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Development of an Azanoradamantane-Type Nitroxyl Radical Catalyst for Class-Selective Oxidation of Alcohols

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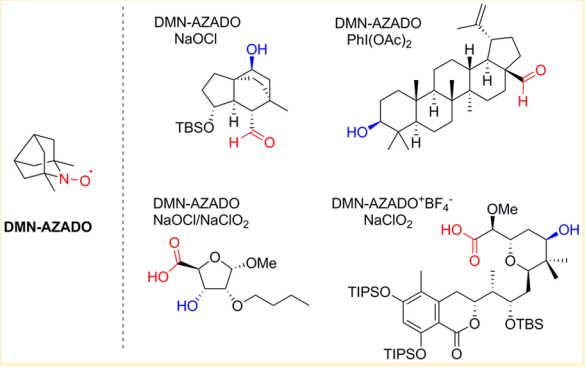
Supporting Information

ABSTRACT: The development of 1,5-dimethyl-9-azanoradamantane *N*-oxyl (DMN-AZADO; 1,5-dimethyl-Nor-AZADO, **2**) as an efficient catalyst for the selective oxidation of primary alcohols in the presence of secondary alcohols is described. The compact and rigid structure of the azanoradamantane nucleus confers potent catalytic ability to DMN-AZADO (**2**). A variety of hindered primary alcohols such as neopentyl primary alcohols were efficiently oxidized by DMN-AZADO (**2**) to the corresponding aldehydes, whereas secondary alcohols remained intact. DMN-AZADO (**2**) also has high catalytic efficiency for one-pot oxidation from primary alcohols to the corresponding carboxylic acids in the presence of secondary alcohols and for oxidative lactonization from diols.



INTRODUCTION

In the field of synthetic organic chemistry, selective transformations of intended functional groups are necessary to synthesize target molecules having multifunctional groups. The use of protecting groups has been the standard means of achieving this, which enables the desired selective transformation by masking the other reactive functional groups. However, it requires counterproductive protection−deprotection operations.[1] The development of alternative methodologies for selective transformations would contribute to the further improvement of organic synthesis.[2] From this perspective, site-selective conversions are a promising strategy.[3] The class-selective oxidation of alcohols can be regarded as one of the most important site-selective oxidations. Several of the known alcohol oxidation methods have selectivity to a particular class of alcohols. (i) MnO_2 oxidation and some other methods are selective oxidation methods for activated alcohols, such as allylic alcohols and benzylic alcohols, in the presence of aliphatic alcohols.[4,5] (ii) Certain halogen- and transition-metal-based oxidation methods show a preference for secondary alcohols in the presence of primary alcohols.[6,7] (iii) TEMPO (2,2,6,6-tetramethylpiperidine *N*-oxyl, **1**)-catalyzed oxidation is also utilized for the selective oxidation of primary alcohols in the presence of secondary alcohols.[8−11] These class-selective oxidation methods have been successfully applied to organic syntheses to discriminate between a desired hydroxy group and other hydroxy groups without the need for protecting groups and have contributed to improving the efficiency of syntheses.[5,7,10] However, the applicability of such synthetic strategies based on class-selective oxidation is still limited. The development of new versatile methods could increase the effectiveness of synthetic strategies employing class-selective oxidation. Herein, we report the high catalytic efficiency of newly synthesized 1,5-dimethyl-9-azanoradamantane *N*-oxyl (DMN-AZADO, 1,5-dimethyl-Nor-AZADO, **2**) for the class-selective oxidation of primary alcohols.

The selectivity of TEMPO (**1**) to primary alcohols originates from the steric repulsion between the four methyl groups around the nitroxyl radical moiety and the alcohols;[10a,11a] that is, because of steric repulsion, the oxidation rate of relatively hindered secondary alcohols is lower than that of primary alcohols. Here, we focus on the fact that the four methyl groups surrounding the nitroxyl radical were originally introduced to increase stability rather than to achieve selectivity.[12] Thus, the relationship between the steric environment around the nitroxyl radical and the catalytic efficiency for the class-selective oxidation of primary alcohols has not yet been clarified in detail. We envisaged that, although two tetrasubstituted α-carbons, one on each side of the nitroxyl radical, are essential for selectivity, reducing the steric hindrance around the nitroxyl radical moiety could enhance catalytic activity while maintaining selectivity to primary alcohols. In this context, we newly designed DMN-AZADO (**2**) as an efficient class-selective catalyst for the oxidation of primary alcohols in the presence of

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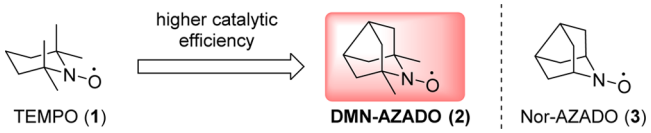


Figure 1. Design of DMN-AZADO.

secondary alcohols (Figure 1). DMN-AZADO (**2**) has two additional methyl groups, one on each side of the nitroxyl radical moiety, compared with Nor-AZADO (**3**),[13d] which is the most compact nucleus among the caged nitroxyl radical catalysts.[13,14]

RESULTS AND DISCUSSION

Figure 2 shows the structures of the oxoammonium species of TEMPO and DMN-AZADO ($TEMPO^+$ and $DMN\text{-}AZADO^+$)

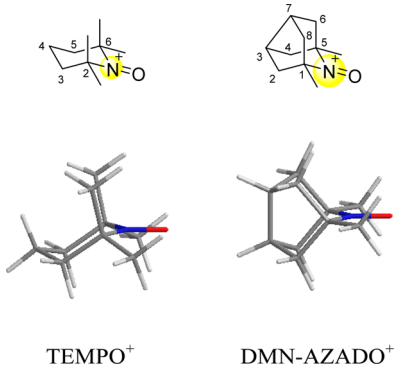


Figure 2. Structures of $TEMPO^+$ and $DMN\text{-}AZADO^+$.

optimized by density functional theory (DFT) calculation.[15] Both catalysts have two tetrasubstituted α-carbons, one on each side of the nitroxyl radical moiety. Owing to the fixation by the azanoradamantane nucleus, the angle C2−C1−C8 (C4−C5−C6) of DMN-AZADO is smaller than the angle C3−C2−Me_{ax} (C5−C6−Me_{ax}) of TEMPO [$\angle$C2−C1−C8 = 99.8° (DMN-AZADO), $\angle$C3−C2−Me_{ax} = 112.6° (TEMPO)], meaning that the former provides a wider reaction space around the active sites. Additionally, the flexible structure of TEMPO can amplify the steric hindrance by its molecular vibration including the flip of its piperidine ring.

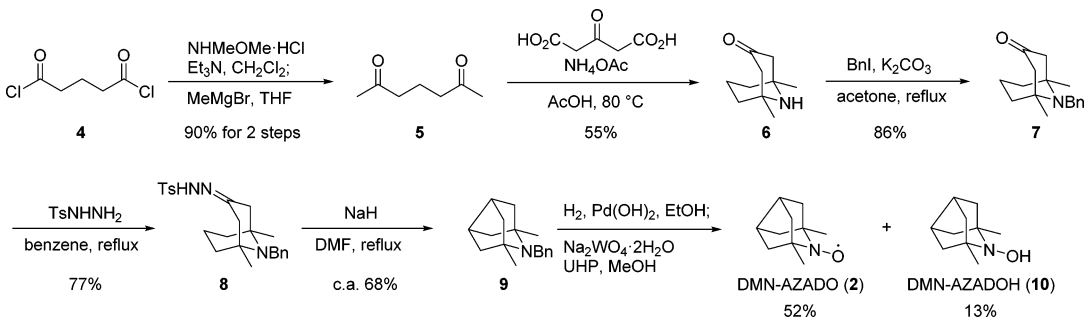
DMN-AZADO was prepared by the following eight-step operation (Scheme 1), which commenced with the preparation of heptane-2,6-dione (**5**) from glutaryl chloride (**4**) via the formation of a Weinreb amide, followed by MeMgBr addition. The three-component condensation of diketone **5**, acetonedicarboxylic acid, and NH_4OAc gave azabicyclononane **6** in moderate yield under a modified Momose's condition.[16] The steric hindrance around the nitrogen atom of azabicyclononane **6** inhibited the subsequent *N*-protection. After considerable experimentation, we found that freshly prepared BnI effectively afforded benzylamine **7**. After the formation of tosylhydrazone **8** by the condensation of ketone **7** with tosylhydrazine in refluxing benzene, treatment with NaH in refluxing DMF promoted ring closing by transannular C−H insertion to give azanoradamantane **9**.[13d,14a,17] Finally, the deprotection and oxidation sequence yielded DMN-AZADO[18] accompanied by 13% DMN-AZADOH (**10**), which is the hydroxylamine of DMN-AZADO (**2**). This synthetic procedure enabled the gram-scale preparation of DMN-AZADO (**2**).[19]

First, we evaluated the catalytic activity of DMN-AZADO (**2**) compared with those of TEMPO (**1**) and 1-Me-AZADO (**11**) for the oxidation of a primary alcohol to an aldehyde using 4-phenyl-1-butanol (**12**) as a substrate and conventional NaOCl as a cooxidant (Figure 3).[13a,20] Despite having steric hindrance, DMN-AZADO (**2**) displayed high catalytic efficiency comparable to that of 1-Me-AZADO (**11**). 0.01 mol % DMN-AZADO (**2**) gave aldehyde **13** in high yield, whereas a considerable decrease in productivity was observed for the same amount of TEMPO (**1**).

The following evaluation using 2,2,4-trimethylpentane-1,3-diol (**14a**), which contains a congested neopentyl primary alcohol, demonstrates the potent catalytic efficiency of DMN-AZADO (**2**) for the class-selective oxidation of a primary alcohol in the presence of a secondary alcohol (Figure 4).[22] 1 mol % DMN-AZADO (**2**) consistently afforded the desired hydroxyaldehyde **15a** in high yield for a wide range of NaOCl amounts. A yield of **15a** of more than 80% was obtained using 1.1−1.5 equiv of NaOCl, and the treatment with more than 1.7 equiv of NaOCl hardly promoted the oxidation of secondary alcohols, although the yield of hydroxy acid **16a** increased. Interestingly, severely controlling the amount of NaOCl to 1.1−1.2 equiv also resulted in highly selective oxidation under a 1-Me-AZADO-catalyzed condition.[10e] However, a slight excess of NaOCl critically reduced the yield of **15a** because of the nonselective oxidation of the secondary alcohol. On the other hand, TEMPO-catalyzed oxidation afforded **15a** in moderate yield, accompanied by the recovery of **14a**.

In view of the application of DMN-AZADO (**2**) to the synthesis of complex molecules, we examined its applicability to the oxidation of betulin (**14b**) using $PhI(OAc)_2$ as a cooxidant [10 mol % catalyst, 1.5 equiv of $PhI(OAc)_2$] (Figure 5).[23] The results showed the efficiency of DMN-AZADO (**2**) for class-selective oxidation. The desired hydroxyaldehyde **15b** was provided in 97% yield together with a negligible amount of

Scheme 1. Preparation of DMN-AZADO



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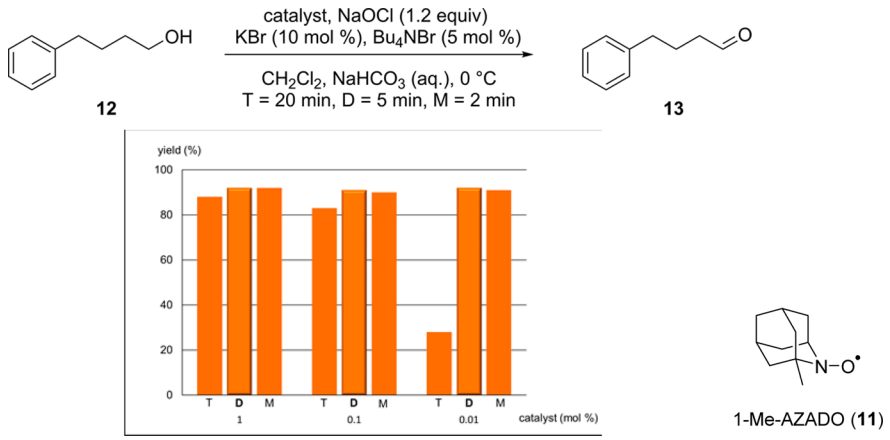

Figure 3. Catalytic activities of TEMPO, DMN-AZADO, and 1-Me-AZADO for the oxidation of a primary alcohol[21] [T = TEMPO (**1**), D = DMN-AZADO (**2**), M = 1-Me-AZADO (**11**)].

