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An Atom-Transfer Radical Addition of Alcohol to Aliphatic Alkyne

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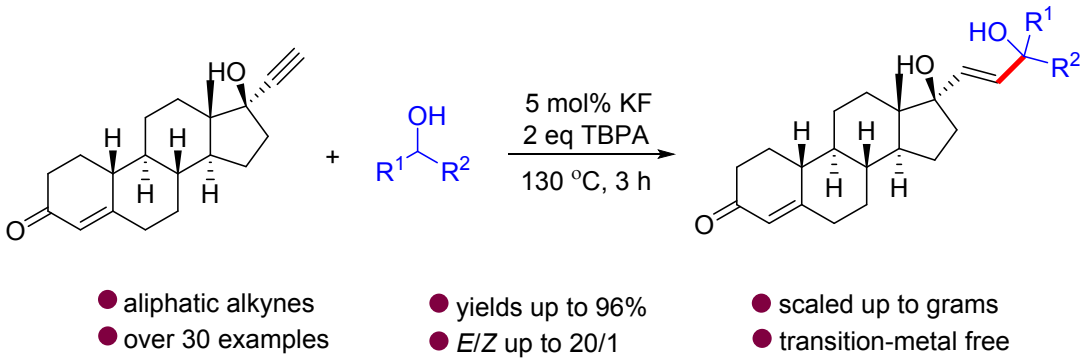
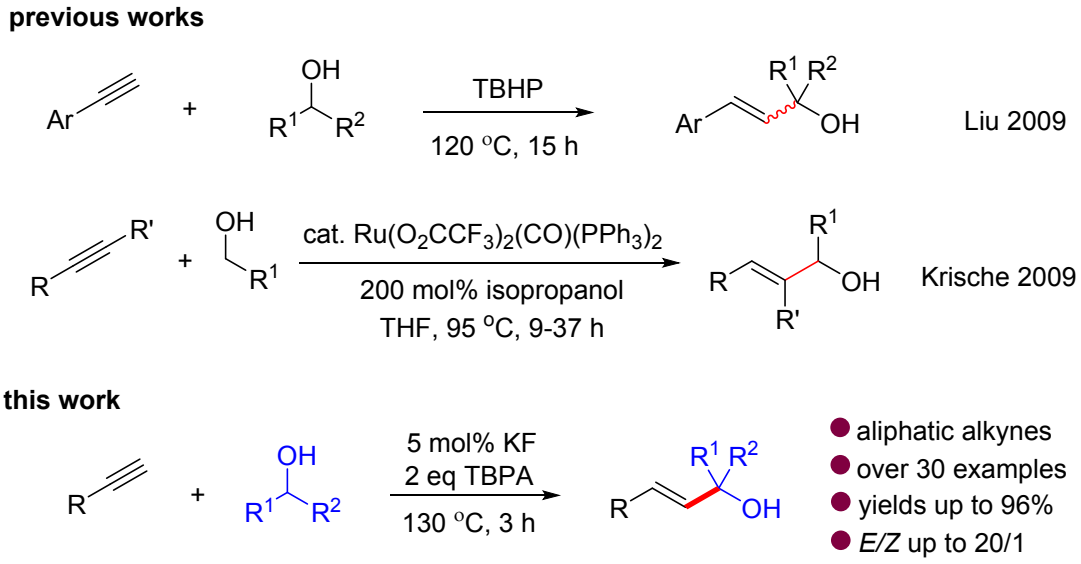


Abstract: An intermolecular hydrogen bond promoted atom-transfer radical addition of simple alcohol to aliphatic alkyne is demonstrated here. Through this strategy, a variety of allyl alcohols can be synthesized in high selectivity and yields. Furthermore, this work reveals the relationship between the selectivity and the substrate.

INTRODUCTION

The construction of a C-C bond by selective cleavage of the α-hydroxy (sp^3)C-H bond in simple aliphatic alcohol is attractive and valuable for organic synthesis.[1] In the past decades, a series of efficient C-C forming methods via atom-transfer radical addition (ATRA) of alcohols with alkenes have been successfully achieved by Tu,[2] Liu,[3] Han and Pan[4] et al.[5] However, ATRA reaction of alcohols with alkynes to produce allylic alcohols has rarely been investigated. In 2009, a first Ru-catalyzed alkenylation of alcohols using alkynes was developed by Krische et al.[6] Subsequently, Liu et al. reported an ATRA of simple alcohols and ethers to aryl alkyne in the same year.[3a] Nevertheless, there are limitations in both systems. For example, only aryl alkynes could be amenable to Liu's system. In addition, the allyl alcohols were obtained in mixed isomers (*E*/*Z* ≈ 1/1). And Krische's work was limited in primary alcohols. Hence, efficient strategy for alkenylation of alcohol is highly desirable. Herein we demonstrated an effective ATRA reaction of simple alcohols with aliphatic

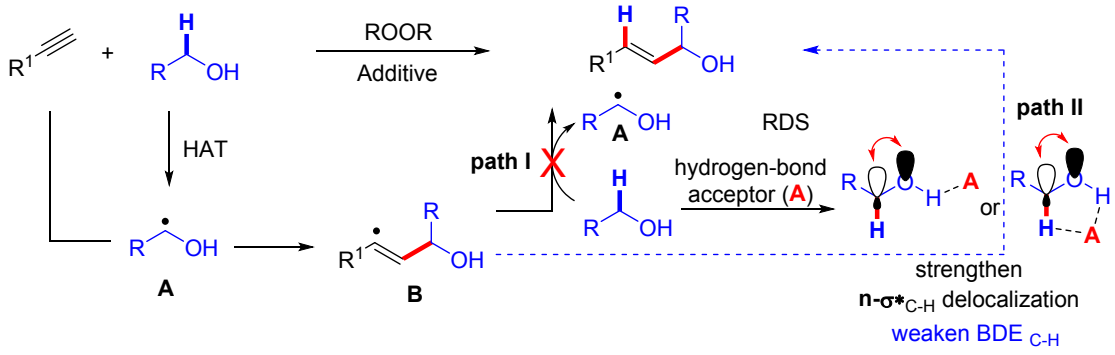
alkynes (Scheme 1).



Scheme 1. Alkenylation of alcohols with alkynes.

RESULTS AND DISCUSSION

As shown in Scheme 2, the rate-determining step (RDS) in this conversion should be the hydrogen-atom transfer (HAT) from alcohol to the alkenyl radical B and then regenerating radical A. It might be energetically unfavorable for cleavage of a relatively strong (sp^3)C-H bond (BDE > 91 kcal/mol)(path I).[7] Inspired by our previous resolution for the ATRA of simple alcohol to unactivated alkene,[8] we began to wonder whether an hydrogen-bond donor could facilitate the HAT process. Since the hydrogen bond (RO-H···A) might strengthen the n-σ*C-H delocalization,[9] and thus the α-hydroxy (sp^3)C-H would be weakened. Subsequently the path II would be favorable to afford the allyl alcohol.

