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Two types of cross-coupling reactions between electron-rich and electron–deficient alkenes assisted by nucleophilic addition using an organic photoredox catalyst

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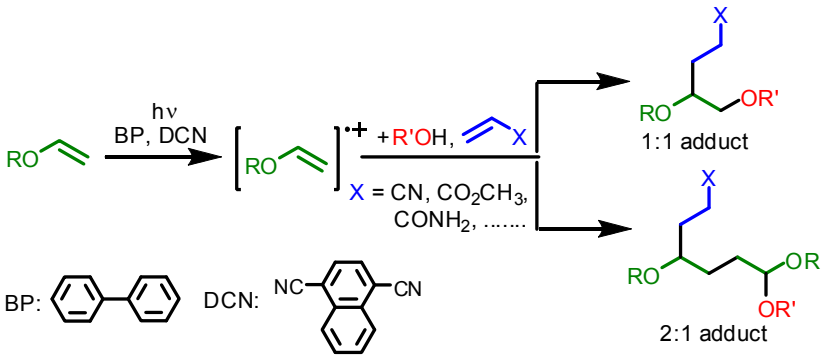


Abstract

Two types of photoreactions between electronically-differentiated donor and acceptor alkenes assisted by nucleophilic addition using an organic photoredox catalyst efficiently afforded 1:1 or 2:1 cross-coupling adducts. A variety of alkenes and alcohols were employed in the photoreaction. Control of the reaction pathway (i.e., the formation of the 1:1 or 2:1 adduct) was achieved by varying the concentration of the alcohol used. Detailed mechanistic studies

suggested that the organic photoredox catalyst acts as an effective electron mediator to promote the formation of the cross-coupling adducts.

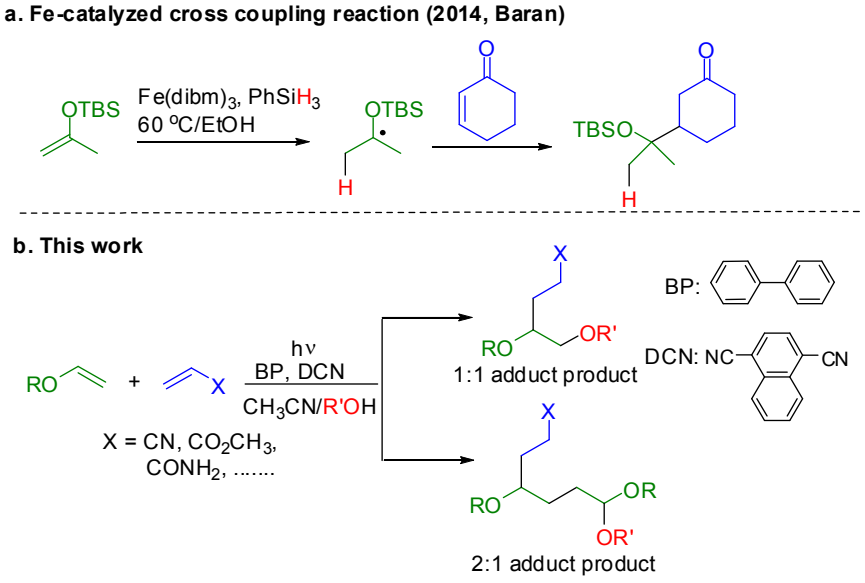
Introduction

Cross-coupling reactions between alkenes are increasingly attracting attention for use in the construction of molecular framework because the simple alkenes starting materials are commercially available, inexpensive, or readily prepared.[1] For example, an elegant Fe-catalyzed cross-coupling reaction between electronically-differentiated donor and acceptor alkenes with phenylsilane was reported by P. S. Baran (Scheme 1a).[2] This type of coupling is rare because copolymerization between the alkenes is a common occurrence. In this reaction, alkyl radical, which was generated from the electron-rich alkene by hydrofunctionalization using an Fe catalyst and silane at 60 °C, reacted with the electron-deficient alkene to afford coupling product after reduction of the adduct radical. This type of cross-coupling reaction has become a powerful and versatile tool for the transformation of alkenes to complex molecules,[3] and milder conditions and a more environmentally friendly method for the cross-coupling reaction, such as reaction without heating and metal, is desirable.

We have recently reported on the photoinduced decarboxylative radical addition of carboxylic acids to alkenes by organic photoredox catalysts such as a combination of phenanthrene (Phen)

and 1,4-dicyanobenzene (DCB), or biphenyl (BP) and 1,4-dicyanonaphthalene (DCN) through photoinduced electron transfer (PET).[4] When assessing the influence of the nature of the alkene on the photoinduced decarboxylative radical addition, we observed that the photoinduced cross-coupling reaction assisted by nucleophilic addition between electron-rich and electron–deficient alkenes took place efficiently via PET[5,6] (Scheme 1b). The study described below has demonstrated the new strategy for cross-coupling between electronically-differentiated alkenes employing organic photoredox catalysts under mild conditions, and the successful control of the formation of two types of cross-coupling products (1:1 or 2:1 adducts) by varying the concentration of nucleophile (R'OH).

Scheme 1. Cross-coupling reactions between electron-rich and electron-deficient alkenes

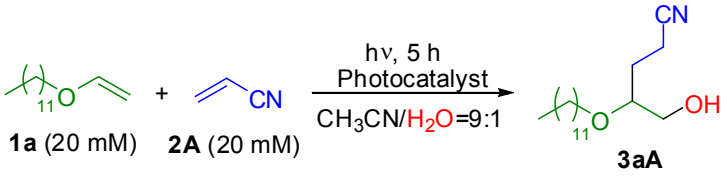


Results and Discussion

Optimization of the photoinduced cross-coupling reaction between dodecyl vinyl ether **1a** as an electron-rich alkene and acrylonitrile **2A** as an electron-deficient alkene using organic photoredox catalysts was carried out (Table 1). Irradiation of an aqueous acetonitrile solution (CH_3CN/H_2O=9:1) containing **1a** (20 mM), **2A** (20 mM), BP (5 mM, 25 mol%), and DCN (5 mM, 25 mol%) in Pyrex vessel (15 x 180 mm) under argon atmosphere using a 100 W high-pressure mercury lamp (>280 nm) for 5 h at room temperature led to the formation of cross-coupling product **3aA** as a racemic mixture in 72% yield (Entry 1, Table 1). Photoreaction using lower concentrations of BP (1 mM, 5 mol%) and DCN (1 mM, 5 mol%) and employing longer irradiation times (24 h) were found to produce **3aA** in the similar yield (66%, Entry 2). In the absence of light, water, DCN, and both BP and DCN, **3aA** was not generated (data not shown). However, with light, water, and DCN but in the absence of BP, a 2% yield of **3aA** was observed (Entry 3). The use of Phen and DCB or Phen and DCN instead of BP and DCN decreased the yield of **3aA** (Entries 4 and 5), because the photoreaction side-products such as [2+2] cycloadducts between Phen and **1a** were obtained. The blue LED (18 W, 405 nm) derived visible light-induced reaction of **1a** (20 mM) and **2A** (20 mM) using BP (2 mM) and 9,10-dicyanoanthracene (DCA, 2 mM) for 24 h also led to decreased yield of **3aA** (35%, Entry 6). The use of aqueous DMF or DMSO (DMF/H_2O or $DMSO/H_2O$=9:1) as the solvent in the

place of aqueous acetonitrile failed to produce the adduct **3aA**, and the use of aqueous acetone (acetone/H_2O=9:1) resulted in a reduced yield of **3aA** (Entry 7). Increasing the proportion of water in the aqueous acetonitrile gradually decreased the yield of **3aA** (Entries 8 and 9, CH_3CN/H_2O=7:3 and 5:5) due to the low solubilities of **1a** and DCN in water. Thus, the highest yield of **3aA** from the photoreaction of **1a** and **2A** was observed using BP and DCN as the organic photoredox catalyst and aqueous acetonitrile (CH_3CN/H_2O=9:1) as the solvent.

Table 1. Photoinduced cross-coupling reaction between **1a** and **2A** assisted by water addition.



1a (20 mM) **2A** (20 mM) **3aA**

Entry	Photocatalyst	Yield of **3aA**/%
1	BP (5 mM), DCN (5 mM)	72
2[a]	BP (1 mM), DCN (1 mM)	66
3	DCN (5 mM)	2
4	Phen (5 mM), DCB (5 mM)	45
5	Phen (5 mM), DCN (5 mM)	46
6[b]	BP (2 mM), DCA (2 mM)	35
7[c]	BP (5 mM), DCN (5 mM)	58
8[d]	BP (5 mM), DCN (5 mM)	66
9[e]	BP (5 mM), DCN (5 mM)	12

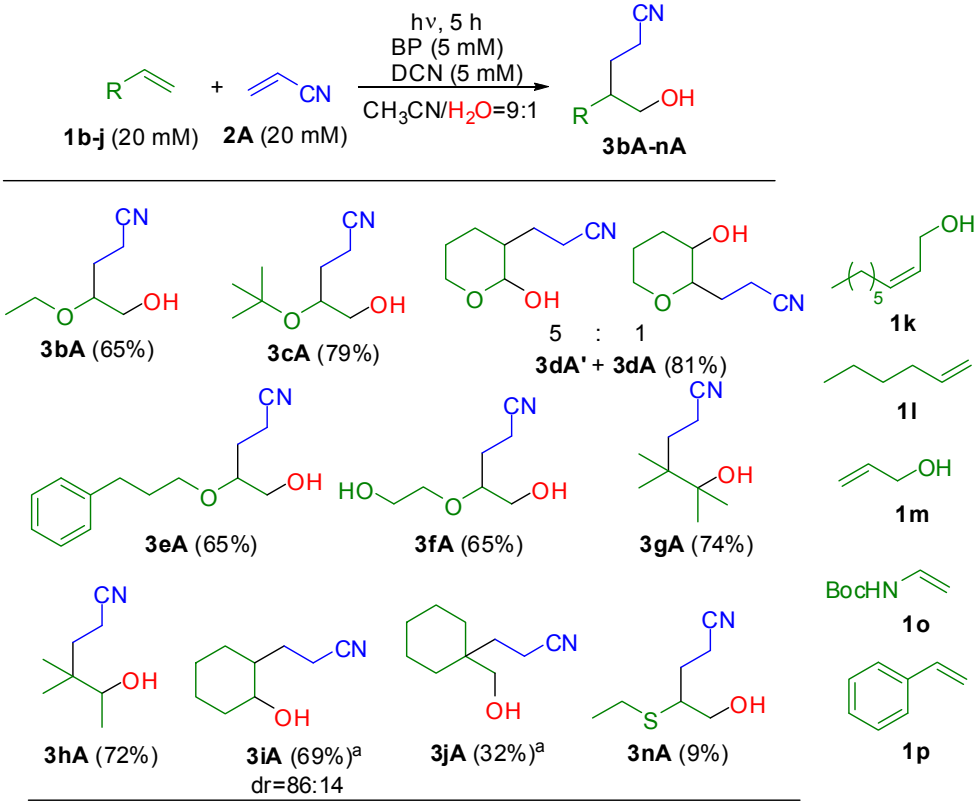
[a]Irradiation time was 24 h. [b]Visible blue LED (405 nm) was used as light source, and irradiation time was 24 h. [c]Acetone/H_2O=9:1. [d]CH_3CN/H_2O=7:3. [e]CH_3CN/H_2O=5:5.

