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Regioselective Addition of Allylindium Reagents to Allenes in Functionalized 1,6-Diols Bearing Allenynes

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Addition reactions of allylindium reagents generated in situ from indium and allyl halides to functionalized allenyne 1,6-diols proceeded regioselectively through anti-Markovnikov addition to produce exclusively dienyne 1,6-diols in good yields in THF at 70 °C. In the case of 3-bromo-2-methylpropene, lithium iodide was used as an additive.

Introduction

The carbometalation of C–C multiple bonds such as alkenes, alkynes, and allenes is a very important organic transformation.[1] In particular, the addition of allylmetal compounds to C–C multiple bonds is a significant method for constructing carbon skeletons. To date, various allylmetalations have been reported on the basis of the nucleophilic character of allylmetals generated from allyl halides and metals (Ta, Zr, Zn, Al, Ti, Si, Sn, and Ga).[2] Recently, indium metal has emerged as the metal with the most potential, because of its advantages with regard to ease of preparation, handling, toxicity, and availability.[3] Although a variety of addition reaction of allylindiums with carbonyl- and imine-derived functional groups have been reported,[4] the addition of allylindiums to C–C multiple bonds have received relatively little attention. Therefore, there is still strong need for efficient addition reactions of allylindiums to C–C multiple bonds. Reactions of allylindiums with homoallenyl alcohols (**1** and **2**) bearing a methyl or isopropyl group at the C1 or C4 position afforded the corresponding allylation products with anti-Markovnikov selectivity.[5] However, because the presence of a hydroxy group was essential for accelerating the allylation reaction, the addition reaction of allylindiums with nonfunctionalized or hydroxy-protected alkynes and allenes did not proceed. In DMF, treatment of allylindiums with propargyl alcohol and homopropargyl alcohol gave the corresponding allylation products with mainly anti-Markovnikov selectivity.[6] Although the reaction of propargyl alcohol with allylindium gave predominantly the anti-Markovnikov product in THF, homologs of propargyl alcohol (**3**, n = 2, 3, and 4) afforded the addition products with Markovnikov selectivity.[7] More recently, it was reported that allylation of unactivated terminal alkynes by treatment with allylindiums provided branched 1,4-dienes through regioselective Markovnikov addition.[8] As part of our continuing effort to expand the synthetic utility of indium, we report herein stereoselective allylindation of allenyne 1,6-diols having an allenol and two alkynol moieties with an allylindium reagent (Figure 1).

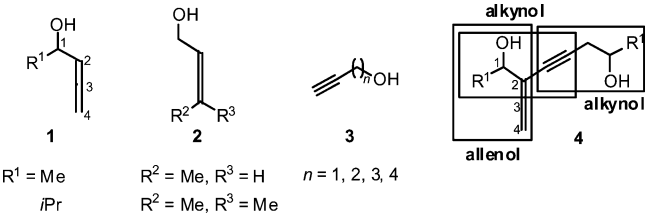

Figure 1. Structures of allenol, alkynol, and allenyne 1,6-diol.

Results and Discussion

We first investigated various experimental conditions in a model reaction of functionalized allenyne 1,6-diol **4c** with allylindium generated in situ from 3-bromo-2-methylpropene and indium (Table 1). 1,6-Diol **4c** was prepared from highly selective addition of the 3,6-dianion reagent derived from 1,6-dibromo-2,4-hexadiyne and indium to benzaldehyde (2 equiv.) in THF.[9] Treatment of **4c** with allylindium produced addition product **5d** in 55% yield in DMF at 100 °C after 15 h (Table 1, Entry 1). The use of LiI as an additive did not give the desired product (Table 1, Entry 2). However, by heating the reaction mixture at reflux (70 °C) in THF gave regioselectively dienyne 1,6-diol **5d** in 30% yield together with starting material **4c** (43%; Table 1, Entry 3). The allylindium reagent obtained from indium (1.5 equiv.) and 3-bromo-2-methylpropene (2.25 equiv.) in-