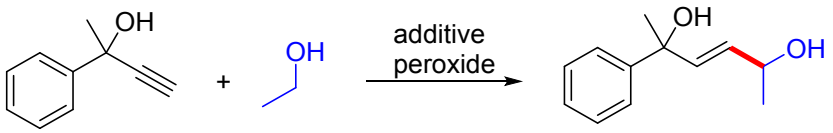


Scheme 2. Possible resolution by addition of hydrogen-bond acceptors.

In order to evaluate the hypothesis, a set of experiments were carried out. Initially,

the 2-phenyl-3-butyn-2-ol and ethanol were chosen as the model substrates to optimize suitable conditions for this reaction (Table 1). Without any additives, no reaction occurred by using TBPB as the initiator (entry 1). But the desired product was obtained in 38% yield with DTBP at 130 °C (entry 2). It is noteworthy that only E allylic product was observed. To our delight, the catalytic amount of KF (from 1 mol% to 20 mol%) could dramatically facilitate this reaction (entries 3-10). With 5 mol% KF, 2 equiv. of TBPA afforded the desired product in nearly quantitative yields (entry 6). The product was isolated in 70% yield even with 1 mol% KF (entry 10).

Table 1. Optimization of the radical addition of alcohols to alkynes [a]



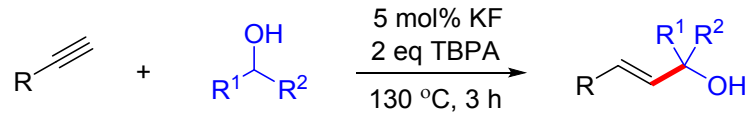
Entry	Peroxide (equiv)	Additive (mol%)	Temp. (°C)	Sol. (mL)	Yield [b] (%)
1	TBPB (3)	-	130	5	-
2	DTBP (2)	-	130	5	38
3	DTBP (2)	KF (20)	130	5	87
4	TBPB (3)	KF (20)	130	5	67
5	TBPA (3)	KF (20)	130	5	91
6	**TBPA (2)**	**KF (5)**	**130**	**5**	**96**
7	TBPA (1)	KF (5)	130	5	75
8	TBPA (2)	KF (5)	120	5	53
9	TBPA (2)	KF (5)	130	3	80
10[c]	TBPA (2)	KF (1)	130	25	70

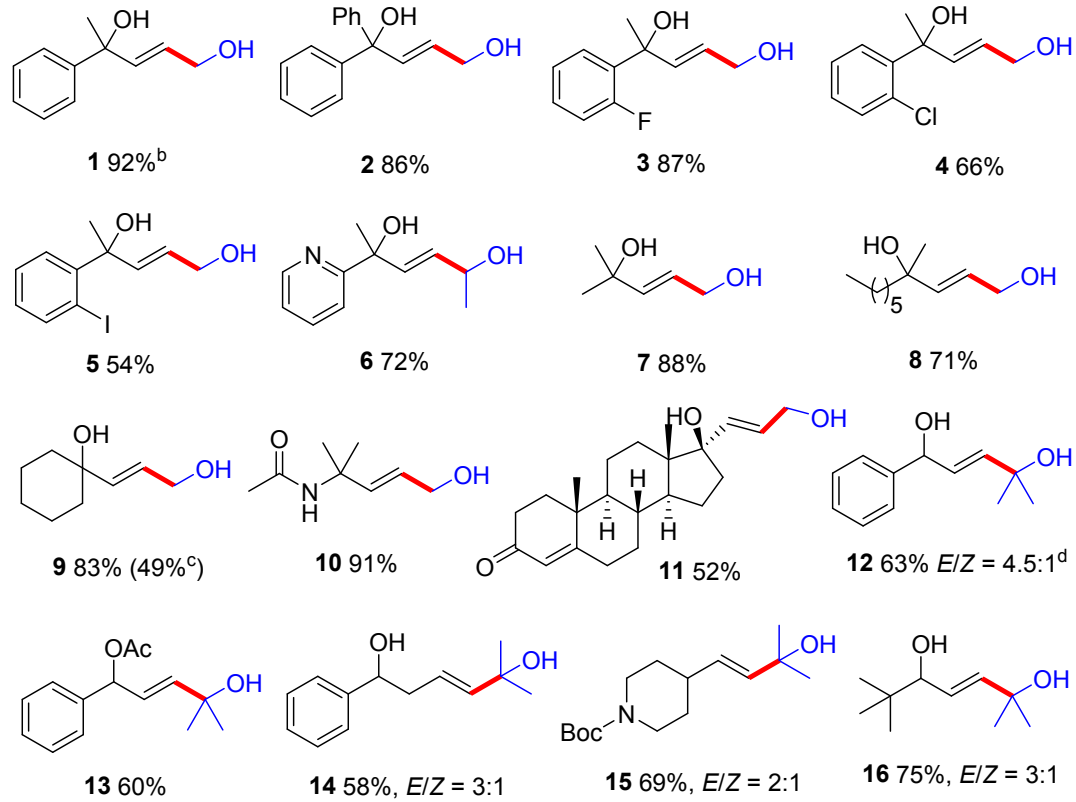
[a] Reaction conditions: Alkynes (1 equiv., 0.20 mmol), ethanol as solvent, sealed tube, 3 h, unless otherwise noted. [b] Isolated yield. [c] Alkynes (1 equiv., 1.0 mmol). TBPB = *tert*-butyl peroxybenzoate; DTBP = Di-*tert*-butyl peroxide; TBPA = *tert*-butyl peroxyacetate.

