

Accepted Manuscript

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PII: S0040-4020(15)00245-8

DOI: [10.1016/j.tet.2015.02.064](https://doi.org/10.1016/j.tet.2015.02.064)

Reference: TET 26453

To appear in: *Tetrahedron*

Received Date: 20 January 2015

Revised Date: 7 February 2015

Accepted Date: 17 February 2015

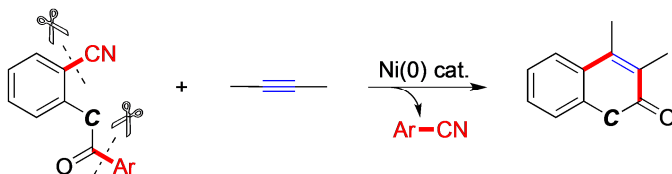
Please cite this article as: Nakai K, Kurahashi T, Matsubara S, Nickel-Catalyzed Dual C–C σ Bond Activation to Construct Carbocyclic Skeletons, *Tetrahedron* (2015), doi: 10.1016/j.tet.2015.02.064.

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Graphical Abstract

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Tetrahedron
journal homepage: www.elsevier.com



Nickel-Catalyzed Dual C–C σ Bond Activation to Construct Carbocyclic Skeletons

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ARTICLE INFO

Article history:

Received

Received in revised form

Accepted

Available online

Keywords:

C–C Bond Activation

Nickel Catalyst

Heterocyclic Compound

Carbocyclic Compound

ABSTRACT

A nickel/Lewis acid catalyzed intermolecular cycloaddition reaction of *o*-cyanobenzylarylketones with alkynes to form naphthalenones is developed. This reaction is promoted by the nickel/Lewis Acid catalyst pair and involves the cleavage of two C–C σ bonds to eliminate arylcyanide and the formation of different two C–C σ bonds with alkyne insertion.

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1. Introduction

Cycloaddition involving the cleavage of a C–C σ bond enables unprecedented, divergent, and direct transformations in organic syntheses. However, such reactions have not been successfully extended to the synthesis of carbocycles because the reaction conditions and mechanism have not yet been clearly established.^{1–2} For the successful application of this cycloaddition to carbocycles, it is necessary that the starting materials have high ring strain so that they readily undergo C–C bond cleavage; for this reason, the substrates used for the reaction thus far have been limited to cyclopropane^{2a–d} and cyclobutane derivatives.^{2e–i}

During the course of our study on nickel-catalyzed cycloadditions through the elimination of a small molecule to form heterocyclic compounds,^{3–5} we have recently reported cycloaddition reactions of nitriles with alkynes through the cleavage of two C–C σ bonds of esters and amides to form the corresponding heterocycles, coumarins, and quinolones.⁴ This new concept motivated us to investigate the [4+2] cycloaddition through two C–C σ bond cleavages to obtain carbocyclic compounds.

Herein, we report the cycloaddition of cyanoketones with alkynes to form naphthalenone derivatives.^{6–8} This reaction may open a new route for the divergent synthesis of highly substituted naphthalenone derivatives.

2. Results and Discussion

Initially we performed the reaction with cyanoketones **1** and 4-octyne **2a** in the presence of Ni(cod)₂/PMe₃/MAD⁹ (methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide)) in toluene at 120 °C (Table 1). The reaction of simple cyanoketone **1a** with **2a** (entry 1) afforded the corresponding naphthalenone derivative **3aa** in 73% yield (entry 1). Then, we investigated the effect of the leaving group of the substrate in greater detail. Substrates with an electron-donating group, such as **1b** or **1c**, resulted in lower yields (entries 2 and 3) presumably because of the stronger coordination of the Lewis acid MAD with the eliminated nitrile than with the substrate (ArCN; shown in the scheme above Table 1). Substrates with an electron-withdrawing group, **1d** or **1e**, did not result in any notable improvement in the product yield because of the poor leaving ability of the aryl group.

Table 1. Effect of the leaving aryl group of the substrate^a

entry	1	R	yield ^b (%)
1	1a	H	73
2	1b	OMe	59
3	1c	Me	65
4	1d	F	72
5	1e	CF ₃	28

^a Reactions were carried out using Ni(cod)₂ (10 mol %), PMe₃ (20 mol %), MAD: methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (30 mol %), **1** (0.2 mmol), and **2a** (0.6 mmol, 3.0 equiv) in 1.2 mL of toluene for 12 h. ^b GC yields based on **1**. Decane is used as an internal standard.

Table 2. Optimization of reaction conditions^a

entry	Lewis acid	ligand(mol %)	yield ^b (%)
1	MAD	PMe ₃ (20)	73
2	AlMe ₃	PMe ₃ (20)	0
3	AlMe ₂ Cl	PMe ₃ (20)	0
4	BPh ₃	PMe ₃ (20)	20
5	B(C ₆ F ₅) ₃	PMe ₃ (20)	10
6	none	PMe ₃ (20)	0
7	MAD	P(CH ₂ Ph) ₃ (20)	35
8	MAD	PMe ₂ Ph (20)	50
9	MAD	PPh ₃ (20)	16
10	MAD	dmpe ^c (20)	4
11	MAD	IPr ^d (20)	20
12	MAD	PMe ₃ (30)	73
13	MAD	PMe ₃ (40)	69
14	MAD	PMe ₃ (30)	86 ^{e,f}