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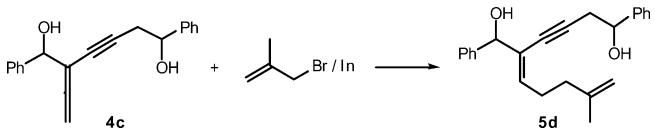
creased the yield (39%) of **5d**, but starting material **4c** did not disappear (Table 1, Entry 4). A variety of additives such as LiI, LiBr, and I_2 were examined to increase the product yield. Among them, the use of lithium iodide (1.5 equiv.) afforded dienyne 1,6-diol **5d** in 65% yield in THF at 70 °C after 16 h, which indicates that the present method proceeded regioselectively via anti-Markovnikov addition (Table 1, Entry 5). No trace of the corresponding Markovnikov addition product was detected by NMR spectroscopy in this reaction. 3-Iodo-2-methylpropene was detected in the ^{1}H NMR spectrum after treatment with lithium iodide in THF, which indicates that the bromine atom in 3-bromo-2-methylpropene was substituted for an iodine atom, and the reaction of the corresponding iodide then proceeded smoothly with indium to produce the organoindium reagent. Surprisingly, addition products resulting from addition of the allylindium to the triple bond were not observed. These results imply that homoallenyl alcohol is more reactive than homopropargyl alcohols directed towards the allylindium reagent. THF was the best solvent among several reaction media (DMF, THF, $PhCH_3$, CH_3CN, THF/H_2O, and DMF/H_2O) that were evaluated. The stereochemistry of the double bond in dienyne 1,6-diol **5d** was proved to be (*E*) by NOE experiments.

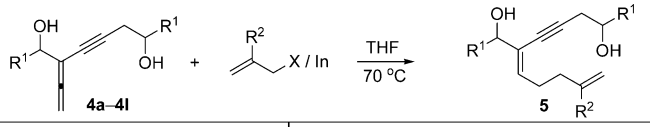
Table 1. Reaction optimization.[a]

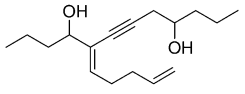
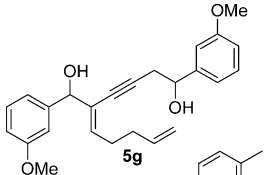
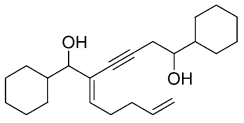
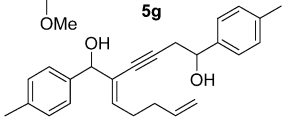
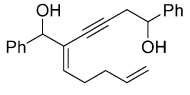
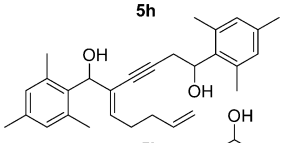
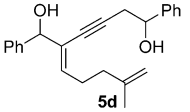
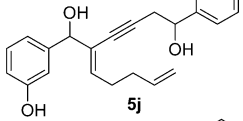
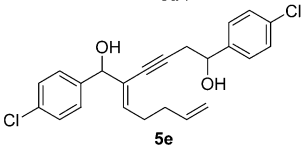
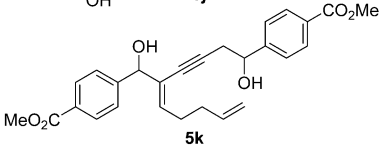
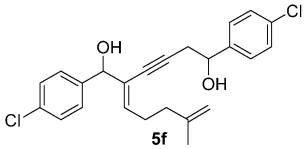
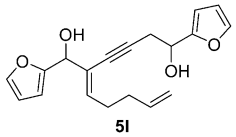


Entry	Solvent	Additive	*T* [°C]	*t* [h]	Yield [%][b]
1	DMF	–	100	15	55
2	DMF	LiI[c]	140	15	trace
3	THF	–	70	18	30(43)[d]
4[e]	THF	–	70	18	39(30)[d]
5	THF	LiI[c]	70	16	65

[a] In (1.0 equiv.) and 3-bromo-2-methylpropene (1.5 equiv.) were used. [b] Isolated yield. [c] LiI (1.5 equiv.) was used. [d] Recovery yield of **4c**. [e] In (1.5 equiv.) and 3-bromo-2-methylpropene (2.25 equiv.) were used.

