion, we have reported an efficient three-component reaction of aryldiazoacetates with alcohols/water and alkynals to afford β-alkynyl α,β-dihydroxy acid esters in good yield with high diastereoselectivity. The advantage of introducing an alkynyl functionality in the three-component product was demonstrated by converting this versatile group to other useful molecules. Dihydroxy enelactones can be efficiently made by simple transformation of the three-component coupling products. Further investigation to develop an enantioselective version of the current reaction is in progress in our laboratory.

Experimental section

General

All reactions were performed under an argon atmosphere in a well-dried reaction flask. ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz with Brucker-400 MHz spectrometer. HRMS (ESI) Mass spectra were recorded on Agilent G1969A LC/MSD TOF. Low-resolution mass spectra were recorded on Waters UPLC Acquity SQD. IR spectra were recordered on NICOLET AVATAR 370 DTGS. Dichloromethane was distilled over calcium hydride.

General procedure for three-component reaction of aryl diazoacetates, alcohols or water, and 2-alkynals

To a flask was charged with 2-alkynal **3** (0.10 mmol, 1.0 eq), alcohol or water **2** (0.12 mmol, 1.2 eq), $Rh_2(OAc)_4$ (1.0 mol%) and dichloromethane (1.5 mL). The reaction mixture was stirred at room temperature, and diazo compound **1** (0.12 mmol, 1.2 eq) in 0.5 mL of dichloromethane was added to the reaction mixture over 0.5 h period of time *via* a syringe pump. The crude reaction mixture was subjected to LC/MS analysis for the determination of diastereoselectivity of the product **4**. The reaction mixture was purified by flash chromatography on silica gel (eluent: EtOAc: light petroleum ether = 1 : 50 to 1 : 10) to give pure **4**.

(2*R, 3*R**)-2-Benzyloxyl-2-phenyl-3-hydroxyl-pent-4-ynoic acid methyl ester (*syn*-4a).** Yield 73%, dr 96/4 (*syn*/*anti*): IR 1497, 1449, 1386, 1245, 1066, 1027, 738, 698; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.66–7.59 (m, 2 H), 7.48–7.30 (m, 8 H), 5.12 (d, *J* = 2.3 Hz, 1 H), 4.87 (d, *J* = 11.4 Hz, 1 H), 4.56 (d, *J* = 11.4 Hz, 1 H), 3.88 (s, 3 H), 2.86 (br s, 1 H), 2.49 (d, *J* = 2.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 170.96, 137.99, 135.08, 128.87, 128.38, 128.17, 127.85, 127.68, 127.50, 86.58, 80.82, 75.30, 68.51, 67.68, 52.53; MS (ES^+) *m*/*z* (%) 311 (40 $[M + H]^+$), 233 (100); HRMS (ESI) calcd for $C_{19}H_{19}O_4$ $[M + H]^+$ = 311.1278, found 311.1284. **(2*S**, 3*R**)-2-Benzyloxyl-2-phenyl-3-hydroxyl-pent-4-ynoic acid methyl ester (*anti*-4a)**: IR 1732, 1497, 1449, 1386, 1257, 1144, 1063, 1025, 737, 697, 677; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.61–7.56 (m, 2 H), 7.29–7.46 (m, 8 H), 5.07 (d, *J* = 2.0 Hz, 1 H), 4.98 (d, *J* = 11.6 Hz, 1 H), 4.56 (d, *J* = 11.6 Hz, 1 H), 3.90 (s, 3 H), 3.18 (br s., 1 H), 2.51 (d, *J* = 2.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 171.97, 138.46, 134.96, 128.90, 128.36, 128.29, 127.45, 127.39, 127.26, 86.93, 80.74, 75.52, 68.89, 68.69, 52.67; MS (ES^+) *m*/*z* (%) 311 (82 $[M + H]^+$), 233 (100); HRMS (ESI) calcd for $C_{19}H_{19}O_4$ $[M + H]^+$ = 311.1278, found 311.1284.