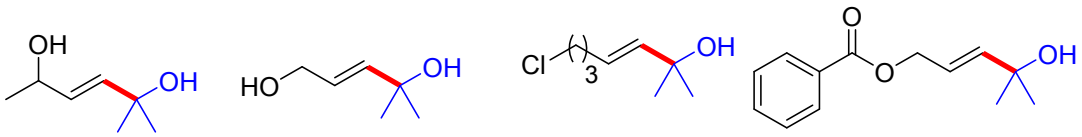
Next we began to evaluate the substrate scope under the typical conditions (Scheme 3). A wide range of alkynes afforded the desired allyl alcohols in good to excellent yields (**1**-**20**). Aryl halides such as fluorine, chlorine and iodine as well as heteroarene can be well tolerated in the system (**3**-**6**). Simple cyclic and acyclic alkyl alkynes were effective substrates (**7**-**9**). Furthermore, amide was also compatible with this system

(**10**). Gratifyingly, alkynes with complex natural product motif also gave the desired compound in good yield (**11**). It is noteworthy that only *E*-allyl alcohols were observed in these substrates (**1**-**11**). Why is the selectivity so high? Whether is it related to the size of vicinal substituent on the triple bond? Then we examined other type of alkynes (**12**-**20**). The 1-phenylprop-2-yn-1-ol afforded a mixture of isomers with *E*/*Z* = 4.5/1 (**12**). But only *E*-product was isolated with 1-phenylprop-2-yn-1-yl acetate (**13**). In addition, substituents with different size of groups were screened (**14**-**20**). As a result, the approximate trend is that the larger substituent on triple bond is, the higher selectivity would be obtained. As a comparison, several randomly chosen examples demonstrated that KF facilitates this reaction (**9** and **20**).

Scheme 3. Examine the scope of unactivated alkynes [a]





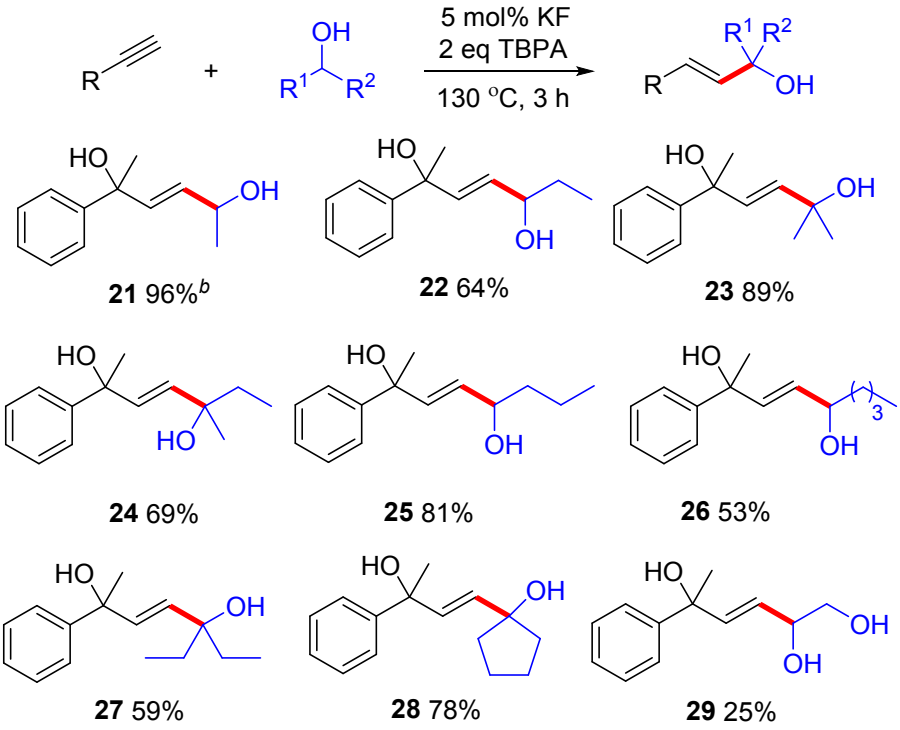


17 71%, *E*/*Z* = 1.4:1 **18** 81%, *E*/*Z* = 2.7:1 **19** 71%, *E*/*Z* = 2.3:1 **20** 75% (49%[c]), *E*/*Z* = 2:1

[a] Reaction conditions: Alkynes (1 equiv., 0.20 mmol), KF (0.6 mg, 5 mol%, 0.01 mmol), TBPA (53 mg, 2 equiv., 0.40 mmol), 5 mL of alcohol as solvent, sealed tube, 130 °C (measured temperature of the oil bath), 3 h, unless otherwise noted. [b] Isolated yield. [c] Isolated yield without KF. [d] The ratio of the E/Z isomers was determined by crude ^{1}H NMR.

Then we tested a series of alcohols, and we found that diverse primary and secondary alcohols as well as diol were amenable to this system (Scheme 4). Both linear and cyclic alcohols were effective substrates (**21**-**29**). Glycol also gave the expected product in 25% yield (**29**). Furthermore we found that this reaction could be scaled up to gram level without decreasing efficiency. For example, reaction of 1,1-diphenylprop-2-yn-1-ol (1.04 g, 5 mmol) with ethanol produced the corresponding product (*E*)-1,1-diphenylpent-2-ene-1,4-diol (**30**) in 87% yield.

Scheme 4. Scope of alcohols.[a]



21 96%[b] **22** 64% **23** 89%

24 69% **25** 81% **26** 53%

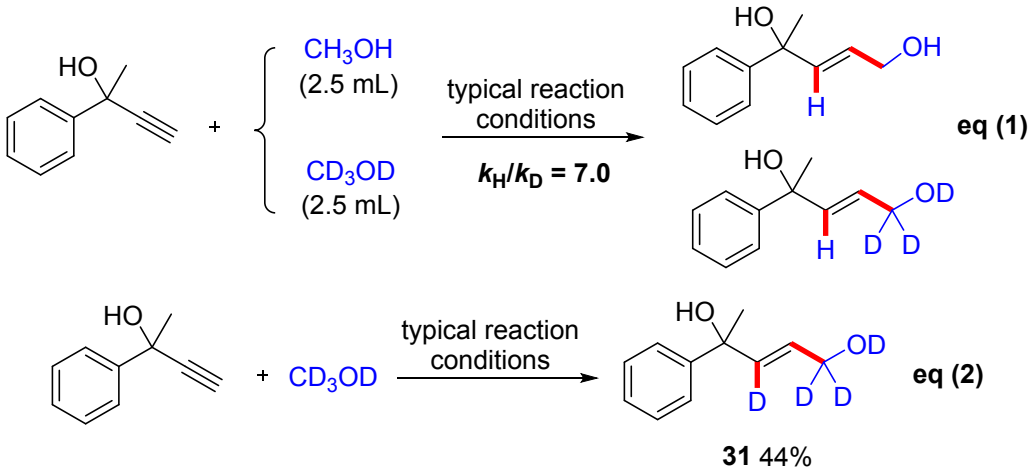
27 59% **28** 78% **29** 25%

[a] Typical reaction conditions. [b] Isolated yield.

Finally, a series of experiments were carried out to verify the mechanism we

proposed previously (Scheme 5). Firstly, kinetic isotope effect experiments were conducted. The results showed that it should be a primary isotope effect (k_H/k_D = 7.0), which suggested that the cleavage of C-H bond might be involved in the RDS (eq. 1). Ultimately, an isotopic tracer experiment further confirmed that it should be a typical ATRA process (eq. 2).

