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Synthesis of Alkynyl-Glycinols by Lewis Acid Catalyzed Propargylic Substitution of Bis-Imidates

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Racemic and enantioenriched alkynyl-glycinols can be synthesized by Lewis acid catalyzed cyclization reaction of bis-trichloracetimidates derived from alkynyl-glycols. The cyclization proceeds selectively to give 4-alkynyl-oxazolines as the propargylic substitution products. Enantioenriched bis-imidates that contain an alkyl or trimethylsilyl substituent at the acetylene gave oxazolines with complete inversion of configuration. In turn, considerable racemization was observed in the cyclization of bis-imidates that contain a phenyl substituent. The racemization for these substrates can be suppressed by introduction of the electronegative substituent at the phenyl ring. Oxazolines prepared by bis-imidate cyclization reaction can be readily transformed to protected alkynyl-glycol derivatives.

Introduction

Alkynyl-glycinols **3** (Figure 1) have found application as important multifunctional building blocks for the construction of complex molecules.[1–10] Nevertheless, the literature review revealed that there is a limited number of methods for the synthesis of such compound types.[11–19] Of particular interest is the access to enantioenriched alkynyl-glycinols that typically relies on derivatization of Garner's aldehyde[5,11,12,20,21] and Ellman-type addition reactions of terminal alkynes to *N*-sulfinyl imines.[14,17]

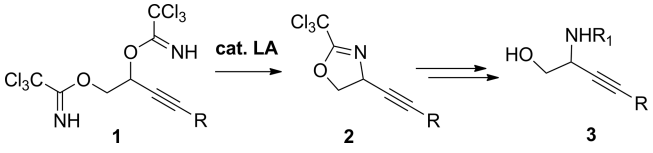

Figure 1. Alkynyl-glycinols **3** by propargylic substitution of bis-imidates **1**.

Previously we developed the synthesis of unsaturated amino alcohols based on allylic substitution in bis-imidates.[22–27] In these systems, one of the imidates serves as an *N*-nucleophile and the other as a leaving group when activated by the acid catalyst. Here we report investigation of the propargylic substitution reaction of bis-imidates **1** derived from alkynyl-glycols (Figure 1). Both regioselectivity and chirality transfer of the cyclization were explored with an aim to prepare alkynyl-oxazolines **2**, which are precursors of alkynyl-glycinols **3**.

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Results and Discussion

Racemic alkynyl-glycols **6a**–**6j** required for the synthesis of bis-imidate **1** were prepared by addition of magnesium or lithium acetylenides to protected acetaldehydes **4a** and **4b** followed by deprotection of intermediates **5a**–**5j**.

For the synthesis of diinyl-glycols **6k** and **6l**, intermediate **5b** was first de-silylated and then subjected to Glaser coupling with bromoalkynes (Table 1). For the synthesis of vinylacetylenyl-glycol **6m**, de-silylation of intermediate **5b** was followed by Sonogashira coupling with vinyl bromide (Table 1).[28]

Enantioenriched ethynyl-glycols *R*-**6a**–**6e** were prepared by using Noyori asymmetric hydrogenation reaction of protected hydroxyl ketones **7a**–**7f** as a key step (Table 2).[29] Ketones **7a**–**7e** were prepared by oxidation of protected diols **5a**–**5e**.

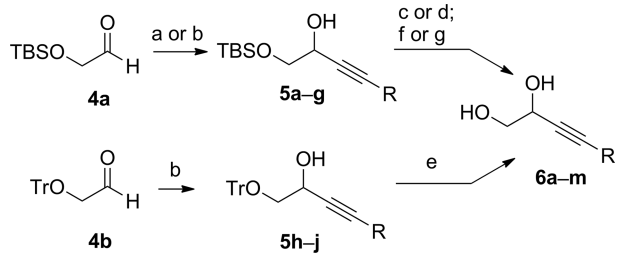
Carreira's asymmetric addition of alkynes to protected hydroxy ketone **4b**[30] was found to be the method of choice for the synthesis of enantioenriched aryl-substituted ethynyl-glycols *R*-**6h**–**6j** (Table 3).

The absolute configuration for representative diols *R*-**6b** and *R*-**6j** was determined by analysis of the ^{1}H NMR spectroscopic data of the diastereoisomeric diesters that resulted from derivatization with *R*- and *S*-α-metoxyphenylacetic acids (see Supporting Information).[31]

Diols **6a**–**6m** were converted into bis-imidates **1a**–**1m** in good yields by the reaction with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; Table 4).

Cyclization of bis-imidates **1a**–**1m** was achieved in good yields with a wide range of Lewis acid catalysts: trimethylsilyl (TMS)OTf, $BF_3{\cdot}Et_2O$, $AlCl_3$, $FeCl_3$ (Table 5). In this reaction, 4-alkynyloxazolines **2a**–**2m** typically were obtained with high selectivity over regioisomers **7a**–**7m**. In the

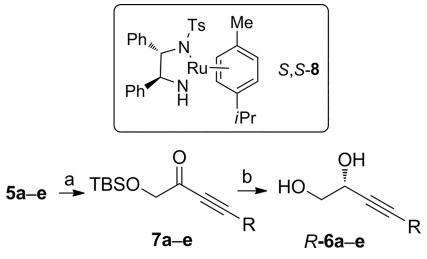
Table 1. Preparation of racemic alkynyl-glycols **6**.[a]



Entry	R	**5**, yield [%]	**6**, yield [%]
1	Me	**5a**, 87	**6a**, 81
2	TMS	**5b**, 81	**6b**, 94
3	$BnOCH_2$	**5c**, 27	**6c**, 93
4	$BnOCH_2CH_2$	**5d**, 45	**6d**, > 99
5	*t*Bu	**5e**, 78	**6e**, 88
6	Pent	**5f**, 76	**6f**, 90
7	TIPS	**5g**, 60	**6g**, 97
8	Ph	**5h**, 70	**6h**, 91
9	2-ClC_6H_4	**5i**, 70	**6i**, 95
10	3,5-ClC_6H_3	**5j**, 56	**6j**, 82
11	PentC≡C	–	**6k**, 88[b]
12	TIPSC≡C	–	**6l**, 79[b]
13	CH_2=CH	–	**6m**, 88[b]

[a] Reagents and conditions: (a) **4a**, MeC≡CMgBr, Et_2O, 0 °C for **5a**; (b) **4a** or **4b**, RC≡CH, *n*BuLi, THF, –78 °C for **5b**–**5j**; (c) **5a** and **5c**–**5f**, TBAF, AcOH, THF room temp. for **6a** and **6c**–**6f**; (d) **5b**, **g**, 1% HCl, MeOH, room temp. for **6b**, **g**; (e) **5h**–**5j**, 15 mol-% *p*TsOH·H_2O, MeOH, CH_2Cl_2, room temp. for **6h**–**6j**; (f) **5b**, KF, MeOH 50 °C then PentC≡CBr or triisopropylsilyl (TIPS)C≡CBr, NH_2OH·HCl, 20 mol-% CuCl, $BuNH_2$, room temp. for **6k** and **6l**; (g) **5b**, KF, MeOH 50 °C then 10 mol-% CuI, 2 mol-% $Pd(PPh_3)_4$, diethanolamine, vinyl bromide, THF, room temp. for **6m**. [b] Diols **6k**–**6m** were prepared from intermediate **5b**.

Table 2. Preparation of enantioenriched alkynyl-glycols **6** by using Noyori asymmetric reduction reaction.[a]

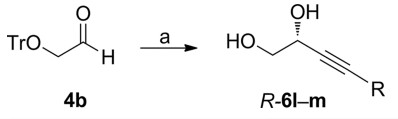


Entry	R	**7**, yield [%]	**6**, yield [%] (*ee* [%])[b]
1	Me	**7a**, 70	*R*-**6a**, 72 (90)
2	TMS	**7b**, 70	*R*-**6b**, 68 (96)
3	$BnOCH_2$	**7c**, 83	*R*-**6c**, 61 (92)
4	$BnOCHCH_2$	**7d**, 70	*R*-**6d**, 43 (93)
5	*t*Bu	**7e**, 50	*R*-**6e**, 63 (93)

[a] Reagents and conditions: (a) Dess–Martin periodinane, CH_2Cl_2, room temp. (b) Cat. **8** (6 mol-%), *i*PrOH room temp., then TBAF, AcOH, THF room temp. [b] *ee* was determined by chiral GC for **6a**, **6b**, and **6e**, or by HPLC by using chiral column Chiralpak IB for **6c** and **6d**.

case of TMS-substituted substrate **1b**, the desired selectivity for oxazoline **2b** formation was improved by replacing the TMSOTf catalyst with $AlCl_3$ (Table 5, Entries 2 and 3).

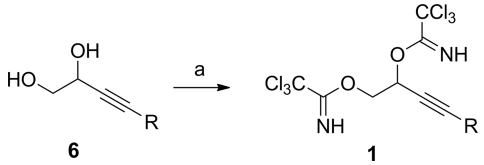
Table 3. Preparation of enantioenriched alkynyl-glycols by using Carreira's asymmetric alkynylation.[a]



Entry	R	**6**, yield [%] (*ee* [%])[b]
1	Ph	*R*-**6h**, 79 (88)
2	2-ClC_6H_4	*R*-**6i**, 88 (90)
3	3,5-ClC_6H_3	*R*-**6j**, 60 (93)

[a] Reagents and conditions: (a) RC≡CH (2.5 equiv.), (–)-*N*-methylephedrine (2.2 equiv.), $Zn(OTf)_2$ (2.0 equiv.), TEA (2.2 equiv.), toluene room temp. then *p*TsOH·H_2O (15 mol-%), MeOH, CH_2Cl_2, room temp. [b] *ee* was determined by HPLC by chiral column Chiralpak IB.