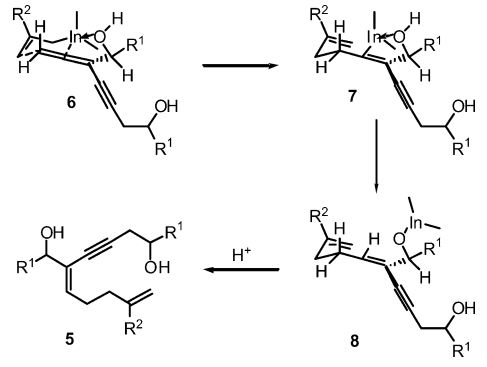
Table 2. Regioselective allylation of allylindium to allenes in 1,6-diols having allenynes.[a]



Entry	X	*t* [h]	Product	Yield [%]	Entry	X	*t* [h]	Product	Yield [%]
1	I	1	 **5a**	65	7	I	2	 **5g**	72
2	I	2	 **5b**	69	8	I	2	 **5h**	74
3	I	1	 **5c**	72	9	I	3	 **5i**	71
4[b]	Br	16	 **5d**	65	10	I	3	 **5j**	80
5	I	2	 **5e**	68	11	I	1	 **5k**	81
6[b]	Br	16	 **5f**	73	12	I	2	 **5l**	62

[a] In (1.0 equiv.) and allyl iodide (1.5 equiv.) were used. [b] In (1.0 equiv.), allyl halide (1.5 equiv.), and LiI (1.5 equiv.) were used.

To demonstrate the efficiency and scope of the present method, allylindium reagents generated in situ from the reaction of indium with allyl bromide and 3-bromo-2-methylpropene were treated with a variety of allenyne 1,6-diols, and the results are summarized in Table 2. Under the optimized conditions, allylindium added to diol **4a** in THF to give dienyne–1,6-diol **5a** in 65% yield (Table 2, Entry 1). Compound **4b** obtained from cyclohexanecarboxaldehyde produced desired compound **5b** in 69% yield (Table 2, Entry 2). Reaction of **4c** with allylindium afforded **5c** in 72% yield under the optimum conditions (Table 2, Entry 3). The presence of various substituents such as chloride, methoxy, methyl, hydroxy, and methoxycarbonyl groups on the aromatic rings did not affect the efficiency of the present reactions (Table 2, Entries 5–11). It is noteworthy that protection of the hydroxy group is not necessary under the present reaction conditions (Table 2, Entry 10). The reaction of allenyne 1,6-diol **4e** obtained from 4-chlorobenzaldehyde, indium, and 1,6-dibromo-2,4-hexadiyne with allylindium and 2-methylallylindium provided regioselectively functionalized dienyne 1,6-diols **5e** and **5f** in 68 and 73% yield, respectively (Table 2, Entries 5 and 6). In the case of the allylindium reagent obtained from 3-bromo-2-methylpropene and indium, a longer reaction time (16 h) was needed to complete the reaction (Table 2, Entries 4 and 6). Allenyne 1,6-diol **4i** derived from 2,4,6-trimethylbenzaldehyde turned out to be compatible with the employed reaction conditions (Table 2, Entry 9). Compound **4l** obtained from 2-furaldehyde worked equally well with indium and allyl iodide (Table 2, Entry 12). In all cases, no corresponding Markovnikov addition products to the allene group or addition products of allylindium reagents to the triple bond were formed in any of the reactions. Although the present reaction mechanism has not been established, a possible reaction pathway is described in Scheme 1. Addition of allylindiums to allenyne 1,6-diols can occur regioselectively and stereoselectively through hydroxy-chelated bicyclic transition state **6** to afford (*E*)-1,5-dienynes **5**. The hydroxy group in homoallenyl alcohol can coordinate to the indium atom in the allylindium reagent, which would produce bicyclic transition state **6** composed of chelated five- and six-membered rings (Zimmerman–Traxler model). The resulting vinylindium compound **7** could be spontaneously protonated by the hydroxy proton to afford (*E*)-allyl alcohol indium salt **8** followed by aqueous workup to provide dienyne 1,6-diol **5**.



Scheme 1. Plausible mechanism for the addition of allylindiums to allenyne 1,6-diol.