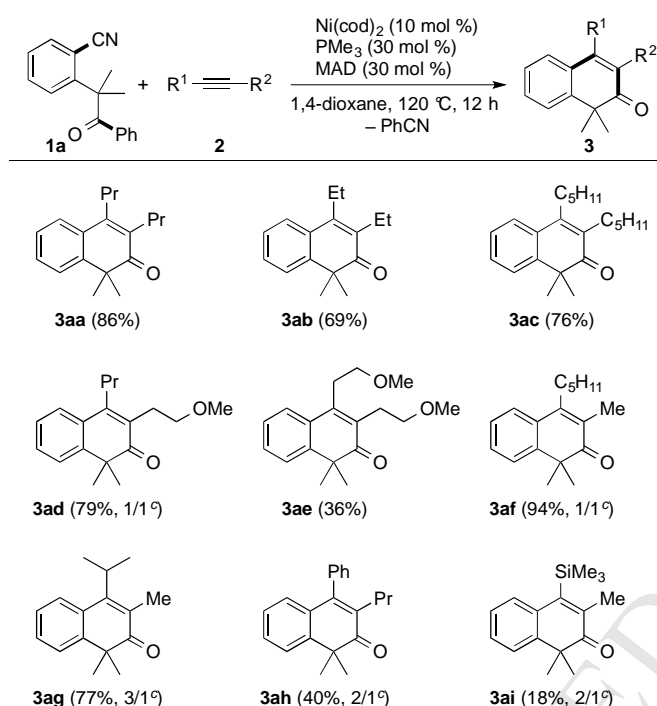
^a Reactions were carried out using Ni(cod)₂ (10 mol %), ligand, Lewis acid (30 mol %), **1a** (0.2 mmol), and **2a** (0.6 mmol, 3.0 equiv) in 1.2 mL of toluene for 12 h otherwise noted. ^b GC yields based on **1a**. Decane was used as an internal standard. ^c dmpe: 1,2-bis(dimethyl-phosphino)ethane. ^d IPr: 1,3-bis(2,6-diisopropylphenyl)-imidazol-2-ylidene. ^e 1,4-dioxane was used as solvent instead of toluene. ^f Isolated yield was given.

We next focused on optimizing the reaction conditions (Table 2). The reaction without any Lewis acid or with Lewis acids other than MAD led to low or zero yield (entries 2–6). P(CH₂Ph)₃ and PMe₂Ph, which were the best ligands for the synthesis of coumarins^{4a} and quinolones,^{4b} resulted in only moderate yields (entries 7 and 8). A relatively electron-deficient phosphine ligand, PPh₃, indicated no positive effect (entry 9). An electron-rich bidentate ligand, DMPE, and an *N*-heterocyclic carbene ligand, IPr, gave poor yields (entries 10 and 11). Finally it was found that using 30 mol% of PMe₃ and 1,4-dioxane as the solvent improved the yield to 86% (entries 12–14).

With the optimized conditions in hand, we performed the cycloaddition reaction with various alkynes (Table 3). The reaction of cyanoketone **1a** with 4-octyne **2a** afforded naphthalenone **3aa** in 86% yield, as shown above. Other symmetric alkynes such as 3-hexyne **2b** and 6-dodecyne **2c**, too, afforded the desired products in good-to-excellent yields. Alkynes bearing methoxy substituents (**2d**, **2e**) could participate in the reaction, but the yield was decreased when using an alkyne bearing two methoxy groups. In addition, no orientational effect of the methoxy group was observed in the reaction with alkyne **2d**. With 2-octyne **2f**, a 1:1 mixture of regioisomers was obtained in 94% yield. When 4-methyl-2-pentyne **2g**, a relatively bulkier alkyne, was used for the reaction, the regioselectivity of the isomers increased to 3:1, and the bulky substituents tended to be oriented close to the aryl ring. An aryl-substituted alkyne **2h** was tolerated in the reaction, although the product yield was only moderate. The major regioisomer of **3ah**

was confirmed by X-ray crystal structure analysis (Figure 1). On the other hand, an alkyne bearing a trimethylsilyl group **2i** was hardly transformed into naphthalenone **3ai**, and about 80% of **1a** remained intact under these reaction conditions. This is supposed to be due to steric as well as electronic factors in **2i**. Terminal alkynes such as 1-octyne and phenylacetylene failed to participate in the reaction because they underwent rapid oligomerization. Furthermore, as shown in Scheme 2, cyclopentane derivative **1f** proved to be highly reactive under the reaction conditions, and the corresponding spirocyclic naphthalenone derivative **3fa** was obtained in 87% yield, while the reaction of non-substituted cyanoketone **1g** afforded naphthol **4ga** in 31% yield.

Table 3. Cycloaddition to form naphthalenones^{a,b}



^a Reactions were carried out using Ni(cod)₂ (10 mol %), PMe₃ (30 mol %), MAD (30 mol %), **1a** (0.2 mmol), and **2** (0.6 mmol, 3.0 equiv) in 1.2 mL of 1,4-dioxane for 12 h. ^b Isolated yield based on **1a** was given. ^c Ratio of regioisomers.

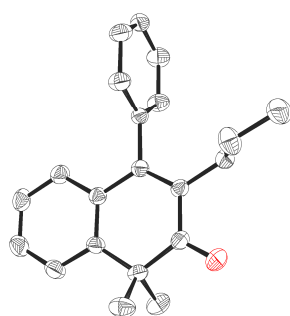
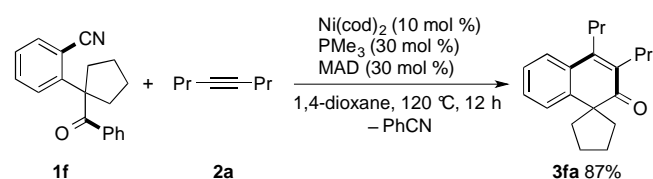
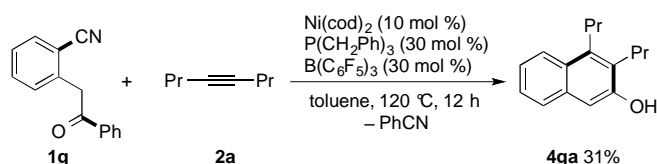


Figure 1. ORTEP drawing of **3ah**



Scheme 2. Synthesis of spirocyclic naphthalenone **3fa**



Scheme 4. Synthesis of naphthol **4ga**

In conclusion, we have developed a nickel-catalyzed cycloaddition reaction of cyanoketones with alkynes to form naphthalenone derivatives through the cleavage of two C–C σ bonds. The reaction requires both a nickel catalyst and a Lewis acid cocatalyst. Various naphthalenones, including a spirocyclic moiety, could be synthesized by using this catalytic system. Efforts for broadening the substrate scope and elucidating the reaction mechanism in detail are currently underway.