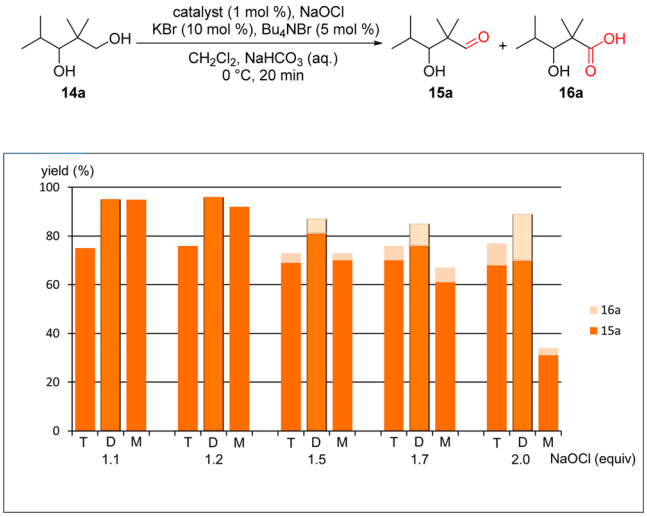

Figure 4. Catalytic efficiencies of TEMPO, DMN-AZADO, and 1-Me-AZADO for the class-selective oxidation of a primary alcohol[21] [T = TEMPO (**1**), D = DMN-AZADO (**2**), M = 1-Me-AZADO (**11**)].

ketoaldehyde **17b** via DMN-AZADO-catalyzed oxidation. Relatively dilute 0.2 M CH_2Cl_2 condition gave slightly better results than 1.0 M CH_2Cl_2, and the amount of ketoaldehyde decreased to less than 1%. In contrast, TEMPO-catalyzed oxidation recovered 26% betulin after 2 h. Increasing the reaction time led to the decomposition of **15b**. 1-Me-AZADO (**11**) was accompanied by the overoxidation of secondary alcohols to produce ketoaldehyde **17b** in more than 40% yield. Entry using 10 mol % 1-Me-AZADO (**11**) and 1.0 equiv of $PhI(OAc)_2$ provided 13% ketoaldehyde **17b** and 10% recovered betulin **14b** together with 75% hydroxyaldehyde **15b**, suggesting that overoxidation is inevitable even with careful operation (Table S4, entry 5, Supporting Information). Oxidation with Dess–Martin periodinane (DMP)[24] resulted in low selectivity and low productivity.

Table 1 shows the results of using various substrates for the class-selective oxidation of a primary alcohol catalyzed by DMN-AZADO (**2**) and TEMPO (**1**) [Method A: catalyst (1 mol %)/NaOCl (1.2 equiv)/KBr (10 mol %)/Bu_4NBr (5 mol %)/CH_2Cl_2/aq. $NaHCO_3$. Method B: catalyst (2–5 mol %)/$PhI(OAc)_2$ (1.2–1.5 equiv)/CH_2Cl_2]. DMN-AZADO (**2**) generally exhibited higher reactivity than TEMPO (**1**), and a significant loss of selectivity compared with TEMPO (**1**) was not observed. The superior catalytic performance of DMN-AZADO (**2**) became much more prominent in the oxidation of hindered primary alcohols such as neopentyl alcohols (entries 3–10). It is also notable that increasing the reaction time promoted the degradation of the desired products under TEMPO catalysis instead of increasing the yields of the desired products (entries 2–5, 7–9). Neither TEMPO (**1**) nor DMN-AZADO (**2**) provided satisfying results for the oxidation of **14k**, which is presumably due to the small difference in steric hindrance between the primary alcohol and the secondary alcohol (entry 11).

Next, we examined the applicability of DMN-AZADO (**2**) to the class-selective one-pot oxidation of primary alcohols to carboxylic acids in the presence of secondary alcohols under a cat. NaOCl/$NaClO_2$ condition [catalyst (10 mol %)/NaOCl (10 mol %)/$NaClO_2$ (3.0 equiv)].[25,26] Note that high selectivity to primary alcohols is required for the full conversion (Scheme 2). Under this condition, the catalytic oxoammonium species is generated from the corresponding nitroxyl radicals and/or hydroxylamine by oxidation with NaOCl, which is catalytically generated from $NaClO_2$ in the oxidation of aldehydes to the corresponding carboxylic acids (Scheme 2a). Hence, the oxidation of secondary alcohols does not generate NaOCl, which leads to the deactivation of the catalytic system (Scheme 2b). In the evaluation using 10 mol % catalyst for the one-pot oxidation of diol **14e**, the typical properties of each catalyst was exhibited (Table 2). The TEMPO-catalyzed oxidation was slow because of steric hindrance, and 31% diol **14e** was recovered after 24 h. 1-Me-AZADO-catalyzed oxidation stopped at 65% conversion along with 9% keto acid **18e**, which is due to the shortage of NaOCl (entry 2). Therefore, the addition of another 10 mol % NaOCl increased the yields of hydroxy acid **16e** and keto acid **18e** (entry 3). In contrast, the desired selective oxidation efficiently proceeded via DMN-AZADO (**2**) catalysis to afford hydroxy acid **16e** in high yield; 5 mol % DMN-AZADO (**2**) sufficiently catalyzed the one-pot selective oxidation.

We examined the possibility of the selective one-pot oxidation of diols to the corresponding hydroxy acids [catalyst (5 mol %)/NaOCl (5 mol %)/$NaClO_2$ (3.0 equiv)] (Table 3). DMN-AZADO (**2**) exhibited superior efficiency to TEMPO (**1**), except for the very simple diol **14d**. The TEMPO-catalyzed condition recovered a small amount of starting materials even

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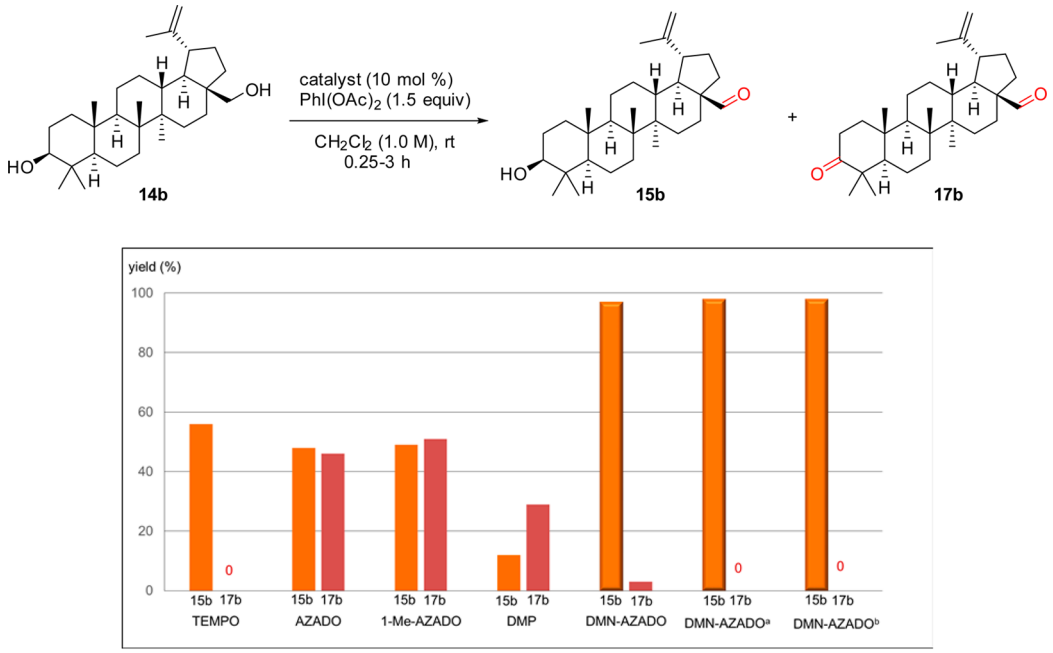

[a] 0.2 M CH_2Cl_2, [b] 2 mol % DMN-AZADO

Figure 5. Catalytic efficiencies of TEMPO, DMN-AZADO, and 1-Me-AZADO for class-selective oxidation of betulin (**14b**).[21]

after 24 h, while the DMN-AZADO-catalyzed condition smoothly led to complete oxidation within a reasonable time (entries 3–5 and 7). DMN-AZADO (**2**) was also successfully applied to the selective oxidation of the advanced intermediate **14o** in the total synthesis of psymberin/irciniastatin A to provide the corresponding hydroxy acid **16o** (Scheme 3).[27] DMN-AZADO$^+BF_4^-$ clearly gave a better result than TEMPO$^+BF_4^-$.[13b]

We also investigated oxidative lactonization from diols to the corresponding lactones via the class-selective oxidation of primary alcohols.[28] DMN-AZADO (**2**) efficiently catalyzed oxidative lactonization. The reaction rate of DMN-AZADO-catalyzed oxidation was significantly higher than that of TEMPO-catalyzed oxidation (Scheme 4).

CONCLUSION

We have found DMN-AZADO (**2**) to be a highly effective organocatalyst for the class-selective oxidation of primary alcohols. DMN-AZADO (**2**) can be prepared on the gram scale in an eight-step sequence. The catalytic efficiency of DMN-AZADO is considerably higher than that of TEMPO without significant loss of selectivity. DMN-AZADO (**2**) gave superior results to TEMPO (**1**) and 1-Me-AZADO (**11**) not only for the class-selective oxidation of primary alcohols to the corresponding aldehydes in the presence of secondary alcohols but also for the selective one-pot oxidation from primary alcohols to carboxylic acids and for oxidative lactonization. The higher catalytic potency of DMN-AZADO (**2**) is particularly noteworthy for congested neopentyl primary alcohols. These results indicate that the selectivity and efficiency of a nitroxyl radical catalyst can be modulated by tuning the steric environment around the nitroxyl radical. Owing to its high potential for application to organic synthesis, we are preparing to make DMN-AZADO (**2**) commercially available.

EXPERIMENTAL SECTION

General Experimental Procedure. All reactions were carried out under an atmosphere of argon unless otherwise specified. Reagents were purchased from commercial suppliers and used without further purification unless otherwise stated. The concentration of aq. NaOCl was determined by standard redox titration (KI). Reactions were monitored by thin-layer chromatography (TLC) carried out on silica gel plates. Column chromatography was performed on silica gel 60N (spherical, neutral, 40–50 μm and 63-210 μm). Optical rotations were measured using a digital polarimeter at room temperature using the sodium D line. Melting points (uncorrected) were determined using melting point apparatus. ^{1}H NMR spectra were recorded on 400 and 600 MHz spectrometers. Chemical shifts (δ) are given in ppm relative to 0.00 ppm for tetramethylsilane (TMS). Coupling constants (J) are reported in Hz. Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, double doublet; dt, double triplet; dq, double quartet. ^{13}C NMR spectra were recorded on 100 and 150 MHz spectrometers. Chemical shifts are given in ppm relative to 77.0 ppm for $CDCl_3$. Low-resolution mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded using electron impact (EI) with a magnetic sector or time-of-flight mass analyzer or by electrospray ionization (ESI) with an ion-trap mass analyzer. Diols **14a–14d** are commercially available. Diols **14e**,[29] **14h**,[30] **14i**,[31] **14k**,[32] **14l**,[33] **14m**,[34] and **14p**[35] were prepared in accordance with known procedures.

Heptane-2,6-dione (5).[36] To a solution of *N*,*O*-dimethylhydroxylamine hydrochloride (47.8 g, 0.490 mol) in CH_2Cl_2 (500 mL), Et_3N (140 mL, 0.980 mol) followed by glutaryl chloride **4** (25 mL, 0.196 mol) at 0 °C was slowly added. The reaction mixture was stirred at 0 °C for 0.5 h and allowed to warm to room temperature. The reaction mixture was stirred at room temperature for 1 h and then washed with water, 1 N HCl, sat. $NaHCO_3$, and brine. The organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The residue was used in the subsequent reaction without further purification. To a solution of the amide in THF (500 mL), MeMgBr (3.0 M in Et_2O, 160 mL, 0.470 mol) was added dropwise at 0 °C. The mixture was stirred for 4 h at room temperature and quenched with sat. NH_4Cl. The mixture was extracted with AcOEt (four times). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (Et_2O:hexane = 2:1) to yield diketone **5**

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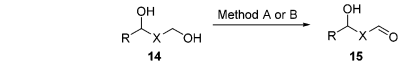
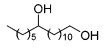
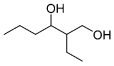
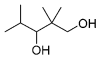
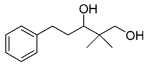
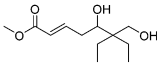
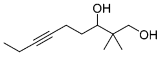
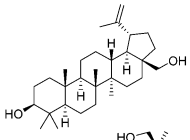
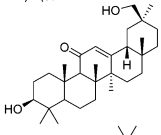
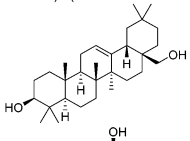
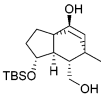
Table 1. Results of Using Various Substrates in Class-Selective Oxidation of Diols to Hydroxyaldehydes[a,b,c,d,e,f]

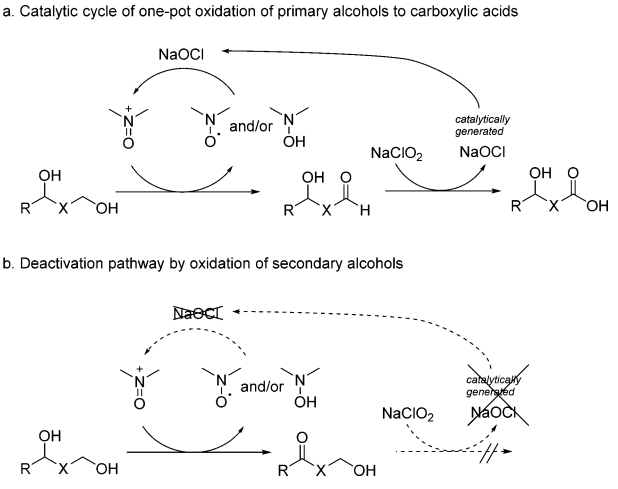


Method A : catalyst (1 mol %), NaOCl (1.2 equiv), KBr (10 mol %), Bu_4NBr (5 mol %) CH_2Cl_2 (0.375 M), $NaHCO_3$ (aq.) (0.375 M) 0 °C
Method B : catalyst (5 mol %), $PhI(OAc)_2$ (1.5 equiv), CH_2Cl_2 (0.2 M), rt

entry	substrate		method	yield / time TEMPO	yield / time DMN-AZADO
1		**14c**	A	93% / 20 min[a,b]	89% / 15 min[a,c]
			B	68% / 3 h[d] (88% / 1.5 h[e])	84% / 2 h[d]
2		**14d**	A	94% / 10 min	95% / 5 min
			B	58% / 4 h[d]	85% / 3 h[d]
3		**14a**	A	76% / 20 min	96% / 20 min
			B	21% / 2 h	80% / 1 h
4		**14e**	A	70% / 20 min	93% / 4 min
			B	26% / 1.5 h[f]	92% / 15 min[f]
5		**14f**	A	67% / 20 min	90% / 10 min
6		**14g**	A	79% / 20 min	94% / 5 min
7		**14b**	B	32% / 4 h	97% / 45 min
8		**14h**	A	78% / 10 min	91% / 3 min
			B	62% / 2 h	99% / 1 h
9		**14i**	B	41% / 2.5 h	95% / 30 min
10		**14j**	A	70% / 20 min	84% / 4 min
11		**14k**		——	——

[a]0.05 M CH_2Cl_2 and 0.1 M $NaHCO_3$ (aq.) were used as solvents. [b]5% ketoaldehyde was obtained with TEMPO. [c]7% ketoaldehyde was obtained with DMN-AZADO. [d]2 mol % catalyst and 1.2 equiv of $PhI(OAc)_2$ were used. [e]5 mol % catalyst and 1.2 equiv of $PhI(OAc)_2$ were used. [f]1.0 M CH_2Cl_2 was used.