The scope and limitations of the electron-rich alkenes were then explored (Table 2). A variety of vinyl ethers such as ethyl vinyl ether **1b**, *t*-butyl vinyl ether **1c**, 3,4-dihydro-2*H*-pyran **1d**,

3-phenylpropyl vinyl ether **1e**, and 2-hydroxyethyl vinyl ether **1f** reacted with **2A** under the optimized photochemical conditions, providing cross-coupling adducts **3bA–fA** as racemic and diastereomeric mixtures in good yields. In the case of **1d**, the regioisomers (**3dA'** and **3dA**) were observed, as was the case in a similar photoinduced nucleophilic addition.[6] The observation of good yield of **3fA** shows that a hydroxy group in **1** is tolerated in this photoreaction. In comparison with the products from **1a**,**b**,**e**, and **f**, the product **3cA** from *t*-butyl vinyl ether **1c** was obtained in a slightly higher yield because a slightly more electron-rich radical was generated (see intermediate **16** in the plausible mechanism described in Scheme 4). The tetra-, and tri-substituted alkenes **1g**,**h** provided good yields of **3gA**,**hA**, respectively, and the photoreaction of cyclohexene **1i** provided a similar yield of **3iA**, even though an increased concentration of DCN (10 mM) was required. In constrast, the photoreaction of methylenecyclohexane **1j** resulted in significantly decreased product yield, even with an increased concentration of DCN (10 mM). The use of di-substituted alkene ((*Z*)-2-nonen-1-ol) **1k**, the less-substituted alkene (1-hexene) **1l**, and allyl alcohol **1m** resulted in no reaction, indicating the photoreaction is strongly dependent on the oxidation potential of the electron-rich alkenes (oxidation potential vs. SCE in acetonitrile: **1b** +1.99 V, **1g** +1.56 V, **1h** +2.08 V, **1i** +2.25 V, **1j** +2.62 V, **1l** +2.85 V)[7]. When ethyl vinyl thioether **1n** was subjected to the photoreaction, cross-coupling product **3nA** was obtained in a significantly lower yield, because

the highly reactive thioether **3nA** under the photochemical conditions gave the secondary photoproduct. The use of *t*-butyl vinylcarbamate **1o** and styrene **1p** as the electron-rich alkene resulted in a complex mixture. Thus, a variety of vinyl ethers and alkyl substituted alkenes can be employed as the electron-rich alkene for the photoinduced cross-coupling, with the exception of those having a high oxidation potential or having high reactivity under the photochemical conditions.

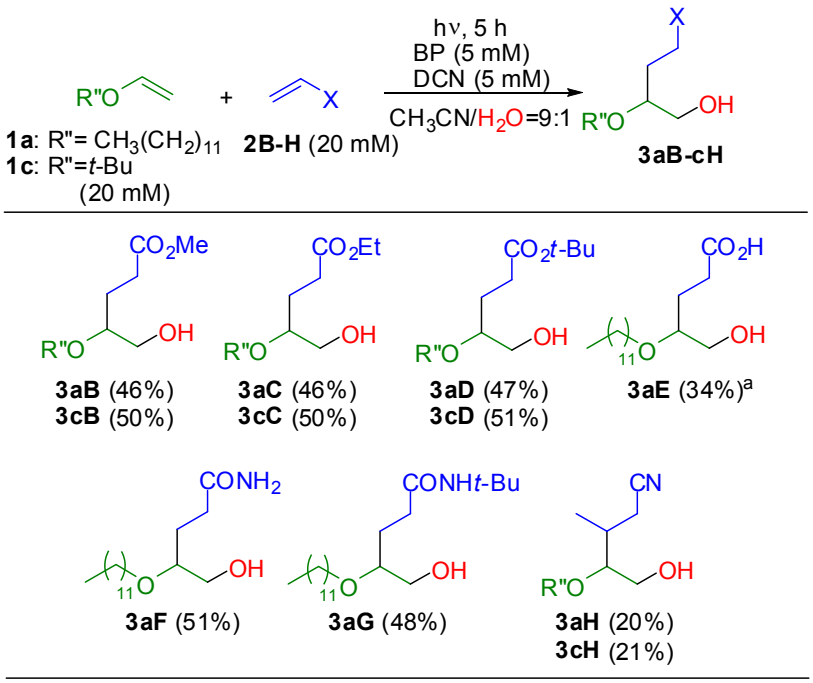
Table 2. Scope of electron-rich alkene **1** in the photoreaction with **2A**.



[a]BP (5 mM) and DCN (10 mM) were used as the photocatalyst.

To determine the scope of the electron-deficient alkene, we explored the reactions of **1a**,**c** with methyl acrylate **2B**, ethyl acrylate **2C**, *t*-butyl acrylate **2D**, acrylic acid **2E**, acrylamide **2F**, *N*-*t*-butyl acrylamide **2G**, and crotononitrile **2H** under the same photochemical conditions (Table 3). The use of the relatively poorly electron-deficient alkenes **2B–H** in the place of **2A** led to lower yields of products **3aB–cH** along with the formation of polymeric materials as previously reported by us.[8] In the case of **2E**, a secondary photoreaction (photoinduced decarboxylation) of the photoproduct **3aE** took place to decrease the yield of **3aE**, and the yield was improved by carrying out the reaction for a shorter time (4 h). Similar to the results seen in Table 2, slightly increased yields of **3cB–cD** were observed using **1c** as the electron-rich alkene in comparison with those using **1a**. The combined results show that a variety of electron-rich and electron-deficient alkenes can efficiently participate in the formation of cross-coupling product **3** using the organic photoredox catalyst.

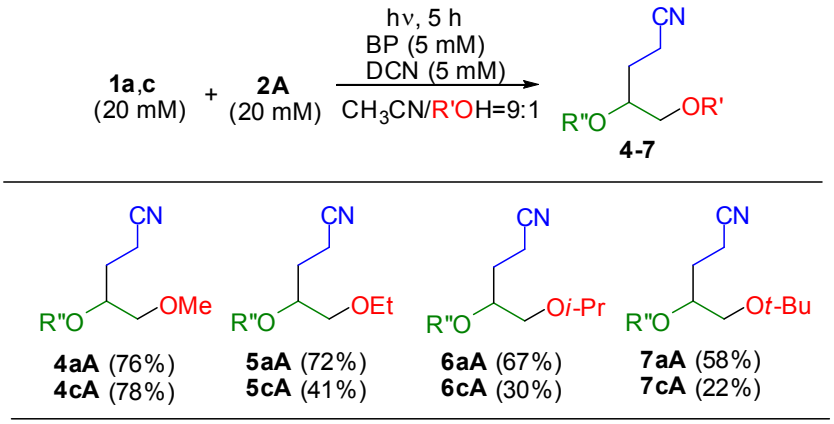
Table 3. Scope of electron-deficient alkene **2** in the photoreaction with **1a** or **1c**.



[a]Irradiation time was 4 h.

To elucidate the roll of the nucleophile, photoreactions of **1a**,**c** with **2A** in a 9:1 solvent mixture of acetonitrile and an alcohol such as MeOH, EtOH, *i*-PrOH, and *t*-BuOH were carried out (Table 4). Similar yields of **4aA**,**cA** were obtained in the photoreactions of **1a**,**c** using MeOH instead of water. The yields of coupling products **5aA–7cA** were strongly dependent on the steric hindrance of both **1** and the alcohol used. In fact, the photoreaction of the hindered vinyl ether **1c** was strongly affected by the steric hindrance of *t*-BuOH to cause the low yield of **7cA**.

Table 4. Scope of the nucleophile in the photoinduced cross-coupling reactions of **1a**,**c** with **2A**.



We next determined if a low concentration of alcohol could promote this reaction (Table 5). The photoreaction of **1a** (20 mM) and **2A** (20 mM) in the presence of a low concentration of alcohol (MeOH, 200 mM) as the nucleophile in dry acetonitrile led to the surprising formation of 2:1 adduct **8aA**. Optimization of the concentrations of **1a** and **2A** (**1a**: 20 mM, **2A**: 10 mM) resulted in a high yield of **8aA** (88%). Similar photoreactions of **1a**,**c** (20 mM) and **2A**,**B** (10 mM) in the presence of a low concentration of alcohols (MeOH, EtOH, and *i*-PrOH: 200 mM) provided 2:1 adducts **8cA–11aA**. Similar to the abovementioned trends, the use of poorly electron-deficient alkenes such as **2B** and more sterically hindered alcohols such as *i*-PrOH decreased the yield of the adducts. When water was used as a nucleophile, aldehydes **12aA–cB** were obtained through the formation of hemiacetal **13** (Table 6). In contrast, the use of alkyl substituted alkenes **1g**,**h** in the place of vinyl ethers **1a**,**c** with a low concentration of water did

not lead to the formation of the 2:1 adduct (Scheme 2); instead, **1g** formed the substituted cyanonaphthalene **14** in 19% yield based on DCN and **1h** formed the 1:1 adduct **3hA** in the almost same yield as that with higher amount of water (Table 2). Thus, the formation of 2:1 adducts was observed only in the photoreaction of vinyl ethers with a low concentration of the nucleophile.

Table 5. Formation of 2:1 adducts **8-11** in the photoreaction of **1** and **2** with a low concentration of R'OH.