3. Experimental

3.1. General

All manipulations of oxygen- and moisture-sensitive materials were conducted in a dry box or with a standard Schlenk technique under a purified argon atmosphere. Nuclear magnetic resonance spectra were taken on Varian UNITY INOVA 500 (¹H, 500 MHz; ¹³C, 125.7 MHz) spectrometer using tetramethylsilane (¹H) as an internal standard. ¹H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, br = broad, m = multiplet), coupling constants (Hz), integration, and identification. Mass spectra were recorded on a SHIMADZU GCMS-QP2010 Plus (EI) and a Thermo Scientific Exactive (ESI) spectrometers. Infrared (IR) spectra were determined on a SHIMADZU IR Affinity-1 spectrometer. Melting points were determined using a YANAKO MP-500D. X-ray data were taken on a Rigaku XtaLAB mini diffractometer equipped with a CCD detector. TLC analyses were performed by means of Merck Kieselgel 60 F₂₅₄ (0.25 mm) Plates. Visualization was accomplished with UV light (254 nm) and/or an aqueous alkaline KMnO₄ solution followed by heating. Flash column chromatography was carried out using Kanto Chemical silica gel (spherical, 40–50 μ m). Unless otherwise noted, commercially available reagents were used without purification. Bis(1,5-cyclooctadiene)nickel and trimethylphosphine were purchased from Strem Chemicals, Inc. Methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD) was purchased as a solution in toluene from Tokyo Chemicals Industry Co., Ltd. Cyanobenzylarylketones **1** were prepared according to the literature.¹⁰

3.2. Experimental Procedure and Characterization Data for Substrates.

General procedure. Preparation of the compounds was accomplished by a similar procedure to the patent.¹¹ To a solution of sodium hydride (0.9 g of 60% in oil, 22.5 mmol) and tetrahydrofuran (10 mL) was portionwise added a solution of deoxybenzoin derivative (10 mmol) and methyl iodide (1.56 mL, 25 mmol) in tetrahydrofuran (10 mL) at 0 °C, warmed to 25 °C, stirred at 25 °C for 18 hours, cooled to 0 °C, and quenched by addition of acetic acid (1 drop). A solution of the residue in ethyl acetate was washed with water, saturated sodium bicarbonate solution (twice) and saturated sodium chloride solution, dried (Na₂SO₄), filtered and concentrated in vacuo to afford an oil,

which was purified by flash silica gel column chromatography to give the dimethylated substrate (**1a–1e**).

2-(2-Methyl-1-oxo-1-phenyl-2-propyl)benzonitrile (1a).

¹H NMR (CDCl₃) δ 7.70–7.64 (m, 2H; Ar–H), 7.58 (dd, *J* = 1.5, 6.5 Hz, 2H; Ar–H), 7.54 (dd, *J* = 1.0, 7.5 Hz, 1H; Ar–H), 7.38 (tt, *J* = 1.0, 7.0 Hz, 1H; Ar–H), 7.35 (ddd, *J* = 2.0, 7.0, 7.5 Hz, 1H; Ar–H), 7.23 (ddd, *J* = 1.0, 7.5, 7.5 Hz, 1H; Ar–H), 1.79 (s, 6H; 2CH₃). ¹³C NMR (CDCl₃) δ 201.4, 149.2, 135.4, 135.2, 133.6, 132.3, 129.9, 128.2, 127.4, 126.2, 118.0, 111.9, 52.1, 27.9.

2-(1-(4-Methoxyphenyl)-2-methyl-1-oxo-2-propyl)benzonitrile (1b).

¹H NMR (CDCl₃) δ 7.69–7.64 (m, 2H; Ar–H), 7.57 (d, *J* = 9.5 Hz, 2H; Ar–H), 7.56 (tt, *J* = 1.0, 7.0 Hz, 1H; Ar–H), 7.35 (ddd, *J* = 2.5, 6.5, 6.5 Hz, 1H; Ar–H), 6.70 (d, *J* = 9.5 Hz, 2H; Ar–H), 3.77 (s, 3H; OCH₃), 1.77 (s, 6H; 2CH₃). ¹³C NMR (CDCl₃) δ 199.7, 162.7, 149.7, 135.3, 133.6, 132.4, 128.1, 127.3, 126.1, 118.0, 113.4, 112.0, 55.5, 51.8, 28.0.

2-(2-Methyl-1-oxo-1-(*p*-tolyl)-2-propyl)benzonitrile (1c).

¹H NMR (CDCl₃) δ 7.69–7.64 (m, 1H; Ar–H), 7.65 (ddd, *J* = 1.5, 7.0, 8.0 Hz, 1H; Ar–H), 7.55 (dd, *J* = 1.0, 8.5 Hz, 1H; Ar–H), 7.48 (d, *J* = 8.0 Hz, 2H; Ar–H), 7.34 (ddd, *J* = 2.0, 6.5, 8.0 Hz, 1H; Ar–H), 7.02 (d, *J* = 8.0 Hz, 2H; Ar–H), 2.29 (s, 3H; CH₃), 1.78 (s, 6H; 2CH₃). ¹³C NMR (CDCl₃) δ 200.9, 149.6, 143.1, 135.3, 133.5, 132.8, 130.2, 128.9, 127.3, 126.2, 118.0, 112.0, 52.0, 28.0, 21.7.

2-(1-(4-Fluorophenyl)-2-methyl-1-oxo-2-propyl)benzonitrile (1d).

¹H NMR (CDCl₃) δ 7.70–7.65 (m, 2H; Ar–H), 7.60 (ddd, *J* = 2.5, 5.5, 9.5 Hz, 2H; Ar–H), 7.56 (ddd, *J* = 1.0, 1.5, 7.5 Hz, 1H; Ar–H), 7.39–7.34 (m, 1H; Ar–H), 6.90 (ddd, *J* = 2.5, 8.5, 9.0 Hz, 1H; Ar–H), 1.78 (s, 6H; 2CH₃). ¹³C NMR (CDCl₃) δ 199.8, 165.0 (d, *J* = 255 Hz, C–F), 149.1, 135.3, 133.7, 132.6 (d, *J* = 9.2 Hz, CCC–F), 131.7 (d, *J* = 3.4 Hz, CCCC–F), 127.6, 126.1, 117.9, 115.4 (d, *J* = 21.6 Hz, CC–F), 112.0, 52.0, 27.9. ¹⁹F NMR (CDCl₃) δ –106.4.

2-(2-Methyl-1-oxo-1-(4-(trifluoromethyl)phenyl)-2-propyl)benzonitrile (1e).