Scheme 2. Catalytic Pathway of Selective One-Pot Oxidation of Diols to Hydroxy Acids



(22.5 g, 90%) as a pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (t, J = 7.2 Hz, 4H), 2.13 (s, 6H), (quint, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.3, 42.4, 29.9, 17.6; IR (neat, cm^{-1}): 1714; MS m/z 128 $[M]^+$, 43 (100%); HRMS (EI): calcd. for $C_7H_{12}O_2$ 128.0837 $[M]^+$, found 128.0835.

1,5-Dimethyl-9-azabicyclo[3.3.1]nonan-3-one (6). To a solution of diketone **5** (5.07 g, 39.6 mmol) in AcOH (49 mL), NH_4OAc (18.3 g, 0.238 mol) and acetone dicarboxylic acid (34.7 g, 0.238 mol) were added at room temperature. The reaction mixture was stirred for 3 h at 80 °C and then cooled to 0 °C. After the solution was diluted with CH_2Cl_2 and water until it separated into two layers, it was acidified with 10% HCl aq. (pH 1) and then diluted with AcOEt. The resultant mixture was extracted with water. The combined aqueous layers were basified with 20% NaOH (pH 11) and extracted with CH_2Cl_2 (three times). Then, the combined organic layers were dried over K_2CO_3 and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (AcOEt:hexane = 1:1 to MeOH:$CHCl_3$ = 1:8) to yield amine **6** (3.65 g, 55%) as a dark red oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (d, J = 16.2 Hz, 2H), 2.11 (d, J = 16.2 Hz, 2H), 1.70−1.62 (m, 3H), 1.58−1.41 (m, 1H), 1.41−1.28 (m, 3H), 1.21 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.3, 52.9, 52.4, 37.9, 31.5, 19.4; IR (neat, cm^{-1}): 1704, 850; MS m/z 167 $[M]^+$, 124 (100%); HRMS (EI): calcd. for $C_{10}H_{17}NO$ 167.1310 $[M]^+$, found 167.1292.

***N*-Benzyl 1,5-Dimethyl-9-azabicyclo[3.3.1]nonan-3-one (7).** To a solution of amine **6** (1.06 g, 6.34 mmol) and freshly prepared benzyl iodide (1.26 mL, 10.1 mmol)[37] in acetone (11 mL), K_2CO_3 (1.40 g, 10.1 mmol) was added at room temperature. The reaction mixture was refluxed for 2 days. After cooling to 0 °C, the reaction mixture was diluted with CH_2Cl_2 and quenched with water. The mixture was extracted with CH_2Cl_2 (three times). The combined organic layers were dried over K_2CO_3 and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (AcOEt:hexane = 1:12 to 1:8) to yield benzyl amine **7** (1.40 g, 86%) as a white solid; mp 100−101 °C (recrystallized from hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 7.8 Hz, 2H), 7.31 (t, J = 7.8 Hz, 2H), 7.19 (t, J = 7.8 Hz, 1H), 3.94 (s, 2H), 2.42 (d, J = 15.9 Hz, 2H), 2.25 (d, J = 15.9 Hz, 2H), 1.78−1.65 (m, 2H), 1.62−1.43 (m, 4H), 1.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.8, 144.2, 128.1, 126.6, 126.0, 57.9, 49.3, 47.3, 37.8, 29.8, 19.6; IR (neat, cm^{-1}): 1702, 1202, 719, 695; MS m/z 257 $[M]^+$, 257 (100%); HRMS (EI): calcd. for $C_{17}H_{23}NO$ 257.1780 $[M]^+$, found 257.1762.

***N*-Benzyl 1,5-Dimethyl-9-azabicyclo[3.3.1]nonan-3-ylidene)-4-methylbenzene-sulfonohydrazide (8).** To a solution of benzyl amine **7** (5.46 g, 21.2 mmol) in benzene (106 mL), *p*-toluenesulfonyl hydrazine (9.48 g, 50.9 mmol) was added, and the reaction mixture was refluxed with a Dean−Stark water separator for 9 h. After the solution was cooled to 0 °C, it was extracted with AcOEt (three times). The combined organic layers were washed with brine and dried over $MgSO_4$ and then concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (AcOEt:hexane = 1:4) to yield hydrazone **8** (6.93 g, 77%) as a yellow solid; mp 168−169 °C (recrystallized from hexane-$CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90−7.83 (m, 2H), 7.63 (br s, 1H), 7.44−7.37 (m, 2H), 7.35−7.28 (m, 2H), 7.28−7.22 (m, 2H), 7.20−7.12 (m, 1H), 3.90−3.72 (m, 2H), 2.43 (s, 3H), 2.41−2.25 (m, 3H), 2.01 (d, J = 16.1 Hz, 1H), 1.67−1.55 (m, 2H), 1.55−1.40 (m, 2H), 1.40−1.28 (m, 2H), 0.983 (s, 3H), 0.979 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 144.4, 143.9, 135.7, 129.5, 127.99, 127.98, 126.6, 125.9, 56.2, 56.1, 47.0, 30.1, 29.9, 21.6, 19.3; IR (neat, cm^{-1}): 3218, 1166; MS m/z 425 $[M]^+$, 240 (100%); HRMS (EI): calcd. for $C_{24}H_{31}N_3O_2S$ 425.2137 $[M]^+$, found 425.2118.

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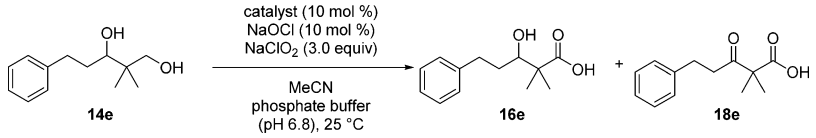
Table 2. Catalytic Efficiencies of TEMPO, 1-Me-AZADO, and DMN-AZADO for the One-Pot Class-Selective Oxidation of Diols to Hydroxy Acids



			yield (%)[a]		
entry	catalyst	time (h)	**16e**	**18e**	**14e**
1	TEMPO	24	58	0	31
2	1-Me-AZADO	2	47	9	35
3	1-Me-AZADO[b]	4	63	17	19
4	DMN-AZADO	1	90	0	0
5	DMN-AZADO[c]	3	91	0	0

[a]Isolated as methyl esters after treatment with CH_2N_2. [b]10 mol % NaOCl was added after 1.5 h. [c]5 mol % DMN-AZADO and NaOCl were used.

***N*-Benzyl 1,5-Dimethyl-9-azanoradamantane (9).** To a solution of hydrazone **8** (2.50 g, 5.87 mmol) in DMF (59 mL), NaH (60% dispersion in mineral oil, 704 mg, 17.6 mmol) was added, and the reaction mixture was stirred at room temperature for 15 min and then refluxed for 15 min before quenching with water at 0 °C. The reaction mixture was extracted with Et_2O (three times), and the organic layers were washed with brine and dried over Na_2SO_4 and then concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (only hexane to AcOEt:hexane = 1:8) to yield *N*-benzyl azanoradamantane **9** and *N*-benzyl-1,5-dimethyl-9-azabicyclo[3.3.1]non-2-ene (**20**) (1.10 g, 77% (**9** + **20**), ca. 8:1) as an inseparable mixture.

N-Benzyl 1,5-Dimethyl-9-azanoradamantane (9).[38,39] Pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51−7.42 (m, 2H), 7.32−7.24 (m, 2H), 7.18−7.11 (m, 1H), 3.76 (s, 2H), 2.54 (quint, J = 5.0 Hz, 2H), 1.62 (d, J = 10.0 Hz, 4H), 1.48 (dd, J = 10.0, 5.0 Hz, 4H), 1.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 127.8, 127.0, 125.5, 65.3, 50.8, 47.3, 38.6, 23.7; IR (neat, cm^{-1}): 719; MS m/z 241 [M]$^+$, 241 (100%); HRMS (EI): calcd. for $C_{17}H_{23}N$ 241.1831 [M]$^+$, found 241.1815.

1,5-Dimethyl-9-azanoradamantane *N*-Oxyl (2). To a solution of 20% $Pd(OH)_2/C$ (wetted with 50% water, 620 mg) in EtOH (130 mL), a mixture of azanoradamantane **9** and azabicyclononene **20** (6.20 g, ca. 8:1) was added. The reaction flask was purged with H_2 three times, and then the reaction mixture was stirred at room temperature under H_2 atmosphere for 1 day. The catalyst was removed by filtration through Celite. The filtrate was concentrated under reduced pressure. The residue was dissolved in $CHCl_3$ and sat. Na_2CO_3 and then extracted with $CHCl_3$ (twice). The combined organic layers were dried over K_2CO_3 and concentrated under reduced pressure. The residue was used in the subsequent reaction without further purification. To a solution of the crude amine in MeOH (51 mL), $Na_2WO_4{\cdot}2H_2O$ (4.24 g, 12.9 mmol) was added. After the suspension was stirred at room temperature for 30 min, UHP (7.25 g, 77.1 mmol) was added, which was followed by stirring for an additional 2 h. Sat. $NaHCO_3$ was added to the reaction mixture, and then the mixture was extracted with $CHCl_3$ (three times). The organic layers were dried over K_2CO_3 and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography to yield an inseparable mixture of 1,5-dimethyl-9-azanoradamantane *N*-oxyl (DMN-AZADO) (**2**) and 1,5-dimethyl-9-azabicyclo[3.3.1]nonane *N*-oxyl (2.24 g, ca. 52%) as a red oil from the eluent of Et_2O:hexane = 1:4, and an inseparable mixture of *N*-hydroxy-1,5-dimethyl-9-azanoradamantane (**10**) and *N*-hydroxy-1,5-dimethyl-9-azabicyclo-[3.3.1]nonane (570 mg, ca. 13%) as a white solid from the eluent of AcOEt:hexane = 1:2 to only AcOEt.

DMN-AZADO (2).[38] Dark red oil (142 mg, 50%);[39] IR (neat, cm^{-1}): 1456, 1374, 1337; MS m/z 166 [M]$^+$, 93 (100%); HRMS (EI): calcd. for $C_{10}H_{16}NO^{\bullet}$ 166.1232 [M]$^+$, found 166.1232; Anal: calcd. for $C_{10}H_{16}NO^{\bullet}$: C, 72.25; H, 9.70; N, 8.43, found: C, 72.06; H, 9.91; N, 8.40.

DMN-AZADOH (10).[38] White solid (38 mg, 13%);[39] ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.53−2.38 (m, 2H), 1.89 (dd, J = 11.2, 2.9 Hz, 2H), 1.66−1.56 (m, 2H), 1.54−1.44 (m, 2H), 1.36 (dd, J = 11.2, 6.6 Hz, 2H), 1.26 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 68.6, 47.9, 42.4, 37.6, 37.2, 21.7; IR (neat, cm^{-1}): 3366; MS m/z 167 [M]$^+$, 167 (100%); HRMS (EI): calcd. for $C_{10}H_{17}NO$ 167.1310 [M]$^+$, found 167.1296.

Preparation of DMN-AZADO$^+BF_4^-$.[13b] To a solution of DMN-AZADO (294 mg, 1.77 mmol) in H_2O (0.45 mL), 42% HBF_4 (0.37 mL, 1.77 mmol) in H_2O (0.15 mL) was added dropwise at room temperature. After cooling to 0 °C, aqueous NaOCl (0.885 mmol) was added slowly and the reaction mixture was stirred for 30 min at 0 °C. It was then filtered, and the precipitate was washed with ice-cold 5% $NaHCO_3$, water, and Et_2O. The obtained solid was dried under reduced pressure to afford DMN-AZADO$^+BF_4^-$ (219 mg, 49%) as a yellow solid; Anal: calcd. for $C_{10}H_{16}NOBF_4$: C, 47.46; H, 6.37; N, 5.54, found: C, 47.50; H, 6.41; N, 5.51.