(2*R, 3*R**)-2-Benzyloxy-3-hydroxy-2-phenyl-5-trimethylsilanyl-pent-4-ynoic acid methyl ester (*syn*-4b).** Yield 75%, dr 96/4 (*syn*/*anti*): IR 1743, 1497, 1449, 1250, 1073, 1019, 843, 760, 726, 697; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.59–7.57 (m, 2 H), 7.47–7.30 (m, 8 H), 5.08 (s, 1 H), 4.84 (d, *J* = 11.4 Hz, 1 H), 4.59 (d, *J* = 11.4 Hz, 1 H), 3.87 (s, 3 H), 0.16 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 171.03, 138.11, 135.11, 128.70, 128.33, 127.94, 127.89, 127.58, 127.36, 102.48, 86.55, 77.02, 68.36, 67.88, 52.43, –0.35; MS (ES^+) *m*/*z* (%) 383 (53 $[M + H]^+$), 293 (100); HRMS (ESI) calcd for $C_{22}H_{27}O_4Si$ $[M + H]^+$ = 383.1673, found 383.1668.

(2*R, 3*R**)-2-Benzyloxy-3-hydroxy-2-phenyl-dec-4-ynoic acid methyl ester (*syn*-4c).** Yield 59%, dr 92/8 (*syn*/*anti*): IR 1743, 1497, 1449, 1380, 1245, 1104, 1068, 1027, 735, 699; ^{1}H NMR ($CDCl_3$, 400 MHz), δ ppm 7.65–7.58 (m, 2 H), 7.49–7.29 (m, 8 H), 5.11 (t, *J* = 2.0 Hz, 1 H), 4.85 (d, *J* = 11.4 Hz, 1 H), 4.58 (d, *J* = 11.4 Hz, 1 H), 3.87 (s, 3 H), 2.84 (br s, 1 H), 2.19 (td, *J* = 7.1, 2.0 Hz, 2 H), 1.41–1.53 (m, 2 H), 1.26–1.38 (m, 4 H), 0.86–0.95 (m, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 171.22, 138.21, 135.59, 128.57, 128.33, 128.25, 127.96, 127.91, 127.58, 127.48, 88.13, 86.82, 77.17, 68.36, 67.83, 52.39, 30.91, 28.09, 22.21, 18.73, 13.97; MS (ES^+) *m*/*z* (%) 381 (45 $[M + H]^+$), 363 (100); HRMS (ESI) calcd for $C_{24}H_{29}O_4$ $[M + H]^+$ = 381.2060, found 381.2060.

(2*R, 3*R**)-2-Benzyloxy-3-hydroxy-2,5-diphenyl-pent-4-ynoic acid methyl ester (4d).** Yield 78%, dr 95/5 (*syn*/*anti*): IR 1741, 1491, 1448, 1242, 1068, 1027, 757, 735, 693; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.73–7.63 (m, 2 H), 7.53–7.29 (m, 13 H), 5.35 (s, 1 H), 4.92 (d, *J* = 11.4 Hz, 1 H), 4.65 (d, *J* = 11.4 Hz, 1 H), 3.90 (s, 3 H), 2.79 (br s, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 171.15, 138.12, 135.39, 131.71, 128.79, 128.55, 128.41, 128.26, 128.09, 127.93, 127.66, 127.50, 122.47, 87.04, 86.94, 86.39, 68.52, 68.27, 52.57; MS (ES^+) *m*/*z* (%) 387 (42 $[M + H]^+$), 369 (100); HRMS (ESI) calcd for $C_{25}H_{23}O_4$ $[M + H]^+$ = 387.1591, found 387.1597.

(2*R, 3*R**)-2-(Anthracen-9-ylmethoxy)-3-hydroxy-2-phenyl-5-trimethylsilanyl-pent-4-ynoic acid methyl ester (4e).** Yield 75%, dr > 99/1 (*syn*/*anti*): IR 1718, 1448, 1330, 1248, 1208, 1070, 1049, 1018, 993, 898, 839, 757, 733, 698; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 8.51 (s, 1 H), 8.42 (d, *J* = 8.3 Hz, 2 H), 8.04 (d, *J* = 7.8 Hz, 2 H), 7.71–7.64 (m, 2 H), 7.58–7.45 (m, 4 H), 7.45–7.38 (m, 3 H), 6.02 (d, *J* = 10.1 Hz, 1 H), 5.46 (d, *J* = 10.3 Hz, 1 H), 5.17 (s, 1 H), 3.99 (s, 3 H), 0.12–0.19 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 171.39, 135.95, 131.53, 131.21, 128.94, 128.64, 128.50, 128.19, 128.07, 126.24, 124.99, 124.71, 102.79, 92.11, 86.75, 67.79, 60.78, 52.47, –0.28; MS (ES^+) *m*/*z* (%) 483 (100 $[M + H]^+$); HRMS (ESI) calcd for $C_{30}H_{30}NaO_4Si$ $[M + Na]^+$ = 505.1806, found 505.1818.