¹H NMR (CDCl₃) δ 7.72–7.66 (m, 4H; Ar–H), 7.55 (d, *J* = 7.5 Hz, 1H; Ar–H), 7.49 (d, *J* = 8.0 Hz, 2H; Ar–H), 7.35 (ddd, *J* = 3.0, 6.0, 8.0 Hz, 1H; Ar–H), 1.80 (s, 6H; 2CH₃). ¹³C NMR (CDCl₃) δ 200.6, 148.5, 138.7, 135.3, 133.8, 133.5 (q, *J* = 32.7 Hz, C–CF₃), 130.0, 127.8, 126.2, 125.2 (q, *J* = 3.9 Hz, C–CCF₃), 123.7 (q, *J* = 273 Hz, CF₃), 117.9, 112.0, 52.3, 27.7. ¹⁹F NMR (CDCl₃) δ –63.7.

2-(1-Benzoylcyclopentyl)benzonitrile (1f).

The general procedure was followed using 1,4-dibromobutane (12.5 mmol) instead of methyl iodide, which afforded the compound **1f**. ¹H NMR (CDCl₃) δ 7.64–7.56 (m, 4H; Ar–H), 7.54 (dd, *J* = 1.0, 7.5 Hz, 1H; Ar–H), 7.36 (tt, *J* = 1.5, 7.5 Hz, 1H; Ar–H), 7.28 (ddd, *J* = 2.5, 6.5, 9.0 Hz, 1H; Ar–H), 7.23 (ddd, *J* = 2.0, 7.5, 7.5 Hz, 1H; Ar–H), 2.77–2.70 (m, 2H; CH₂), 2.32–2.25 (m, 2H; CH₂), 1.91–1.80 (m, 4H; 2CH₂). ¹³C NMR (CDCl₃) δ 200.2, 148.7, 136.0, 135.4, 133.1, 132.1, 129.9, 128.2, 127.1, 126.8, 118.1, 112.1, 110.0, 63.4, 38.0, 25.6.

2-(2-Oxo-2-phenylethyl)benzonitrile (1g) : CAS RN [10517-64-3].

¹H NMR (CDCl₃) δ 8.05 (dd, *J* = 1.0, 8.5 Hz, 2H; Ar–H), 7.69 (dd, *J* = 1.0, 8.5 Hz, 1H; Ar–H), 7.61 (tt, *J* = 2.0, 7.5 Hz, 1H; Ar–

H), 7.57 (ddd, *J* = 1.0, 8.0, 8.0 Hz, 1H; Ar–H), 7.51 (ddd, *J* = 2.0, 7.5, 8.0 Hz, 2H; Ar–H), 7.39 (ddd, *J* = 1.0, 6.0, 8.0 Hz, 2H; Ar–H), 4.55 (s, 2H; CH₂). ¹³C NMR (CDCl₃) δ 195.6, 138.8, 136.5, 133.8, 133.0, 132.9, 131.2, 129.0, 128.6, 127.8, 118.0, 113.9, 43.8.

3.3. Experimental Procedure and Characterization Data for Products.

General procedure. The reaction was performed in a 15 mL sealed tube equipped with a Teflon-coated magnetic stirrer. A ketone (0.2 mmol) and an alkyne (0.6 mmol) were added to a solution of bis(1,5-cyclooctadiene)nickel (5.5 mg, 0.02 mmol), trimethylphosphine (0.06 mmol), and methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD) (0.06 mmol) in 1,4-dioxane (1.2 mL) in a dry box. The tube was taken outside the dry box and heated at 120 °C for the indicated time under argon atmosphere. The resulting reaction mixture was cooled to ambient temperature and filtered through a silica gel pad, concentrated in vacuo. The residue was purified by flash silica gel column chromatography (20 g, 2x15 cm, hexane/ethyl acetate = 20:1, hexane/toluene = 2:1, or hexane/triethylamine = 40:1) to give the corresponding naphthalenone.

1,1-Dimethyl-3,4-dipropylnaphthalen-2(1H)-one (3aa).

Yield: 86%, colorless oil. TLC: R_f 0.32 (hexane/ethyl acetate=20/1). ¹H NMR (CDCl₃) δ 7.54 (dd, *J* = 1.5, 7.5 Hz, 1H; Ar–H), 7.43 (dd, *J* = 1.0, 7.5 Hz, 1H; Ar–H), 7.33 (ddd, *J* = 2.0, 7.5, 8.0 Hz, 1H; Ar–H), 7.28 (ddd, *J* = 1.0, 7.5, 8.0 Hz, 1H; Ar–H), 2.73 (t, *J* = 8.0 Hz, 2H; CH₂), 2.49 (t, *J* = 8.0 Hz, 2H; CH₂), 1.65 (tq, *J* = 7.5, 8.0 Hz, 2H; CH₂), 1.44 (tq, *J* = 7.5, 8.0 Hz, 2H; CH₂), 1.44 (s, 6H; 2CH₃), 1.09 (t, *J* = 7.5 Hz, 3H; CH₃), 0.98 (t, *J* = 7.5 Hz, 3H; CH₃). ¹³C NMR (CDCl₃) δ 204.2, 149.2, 146.9, 133.6, 130.1, 128.7, 126.6, 126.1, 125.7, 46.8, 31.8, 28.7, 28.0, 23.0, 22.8, 14.8, 14.6. IR (neat): 2963, 2931, 2871, 1654, 1608, 1459, 1378, 1085, 757 cm⁻¹. MS *m/z* (%): 257/256 (13/70) [M⁺], 242/241 (14/82) [M⁺–Me], 228/227 (2/5) [M⁺–Et], 214/213 (19/100) [M⁺–Pr], 199 (68), 185 (36), 171 (69), 157 (58), 143 (73), 128 (42), 115 (28). HRMS (ESI⁺) Calcd for C₁₈H₂₅O [M+H]⁺ 257.1900, found 257.1897.

3,4-Diethyl-1,1-dimethylnaphthalen-2(1H)-one (3ab).