Conclusions

We demonstrated that the addition of allylindium reagents to functionalized allenyne 1,6-diols proceeds regioselectively through anti-Markovnikov addition to produce exclusively dienyne 1,6-diols in good yields. These results should open more opportunities in the search of efficient and selective new C–C bond-forming reactions because of the possible applications of the functionalized dienyne 1,6-diols.

Experimental Section

Typical Experimental Procedures for 5d: Indium (57.4 mg, 0.5 mmol) and lithium iodide (100.0 mg, 0.75 mmol) in dry THF (1 mL) was slowly added to 3-bromo-2-methylpropene (101.0 mg, 0.75 mmol) at room temperature under a nitrogen atmosphere. After 15 min, compound **1c** (145.0 mg, 0.5 mmol) was added to the indium reagent in dry THF (1 mL), and the mixture was then stirred at 70 °C for 16 h. After cooling to room temperature, the reaction mixture was quenched with 10% HCl (1 mL). The aqueous layer was extracted with diethyl ether (3 × 10 mL), and the combined organic phase were washed with water and brine, dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexane, 1:3; R_f = 0.3) to give **5d** (108.0 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.26–7.17 (m, 10 H), 5.86 (t, J = 7.23 Hz, 1 H), 5.04 (s, 1 H), 4.67–4.62 (m, 1 H), 4.65 (s, 1 H), 4.60 (s, 1 H), 2.68–2.63 (m, 4 H), 2.33–2.28 (m, 2 H), 2.01 (t, J = 7.53 Hz, 2 H), 1.62 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) Isomer A: δ = 145.4, 143.0, 142.5, 138.13, 128.8, 128.7, 128.24, 128.1, 126.74, 126.7, 126.2, 110.9, 93.6, 79.3, 77.1, 72.8, 37.2, 30.9, 28.7, 22.8 ppm. Isomer B: δ = 145.4, 143.0, 142.5, 138.09, 128.8, 128.7, 128.22, 128.1, 126.72, 126.7, 126.2, 110.9, 93.6, 79.3, 77.1, 72.8, 37.2, 30.9, 28.7, 22.8 ppm. IR (KBr, neat): $\tilde{\nu}$ = 3388, 3064, 3029, 2907, 1451, 1043 cm^{-1}. HRMS (EI): calcd. for $C_{24}H_{26}O_2$ $[M]^+$ 346.1933; found 346.1935.

(*E*)-5-Pent-4-enylidenedodec-6-yne-4,9-diol (5a): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 5.87–5.26 (m, 2 H), 5.03 (d, J = 17.1 Hz, 1 H), 4.98 (d, J = 10.2 Hz, 1 H), 4.00 (t, J = 6.77 Hz, 1 H), 3.81–3.76 (m, 1 H), 2.75 (s, 1 H), 2.61 (dd, J = 4.75, 4.75 Hz, 1 H), 2.50 (dd, J = 6.52, 6.52 Hz, 1 H), 2.34 (q, J = 7.32 Hz, 2 H), 2.18–2.13 (m, 2 H), 1.65–1.61 (m, 2 H), 1.60–1.46 (m, 4 H), 1.41–1.28 (m, 3 H), 0.93 (q, J = 7.4 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) Isomer A: δ = 138.3, 136.98, 127.6, 115.4, 93.3, 78.7, 75.65, 70.3, 38.9, 38.5, 33.4, 29.8, 28.9, 19.26, 14.4, 14.3 ppm. Isomer B: δ = 138.3, 136.96, 127.6, 115.4, 93.3, 78.7, 75.7, 70.2, 38.9, 38.5, 33.4, 29.8, 28.9, 19.25, 14.4, 14.3 ppm. IR (KBr, neat): $\tilde{\nu}$ = 3357, 3077, 2958, 2932, 2872, 1640, 1464, 1016 cm^{-1}. HRMS (EI): calcd. for $C_{17}H_{28}O_2$ $[M]^+$ 264.2089; found 264.2091.