(2*R, 3*R**)-2-(3-Chloro-benzyloxy)-3-hydroxy-2-phenyl-5-trimethylsilanyl-pent-4-ynoic acid methyl ester (4f).** Yield 65%, dr 95/5 (*syn*/*anti*): IR 1740, 1250, 1074, 999, 843, 759, 698; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.63 (s, 1 H), 7.49–7.30 (m, 8 H), 5.08 (s, 1 H), 4.81 (d, *J* = 11.4 Hz, 1 H), 4.59 (d, *J* = 11.4 Hz, 1 H), 3.87 (s, 3 H), 2.48 (br s, 1 H), 0.17 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 170.66, 137.64, 137.20, 133.93, 128.82, 128.35, 127.77, 127.53, 127.44, 126.12, 101.80, 92.96, 86.87, 85.99, 68.51, 67.60, –0.31, –0.35, –0.37; MS (ES^+) *m*/*z* (%) 417 (50 $[M + H]^+$), 327 (100); HRMS (ESI) calcd for $C_{22}H_{26}ClO_4Si$ $[M + H]^+$ = 417.1283, found 417.1271.

(2*R, 3*R**)-2-(3-Bromo-benzyloxy)-3-hydroxy-2-phenyl-5-trimethylsilanyl-pent-4-ynoic acid methyl ester (4g).** Yield 62%, dr 90/10 (*syn*/*anti*): IR 1741, 1250, 1074, 997, 843, 760, 697; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.79 (s, 1 H), 7.56–7.23 (m, 8 H), 5.08 (s, 1 H), 4.80 (d, *J* = 11.1 Hz, 1 H), 4.59 (d, *J* = 11.1 Hz, 1 H), 3.87 (s, 3 H), 2.49 (br s, 1 H), 0.17 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 170.64, 137.61, 137.43, 131.85, 131.17, 131.07, 129.31, 128.41, 127.79, 127.48, 126.66, 122.08, 101.76, 92.99, 85.91, 68.52, 67.59, –0.29, –0.36; MS (ES^+) *m*/*z* (%) 461 (95 $[M + H]^+$), 463 (100); HRMS (ESI) calcd for $C_{22}H_{25}BrNaO_4Si$ $[M + Na]^+$ = 483.0598, found 483.0596.

(2*R, 3*R**)-3-Hydroxy-2-(4-methoxy-benzyloxy)-2-phenyl-5-trimethylsilanyl-pent-4-ynoic acid methyl ester (4h).** Yield 76%, dr 96/4 (*syn*/*anti*): IR 1742, 1609, 1512, 1454, 1250, 1179, 1074, 1025, 843, 761, 736, 698; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.52–7.27 (m, 7 H), 6.93 (d, *J* = 8.8 Hz, 2 H), 5.05 (s, 1 H), 4.83 (d, *J* = 11.4 Hz, 1 H), 4.57 (d, *J* = 11.4 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 2.56 (br s, 1 H), 0.17 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 171.20, 159.82, 138.24, 129.37, 129.20, 128.31, 127.45, 127.11, 113.36, 102.71, 92.04, 86.26, 68.18, 67.97, –0.25, –0.30, –0.34; MS (ES^+) *m*/*z* (%) 413 (15 $[M + H]^+$), 305 (100); HRMS (ESI) calcd for $C_{23}H_{28}NaO_5Si$ $[M + Na]^+$ = 435.1598, found 435.1594.