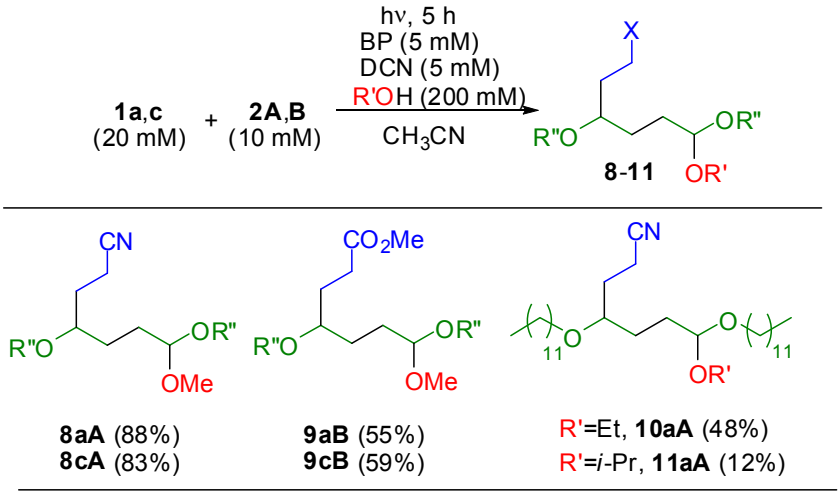
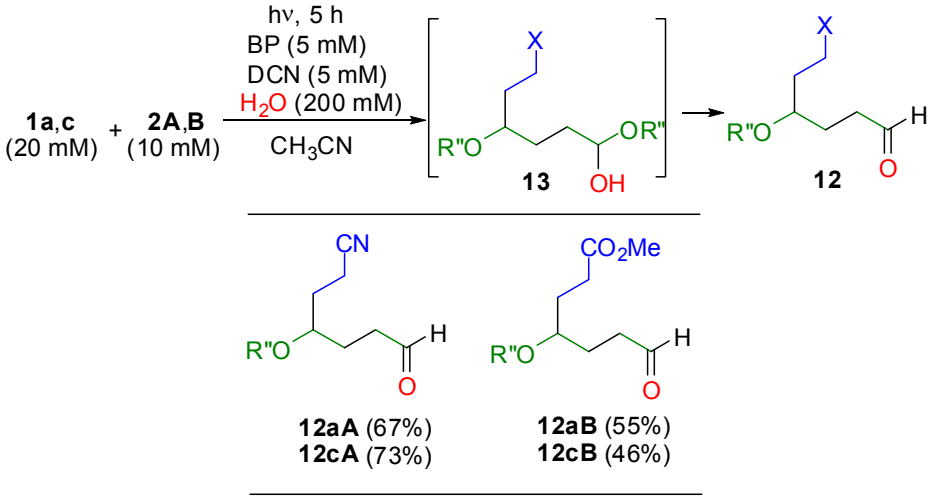
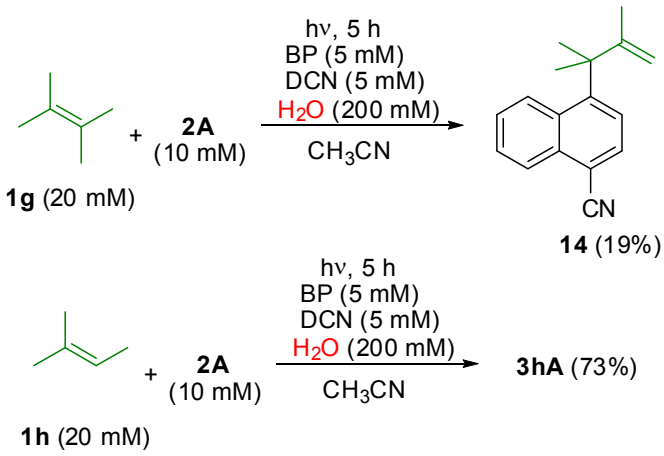


Table 6. Formation of aldehyde **12** in the photoreaction of **1** and **2** with a low concentration of water through the formation of intermediate **13**.



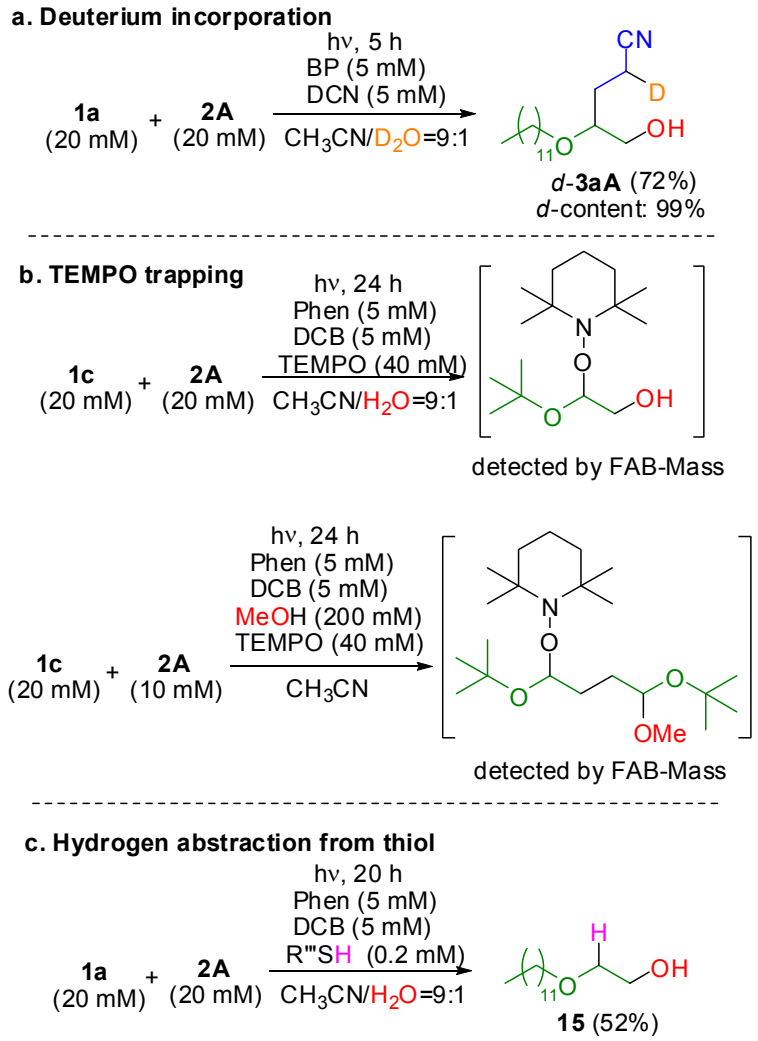
Scheme 2. Photoreactions of **1g**,**h** with a low concentration of water.



Mechanistic insight into this process was obtained from deuterium incorporation and radical trapping experiments (Scheme 3). The result of the photoinduced reaction of **1a** and **2A** in CH_3CN/D_2O=9:1 showed that deuterated product *d*-**3aA** was obtained with a high *d*-content

(99%) and in similar yield (72%) to that with un-deuterated water (Scheme 3a). This result indicates that protonation occurs after carbanion formation at the α-carbon attached to the cyano group. TEMPO radical trapping was performed for the reaction of **1c** and **2A** in the presence of 2 equiv of TEMPO (40 mM) employing a long irradiation time (24 h) (Scheme 3b). Phen/DCB as photocatalyst was used as the photocatalyst in this experiment because the high oxidation ability of the excited state of DCN prevented TEMPO trapping. The formation of the corresponding adduct **3cA** was disturbed by the addition of TEMPO, and the TEMPO coupling product was detected by FAB-Mass spectrometry (see Experimental section and Figure S2 (^{1}H NMR spectrum of crude product) in SI). The TEMPO product was not isolated because the TEMPO coupling product was unstable for isolation. The corresponding TEMPO coupling product produced under the photochemical conditions used the 2:1 adduct formation was also detected by FAB-Mass spectrometry (see Experimental section and Figure S3 (^{1}H NMR spectrum of crude product) in SI). Addition of the radical trapping reagent *t*-dodecanethiol (R"'SH, 0.2 mM) into aqueous acetonitrile solution of **1a** and **2A** catalyzed by Phen and DCB provided reduction product **15** in 52% yield after extended irradiation (20 h). These results show that the radical at the α-carbon attached to the ether oxygen is generated after the nucleophilic addition.

Scheme 3. Deuterium incorporation, TEMPO trapping, and thiol trapping experiments in the photoreaction of **1** and **2**.



Additional information about the photoreaction mechanism was obtained by the fluorescence quenching (Figure 1). The fluorescence of DCN in the aqueous acetonitrile solution was efficiently quenched by both BP (Figure 1a) and vinyl ether **1a** (Figure 1b). The rate constants for fluorescence quenching (k_q) by BP and **1a** were calculated as 7.48×10^8 and 7.18×10^8

$M^{-1}s^{-1}$, respectively, from the Stern-Volmer plot $I_0/I = 1 + k_q\tau[Q]$ (I_0: fluorescence intensity of DCN at 386 nm, I: observed fluorescence intensity of DCN at 386 nm with BP or **1a**, τ = 10.1 ns (fluorescence lifetime of DCN)[9], [Q]: concentration of BP or **1a**). The Rehm-Weller equation[10] confirms that both PET process are exothermic, as indicated by the negative ΔG values (–31 and –17 $kJmol^{-1}$, $\Delta G = 96.49[E(D^{\bullet+}/D)–E(A/A^{\bullet-})]–Es$) that were calculated using the reduction potential ($E(A/A^{\bullet-})$): –1.28 V vs. SCE in acetonitrile)[11] and excited singlet energy (Es: 333 $kJmol^{-1}$)[11] of DCN and the oxidation potential of BP and **1a** ($E(D^{\bullet+}/D)$: +1.85 and +1.99 V vs. SCE in acetonitrile)[12]. These results indicate that the PET from both BP and **1a** to the excited state of DCN occurs smoothly, and the rate of PET between BP and DCN is slightly faster than that between **1a** and DCN, because BP has a lower oxidation potential than **1a**.

a. Fluorescence quenching of DCN with BP **b. Fluorescence quenching of DCN with 1a**