Representative Procedure for the Selective Oxidation of Diols to Hydroxyaldehydes Using NaOCl as a Cooxidant (Method A). To a solution of 2,2-dimethyl-5-phenylpentane-1,3-diol (**14e**) (42.5 mg, 0.204 mmol) and DMN-AZADO (**2**) (0.339 mg, 0.0020 mmol) in CH_2Cl_2 (0.54 mL), sat. $NaHCO_3$ (0.32 mL) containing KBr (2.43 mg, 0.020 mmol) and *n*-Bu_4NBr (3.29 mg, 0.010 mmol) was added. While the reaction mixture was vigorously stirred at 0 °C, a premixed solution of aqueous NaOCl (0.245 mmol) and sat. $NaHCO_3$ (0.22 mL) was added dropwise over 2 min. After stirring for 4 min at 0 °C, the reaction mixture was quenched with sat. $Na_2S_2O_3$ (1 mL). The layers were separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by flash silica gel column chromatography (AcOEt:hexane = 1:4) to give 3-hydroxy-2,2-dimethyl-5-phenylpentanal (**15e**) (39.3 mg, 93%).

Representative Procedure for the Selective Oxidation of Diols to Hydroxyaldehydes Using PhI(OAc)$_2$ as a Cooxidant (Method B). To a solution of 2,2,4-trimethylpentane-1,3-diol (**14a**) (41.7 mg, 0.285 mmol) and DMN-AZADO (**2**) (2.37 mg, 0.0143 mmol) in CH_2Cl_2 (1.4 mL), $PhI(OAc)_2$ (138 mg, 0.428 mmol) was added in a single portion. After stirring for 1 h at room temperature, the reaction mixture was diluted with Et_2O and quenched with sat. $NaHCO_3$ (1 mL) and sat. $Na_2S_2O_3$ (1 mL), and the layers were separated. The aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude material was purified by flash silica gel column chromatography (AcOEt:hexane = 1:4) to give 3-hydroxy-2,2,4-trimethylpentanal (**15a**) (32.8 mg, 80%).

Representative Procedure for the Selective One-Pot Oxidation of Diols to Hydroxy Acids Using NaOCl and NaClO$_2$. To a solution of 2,2-dimethyl-5-phenylpentane-1,3-diol (**14e**) (49.6 mg, 0.238 mmol) in MeCN (1.2 mL) and phosphate buffer (0.8 mL, pH = 6.8, 1 M) at 25 °C, a MeCN solution of DMN-AZADO (**2**) (1.98 mg, 0.012 mmol) was added. Then, $NaClO_2$

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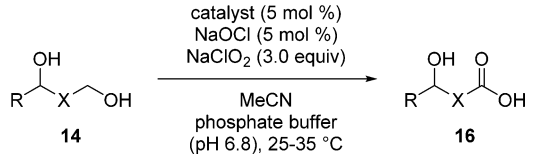
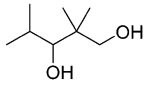
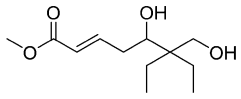
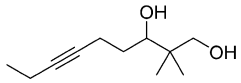
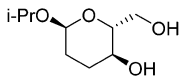
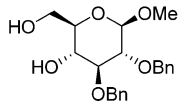
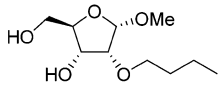
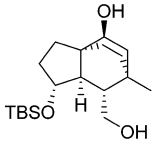
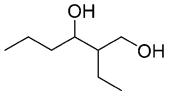
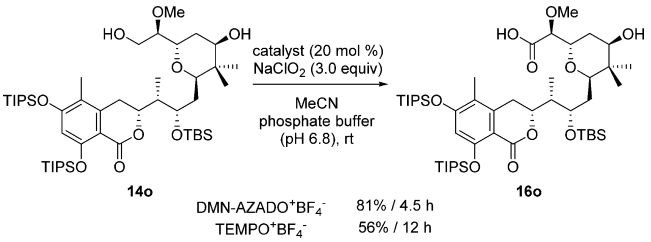
Table 3. Results of Using Various Substrates in One-Pot Class-Selective Oxidation of Diols to Hydroxy Acids[a,b,c,d]



entry	substrate		yield[a] / time	
			TEMPO	DMN-AZADO
1		**14a**	49% / 24 h (45%)[b]	92% / 7 h
2		**14f**	93% / 20 h[c]	93% / 8 h[c]
3		**14g**	82% / 24 h (13%)[b]	98% / 4.5 h
4		**14l**	81% / 24 h (12%)[b]	95% / 12 h
5		**14m**	85% / 24 h	94% / 14 h
6		**14n**	77% / 24 h (13%)[b]	83% / 9 h (8%)[b]
7		**14j**	86% / 24 h[d] (2%)[b]	92% / 6 h[d]
8		**14d**	88% / 3 h	70% / 3 h (17%)[b]

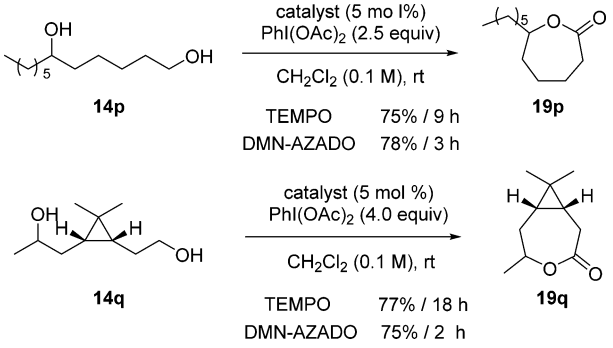
[a]Isolated as methyl esters after treatment with CH_2N_2. [b]The numbers in parentheses are the yields of the recovered diols. [c]10 mol % catalyst and 10 mol % NaOCl were used. [d]0.6 M $CHCl_3$ was added. Isolated as carboxylic acids.

Scheme 3. Class-Selective Oxidation of Intermediate 14o in Synthesis of Psymberin/Irciniastatin A



(80.8 mg, 80%, 0.714 mmol) in H_2O (0.4 mL) and dilute aq. NaOCl solution (0.09 mL, 0.0119 mmol) were simultaneously added over 30 s. After stirring at 25 °C for 3 h, the reaction mixture was acidified with phosphate buffer (3 mL, pH = 2.3), NaCl and CH_2Cl_2 were added, and the two layers were separated. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. After the treatment of CH_2N_2 in Et_2O, the crude product was purified by flash silica gel column chromatography (AcOEt:hexane = 1:4) to give methyl 3-hydroxy-2,2-dimethyl-5-phenylpentanoate (**16e′**) (51.2 mg, 91%).

Scheme 4. Oxidative Lactonization Employing Class-Selective Oxidation of Primary Alcohols



Representative Procedure for the Oxidative Lactonization of Diols. To a solution of dodecane-1,6-diol (**14p**) (40.7 mg, 0.201 mmol) and DMN-AZADO (**2**) (1.68 mg, 0.010 mmol) in CH_2Cl_2 (2.0 mL), $PhI(OAc)_2$ (162 mg, 0.503 mmol) was added in a single portion. After the reaction mixture was stirred for 3 h at room temperature, it was diluted with Et_2O and quenched with sat. $NaHCO_3$ (1 mL), followed by sat. $Na_2S_2O_3$ (1 mL). The layers were separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by flash silica gel column chromatography (AcOEt:hexane = 1:4) to give 7-hexyloxepan-2-one (**19p**) (31.0 mg, 78%).

Syntheses of Diols and Compound Characterization. *3-Hydroxy-2,2,4-trimethylpentanal (**15a**).*[40] Pale yellow oil (49.2 mg, 96%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H), 3.55 (dd, J = 5.8, 3.9 Hz, 1H), 1.96 (d, J = 5.8 Hz, 1H), 1.88 (sept d, J = 6.8, 3.9 Hz, 1H), 1.13 (s,, 3H), 1.12 (s, 3H), 0.97 (d, J = 6.8 Hz, 3H), 0.91 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.7, 80.2, 50.5, 29.9, 21.7, 19.8, 18.6, 17.2; IR (neat, cm^{-1}): 3421, 1717; MS m/z 144 [M]$^+$, 72 (100%); HRMS (EI) calcd. for $C_8H_{16}O_2$: 144.1150 [M]$^+$, found: 144.1150.

*Methyl 3-Hydroxy-2,2,4-trimethylpentanoate (**16a′**).*[41] Pale orange oil (48.2 mg, 92%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.69 (s, 3H), 3.39 (dd, J = 8.7, 3.6 Hz, 1H), 2.81 (d, J = 8.7 Hz, 1H), 1.86 (sept d, J = 6.9, 3.6 Hz, 1H), 1.28 (s, 3H), 1.19 (s, 3H), 0.97 (d, J = 6.9 Hz, 3H), 0.81 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 81.2, 51.6, 45.8, 29.8, 23.0, 22.3, 21.3, 16.2; IR (neat, cm^{-1}): 3506, 1729, 1264, 1143; HRMS (ESI) calcd. for $C_9H_{18}O_3Na$: 197.1148 [M + Na]$^+$, found: 197.1156.

*Betulinal (**15b**).*[42] White solid (48.3 mg, 97%); $[\alpha]_D^{26}$ +14.7 (c 1.67, $CHCl_3$); mp 168−169 °C ($CHCl_3$-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1H), 4.76 (s, 1H), 4.63 (s, 1H), 3.18 (dd, J = 10.6, 4.4 Hz, 1H), 2.86 (td, J = 11.1, 5.8 Hz, 1H), 2.12−2.04 (m, 1H), 2.02 (td, J = 12.1, 3.4 Hz, 1H), 1.96−1.82 (m, 1H), 1.82−0.84 (m, 33H), 0.82 (s, 3H), 0.75 (s, 3H), 0.67 (d, J = 9.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.7, 149.7, 110.1, 78.9, 59.3, 55.3, 50.4, 48.0, 47.5, 42.5, 40.8, 38.8, 38.71, 38.67, 37.2, 34.3, 33.2, 29.8, 29.2, 28.8, 28.0, 27.4, 25.5, 20.7, 19.0, 18.2, 16.1, 15.9, 15.3, 14.2; IR (neat, cm^{-1}): 3419, 1724, 910; MS m/z 440 [M]$^+$, 440 (100%); HRMS (EI) calcd. for $C_{30}H_{48}O_2$: 440.3654 [M]$^+$, found: 440.3656.

*Betulonal (**17b**).*[42] White solid (25.0 mg, 51%); $[\alpha]_D^{24}$ +42.7 (c 1.30, $CHCl_3$); mp 138−139 °C ($CHCl_3$-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1H), 4.76 (s, 1H), 4.64 (s, 1H), 2.88 (td, J = 11.1, 5.8 Hz, 1H), 2.58−2.34 (m, 2H), 2.19−2.01 (m, 2H), 1.98−1.85 (m, 2H), 1.85−1.66 (m, 6H), 1.57−1.18 (m, 14H), 1.18−0.77 (m, 16H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 217.9, 206.5, 149.6, 110.2, 59.3, 54.9, 49.8, 47.9, 47.5, 47.3, 42.6, 40.8, 39.6, 38.7, 36.9, 34.1, 33.6, 33.2, 29.8, 29.1, 28.8, 26.6, 25.5, 21.3, 21.0, 19.6, 19.0, 15.9, 15.7, 14.2; IR (neat, cm^{-1}): 1705, 1454; MS m/z 438 [M]$^+$, 410 (100%); HRMS (EI) calcd. for $C_{30}H_{46}O_2$: 438.3498 [M]$^+$, found: 438.3481.

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*12-Hydroxyoctadecanal (**15c**).* White solid (37.0 mg, 89%); mp 53−54 °C (Et_2O-hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 9.76 (t, J = 1.8 Hz, 1H), 3.58 (br s, 1H), 2.42 (td, J = 7.2, 1.8 Hz, 2H), 1.63 (quint, J = 7.2 Hz, 2H), 1.49−1.30 (m, 6H), 1.42−1.20 (m, 21H), 0.88 (t, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.9, 71.8, 43.8, 37.41, 37.38, 31.8, 29.6, 29.5, 29.4, 29.31, 29.25, 29.1, 25.6, 25.5, 22.5, 22.0, 14.0; IR (neat, cm^{-1}): 3300, 1712, 1469; MS m/z 283 $[M - H]^+$, 199 (100%); HRMS (EI) calcd. for $C_{18}H_{35}O_2$: 283.2637 $[M - H]^+$, found: 283.2622.

*2-Ethyl-3-hydroxyhexanal (**15d**).* Colorless oil (49.9 mg, 95%); ^1H NMR (400 MHz, $CDCl_3$) δ9.78 (d, J = 2.4 Hz, 0.4H), 9.76 (d, J = 2.9 Hz, 0.6H), 3.98 (dt, J = 8.7, 4.4 Hz, 0.4H), 3.88 (dt, J = 5.8, 5.8 Hz, 0.6H), 2.37−2.23 (m, 1H), 2.06 (br s, 0.6H), 1.86 (br s, 0.4H), 1.84−1.73 (m, 1H), 1.73−1.61 (m, 1H), 1.58−1.42 (m, 3H), 1.42−1.29 (m, 1H), 1.05−0.89 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ major 205.9, 70.8, 58.7, 37.1, 19.3, 18.6, 13.8, 11.4, minor 205.7, 70.5, 58.8, 36.5, 19.1, 17.4, 13.8, 12.1; IR (neat, cm^{-1}): 3428, 1719, 1463; MS m/z 145 $[M + H]^+$, 72 (100%); HRMS (EI) calcd. for $C_8H_{17}O_2$: 145.1229 $[M + H]^+$, found: 145.1215.