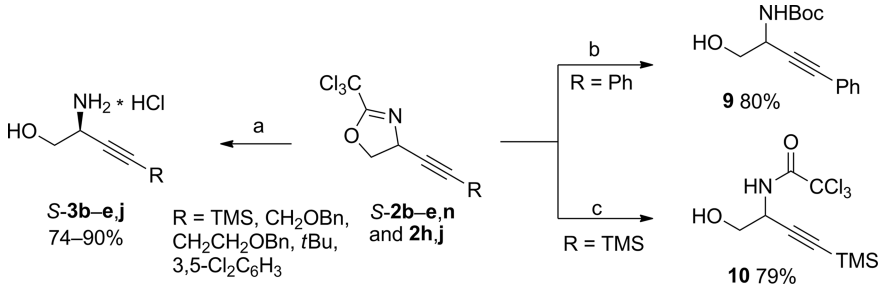
Table 4. Preparation of bis-imidates **1** from alkynyl-glycols **6**.[a]



Entry	R	**1**, yield [%][b]
1	Me	**1a**, 73
2	TMS	**1b**, 85
3	$BnOCH_2$	**1c**, 92
4	$BnOCH_2CH_2$	**1d**, 97
5	*t*Bu	**1e**, 90
6	Pent	**1f**, 88
7	TIPS	**1g**, 99
8	Ph	**1h**, 80
9	2-ClC_6H_4	**1i**, 85
10	3,5-ClC_6H_3	**1j**, 88
11	Pent–C≡C	**1k**, 83
12	TIPS–C≡C	**1l**, 50
13	CH_2=CH	**1m**, 85

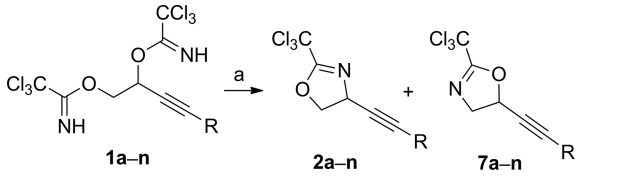
[a] Reagents and conditions: (a) CCl_3CN, 20 mol-% DBU, molecular sieves (4 Å), CH_2Cl_2, 0 °C. [b] Enantioenriched bis-imidates *R*-**1** were prepared by the same procedure as the racemic compound in similar yields.

Chirality transfer in the cyclization reaction of enantioenriched bis-imidates *R*-**1** was investigated. Substrates *R*-**1a**–**1e** that contained an alkyl or TMS substituent gave oxazolines *S*-**2a**–**2e** with complete inversion of configuration at the stereocenter (Table 6, Entries 1–5). This stereochemical outcome indicates that the S_N2 type substitution of the Lewis acid complexed propargylic imidate with the uncomplexed imidate (Figure 2). Notably, this is different from allylic substitution reaction with bis-imidates, which proceed by an S_N1 type reaction mechanism.[22,24,26] In turn, phenyl-substituted bis-imidate *R*-**1h** formed oxazoline **2h** with a considerable degree of racemization (Table 6, Entry 6). One chlorine substituent in the phenyl ring in substrate *R*-**1i** slightly suppressed the racemization in the cyclization to oxazoline **2i** (Table 6, Entries 7–9). With two chlorines in the phenyl ring in substrate *R*-**1j** the racemization was minimal with all the catalysts explored and oxazoline *S*-**2j** was



Scheme 1. Transformation of oxazolines **2** into amino alcohol derivatives **3**, **9**, and **10**. Reagents and conditions: (a) Aqueous HCl (6 M), MeOH, room temp.; (b) Aqueous HCl (6 M), MeOH room temp. then Boc_2O, $NaHCO_3$, THF room temp.; (c) *p*TsOH, pyridine, H_2O 80 °C.

Table 5. Substrate scope in the cyclization reaction of bis-imidates **1** to oxazolines **2**.[a]



Entry	R	Cat.[b]	**2**/**7**	**2**, yield [%]
1	Me	TMSOTf	> 50:1	**2a**, 71
2	TMS	TMSOTf	9:1	**2b**, 82
3	TMS	$AlCl_3$	35:1	**2b**, 91
4	$BnOCH_2$	$AlCl_3$	8:1	**2c**, 75
5	$BnOCH_2CH_2$	$AlCl_3$	41:1	**2d**, 80
6	*t*Bu	$AlCl_3$	> 50:1	**2e**, 84
7	Pent	TMSOTf	> 50:1	**2f**, 82
8	TIPS	$AlCl_3$	23:1	**2g**, 73
9	Ph	TMSOTf	25:1	**2h**, 79
10	2-ClC_6H_4	TMSOTf	> 50:1	**2i**, 70
11	3,5-ClC_6H_3	$AlCl_3$	32:1	**2j**, 95
12	PentC≡C	$AlCl_3$	11:1	**2k**, 86
13	TIPSC≡C	$AlCl_3$	> 50:1	**2l**, 69
14	CH_2=CH	$AlCl_3$	> 50:1	**2m**, 80

[a] Reagents and conditions: (a) Lewis acid, CH_2Cl_2, room temp. [b] From the range of catalysts screened (TMSOTf, $BF_3{\cdot}Et_2O$, $AlCl_3$, $FeCl_3$) only the result for the best performing catalyst is shown.

Table 6. Chirality transfer in the cyclization reaction of enantioenriched bis-imidates **1** to oxazolines **2**.

Entry	R	**1**, (*ee* [%])	Cat.	**2**, yield [%] (*ee* [%])
1	Me	*R*-**1a**, (90)	$AlCl_3$	*S*-**2a**, 80 (90)
2	TMS	*R*-**1b**, (96)	$AlCl_3$	*S*-**2b**, 90[a] (96)
3	$BnOCH_2$	*R*-**1c**, (92)	$AlCl_3$	*S*-**2c**, 70 (92)
4	$BnOCHCH_2$	*R*-**1d**, (93)	$AlCl_3$	*S*-**2d**, 75 (92)
5	*t*Bu	*R*-**1e**, (93)	TMSOTf	*S*-**2e**, 84 (93)
6	Ph	*R*-**1h**, (88)	$BF_3{\cdot}Et_2O$	*S*-**2h**, 80 (36)
7	2-ClC_6H_4	*R*-**1i**, (90)	$BF_3{\cdot}Et_2O$	*S*-**2i**, 90 (52)
8			TMSOTf	*S*-**2i**, 75 (57)
9			$AlCl_3$	*S*-**2i**, 89 (52)
10	3,5-ClC_6H_3	*R*-**1j**, (93)	$BF_3{\cdot}Et_2O$	*S*-**2j**, 56 (86)
11			TMSOTf	*S*-**2j**, 50 (89)
12			$AlCl_3$	*S*-**2j**, 79 (76)

[a] ^{1}H NMR yield. 1,4-bis(trichloromethyl)benzene was used as an internal standard.

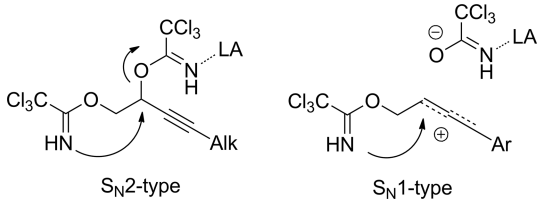


Figure 2. Proposed mechanisms for bis-imidate **1** cyclization reaction in the case of alkyl and aryl substitution.

observed in high enantiopurity (Table 6, Entries 10–12). These results indicate a mixed S_N1/S_N2 type mechanism in the case of substrates that bear a phenyl group in acetylenic position (Figure 2). The S_N1 pathway is obviously diminished by decreasing the carbenium ion stabilizing effect of the phenyl group in substrates *R*-**1i** and *R*-**1j**.

The synthetic utility of oxazolines **2** was demonstrated by transforming them into alkynyl-glycinol derivatives (Scheme 1). Strong acidic hydrolysis of oxazolines *S*-**2b**–**2e** and *S*-**2j** led to alkynyl-glycinols *S*-**3b**–**3e** and *S*-**3j**. The absolute configuration for the representative amino alcohols *S*-**3b** and *S*-**3j** was determined by analysis of the ^{1}H NMR spectra of the diastereoisomeric arylamines resulting from derivatization with *R*- and *S*-1-fluoro-2,4-dinitrophenyl-5-phenylethylamines (see Supporting Information).[32]

The hydrolysis of oxazoline **2h** was followed by *tert*-butoxycarbonyl (Boc)-protection without isolation of an intermediate to give protected amino alcohol **9**. Mild acidic hydrolysis of oxazoline **2b** provided *N*-trichloroacetyl amino alcohol **10**.

Conclusions

In summary, we have developed a new approach to enantioenriched alkynyl-glycinols based on cyclization reaction of bis-trichloroacetimidates derived from alkynyl-glycols. The cyclization reaction of bis-imidates proceeds selectively to give 4-alkynyl-oxazolines as propargylic substitution products. Enantioenriched bis-imidates that contain an alkyl or TMS substituent at acetylene give oxazolines with complete inversion of configuration. In turn, considerable racemization was observed in the cyclization reaction of bis-imidates that contain a phenyl substituent. The race-

mization for these substrates can be suppressed by introduction of electronegative substituents in the phenyl ring. The oxazolines prepared by bis-imidate cyclization can be readily transformed into alkynyl-glycinol derivatives.