(*E*)-1,6-Dicyclohexyl-2-pent-4-enylidenehex-3-yne-1,6-diol (5b): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 5.85–5.76 (m, 1 H), 5.78 (t, J = 7.26 Hz, 1 H), 5.04 (d, J = 17.1 Hz, 1 H), 4.98 (d, J = 10.1 Hz, 1 H), 3.65 (d, J = 7.87 Hz, 1 H), 3.53–3.48 (m, 1 H), 2.64 (dd, J = 4.5, 4.5 Hz, 1 H), 2.55 (dd, J = 6.87, 6.87 Hz, 1 H), 2.41–2.33 (m, 2 H), 2.19–2.14 (m, 2 H), 2.01–1.92 (m, 3 H), 1.77–1.66

(m, 9 H), 1.58–1.46 (m, 4 H), 1.30–0.85 (m, 10 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) Isomer A: δ = 138.3, 138.0, 126.5, 115.4, 93.4, 80.8, 78.8, 74.6, 43.0, 42.4, 33.5, 29.9, 29.8, 29.5, 29.3, 28.67, 26.9, 26.8, 26.6, 26.5, 26.4, 26.3, 26.26 ppm. Isomer B: δ = 138.3, 137.9, 126.6, 115.4, 93.4, 80.9, 78.8, 74.6, 43.0, 42.3, 33.5, 29.9, 29.8, 29.6, 29.4, 28.74, 26.9, 26.8, 26.6, 26.5, 26.4, 26.3, 26.26 ppm. IR (KBr, neat): $\tilde{\nu}$ = 3366, 2923, 2851, 1448, 1263 cm^{-1}. HRMS (EI): calcd. for $C_{23}H_{36}O_2$ [M]$^+$ 344.2715; found 344.2714.

(*E*)-2-Pent-4-enylidene-1,6-diphenylhex-3-yne-1,6-diol (5c): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.37–7.27 (m, 10 H), 5.98 (t, *J* = 7.27 Hz, 1 H), 5.84–5.74 (m, 1 H), 5.14 (s, 1 H), 5.03 (d, *J* = 17.1 Hz, 1 H), 4.98 (d, *J* = 10.5 Hz, 1 H), 4.75–4.72 (m, 1 H), 2.75–2.73 (m, 2 H), 2.37–2.32 (m, 4 H), 2.15 (q, *J* = 7.15 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) Isomer A: δ = 142.5, 142.0, 137.8, 137.41, 128.4, 128.3, 127.83, 127.7, 126.4, 126.3, 125.7, 115.1, 93.1, 78.9, 76.7, 72.3, 33.0, 30.5, 29.5 ppm. Isomer B: δ = 142.5, 142.0, 137.8, 137.38, 128.4, 128.3, 127.85, 127.7, 126.4, 126.3, 125.7, 115.1, 93.0, 78.9, 76.7, 72.3, 33.0, 30.5, 29.5 ppm. IR (KBr, neat): $\tilde{\nu}$ = 3407, 3064, 3029, 2926, 1454, 1049 cm^{-1}. HRMS (EI): calcd. for $C_{23}H_{24}O_2$ [M]$^+$ 332.1776; found 332.1779.

(*E*)-1,6-Bis(4-chlorophenyl)-2-pent-4-enylidenehex-3-yne-1,6-diol (5e): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.30–7.18 (m, 8 H), 5.94 (t, *J* = 7.27 Hz, 1 H), 5.82–5.71 (m, 1 H), 5.08 (s, 1 H), 5.02 (d, *J* = 17.0 Hz, 1 H), 4.98 (d, *J* = 11.2 Hz, 1 H), 4.71 (t, *J* = 6.58 Hz, 1 H), 2.84 (s, 1 H), 2.75 (s, 1 H), 2.70 (d, *J* = 6.58 Hz, 2 H), 2.32–2.27 (m, 2 H), 2.13 (q, *J* = 6.62 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) Isomer A: δ = 141.0, 140.4, 138.0, 137.7, 133.53, 133.3, 128.5, 128.4, 127.7, 127.65, 127.2, 126.04, 92.8, 78.8, 76.1, 71.64, 32.9, 30.3, 29.4 ppm. Isomer B: δ = 141.0, 140.4, 138.0, 137.7, 133.51, 133.3, 128.5, 128.4, 127.7, 127.65, 127.2, 126.00, 92.8, 78.8, 76.1, 71.59, 32.9, 30.3, 29.4 ppm. IR (KBr, neat): $\tilde{\nu}$ = 3379, 3076, 2977, 2909, 1490, 1090, 1013 cm^{-1}. HRMS (EI): calcd. for $C_{23}H_{22}Cl_2O_2$ [M]$^+$ 400.0997; found 400.0994.