*Methyl 2-Ethyl-3-hydroxyhexanoate (**16d′**).* Pale yellow oil (39.3 mg, 70%); ^1H NMR (400 MHz, $CDCl_3$) δ 3.81 (td, J = 8.6 Hz, 4.3 Hz, 0.4H), 3.76−3.65 (m, 0.6H), 3.72 (s, 3H), 2.45−2.34 (m, 1.6H), 2.30 (d, J = 4.3 Hz, 0.4H), 1.74 (qd, J = 15.6, 7.8, 0.8H), 1.68 (qd, J = 14.4, 7.2, 1.2H), 1.60−1.28 (m, 4H), 0.93 (t, J = 7.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ major: 176.0, 71.6, 52.6, 51.4, 37.7, 22.6, 18.8, 13.9, 11.8, minor: 175.8, 71.6, 52.8, 51.5, 36.5, 20.3, 19.0, 13.9, 12.1; IR (neat, cm^{-1}): 3460, 1736, 1170; MS m/z 175 $[M + H]^+$, 102 (100%); HRMS (EI) calcd. for $C_9H_{19}O_3$: 175.1334 $[M + H]^+$, found: 175.1349.

*2,2-Dimethyl-5-phenylpentane-1,3-diol (**14e**).*[29] White solid (556 mg, 95%); mp 80−81 °C ($CHCl_3$-hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37−7.15 (m 5H), 3.58 (dd, J = 10.6, 5.3 Hz, 1H), 3.52 (ddd, J = 10.6, 4.6, 1.2 Hz, 1H), 3.46 (dd, J = 10.6, 4.8 Hz, 1H), 2.93 (ddd, J = 14.2, 9.7, 4.8 Hz, 1H), 2.64 (ddd, J = 14.2, 9.7, 6.8 Hz, 1H), 2.59−2.52 (m, 1H), 2.47−2.32 (m, 1H), 1.89−1.78 (m, 1H), 1.76−1.63 (m, 1H), 0.89 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2, 128.5, 128.4, 125.9, 78.9, 72.4, 38.5, 33.8, 33.0, 22.5, 18.9; IR (neat, cm^{-1}): 3362, 748, 700; MS m/z 208 $[M]^+$, 134 (100%); HRMS (EI) calcd. for $C_{13}H_{20}O_2$: 208.1463 $[M]^+$, found: 208.1463.

*3-Hydroxy-2,2-dimethyl-5-phenylpentanal (**15e**).*[40] Pale yellow oil (39.3 mg, 93%); ^1H NMR (400 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.36−7.17 (m, 5H), 3.77 (d, J = 9.7 Hz, 1H), 2.96 (ddd, J = 14.0, 9.7, 5.4 Hz, 1H), 2.67 (ddd, J = 14.0, 9.2, 7.3 Hz, 1H), 2.29 (br s, 1H), 1.83−1.64 (m, 2H), 1.11 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6, 141.6, 128.3, 125.8, 74.0, 50.3, 33.0, 32.5, 18.8, 16.3; IR (neat, cm^{-1}): 3466, 1721, 750, 700; MS m/z 188 $[M - H_2O]^+$, 72 (100%); HRMS (EI) calcd. for $C_{13}H_{16}O$: 188.1201 $[M - H_2O]^+$, found: 188.1189.

*Methyl 3-Hydroxy-2,2-dimethyl-5-phenylpentanoate (**16e′**).*[29] pale yellow oil (51.0 mg, 90%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.15 (m, 5H), 3.69 (s, 3H), 3.62 (ddd, J = 10.4, 7.0, 1.7 Hz, 1H), 2.95 (ddd, J = 14.2, 9.8, 4.9 Hz, 1H), 2.65 (ddd, J = 14.2, 9.2, 6.8 Hz, 1H), 2.57 (d, J = 7.0 Hz, 1H), 1.87−1.70 (m, 1H), 1.70−1.50 (m, 1H), 1.19 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 142.0, 128.4, 128.3, 125.8, 76.0, 51.8, 47.1, 33.6, 32.8, 22.3, 20.3; IR (neat, cm^{-1}): 3501, 1723, 750, 701; MS m/z 236 $[M]^+$, 117 (100%); HRMS (EI) calcd. for $C_{14}H_{20}O_3$: 236.1413 $[M]^+$, found: 236.1401.

*Methyl (E)-6-Ethyl-5-hydroxy-6-(hydroxymethyl)oct-2-enoate (**14f**).* To a solution of 2,2-diethyl-1,3-propanediol (5.00 g, 37.8 mmol) in DMF (190 mL), TBSCl (6.84 g, 45.4 mmol) and imidazole (10.3 g, 151 mmol) were added at room temperature. The reaction mixture was stirred for 20 min and quenched with water at 0 °C and then extracted with Et_2O (three times). The organic layers were washed with brine and dried over $MgSO_4$ and then concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (AcOEt:hexane = 1:8) to yield the corresponding silyl ether (8.84 g, 95%) as a colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 3.52 (s, 2H), 3.51 (d, J = 5.3 Hz, 2H), 2.85 (t, J = 5.3 Hz, 1H), 1.34 (dq, J = 14.4, 7.2 Hz, 2H), 1.26 (dq, J = 14.4, 7.2 Hz, 2H), 0.90 (s, 9H), 0.81 (t, J = 7.2 Hz, 6H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 69.7, 68.9, 40.9, 25.8, 22.6, 18.1, 7.3, −5.7; IR (neat, cm^{-1}): 3452, 1254, 1096, 837; MS m/z 189 $[M - t\mathrm{Bu}]^+$, 75 (100%); HRMS (EI) calcd. for $C_9H_{21}O_2Si$: 189.1311 $[M - t\mathrm{Bu}]^+$, found: 189.1294.

To a solution of the silyl ether (1.98 g, 8.03 mmol) and 1-Me-AZADO (13.3 mg, 0.0803 mmol) in CH_2Cl_2 (21.5 mL), sat. $NaHCO_3$ (13.0 mL) containing KBr (95.6 mg, 0.803 mmol) and n-Bu_4NBr (129.4 mg, 0.402 mmol) was added. To this cooled (0 °C, water-ice bath) and vigorously stirred reaction mixture, a premixed solution of aqueous NaOCl (9.64 mmol) and sat. $NaHCO_3$ (16.0 mL) was added dropwise over 7 min. The reaction was stirred for 8 min at 0 °C and then quenched with sat. $Na_2S_2O_3$ (5 mL). The aqueous layer was separated and extracted with Et_2O (twice). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was used in the subsequent reaction without further purification. To zinc powder (1.05 g, 16.1 mmol) in benzene (8 mL), a solution of the crude aldehyde and methyl 4-bromocrotonate (purity > 85%) (1.15 mL, 8.03 mmol) in benzene (3.5 mL) was added. Then, a small piece of iodine was added and the mixture was refluxed for 2 h.[43] After the solution was cooled with an ice bath, it was quenched with sat. NH_4Cl and extracted with Et_2O (three times). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude material was purified by flash silica gel column chromatography (AcOEt:hexane = 1:8) to give the corresponding siloxy ester (1.49 g, 54%) as a colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.15 (dt, J = 15.6, 7.1 Hz, 1H), 5.90 (dt, J = 15.6, 1.5 Hz, 1H), 3.72 (s, 3H), 3.68−3.55 (m, 2H), 3.61 (d, J = 10.2 Hz, 1H), 3.54 (d, J = 10.2 Hz, 1H), 2.45 (ddt, J = 14.6, 7.1, 1.5 Hz, 1H), 2.37−2.25 (m, 1H), 1.58 (dq, J = 14.6, 7.3 Hz, 1H), 1.57 (dq, J = 14.6, 7.3 Hz, 1H), 1.33 (dq, J = 14.6, 7.3 Hz, 1H), 1.17 (dq, J = 14.6, 7.3 Hz, 1H), 0.90 (s, 9H), 0.83 (t, J = 7.3 Hz, 3H), 0.79 (t, J = 7.3 Hz, 3H), 0.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 148.1, 122.3, 76.0, 68.0, 51.3, 42.5, 35.4, 25.8, 23.1, 22.8, 18.0, 7.44, 7.35, −5.79, −5.80; IR (neat, cm^{-1}): 3500, 1727, 1258, 1075, 838; MS m/z 345 $[M + H]^+$, 135 (100%); HRMS (EI) calcd. for $C_{18}H_{37}O_4Si$: 345.2456 $[M + H]^+$, found: 345.2450.

To a solution of the obtained siloxy ester (1.95 g, 5.66 mmol) in MeOH (28 mL), PPTS (142 mg, 0.566 mmol) was added at 50 °C, and the reaction mixture was stirred for 2.5 h. It was then cooled to room temperature, diluted with H_2O, and extracted with AcOEt (three times). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude material was purified by flash silica gel column chromatography (AcOEt:hexane = 1:4 to 1:2) to give diol **14f** (1.02 g, 78%) as a colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.08 (ddd, J = 15.8, 7.8, 6.8 Hz, 1H), 5.95 (d, J = 15.8 Hz, 1H), 3.79−3.69 (m, 1H), 3.74 (s, 3H), 3.69 (dd, J = 11.1, 3.9 Hz, 1H), 3.58 (dd, J = 11.1, 5.3 Hz, 1H), 2.66 (d, J = 5.8 Hz, 1H), 2.51−2.32 (m, 3H), 1.62 (dq, J = 14.6, 7.3 Hz, 1H), 1.60 (dq, J = 14.6, 7.3 Hz, 1H), 1.37 (dq, J = 14.6, 7.3 Hz, 1H), 1.12 (dq, J = 14.6, 7.3 Hz, 1H), 0.87 (t, J = 7.3 Hz, 3H), 0.83 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 147.3, 123.1, 76.3, 67.1, 51.5, 42.6, 34.9, 23.1, 22.7, 7.41, 7.37; IR (neat, cm^{-1}): 3384, 1724, 1271; MS m/z 231 $[M + H]^+$, 100 (100%); HRMS (EI) calcd. for $C_{12}H_{23}O_4$: 231.1591 $[M + H]^+$, found: 231.1582.

*Methyl (E)-6-Ethyl-6-formyl-5-hydroxyoct-2-enoate (**15f**).* Colorless oil (45.6 mg, 90%); ^1H NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H), 7.03 (dt, J = 14.4, 7.2 Hz, 1H), 5.94 (d, J = 14.4 Hz, 1H), 3.98 (ddd, J = 10.4, 4.8, 2.4 Hz, 1H), 3.74 (s, 3H), 2.44−2.21 (m, 2H), 2.29 (d, J = 4.8 Hz, 1H), 1.80 (dq, J = 14.8, 7.4 Hz, 1H), 1.78 (dq, J = 14.8, 7.4 Hz, 1H), 1.70 (dq, J = 14.8, 7.4 Hz, 1H), 1.58 (dq, J = 14.8, 7.4 Hz, 1H), 0.94 (t, J = 7.4 Hz, 3H), 0.87 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.2, 166.7, 146.2, 123.3, 72.0, 55.4, 51.5, 34.6, 23.0, 22.0, 8.27, 7.97; IR (neat, cm^{-1}): 3500, 1722, 1658, 1275; MS m/z 229 $[M + H]^+$, 100 (100%); HRMS (EI) calcd. for $C_{12}H_{21}O_4$: 229.1434 $[M + H]^+$, found: 229.1426.

*Dimethyl (E)-6,6-Diethyl-5-hydroxyhept-2-enedioate (**16f′**).* Colorless oil (30.1 mg, 93%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.06 (dt, J = 15.5, 7.2 Hz 1H), 5.92 (d, J = 15.5 Hz, 1H), 3.87 (ddd, J = 10.1, 7.2, 2.4 Hz, 1H), 3.73 (s, 6H), 2.98 (d, J = 7.2 Hz, 1H), 2.43 (dd, J = 14.4, 7.2 Hz, 1H), 2.28−2.17 (m, 1H), 1.83 (dq, J = 14.4, 7.2 Hz, 1H), 1.764 (q, J = 7.7 Hz, 1H), 1.758 (q, J = 7.7 Hz, 1H), 1.56 (dq,

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J = 14.4, 7.2 Hz, 1H), 0.89 (t, J = 7.2 Hz, 3H), 0.84 (t, J = 7.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 166.7, 146.5, 122.9, 72.9, 53.6, 51.7, 51.4, 34.9, 25.6, 24.0, 8.7, 8.6; IR (neat, cm^{-1}): 3517, 1725, 1225; MS m/z 259 $[M + H]^+$, 130 (100%); HRMS (EI) calcd. for $C_{13}H_{23}O_5$: 259.1540 $[M + H]^+$, found: 259.1547.

2,2-Dimethylnon-6-yne-1,3-diol (**14g**). To a solution of 2,2-dimethylpropane-1,3-diol (5.00 g, 48.0 mmol) and TBSCl (3.62 g, 24.0 mmol) in THF (40 mL), DIPEA (8.36 mL, 48.0 mmol) was added dropwise at 0 °C over 2 h, and the reaction mixture was stirred at room temperature for 12 h. After the reaction mixture was concentrated under reduced pressure, CH_2Cl_2 was added and the solution was washed with sat. NH_4Cl. Then, the organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (AcOEt:hexane = 1:16) to yield the corresponding silyl ether (4.34 g, 41%) as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.46 (d, J = 5.8 Hz, 2H), 3.46 (s, 2H), 2.81 (t, J = 5.8 Hz, 1H), 0.90 (s, 9H), 0.89 (s, 6H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 72.6, 72.1, 36.4, 25.8, 21.4, 18.1, −5.7; IR (neat, cm^{-1}): 3391, 1255, 1097, 837; MS m/z 219 $[M + H]^+$, 75 (100%); HRMS (EI) calcd. for $C_{11}H_{27}O_2Si$: 219.1780 $[M + H]^+$, found: 219.1772.