Experimental Section

General Information: Commercially available reagents were used without further purification. Ru(p-cymene)[(*S*,*S*)-TsDPEN] catalyst *S*,S-**8**[33] and protected aldehydes **4a**[34] and **4b**[35] were prepared in accordance with the procedures described in the literature. *i*PrOH was distilled from CaH_2. All air- or moisture-sensitive reactions were carried out under an argon atmosphere with oven-dried glassware. Flash chromatography was carried out with Merck Kieselgel 60 (230–400 mesh). Thin-layer chromatography was performed on silica gel and was visualized by staining with $KMnO_4$. NMR spectra were recorded with a Varian Mercury spectrometer (400 MHz) and a Bruker Fourier spectrometer (300 MHz) with chemical shift values reported relative to tetramethylsilane by using the residual chloroform signal as an internal standard. Elemental analyses were performed with a Carlo-Erba EA1108 Elemental Analyzer. HRMS were obtained with a Q-TOF micro high-resolution mass spectrometer with ESI (ESI+/ESI–). Chiral HPLC was carried out with a Chiralpak IB column. Chiral GC was carried out with 6-TBDMS-2,3-Me-β-CD 50%, 25 m as the chiral stationary phase.

General Procedure for the Synthesis of Protected Diols 5a–5j: *n*BuLi solution in hexanes (2.5 M, 0.44 mL, 1.2 mmol) was added dropwise to a solution of alkyne (1.1 mmol) in tetrahydrofuran (THF; 8 mL) at –78 °C. The resulting reaction mixture was stirred at –78 °C for 30 min, then a solution of aldehyde **4a** (174 mg, 1.0 mmol) in THF (2 mL) was added dropwise. The reaction mixture was stirred at –78 °C for 2 h (TLC control) then saturated aqueous NH_4Cl (5 mL) and Et_2O (10 mL) were added. The organic phase was separated and the aqueous phase was extracted with Et_2O (2 × 20 mL). The combined organic phase was washed with brine, dried with Na_2SO_4, filtered, and the solvents evaporated. The crude residue was purified by chromatography on silica gel (ethyl acetate/hexanes, 1:10–1:6) to afford alcohols **rac-5**.

Compounds **5a**,[36] **5b**,[37] and **5e**[38] are known.

5-(Benzyloxy)-1-(*tert*-butyldimethylsilyloxy)pent-3-yn-2-ol (5c): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.26 (m, 5 H, -C_6H_5), 4.59 (s, 2 H, -OCH_2Ph), 4.49–4.43 (m, 1 H, -CHO-), 4.21 (d, J = 1.7 Hz, 2 H, -CH_2OBn), 3.79 (dd, J = 10.0, 3.8 Hz, 1 H, -CH_2O-), 3.67 (dd, J = 10.0, 7.1 Hz, 1 H, -CH_2O-), 2.74–2.62 (m, 1 H, -O*H*), 0.91 [s, 9 H, -SiC(CH_3)$_3$], 0.11 [s, 6 H, -Si(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.5, 128.5, 128.2, 128.0, 84.6, 81.5, 71.7, 67.0, 63.3, 57.5, 25.8, 18.5, –5.2 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{18}H_{29}O_3Si$ [M + H]$^+$ 321.1880; found 321.1889.

6-(Benzyloxy)-1-(*tert*-butyldimethylsilyloxy)hex-3-yn-2-ol (5d): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.26 (m, 5 H, -C_6H_5), 4.54 (s, 2 H, -OCH_2Ph), 4.41–4.34 (m, 1 H, -C*H*O-), 3.74 (dd, J = 10.0, 3.7 Hz, 1 H, -CH_2OTBS), 3.63–3.55 (m, 3 H, two signals overlapping, -CH_2OTBS, -CH_2CH_2OBn), 2.53 (td, J = 7.1, 2.0 Hz, 2 H, -C$H_2$$CH_2$OBn), 0.91 [s, 9 H, -SiC(CH_3)$_3$], 0.09 [s, 6 H, -Si(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.2, 128.6, 128.2, 128.0, 83.0, 79.1, 73.1, 68.4, 67.4, 63.4, 26.0, 20.3, 18.5, –5.2 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{19}H_{31}O_3Si$ [M + H]$^+$ 335.2037; found 335.2034.

1-(*tert*-Butyldimethylsilyloxy)non-3-yn-2-ol (5f): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.41–4.34 (m, 1 H, -C*H*O-), 3.74 (dd, J = 10.0, 3.7 Hz, 1 H, -CH_2O-), 3.60 (dd, J = 10.0, 7.5 Hz, 1 H, -CH_2O-), 2.54 (d, J = 4.2 Hz, 1 H, -OH), 2.20 [td, J = 7.2, 2.0 Hz, 2 H, -C$H_2$$(CH_2)_3CH_3$], 1.54–1.46 [m, 2 H, -$CH_2CH_2$-$(CH_2)_2CH_3$], 1.40–1.25 [m, 4 H, -$CH_2CH_2$$(CH_2)_2CH_3$], 0.93–0.87 [two signals overlapping, 12 H, -SiC(CH_3)$_3$, -$(CH_2)_4$CH_3], 0.09 [s, 6 H, -Si(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 86.5, 77.9, 67.5, 63.5, 31.2, 28.4, 26.0, 22.3, 18.8, 18.5, 14.1, –5.2 ppm. GC–MS (EI): *m*/*z* = 270 [M]$^+$. No ionization under HRMS conditions.

1-[(*tert*-Butyldimethylsilyl)oxy]-4-(triisopropylsilyl)but-3-yn-2-ol (5g): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.46–4.38 (m, 1 H, -C*H*O-), 3.77 (dd, J = 9.9, 3.9 Hz, 1 H, -CH_2O-), 3.65 (dd, J = 9.9, 6.5 Hz, 1 H, -CH_2O-), 2.53 (d, J = 5.4 Hz, 1 H, -OH), 1.11–1.02 {m, 23 H, -Si[C*H*(CH_3)$_2$]$_3$} 0.91 [s, 9 H, -SiC(CH_3)$_3$], 0.10 [s, 6 H, -Si(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 105.78, 86.29, 67.21, 63.75, 25.99, 18.72, 18.45, 11.26, –5.23 ppm. GC–MS (EI): *m*/*z* = 299.1[M – *t*Bu]$^+$.

4-Phenyl-1-(trityloxy)but-3-yn-2-ol (5h): Viscous colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57–7.21 [m, 20 H, C_6H_5-, -C(C_6H_5)$_3$], 4,78–4.69 (br., 1 H, -C*H*O-), 3.50–3.36 (m, 2 H, -CH_2O-), 2.68–2.56 (br., 1 H, -O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.6, 131.8, 128.7, 128.5, 128.3, 128.0, 127.2, 122.4, 87.4, 86.9, 85.5, 67.3, 62.6 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{29}H_{25}O_2$ 405.1849; found 405.1846 [M + H]$^+$.

4-(2-Chlorophenyl)-1-(trityloxy)but-3-yn-2-ol (5i): Viscous colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 [m, 19 H, 2-ClC_6H_4-, -C(C_6H_5)$_3$], 4.77 (m, 1 H, -C*H*O-), 3.50 (dd, J = 9.3, 6.1 Hz, 1 H, -CH_2O-), 3.43 (dd, J = 9.3, 4.1 Hz, 1 H, -CH_2O-), 2.68 (d, J = 5.5 Hz, 1 H, -O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.7, 136.1, 133.7, 129.6, 129.3, 128.8, 128.0, 127.3, 126.5, 122.5, 93.0, 87.0, 82.2, 67.2, 62.7 ppm. No ionization under HRMS conditions.

4-(3,5-Dichlorophenyl)-1-(trityloxy)but-3-yn-2-ol (5j): Viscous colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.43 [m, 6 H, 3,5-$Cl_2C_6H_3$-, -C(C_6H_5)$_3$], 7.34–7.22 [m, 12 H, -C(C_6H_5)$_3$], 4.66 (td, J = 6.0, 4.3 Hz, 1 H, -C*H*O-), 3.43–3.35 (m, 2 H, -CH_2O-), 2.57 (d, J = 5.7 Hz, 1 H, -O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.6, 135.0, 130.1, 129.1, 128.8, 128.1, 127.4, 125.4, 90.0, 87.2, 83.0, 67.1, 62.6 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{29}H_{22}Cl_2O_2Na$ [M + Na]$^+$ 495.0889; found 495.0891.

General Procedure for the Synthesis of Diols 6a, 6c–6f: To a solution of substrate **5a**, or **5c**–**5f** (1.00 mmol) in THF (12 mL), AcOH (0.17 mL, 3.00 mmol) and tetra-*n*-butylammonium fluoride (TBAF; 0.95 g, 3.00 mmol) were added. The reaction mixture was stirred until complete conversion (TLC control). Then triethylamine (TEA; 0.40 mL) and silica gel were added and the solvent was evaporated. The residue was purified by chromatography on a short silica gel column (light petroleum ether/ethyl acetate, 2:1) to afford the product.

Compound ***R*-6a**[39] is known. NMR spectroscopic data for racemic compound **6a** matched these reported for enantioenriched compound ***R*-6a**.