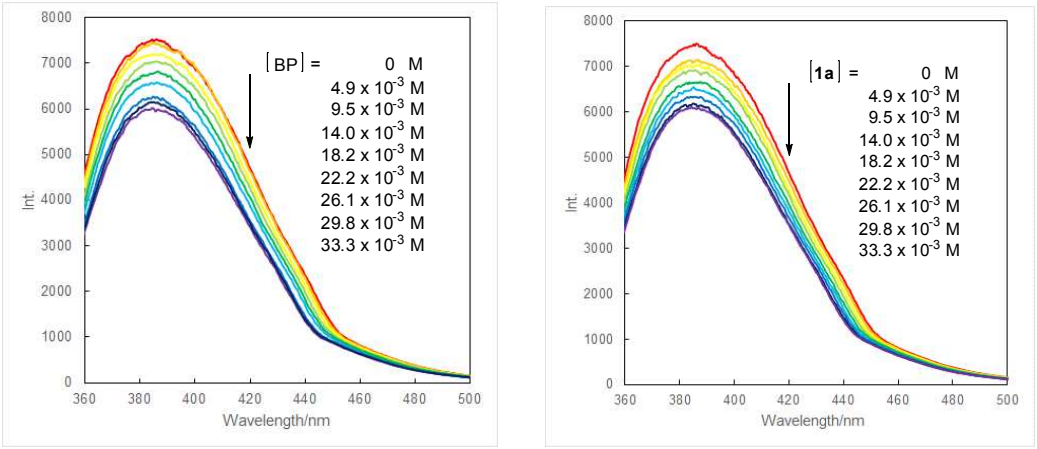
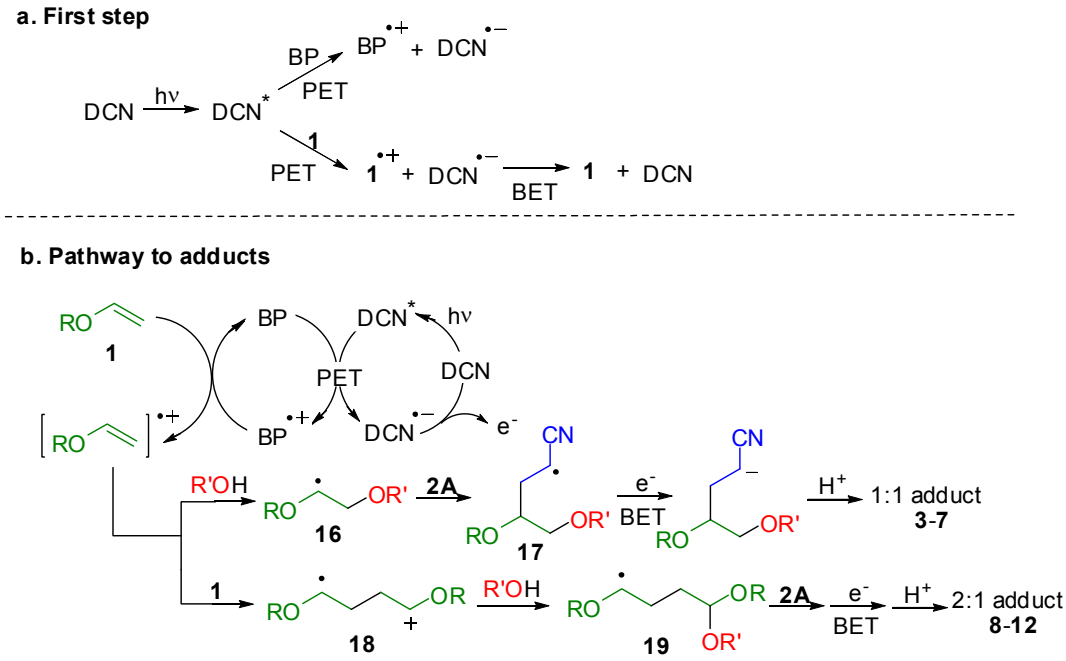


Figure 1. Fluorescence quenching of DCN with BP (a) and **1a** (b) excited at 310 nm in aqueous acetonitrile solution (CH_3CN/H_2O=9:1).

Based on the aforementioned results and the results from a similar three-component coupling photoreaction reported by D. R. Arnold[13] and K. Mizuno[14], a plausible mechanism for the photoinduced cross-coupling reaction between **1** and **2** is shown in Scheme 4. First, PET between BP and the excited state of DCN by light absorption (>280 nm, see absorption spectra of BP, DCN, and **1a** (Figure S1 in SI)) generates the radical cation of BP and the radical anion of DCN. Also, PET between **1** and the excited state of DCN generates the radical cation of **1** and the radical anion of DCN (Scheme 4a). As shown in Entry 3 in Table 3, the efficiency of photoreaction through the formation of the radical ion pair between **1** and DCN was quite low, probably because back electron transfer (BET) was faster than nucleophilic attack to the radical cation of **1**. This means that the adducts are primarily obtained through the formation of the BP/DCN radical ion pair as shown in Scheme 4b. A second electron transfer between **1** and the radical cation of BP forms the radical cation of **1** and BP, even though it is estimated from the oxidation potential of BP (+1.85 V)[7] and **1** (e.g., **1b**: +1.99 V)[7] that the electron transfer is an endothermic process. A similar electron transfer process between the radical cation of polycyclic aromatic compounds such as BP and electron-rich alkenes such as **1b** has been reported, and the formation of a π-complex between the radical cation of BP and **1b** was considered to promote the electron transfer.[15] However, the efficiency of the electron transfer between the radical

cation of BP and alkenes having a high oxidation potential such as **1k**,**l**,**m** is quite low and therefore the adducts are not formed. Thus, BP serve as an electron mediator both to separate the radical ion pair between **1** and DCN and to prevent fast BET in the photoreaction. When an electron-rich alkene having a low oxidation potential (less than +2.62 V, for example **1j**) is used with a high concentration of the nucleophile R'OH, the high rate of nucleophilic addition to the radical cation of **1** leads to the formation of the electron-rich radical **16**, and subsequently radical addition of **16** to **2A** forms electron-deficient radical **17**. BET from the radical anion of DCN to radical **17** generates the carbanion, as mentioned in the deuterium incorporation experiment, followed by protonation to yield 1:1 adducts **3–7**. However, when the concentration of R'OH is low, the low rate of nucleophilic addition to the radical cation results in the dimerization of vinyl ethers **1**, as was reported in the similar PET-promoted addition of vinyl ethers to generate the radical cation of dimer **18**.[5g,16] Nucleophilic addition of R'OH to **18** forms electron-rich radical **19**, and the same radical and BET process provides 2:1 adducts **8–12**. When alkyl-substituted alkenes **1g,h** are employed in the place of vinyl ethers as the electron-rich alkene in a low concentration of R'OH, the 2:1 adduct is not formed due to the low rate of dimerization of the radical cations of **1g,h**. In the case of **1g**, substitution between the radical cations of **1g** and the radical anion of DCN takes place after decyanation to yield **14** as previously reported.[13b]

Scheme 4. Plausible mechanism for the photoreaction.

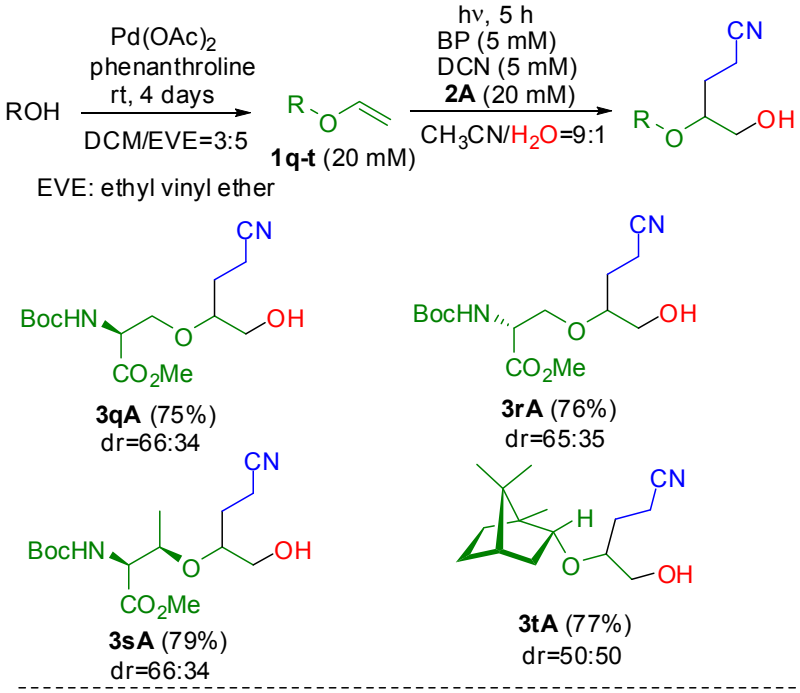


Finally, the applicability of this process to the use of vinyl ethers from bioactive alcohols[17] and the conversion of the photoproducts to lactones[18] was examined (Scheme 5). Vinyl ethers **1q–t** derived from bioactive alcohols such as L-serine, D-serine, L-threonine, and D-borneol were converted to diastereomeric mixture of cross-coupling products **3qA–tA** under the same photochemical conditions as used previously (Scheme 5a). In addition, the hydrolysis of photoproduct **3cA** by NaOH and the sequential treatment by TFA led to the formation of 6-membered lactone **20**, which is an intermediate for the preparation of an antineoplastic drug.[19] Similarly, the hydrolysis of **3iA** without TFA treatment provided the bicyclic lactone **21**, which

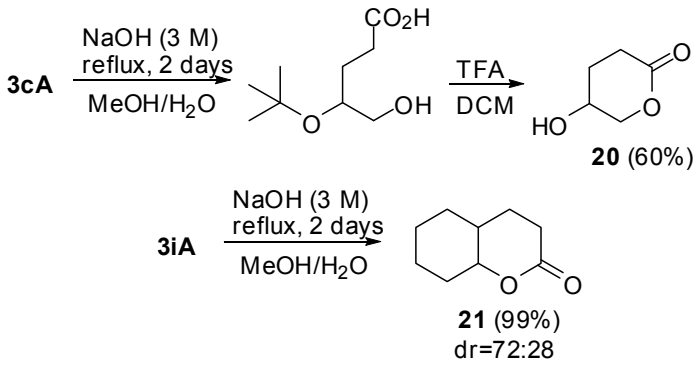
is an intermediate in the synthesis of an α_2-adrenoreceptor agonist.[20]

Scheme 5. Photoreaction of vinyl ethers prepared from bioactive alcohols and conversion of the photoproducts to lactones.

a. Preparation of vinyl ethers from bioactive alcohols and their photoreaction



b. Modification of the photoproduct



Conclusion

This study has led to the development of a new general method for the preparation of cross-coupling adducts between electronically-differentiated donor and acceptor alkenes containing a nucleophile by using an organic photocatalyst (BP/DCN) under mild conditions. This process can be employed with a variety of alkenes and alcohols as the substrates, and the limitations of the alkenes were described. The selective formation of 1:1 or 2:1 adducts in the photoreaction of vinyl ethers depends on the concentration of the nucleophile. The photoinduced redox system using BP and DCN was found to be superior to the direct PET process between **1** and DCN. Vinyl ethers are easily accessible from alcohols; therefore, this method can be applied to the construction of the fundamental framework of complex molecules from alcohols and alkenes. Further investigations for the application of this methodology to the preparation of stereoselective adducts are underway.

Experimental Section

General Information. All reagents and solvents were used as received from commercial suppliers. IR spectra were recorded on an FT-IR spectrometer. ^{1}H NMR spectra were recorded in $CDCl_3$ containing tetramethylsilane as an internal standard, and were acquired on either a 500 MHz spectrometer. $^{13}C\{^{1}H\}$ NMR spectra were acquired on a 125 MHz spectrometer.

High-resolution mass spectra were obtained using double-focusing magnetic sector mass spectrometer coupled with FAB. The light source was a high-pressure (100 W) mercury arcs and blue LED (18 W, 405 nm). Column chromatography was performed on Wakogel C-300, particle size 45-75 μm.

General procedure for the photoreaction of 1 with 2. An aqueous CH_3CN solution (CH_3CN 36 mL, H_2O 4 mL) of **1** (20 mM), **2** (20 mM), BP (5 mM), and DCN (5 mM) in Pyrex vessels (18 mm x 180 mm) was purged with Ar for 10 min. The mixture was irradiated with a 100 W high-pressure mercury lamp for 5 h, and then the solvent was removed under reduced pressure. The crude product was purified by silica-gel column chromatography using hexane/EtOAc = 1:1 as the eluent to give adduct **3**.