Yield: 69%, colorless oil. TLC: R_f 0.29 (hexane/ethyl acetate=20/1). ¹H NMR (CDCl₃) δ 7.58 (dd, *J* = 1.0, 8.0 Hz, 1H; Ar–H), 7.44 (dd, *J* = 1.5, 7.5 Hz, 1H; Ar–H), 7.34 (ddd, *J* = 1.0, 7.5, 8.0 Hz, 1H; Ar–H), 7.29 (ddd, *J* = 1.5, 7.0, 8.0 Hz, 1H; Ar–H), 2.80 (q, *J* = 7.5 Hz, 2H; CH₂), 2.54 (q, *J* = 7.5 Hz, 2H; CH₂), 1.45 (s, 6H; 2CH₃), 1.27 (t, *J* = 7.5 Hz, 3H; CH₃), 1.06 (t, *J* = 7.5 Hz, 3H; CH₃). ¹³C NMR (CDCl₃) δ 203.9, 150.3, 147.1, 134.5, 129.9, 128.7, 126.6, 126.1, 125.6, 46.8, 28.0, 22.6, 19.7, 14.1, 13.9. IR (neat): 2970, 1654, 1648, 1610, 1459, 1379, 1347, 1262, 1061, 760 cm⁻¹. MS *m/z* (%): 229/228 (10/65) [M⁺], 214/213 (6/36) [M⁺–Me], 200/199 (4/8) [M⁺–Et], 186/185 (23/100), 171 (69), 157 (89), 143 (37), 128 (31). HRMS (ESI⁺) Calcd for C₁₆H₂₁O [M+H]⁺ 229.1587, found 229.1585.

1,1-Dimethyl-3,4-dipentyl-naphthalen-2(1H)-one (3ac).

Yield: 76%, colorless oil. TLC: R_f 0.35 (hexane/ethyl acetate=20/1). ¹H NMR (CDCl₃) δ 7.54 (dd, *J* = 1.5, 8.0 Hz, 1H; Ar–H), 7.43 (dd, *J* = 1.5, 7.5 Hz, 1H; Ar–H), 7.33 (ddd, *J* = 1.5, 7.5, 7.5 Hz, 1H; Ar–H), 7.28 (ddd, *J* = 1.5, 7.5, 8.0 Hz, 1H; Ar–H), 2.73 (dd, *J* = 8.0, 8.5 Hz, 2H; CH₂), 2.50 (dd, *J* = 6.5, 9.0 Hz, 2H; CH₂), 1.65–1.56 (m, 2H; CH₂), 1.52–1.33 (m, 10H; CH₂), 1.44 (s, 6H; 2CH₃), 0.94 (t, *J* = 7.5 Hz, 3H; CH₃), 0.91 (t, *J* = 7.0 Hz, 3H; CH₃). ¹³C NMR (CDCl₃) δ 204.1, 149.3, 147.0, 133.7, 130.2, 128.7, 126.6, 126.1, 125.6, 46.8, 32.6, 32.4, 30.0, 29.4,

29.2, 28.1, 26.7, 22.7, 22.7, 14.2, 14.2. IR (neat): 2958, 2929, 2860, 1654, 1608, 1466, 1378, 1351, 1262, 1092, 757 cm^{-1} . MS m/z (%): 313/312 (2/5) $[\text{M}^+]$, 298/297 (3/12) $[\text{M}^+-\text{Me}]$, 270/269 (3/13) $[\text{M}^+-\text{Pr}]$, 242/241 (21/100) $[\text{M}^+-\text{C}_5\text{H}_{11}]$, 185 (26), 157 (17), 143 (26). HRMS (ESI^+) Calcd for $\text{C}_{22}\text{H}_{33}\text{O}$ $[\text{M}+\text{H}]^+$ 313.2526, found 313.2522.

3-(2-Methoxyethyl)-1,1-dimethyl-4-propylnaphthalen-2(1H)-one (3ad).

Yield: 40%, pale yellow oil. TLC: R_f 0.34 (hexane/ethyl acetate=10/1). ^1H NMR (CDCl_3) δ 7.56 (dd, $J = 1.5, 7.5$ Hz, 1H; Ar-H), 7.44 (dd, $J = 1.5, 7.5$ Hz, 1H; Ar-H), 7.34 (ddd, $J = 1.5, 7.5, 8.0$ Hz, 1H; Ar-H), 7.29 (ddd, $J = 1.5, 7.5, 8.0$ Hz, 1H; Ar-H), 3.44 (t, $J = 7.5$ Hz, 2H; OCH_2), 3.34 (s, 3H; OCH_3), 2.84 (t, $J = 7.5$ Hz, 2H; CH_2), 2.78 (t, $J = 8.0$ Hz, 2H; CH_2), 1.65 (tq, $J = 7.5, 8.0$ Hz, 2H; CH_2), 1.45 (s, 6H; 2CH_3), 1.09 (t, $J = 7.5$ Hz, 3H; CH_3). ^{13}C NMR (CDCl_3) δ 204.1, 151.2, 147.0, 130.0, 129.8, 129.0, 126.7, 126.1, 125.9, 71.8, 58.7, 46.9, 31.9, 28.0, 27.4, 23.0, 14.7. IR (neat): 2966, 2930, 2872, 1654, 1608, 1459, 1379, 1349, 1261, 1115, 759 cm^{-1} . MS m/z (%): 273/272 (11/50) $[\text{M}^+]$, 258/257 (2/10) $[\text{M}^+-\text{Me}]$, 240 (30), 225 (100), 197 (41), 183 (31), 157 (43), 143 (30), 45 (37), 43 (40). HRMS (ESI^+) Calcd for $\text{C}_{18}\text{H}_{25}\text{O}_2$ $[\text{M}+\text{H}]^+$ 273.1849, found 273.1845.

4-(2-Methoxyethyl)-1,1-dimethyl-3-propylnaphthalen-2(1H)-one (3ad').