To a solution of the silyl ether (1.35 g, 6.18 mmol) and DMN-AZADO (20.5 mg, 0.124 mmol) in CH_2Cl_2 (16.5 mL), sat. $NaHCO_3$ (10.0 mL) containing KBr (73.5 mg, 0.618 mmol) was added. To this cooled (0 °C, water-ice bath) and vigorously stirred reaction mixture, a premixed solution of aqueous NaOCl (6.80 mmol) and sat. $NaHCO_3$ (12.0 mL) was added dropwise. After stirring at 0 °C for 25 min, the reaction mixture was quenched with sat. $Na_2S_2O_3$. The aqueous layer was separated and extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was used in the subsequent reaction without further purification. To magnesium turnings (174 mg, 7.15 mmol) in THF (2.0 mL), a small piece of iodine was added. After the mixture was stirred for 15 min, 1-bromo-3-hexyne (960 mg, 5.96 mmol) in THF (3.0 mL) was added. The reaction mixture was refluxed for 30 min and cooled to −40 °C, and then the aldehyde in THF (1.0 mL) was added dropwise. After stirring for 1 h, the reaction mixture was quenched with sat. NH_4Cl and extracted with Et_2O (twice). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude material was purified by flash silica gel column chromatography (AcOEt:hexane = 1:30) to give the corresponding alkyne (384 mg, 22%) as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (br s, 2H), 3.52 (d, J = 9.7 Hz, 1H), 3.45 (d, J = 9.7 Hz, 1H), 2.41 (dddt, J = 16.4, 7.2, 4.8, 2.4 Hz, 1H), 2.25 (tt, J = 7.7, 2.4 Hz, 1H), 2.16 (qt, J = 7.5, 2.4 Hz, 2H), 1.70−1.60 (m, 1H), 1.56−1.44 (m, 1H), 1.12 (t, J = 7.5 Hz, 3H), 0.90 (s, 9H), 0.87 (s, 3H), 0.86 (s, 3H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 81.7, 79.5, 77.9, 73.1, 38.2, 31.6, 25.8, 22.4, 19.1, 18.1, 15.9, 14.4, 12.4, −5.70, −5.71; IR (neat, cm^{-1}): 3502, 1254, 1088, 838; MS m/z 298 $[M]^+$, 75 (100%); HRMS (EI) calcd. for $C_{17}H_{34}O_2Si$: 298.2328 $[M]^+$, found: 298.2336.

To a solution of the alkyne (479 mg, 1.60 mmol) in THF (16 mL), TBAF (1.0 M in THF) (2.4 mL, 2.4 mmol) was added at room temperature. The reaction mixture was stirred for 30 min and diluted with AcOEt, washed with sat. NH_4Cl, and extracted with AcOEt (three times). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude material was purified by flash silica gel column chromatography (AcOEt:hexane = 1:4 to 1:2) to give diol **14g** (286 mg, 97%) as a pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 (d, J = 10.6 Hz, 1H), 3.57 (d, J = 10.6 Hz, 1H), 3.47 (d, J = 10.6 Hz, 1H), 3.18 (s, 1H), 3.07 (s, 1H), 2.43−2.24 (m, 2H), 2.17 (dt, J = 14.7, 2.4 Hz, 1H), 2.16 (dt, J = 14.7, 2.4 Hz, 1H), 1.76−1.65 (m, 1H), 1.62−1.48 (m, 1H), 1.12 (t, J = 7.6 Hz, 3H), 0.91 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 82.8, 79.1, 79.0, 72.3, 38.3, 31.0, 22.5, 18.8, 16.2, 14.2, 12.3; IR (neat, cm^{-1}): 3357, 1040; HRMS (ESI) calcd. for $C_{11}H_{20}O_2Na$: 207.1356 $[M + Na]^+$, found: 207.1363.

3-Hydroxy-2,2-dimethylnon-6-ynal (**15g**). Pale yellow oil (30.3 mg, 94%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 3.89 (d, J = 10.1 Hz, 1H), 2.51 (s, 1H), 2.43−2.27 (m, 2H), 2.17 (dt, J = 14.9, 2.4 Hz, 1H), 2.15 (dt, J = 14.9, 2.4 Hz, 1H), 1.64 (dtd, J = 14.0, 7.2, 1.9 Hz, 1H), 1.59−1.48 (m, 1H), 1.12 (t, J = 7.7 Hz, 3H), 1.10 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.5, 82.9, 78.6, 74.3, 50.3, 30.5, 18.9, 16.4, 16.0, 14.2, 12.4; IR (neat, cm^{-1}): 3508, 1724, 1063; MS m/z 167 $[M - Me]^+$, 72 (100%); HRMS (EI) calcd. for $C_{10}H_{15}O_2$: 167.1072 $[M - Me]^+$, found: 167.1081.

Methyl 3-Hydroxy-2,2-dimethylnon-6-ynoate (**16g′**). Pale yellow oil (36.0 mg, 98%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (ddd, J = 10.5, 6.2, 1.9 Hz, 1H), 3.71 (s, 3H), 2.61 (d, J = 6.2 Hz, 1H), 2.45−2.23 (m, 2H), 2.17 (dt, J = 15.0, 2.4 Hz, 1H), 2.15 (dt, J = 15.0, 2.4 Hz, 1H), 1.66 (dtd, J = 13.5, 5.8, 1.9 Hz, 1H), 1.53−1.41 (m, 1H), 1.20 (s, 3H), 1.18 (s, 3H), 1.11 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 82.4, 78.9, 75.8, 51.9, 47.0, 31.2, 22.3, 20.3, 16.1, 14.3, 12.4; IR (neat, cm^{-1}): 3509, 1726, 1134; MS m/z 212 $[M]^+$, 102 (100%); HRMS (EI) calcd. for $C_{12}H_{20}O_3$: 212.1412 $[M]^+$, found: 212.1415.

Glycyrrhetol (**14h**).[30] White solid (235 mg, 79%); $[\alpha]_D^{25}$ +110.3 (c 0.55, $CHCl_3$); mp 254−255 °C (Acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.59 (s, 1H), 3.55 (d, J = 10.6 Hz, 1H), 3.46 (d, J = 10.6 Hz, 1H), 3.22 (dd, J = 10.6, 5.3 Hz, 1H), 2.78 (dt, J = 13.6, 3.4 Hz, 1H), 2.34 (s, 1H), 2.14−2.02 (m, 2H), 1.82 (td, J = 13.5, 4.4 Hz, 1H), 1.72−1.53 (m, 7H), 1.53−1.24 (m, 7H), 1.38 (s, 3H), 1.24−1.10 (m, 1H), 1.131 (s, 3H), 1.126 (s, 3H), 1.10−0.88 (m, 2H), 1.00 (s, 3H), 0.92 (s, 3H), 0.86 (s, 3H), 0.80 (s, 3H), 0.70 (d, 12.0 Hz, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.2, 169.8, 128.3, 78.7, 66.2, 61.7, 54.9, 47.0, 45.4, 43.4, 40.3, 39.1, 37.1, 35.9, 35.4, 32.7, 32.3, 29.4, 28.5, 28.1, 27.3, 27.2, 26.7, 26.4, 23.4, 18.7, 17.5, 16.3, 15.5; IR (neat, cm^{-1}): 3398, 1650, 732; MS m/z 456 $[M]^+$, 289 (100%); HRMS (EI) calcd. for $C_{30}H_{48}O_3$: 456.3604 $[M]^+$, found: 456.3606.

Glycyrrhetaldehyde (**15h**).[44] White foam (42.8 mg, 99%); $[\alpha]_D^{26}$ +140.8 (c 0.51, $CHCl_3$); mp 246−247 °C ($CHCl_3$-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.42 (s, 1H), 5.66 (s, 1H), 3.23 (dd, J = 10.6, 5.3 Hz, 1H), 2.79 (dt, J = 13.6, 3.4 Hz, 1H), 2.34 (s, 1H), 2.14−1.96 (m, 2H), 1.96−1.77 (m, 3H), 1.77−1.52 (m, 6H), 1.52−1.34 (m, 7H), 1.34−1.09 (m, 8H), 1.09−0.90 (m, 8H), 0.81 (s, 3H), 0.80 (s, 3H), 0.70 (d, J = 10.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.6, 200.0, 168.5, 128.6, 78.7, 61.8, 54.9, 47.6, 46.8, 45.4, 43.2, 39.13, 39.11, 38.4, 37.1, 32.7, 31.9, 28.5, 28.3, 28.1, 27.3, 26.4, 26.1, 24.0, 23.7, 18.7, 17.5, 16.3, 15.5; IR (neat, cm^{-1}): 3461, 1728, 1655, 755; MS m/z 454 $[M]^+$, 287 (100%); HRMS (EI) calcd. for $C_{30}H_{46}O_3$: 454.3447 $[M]^+$, found: 454.3436.

Erythrodiol (**14i**).[31] White solid (373 mg, 48%); $[\alpha]_D^{25}$ +76.3 (c 0.68, $CHCl_3$); mp 227−228 °C ($CHCl_3$-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.20 (t, J = 3.4 Hz, 1H), 3.56 (d, J = 11.1 Hz, 1H), 3.22 (d, J = 10.6 Hz, 2H), 1.99 (dd, J = 13.3, 4.2 Hz, 1H), 1.95−1.84 (m, 3H), 1.80−1.50 (m, 10H), 1.50−1.13 (m, 10H), 1.12−0.70 (m, 22H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2, 122.4, 79.0, 69.7, 55.2, 47.6, 46.5, 42.3, 41.7, 39.8, 38.8, 38.6, 36.9, 34.1, 33.2, 32.6, 31.0, 30.9, 28.1, 27.2, 25.9, 25.5, 23.57, 23.55, 23.51, 22.0, 18.3, 16.7, 15.6, 15.5; IR (neat, cm^{-1}): 3353, 1043, 1003; MS m/z 442 $[M]^+$, 203 (100%); HRMS (EI) calcd. for $C_{30}H_{50}O_2$: 442.3811 $[M]^+$, found: 442.3815.

Oleanolaldehyde (**15i**).[45] White solid (41.7 mg, 95%); $[\alpha]_D^{22}$ +68.7 (c 0.41, $CHCl_3$); mp 184−185 °C ($CHCl_3$-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.40 (s, 1H), 5,34 (t, J = 3.5 Hz, 1H), 3.21 (dd, J = 11.2, 4.4 Hz, 1H), 2.63 (dd, J = 13.7, 4.4 Hz, 1H), 1.98 (td, J = 13.6, 3.9 Hz, 1H), 1.89 (t, J = 3.9 Hz, 1H), 1.87 (m, 1H), 1.80−0.60 (m, 41H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.5, 142.9, 123.2, 78.9, 55.2, 49.1, 47.5, 45.6, 41.7, 40.4, 39.5, 38,7, 38.4, 37.0, 33.1, 33.0, 32.7, 30.6, 28.1, 27.7, 27.1, 26.7, 25.5, 23.40, 23.38, 22.1, 18.3, 17.0, 15.6, 15.3; IR (neat, cm^{-1}): 3509, 1712, 753; MS m/z 440 $[M]^+$, 203 (100%); HRMS (EI) calcd. for $C_{30}H_{48}O_2$: 440.3654 $[M]^+$, found: 440.3649.

(1R,3aR,4S,6S,7R,7aR)-1-((tert-Butyldimethylsilyl)oxy)-7-(hydroxymethyl)-6-methyloctahydro-3a,6-ethanoinden-4-ol (**14j**). To a solution of ethyl (1*R*,3a*R*,6*S*,7*R*,7a*R*)-1-((*tert*-butyldimethylsilyl)-oxy)-6-methyl-4-oxooctahydro-3a,6-ethanoindene-7-carboxylate[18] (300 mg, 0.788 mmol) in MeOH (0.8 mL) and THF (8 mL), $LiBH_4$ (3.0 M in THF, 2.6 mL, 7.9 mmol) was added dropwise at 0 °C, and then the reaction mixture was stirred at 50 °C for 13 h. After cooling to 0 °C, the solution was quenched with sat. NH_4Cl and extracted with AcOEt (three times). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was

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purified by flash silica gel column chromatography (AcOEt:hexane = 1:8 to 1:4) to yield diol **14j** (180 mg, 67%) as a white solid; $[\alpha]_D^{24}$ +12.9 (*c* 0.60, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 4.96 (d, *J* = 11.1 Hz, 1H), 4.34 (dd, *J* = 5.6, 5.6 Hz, 1H), 3.80 (dd, *J* = 10.5, 5.6 Hz, 1H), 3.53 (dd, *J* = 10.5, 7.2 Hz, 1H), 3.49 (ddd, *J* = 11.1, 9.8, 2.2 Hz, 1H), 2.12−2.04 (m, 1H), 2.01−1.94 (m, 1H), 1.87 (dd, *J* = 14.1, 9.8 Hz, 1H), 1.82−1.73 (m, 2H), 1.68−1.60 (m, 1H), 1.60−1.52 (m, 2H), 1.35−1.14 (m, 3H), 1.28 (d, *J* = 14.1 Hz, 1H), 1.09−1.02 (m, 1H), 0.93 (s, 9H), 0.88 (s, 3H), 0.13 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 74.6, 72.9, 64.4, 53.0, 50.7, 45.0, 42.9, 36.1, 34.7, 32.8, 31.3, 29.2, 25.8, 24.7, 18.0, −4.7, −4.9; IR (neat, cm^{-1}): 3408, 3298, 991; MS *m*/*z* 283 $[M - t\text{Bu}]^+$, 191 (100%); HRMS (EI) calcd. for $C_{15}H_{27}O_3Si$: 283.1730 $[M - t\text{Bu}]^+$, found: 283.1733.