5-(Benzyloxy)pent-3-yne-1,2-diol (6c): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.26 (m, 5 H, -$CH_2C_6H_5$), 4.57 (s, 2 H, -OCH_2Ph), 4.51–4.44 (m, 1 H, -C*H*OH), 4.19 (d, J = 1.7 Hz, 2 H, -CH_2OBn), 3.76–3.60 (m, 2 H, -CH_2OH), 3.45–3.33 (br., 1 H, -O*H*), 3.12–3.00 (br., 1 H, -O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.2, 128.6, 128.2, 128.1, 84.6, 82.0, 72.1, 66.5, 63.3, 57.5 ppm. (***R*-6c**): $[\alpha]_D^{20}$ = –13.1 (c = 1, CH_2Cl_2).

6-(Benzyloxy)hex-3-yne-1,2-diol (6d): Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39–7.33 (m, 5 H, -$CH_2C_6H_5$), 4.57 (s, 2

H, -OCH_2Ph), 4.50–4.40 (m, 1 H, -C*H*OH), 3.77–3.64 (m, 2 H, -CH_2OH), 3.60 (t, J = 6.9 Hz, 2 H, -CH_2CH_2OBn), 2.56 (td, J = 6.9, 1.9 Hz, 2 H, -CH_2CH_2OBn), 2.16 (br., 1 H, -O*H*), 2.06–1.97 (br., 1 H, -O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.8, 128.5, 127.9, 127.8, 83.4, 79.4, 73.0, 68.2, 66.7, 63.3, 20.1 ppm. (*R*-**6d**): $[\alpha]_D^{20}$ = –9.3 (c = 0.8, CH_2Cl_2).

5,5-Dimethylhex-3-yne-1,2-diol (6e): White powder, m.p. 74–76 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.37 (dd, J = 7.5, 3.6 Hz, 1 H, -C*H*OH), 3.62 (dd, J = 11.4, 3.6 Hz, 1 H, -CH_2OH), 3.53 (dd, J = 11.4, 7.5 Hz, 1 H, -CH_2OH), 3.47–3.19 (br., 2 H, two signals overlapping, -O*H*), 1.15 [s, 9 H, -C(CH_3)$_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 95.5, 76.2, 67.0, 63.5, 31.0, 27.5 ppm. No ionization under HRMS conditions. (*R*-**6e**): $[\alpha]_D^{20}$ = –18.6 (c = 1, CH_2Cl_2). $C_8H_{14}O_2$: C 67.57, H 9.92; found C 67.16, H 9.96.

Non-3-yne-1,2-diol (6f): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.47–4.40 (br., 1 H, HOC*H*-), 3.75–3.67 (br., 1 H, HOCH_2-), 3.63 (dd, 1 H, HOCH_2-), 2.39–2.28 (m, 1 H, *H*O-), 2.20 [td, J = 7.2, 2.0 Hz, 3 H, two signals overlapping: *H*O- un -CH_2-(CH_2)$_3$CH_3], 1.56–1.45 [m, 2 H, -CH_2CH_2(CH_2)$_2$CH_3], 1.40–1.25 [m, 4 H, -(CH_2)$_2$(CH_2)$_2$CH_3], 0.89 [t, J = 7.1 Hz, 3 H, -(CH_2)$_4$-CH_3] ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 87.6, 77.9, 67.1, 63.7, 31.3, 28.4, 22.4, 18.9, 14.2 ppm. No ionization under HRMS conditions.

General Procedure for the Synthesis of Diols 6b, and 6g: Substrate **5b**, or **5g** (1.00 mmol) was dissolved in a methanolic HCl solution (1%, 10 mL). The reaction mixture was stirred until complete conversion (TLC control). Then TEA (0.40 mL) and silica gel were added and the solvent was evaporated. The residue was purified by chromatography on a short silica-gel column (light petroleum ether/ethyl acetate, 1:1) to afford the product.

Compound **6g**[40] is known.

4-(Trimethylsilyl)but-3-yne-1,2-diol (6b): White powder, m.p. 53–54 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.52–4.39 (br., 1 H, -C*H*OH), 3.81–3.59 (m, 2 H, -CH_2OH), 2.36–2.22 (br., 1 H, -O*H*), 2.15–1.98 (br., 1 H, -O*H*), 0.18 [s, 9 H, -Si(CH_3)$_3$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 103.1, 91.7, 66.6, 63.9, –0.1 ppm. No ionization under HRMS conditions. (*R*-**6b**): $[\alpha]_D^{20}$ = –24.3 (c = 1, CH_2Cl_2). $C_7H_{14}O_2Si$: C 53.12, H 8.92; found C 53.00, H 8.91.

General Procedure for the Synthesis of Diols 6h–6j: To a solution of substrate **5h**–**5j** (1 mmol) in a mixture of CH_2Cl_2 and MeOH (2.5 mL/1.35 mL), *p*TsOH·H_2O (0.15 mmol) was added. The reaction mixture was stirred until complete conversion (TLC control), typically overnight. Then TEA (20 μL) and silica gel were added and the solvent evaporated. The residue was purified by chromatography on a short silica-gel column (light petroleum ether/ethyl acetate, 1:1) to afford the product.

Racemic compound **6h**[41] is known.

4-(Phenyl)but-3-yne-1,2-diol (*R*-6h): NMR spectroscopic data corresponded to these reported in the literature for the racemic compound. White powder, m.p. 60–62 °C. $[\alpha]_D^{20}$ = –26.8 (c = 1.0, CH_2Cl_2). No ionization under HRMS conditions. $C_{10}H_{10}O_2$·1/6H_2O: C 72.71, H 6.31; found C 72.94, H 6.24.

4-(2-Chlorophenyl)but-3-yne-1,2-diol (6i): White powder, m.p. 110–112 °C. ^{1}H NMR (400 MHz, CD_3OD): δ = 7.51 (dd, J = 7.4, 2.0 Hz, 1 H, -C$_6H_4$), 7.43 (dd, J = 7.7, 1.5 Hz, 1 H, -C$_6H_4$), 7.32 (td, J = 7.7, 2.0 Hz, 1 H, -C$_6H_4$), 7.26 (td, J = 7.4, 1.5 Hz, 1 H, -C$_6H_4$), 4.59 (dd, J = 7.2, 4.7 Hz, 1 H, -C*H*OH), 3.73 (dd, J = 11.2, 4.7 Hz, 1 H, -CH_2OH), 3.67 (dd, J = 11.2, 7.2 Hz, 1 H, -CH_2OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.8, 134.6, 130.8, 130.3, 127.8, 123.9, 94.6, 82.4, 67.3, 64.7 ppm. (*R*-**6i**): $[\alpha]_D^{20}$ = –13.3 (c = 0.7, CH_2Cl_2). No ionization under HRMS conditions.

4-(3,5-Dichlorophenyl)but-3-yne-1,2-diol (6j): White powder, m.p. 115–117 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.29 (m, 3 H, -C$_6H_3$), 4.67 (dd, J = 6.4, 3.7 Hz, 1 H, -C*H*OH), 3.84 (dd, J = 11.4, 3.7 Hz, 1 H, -CH_2OH), 3.77 (dd, J = 11.4, 6.4 Hz, 1 H, -CH_2OH), 2.46–2.33 (br., 1 H, -O*H*), 2.16–1.96 (br., 1 H, -O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.1, 130.131, 129.3, 125.0, 89.2, 83.7, 66.4, 63.7 ppm. No ionization under HRMS conditions. (*R*-**6j**): $[\alpha]_D^{20}$ = –5.4 (c = 0.7, MeOH).

Undeca-3,5-diyne-1,2-diol (6k): To a solution of substrate **5b** (0.20 g, 0.73 mmol) in MeOH (8 mL) KF (0.11 g, 1.83 mmol) was added. The reaction mixture was heated at 50 °C for 7 h. After the desilylation reaction was complete (TLC control), the reaction mixture was cooled to room temp. and CuCl (14 mg, 0.15 mmol), NH_2OH·HCl (76 mg, 1.1 mmol), and $PentNH_2$ (0.85 mL) were added. The reaction mixture was stirred at room temp. for 10 min. A solution of 1-bromoalkyne (0.19 g, 1.1 mmol) in MeOH (3 mL) was added and stirring was continued for an additional 40 min until TLC showed complete conversion. The reaction mixture was poured into water (15 mL) and extracted with Et_2O (3 × 15 mL). The combined organic phase was washed with saturated aqueous $KHSO_4$ (10 mL), saturated aqueous NaCl (10 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc, 1:1) to give diol **6k** (115 mg, 88%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.52–4.47 (m, 1 H, HOC*H*-), 3.70–3.57 (m, 2 H, HOCH_2-), 2.47–2.37 (br., 1 H, *H*O-), 2.28 [td, J = 7.0, 0.9 Hz, 2 H, -CH_2(CH_2)$_3$CH_3], 2.21–2.09 (m, 1 H, *H*O-), 1.53 [m, 2 H, -CH_2CH_2(CH_2)$_2$CH_3], 1.42–1.27 [m, 4 H, -(CH_2)$_2$-(CH_2)$_2$CH_3], 0.90 [t, J = 7.1 Hz, 3 H, -(CH_2)$_4$CH_3] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 82.3, 72.9, 71.3, 66.3, 64.1, 63.6, 30.9, 27.7, 22.1, 19.2, 13.9 ppm.

