Synthesis S. Kamijo et al. Paper

Synthesis of Aliphatic Azides by Photoinduced C(sp³)–H Azidation

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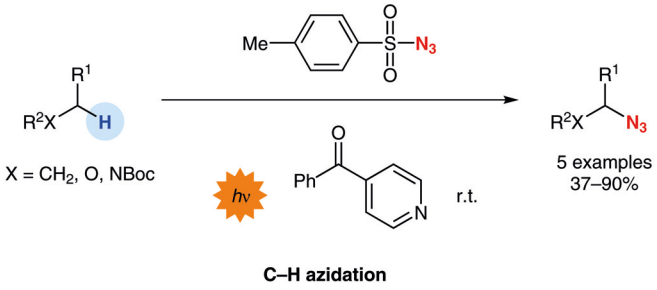
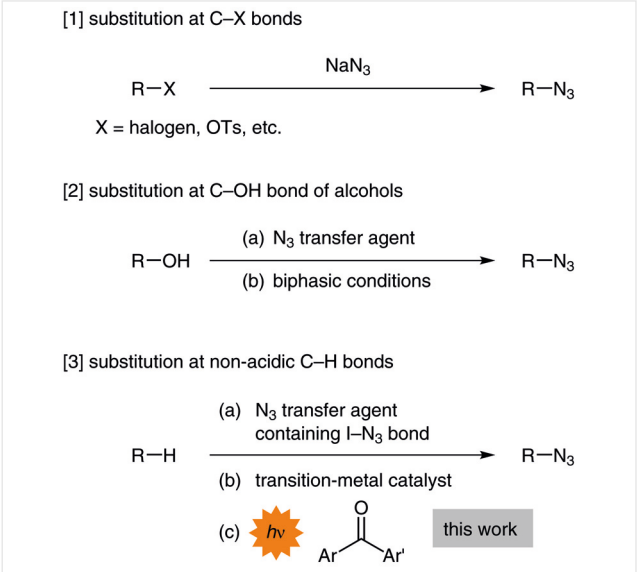


Received: 31.08.2015
Accepted after revision: 17.09.2015
Published online: 20.10.2015
DOI: 10.1055/s-0035-1560705; Art ID: ss-2015-f0508-op

Abstract A photoinduced synthesis of aliphatic azides was achieved in a single step starting from the parent cyclic alkanes, as well as from tetrahydrofuran and pyrrolidine derivatives. The reaction proceeds via direct azidation of C(sp³)–H bonds in the presence of 4-benzoylpyridine under photoirradiation conditions utilizing tosyl azide as the azide source. The chemoselective C–H mono-azidation at room temperature and the formation of azide compounds in spite of their potential photolability are the key features of the present transformation.

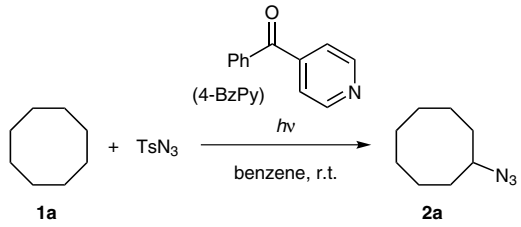
Key words C–H functionalization, azidation, photoreaction, aliphatic azides, sulfonyl azide, aryl ketone

Organic azides constitute an important class of compounds[1] in the field of synthetic organic chemistry as convenient precursors for a variety of nitrogen-containing molecules, including aza-heteroaromatics such as indoles and pyrroles, aliphatic azacycles like pyrrolidine and piperidine analogues, and naturally occurring alkaloids.[2] Among the reactions involving the azide functionality, [3+2] cycloaddition between organic azides and terminal alkynes has been recently re-investigated and copper catalysis was found to facilitate the triazole formation (CuAAC, click reaction).[3] Under the copper catalysis, the triazole-forming reaction proceeds even in the presence of water and air at ambient temperature. The mildness of the reaction conditions as well as the high reliability and robustness of the covalent-bond formation has made the click reaction an indispensable tool in a wide range of scientific fields, especially in chemical biology and material science.[1,4] Accordingly, the above mentioned new synthetic methodology has greatly expanded the utility of azide compounds. In spite of this marked increase in the demand of organic azide species, advancements in their preparative methods continue to be rather sluggish. The classical and most frequently applied method to obtain alkyl azides is a substitution reaction starting from alkyl halides and their analogues using sodium azide as a nucleophile (Scheme 1, eq. 1).[1,5] Substitutions of the hydroxy functionality in alcohols, a poor leaving group, were achieved by treatment with an elaborated azide transfer agent, such as 2-azido-1,3-dimethylimidazolium hexafluorophosphate (ADMP)[6] and diphenylphosphoryl azide,[7] or by conducting the reaction under finely tuned biphasic conditions[8] (Scheme 1, eq. 2).[9] Recent investigations allowed direct substitution of nonacidic C(sp³)–H bonds, generally unreactive moieties in organic substances, by applying reactive iodine-based agents, such as iodonium azide (IN_3)[10] and azidoiodinane[11] (Scheme 1,