Scheme 5. Mechanistic studies.



CONCLUSIONS

In summary, we have developed herein a metal-free ATRA reaction of simple alcohols with aliphatic alkynes. By addition of 5 mol% of KF, a wide range of allylic alcohols can be facilely synthesized via intermolecular H-bonding. Additionally, this work revealed that the *E*/*Z* selectivity in this type of reaction is not related to alcohol but the size of substituent on the triple bond. The more sterically crowded alkyne is, the higher selectivity will be. Hence this method is expected to have wide applications in material science and medicinal chemistry community.

EXPERIMENTAL SECTION

General Information: All chemicals were commercially available and used as received without further purification. Reactions were monitored by thin-layer chromatography (TLC). ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded at 400, 100, and 375 MHz, respectively. Mass spectra were determined on a Hewlett Packard 5988A spectrometer by direct inlet at 70 eV. High-resolution mass spectral

analysis (HRMS) data were measured on a Bruker Apex II with a Q-TOF detector. All products were identified by ^{1}H and ^{13}C NMR, MS or HRMS. The starting materials were purchased from Energy chemistry, Aldrich, Acros Organics, J&K Chemicals or TCI and used without further purification. Chemical shifts (δ) are given relative to internal TMS. The NMR data are presented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constant J (Hz), and integration.

Typical Experimental Procedure for the Synthesis of 1-31.

A mixture of alkynes (1 equiv., 0.20 mmol), alcohols (5 mL), KF (0.6 mg, 5 mol%, 0.01 mmol), and TBPA (53 mg, 2 equiv., 0.40 mmol) was heated at 130 ^{o}C (the measured temperature of the oil bath) for 3 h in a sealed tube (35 mL). After the reaction finished, the mixture was evaporated under vacuum and purified by column chromatography to afford the desired product.

A scaled-up experimental procedure: A mixture of 1,1-diphenylprop-2-yn-1-ol (1.04 g, 1 equiv., 5.0 mmol), ethanol (125 mL), KF (14.5 mg, 5 mol%, 0.25 mmol), and TBPA (1.32 g, 2 equiv., 10.0 mmol) was heated at 130 ^{o}C (the measured temperature of the oil bath) for 3 h in a sealed tube (300 mL). After the reaction finished, the mixture was evaporated under vacuum and purified by column chromatography to afford the desired product (**30**, (*E*)-1,1-diphenylpent-2-ene-1,4-diol, 1.04 g, isolated yield: 87%).

(E)-4-phenylpent-2-ene-1,4-diol[10] (1). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 32.7 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (m, 2H), 7.35 (m, 2H), 7.26 (m, 1H), 6.04 (dt, *J* = 15.6, 1.2 Hz, 1H), 5.88 (dt, *J* = 15.6, 5.2 Hz, 1H), 4.19 (dd, *J* = 5.2, 1.3 Hz, 2H), 1.98 (s, 1H), 1.68 (s, 3H), 1.26 (s, 1H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 146.5, 138.2, 128.3, 127.2, 127.0, 125.1, 74.2, 63.0, 29.7. MS(EI): m/z(%): 178(0.05), 160(10.8), 147(67.4), 117(100.0), 43(50.1).

(E)-1,1-diphenylbut-2-ene-1,4-diol (2). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 2/1, 41.3 mg, 86%)**.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.17 (m, 10H), 6.30 (dt, *J* = 15.6, 1.6 Hz, 1H), 5.81

(dt, *J* = 15.6, 5.2 Hz, 1H), 4.16 (dd, *J* = 5.2, 1.2 Hz, 2H), 2.35 (s, 1H), 1.52 (s, 1H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 145.9, 136.6, 128.9, 128.2, 127.3, 126.8, 78.8, 63.0. HRMS (ESI, m/z): Calculated for $C_{16}H_{17}O_2$ $(M+H)^+$ 241.1233, found 241.1231.

(E)-4-(2-fluorophenyl)pent-2-ene-1,4-diol (3). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 34.1 mg, 87%)**.** ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (t, *J* = 8.0 Hz, 1H), 7.28 – 7.22 (m, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 7.01 (dd, *J* = 12.0, 8.0 Hz, 1H), 6.13 (d, *J* = 15.6 Hz, 1H), 5.81 (dt, *J* = 15.6, 5.2 Hz, 1H), 4.15 (d, *J* = 5.2 Hz, 2H), 2.52 (s, 1H), 1.87 (s, 1H), 1.71 (s, 3H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 161.1, 158.7, 136.9, 136.8, 133.3, 133.2, 129.0, 128.9, 127.5, 126.8, 126.7, 124.1, 124.0, 116.2, 115.9, 73.1, 73.0, 62.9, 28.5, 28.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.05, -112.08, -112.10, -112.12. HRMS (ESI, m/z): Calculated for $C_{11}H_{14}FO_2$ $(M+H)^+$ 197.0972, found 197.0975.

(E)-4-(2-chlorophenyl)pent-2-ene-1,4-diol (4). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 30.0 mg, 66%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.34 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.29 – 7.25 (m, 1H), 7.21 (td, *J* = 7.6, 1.6 Hz, 1H), 6.15 (dt, *J* = 15.6, 1.6 Hz, 1H), 5.76 (dt, *J* = 15.6, 5.4 Hz, 1H), 4.17 (dd, *J* = 5.4, 1.6 Hz, 2H), 2.95 (s, 1H), 1.78 (s, 3H), 1.75 (s, 1H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.9, 136.8, 131.7, 131.2, 128.6, 128.6, 127.4, 126.9, 74.4, 63.0, 27.9. HRMS (ESI, m/z): Calculated for $C_{11}H_{14}ClO_2$ $(M+H)^+$ 213.0677, found 213.0675.

(E)-4-(2-iodophenyl)pent-2-ene-1,4-diol (5). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 32.8 mg, 54%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.05 (t, *J* = 7.8 Hz, 1H), 5.96 (d, *J* = 15.6 Hz, 1H), 5.84 (dt, *J* = 15.6, 7.8 Hz, 1H), 4.14 (dd, *J* = 5.2, 1.2 Hz, 2H), 2.39 (s, 1H), 2.28 (s, 1H), 1.61 (s, 3H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 149.0, 137.4, 136.0, 134.2, 130.0, 127.7, 124.5, 94.42, 73.7, 62.7, 29.7. HRMS (ESI, m/z): Calculated for $C_{11}H_{14}IO_2$ $(M+H)^+$ 305.0033, found 305.0032.