Yield: 39%, colorless oil. TLC: R_f 0.40 (hexane/ethyl acetate=10/1). ^1H NMR (CDCl_3) δ 7.61 (dd, $J = 1.5, 8.0$ Hz, 1H; Ar-H), 7.44 (dd, $J = 1.5, 7.0$ Hz, 1H; Ar-H), 7.34 (ddd, $J = 1.5, 7.5, 7.5$ Hz, 1H; Ar-H), 7.30 (ddd, $J = 1.5, 7.5, 7.5$ Hz, 1H; Ar-H), 3.60 (t, $J = 7.5$ Hz, 2H; OCH_2), 3.39 (s, 3H; OCH_3), 3.10 (t, $J = 7.5$ Hz, 2H; CH_2), 2.52 (t, $J = 8.0$ Hz, 2H; CH_2), 1.45 (tq, $J = 7.5, 8.0$ Hz, 2H; CH_2), 1.44 (s, 6H; 2CH_3), 0.99 (t, $J = 7.5$ Hz, 3H; CH_3). ^{13}C NMR (CDCl_3) δ 204.0, 146.8, 144.9, 135.2, 130.1, 128.9, 126.8, 126.1, 125.6, 71.6, 59.0, 47.0, 30.2, 28.8, 28.0, 22.8, 14.6. IR (neat): 2964, 2930, 2871, 1648, 1608, 1458, 1379, 1261, 1113, 758 cm^{-1} . MS m/z (%): 273/272 (12/53) $[\text{M}^+]$, 258/257 (4/20) $[\text{M}^+-\text{Me}]$, 225 (54), 197 (53), 211 (24), 197 (52), 183 (27), 169 (34), 155 (32), 45 (100). HRMS (ESI^+) Calcd for $\text{C}_{18}\text{H}_{25}\text{O}_2$ $[\text{M}+\text{H}]^+$ 273.1849, found 273.1844.

3,4-Bis(2-methoxyethyl)-1,1-dimethylnaphthalen-2(1H)-one (3ae).

Yield: 36%, colorless oil. TLC: R_f 0.13 (hexane/ethyl acetate=10/1). ^1H NMR (CDCl_3) δ 7.63 (dd, $J = 1.0, 8.0$ Hz, 1H; Ar-H), 7.44 (dd, $J = 1.5, 7.5$ Hz, 1H; Ar-H), 7.35 (ddd, $J = 1.0, 7.5, 7.5$ Hz, 1H; Ar-H), 7.30 (ddd, $J = 1.5, 7.5, 7.5$ Hz, 1H; Ar-H), 3.61 (t, $J = 7.5$ Hz, 2H; CH_2), 3.45 (t, $J = 7.0$ Hz, 2H; CH_2), 3.37 (s, 3H; OCH_3), 3.32 (s, 3H; OCH_3), 3.15 (t, $J = 7.5$ Hz, 3H; CH_2), 2.87 (t, $J = 7.0$ Hz, 3H; CH_2), 1.45 (s, 6H; 2CH_3). ^{13}C NMR (CDCl_3) δ 203.9, 147.0, 146.8, 131.6, 130.0, 129.1, 126.8, 126.1, 125.8, 71.6, 71.5, 59.0, 58.7, 47.0, 30.4, 27.9, 27.5. IR (neat): 2975, 2928, 2873, 2826, 2360, 1654, 1610, 1459, 1380, 1347, 1261, 1192, 1113, 759 cm^{-1} . MS m/z (%): 289/288 (2/12) $[\text{M}^+]$, 257/256 (4/19), 241 (15), 229 (30), 211 (30), 209 (30), 45 (100). HRMS (ESI^+) Calcd for $\text{C}_{18}\text{H}_{25}\text{O}_3$ $[\text{M}+\text{H}]^+$ 289.1798, found 289.1794.

1,1,3-Trimethyl-4-pentylnaphthalen-2(1H)-one (3af).

Yield: 47%, colorless oil. TLC: R_f 0.19 (hexane/ethyl acetate=20/1). ^1H NMR (CDCl_3) δ 7.55 (dd, $J = 1.5, 8.0$ Hz, 1H; Ar-H), 7.45 (dd, $J = 1.5, 7.5$ Hz, 1H; Ar-H), 7.34 (ddd, $J = 1.5, 7.5, 7.5$ Hz, 1H; Ar-H), 7.29 (ddd, $J = 1.5, 7.5, 7.5$ Hz, 1H; Ar-H), 2.75 (t, $J = 8.0$ Hz, 2H; CH_2), 2.04 (s, 3H; CH_3), 1.59 (tq, $J =$

7.5, 8.0 Hz, 2H; CH_2), 1.50–1.37 (m, 4H; 2CH_2), 1.45 (s, 6H; 2CH_3), 0.93 (t, $J = 7.0$ Hz, 3H; CH_3). ^{13}C NMR (CDCl_3) δ 204.2, 150.3, 147.0, 129.9, 128.8, 128.8, 126.6, 126.3, 125.4, 46.6, 32.5, 30.1, 28.5, 28.5, 22.7, 14.2, 12.3. IR (neat): 2959, 2929, 2862, 2360, 1652, 1611, 1566, 1491, 1466, 1445, 1379, 1340, 1268, 1035, 756 cm^{-1} . MS m/z (%): 257/256 (8/41) $[\text{M}^+]$, 242/241 (6/35) $[\text{M}^+-\text{Me}]$, 214/213 (7/21) $[\text{M}^+-\text{Pr}]$, 200 (10), 185 (17), 171 (28), 157 (100), 143 (34). HRMS (ESI^+) Calcd for $\text{C}_{18}\text{H}_{25}\text{O}$ $[\text{M}+\text{H}]^+$ 257.1900, found 257.1894.

1,1,4-Trimethyl-3-pentylnaphthalen-2(1H)-one (3af').

Yield: 47%, pale yellow oil. TLC: R_f 0.20 (hexane/ethyl acetate=20/1). ^1H NMR (CDCl_3) δ 7.58 (dd, $J = 1.5, 7.5$ Hz, 1H; Ar-H), 7.43 (dd, $J = 1.5, 7.5$ Hz, 1H; Ar-H), 7.34 (ddd, $J = 1.5, 7.5, 7.5$ Hz, 1H; Ar-H), 7.29 (ddd, $J = 1.5, 7.5, 7.5$ Hz, 1H; Ar-H), 2.54 (t, $J = 7.0$ Hz, 2H; CH_2), 2.36 (s, 3H; CH_3), 1.45 (s, 6H; 2CH_3), 1.43–1.30 (m, 6H; 3CH_2), 0.89 (t, $J = 7.5$ Hz, 3H; CH_3). ^{13}C NMR (CDCl_3) δ 203.6, 146.4, 145.2, 134.2, 131.2, 128.8, 126.6, 125.8, 125.5, 46.7, 32.2, 29.0, 28.1, 26.6, 22.7, 16.5, 14.3. IR (neat): 2958, 2929, 2860, 2360, 1651, 1613, 1458, 1380, 1261, 1097, 755 cm^{-1} . MS m/z (%): 257/256 (2/12) $[\text{M}^+]$, 242/241 (13/67) $[\text{M}^+-\text{Me}]$, 214/213 (6/29) $[\text{M}^+-\text{Pr}]$, 185 (37), 171 (18), 157 (100), 141 (26). HRMS (ESI^+) Calcd for $\text{C}_{18}\text{H}_{25}\text{O}$ $[\text{M}+\text{H}]^+$ 257.1900, found 257.1894.