(1R,3aR,4S,6S,7R,7aR)-1-((tert-Butyldimethylsilyl)oxy)-4-hydroxy-6-methyloctahydro-3a,6-ethanoindene-7-carbaldehyde (**15j**). Pale yellow oil (25.2 mg, 84%); $[\alpha]_D^{25}$ +60.7 (*c* 1.10, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 9.87 (d, *J* = 2.4 Hz, 1H), 4.88 (d, *J* = 11.6 Hz, 1H), 4.16 (t, *J* = 5.8 Hz, 1H), 3.60−3.47 (m, 1H), 2.50 (d, *J* = 9.7 Hz, 1H), 2.27−2.07 (m, 2H), 2.07−1.86 (m, 2H), 1.86−1.74 (m, 1H), 1.64−1.48 (m, 2H), 1.48−1.22 (m, 3H), 1.22−1.10 (m, 1H), 1.10 (s, 3H), 0.92 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.6, 73.2, 72.5, 54.5, 50.2, 46.6, 44.3, 36.1, 34.6, 34.0, 31.2, 29.9, 25.7, 24.7, 18.0, −4.9, −5.1; IR (neat, cm^{-1}): 3410, 1718, 1255; MS *m*/*z* 281 $[M - t\text{Bu}]^+$, 263 (100%); HRMS (EI) calcd. for $C_{15}H_{25}O_3Si$: 281.1573 $[M - t\text{Bu}]^+$, found: 281.1576.

(1R,3aR,4S,6S,7R,7aR)-1-((tert-Butyldimethylsilyl)oxy)-4-hydroxy-6-methyloctahydro-3a,6-ethanoindene-7-carboxylic Acid (**16j**). White solid (29.2 mg, 92%); $[\alpha]_D^{21}$ +16.5 (*c* 0.57, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.96 (d, *J* = 11.2 Hz, 1H), 4.18 (dd, *J* = 5.2, 5.2 Hz, 1H), 3.61−3.51 (m, 1H), 2.58 (d, *J* = 10.2 Hz, 1H), 2.19 (dd, *J* = 9.8, 5.4 Hz, 1H), 2.15−1.87 (m, 3H), 1.87−1.73 (m, 1H), 1.65−1.52 (m, 2H), 1.52−1.40 (m, 1H), 1.40−1.22 (m, 2H), 1.12−1.01 (m, 1H), 0.96 (s, 3H), 0.93 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.7, 73.2, 72.6, 50.6, 49.4, 47.4, 44.2, 35.8, 34.1, 33.9, 30.9, 28.6, 25.7, 24.7, 18.0, −4.9, −5.3; IR (neat, cm^{-1}): 3284, 1718, 1259, 1178; MS *m*/*z* 353 $[M - H]^+$, 205 (100%); HRMS (EI) calcd. for $C_{19}H_{33}O_4Si$: 353.2148 $[M - H]^+$, found: 353.2144.

1-Hydroxymethyl-7,7-dimethylbicyclo[2.2.1]heptan-2-ol (**14k**).[32] White solid (524 mg, 74%); mp 159−160 °C ($CHCl_3$-hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 4.00 (dd, *J* = 8.1 Hz, 3.7 Hz, 1H), 3.93 (d, *J* = 11.1 Hz, 1H), 3.75 (d, *J* = 11.1 Hz, 1H), 2.76 (br s, 1H), 2.35 (br s, 1H), 1.88−1.65 (m, 4H), 1.56−1.43 (m, 1H), 1.19 (s, 3H), 1.17−1.00 (m, 2H), 0.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 78.6, 63.3, 52.9, 46.5, 46.0, 40.4, 30.0, 26.9, 21.0, 20.6; IR (neat, cm^{-1}): 3343, 1067; MS *m*/*z* 152 $[M - H_2O]^+$, 108 (100%); HRMS (EI) calcd. for $C_{10}H_{16}O$: 152.1201 $[M - H_2O]^+$, found: 152.1203.

Isopropyl 2,3-Dideoxy-α-D-glucopyranoside (**14l**). White solid (780 mg, 56%); mp 66−67 °C (Et_2O-hexane); $[\alpha]_D^{22}$ +159.7 (*c* 0.56, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.90 (d, *J* = 1.9 Hz, 1H), 3.89 (sept, *J* = 6.3 Hz, 1H), 3.85−3.74 (m, 2H), 3.68−3.56 (m, 2H), 2.65 (br s, 1H), 2.49 (br s, 1H), 1.91−1.79 (m, 2H), 1.87−1.67 (m, 2H), 1.21 (d, *J* = 6.3 Hz, 3H), 1.14 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 93.7, 72.8, 68.0, 67.3, 63.1, 29.7, 27.1, 23.3, 21.3; IR (neat, cm^{-1}): 3284, 1124; HRMS (ESI) calcd. for $C_9H_{18}O_4Na$: 213.1097 $[M + Na]^+$, found: 213.1105.

Methyl (Isopropyl 2,3-dideoxy-α-D-glucopyranoside)urinate (**16l′**). Colorless oil (51.2 mg, 95%); $[\alpha]_D^{29}$ +95.9 (*c* 2.56, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.01 (t, *J* = 2.4 Hz, 1H), 4.19 (d, *J* = 9.2 Hz, 1H), 3.95 (sept, *J* = 6.3 H, 1H), 3.83 (s, 3H), 3.84−3.74 (m, 1H), 3.15 (s, 1H), 1.98−1.81 (m, 2H), 1.81−1.72 (m, 2H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.15 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 94.3, 72.2, 68.7, 67.4, 52.4, 28.9, 25.8, 23.2, 21.3; IR (neat, cm^{-1}): 3476, 1750, 1126; MS *m*/*z* 175 $[M - i\text{Pr}]^+$, 129 (100%); HRMS (EI) calcd. for $C_7H_{11}O_5$:175.0607 $[M - i\text{Pr}]^+$, found: 175.0607.

Methyl 2,3-Di-O-benzyl-β-D-glucopyranoside (**14m**).[33] White solid (603 mg, 92%); $[\alpha]_D^{24}$ +20.3 (*c* 0.20, CH_3CN); mp 118−120 °C ($CHCl_3$-hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.26 (m, 10H), 4.97 (d, *J* = 11.2 Hz, 1H), 4.93 (d, *J* = 11.2 Hz, 1H), 4.71 (d, *J* = 11.2 Hz, 1H), 4.67 (d, *J* = 11.2 Hz, 1H), 4.37 (d, *J* = 7.3 Hz, 1H), 3.89 (ddd, *J* = 12.0, 6.3, 3.9 Hz, 1H), 3.77 (ddd, *J* = 12.0, 7.0, 5.3 Hz, 1H), 3.58 (s, 3H), 3.55 (td, *J* = 9.0, 2.4 Hz, 1H), 3.45 (t, *J* = 9.0 Hz, 1H), 3.39 (t, *J* = 7.3 Hz, 1H), 3.34 (ddd, *J* = 9.0, 5.3, 3.9 Hz, 1H), 2.24 (d, *J* = 2.4 Hz, 1H), 2.01 (dd, *J* = 7.0, 6.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 138.3, 128.6, 128.4, 128.1, 128.0, 127.9, 127.7, 105.0, 83.8, 82.0, 75.2, 74.8, 74.6, 70.4, 62.7, 57.3; IR (neat, cm^{-1}): 3420, 1061, 737, 698; MS *m*/*z* 283 $[M - Bn]^+$, 91 (100%); HRMS (EI) calcd. for $C_{14}H_{19}O_6$:283.1182 $[M - Bn]^+$, found: 283.1184.

Methyl (Methyl 2,3-Di-O-benzyl-β-D-glucopyranoside)urinate (**16m′**).[46] Colorless oil (42.3 mg, 94%); $[\alpha]_D^{29}$ −14.5 (*c* 2.05, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.25 (m, 10H), 4.90 (d, *J* = 11.2 Hz, 1H), 4.89 (d, *J* = 11.2 Hz, 1H), 4.80 (d, *J* = 11.2 Hz, 1H), 4.71 (d, *J* = 11.2 Hz, 1H), 4.37 (d, *J* = 8.3 Hz, 1H), 3.87−3.81 (m, 2H), 3.83 (s, 3H), 3.59 (s, 3H), 3.52 (dd, *J* = 8.3, 8.3 Hz, 1H), 3.44 (dd, *J* = 8.3, 8.3 Hz, 1H), 2.80 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 138.4, 138.3, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 105.0, 83.0, 81.1, 75.3, 74.8, 74.2, 71.7, 57.4, 52.7; IR (neat, cm^{-1}): 3490, 1749, 1069, 738, 698; HRMS (ESI) calcd. for $C_{22}H_{26}O_7Na$: 425.1571 $[M + Na]^+$, found: 425.1581.

Methyl 2-O-n-Butyl-α-D-ribofuranoside (**14n**). To a solution of methyl 3,5-di-*O*-benzyl-α-D-ribofuranoside[47] (1.59 g, 4.62 mmol) in DMF (12 mL), NaH (60% dispersion in mineral oil, 462 mg, 11.6 mmol) was added at 0 °C. After the reaction mixture was stirred for 10 min at 0 °C, *n*-butyl bromide (1.09 mL, 10.2 mmol) was added and the reaction mixture was stirred for 30 min at room temperature. It was then quenched with water at 0 °C. The solution was extracted with Et_2O (twice), and the organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (AcOEt:hexane = 1:4) to yield the corresponding ether (1.76 g, 95%) as a pale yellow oil; $[\alpha]_D^{25}$ +103 (*c* 0.280, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.21 (m, 10H), 4.97 (d, *J* = 4.4 Hz, 1H), 4.70 (d, *J* = 12.7 Hz, 1H), 4.59 (d, *J* = 12.7 Hz, 1H), 4.52 (d, *J* = 12.2 Hz, 1H), 4.46 (d, *J* = 12.2 Hz, 1H), 4.23 (ddd, *J* = 4.4, 3.9, 2.9 Hz, 1H), 3.84 (dd, *J* = 6.8, 2.9 Hz, 1H), 3.72 (dd, *J* = 6.8, 4.4 Hz, 1H), 3.58−3.42 (m, 2H), 3.46 (s, 3H), 3.44 (dd, *J* = 10.3, 3.9 Hz, 1H), 3.38 (dd, *J* = 10.3, 4.4 Hz, 1H), 1.73−1.58 (m, 2H), 1.48−1.31 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 138.0, 128.4, 128.21, 128.19, 127.7, 127.5, 102.4, 82.1, 79.5, 75.0, 73.5, 72.3, 70.8, 70.2, 55.4, 31.8, 19.2, 13.9; IR (neat, cm^{-1}): 1109, 1028, 736, 698; MS *m*/*z* 400 $[M]^+$, 219 (100%); HRMS (EI) calcd. for $C_{24}H_{32}O_5$:400.2250 $[M]^+$, found: 400.2250.

To a solution of 20% $Pd(OH)_2/C$ (wetted with 50% water, 170 mg) in MeOH (5 mL) and AcOEt (35 mL), ether (1.70 g, 4.24 mmol) was added. After the reaction flask was purged with H_2 three times, the reaction mixture was stirred at room temperature under a H_2 atmosphere for 50 min. The catalyst was removed by filtration through Celite. The filtrate was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (AcOEt:hexane = 1:1) to yield diol **14n** (730 mg, 78%) as a colorless oil; $[\alpha]_D^{28}$ +88.8 (*c* 1.04, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.98 (d, *J* = 3.9 Hz, 1H), 4.21−4.14 (m, 1H), 4.09 (dd, *J* = 6.3, 1.9 Hz, 1H), 3.81 (dd, *J* = 11.7, 2.9 Hz, 1H), 3.78 (dd, *J* = 6.3, 4.4 Hz, 1H), 3.70 (dd, *J* = 11.7, 2.9 Hz, 1H), 3.64 (dt, *J* = 9.2, 6.8 Hz, 1H), 3.57 (dt, *J* = 9.2, 6.8 Hz, 1H), 3.45 (s, 3H), 1.65 (q, *J* = 6.8 Hz, 1H), 1.63 (q, *J* = 6.8 Hz, 1H), 1.40 (sext, *J* = 7.3 Hz, 2H), 0.93 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 102.6, 86.4, 79.3, 70.7, 69.6, 62.9, 55.1, 31.7, 19.1, 13.8; IR (neat, cm^{-1}): 3375, 1033; HRMS (ESI) calcd. for $C_{10}H_{20}O_5Na$: 243.1203 $[M + Na]^+$, found: 243.1209.

Methyl (Methyl 2-O-n-Butyl-α-D-ribofuranoside)urinate (**16n′**). Colorless oil (38.8 mg, 83%); $[\alpha]_D^{28}$ +83.9 (*c* 1.13, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.11 (d, *J* = 4.4 Hz, 1H), 4.65 (d, *J* = 2.0 Hz, 1H), 4.29 (ddd, *J* = 8.8, 5.9, 2.0 Hz, 1H), 3.86 (dd, *J* = 5.9, 4.4 Hz, 1H), 3.79 (s, 3H), 3.63 (dt, *J* = 9.3, 6.8 Hz, 1H), 3.56 (dt, *J* = 9.3, 6.8 Hz, 1H), 3.48 (s, 3H), 3.21 (d, *J* = 8.8 Hz, 1H), 1.65 (q, *J* = 6.8 Hz, 1H), 1.63 (q, *J* = 6.8 Hz, 1H), 1.39 (sext, *J* = 7.3 Hz, 2H), 0.93 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 102.6, 83.7, 78.2, 71.8, 70.6, 55.5, 52.4, 31.6, 19.0, 13.7; IR (neat, cm^{-1}): 3528, 1753, 1055; MS *m*/*z* 247 $[M - H]^+$, 159 (100%); HRMS (EI) calcd. for $C_{11}H_{19}O_6$:247.1182 $[M - H]^+$, found: 247.1179.