6-(Triisopropylsilyl)hexa-3,5-diyne-1,2-diol (6l): Prepared similar to compound **6k** from but-3-yne-1,2-diol (41 mg), yield 101 mg (79%), slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.50–4.41 (m, 1 H, HOC*H*-), 3.76–3.61 (m, 2 H, HOCH_2-), 2.45–2.33 (br., 1 H, *H*O-), 2.14–2.02 (br., 1 H, *H*O-), 1.02 (s, 21 H, 3 *i*Pr) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 90.5, 87.3, 76.0, 73.2, 68.1, 65.5, 20.5, 13.2 ppm. No ionization under HRMS conditions.

Hex-5-en-3-yne-1,2-diol (6m): Following the reported procedure,[28] CuI (12.8 mg, 0.067 mmol, 10 mol-%) and $Pd(PPh_3)_4$ (15.6 mg, 0.013 mmol, 2 mol-%) were dissolved in diethylamine (0.6 mL) at room temp. under an argon atmosphere. To this reaction mixture, a solution of but-3-yne-1,2-diol (58 mg, 0.67 mmol, 1.0 equiv.) in THF and vinyl bromide in THF (1 M, 1.0 mL, 1.01 mmol, 1.5 equiv.) were sequentially added dropwise and the resulting suspension was stirred at room temp. for 4 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/EtOAc, 1:1) as an eluent to give diol **6m** (66 mg, 88%) as a colorless oil. ^{1}H NMR (400 MHz, CD_3OD): δ = 5.84 (ddd, J = 17.6, 11.1, 1.8 Hz, 1 H, -C*H*=CH_2), 5.59 (dd, J = 17.6, 2.2 Hz, 1 H, -CH=CH_2), 5.46 (dd, J = 11.1, 2.2 Hz, 1 H, -CH=CH_2), 4.40 (ddd, J = 6.9, 4.9, 1.8 Hz, 1 H, -C*H*O-), 3.58 (dd, J = 11.2, 4.9 Hz, 1 H, -CH_2O-), 3.53 (dd, J = 11.2, 6.9 Hz, 1 H, -CH_2O-) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 127.6, 118.0, 89.7, 84.5, 67.3, 64.5 ppm. No ionization under HRMS conditions.

General Procedure for the Synthesis of Ketones 7a–7e: To a solution of alcohol **5a**–**5e** (0.28 g, 1.31 mmol) in CH_2Cl_2 (7 mL) Dess–Martin periodinane (0.406 M in CH_2Cl_2, 4.8 mL, 1.97 mmol) was slowly added. The reaction mixture was stirred until complete conversion (TLC control). Then the mixture was diluted with Et_2O (15 mL),

filtered through a short Celite® column and the filtrate was evaporated. The residue was purified by flash column chromatography (petroleum ether/EtOAc, 15:1) to give ketone **7a**–**7e**.

Compounds **7b**,[37] and **7e**[38] are known.

1-[(*tert*-Butyldimethylsilyl)oxy]pent-3-yn-2-one (7a): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.30 (s, 2 H, -CH_2OTBS), 2.03 (s, 3 H, -CH_3), 0.92 [s, 9 H, -SiC(CH_3)$_3$], 0.10 [s, 6 H, -Si(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.8, 93.3, 78.2, 70.6, 25.9, 18.6, 4.3, –5.2 ppm.

5-(Benzyloxy)-1-(*tert*-butyldimethylsilyloxy)pent-3-yn-2-one (7c): Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.28 (m, 5 H, -C$_6H_5$), 4.62 (s, 2 H, -CH_2OTBS), 4.38–4.31 (m, 4 H, two signals overlapping, -CH_2OBn, -OCH_2Ph), 0.93 [s, 9 H, -SiC(CH_3)$_3$], 0.11 [s, 6 H, -Si(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.1, 136.8, 128.7, 128.3, 128.2, 90.6, 83.4, 72.3, 70.5, 57.1, 25.9, 18.5, –5.3 ppm.

6-(Benzyloxy)-1-(*tert*-butyldimethylsilyloxy)hex-3-yn-2-one (7d): Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.14 (m, 5 H, -C$_6H_5$), 4.45 (s, 2 H, -CH_2OTBS), 4.22 (s, 2 H, -OCH_2Ph), 3.54 (t, J = 6.8 Hz, 2 H, -CH$_2$CH_2OBn), 2.58 (t, J = 6.8 Hz, 2 H, -CH_2CH$_2$OBn), 0.83 [s, 9 H, -SiC(CH_3)$_3$], 0.00 [s, 6 H, -Si(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.4, 137.8, 128.5, 127.9, 127.8, 93.7, 79.3, 73.2, 70.6, 67.1, 25.8, 20.7, 18.5, –5.3 ppm.

General Procedure for the Synthesis of Enantioenriched Alcohols *R*-5a–5e: To a solution of catalyst **8** (20 mg, 0.03 mmol) in degassed *i*PrOH (8 mL) a solution of ketone **7a**–**7e** (0.49 mmol) in *i*PrOH (2 mL) was added. The reaction mixture was stirred until TLC showed complete conversion (from 40 min to 15 h). Then the reaction mixture was evaporated and the residue was purified by flash column chromatography (petroleum ether/EtOAc, 15:1) to give diol ***R*-5a**–**5e**.

1-[(*tert*-Butyldimethylsilyl)oxy]pent-3-yn-2-ol (*R*-5a): Enantiomeric excess (90%) was determined by chiral GC analysis [β-DEX™ 120; 30 m × 0.25 mm, d_f 0.25 μm; 160 °C to 220 °C; t_r (major) 19.4 min, t_r (minor) 19.6 min].

1-[(*tert*-Butyldimethylsilyl)oxy]-4-(trimethylsilyl)but-3-yn-2-ol (*R*-5b): $[\alpha]_D^{20}$ = –9.0 (c = 1.0, CH_2Cl_2). Enantiomeric excess (96%) was determined by chiral GC analysis [β-DEX™ 120; 30 m × 0.25 mm, d_f 0.25 μm; 160 °C to 220 °C; t_r (major) 26.5 min, t_r (minor) 26.2 min].

5-(Benzyloxy)-1-(*tert*-butyldimethylsilyloxy)pent-3-yn-2-ol (*R*-5c): $[\alpha]_D^{20}$ = –2.6 (c = 0.4, CH_2Cl_2). Enantiomeric excess (92%) was determined by supercritical fluid chromatography (SFC) analysis on chiral phase [Lux Cellulose 1; 4.6 × 150 mm; F = 2 mL/min, 10% IPA + 90% Hex; T = 25 °C; t_r (major) 9.3 min, t_r (minor) 7.2 min].

6-(Benzyloxy)-1-(*tert*-butyldimethylsilyloxy)hex-3-yn-2-ol (*R*-5d): $[\alpha]_D^{20}$ = –2.6 (c = 0.3, CH_2Cl_2). Enantiomeric excess (93%) was determined by SFC analysis on chiral phase [Chiralpak IB; 4.6 × 250 mm; F = 1 mL/min, 10% IPA + 90% Hex; T = 25 °C; t_r (major) 7.6 min, t_r (minor) 6.6 min].

1-[(*tert*-Butyldimethylsilyl)oxy]-5,5-dimethylhex-3-yn-2-ol (*R*-5e): $[\alpha]_D^{20}$ = –4.2 (c = 0.3, CH_2Cl_2) Enantiomeric excess (93%) was determined by chiral GC analysis [β-DEX™ 120; 30 m × 0.25 mm, d_f 0.25 μm; 160 °C to 220 °C; t_r (major) 31.0 min, t_r (minor) 30.8 min].

General Procedure for the Synthesis of Enantioenriched Alcohols *R*-5h–5j: $Zn(OTf)_2$ (2.0 mmol, 2.0 equiv.) was dried under vacuum at 125 °C for 2 h. Then the flask was cooled to room temperature, the vacuum was released and (–)-*N*-methylephedrine (2.2 mmol, 2.2 equiv.) was added. The vacuum was applied for 30 min and then released. Toluene (3 mL) and triethylamine (2.2 mmol, 2.2 equiv.) were added and the reaction mixture was stirred at room temperature for 2 h (in some cases overnight). Alkyne (3.0 mmol, 3.0 equiv.) was added dropwise and the reaction mixture was stirred at room temp. for 15 min. A solution of aldehyde (1.0 mmol, 2.2 equiv.) in toluene (1 mL) was added slowly by means of a syringe pump (within 1 h). The reaction mixture was stirred until TLC showed complete conversion. The reaction mixture was filtered through a short silica gel column (toluene) to afford products **5h**–**5j**.

4-Phenyl-1-(trityloxy)but-3-yn-2-ol (*R*-5h): $[\alpha]_D^{20}$ = 12.4 (c = 1.0, CH_2Cl_2). Enantiomeric excess (88%) was determined by SFC analysis on chiral phase [Chiralpak IB; 4.6 × 250 mm; F = 1 mL/min, 10% IPA + 90% Hex; T = 25 °C; t_r (major) 11.0 min, t_r (minor) 8.0 min].

4-(3-Chlorophenyl)-1-(trityloxy)but-3-yn-2-ol (*R*-5i): $[\alpha]_D^{20}$ = 2.6 (c = 1.2, CH_2Cl_2). Enantiomeric excess (90%) was determined by SFC analysis on chiral phase [Lux Cellulose 1; 4.6 × 150 mm; F = 1 mL/min, 10% IPA + 90% Hex; T = 25 °C; t_r (major) 7.0 min, t_r (minor) 9.1 min].