(*E*)-1,6-Bis(4-chlorophenyl)-2-(4-methylpent-4-enylidene)hex-3-yne-1,6-diol (5f): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.31–7.21 (m, 8 H), 5.96 (t, *J* = 7.24 Hz, 1 H), 5.10 (s, 1 H), 4.75–4.73 (m, 1 H), 4.74 (s, 1 H), 4.67 (s, 1 H), 2.74–2.72 (m, 2 H), 2.54 (s, 1 H), 2.45 (s, 1 H), 2.37 (q, *J* = 7.24 Hz, 2 H), 2.09 (q, *J* = 7.45 Hz, 2 H), 1.70 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) Isomer A: δ = 144.8, 140.9, 140.4, 138.3, 133.57, 133.4, 128.6, 128.4, 127.6, 127.2, 125.82, 92.7, 78.8, 76.1, 71.7, 36.7, 30.4, 28.2, 22.3 ppm. Isomer B: δ = 144.8, 140.9, 140.4, 138.3, 133.56, 133.4, 128.6, 128.4, 127.7, 127.2, 125.79, 92.7, 78.8, 76.1, 71.6, 36.7, 30.3, 28.2, 22.3 ppm. IR (KBr, neat): $\tilde{\nu}$ = 3375, 3073, 2911, 1490, 1090, 1013 cm^{-1}. HRMS (EI): calcd. for $C_{24}H_{24}Cl_2O_2$ [M]$^+$ 414.1153; found 414.1153.

(*E*)-1,6-Bis(3-methoxyphenyl)-2-pent-4-enylidenehex-3-yne-1,6-diol (5g): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.25–7.19 (m, 2 H), 6.94–6.84 (m, 4 H), 6.82–6.79 (m, 2 H), 5.95 (t, *J* = 7.23 Hz, 1 H), 5.83–5.73 (m, 1 H), 5.09 (s, 1 H), 5.02 (d, *J* = 17.1 Hz, 1 H), 4.97 (d, *J* = 10.1 Hz, 1 H), 4.72 (q, *J* = 6.1 Hz, 1 H), 3.77 (s, 3 H), 3.76 (s, 3 H), 2.76–2.71 (m, 4 H), 2.33 (q, *J* = 7.37 Hz, 2 H), 2.14 (q, *J* = 7.07 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) Isomer A: δ = 159.7, 159.5, 144.3, 143.8, 137.8, 137.43, 129.4, 129.2, 126.38, 118.6, 118.1, 115.1, 113.27, 113.1, 111.9, 111.2, 93.16, 78.8, 76.6, 72.3, 55.2, 32.9, 30.5, 29.4 ppm. Isomer B: δ = 159.7, 159.5, 144.3, 143.8, 137.8, 137.38, 129.4, 129.2, 126.36, 118.6, 118.1, 115.1, 113.29, 113.2, 111.9, 111.2, 93.19, 78.8, 76.6, 72.3, 55.2, 32.9, 30.5, 29.4 ppm. IR (KBr, neat): $\tilde{\nu}$ = 3407, 3074, 2917, 2835, 1600, 1260, 1042 cm^{-1}. HRMS (EI): calcd. for $C_{25}H_{28}O_4$ [M]$^+$ 392.1988; found 392.1987.