(E)-2-(pyridin-2-yl)hex-3-ene-2,5-diol (6). A colorless solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/2, 27.8 mg, 72%). ^1H

NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, *J* = 5.6, 4.4 Hz, 2H), 7.30 (dd, *J* = 5.6, 1.2 Hz, 2H), 5.89 (d, *J* = 15.6 Hz, 1H), 5.77 (ddd, *J* = 15.6, 7.6, 5.6 Hz, 1H), 4.31 (p, *J* = 6.4 Hz, 1H), 3.80 (s, 2H), 1.58 (d, *J* = 1.2 Hz, 3H), 1.24 (dd, *J* = 6.4, 2.4 Hz, 4H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ 156.9, 148.7, 134.6, 133.4, 120.6, 73.1, 67.6, 29.19, 23.27. HRMS (ESI, m/z): Calculated for $C_{11}H_{16}NO_2$ $(M+H)^+$ 194.1176, found 194.1175.

(E)-2-methylhex-3-ene-2,5-diol (7). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 20.4 mg, 88%). ^1H NMR (400 MHz, $CDCl_3$) δ 5.85 (d, *J* = 15.6 Hz, 1H), 5.79 (dd, *J* = 15.6, 4.4 Hz, 1H), 4.14 (d, *J* = 4.4 Hz, 2H), 2.05 (s, 1H), 2.03 (s, 1H), 1.32 (s, 6H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 139.4, 125.8, 70.5, 63.0, 29.6. HRMS (ESI, m/z): Calculated for $C_6H_{13}O_2$ $(M+H)^+$ 117.0910, found 117.0912.

(E)-4-methyldec-2-ene-1,4-diol (8). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 18.5 mg, 71%). ^1H NMR (400 MHz, $CDCl_3$) δ 5.88 – 5.80 (m, 1H), 5.78 (d, *J* = 15.6 Hz, 1H), 4.18 (d, *J* = 4.4 Hz, 2H), 1.53 (m, 2H), 1.44 (s, 1H), 1.28 (m, 11H), 0.88 (t, *J* = 6.4 Hz, 3H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 138.7, 126.4, 72.7, 63.2, 42.7, 31.8, 29.7, 27.9, 23.9, 22.6, 14.0. HRMS (ESI, m/z): Calculated for $C_{11}H_{23}O_2$ $(M+H)^+$ 187.1693, found 187.1694.

(E)-1-(3-hydroxyprop-1-en-1-yl)cyclohexan-1-ol (9). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 2/1, 25.9 mg, 83%). ^1H NMR (400 MHz, $CDCl_3$) δ 5.87 (dd, *J* = 15.6, 4.4 Hz, 1H), 5.81 (d, *J* = 15.6 Hz, 1H), 4.15 (d, *J* = 4.0 Hz, 2H), 1.81 (s, 2H), 1.63 – 1.24 (m, 10H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 139.3, 126.5, 71.2, 63.2, 37.8, 25.4, 22.0. HRMS (ESI, m/z): Calculated for $C_9H_{17}O_2$ $(M+H)^+$157.1223, found 157.1224.

(E)-N-(5-hydroxy-2-methylpent-3-en-2-yl)acetamide (10). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 28.6 mg, 91%). ^1H NMR (400 MHz, $CDCl_3$) δ 5.88 (d, *J* = 15.6 Hz, 1H), 5.69 (dt, *J* = 15.6, 5.6 Hz, 2H), 4.12 (dd, *J* = 5.6, 0.8 Hz, 2H), 2.80 (s, 1H), 1.93 (s, 3H), 1.42 (s, 6H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 139.4, 125.8, 70.5, 63.0, 29.6. HRMS (ESI, m/z): Calculated for $C_8H_{16}NO_2$ $(M+H)^+$ 158.1176, found 158.1174.

(8R,9S,10R,13S,14S,17R)-17-hydroxy-17-((E)-3-hydroxyprop-1-en-1-yl)-10,13-dimethyl-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3H-cyclopenta[a]phenanthren-3-one (11). A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/2, 34.7mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89 (d, *J* = 15.6 Hz, 1H), 5.77 (dt, *J* = 15.6, 5.2 Hz, 1H), 5.72 (s, 1H), 4.25 – 4.15 (m, 2H), 2.43 – 2.24 (m, 4H), 2.03 – 1.94 (m, 2H), 1.86 (m, 2H), 1.68 – 1.47 (m, 6H), 1.43 – 1.35 (m, 2H), 1.25 – 1.20 (m, 2H), 1.18 (s, 3H), 0.95 (s, 3H). ^{13}C{1H} NMR (101 MHz, $CDCl_3$) δ 199.5, 171.2, 136.1, 127.1, 123.8, 83.3, 63.2, 53.6, 49.6, 46.4, 38.6, 36.6, 36.3, 35.7, 33.9, 32.8, 32.0, 31.6, 23.4, 20.6, 17.4, 14.0. HRMS (ESI, m/z): Calculated for $C_{22}H_{33}O_3$ $(M+H)^+$ 345.2424, found 345.2423

(E)-4-methyl-1-phenylpent-2-ene-1,4-diol (12). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 19.8 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 5H), 5.94 (d, *J* = 15.6 Hz, 1H), 5.86 (dd, *J* = 15.6, 6.0 Hz, 1H), 5.21 (d, *J* = 6.0 Hz, 1H), 2.04 (s, 1H), 1.33 (d, *J* = 1.6 Hz, 6H), 1.25 (s, 1H). ^{13}C{1H} NMR (101 MHz, $CDCl_3$) δ 142.9, 139.1, 129.0, 128.6, 127.7, 126.2, 74.6, 70.6, 29.7. HRMS (ESI, m/z): Calculated for $C_{12}H_{17}O_2$ $(M+H)^+$ 193.1223, found 193.1223.