4-(3,5-Dichlorophenyl)-1-(trityloxy)but-3-yn-2-ol (*R*-5j): $[\alpha]_D^{20}$ = 19.9 (c = 1.7, CH_2Cl_2). Enantiomeric excess (93%) was determined by SFC analysis on chiral phase [Lux Cellulose 1; 4.6 × 150 mm; F = 2 mL/min, 10% IPA + 90% Hex; T = 25 °C; t_r (major) 6.1 min, t_r (minor) 10.2 min].

General Procedure for the Synthesis of Bis-imidates 1: To a solution of diol **6a**–**6m** (1.0 mmol) in CH_2Cl_2 or THF (10 mL) molecular sieves (4 Å) were added. The reaction mixture was cooled to 0 °C and DBU (0.25 mmol, 25 mol-%) was added. The solution was stirred at 0 °C for 30 min, trichloroacetonitrile (4 mmol, 4 equiv.) was added. The reaction mixture was stirred until complete conversion of the starting material (TLC control). The solvent was removed and the residue was purified by filtering through a short silica-gel column (CH_2Cl_2). If needed, the product was purified by flash column chromatography on silica gel (petroleum ether/EtOAc, 10:1) to give bis-trichloroacetimidate **1a**–**1m**.

Pent-3-yne-1,2-diyl Bis-trichloroacetimidate (1a): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (s, 1 H, =N*H*), 8.43 (s, 1 H, =N*H*), 5.88–5.84 (m, 1 H, -C*H*O-), 4.67–4.53 (m, 2 H, CH_2O-), 1.89 (s, 3 H, -CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.3, 161.6, 91.1, 91.1, 84.7, 71.9, 69.2, 66.6, 3.7 ppm. HRMS (ESI-TOF): m/z calcd. for $C_9H_9Cl_6N_2O_2$ $[M + H]^+$ 386.8790; found 386.8786.

4-(Trimethylsilyl)but-3-yne-1,2-diyl Bis-trichloroacetimidate (1b): White powder, m.p. 46–48 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54 (s, 1 H, =N*H*), 8.43 (s, 1 H, =N*H*), 5.93 (dd, J = 7.7, 4.1 Hz, 1 H, -C*H*O-), 4.68–4.57 (m, 2 H, -CH_2O-), 0.17 [s, 9 H, -Si(CH_3)$_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.5, 161.5, 97.3, 93.8, 77.4, 69.0, 66.6, –0.2 ppm. HRMS (ESI-TOF): m/z calcd. for $C_{11}H_{15}Cl_6N_2O_2Si$ $[M + H]^+$ 444.9028; found 444.9029.

5-(Benzyloxy)pent-3-yne-1,2-diyl Bis-trichloroacetimidate (1c): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.57 (s, 1 H, =N*H*), 8.46 (s, 1 H, =N*H*), 7.37–7.26 (m, 5 H, -C$_6H_5$), 6.00–5.94 (m, 1 H, -C*H*O-), 4.68 (dd, J = 11.7, 3.9 Hz, 1 H, -CH_2O-), 4.62 (dd, J = 11.7, 7.7 Hz, 1 H, -CH_2O-), 4.58 (s, 2 H, -CH_2Ph), 4.21 (d, J = 1.7 Hz, 2 H, -CH_2OBn) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.3, 161.4, 137.2, 128.6, 128.3, 128.1, 90.9, 84.0, 79.5, 71.6, 68.8, 66.0, 57.2 ppm. Unstable under HRMS analysis conditions.

6-(Benzyloxy)hex-3-yne-1,2-diyl Bis-trichloroacetimidate (1d): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (s, 1 H, =N*H*),

8.42 (s, 1 H, =N*H*), 7.37–7.24 (m, 5 H, -C_6H_5), 5.90 (ddt, *J* = 5.9, 4.0, 2.0 Hz, 1 H, -C*H*O-), 4.64–4.56 (m, 2 H, -CH_2O-), 4.52 (s, 2 H, -OCH_2Ph), 3.57 (t, *J* = 7.0 Hz, 2 H, -CH_2CH_2OBn), 2.55 (td, *J* = 7.0, 2.0 Hz, 2 H, -CH_2CH_2OBn) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 162.7, 161.9, 138.4, 128.9, 128.2, 128.1, 91.3, 86.2, 74.3, 73.4, 69.5, 68.3, 66.9, 20.7 ppm. Unstable under HRMS analysis conditions.

5,5-Dimethylhex-3-yne-1,2-diyl Bis-trichloroacetimidate (1e): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 8.49 (s, 1 H, =N*H*), 8.41 (s, 1 H, =N*H*), 5.91 (dd, *J* = 7.0, 4.8 Hz, 1 H, -C*H*O-), 4.61–4.53 (m, 2 H, -CH_2O-), 1.21 [s, 9 H, -C(CH_3)$_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 162.6, 161.5, 97.2, 91.2, 91.1, 71.4, 69.4, 66.7, 30.8, 27.6 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{12}H_{15}C_{16}N_2O_2$ [M + H]$^+$ 428.9259; found 428.9248.

Non-3-yne-1,2-diyl Bis-trichloroacetimidate (1f): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 8.49 (s, 1 H, =N*H*), 8.40 (s, 1 H, =N*H*), 5.87 (dd, *J* = 9.2, 4.3 Hz, 1 H, -C*H*O-), 4.63–4.56 (m, 2 H, -CH_2O-), 2.21 [td, *J* = 7.1, 2.0 Hz, 2 H, -CH_2(CH$_2$)$_3$CH$_3$], 1.54–1.45 [m, 2 H, -CH_2CH_2(CH$_2$)$_2$CH$_3$], 1.38–1.22 [m, 4 H, -CH_2CH_2(CH_2)$_2$CH$_3$], 0.87 [t, *J* = 7.1 Hz, 3 H, -(CH$_2$)$_4$CH_3] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 162.5, 161.7, 89.4, 72.9, 69.4, 66.9, 31.1, 28.1, 22.3, 18.9, 14.1 (-*C*Cl$_3$ not detected) ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{13}H_{17}C_{16}N_2O_2$ [M + H]$^+$ 442.9416; found 442.9408.

4-(Triisopropylsilyl)but-3-yne-1,2-diyl Bis-trichloroacetimidate (1g): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 8.53 (s, 1 H, =N*H*), 8.41 (s, 1 H, =N*H*), 5.90 (dd, *J* = 7.6, 4.2 Hz, 1 H, -C*H*O-), 4.70–4.55 (m, 2 H, -CH_2O-), 1.04 {s, 21 H, -Si[C*H*(CH_3)$_2$]$_3$} ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 162.5, 161.3, 110.2, 99.4, 91.1, 90.2, 69.0, 66.7, 18.6, 11.2 ppm. Unstable under HRMS analysis conditions.

4-Phenylbut-3-yne-1,2-diyl Bis-trichloroacetimidate (1h): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 8.57 (s, 1 H, =N*H*), 8.45 (s, 1 H, =N*H*), 7.56–7.41 (m, 2 H, -C_6H_5), 7.41–7.25 (m, 3 H, -C_6H_5), 6.13 (dd, *J* = 7.6, 4.1 Hz, 1 H, -C*H*O-), 4.79–4.65 (m, 2 H, -CH_2O-) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 162.5, 161.6, 132.2, 129.2, 128.5, 121.8, 91.1, 87.8, 81.7, 69.0, 66.9 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{12}H_9Cl_3NO$ [M – C_2HNOCl_3]$^+$ 287.9752; found 287.9750.

4-(2-Chlorophenyl)but-3-yne-1,2-diyl Bis-trichloroacetimidate (1i): Colorless oil. ^{1}H NMR (400 MHz, cdcl$_3$): *δ* = 8.55 (s, 1 H, =N*H*), 8.41 (s, 1 H, =N*H*), 7.40 (d, *J* = 7.6 Hz, 1 H, -C_6H_4Cl), 7.31 (d, *J* = 8.0 Hz, 1 H, -C_6H_4Cl), 7.24–7.17 (m, 1 H, -C_6H_4Cl), 7.17–7.10 (m, *J* = 7.5 Hz, 1 H, -C_6H_4Cl), 6.12 (dd, *J* = 7.7, 4.0 Hz, 1 H, -C*H*O-), 4.76–4.63 (m, 2 H, -CH_2O-) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 162.4, 161.5, 136.5, 133.8, 130.2, 129.5, 126.5, 121.8, 91.0, 91.0, 86.9, 84.4, 68.8, 66.8 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{12}H_8NOCl_4$ [M – C_2HNOCl_3]$^+$ 321.9360; found 321.9360.

4-(3,5-Dichlorophenyl)but-3-yne-1,2-diyl Bis-trichloroacetimidate (1j): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 8.60 (s, 1 H, =N*H*), 8.48 (s, 1 H, =N*H*), 7.39–7.27 (m, 3 H, -C_6H_3), 6.10 (dd, *J* = 7.5, 4.1 Hz, 1 H, -C*H*O-), 4.72 (dd, *J* = 11.7, 4.1 Hz, 1 H, -CH_2O-), 4.68 (dd, *J* = 11.7, 7.5 Hz, 1 H, -CH_2O-) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 162.4, 161.5, 135.1, 130.3, 129.7, 124.5, 91.0, 90.9, 85.0, 84.2, 68.6, 66.5 ppm. Unstable under HRMS analysis conditions.