*(R)-3-((2S,3S)-3-((tert-Butyldimethylsilyl)oxy)-4-((2R,4R,6S)-4-hydroxy-6-((R)-2-hydroxy-1-methoxyethyl)-3,3-dimethyltetrahydro-2H-pyran-2-yl)butan-2-yl)-5-methyl-6,8-bis((triisopropylsilyl)oxy)-isochroman-1-one (**14o**).* White solid (58.4 mg, 95%); $[\alpha]_D^{27}$ +58.3° (*c* 0.53, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 6.28 (s, 1H), 4.27−4.19 (m, 2H), 4.04 (d, *J* = 12.0 Hz, 1H), 3.83 (dt, *J* = 9.2, 4.8 Hz, 1H), 3.63−3.61 (m, 2H), 3.53 (s, 3H), 3.45 (ddd, *J* = 12.0, 6.0, 2.6 Hz, 1H), 3.37 (br s, 1H), 3.21 (d, *J* = 10.4 Hz, 1H), 2.96 (dd, *J* = 16.4, 2.0 Hz, 1H), 2.74 (dd, *J* = 16.8, 12.8 Hz, 1H), 2.08 (s, 3H), 2.02−1.91 (m, 3H), 1.77−1.65 (m, 2H), 1.48 (br s, 1H), 1.29 (sept, *J* = 7.2 Hz, 6H), 1.11−1.07 (m, 36H), 1.04 (s, 3H), 0.95 (s, 3H), 0.88 (s, 3H), 0.83 (s, 9H), 0.08 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 159.0, 157.7, 141.6, 118.1, 109.7, 109.5, 80.8, 79.4, 75.8, 72.5, 67.9, 62.2, 59.0, 39.8, 38.0, 34.5, 30.4, 29.1, 25.9, 25.8, 24.1, 18.0, 18.0, 17.9, 13.3, 13.1, 11.7, 8.6, −3.2, −4.7; IR (neat, cm^{-1}): 3440, 1705, 1172, 1085; HRMS (ESI) calcd. for $C_{48}H_{91}O_9Si_3$: 895.5965 $[M + H]^+$, found: 895.5941.

*(S)-2-((2S,4R,6R)-6-((2S,3S)-2-((tert-Butyldimethylsilyl)oxy)-3-((R)-5-methyl-1-oxo-6,8-bis((triisopropylsilyl)oxy)isochroman-3-yl)-butyl)-4-hydroxy-5,5-dimethyltetrahydro-2H-pyran-2-yl)-2-methoxyacetic Acid (**16o**).* White solid (14.4 mg, 81%); $[\alpha]_D^{28}$ +62.8° (*c* 0.96, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 6.29 (s, 1H), 4.45 (dd, *J* = 11.0, 3.8 Hz, 1H), 4.25 (dq, *J* = 13.0, 2.8 Hz, 1H) 4.19−4.14 (m, 1H), 3.77 (d, *J* = 8.4 Hz, 1H), 3.70 (dd, *J* = 5.6, 3.2 Hz, 1H), 3.46−3.42 (m, 1H), 3.42 (s, 3H), 2.97 (dd, *J* = 16.8, 13.2 Hz, 1H), 2.85 (dd, *J* = 16.6, 2.6 Hz, 1H), 2.42 (t, *J* = 11.2 Hz, 1H), 2.17 (t, *J* = 6.6 Hz, 1H), 2.07 (s, 3H), 2.00−1.94 (m, 1H), 1.87−1.84 (m, 1H), 1.55 (td, *J* = 10.8, 3.2 Hz, 1H), 1.30 (sept, *J* = 8.0 Hz, 6H), 1.34−1.26 (m, 1H), 1.13−1.08 (m, 36H), 1.03 (s, 3H), 0.97 (d, *J* = 7.2 Hz, 3H), 0.93 (s, 3H), 0.88 (s, 9H), 0.15 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.4, 166.2, 159.3, 157.8, 142.2, 118.1, 109.2, 109.2, 83.1, 79.8, 72.6, 68.1, 66.4, 58.2, 37.2, 36.9, 33.4, 31.7, 28.2, 26.1, 25.8, 18.0, 18.0, 18.0, 17.9, 13.2, 13.1, 11.7, 8.1, −3.1, −4.5; IR (neat, cm^{-1}): 3405, 1727, 1173, 1090; HRMS (ESI) calcd. for $C_{48}H_{89}O_{10}Si_3$: 909.5764 $[M + H]^+$, found: 909.5765.

*Dodecane-1,6-diol (**14p**).*[35] White solid (421 mg, 64%); mp 43−45 °C ($CHCl_3$-hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 3.63 (t, *J* = 6.5 Hz, 2H), 3.64−3.47 (m, 1H), 1.98 (br s, 1H), 1.77 (br s, 1H), 1.58 (quint, *J* = 6.5 Hz, 2H), 1.56−1.20 (m, 16H), 0.88 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 71.8, 62.7, 37.5, 37.3, 32.6, 31.8, 29.3, 25.7, 25.6, 25.3, 22.6, 14.0; IR (neat, cm^{-1}): 3317; HRMS (ESI) calcd. for $C_{12}H_{26}O_2Na$: 225.1825 $[M + Na]^+$, found: 225.1834.

*7-Hexyloxepan-2-one (**19p**).*[28c] Pale yellow oil (31.0 mg, 78%); ^1H NMR (400 MHz, $CDCl_3$) δ 4.23 (td, *J* = 7.8, 3.9 Hz, 1H), 2.78−2.48 (m, 2H), 2.06−1.81 (m, 3H), 1.81−1.40 (m, 6H), 1.40−1.18 (m, 7H), 0.88 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 80.5, 36.3, 34.9, 34.5, 31.6, 29.0, 28.2, 25.3, 23.0, 22.5, 14.0; IR (neat, cm^{-1}): 1730; MS *m*/*z* 199 $[M + H]^+$, 85 (100%); HRMS (EI) calcd. for $C_{12}H_{23}O_2$: 199.1698 $[M + H]^+$, found: 199.1688.

*1-((1S,3R)-3-(2-Hydroxyethyl)-2,2-dimethylcyclopropyl)propan-2-ol (**14q**).* A solution of (+)-3-carene (128 mg, 0.940 mmol) in pyridine (0.24 mL) and CH_2Cl_2 (5 mL) was cooled to −78 °C, and excess ozone was bubbled into the solution for 30 min. After argon gas was bubbled into the reaction mixture to purge the ozone, THF (5 mL) and $NaBH_4$ (533 mg, 14.1 mmol) were added portionwise. The reaction mixture was stirred at 0 °C for 2 h and then quenched with H_2O. The solution was extracted with CH_2Cl_2 (three times), and the organic layers were dried over $MgSO_4$ and then concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (AcOEt:hexane = 1:2 to 1:1) to yield diol **14q**[48] (97.5 mg, 60%) as a colorless oil (a mixture of two diastereomers); ^1H NMR (400 MHz, $CDCl_3$) δ 3.87 (sext, *J* = 6.0 Hz, 0.5H), 3.86 (sext, *J* = 6.0 Hz, 0.5H), 3.77−3.63 (m, 1H), 3.67 (t, *J* = 6.8 Hz, 1H), 2.13 (br s, 1H), 1.74 (br s, 1H), 1.59−1.44 (m, 1H), 1.52 (q, *J* = 6.8 Hz, 1H), 1.44−1.34 (m, 2H), 1.22 (d, *J* = 6.0 Hz, 1.5H), 1.21 (d, *J* = 6.0 Hz, 1.5H), 1.06 (s, 1.5H), 1.05 (s, 1.5H), 0.94 (s, 1.5H), 0.91 (s, 1.5H), 0.61−0.47 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 68.5, 67.6, 62.52, 62.47, 33.5, 33.4, 28.9, 27.6, 27.3, 23.3, 23.0, 22.6, 22.5, 22.1, 16.3, 15.9, 15.00, 14.96; IR (neat, cm^{-1}): 3316, 1057; MS *m*/*z* 172 $[M]^+$, 128 (100%); HRMS (EI) calcd. for $C_{10}H_{20}O_2$: 172.1463 $[M]^+$, found: 172.1446.

*(1R,7S)-5,8,8-Trimethyl-4-oxabicyclo[5.1.0]octan-3-one (**19q**).*[49] Colorless oil (32.7 mg, 75%); ^1H NMR (400 MHz, $CDCl_3$) δ 4.63 (dq, *J* = 10.1, 6.3 Hz, 0.5H), 4.14 (dqd, *J* = 12.0, 6.0, 3.0 Hz, 0.5H), 3.17 (dd, *J* = 15.5, 4.8 Hz, 0.5H), 2.97 (dd, *J* = 15.5, 4.1 Hz, 0.5H), 2.77 (dd, *J* = 14.5, 8.0 Hz, 0.5H), 2.42 (dd, *J* = 14.5, 10.1 Hz, 0.5H), 2.20−2.02 (m, 1H), 1.87 (dd, *J* = 15.5, 1.9 Hz, 0.5H), 1.80 (ddd, *J* = 15.9, 10.6, 5.3 Hz, 0.5H), 1.32 (d, *J* = 6.0 Hz, 1.5H), 1.31 (d, *J* = 6.0 Hz, 1.5H), 1.074 (s, 1.5H), 1.067 (s, 1.5H), 1.05 (s, 1.5H), 1.04 (s, 1.5H), 1.03−0.85 (m, 1H), 0.78−0.65 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 173.1, 76.9, 73.9, 33.0, 30.7, 30.6, 29.1, 29.0, 28.5, 22.1, 22.0, 21.7, 20.7, 19.9, 19.8, 18.7, 18.0, 14.8, 14.7; IR (neat, cm^{-1}): 1734; MS *m*/*z* 168 $[M]^+$, 81 (100%); HRMS (EI) calcd. for $C_{10}H_{16}O_2$: 168.1150 $[M]^+$, found: 168.1143.

■ ASSOCIATED CONTENT

Supporting Information

Numerical data of Figures 3−5, comparison of the catalytic efficiencies of *practical* DMN-AZADO and pure DMN-AZADO, and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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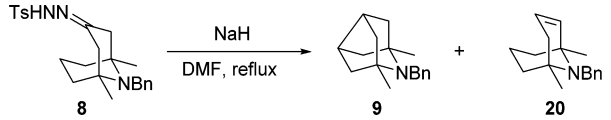
(18) The formal redox potential ($E^{o\prime}$) of DMN-AZADO (**2**) was determined as 144 mV by cyclic voltammetry (CV) measurement (working electrode: glassy carbon; reference electrode: Ag/Ag^{+}).[13g]
(19) In a small-scale preparation, the treatment of tosylhydrazone **8** with NaH in refluxing DMF gave *N*-Bn azanoradamantane **9** as a single product. However, in a gram-scale preparation, the treatment of tosylhydrazone **8** with NaH in refluxing DMF afforded *N*-Bn azanoradamantane **9** as a 7:1 to 8:1 inseparable mixture with azabicyclo[3.3.1]nonene **20** after purification by silica gel column chromatography.[17] Without further purification, *practical* DMN-AZADO (**2**) was prepared. Thus, the *practical* DMN-AZADO (**2**) contained the bicyclic radical derived from **20** in the gram-scale preparation. Comparison of the catalytic efficiencies of the *practical* DMN-AZADO (**2**) and pure DMN-AZADO showed no significant difference. In this study, we used the bicyclic-radical-containing *practical* DMN-AZADO (**2**). Details are provided in the Supporting Information.



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(21) The numerical data are given in the Supporting Information.
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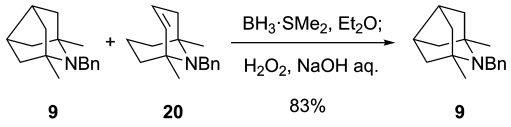
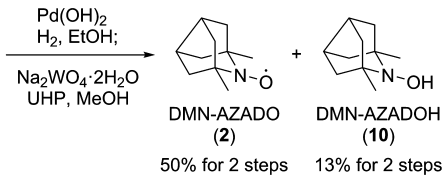
(38) Characterization data were obtained after purification.[39]
(39) Pure DMN-AZADO (**2**) was prepared by the following methods.





To a solution of a ca. 8:1 mixture of *N*-Bn 9-azanoradamantane **9** and *N*-Bn 9-azabicyclo[3.3.1]nonene **20** (497 mg, 2.06 mmol) in Et_2O (4.1 mL) at 0 °C, $BH_3·SMe_2$ (2.0 M in Et_2O, 2.1 mL, 4.2 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 1.5 h. After cooling to 0 °C, 2 N NaOH (5.2 mL) and H_2O_2 (0.69 mL) were added dropwise. After the reaction mixture was stirred for 3 h at room temperature, it was quenched with sat. NH_4Cl at 0 °C and extracted with Et_2O (three times). The organic layers were washed with brine, then dried over K_2CO_3, and then concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (AcOEt:hexane = 1:8 to 1:2) to recover *N*-benzyl-1,5-dimethyl-9-azanoradamantane (**9**) (411 mg, 83%) as a single compound. After the subsequent deprotection and oxidation, pure DMN-AZADO (142 mg, 50%) and DMN-AZADOH (38 mg, 13%) were provided.

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