4-dodecyloxy-5-hydroxypentanenitrile (3aA): 0.164 g, 72%, white solid, mp 36–37 °C; IR (KBr, cm^{-1}) 3437, 2923, 2854, 2248; ^1H NMR (500 MHz, $CDCl_3$) δ 3.77–3.74 (m, 1H), 3.61–3.44 (m, 4H), 2.51–2.44 (m, 2H), 2.24 (s (br), 1H), 1.94–1.84 (m, 2H), 1.60–1.55 (m, 2H), 1.38–1.14 (m, 18H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.7, 77.5, 70.3, 62.9, 31.9, 30.0, 29.7, 29.6, 29.5, 29.4, 27.3, 26.2, 22.7, 14.1, 13.4; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{17}H_{34}NO_2$: 284.2590, found: 284.2607.

4-ethoxy-5-hydroxypentanenitrile (3bA): 0.075 g, 65%, colorless oil; IR (neat, cm^{-1}) 3435, 2976, 2934, 2879, 2248; ^1H NMR (500 MHz, $CDCl_3$) δ 3.74–3.64 (m, 2H), 3.57–3.46 (m, 3H), 2.54–2.40 (m, 3H), 1.93–1.863 (m, 2H), 1.23 (t, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.8, 77.4, 65.5, 63.0, 27.2, 15.5, 13.4; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_7H_{14}NO_2$: 144.1025, found: 144.1013.

4-tert-butoxy-5-hydroxypentanenitrile (3cA): 0.108 g, 79%, colorless oil; IR (neat, cm^{-1}) 3462,

2978, 2881, 2248; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.73–3.69 (m, 1H), 3.59–3.50 (m, 2H), 2.49–2.42 (m, 3H), 2.28 (s (br), 1H), 1.92–1.87 (m, 2H), 1.26 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.1, 74.5, 69.3, 64.8, 28.9, 28.5, 13.3; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_9H_{18}NO_2$: 172.1338, found: 172.1322.

3-(tetrahydro-2-hydroxy-pyran-3-yl)propanenitrile (3dA'): 0.078 g, 68%, colorless oil; IR (neat, cm^{-1}) 3432, 2931, 2858, 2247; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.09 (s, 0.4H), 4.43 (t, *J* = 6.0 Hz, 0.6H), 4.02–3.93 (m, 1H), 3.83 (d, *J* = 6.0 Hz, 0.6H), 3.60–3.57 (m, 0.4H), 3.52–3.47 (m, 0.6H), 3.30 (s, 0.4H), 2.51–2.47 (m, 1.2H), 2.45–2.36 (m, 0.8H), 1.97–1.89 (m, 1.2H), 1.84–1.78 (m, 0.8H), 1.68–1.49 (m, 3H), 1.26–1.19 (m, 2H), 0.89–0.84 (m, 0.4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.0, 119.8, 99.5, 93.0, 65.6, 60.0, 40.9, 38.4, 29.7, 27.7, 27.0, 24.7, 23.3, 15.4, 14.6; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_8H_{14}NO_2$: 156.1025, found:156.1026.

3-(tetrahydro-3-hydroxy-pyran-2-yl)propanenitrile (3dA): 0.022 g, 13%, colorless oil; IR (neat, cm^{-1}) 3439, 2940, 2853, 2247; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.01–3.98 (m, 1H), 3.65–3.63 (m, 1H), 3.51–3.43 (m, 2H), 2.50–2.47 (m, 2H), 2.07–1.86 (m, 4H), 1.79–1.69 (m, 2H), 1.47–1.43 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.7, 77.6, 68.6, 66.7, 30.6, 27.8, 20.0, 13.6; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_8H_{14}NO_2$: 156.1025, found: 156.1005.

5-hydroxy-4-(3-phenylpropoxy)pentanenitrile (3eA): 0.121 g, 65%, colorless oil; IR (neat, cm^{-1}) 3441, 3060, 3026, 2940, 2247; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31–7.18 (m, 5H), 3.76–3.73 (m, 1H), 3.63–3.58 (m, 1H), 3.53–3.45 (m, 3H), 2.72–2.69 (m, 2H), 2.52–2.41 (m, 2H), 1.96–1.79 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.5, 128.41, 128.37, 126.0, 119.7, 77.5, 69.2, 62.9, 32.33, 31.4, 27.2, 13.4; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{14}H_{20}NO_2$: 234.1494, found: 234.1492.

5-hydroxy-4-(2-hydroxyethoxy)pentanenitrile (3fA): 0.083 g, 65%, colorless oil; IR (neat, cm^{-1}) 3424, 2937, 2876, 2248; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.84–3.70 (m, 5H), 3.60–3.54 (m, 2H), 3.02 (s (br), 1H), 2.85 (s (br), 1H), 2.58–2.44 (m, 2H), 1.97–1.81 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.8, 78.7, 71.4, 63.4, 62.2, 27.2, 13.6; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_7H_{14}NO_3$: 160.0974, found:160.0968.

5-hydroxy-4,4,5-trimethylhexanenitrile (3gA): 0.092 g, 74%, colorless oil; IR (neat, cm^{-1}) 3438, 2970, 2881, 2246; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.43–2.40 (m, 2H), 1.82–1.78 (m, 2H), 1.42 (s (br), 1H), 1.21 (s, 6H), 0.93 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 121.0, 75.3, 39.6, 33.6, 25.7, 21.7, 13.3; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_9H_{18}NO$: 156.1389, found: 156.1375.

5-hydroxy-4,4-dimethylhexanenitrile (3hA): 0.081 g, 72%, colorless oil; IR (neat, cm^{-1}) 3456, 2973, 2248; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.52 (q, *J* = 6.4 Hz, 1H), 2.43–2.31 (m, 2H), 2.02 (s (br), 1H), 1.84–1.78 (m, 1H), 1.66–1.60 (m, 1H), 1.14 (d, *J* = 6.4 Hz, 3H), 0.92–0.85 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.8, 73.6, 37.2, 34.3, 22.9, 21.8, 18.0, 12.5; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_8H_{16}NO$: 142.1232, found: 142.1227.

3-(2-hydroxycyclohexyl)propanenitrile (3iA): 0.085 g, 69%, colorless oil; IR (neat, cm^{-1}) 3435, 2929, 2858, 2248; ^1H NMR (500 MHz, $CDCl_3$) δ 3.92–3.90 (m, 0.1H), 3.24–3.22 (m, 0.9H), 2.55–2.40 (m, 2H), 2.16–2.09 (m, 0.9H), 1.99–1.95 (m, 0.9H), 1.83–1.16 (m, 9.3H), 1.00–0.92 (m, 0.9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.4, 74.8, 68.3, 44.1, 39.9, 36.2, 33.1, 30.3, 29.0, 27.5, 26.1, 25.3, 24.7, 20.2, 15.2, 14.8; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_9H_{16}NO$: 154.1232, found:154.1252.

3-(1-(hydroxymethyl)cyclohexyl)propanenitrile (3jA): 0.043 g, 32%, colorless oil; IR (neat, cm^{-1}) 3443, 2876, 2249; ^1H NMR (500 MHz, $CDCl_3$) δ 3.46 (s, 2H), 2.36 (t, J = 8.0 Hz, 2H), 1.79 (t, J = 8.0 Hz, 2H), 1.67 (s (br), 1H), 1.51–1.26 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.9, 67.7, 36.9, 32.2, 31.4, 26.1, 21.3, 11.8; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{10}H_{18}NO$: 168.1389, found: 168.1376.

4-ethylthio-5-hydroxypentanenitrile (3nA): 0.011 g, 9%, colorless oil; IR (neat, cm^{-1}) 3436, 2932, 2248; ^1H NMR (500 MHz, $CDCl_3$) δ 3.70–3.67 (m, 1H), 3.65–3.61 (m, 1H), 2.89–2.83 (m, 1H), 2.65–2.55 (m, 4H), 2.30–2.26 (m, 1H), 2.09–2.02 (m, 1H), 1.81–1.74 (m, 1H), 1.29 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.4, 64.1, 47.4, 27.5, 25.0, 15.1; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_7H_{14}NOS$: 160.0796, found: 160.0774.

methyl 4-dodecyloxy-5-hydroxypentanoate (3aB): 0.117 g, 46%, colorless oil; IR (neat, cm^{-1}) 3460, 2925, 2858, 1741; ^1H NMR (500 MHz, $CDCl_3$) δ 3.68–3.65 (m, 4H), 3.52–3.46 (m, 3H), 3.40–3.38 (m, 1H), 2.41 (t, J = 7.5 Hz, 2H), 2.10 (s (br), 1H), 1.91–1.81 (m, 2H), 1.59–1.53 (m, 2H), 1.38–1.14 (m, 18H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1, 78.6, 69.9, 63.7, 51.7, 31.9, 30.1, 29.67, 29.65, 29.63, 29.5, 29.4, 26.2, 26.0, 22.7, 14.1; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{18}H_{37}O_4$: 317.2692, found: 317.2680.

methyl 4-tert-butoxy-5-hydroxypentanoate (3cB): 0.082 g, 50%, colorless oil; IR (neat, cm^{-1}) 3466, 2974, 2824, 1739; ^1H NMR (500 MHz, $CDCl_3$) δ 3.68–3.66 (m, 4H), 3.57–3.54 (m, 1H), 3.46–3.44 (m, 1H), 2.39 (t, J = 7.5 Hz, 2H), 2.07 (s (br), 1H), 1.89–1.83 (m, 2H), 1.24 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 74.2, 69.9, 64.9, 51.6, 29.6, 28.6, 28.0; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{10}H_{21}O_4$: 205.1440, found: 205.1423.

ethyl 4-dodecyloxy-5-hydroxypentanoate (3aC): 0.124 g, 46%, colorless oil; IR (neat, cm^{-1}) 3457, 2927, 2849, 1738; ^1H NMR (500 MHz, $CDCl_3$) δ 4.13 (q, J = 7.2 Hz, 2H), 3.66–3.64 (m, 1H), 3.52–3.47 (m, 3H), 3.41–3.37 (m, 1H), 2.39 (t, J = 7.5 Hz, 2H), 2.28 (s (br), 1H), 1.90–1.81 (m, 2H), 1.57–1.53 (m, 2H), 1.38–1.14 (m, 21H), 0.88 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 78.7, 69.9, 63.7, 60.4, 31.9, 30.1, 30.0, 29.69, 29.65, 29.52, 29.4, 26.2, 26.0, 22.7, 14.2, 14.1; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{19}H_{39}O_4$: 331.2848, found: 331.2846.

ethyl 4-tert-butoxy-5-hydroxypentanoate (3cC): 0.087 g, 50%, colorless oil; IR (neat, cm^{-1}) 3466, 2972, 2876, 1732; ^1H NMR (500 MHz, $CDCl_3$) δ 4.13 (q, J = 7.0 Hz, 2H), 3.68–3.66 (m,