Undeca-3,5-diyne-1,2-diyl Bis-trichloroacetimidate (1k): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 8.57 (s, 1 H, =N*H*), 8.46 (s, 1 H, =N*H*), 5.94 (dd, *J* = 7.8, 3.9 Hz, 1 H, -C*H*O-), 4.71–4.57 (m, 2 H, -CH_2O-), 2.28 [t, *J* = 7.1 Hz, 2 H, -CH_2(CH$_2$)$_3$CH$_3$], 1.58–1.48 [m, 4 H, -(CH_2)$_2$(CH$_2$)$_2$CH$_3$], 1.41–1.24 [m, 4 H, -CH_2CH_2(CH_2)$_2$CH$_3$], 0.90 [t, *J* = 7.1 Hz, 3 H, -(CH$_2$)$_4$CH_3] ppm. ^{13}C NMR (101 MHz, $CDCl_3$): *δ* = 162.4, 161.4, 90.9, 90.8, 83.3, 73.0, 68.7, 67.7, 66.7, 64.2, 31.1, 27.8, 22.3, 19.4, 14.0 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{15}H_{17}C_{16}N_2O_2$ [M + H]$^+$ 466.9416; found 466.9413.

6-(Triisopropylsilyl)hexa-3,5-diyne-1,2-diyl Bis-trichloroacetimidate (1l): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 8.53 (s, 1 H, =N*H*), 8.40 (s, 1 H, =N*H*), 5.91 (dd, *J* = 8.0, 3.8 Hz, 1 H, -C*H*O-), 4.62 (dd, *J* = 11.7, 3.8 Hz, 1 H, -CH_2O-), 4.56 (dd, *J* = 11.7, 8.0 Hz, 1 H, -CH_2O-), 1.01 {s, 21 H, -Si[C*H*(CH_3)$_2$]$_3$} ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 162.1, 161.2, 90.7, 90.6, 88.2, 86.7, 72.9, 68.6, 68.4, 66.3, 18.5, 11.2 ppm. Unstable under HRMS analysis conditions.

Hex-5-en-3-yne-1,2-diyl Bis-trichloroacetimidate (1m): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = ppm. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 8.55 (s, 1 H, =N*H*), 8.45 (s, 1 H, =N*H*), 6.03 (ddd, *J* = 7.7, 4.1, 1.6 Hz, 1 H, -C*H*O-), 5.82 (ddd, *J* = 17.5, 10.8, 1.6 Hz, 1 H, -C*H*=CH$_2$), 5.72 (dd, *J* = 17.5, 2.5 Hz, 1 H, -CH=CH_2), 5.57 (dd, *J* = 10.8, 2.5 Hz, 1 H, -C*H*=CH_2), 4.70–4.60 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 162.5, 161.6, 129.4, 116.1, 91.0, 91.0, 86.4, 82.2, 68.9, 66.7 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{10}H_8Cl_6N_2O_2$ [M + H]$^+$ 398.8790; found 398.8793.

General Procedure for the Cyclization Reaction of Bis-trichloroacetimidates 1a–1m: Molecular sieves (4 Å) and a Lewis acid catalyst (0.05 mmol, 10 mol-%) were added to a stirred solution of bis-imidate **1a**–**1m** (0.50 mmol) in solvent (5 mL) at room temp. After the reaction was complete (TLC control in the first minute of the reaction), TEA (50 mol-%) was added to the reaction mixture and the solvent was evaporated. The residue was purified by chromatography on a short silica-gel column (light petroleum ether/ethyl acetate, 10:1) to afford product **2a**–**2m**.

4-(Prop-1-yn-1-yl)-2-(trichloromethyl)oxazoline (2a): Colorless oil. ^{1}H NMR (400 MHz, [D$_6$]dimethyl sulfoxide): *δ* = 5.19–5.12 (m, 1 H, -C*H*N-), 4.86 (dd, *J* = 10.0, 8.2 Hz, 1 H, -CH_2O-), 4.47 (t, *J* = 8.2 Hz, 3 H, -CH_2O-), 1.84 (d, *J* = 2.3 Hz, 3 H, -CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ dried with K_2CO_3): *δ* = 163.7, 86.5, 82.7, 75.8, 58.0, 3.9 ppm. GC–MS (EI): *m*/*z* = 225 [M]$^+$. Enantiomeric excess (90%) was determined by chiral GC analysis [β-DEX™ 120; 30 m × 0.25 mm, d_f 0.25 μm; 160 °C to 220 °C; t_r (major) 19.2 min, t_r (minor) 18.8 min].

4-[(Trimethylsilyl)ethynyl]-2-(trichloromethyl)oxazoline (2b): White powder, m.p. 53–54 °C. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 5.07 (dd, *J* = 10.2, 9.1 Hz, 1 H, -C*H*N-), 4.82 (dd, *J* = 10.2, 8.2 Hz, 1 H, -CH_2O-), 4.54 (dd, *J* = 9.1, 8.2 Hz, 1 H, -CH_2O-), 0.19 [s, 9 H, -Si(CH_3)$_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 164.0, 101.2, 91.2, 86.2, 76.4, 58.3, –0.3 ppm. GC–MS (EI): *m*/*z* = 283 [M]$^+$. HRMS (ESI-TOF): *m*/*z* calcd. for $C_9H_{13}Cl_3NOSi$ [M + H]$^+$ 283.9827; found 283.9833. Enantiomeric excess (96%) was determined by chiral GC analysis [β-DEX™ 120; 30 m × 0.25 mm, d_f 0.25 μm; 160 °C to 220 °C; t_r (major) 23.4 min, t_r (minor) 22.9 min].

4-[3-(Benzyloxy)prop-1-yn-1-yl]-2-(trichloromethyl)oxazoline (2c): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.37–7.27 (m, 5 H, -C_6H_5), 5.12 (ddt, *J* = 10.3, 8.7, 1.8 Hz, 1 H, -C*H*O-), 4.82 (dd, *J* = 10.3, 8.3 Hz, 1 H, -CH_2O-), 4.59–4.53 (two signals overlapping, 3 H, -OCH_2Ph, -CH_2O-), 4.23 (d, *J* = 2.0 Hz, 2 H, -CH_2OBn) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 164.4, 137.3, 128.6, 128.2, 128.1, 82.9, 82.3, 77.4, 76.5, 72.1, 57.9, 57.6 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{14}H_{13}Cl_3NO_2$ [M + H]$^+$ 332.0006; found 332.0011. Enantiomeric excess (92%) was determined by SFC analysis on chiral

phase [Chiralpak IB; 4.6 × 250 mm; F = 1 mL/min, 10% IPA + 90% Hex; T = 25 °C; t_r (major) 13.0 min, t_r (minor) 14.0 min].

4-[4-(Benzyloxy)but-1-yn-1-yl]-2-(trichloromethyl)oxazoline (2d): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.26 (m, 5 H, -C_6H_5), 5.04 (ddt, J = 10.1, 9.0, 2.1 Hz, 1 H, -C*H*N-), 4.78 (dd, J = 10.1, 8.2 Hz, 1 H, -CH_2O-), 4.56–4.46 (two signals overlapping, 3 H, -CH_2O-, -OCH_2Ph), 3.59 (t, J = 6.9 Hz, 2 H, -CH_2CH_2OBn), 2.55 (td, J = 6.9, 2.1 Hz, 2 H, -CH_2CH_2OBn) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.0, 138.1, 128.6, 127.9, 127.8, 86.4, 83.8, 77.7, 76.8, 73.1, 68.1, 58.0, 20.4 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{15}H_{15}Cl_3NO_2$ $[M + H]^+$ 346.0163; found 346.0160. Enantiomeric excess (92%) was determined by SFC analysis on chiral phase [Chiralpak IB; 4.6 × 250 mm; F = 1 mL/min, 10% IPA + 90% Hex; T = 25 °C; t_r (major) 11.9 min, t_r (minor) 9.7 min].

4-(3,3-Dimethylbut-1-yn-1-yl)-2-(trichloromethyl)oxazoline (1e): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.02 (dd, J = 10.0, 9.1 Hz, 1 H, -C*H*N-), 4.78 (dd, J = 10.0, 8.1 Hz, 1 H, -CH_2O-), 4.43 (dd, J = 9.1, 8.1 Hz, 1 H, -CH_2O-), 1.20 [s, 9 H, -C-(CH_3)$_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 95.0, 86.5, 77.1, 75.1, 58.1, 30.9, 27.6 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{10}H_{13}Cl_3NO$ $[M + H]^+$ 268.0057; found 268.0064. Enantiomeric excess (93%) was determined by chiral GC analysis [β-DEX™ 120; 30 m × 0.25 mm, d_f 0.25 μm; 160 °C to 220 °C; t_r (major) 26.3 min, t_r (minor) 26.1 min].

4-(Hept-1-yn-1-yl)-2-(trichloromethyl)oxazoline (2f): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.02 (ddt, J = 9.9, 8.8, 2.1 Hz, 1 H, -C*H*N-), 4.77 (dd, J = 9.9, 8.2 Hz, 1 H, -CH_2O-), 4.47 (dd, J = 8.8, 8.2 Hz, 1 H, -CH_2O-), 2.19 [td, J = 7.2, 2.1 Hz, 3 H, -CH_2(CH_2)$_3$$CH_3$], 1.50 [p, J = 7.2 Hz, 2 H, -CH_2CH_2(CH_2)$_2$$CH_3$], 1.38–1.22 [m, 4 H, -($CH_2$)$_2$(C$H_2$)$_2$$CH_3$], 0.92–0.81 [m, 3 H, -($CH_2$)$_4$-C$H_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.9, 87.3, 86.5, 77.0, 76.6, 58.1, 31.2, 28.2, 22.3, 18.9, 14.1 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{11}H_{15}Cl_3NO$ $[M + H]^+$ 282.0214; found 282.0219.