(E)-4-hydroxy-4-methyl-1-phenylpent-2-en-1-yl acetate (13). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 2/1, 28.1 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 5H), 6.27 (d, *J* = 4.7 Hz, 1H), 5.88 (d, *J* = 15.6 Hz, 1H), 5.83 (dd, *J* = 15.6, 4.8 Hz, 1H), 2.10 (s, 3H), 1.31 (d, *J* = 4.4 Hz, 6H). ^{13}C{1H} NMR (101 MHz, $CDCl_3$) δ 169.9, 140.9, 139.3, 128.5, 128.1, 127.0, 125.2, 75.6, 70.5, 29.6, 21.3. HRMS (ESI, m/z): Calculated for $C_{14}H_{19}O_3$ $(M+H)^+$ 235.1329, found 235.1328

(Z)-5-methyl-1-phenylhex-3-ene-1,5-diol (14'). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 4.5 mg, 14.5%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 4H), 7.27 – 7.24 (m, 1H), 5.64 (d, *J* = 12.0 Hz, 1H), 5.37 (ddd, *J* = 12.0, 9.2, 7.6 Hz, 1H), 4.73 (dd, *J* = 8.4, 3.6 Hz, 1H), 3.01 – 2.94 (m, 1H), 2.80 (s, 1H), 2.62 – 2.55 (m, 1H), 1.33 (d, *J* = 2.0 Hz, 6H), 1.23 (s, 1H). ^{13}C{1H} NMR (101 MHz, $CDCl_3$) δ 144.4, 140.1, 128.4, 127.4, 125.7, 124.8,

73.1, 72.0, 37.3, 32.0, 31.2. HRMS (ESI, m/z): Calculated for $C_{13}H_{19}O_2$ $(M+H)^+$ 207.1038, found 207.1036.

(E)-5-methyl-1-phenylhex-3-ene-1,5-diol (14). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 17.9 mg, 43.5%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 4H), 7.26 – 7.22 (m, 1H), 5.68 (d, *J* = 15.6 Hz, 1H), 5.60 (dt, *J* = 15.6, 6.4 Hz, 1H), 4.68 (dd, *J* = 7.2, 5.6 Hz, 1H), 2.46 – 2.38 (m, 2H), 2.19 (d, *J* = 6.8 Hz, 1H), 1.69 (s, 1H), 1.26 (s, 6H). ^{13}C{1H} NMR (101 MHz, $CDCl_3$) δ 143.9, 141.9, 128.4, 127.5, 125.8, 122.6, 73.7, 70.6, 42.1, 29.8, 29.7. HRMS (ESI, m/z): Calculated for $C_{13}H_{19}O_2$ $(M+H)^+$ 207.1038, found 207.1037.

tert-butyl (E)-4-(3-hydroxy-3-methylbut-1-en-1-yl)piperidine-1-carboxylate (15'). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 12.4 mg, 23%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.44 (d, *J* = 12.0 Hz, 1H), 5.1 (t, *J* = 6.4 Hz,1H), 4.07 (s, 2H), 3.02 (dt, *J* = 15.0, 11.2 Hz, 1H), 2.73 (s, 2H), 1.60 (d, *J* = 10.4 Hz, 2H), 1.45 (s, 9H), 1.37 (s, 6H), 1.22 (dd, *J* = 13.6, 5.3 Hz, 2H). ^{13}C{1H} NMR (101 MHz, $CDCl_3$) δ 154.8, 136.0, 135.2, 79.3, 71.7, 43.23, 34.9, 32.3, 31.6, 28.5. HRMS (ESI, m/z): Calculated for $C_{15}H_{28}NO_3$ $(M+H)^+$ 270.2064, found 270.2062

tert-butyl (E)-4-(3-hydroxy-3-methylbut-1-en-1-yl)piperidine-1-carboxylate (15). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 24.8 mg, 46%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.59 (d, *J* = 15.6 Hz, 1H), 5.54 (d, *J* = 15.6 Hz, *J* = 6.4 Hz, 1H), 4.07 (s, 2H), 2.71 (t, *J* = 11.6 Hz, 2H), 2.12 – 2.01 (m, 1H), 1.64 (d, *J* = 12.8 Hz, 2H), 1.58 (d, *J* = 10.7 Hz, 1H), 1.44 (s, 9H), 1.28 (s, 6H), 1.27 – 1.20 (m, 2H). ^{13}C{1H} NMR (101 MHz, $CDCl_3$) δ 154.8, 136.6, 130.8, 79.3, 70.5, 43.9, 38.4, 31.8, 29.8, 28.4. HRMS (ESI, m/z): Calculated for $C_{15}H_{28}NO_3$ $(M+H)^+$ 270.2064, found 270.2065.

(Z)-2,6,6-trimethylhept-3-ene-2,5-diol (16'). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 6.5 mg, 19%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.62 (dd, *J* = 12.4, 1.2 Hz, 1H), 5.50 (dd, *J* = 12.4, 6.8 Hz, 1H), 4.40 (dd, *J* = 6.8, 1.2 Hz, 1H), 2.93 (s, 1H), 1.39 (d, *J* = 4.2 Hz, 6H), 1.25 (s, 1H),

0.94 (s, 9H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 140.3, 126.3, 80.2, 70.5, 34.8, 29.8, 25.5. HRMS (ESI, m/z): Calculated for $C_{10}H_{21}O_2$ $(M+H)^+$ 173.1536, found 173.1537.

(E)-2,6,6-trimethylhept-3-ene-2,5-diol (16). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 19.4 mg, 56%). ^1H NMR (400 MHz, $CDCl_3$) δ 5.82 (d, *J* = 15.6 Hz, 1H), 5.73 (dd, *J* = 15.6, 6.8 Hz, 1H), 3.75 (d, *J* = 6.8 Hz, 1H), 1.51 (s, 1H), 1.49 (s, 1H), 1.33 (s, 6H), 0.90 (s, 9H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 140.5, 126.4, 80.4, 70.7, 35.0, 29.9, 29.8, 25.6. HRMS (ESI, m/z): Calculated for $C_{10}H_{21}O_2$ $(M+H)^+$ 173.1536, found 173.1537.

(Z)-2-methylhex-3-ene-2,5-diol (17'). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 7.7 mg, 30%). ^1H NMR (400 MHz, $CDCl_3$) δ 5.50 (dd, *J* = 12.4, 1.2 Hz, 1H), 5.38 (dd, *J* = 12.4, 6.4 Hz, 1H), 4.87 (pd, *J* = 6.4, 1.2 Hz, 1H), 3.63 (s, 2H), 1.39 (s, 6H), 1.30 (d, *J* = 6.4 Hz, 3H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 138.2, 132.7, 71.8, 64.0, 31.9, 30.8, 23.8. HRMS (ESI, m/z): Calculated for $C_7H_{15}O_2$ $(M+H)^+$ 131.1067, found 131.1065.

(E)-2-methylhex-3-ene-2,5-diol (17). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 10.7 mg, 41%). ^1H NMR (400 MHz, $CDCl_3$) δ 5.80 (d, *J* = 16.0 Hz, 1H), 5.70 (dd, *J* = 15.6, 6.0 Hz, 1H), 4.32 (p, *J* = 6.4 Hz, 1H), 2.35 (s, 2H), 1.32 (s, 6H), 1.28 (d, *J* = 6.4 Hz, 3H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ 137.6, 130.7, 70.4, 68.3, 29.7, 29.5, 23.4. HRMS (ESI, m/z): Calculated for $C_7H_{15}O_2$ $(M+H)^+$ 131.1067, found 131.1066.