(2*R, 3*R**)-2-(4-Fluoro-benzyloxy)-3-hydroxy-2-phenyl-5-trimethylsilanyl-pent-4-ynoic acid methyl ester (4i).** Yield 73%, dr 95/5 (*syn*/*anti*): IR 1742, 1604, 1509, 1249, 1162, 1073, 1014, 832, 761, 736, 697; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.61–7.54 (m, 2 H), 7.46–7.30 (m, 4 H), 7.08 (t, *J* = 8.8 Hz, 2 H), 5.07 (s, 1 H), 4.81 (d, *J* = 11.4 Hz, 1 H), 4.57 (d, *J* = 11.4 Hz, 1 H), 3.87 (s, 3 H), 0.16 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) 170.94, 137.85, 130.94, 130.91, 129.90, 129.81, 128.38, 127.69, 127.34, 114.90, 114.68, 102.13, 92.60, 85.99, 68.31, 67.73, –0.36; MS (ES^+) *m*/*z* (%) 401 (85 $[M + H]^+$), 383 (100); HRMS (ESI) calcd for $C_{22}H_{26}FO_4Si$ $[M + H]^+$ = 401.1579, found 401.1563.

(2*R, 3*R**)-2,3-Dihydroxy-2-phenyl-pent-4-ynoic acid methyl ester (*syn*-4j).** Yield 75%, dr 73/27 (*syn*/*anti*): IR 1732, 1448, 1257, 1188, 1132, 1073, 1033, 990, 903, 812, 788, 740, 697; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.70–7.67 (m, 2 H), 7.44–7.34 (m, 3 H), 5.06 (d, *J* = 2.0 Hz, 1 H), 3.85 (s, 3 H), 3.23 (br s, 2 H), 2.53 (d, *J* = 2.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 172.59, 136.53, 128.56, 128.46, 126.29, 80.67, 80.65, 74.71, 67.31, 53.74; MS (ES^+) *m*/*z* (%) 221 (26 $[M + H]^+$), 203 (100); HRMS (ESI) calcd for $C_{12}H_{12}NaO_4$ $[M + Na]^+$ = 243.0628, found 243.0628; **(2*S**, 3*R**)-2,3-Dihydroxy-2-phenyl-pent-4-ynoic acid methyl ester (*anti*-4j)**: IR 1730, 1437, 1415, 1256, 1198, 1134, 1076, 1038, 996, 940, 788, 735, 698; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.73–7.62 (m, 2 H), 7.46–7.33 (m, 3 H), 5.15 (d, *J* = 2.3 Hz, 1 H), 3.88 (s, 3 H), 3.75 (br s, 1 H), 2.31 (d, *J* = 2.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 173.16, 137.05, 128.41, 128.34, 125.80, 125.69, 81.07, 80.02, 74.90, 74.88, 67.66; MS (ES^+) *m*/*z* (%) 221 (33 $[M + H]^+$), 203 (100); HRMS (ESI) calcd for $C_{12}H_{12}NaO_4$ $[M + Na]^+$ = 243.0628, found 243.0630.

(2*R, 3*R**)-2,3-Dihydroxy-2-phenyl-5-trimethylsilanyl-pent-4-ynoic acid methyl ester (*syn*-4k).** Yield 71%, dr 70/30 (*syn*/*anti*): IR 1736, 1449, 1251, 1178, 1134, 1073, 999, 932, 843, 759, 740, 698; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.69 (d, *J* = 7.1 Hz, 2 H), 7.45–7.32 (m, 3 H), 5.03 (s, 1 H), 3.83 (s, 3 H), 3.59 (br s, 2 H), 0.21 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) 172.66, 136.57, 128.46, 128.38, 126.36, 102.08, 91.77, 80.80, 67.88, 53.56, –0.25, –0.28; MS (ES^+) *m*/*z* (%) 293 (100 $[M + H]^+$); HRMS (ESI) calcd for $C_{15}H_{21}O_4Si$ $[M + H]^+$ = 293.1204, found 293.1214; **(2*S**, 3*R**)-2,3-Dihydroxy-2-phenyl-5-trimethylsilanyl-pent-4-ynoic acid methyl ester (*anti*-4k)**: IR 1732, 1448, 1250, 1191, 1135, 1073, 1039, 1001, 953, 844, 765, 741, 695; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.65 (d, *J* = 7.3 Hz, 2 H), 7.42–7.31 (m, 3 H), 5.10 (s, 1 H), 3.94 (br s, 2 H), 3.88 (s, 3 H), 0.01 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) 173.32, 137.37, 128.38, 128.18, 125.83, 101.48, 92.11, 81.29, 68.39, 53.82, 53.79, –0.47; MS (ES^+) *m*/*z* (%) 293 (21 $[M + H]^+$), 275 (100); HRMS (ESI) calcd for $C_{15}H_{20}NaO_4Si$ $[M + Na]^+$ = 315.1023, found 315.1027.