(*E*)-2-Pent-4-enylidene-1,6-di-*p*-tolylhex-3-yne-1,6-diol (5h): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.23–7.09 (m, 8 H), 5.93 (t, *J* = 7.21 Hz, 1 H), 5.83–5.72 (m, 1 H), 5.07 (d, *J* = 3.74 Hz, 1 H), 5.01 (d, *J* = 17.1 Hz, 1 H), 4.97 (d, *J* = 10.1 Hz, 1 H), 4.72–4.68 (m, 1 H), 2.70 (d, *J* = 6.29 Hz, 2 H), 2.63 (s, 1 H), 2.59 (s, 1 H), 2.34–2.29 (m, 2 H), 2.33 (s, 3 H), 2.32 (s, 3 H), 2.12 (q, *J* = 7.14 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) Isomer A: δ = 140.1, 139.6, 138.3, 137.9, 137.7, 137.39, 129.5, 129.4, 127.05, 126.68, 126.2, 115.5, 93.6, 79.3, 77.0, 72.6, 33.4, 30.9, 29.9, 21.57 ppm. Isomer B: δ = 140.1, 139.6, 138.3, 137.8, 137.7, 137.4, 129.5, 129.4, 127.07, 126.7, 126.2, 93.6, 79.3, 77.0, 72.6, 33.4, 30.9, 29.9, 21.59 ppm. IR (KBr, neat): $\tilde{\nu}$ = 3375, 3022, 2976, 2920, 1513, 1042 cm^{-1}. HRMS (EI): calcd. for $C_{25}H_{28}O_2$ [M]$^+$ 360.2089; found 360.2087.

(*E*)-2-Pent-4-enylidene-1,6-bis(2,4,6-trimethylphenyl)hex-3-yne-1,6-diol (5i): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 6.80 (s, 2 H), 6.79 (s, 2 H), 5.79–5.71 (m, 1 H), 5.68–5.63 (m, 1 H), 5.57 (s, 1 H), 5.18–5.13 (m, 1 H), 4.98 (d, *J* = 17.2 Hz, 1 H), 4.94 (d, *J* = 10.1 Hz, 1 H), 2.97–2.90 (m, 1 H), 2.68–2.60 (m, 1 H), 2.39–2.34 (m, 8 H), 2.32–2.29 (m, 8 H), 2.30 (s, 3 H), 2.29 (s, 3 H), 2.09 (q, *J* = 7.1 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) Isomer A: δ = 138.4, 137.6, 137.5, 137.4, 136.5, 135.5, 135.2, 134.6, 130.56, 130.2, 125.1, 115.3, 93.63, 79.7, 72.1, 70.5, 33.5, 30.1, 27.7, 21.3, 21.2, 21.1 ppm. Isomer B: δ = 138.4, 137.6, 137.5, 137.3, 136.6, 135.6, 135.1, 134.5, 130.58, 130.3, 125.1, 115.3, 93.57, 79.7, 72.0, 70.3, 33.5, 30.1, 27.6, 21.3, 21.2, 21.0 ppm. IR (KBr, neat): $\tilde{\nu}$ = 3398, 2920, 1611, 1447 cm^{-1}. HRMS (EI): calcd. for $C_{29}H_{36}O_2$ [M]$^+$ 416.2715; found 416.2713.

(*E*)-1,6-Bis(3-hydroxyphenyl)-2-pent-4-enylidenehex-3-yne-1,6-diol (5j): ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25 °C, TMS): δ = 9.26 (s, 1 H), 9.23 (s, 1 H), 7.05 (t, *J* = 7.79 Hz, 2 H), 6.77 (s, 1 H), 6.73–6.65 (m, 3 H), 6.60 (t, *J* = 8.3 Hz, 2 H), 5.97 (t, *J* = 7.15 Hz, 1 H), 5.81–5.71 (m, 1 H), 5.43 (dd, *J* = 4.12, 4.34 Hz, 1 H), 5.36 (d, *J* = 4.15 Hz, 1 H), 5.01 (d, *J* = 17.2 Hz, 1 H), 4.95 (d, *J* = 10.6 Hz, 1 H), 4.83 (s, 1 H), 4.53–4.48 (m, 1 H), 2.65–2.59 (m, 1 H), 2.57–2.52 (m, 1 H), 2.17 (q, *J* = 7.15 Hz, 1 H), 2.05 (q, *J* = 6.75 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO) Isomer A: δ = 157.4, 157.2, 146.3, 145.4, 138.4, 134.6, 129.0, 128.9, 128.0, 117.8, 117.3, 115.5, 114.2, 114.1, 113.80, 113.2, 93.4, 79.2, 75.33, 71.77, 33.1, 30.4, 29.0 ppm. Isomer B: δ = 157.4, 157.2, 146.3, 145.4, 138.4, 134.5, 129.0, 128.9, 127.98, 117.9, 117.3, 115.5, 114.2, 114.1, 113.8, 113.2, 93.4, 79.22, 75.27, 71.81, 33.1, 30.4, 29.0 ppm. IR (KBr, neat): $\tilde{\nu}$ = 3268, 2908, 1455, 1277, 1023, 998 cm^{-1}. HRMS (EI): calcd. for $C_{23}H_{24}O_4$ [M]$^+$ 364.1675; found 364.1676.