(Z)-4-methylpent-2-ene-1,4-diol (18'). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1, 5.1 mg, 21.9%). ^1H NMR (400 MHz, $CDCl_3$) δ 5.59 (d, *J* = 12.0 Hz, 1H), 5.51 (dd, *J* = 12.0, 4.8 Hz, 1H), 4.31 (d, *J* = 4.2 Hz, 2H), 3.14 (s, 1H), 3.13 (s, 1H), 1.38 (s, 6H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 139.4, 127.5, 71.9, 59.0, 31.2. HRMS (ESI, m/z): Calculated for $C_6H_{13}O_2(M+H)^+$ 117.0910, found 117.0908.

(E)-4-methylpent-2-ene-1,4-diol (18). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1, 13.7 mg, 59%). ^1H NMR (400 MHz, $CDCl_3$) δ 5.83 (d, *J* = 15.6 Hz, 1H), 5.77 (dd, *J* = 15.6, 4.8 Hz, 1H),

4.11 (d, *J* = 4.4 Hz, 2H), 2.66 (s, 1H), 2.52 (s, 1H), 1.31 (s, 6H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 139.4, 125.8, 70.5, 62.8, 29.5. HRMS (ESI, m/z): Calculated for $C_6H_{13}O_2(M+H)^+$ 117.0910, found 117.0909.

(E)-7-chloro-2-methylhept-3-en-2-ol (19). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 14.8 mg, 49.5%). ^1H NMR (400 MHz, $CDCl_3$) δ 5.67 (d, *J* = 15.6 Hz, 1H), 5.59 (dt, *J* = 15.6, 6.4 Hz, 1H), 3.53 (t, *J* = 6.4 Hz, 2H), 2.19 (q, *J* = 1 6.4 Hz, 2H), 1.82 – 1.89 (m, 2H), 1.38 (s, 1H), 1.31 (s, 6H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 139.4, 125.1, 70.6, 44.3, 32.0, 29.9, 29.2. HRMS (ESI, m/z): Calculated for $C_8H_{15}ClO$ $(M+H)^+$ 163.0884, found 163.0883.

(Z)-4-hydroxy-4-methylpent-2-en-1-yl benzoate (20'). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1, 11 mg, 25%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.00 (m, 2H), 7.60 – 7.52 (m, 1H), 7.48 – 7.41 (m, 2H), 5.67 (dt, *J* = 12.0, 1.2 Hz, 1H), 5.50 (dt, *J* = 12.0, 6.8 Hz, 1H), 5.25 (dd, *J* = 6.8, 1.2 Hz, 2H), 2.85 (s, 1H), 1.39 (s, 6H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 166.9, 140.8, 133.0, 130.3, 129.6, 128.3, 123.0, 72.2, 61.6, 31.0. HRMS (ESI, m/z): Calculated for $C_{13}H_{17}O_3$ $(M+H)^+$ 221.1172, found 221.1171.

(E)-4-hydroxy-4-methylpent-2-en-1-yl benzoate (20). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 2/1, 22 mg, 50%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.00 (m, 2H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 6.00 (d, *J* = 15.7 Hz, 1H), 5.89 (dd, *J* = 13.7, 7.8 Hz, 1H), 4.82 (dd, *J* = 5.8, 0.9 Hz, 2H), 1.69 (s, 1H), 1.35 (s, 6H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 166.3, 142.3, 132.9, 130.2, 129.6, 128.3, 120.9, 70.5, 64.9, 29.6. HRMS (ESI, m/z): Calculated for $C_{13}H_{17}O_3$ $(M+H)^+$ 221.1172, found 221.1170.

(E)-4-phenylpent-2-ene-1,4-diol[3a] (21). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 36.9 mg, 96%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.0 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.26 – 7.21 (m, 1H), 5.98 (ddd, *J* = 15.6, 4.0, 0.8 Hz, 1H), 5.72 (ddd, *J* = 15.6, 6.5, 3.0 Hz, 1H), 4.12 – 3.98 (m, 1H), 2.26 (d, *J* = 16.8 Hz, 1H), 1.87 (s, 1H), 1.64 (t, *J* = 3.2 Hz, 3H), 1.62 – 1.51 (m, 2H), 0.91 (td, *J* = 7.4, 2.8 Hz, 3H). $^{13}C\{1H\}$ NMR (101 MHz,

$CDCl_3$) δ 146.6, 136.6, 132.1, 128.2, 126.9, 125.1, 74.1, 68.3, 29.7, 23.3. **MS (EI): *m/z* (%):** 192(0.1), 177(5.3), 147(100.0),131(79.5), 105(42.8), 91(37.0), 43(88.5).

(E)-2-phenylhept-3-ene-2,5-diol (22). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 26.4 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.0 Hz, 2H), 7.33 (t, *J* = 8.0 Hz, 2H), 7.26 – 7.22 (m, 1H), 5.98 (ddd, *J* = 15.6, 4.0, 0.8 Hz, 1H), 5.72 (ddd, *J* = 15.6, 6.4, 3.2 Hz, 1H), 4.05 (dd, *J* = 6.4, 3.6 Hz, 1H), 2.26 (d, *J* = 16.8 Hz, 1H), 1.87 (s, 1H), 1.65 (d, *J* = 2.8 Hz, 3H), 1.61 – 1.52 (m, 2H), 0.91 (td, *J* = 7.2, 2.8 Hz, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 146.6, 137.7, 130.6, 128.2, 126.9, 125.0, 74.1, 73.7, 30.0, 29.7, 9.8. HRMS (ESI, m/z): Calculated for $C_{13}H_{19}O_2$ $(M+H)^+$ 207.1380, found 207.1380.

(E)-2-methyl-5-phenylhex-3-ene-2,5-diol[11] (23). A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 36.7 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 1H), 5.95 (d, *J* = 15.8 Hz, 1H), 5.83 (d, *J* = 15.8 Hz, 1H), 2.30 (s, 1H), 2.03 (s, 1H), 1.62 (s, 3H), 1.30 (s, 6H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 146.8, 135.8, 133.4, 128.1, 126.8, 125.1, 74.1, 70.6, 29.8, 29.7, 29.6. MS (EI): *m/z*(%): 206(0.02), 191(5.5), 171(16.6), 145(100.0), 105(73.5).