1H), 3.58–3.54 (m, 1H), 3.47–3.43 (m, 1H), 2.37 (t, *J* = 7.5 Hz, 2H), 2.08 (s (br), 1H), 1.88–1.82 (m, 2H), 1.27–1.18 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 74.2, 70.0, 64.9, 60.4, 29.9, 28.6, 28.0, 14.2; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{11}H_{23}O_4$: 219.1596, found: 219.1602.

tert-butyl 4-dodecyloxy-5-hydroxypentanoate (3aD): 0.133 g, 47%, colorless oil; IR (neat, cm^{-1}) 3311, 3080, 2928, 2858, 1731; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.65–3.62 (m, 1H), 3.59–3.47 (m, 3H), 3.40–3.37 (m, 1H), 2.30 (t, *J* = 7.3 Hz, 2H), 2.24 (s (br), 1H), 1.86–1.75 (m, 2H), 1.59–1.54 (m, 2H), 1.45 (s, 9H), 1.38–1.14 (m, 18H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 80.4, 78.8, 69.9, 63.8, 31.9, 31.0, 30.1, 29.7, 29.6, 29.5, 29.4, 28.1, 26.2, 26.0, 22.7, 14.1; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{21}H_{43}O_4$: 359.3162, found: 359.3140.

tert-butyl 4-tert-butoxy-5-hydroxypentanoate (3cD): 0.101 g, 51%, colorless oil; IR (neat, cm^{-1}) 3462, 2964, 1730; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.67–3.65 (m, 1H), 3.56–3.53 (m, 1H), 3.45–3.43 (m, 1H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.15 (s (br), 1H), 1.84–1.77 (m, 2H), 1.45 (s, 9H), 1.21 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.3, 80.4, 74.1, 70.1, 65.0, 31.0, 28.6, 28.11, 28.06; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{13}H_{27}O_4$: 247.1909, found: 247.1919.

4-dodecyloxy-5-hydroxypentanoic acid (3aE): 0.082 g, 34%, white solid, mp 33–35 °C; IR (KBr, cm^{-1}) 3402, 2925, 2854, 1739; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.71–3.68 (m, 1H), 3.53–3.41 (m, 4H), 2.46 (t, *J* = 7.5 Hz, 2H), 1.93–1.83 (m, 2H), 1.58–1.54 (m, 2H), 1.38–1.14 (m, 18H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.3, 78.6, 70.1, 63.6, 31.9, 30.1, 29.67, 29.65, 29.60, 29.5, 29.4, 26.2, 25.8, 22.7, 14.1; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{17}H_{35}O_4$: 303.2535, found: 303.2541.

4-dodecyloxy-5-hydroxypentanamide (3aF): 0.123 g, 51%, white solid, mp 67–68 °C; IR (KBr, cm^{-1}) 3394, 2955, 2923, 2853, 1662, 1615; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 (s (br), 2H), 3.66–3.63 (m, 1H), 3.53–3.40 (m, 4H), 2.56 (s (br), 1H), 2.37–2.28 (m, 2H), 1.92–1.86 (m, 2H), 1.57–1.53 (m, 2H), 1.38–1.14 (m, 18H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.6, 78.8, 69.8, 63.3, 31.9, 31.1, 30.1, 29.67, 29.65, 29.5, 29.4, 26.2, 26.1, 22.7, 14.1; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{17}H_{36}NO_3$: 302.2695, found: 302.2695.

N-tert-butyl-4-dodecyloxy-5-hydroxypentanamide (3aG): 0.139 g, 48%, colorless oil; IR (neat, cm^{-1}) 3311, 3080, 2928, 2858, 1646, 1552; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.43 (s (br), 1H), 3.61–3.59 (m, 1H), 3.51–3.47 (m, 3H), 3.41–3.38 (m, 1H), 2.59 (s (br), 1H), 2.23–2.14 (m, 2H), 1.92–1.82 (m, 2H), 1.59–1.53 (m, 2H), 1.39–1.21 (m, 27H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 78.8, 69.7, 63.3, 51.2, 32.4, 31.9, 30.1, 29.7, 29.6, 29.5, 29.4, 28.8, 26.2, 25.9, 22.7, 14.1; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{21}H_{44}NO_3$: 358.3321, found: 358.3326.

4-dodecyloxy-5-hydroxy-3-methylpentanenitrile (3aH): 0.048 g, 20%, colorless oil; IR (neat,

cm^{-1}) 3449, 2921, 2858, 2248; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.86–3.83 (m, 1H), 3.64–3.56 (m, 2H), 3.45–3.40 (m, 1H), 3.14–3.11 (m, 1H), 2.57–2.46 (m, 2H), 2.22–2.16 (m, 1H), 1.83 (s (br), 1H), 1.62–1.56 (m, 2H), 1.38–1.14 (m, 18H), 1.12 (d, *J* = 6.5 Hz, 3H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 118.9, 82.0, 70.7, 60.2, 31.9, 31.5, 30.1, 29.7, 29.64, 29.62, 29.60, 29.5, 29.4, 26.2, 22.7, 21.1, 16.1, 14.1; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{18}H_{36}NO_2$: 298.2746, found: 298.2754.

4-tert-butoxy-5-hydroxy-3-methylpentanenitrile (3cH): 0.032 g, 21%, colorless oil; IR (neat, cm^{-1}) 3484, 3008, 2865, 2247; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.70–3.43 (m, 3H), 2.65–2.50 (m, 1H), 2.43–2.27 (m, 1H), 2.18–2.15 (m, 1H), 1.94–1.92 (m, 1H), 1.28–1.22 (m, 9H), 1.12 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.7, 119.4, 74.6, 73.5, 72.5, 62.7, 62.1, 34.6, 32.5, 28.8, 28.6, 21.2, 20.3, 16.2, 15.8; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{10}H_{20}NO_2$: 186.1494, found:186.1487.

4-dodecyloxy-5-methoxypentanenitrile (4aA): 0.181 g, 76%, colorless oil; IR (neat, cm^{-1}) 2926, 2854, 2247; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.65–3.61 (m, 1H), 3.51–3.33 (m, 7H), 2.50–2.46 (m, 2H), 1.92–1.84 (m, 2H), 1.60–1.53 (m, 2H), 1.38–1.14 (m, 18H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.8, 76.1, 73.7, 70.5, 59.3, 31.9, 30.0, 29.7, 29.6, 29.5, 29.4, 28.0, 26.1, 22.7, 14.1, 13.4; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{18}H_{36}NO_2$: 298.2746, found: 298.2754.

4-tert-butoxy-5-methoxypentanenitrile (4cA): 0.116 g, 78%, colorless oil; IR (neat, cm^{-1}) 2976, 2933, 2247; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.74–3.72 (m, 1H), 3.41–3.35 (m, 4H), 3.26–3.23 (m, 1H), 2.45–2.42 (m, 2H), 1.95–1.92 (m, 1H), 1.85–1.82 (m, 1H), 1.23 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.3, 75.5, 74.3, 67.8, 59.2, 29.5, 28.4, 13.0; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{10}H_{20}NO_2$: 186.1494, found: 186.1477.

4-dodecyloxy-5-ethoxypentanenitrile (5aA): 0.180 g, 72%, colorless oil; IR (neat, cm^{-1}) 2928, 2855, 2247; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66–3.61 (m, 1H), 3.53–3.47 (m, 4H), 3.44–3.40 (m, 2H), 2.50–2.46 (m, 2H), 1.94–1.75 (m, 2H), 1.60–1.53 (m, 2H), 1.38–1.14 (m, 21H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.9, 76.3, 71.6, 70.5, 66.9, 31.9, 30.1, 29.7, 29.6, 29.5, 29.4, 28.2, 26.1, 22.7, 15.1, 14.1, 13.4; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{19}H_{38}NO_2$:312.2902, found: 312.2888.

4-tert-butoxy-5-ethoxypentanenitrile (5cA): 0.065 g, 41%, colorless oil; IR (neat, cm^{-1}) 2976, 2934, 2871, 2246; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.74–3.72 (m, 1H), 3.51–3.43 (m, 3H), 3.27–3.24 (m, 1H), 2.44 (t, *J* = 7.3 Hz, 2H), 1.98–1.94 (m, 1H), 1.85–1.80 (m, 1H), 1.29–1.17 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.3, 74.3, 73.3, 68.0, 66.8, 29.7, 28.4, 15.1, 13.0; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{11}H_{22}NO_2$: 200.1650, found: 200.1672.

4-dodecyloxy-5-isopropoxypentanenitrile (6aA): 0.175 g, 67%, colorless oil; IR (neat, cm^{-1}) 2927, 2858, 2251; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66–3.54 (m, 2H), 3.49–3.37 (m, 4H),

2.49–2.46 (m, 2H), 1.95–1.90 (m, 1H), 1.84–1.79 (m, 1H), 1.59–1.52 (m, 2H), 1.32–1.21 (m, 18H), 1.14 (d, J = 5.8 Hz, 6H), 0.88 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.0, 76.5, 72.2, 70.5, 69.3, 31.9, 30.1, 29.7, 29.6, 29.5, 29.4, 28.3, 26.1, 22.7, 22.1, 22.0, 14.1, 13.4; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{20}H_{40}NO_2$: 326.3060, found: 326.3062.

4-tert-butoxy-5-isopropoxypentanenitrile (6cA): 0.052 g, 30%, colorless oil; IR (neat, cm^{-1}) 2974, 2927, 2247; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.71–3.68 (m, 1H), 3.56–3.54 (m, 1H), 3.45–3.42 (m, 1H), 3.22–3.19 (m, 1H), 2.43 (t, J = 7.5 Hz, 2H), 1.99–1.95 (m, 1H), 1.83–1.79 (m, 1H), 1.20 (s, 9H), 1.15 (d, J = 6.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.4, 74.2, 72.1, 70.9, 68.3, 29.8, 28.5, 22.1, 22.0, 13.0; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{12}H_{24}NO_2$: 214.1807, found: 214.1793.

5-tert-butoxy-4-dodecyloxypentanenitrile (7aA): 0.158 g, 58%, colorless oil; IR (neat, cm^{-1}) 2925, 2885, 2246; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66–3.61 (m, 1H), 3.46–3.40 (m, 3H), 3.28–3.25 (m, 1H), 2.47 (t, J = 7.5 Hz, 2H), 1.97–1.92 (m, 1H), 1.81–1.76 (m, 1H), 1.59–1.50 (m, 2H), 1.30–1.21 (m, 18H), 1.17 (s, 9H), 0.88 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.0, 76.9, 73.1, 70.6, 63.0, 31.9, 30.1, 29.7, 29.6, 29.5, 29.4, 28.4, 27.4, 26.2, 22.7, 14.1, 13.4; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{21}H_{42}NO_2$: 340.3216, found: 340.3224.