(*E*)-1,6-Bis[(4-methoxycarbonyl)phenyl]-2-pent-4-enylidenehex-3-yne-1,6-diol (5k): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.97–7.91 (m, 4 H), 7.40–7.37 (m, 2 H), 7.34–7.30 (m, 2 H), 5.96 (t, *J* = 7.22 Hz, 1 H), 5.79–5.69 (m, 1 H), 5.15 (s, 1 H), 4.99 (d, *J* = 17.0 Hz, 1 H), 4.96 (d, *J* = 9.91 Hz, 1 H), 4.82–4.76 (m, 1 H), 3.86 (s, 6 H), 3.40 (s, 1 H), 3.35 (s, 1 H), 2.74–2.71 (m, 2 H), 2.32–2.25 (m, 2 H), 2.13–2.08 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) Isomer A: δ = 159.9, 159.72, 138.7, 135.3, 133.8, 133.7, 130.4, 129.1, 127.6, 122.64, 115.3, 114.3, 114.1, 95.34, 80.4, 76.8, 72.58, 55.7, 35.7, 31.0, 30.3 ppm. Isomer B: δ = 159.9, 159.71, 138.7, 135.3, 133.8, 133.7, 130.4, 129.1, 127.6, 122.6, 115.3, 114.3, 114.0, 95.31, 80.4, 76.7, 72.62, 55.7, 35.7, 31.0, 30.3 ppm. IR (KBr, neat): $\tilde{\nu}$ = 3450, 3075, 2951, 1721, 1436, 1282, 1111 cm^{-1}. HRMS (EI): calcd. for $C_{27}H_{28}O_6$ [M]$^+$ 448.1886; found 446.1886.

(*E*)-1,6-Difuran-2-yl-2-pent-4-enylidenehex-3-yne-1,6-diol (5l): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.36 (s, 2 H), 6.35–6.31 (m, 2 H), 6.29–6.26 (m, 2 H), 6.00 (t, *J* = 7.20 Hz, 1 H), 5.85–5.75 (m, 1 H), 5.12 (s, 1 H), 5.03 (d, *J* = 17.1 Hz, 1 H), 4.98 (d, *J* =

10.2 Hz, 1 H), 4.83 (t, J = 6.05 Hz, 1 H), 2.91 (d, J = 6.05 Hz, 2 H), 2.75 (s, 2 H), 2.40–2.34 (m, 2 H), 2.15 (q, J = 7.05 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) Isomer A: δ = 155.3, 155.19, 142.7, 142.62, 138.7, 138.1, 124.03, 115.6, 110.7, 110.6, 107.3, 107.0, 92.7, 79.2, 71.22, 66.6, 33.2, 29.9, 27.7 ppm. Isomer B: δ = 155.2, 155.16, 142.7, 142.59, 138.7, 138.1, 124.0, 115.6, 110.7, 110.6, 107.4, 107.1, 92.6, 79.1, 71.16, 66.6, 33.2, 29.9, 27.7 ppm. IR (KBr, neat): $\tilde{\nu}$ = 3366, 2977, 2914, 1639, 1504, 1143, 1010, 737 cm^{-1}. HRMS (EI): calcd. for $C_{19}H_{20}O_4$ $[M]^+$ 312.1362; found 312.1364.

Supporting Information (see footnote on the first page of this article): Experimental procedure and data of compounds **4a**–**l**; ^{1}H and ^{13}C NMR spectra for compounds **4c**, **4h**, **4k**, **5c**, **5h**, **5k**.

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