(E)-5-methyl-2-phenylhept-3-ene-2,5-diol (24). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 30.4 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.2 Hz, 2H), 7.34 (d, *J* = 7.2 Hz, 2H), 7.25 (d, *J* = 6.8 Hz, 1H), 5.98 (dd, *J* = 15.6, 1.2 Hz, 1H), 5.76 (d, *J* = 15.6 Hz, 1H), 2.03 (s, 1H), 1.65 (s, 3H), 1.60 – 1.54 (m, 2H), 1.28 (d, *J* = 1.6 Hz, 3H), 0.87 (td, *J* = 7.6, 4.4 Hz, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 146.8, 134.7, 134.5, 128.2, 126.9, 125.1, 74.2, 73.0, 35.2, 29.9, 27.4, 8.3. HRMS (ESI, m/z): Calculated for $C_{14}H_{21}O_2$ $(M+H)^+$ 221.1536, found 221.1539.

(E)-2-phenyloct-3-ene-2,5-diol (25). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 35.7 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.8 (d, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.29 – 7.24 (m, 1H), 6.00 (ddd, *J* = 15.6, 3.6, 0.8 Hz, 1H), 5.75 (ddd, *J* = 15.6, 6.4, 3.0 Hz, 1H), 4.16 (q, *J* = 6.4 Hz, 1H), 2.29 (s, 1H), 2.13 (s, 1H), 1.67 (d, *J* = 2.8 Hz, 1H), 1.60

– 1.48 (m, 2H), 1.45 – 1.33 (m, 2H), 0.95 (td, *J* = 7.2, 3.0 Hz, 3H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ 146.6, 137.5, 131.0, 128.2, 126.9, 125.1, 74.1, 72.2, 39.3, 29.7, 18.6, 14.0. HRMS (ESI, m/z): Calculated for $C_{14}H_{21}O_2$ $(M+H)^+$ 221.1536, found 221.1537.

(E)-2-phenylnon-3-ene-2,5-diol (26). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 21.8 mg, 53%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.0 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.26 – 7.22 (m, 1H), 5.98 (dd, *J* = 15.6, 3.2 Hz, 1H), 5.74 (dd, *J* = 15.6, 6.4 Hz, 1H), 4.13 (q, *J* = 6.4 Hz, 1H), 2.12 (s, 1H), 2.03 (s, 1H), 1.66 (d, *J* = 2.8 Hz, 3H), 1.60 – 1.51 (m, 2H), 1.35 – 1.32 (m, 4H), 0.90 (td, *J* = 6.8, 2.4 Hz, 3H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ 146.5, 137.5, 131.1, 128.2, 127.0, 125.1, 74.1, 72.5, 36.9, 29.7, 27.6, 22.6, 14.0. HRMS (ESI, m/z): Calculated for $C_{15}H_{23}O_2$ $(M+H)^+$ 235.1393, found 235.1391.

(E)-5-ethyl-2-phenylhept-3-ene-2,5-diol (27). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 27.6 mg, 59%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.26 – 7.23 (m, 1H), 5.98 (d, *J* = 15.8 Hz, 1H), 5.67 (d, *J* = 15.8 Hz, 1H), 1.94 (s, 1H), 1.66 (s, 3H), 1.59 – 1.52 (m, 4H), 1.39 (s, 1H), 0.86 (q, *J* = 7.2 Hz, 6H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ 146.8, 135.5, 133.4, 128.2, 126.9, 125.2, 75.3, 74.4, 33.2, 30.0, 7.9. HRMS (ESI, m/z): Calculated for $C_{15}H_{23}O_2$ $(M+H)^+$ 235.1393, found 235.1392.

(E)-1-(3-hydroxy-3-phenylbut-1-en-1-yl)cyclopentan-1-ol (28). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 36.2 mg, 78%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.44 (m, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.26 – 7.22 (m, 1H), 6.05 (d, *J* = 15.6 Hz, 1H), 5.88 (d, *J* = 15.6 Hz, 1H), 1.87 – 1.84 (m, 2H), 1.67 (s, 8H), 1.66 (s, 3H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ 146.8, 134.2, 133.8, 128.2, 126.9, 125.1, 81.7, 74.2, 40.6, 40.5, 30.0, 23.6. HRMS (ESI, m/z): Calculated for $C_{15}H_{21}O_2$ $(M+H)^+$ 233.1536, found 233.1535.

(E)-5-phenylhex-3-ene-1,2,5-triol (29). A colorless liquid after purification by flash column chromatography (ethyl acetate, 10.4 mg, 25%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.25 (t, *J* = 7.2 Hz, 1H), 6.12 (d, *J* = 15.6 Hz, 1H), 5.74 (ddd, *J* = 15.6, 12.0, 6.0 Hz, 1H), 4.28 (s, 1H), 3.66 (dd, *J* = 7.2, 4.0 Hz, 1H), 3.51 (dd, *J* = 17.2, 9.2 Hz, 1H), 2.77 (br, 2H), 1.88 (s, 1H),

1.66 (d, J = 2.8 Hz, 3H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ146.3, 139.4, 128.3, 127.1, 126.7, 125.1, 74.2, 72.4, 66.3, 29.7. HRMS (ESI, m/z): Calculated for $C_{12}H_{17}O_3$ $(M+H)^+$ 209.1172, found 209.1175.

(E)-1,1-diphenylpent-2-ene-1,4-diol (30). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 2/1, 1.04 g, 87%). ^1H NMR (300 MHz, $CDCl_3$) δ 7.39 – 7.19 (m, 10H), 6.28 (dd, J = 15.6, 1.2 Hz, 1H), 5.75 (dd, J = 15.6, 6.0 Hz, 1H), 4.42 – 4.26 (m, 1H), 3.02 (s, 2H), 1.25 (d, J = 6.4 Hz, 3H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ 145.9, 135.2, 133.6, 128.1, 127.2, 126.8, 78.6, 68.2, 23.3.HRMS (ESI, m/z): Calculated for $C_{17}H_{19}O_2$ $(M+H)^+$ 255.1380, found 255.1382

(E)-4-phenylpent-2-ene-1,1,3-d3-1,4-diol-d (31). A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1, 16 mg, 44%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.2 Hz, 2H), 7.35 (t, J = 7.2 Hz, 2H), 7.30 – 7.22 (m, 1H), 5.87 (s, 1H), 1.68 (s, 3H), 1.59 (s, 1H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) δ 146.5, 138.2, 128.3, 127.2, 127.0, 125.1, 74.2, 63.0, 29.7. HRMS (ESI, m/z): Calculated for $C_{11}H_{10}D_4O_2Na$ $(M+Na)^+$ 205.1137, found 205.1139.

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Notes

The authors declare no competing financial interest.

Supporting Information

Modification of the conditions, mechanistic studies, and copies of spectra. This material is available free of charge via the Internet at **http://pubs.acs.org**.

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