(2*R, 3*R**)-2,3-Dihydroxy-2-phenyl-dec-4-ynoic acid methyl ester (*syn*-4l).** Yield 56%, dr 59/41 (*syn*/*anti*): IR 2931, 2859, 1736, 1448, 1435, 1380, 1254, 1187, 1149, 1073, 1051, 1005, 785, 736, 696; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.73–7.66 (m, 2 H), 7.42–7.30 (m, 3 H), 5.03 (t, *J* = 2.0 Hz, 1 H), 3.80 (s, 3 H), 2.23 (td, *J* = 7.1, 2.0 Hz, 2 H), 1.46–1.58 (m, 2 H), 1.29–1.46 (m, 4 H), 0.98–0.90 (m, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) 172.86, 137.05, 128.28, 128.27, 126.42, 87.64, 81.00, 77.51, 67.61, 53.41, 30.94, 28.19, 22.18, 18.60, 13.97; MS (ES^+) *m*/*z* (%) 291 (12 $[M + H]^+$), 273 (100); HRMS (ESI) calcd for $C_{17}H_{22}NaO_4$ $[M + Na]^+$ = 313.1410, found 313.1408; **(2*S**, 3*R**)-2,3-Dihydroxy-2-phenyl-dec-4-ynoic acid methyl ester (*anti*-4l)**: IR 2933, 1734, 1449, 1256, 1192, 1153, 1127, 1073, 1039, 964, 787, 735, 698; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.69–7.63 (m, 2 H), 7.41–7.29 (m, 3 H), 5.14 (t, *J* = 2.2 Hz, 1 H), 3.85 (s, 3 H), 3.55 (br s, 2 H), 2.04 (td, *J* = 7.0, 2.2 Hz, 2 H), 1.27–1.02 (m, 6 H), 0.83 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) 173.55, 137.74, 128.22, 128.16, 125.83, 87.73, 81.43, 76.47, 68.11, 53.70, 30.59, 27.90, 22.09, 18.48, 13.89; MS (ES^+) *m*/*z* (%) 291 (15 $[M + H]^+$), 273 (100); HRMS (ESI) calcd for $C_{17}H_{22}NaO_4$ $[M + Na]^+$ = 313.1410, found 313.1406.

(2*R, 3*R**)-2-Benzyloxy-3-hydroxy-2-phenyl-pentanoic acid methyl ester (5).** *syn*-**4a** was hydrogenated using H_2 (1 atm) and 10% Pd/C (10% equivalents) at room temperature for 3 h. The catalyst was filtered and washed with methanol twice. The combined washings and filtrate were evaporated *in vacuo* to give the product (quantitative). IR 1734, 1497, 1448, 1242, 1069, 1028, 980, 734, 699; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.58–7.52 (m, 2 H), 7.45–7.30 (m, 8 H), 4.64 (d, *J* = 11.1 Hz, 1 H), 4.34 (d, *J* = 11.1 Hz, 1 H), 4.19 (dd, *J* = 10.5, 2.2 Hz, 1 H), 3.88 (s, 3 H), 2.58 (br s, 1 H), 1.50 (m, 1 H), 1.31–1.21 (m, 1 H), 0.95 (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 171.95, 138.25, 135.78, 128.35, 128.29, 128.15, 127.71, 127.59, 127.45, 87.98, 78.67, 67.90, 52.21, 52.20, 23.89, 11.06; MS (ES^+) *m*/*z* (%) 315 (36 $[M + H]^+$), 297 (100); HRMS (ESI) calcd for $C_{19}H_{23}O_4$ $[M + H]^+$ = 315.1591, found 315.1593.