4-Isopropyl-1,1,3-trimethylnaphthalen-2(1H)-one (3ag).

Yield: 58%, colorless oil. TLC: R_f 0.16 (hexane/ethyl acetate=20/1). ^1H NMR (CDCl_3) δ 7.72 (dd, $J = 1.5, 8.0$ Hz, 1H; Ar-H), 7.44 (dd, $J = 1.5, 7.5$ Hz, 1H; Ar-H), 7.30 (ddd, $J = 1.5, 8.0, 8.0$ Hz, 1H; Ar-H), 7.25 (ddd, $J = 1.5, 7.5, 8.0$ Hz, 1H; Ar-H), 3.53 (sept, $J = 7.0$ Hz, 1H; CH), 2.08 (s, 3H; CH_3), 1.46 (s, 6H; 2CH_3), 1.45 (d, $J = 7.0$ Hz, 6H; 2CH_3). ^{13}C NMR (CDCl_3) δ 205.4, 154.1, 146.5, 130.2, 128.7, 128.3, 126.4, 126.1, 126.0, 46.7, 30.5, 28.1, 21.0, 12.8. IR (neat): 3062, 2969, 2932, 2875, 2360, 1652, 1600, 1564, 1487, 1458, 1379, 1331, 1260, 1111, 1043, 757 cm^{-1} . MS m/z (%): 229/228 (8/40) $[\text{M}^+]$, 214/213 (4/27) $[\text{M}^+-\text{Me}]$, 186/185 (22/52) $[\text{M}^+-i\text{Pr}]$, 170 (27), 157 (100), 142 (28). HRMS (ESI^+) Calcd for $\text{C}_{16}\text{H}_{21}\text{O}$ $[\text{M}+\text{H}]^+$ 229.1587, found 229.1589.

3-Isopropyl-1,1,4-trimethylnaphthalen-2(1H)-one (3ag').

Yield: 19%, colorless oil. TLC: R_f 0.23 (hexane/ethyl acetate=20/1). ^1H NMR (CDCl_3) δ 7.56 (dd, $J = 1.5, 7.5$ Hz, 1H; Ar-H), 7.40 (dd, $J = 1.0, 7.0$ Hz, 1H; Ar-H), 7.31 (ddd, $J = 2.0, 7.0, 7.5$ Hz, 1H; Ar-H), 7.28 (ddd, $J = 1.5, 7.5, 7.5$ Hz, 1H; Ar-H), 3.20 (sept, $J = 7.0$ Hz, 1H; CH), 2.35 (s, 3H; CH_3), 1.44 (s, 6H; 2CH_3), 1.27 (d, $J = 7.0$ Hz, 6H; 2CH_3). ^{13}C NMR (CDCl_3) δ 204.7, 146.0, 143.3, 138.6, 131.9, 128.6, 126.6, 125.7, 125.4, 47.5, 28.7, 26.8, 20.9, 15.9. IR (neat): 2958, 2872, 2360, 1668, 1604, 1566, 1457, 1382, 1332, 1261, 1086, 932, 858, 755 cm^{-1} . MS m/z (%): 229/228 (5/33) $[\text{M}^+]$, 214/213 (2/9) $[\text{M}^+-\text{Me}]$, 186/185 (18/100) $[\text{M}^+-i\text{Pr}]$, 157 (31), 143 (27). HRMS (ESI^+) Calcd for $\text{C}_{16}\text{H}_{21}\text{O}$ $[\text{M}+\text{H}]^+$ 229.1587, found 229.1587.

1,1-Dimethyl-4-phenyl-3-propylnaphthalen-2(1H)-one (3ah).

Yield: 26%, colorless solid. Mp. 67–68 °C (hexane). TLC: R_f 0.27 (hexane/ethyl acetate=20/1). ^1H NMR (CDCl_3) δ 7.50–7.45 (m, 3H; Ar-H), 7.43 (tt, $J = 2.0, 7.5$ Hz, 1H; Ar-H), 7.30 (ddd, $J = 1.5, 7.5, 7.5$ Hz, 1H; Ar-H), 7.20 (dd, $J = 1.5, 8.0$ Hz, 2H; Ar-H), 7.09 (ddd, $J = 1.5, 7.5, 8.0$ Hz, 1H; Ar-H), 6.77 (dd, $J = 1.0, 7.5$ Hz, 1H; Ar-H), 2.17 (t, $J = 8.0$ Hz, 2H; CH_2), 1.55 (s, 6H; 2CH_3), 1.32 (tq, $J = 7.5, 8.0$ Hz, 2H; CH_2), 0.76 (t, $J = 7.5$ Hz, 3H; CH_3). ^{13}C NMR (CDCl_3) δ 204.4, 150.7, 146.6, 138.0, 134.1, 131.4, 129.0, 128.9, 128.7, 128.6, 127.8, 126.4, 125.9, 47.2, 29.8, 28.1, 22.5, 14.5. IR (KBr): 2960, 1642, 1564, 1486, 1442, 1375, 1353, 768, 757, 707 cm^{-1} . MS m/z (%): 291/290

(23/100) [M⁺], 276/275 (27/97) [M⁺-Me], 247 (84), 231 (35), 219 (57), 203 (59), 44 (90). HRMS (ESI⁺) Calcd for C₂₁H₂₃O [M+H]⁺ 291.1743, found 291.1739.

1,1-Dimethyl-3-phenyl-4-propylnaphthalen-2(1H)-one (3ah').