4,5-di-tert-butoxypentanenitrile (7cA): 0.039 g, 22%, colorless oil; IR (neat, cm^{-1}) 2974, 2247; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66–3.63 (m, 1H), 3.38–3.36 (m, 1H), 3.13–3.10 (m, 1H), 2.43 (t, J = 7.5 Hz, 2H), 2.00–1.96 (m, 1H), 1.82–1.77 (m, 1H), 1.21 (s, 9H), 1.17 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.5, 74.1, 72.9, 68.7, 64.6, 29.8, 28.5, 27.5, 13.0; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{13}H_{26}NO_2$: 228.1964, found: 228.1973.

4,7-didodecyloxy-7-methoxyheptanenitrile (8aA): 0.179 g, 88%, colorless oil; IR (neat, cm^{-1}) 2925, 2853, 2246; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.41–4.40 (m, 1H), 3.59–3.29 (m, 8H), 2.48–2.42 (m, 2H), 1.85–1.50 (m, 10H), 1.38–1.14 (m, 36H), 0.88 (t, J = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.9, 103.7, 103.6, 69.4, 66.0, 52.7, 31.9, 30.1, 29.8, 29.6, 29.5, 29.3, 28.4, 28.2, 26.2, 22.7, 14.1, 13.3; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{32}H_{64}NO_3$: 510.4886, found: 510.4862.

4,7-di-tert-butoxy-7-methoxyheptanenitrile (8cA): 0.094 g, 83%, colorless oil; IR (neat, cm^{-1}) 2974, 2827, 2246; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.66–4.64 (m, 1H), 3.64–3.62 (m, 1H), 3.23 (s, 3H), 2.45–2.37 (m, 2H), 1.83–1.72 (m, 2H), 1.61–1.47 (m, 4H), 1.21 (s, 9H), 1.17 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.20, 120.18, 97.4, 97.3, 73.8, 73.7, 68.8, 68.7, 50.1, 50.0, 31.3, 31.1, 30.7, 29.8, 29.7, 28.7, 28.6, 13.1, 13.0; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{16}H_{32}NO_3$: 286.2382, found: 286.2382.

methyl 4,7-didodecyloxy-7-methoxyheptanoate (9aB): 0.119 g, 55%, colorless oil; IR (neat, cm^{-1}) 2909, 2840, 1739; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.42–4.39 (m, 1H), 3.67 (s, 3H), 3.58–3.54 (m, 1H), 3.43–3.25 (m, 7H), 2.41–2.37 (m, 2H), 1.85–1.46 (m, 10H), 1.38–1.14 (m,

36H), 0.88 (t, J = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 103.8, 77.9, 69.2, 66.0, 65.9, 52.7, 52.6, 51.5, 31.9, 30.2, 30.0, 29.9, 29.69, 29.65, 29.55, 29.51, 29.4, 29.1, 28.7, 26.31, 26.27, 22.7, 14.1; HRMS (FAB, *m/z*) calcd for $(M+H–OMe)^+$ $C_{32}H_{64}O_4$: 512.4804, found: 512.4796.

methyl 4,7-di-tert-butoxy-7-methoxyheptanoate (9cB): 0.075 g, 59%, colorless oil; IR (neat, cm^{-1}) 2947, 2802, 1740; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.66–4.64 (m, 1H), 3.67 (s, 3H), 3.55–3.53 (m, 1H), 3.23 (s, 3H), 2.39–2.36 (m, 2H), 1.84–1.45 (m, 6H), 1.23 (s, 9H), 1.18 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.4, 97.6, 97.4, 73.7, 73.3, 69.7, 69.5, 51.4, 49.83, 49.77, 31.00, 30.95, 30.8, 30.5, 30.0, 29.9, 29.8, 28.7, 28.6; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{17}H_{35}O_5$: 319.2484, found: 319.2465.

4,7-didodecyloxy-7-ethoxyheptanenitrile (10aA): 0.101 g, 48%, colorless oil; IR (neat, cm^{-1}) 2889, 2247; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.47–4.45 (m, 1H), 3.66–3.35 (m, 7H), 2.46–2.42 (m, 2H), 1.83–1.52 (m, 10H), 1.32–1.19 (m, 39H), 0.88 (t, J = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.9, 102.8, 69.5, 65.8, 61.22, 61.17, 31.9, 30.1, 29.9, 29.69, 29.65, 29.5, 29.4, 29.0, 28.3, 26.30, 26.27, 22.7, 15.3, 14.1, 13.4; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{33}H_{66}NO_3$: 524.5042, found: 524.5043.

4,7-didodecyloxy-7-isopropoxyheptanenitrile (11aA): 0.026 g, 12%, colorless oil; IR (neat, cm^{-1}) 2923, 2615, 2246; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.53–4.51 (m, 1H), 3.88–3.84 (m, 1H), 3.54–3.49 (m, 2H), 3.43–3.36 (m, 3H), 2.46–2.43 (m, 2H), 1.86–1.55 (m, 10H), 1.26–1.13 (m, 42H), 0.88 (t, J = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.9, 101.3, 76.9, 69.5, 68.61, 68.55, 64.7, 31.9, 30.1, 29.9, 29.68, 29.65, 29.5, 29.4, 28.42, 28.35, 26.32, 26.27, 23.3, 22.7, 22.3, 14.1, 13.4; HRMS (FAB, *m/z*) calcd for $(M+H–O\textit{i}Pr)^+$ $C_{31}H_{61}NO_2$: 479.4702, found: 479.4677.

4-dodecyloxy-6-formylhexanenitrile (12aA): 0.166 g, 67%, colorless oil; IR (neat, cm^{-1}) 2926, 2858, 2247, 1713; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.78 (s, 1H), 3.46–3.36 (m, 3H), 2.53–2.43 (m, 4H), 1.90–1.76 (m, 4H), 1.56–1.51 (m, 2H), 1.38–1.14 (m, 18H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.6, 119.7, 76.1, 69.7, 39.4, 31.9, 30.0, 29.70, 29.66, 29.64, 29.62, 29.60, 29.5, 29.4, 26.2, 25.6, 22.7, 14.1, 13.2; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{19}H_{36}NO_2$: 310.2746, found: 310.2753.

4-tert-butoxy-6-formylhexanenitrile (12cA): 0.058 g, 73%, colorless oil; IR (neat, cm^{-1}) 2975, 2821, 2246, 1725; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.79 (s, 1H), 3.72–3.70 (m, 1H), 2.57–2.36 (m, 4H), 1.88–1.71 (m, 4H), 1.22 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.9, 119.9, 74.2, 67.8, 39.3, 31.2, 28.6, 27.6, 13.0; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{11}H_{20}NO_2$: 198.1494, found: 198.1513.

methyl 4-dodecyloxy-6-formylhexanoate (12aB): 0.075 g, 55%, colorless oil; IR (neat, cm^{-1}) 2985, 2804, 2718, 1740, 1715; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.77 (s, 1H), 3.68–3.62 (m, 4H),

3.41–3.29 (m, 2H), 2.51 (t, J = 7.0 Hz, 2H), 2.39 (t, J = 7.3 Hz, 2H), 1.85–1.76 (m, 4H), 1.58–1.48 (m, 2H), 1.38–1.17 (m, 18H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.2, 174.0, 77.2, 69.3, 63.0, 51.6, 39.8, 32.7, 31.9, 30.0, 29.7, 29.61, 29.58, 29.44, 29.39, 29.31, 28.8, 26.2, 25.7, 22.6, 14.1; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{20}H_{39}O_4$: 343.2849, found: 343.2854.

methyl 4-tert-butoxy-6-formylhexanoate (12cB): 0.042 g, 46%, colorless oil; IR (neat, cm^{-1}) 2975, 2723, 1734, 1714; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.78 (s, 1H), 3.68–3.61 (m, 4H), 2.53–2.36 (m, 4H), 1.82–1.71 (m, 4H), 1.20 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.6, 174.2, 73.8, 68.7, 51.6, 39.7, 30.7, 29.8, 28.6, 28.5, 28.0; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{12}H_{23}O_4$: 231.1596, found: 231.1603.

1-cyano-4-(1,1,2-trimethylprop-2-enyl)naphthalene (14): 0.005 g, 19%, colorless oil; IR (neat, cm^{-1}) 2985, 2915, 2213, 1583, 1509; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, J = 8.0 Hz, 1H), 8.14 (d, J = 8.5 Hz, 1H), 7.84 (d, J = 7.5 Hz, 1H), 7.71–7.63 (m, 2H), 7.29 (d, J = 7.5 Hz, 1H), 3.88 (s, 2H), 1.82 (s, 3H), 1.75 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.1, 132.6, 132.5, 132.3, 128.1, 128.0, 127.3, 126.0, 124.3, 124.2, 118.3, 108.4, 37.4, 20.7, 20.6, 18.8; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{17}H_{18}N$: 236.1440, found:236.1438.

Procedure for the TEMPO trapping of the photoreactions of 1c and 2A in high and low concentrations of water and MeOH. An aqueous CH_3CN solution (CH_3CN 18 mL, H_2O 2 mL) of **1c** (20 mM), **2A** (20 mM), Phen (5 mM), DCB (5 mM), and TEMPO (40 mM) in a Pyrex vessel (18 mm x 180 mm) was purged with Ar for 10 min. The mixture was irradiated with a 100 W high-pressure mercury lamp for 24 h, and then the solvent was removed without heating by blowing with air. The crude product (1:1 adduct with TEMPO) was measured by ^{1}H NMR (Figure S2 in SI) and FAB-Mass spectrometry. The photoreaction of **1c** (20 mM), **2A** (10 mM), Phen (5 mM), DCB (5 mM), and TEMPO (40 mM) in a low concentration of MeOH (200 mM) was carried out in a similar manner to detect 2:1 adduct with TEMPO by ^{1}H NMR (Figure S3 in SI) and FAB-Mass spectrometry. ***1:1 adduct with TEMPO***: HRMS (FAB, *m/z*) calcd for

$(M+H)^+$ $C_{15}H_{32}NO_3$: 274.2382, found: 274.2404. ***2:1 adduct with TEMPO***: HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{22}H_{46}NO_4$: 388.3427, found: 388.3412.

[2-D]-4-dodecyloxy-5-hydroxypentanenitrile (d-3aA): 0.164 g, 72%, white solid, mp 36–37 °C; IR (KBr, cm^{-1}) 3435, 2922, 2854, 2249; ^1H NMR (500 MHz, $CDCl_3$) δ 3.77–3.74 (m, 1H), 3.61–3.44 (m, 4H), 2.49–2.45 (m, 1H), 2.04–1.83 (m, 3H), 1.61–1.55 (m, 2H), 1.38–1.14 (m, 18H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.7, 77.5, 70.3, 63.0, 31.9, 30.1, 29.66, 29.65, 29.62, 29.5, 29.4, 27.2, 26.2, 22.7, 14.1, 13.2 (t, J = 20.3 Hz); HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{17}H_{33}DNO_2$: 285.2652, found: 285.2653.