(2*R, 3*R**)-2,3-Dihydroxy-2-phenyl-oct-7-en-4-ynoic acid methyl ester (6).** To a stirred solution of *syn*-**4j** (90 mg, 0.4 mmol) in dry DMF 1 mL were sequentially added K_2CO_3 (83 mg, 0.6 mmol), tetrabutylammonium bromide (13 mg, 0.04 mmol), and copper(I) iodide (8 mg, 0.04 mmol) at room temperature. After 15 min, allyl bromide (72 mg, 0.6 mmol) was added. The reaction mixture was stirred for 3 h, then it was partitioned between ether and water. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography to give product (84 mg), Yield 80%. IR 1729, 1449, 1394, 1269, 1242, 1180, 1126, 1060, 1008, 916, 782, 736, 698; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.70 (d, *J* = 7.3 Hz, 2 H), 7.45–7.34 (m, 3 H), 5.75–5.88 (m, 1 H), 5.33 (d, *J* = 16.9 Hz, 1 H), 5.16 (d, *J* = 9.9 Hz, 1 H), 5.08 (s, 1 H), 3.83 (s, 3 H), 3.04 (d, *J* = 3.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) 172.85, 136.92, 131.90, 131.85, 128.36, 126.38, 116.43, 116.40, 84.02, 80.89, 79.44, 67.64, 53.57, 22.94; MS (ES^+) *m*/*z* (%) 261 (15 $[M + H]^+$), 243 (100); HRMS (ESI) calcd for $C_{15}H_{16}NaO_4$ $[M + Na]^+$ = 283.0941, found 283.0943.

(2*R, 3*R**)-2,3-Dihydroxy-2-phenyl-pent-4-ynoic acid (7).** To a solution of *syn*-**4j** (120 mg, 0.55 mmol) in MeOH (4 mL) and water (2 mL) was added LiOH (26 mg, 1.1 mmol). The reaction mixture was stirred at room temperature for 3h, then acidified by diluted hydrochloric acid to pH = 2, extracted with ether for 2 times. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and the solvents were removed under reduced pressure to give product (103 mg, yield 92%) as white solid. IR 3282, 1691, 1450, 1309, 1249, 1192, 1150, 1060, 1019, 953, 903, 801, 714, 691, 679; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 13.12 (br s, 1 H) 7.65–7.51 (m, 2 H), 7.239–7.20 (m, 4 H), 5.64 (br s, 1 H), 4.88 (d, J = 2.0 Hz, 1 H) 3.24 (d, J = 2.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 173.84, 140.35, 127.93, 126.98, 84.01, 81.03, 75.91, 66.73; MS (ES^-) m/z (%) 205 (100 [M - 1] $^-$); HRMS (ESI) calcd for $C_{11}H_{10}NaO_4$ $[M + Na]^+$ = 229.0471, found 229.0476.

(3*R, 4*S**)-3,4-Dihydroxy-5-methylene-3-phenyl-dihydro-furan-2-one (8).** To a suspension of **7** (60 mg, 0.29 mmol) in dichloromethane (5 mL) was added Ag_2CO_3 (10 mg, 0.036 mmol). The reaction mixture was stirred at room temperature for 24h, then purified by flash column chromatography to give product (51 mg). Yield 85%. IR 1740, 1720, 1696, 1449, 1360, 1236, 1150, 1100, 1075, 957, 910, 760, 715; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.50–7.32 (m, 5 H), 5.05 (d, J = 2.8 Hz, 1 H), 4.79 (d, J = 3.0 Hz, 1 H), 4.60 (s, 1 H), 3.75 (br s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm 174.11, 154.53, 136.33, 129.35, 129.00, 125.33, 94.58, 78.61, 74.73; MS (ES^-) m/z (%) 205 (10 [M - 1] $^-$), 223 (100); HRMS (ESI) calcd for $C_{11}H_{11}O_4$ $[M + H]^+$ = 207.0652, found 207.0657.

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Notes and references

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