4-[(Triisopropylsilyl)ethynyl]-2-(trichloromethyl)oxazoline (2g): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.06 (dd, J = 9.9, 8.2 Hz, 1 H, -C*H*N-), 4.79 (dd, J = 9.9, 8.2 Hz, 1 H, -CH_2O-), 4.53 (t, J = 8.2 Hz, 1 H, -CH_2O-), 1.05 {s, 21 H, -Si[CH(CH_2)$_3$]$_3$} ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.2, 103.6, 87.9, 86.5, 77.1, 58.6, 18.7, 11.2 ppm. GC–MS: 368 $[M]^+$.

4-(Phenylethynyl)-2-(trichloromethyl)oxazoline (2h): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.43 (m, 2 H, *o*-C_6H_5-), 7.37–7.28 (m, 3 H, *p*,*m*-C_6H_5-), 5.30 (dd, J = 10.0, 8.5 Hz, 1 H, -C*H*N-), 4.90 (dd, J = 10.0, 8.5 Hz, 1 H, -CH_2O-), 4.66 (t, J = 8.5 Hz, 1 H, -CH_2O-) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.3, 132.0, 129.0, 128.5, 122.2, 86.4, 86.1, 85.4, 76.7, 58.5 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{12}H_9Cl_3NO$ $[M + H]^+$ 287.9750; found 287.9749. Enantiomeric excess (36%) was determined by SFC analysis on chiral phase [Chiralpak IB; 4.6 × 250 mm; F = 1 mL/min, 10% IPA + 90% Hex; T = 25 °C; t_r (major) 6.9 min, t_r (minor) 11.8 min].

4-[(3-Chlorophenyl)ethynyl]-2-(trichloromethyl)oxazoline (2i): Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43 (dd, J = 7.4, 2.0 Hz, 1 H, -C_6H_4), 7.32 (dd, J = 7.9, 1.3 Hz, 1 H, -C_6H_4), 7.25–7.10 (m, 2 H, -C_6H_4), 5.27 (dd, J = 10.0, 8.5 Hz, 1 H, -C*H*N-), 4.85 (dd, J = 10.0, 8.5 Hz, 1 H, -CH_2O-), 4.63 (t, J = 8.5 Hz, 1 H, -CH_2O-) ppm. ^{13}C NMR: δ = 164.5, 136.4, 133.8, 130.0, 129.4, 126.6, 122.2, 90.6, 86.4, 82.8, 58.6 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{12}H_7Cl_4NO$ $[M + H]^+$ 321.9355; found 321.9346. Enantiomeric excess (52–57%) was determined by SFC analysis on chiral phase [Chiralpak IB; 4.6 × 250 mm; F = 1 mL/min, 10% IPA + 90% Hex; T = 25 °C; t_r (major) 9.7 min, t_r (minor) 10.9 min].

4-[(3,5-Dichlorophenyl)ethynyl]-2-(trichloromethyl)oxazoline (2j): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27 (m, 3 H, -C_6H_3), 5.24–5.17 (m, 1 H, -C_6H_3), 4.83 (dd, J = 10.1, 8.4 Hz, 1 H, -C*H*N-), 4.62–4.54 (m, 1 H, -CH_2O-) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.7, 135.1, 130.2, 129.4, 124.9, 87.8, 86.2, 83.4, 76.4, 58.2 ppm. Unstable under HRMS analysis conditions. Enantiomeric excess (76–89%) was determined by SFC analysis on chiral phase [Chiralpak IB; 4.6 × 250 mm; F = 1 mL/min, 10% IPA + 90% Hex; T = 25 °C; t_r (major) 5.8 min, t_r (minor) 6.4 min].

4-(Nona-1,3-diyn-1-yl)-2-(trichloromethyl)oxazoline (2k): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.13–5.07 (m, 1 H, -C*H*N-), 4.79 (dd, J = 10.1, 8.4 Hz, 1 H, -CH_2O-), 4.56 (t, J = 8.4 Hz, 1 H, -CH_2O-), 2.27 [td, J = 7.1, 0.8 Hz, 2 H, -CH_2(CH_2)$_3$$CH_3$], 1.53 [p, J = 7.1 Hz, 2 H, -CH_2CH_2(CH_2)$_2$$CH_3$], 1.42–1.24 [m, 4 H, -($CH_2$)$_2$(C$H_2$)$_2$$CH_3$], 0.89 [t, J = 7.1 Hz, 3 H, -(CH_2)$_4$CH_3] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.6, 86.2, 82.7, 76.2, 71.4, 71.3, 64.5, 58.3, 31.1, 27.9, 22.3, 19.4, 14.1 ppm. GC–MS (EI): *m*/*z* 290 $[M^+ – Me]$. Unstable under HRMS analysis conditions.

4-[(Triisopropylsilyl)buta-1,3-diyn-1-yl]-2-(trichloromethyl)oxazoline (2l) Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.13 (dd, J = 10.2, 8.5 Hz, 1 H, -C*H*N-), 4.81 (dd, J = 10.2, 8.5 Hz, 1 H, -CH_2O-), 4.60 (t, J = 8.5 Hz, 1 H, -CH_2O-), 1.08 {s, 21 H, -Si[C*H*-(CH_3)$_2$]$_3$} ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.6, 88.5, 86.0, 85.9, 75.8, 72.2, 71.2, 58.2, 18.5, 11.2 ppm. Unstable under HRMS analysis conditions.

4-(But-3-en-1-yn-1-yl)-2-(trichloromethyl)oxazoline (2m): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.82 (ddd, J = 17.6, 10.9, 1.8 Hz, 1 H, -C*H*=CH_2), 5.70 (dd, J = 17.6, 2.3 Hz, 1 H, -CH=CH_2), 5.54 (dd, J = 10.9, 2.3 Hz, 1 H, -CH=CH_2), 5.18 (ddd, J = 10.1, 8.6, 1.8 Hz, 1 H, -C*H*N-), 4.83 (dd, J = 10.1, 8.6 Hz, 1 H, -CH_2O-), 4.56 (t, J = 8.6 Hz, 1 H, -CH_2O-) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.3, 128.6, 116.4, 86.4, 86.0, 84.7, 76.6, 58.3 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_8H_7Cl_3NO$ $[M + H]^+$ 237.9593; found 237.9593.

General Procedure for the Synthesis of Alkynyl-Glycinols (*S*-3): Aqueous HCl (6 M, 1 mL) was added dropwise to a solution of oxazoline *S*-**2** (0.15 mmol) in MeOH (1.5 mL) at room temperature. The reaction mixture was stirred at room temperature for 2 h and the solvent was evaporated. Toluene (1 mL) was added to the reaction mixture and the solvents evaporated. This procedure was repeated one more time. The residue was suspended in EtOAc and filtered to give amino alcohol *S*-**3**.

2-Amino-4-(trimethylsilyl)but-3-yn-1-ol Hydrochloride (*S*-3b): White powder, yield 90%, m.p. 136–139 °C. ^{1}H NMR (400 MHz, CD_3OD): δ = 4.11 (dd, J = 8.2, 4.2 Hz, 1 H, -NC*H*-), 3.85 (dd, J = 11.6, 4.2 Hz, 1 H, -CH_2OH), 3.65 (dd, 1 H, -CH_2OH), 0.20 [s, 9 H, -Si(CH_3)$_3$] ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 98.5, 94.4, 63.2, 49.6, 46.6, –0.5 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_7H_{16}NOSi$ $[M]^+$ 158.1001; found 158.0994. $[\alpha]_D^{20}$ = 15.6 (c = 1.0, MeOH).

2-Amino-7-(benzyloxy)hepta-3,5-diyn-1-ol Hydrochloride (*S*-3c): White powder, yield 75%, m.p. 110–114 °C. ^{1}H NMR (400 MHz, CD_3OD): δ = 7.39–7.27 (m, 5 H, -C_6H_5), 4.59 (s, 2 H, -OCH_2Ph), 4.26 (d, J = 1.8 Hz, 2 H, -CH_2OBn), 4.18 (ddt, J = 7.7, 4.0, 1.8 Hz, 1 H, -C*H*N-), 3.87 (dd, J = 11.6, 4.0 Hz, 1 H, -CH_2O), 3.70 (dd, J = 11.6, 7.7 Hz, 1 H, -CH_2O) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 137.3, 128.0, 127.7, 127.6, 84.0, 78.3, 71.5, 61.7, 56.5, 44.7 ppm. HRMS (ESI-TOF): *m*/*z* calcd. for $C_{12}H_{16}NO_2$ $[M]^+$ 206.1181; found 206.1175. $[\alpha]_D^{20}$ = 4.1 (c = 0.4, MeOH).

2-Amino-8-(benzyloxy)octa-3,5-diyn-1-ol Hydrochloride (*S*-3d): White powder, yield 81%, m.p. 120–124 °C. ^{1}H NMR (400 MHz,

CD_3OD): δ = 7.38–7.25 (m, 5 H, -C_6H_5), 4.54 (s, 2 H, -OCH_2Ph), 4.05 (ddt, J = 8.3, 4.1, 2.1 Hz, 1 H, -C*H*OH), 3.83 (dd, J = 11.6, 4.1 Hz, 1 H, -CH_2N-), 3.69–3.57 (m, 3 H, -CH_2CH_2OBn, -CH_2OH), 2.57 (td, J = 6.5, 2.1 Hz, 2 H, -CH_2CH_2OBn) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 137.9, 128.0, 127.5, 127.4 ppm.

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