2-dodecyloxyethanol (15): 0.096 g, 52%, colorless oil; IR (neat, cm^{-1}) 3467, 2896; ^1H NMR (500 MHz, $CDCl_3$) δ 3.74–3.72 (m, 2H), 3.54 (t, J = 4.5 Hz, 2H), 3.47 (t, J = 6.8 Hz, 2H), 2.06 (s (br), 1H), 1.60–1.56 (m, 2H), 1.38–1.14 (m, 18H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 71.7, 71.4, 61.9, 31.9, 29.64, 29.59, 29.47, 29.3, 26.1, 22.7, 14.1; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{14}H_{31}O_2$: 231.2324, found:231.2319.

Procedure for the preparation of vinyl ethers 1q–t from alcohols. Ethyl vinyl ether/CH_2Cl_2 = 5:3 (25:15 mL) solution containing Pd(II) acetate (0.05 g, 0.22 mmol) and 1,10-phenanthroline (0.04 g, 0.22 mmol) was stirred for 15 min. (*S*)-*N*-Boc Ser(OH)OMe (1.62 g, 7.4 mmol) was added, and the solution was stirred for 4 d at room temperature. The mixture was filtered through celite, and the filtrate was evaporated. Purification by column chromatography on silica gel using hexane/EtOAc = 20:1 as the eluent gave the corresponding vinyl ether **1q** (0.70 g, 39%). Vinyl ethers **1r**–**t** were prepared by the same method (**1r**: 38%, **1s**: 14%, **1t**: 73%).

(S)-N-Boc Ser(OCH=CH$_2$)OMe (1q): colorless oil; IR (neat, cm^{-1}) 3381, 3118, 2979, 2886, 1753, 1717; ^1H NMR (500 MHz, $CDCl_3$) δ 6.43 (dd, J = 14.0, 7.0 Hz, 1H), 5.37 (d (br), J = 7.5

Hz, 1H), 4.57–4.55 (m, 1H), 4.20 (dd, *J* = 14.0, 3.0 Hz, 1H), 4.11–4.08 (m, 1H), 4.06 (dd, *J* = 7.0, 3.0 Hz, 1H), 3.92 (dd, *J* = 10.0, 3.5 Hz, 1H), 3.78 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 154.6, 151.2, 87.5, 80.2, 67.9, 53.2, 52.7, 28.3; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{11}H_{20}NO_5$: 246.1342, found: 246.1341.

(R)-N-Boc Ser(OCH=CH$_2$)OMe (1r): colorless oil; IR (neat, cm^{-1}) 3385, 3120, 1754, 1714; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.43 (dd, *J* = 14.0, 7.0 Hz, 1H), 5.42 (d (br), *J* = 7.5 Hz, 1H), 4.57–4.55 (m, 1H), 4.20 (dd, *J* = 14.0, 3.0 Hz, 1H), 4.11–4.08 (m, 1H), 4.06 (dd, *J* = 7.0, 3.0 Hz, 1H), 3.92 (dd, *J* = 10.0, 3.5 Hz, 1H), 3.78 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 155.2, 151.0, 87.3, 80.0, 67.8, 53.1, 52.5, 28.1; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{11}H_{20}NO_5$: 246.1341, found: 246.1347.

(1S,2S)-N-Boc Thr(OCH=CH$_2$)OMe (1s): colorless oil; IR (neat, cm^{-1}) 3395, 3117, 2980, 1758, 1715; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.21 (dd, *J* = 14.0, 7.0 Hz, 1H), 5.31 (d (br), *J* = 9.0 Hz, 1H), 4.50–4.49 (m, 1H), 4.40–4.29 (m, 2H), 4.04–4.02 (m, 1H), 3.74 (s, 3H), 1.46 (s, 9H), 1.27 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 155.8, 149.7, 89.2, 79.7, 75.0, 57.3, 52.2, 28.0, 16.2; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{12}H_{22}NO_5$: 260.1498, found: 260.1479.

(1S,2R,4S)-bornyl vinyl ether (1t): colorless oil; IR (neat, cm^{-1}) 3116, 2982, 2952, 2878; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.40 (dd, *J* = 14.0, 7.0 Hz, 1H), 4.11 (dd, *J* = 14.0, 3.0 Hz, 1H), 4.01 (d, *J* = 10.0 Hz, 1H), 3.94 (dd, *J* = 7.0, 3.0 Hz, 1H), 2.25–2.19 (m, 1H), 2.02–1.96 (m, 1H), 1.75–1.66 (m, 2H), 1.29–1.20 (m, 2H), 1.08–1.05 (m, 1H), 0.90–0.83 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.8, 86.9, 83.7, 49.1, 47.7, 44.9, 36.4, 27.9, 26.7, 19.7, 18.8, 13.7; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{12}H_{21}O$: 181.1592, found: 181.1584.

(S)-N-Boc Ser(OCH(CH$_2$)$_2$CNCH$_2$OH)OMe (3qA): 0.189 g, 75%, colorless oil; IR (neat, cm^{-1}) 3392, 2978, 2881, 2247, 1753, 1714; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.49–5.65 (m, 1H), 4.48–4.46 (m, 1H), 4.01–3.91 (m, 2H), 3.79–3.70 (m, 4H), 3.56–3.51 (m, 2H), 2.49–2.40 (m, 2H), 2.18 (s, 1H), 1.92–1.83 (m, 2H), 1.46–1.43 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 171.2, 155.7, 155.5, 119.6, 119.5, 80.3, 79.1, 78.7, 70.4, 69.7, 63.1, 63.0, 54.2, 52.8, 52.7, 31.0, 28.3, 27.14, 27.08, 13.5, 13.3; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{14}H_{25}N_2O_6$: 317.1712, found: 317.1704.

(R)-N-Boc Ser(OCH(CH$_2$)$_2$CNCH$_2$OH)OMe (3rA): 0.193 g, 76%, colorless oil; IR (neat, cm^{-1}) 3452, 3019, 2872, 2248, 1744, 1714; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.60–5.46 (m, 1H), 4.49–4.47 (m, 1H), 4.01–3.91 (m, 2H), 3.82–3.70 (m, 4H), 3.56–3.51 (m, 2H), 2.50–2.39 (m, 2H), 1.94–1.83 (m, 2H), 1.49–1.43 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 171.2, 155.7, 119.6, 119.5, 80.4, 79.1, 78.7, 70.5, 69.8, 63.1, 63.0, 54.2, 52.8, 52.7, 28.3, 27.1, 27.1, 13.5, 13.3; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{14}H_{25}N_2O_6$: 317.1712, found: 317.1693.

(1S,2S)-N-Boc Thr(OCH(CH$_2$)$_2$CNCH$_2$OH)OMe (3sA): 0.208 g, 79%, colorless oil; IR (neat, cm^{-1}) 3505, 3104, 2248, 1744, 1714; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.30–5.16 (m, 1H),

4.38–4.32 (m, 1H), 4.21–4.16 (m, 1H), 3.82–3.76 (m, 3H), 3.68–3.43 (m, 3H), 2.49–2.36 (m, 2H), 1.93–1.80 (m, 2H), 1.59–1.46 (m, 9H), 1.34–1.25 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 171.6, 156.1, 119.7, 80.3, 80.2, 75.5, 74.7, 73.2, 63.8, 63.1, 58.3, 58.2, 52.7, 52.6, 28.3, 27.5, 27.3, 17.7, 16.3, 13.7, 13.0; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{15}H_{27}N_2O_6$: 331.1869, found: 331.1848.

4-bornyloxy-5-hydroxypentanenitrile (3tA): 0.155 g, 77%, colorless oil; IR (neat, cm^{-1}) 3465, 2974, 2863, 2249; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.76–3.65 (m, 2H), 3.55–3.48 (m, 2H), 2.51–2.48 (m, 2H), 2.20–1.87 (m, 5H), 1.74–1.65 (m, 2H), 1.25–1.21 (m, 2H), 1.02–0.97 (m, 1H), 0.91–0.81 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.9, 84.7, 82.7, 77.7, 75.4, 64.0, 62.5, 49.7, 49.3, 47.9, 47.7, 45.1, 45.0, 37.9, 36.5, 28.3, 28.0, 27.6, 26.6, 19.8, 18.91, 18.88, 14.0, 13.9, 13.7, 13.5; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_{15}H_{26}NO_2$: 252.1964, found: 252.1945.

Procedure for the hydrolysis of 3cA,iA and TFA treatment of 3cA. An aqueous NaOH solution (7.2 g, 180 mmol, 20 mL) was added to a MeOH solution (40 mL) of **3cA** or **3iA** (0.286 g, 1.7 mmol or 0.102 g, 0.6 mmol, respectively), and refluxed for 2 d. The mixture was washed with hexane, and the aqueous solution was acidified by the slow addition of 2.5 M H_2SO_4 at 0 °C until the pH decreased to 3, and then extracted with EtOAc. The organic layer was dried over Na_2SO_4 and the solvent was evaporated. For **3iA**, purification by column chromatography on silica gel using hexane/EtOAc = 10:1 as the eluent gave the corresponding lactone **21** (0.090 g, 99%). For **3cA**, TFA treatment was performed without purification. TFA (10 mL) was slowly added to a CH_2Cl_2 (15 mL) solution containing the hydrolyzed product derived from **3cA**, and stirred overnight at room temperature, and the solvent was evaporated. Purification by column chromatography on silica gel using hexane/EtOAc = 1:1 as the eluent gave the corresponding lactone **20** (0.118 g, 60%, 2 steps).

5-hydroxy-tetrahydropyran-2-one (20): Compound **20** has been previously reported.[21] colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.67–4.62 (m, 1H), 3.90 (dd, *J* = 12.5, 4.0 Hz, 1H), 3.66 (dd, *J* = 12.5, 4.0 Hz, 1H), 3.07 (s (br), 1H), 2.67–2.52 (m, 2H), 2.31–2.12 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.0, 81.0, 64.1, 28.7, 23.2.

octahydrocoumarin (21): Compound **21** has been previously reported.[22] colorless oil; IR (neat, cm^{-1}) 2939, 2860, 1731; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.50–4.46 (m, 0.3H), 3.91–3.86 (m, 0.7H), 2.70–2.50 (m, 2H), 2.18–1.84 (m, 4H), 1.73–1.23 (m, 6.3H), 1.11–1.04 (m, 0.7H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5, 171.6, 83.4, 78.3, 38.8, 32.6, 32.3, 31.1, 30.3, 29.9, 26.9, 26.53, 26.48, 25.2, 24.4, 24.3, 24.1, 20.1; HRMS (FAB, *m/z*) calcd for $(M+H)^+$ $C_9H_{15}O_2$: 155.1072, found:155.1056.

Supporting Information

Absorption spectra of BP, DCN, and **1a**. ^{1}H NMR spectra of the crude products using TEMPO. ^{1}H and ^{13}C NMR spectra for all compounds. This material is available free of charge via Internet at http://pubs.acs.org/.

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