Yield: 13%, colorless solid. Mp. 120 °C (hexane). TLC: R_f 0.15 (hexane/ethyl acetate=20/1). ¹H NMR (CDCl₃) δ 7.63 (dd, *J* = 1.0, 8.0 Hz, 1H; Ar-H), 7.52 (dd, *J* = 1.0, 7.5 Hz, 1H; Ar-H), 7.44–7.38 (m, 3H; Ar-H), 7.34 (ddd, *J* = 1.0, 7.5, 7.5 Hz, 2H; Ar-H), 7.14 (dd, *J* = 1.5, 8.0 Hz, 2H; Ar-H), 2.57 (t, *J* = 8.0 Hz, 2H; CH₂), 1.59 (tq, *J* = 7.5, 8.0 Hz, 2H; CH₂), 1.54 (s, 6H; 2CH₃), 0.87 (t, *J* = 7.5 Hz, 3H; CH₃). ¹³C NMR (CDCl₃) δ 203.3, 151.0, 147.5, 136.9, 134.9, 129.8, 129.6, 129.5, 128.3, 127.4, 126.7, 126.5, 126.3, 47.5, 32.8, 28.0, 23.3, 14.5. IR (KBr): 2960, 2360, 1654, 1346, 769 cm⁻¹. MS *m/z* (%): 291/290 (15/68) [M⁺], 262 (28), 233 (29), 219 (100), 204/203/202 (29/31/33), 91 (32), 44 (48). HRMS (ESI⁺) Calcd for C₂₁H₂₃O [M+H]⁺ 291.1743, found 291.1739.

1,1,3-Trimethyl-4-(trimethylsilyl)naphthalen-2(1H)-one (3ai).

Yield: 12%, colorless oil. TLC: R_f 0.20 (hexane/ethyl acetate=20/1). ¹H NMR (CDCl₃) δ 7.44 (dd, *J* = 1.5, 7.5 Hz, 1H; Ar-H), 7.38 (dd, *J* = 1.5, 7.5 Hz, 1H; Ar-H), 7.23 (ddd, *J* = 1.5, 7.0, 7.5 Hz, 1H; Ar-H), 7.20 (ddd, *J* = 1.5, 7.0, 7.5 Hz, 1H; Ar-H), 2.11 (s, 3H; CH₃), 1.46 (s, 6H; 2CH₃), 0.45 (s, 9H; Si(CH₃)₃). ¹³C NMR (CDCl₃) δ 205.6, 150.4, 144.7, 140.4, 133.9, 129.1, 127.7, 126.0, 125.4, 46.8, 27.3, 17.2, 2.9. IR (neat): 2925, 2358, 1654, 1288, 1122, 985 cm⁻¹. MS *m/z* (%): 259/258 (4/19) [M⁺], 244/243 (2/9) [M⁺-Me], 156 (15), 141 (12), 73 (100) [SiMe₃⁺]. HRMS (ESI⁺) Calcd for C₁₆H₂₃OSi [M+H]⁺ 259.1513, found 259.1515.

1,1,4-Trimethyl-3-(trimethylsilyl)naphthalen-2(1H)-one (3ai').

Yield: 6%, colorless oil. TLC: R_f 0.22 (hexane/ethyl acetate=20/1). ¹H NMR (CDCl₃) δ 7.57 (dd, *J* = 1.5, 7.5 Hz, 1H; Ar-H), 7.42 (dd, *J* = 1.5, 7.5 Hz, 1H; Ar-H), 7.35 (ddd, *J* = 1.5, 7.5, 7.5 Hz, 1H; Ar-H), 7.28 (ddd, *J* = 1.5, 7.5, 8.0 Hz, 1H; Ar-H), 2.42 (s, 3H; CH₃), 1.43 (s, 6H; 2CH₃), 0.30 (s, 9H; Si(CH₃)₃). ¹³C NMR (CDCl₃) δ 209.6, 155.4, 147.0, 136.0, 132.0, 129.6, 126.6, 125.5, 125.3, 47.2, 25.9, 20.3, 1.6. IR (neat): 2925, 2347, 1654, 1560, 1507, 1123 cm⁻¹. MS *m/z* (%): 259/258 (3/7) [M⁺], 244/243 (16/71) [M⁺-Me], 228 (34), 185 (17), 156 (16), 73 (100) [SiMe₃⁺]. HRMS (ESI⁺) Calcd for C₁₆H₂₃OSi [M+H]⁺ 259.1513, found 259.1514.

3',4'-dipropyl-2'H-spiro[cyclopentane-1,1'-naphthalen]-2'-one (3fa).

Yield: 87%, colorless oil. TLC: R_f 0.34 (hexane/ethyl acetate=20/1). ¹H NMR (CDCl₃) δ 7.50 (dd, *J* = 1.0, 8.0 Hz, 1H; Ar-H), 7.35 (dd, *J* = 1.0, 8.0 Hz, 1H; Ar-H), 7.30 (ddd, *J* = 1.0, 7.5, 7.5 Hz, 1H; Ar-H), 7.25 (ddd, *J* = 1.0, 7.5, 7.5 Hz, 1H; Ar-H), 2.72 (t, *J* = 8.0 Hz, 2H; CH₂), 2.49 (t, *J* = 8.0 Hz, 2H; CH₂), 2.42–2.33 (m, 2H; CH₂), 1.99–1.81 (m, 6H; 3CH₂), 1.64 (tq, *J* = 7.5, 8.0 Hz, 2H; CH₂), 1.44 (tq, *J* = 7.5, 8.0 Hz, 2H; CH₂), 1.09 (t, *J* = 7.5 Hz, 3H; CH₃), 0.99 (t, *J* = 7.5 Hz, 3H; CH₃). ¹³C NMR (CDCl₃) δ 204.2, 148.9, 147.8, 134.0, 130.6, 128.6, 126.3, 126.3, 125.4, 58.6, 40.6, 31.7, 29.0, 27.3, 23.0, 22.8, 14.7, 14.6. IR (neat): 2959, 2870, 2360, 1651, 1608, 1449, 1355, 1257, 1229, 1114, 1085, 749 cm⁻¹. MS *m/z* (%): 283/282 (5/24) [M⁺], 242/241 (18/100), 240/239 (4/20) [M⁺-Pr], 211 (11), 169 (14), 141 (13). HRMS (ESI⁺) Calcd for C₂₀H₂₇O [M+H]⁺ 283.2056, found 283.2054.

Acknowledgments

This work was supported by JST, ACT-C and Grants-in-Aid from the Ministry of Education, Culture, Sports, Science and Technology, Japan. T.K. acknowledges the Asahi Glass Foundation, The Sumitomo Foundation, Tokuyama Science Foundation, and Kansai Research Foundation. K.N. also acknowledges the Japan Society for the Promotion of Science for Young Scientists for fellowship support.

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