Scheme 1 Preparation of aliphatic azides via substitution

Table 1 Optimization of Reaction Conditions for Photoinduced C–H Azidation of Cyclooctane (**1a**)[a]



1a **2a**

Entry	**1a** (equiv)	4-BzPy (equiv)	Time (h)	NMR yield (%)[b]
1[c]	8	1	6	26
2	8	1	6	49
3[d]	8	1	6	24[e]
4[f]	8	1	24	44
5[g]	8	1	24	24
6	8	2	24	39
7	8	0.5	24	27
8	5	1	24	29
9[h]	8	1	6	50 (51)[i]

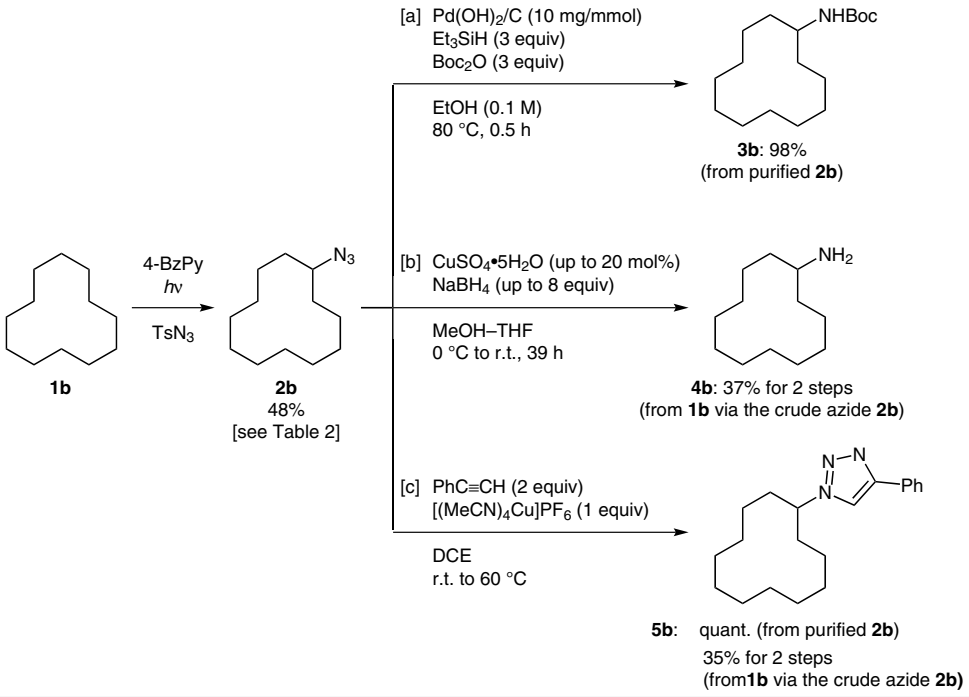
[a] Benzene solution (0.04 M) of cyclooctane (**1a**), TsN_3 (1 equiv), and 4-BzPy was photoirradiated using a LED lamp (365 nm) at r.t.
[b] Yield was calculated based on ^1H NMR analysis of the crude mixture, unless otherwise noted.
[c] Ph_2CO was applied instead of 4-BzPy.
[d] Photoirradiation using a medium-pressure Hg lamp instead of a LED lamp.
[e] A significant amount of TsN_3 was recovered.
[f] The reaction was conducted in CH_2Cl_2.
[g] The reaction was conducted in acetone.
[h] The reaction was conducted in benzene (0.1 M).
[i] Isolated yield is shown in parentheses.

eq. 3a), or by utilizing transition-metal catalysts[12,13] (Scheme 1, eq. 3b). Considering the increasing importance of organic azide species, the development of synthetic variants enabling the preparation of alkyl azides should have great value. We therefore launched a study on a new preparative method of aliphatic azides via direct C–H azidation utilizing a photoexcited aryl ketone[14,15] (Scheme 1, eq. 3c).

At the outset of the investigation, we assumed that one of the key challenges to establish photoinduced azide synthesis should be control of the inherent photolabile nature of both the azide source and azide products.[16] A literature search revealed that: (1) benzyl azide remains intact with exposure to UV light of 365 nm, 302 nm, and 254 nm,[17] and (2) *p*-toluenesulfonyl azide (TsN_3) generates nitrene with exposure to UV light of 300 nm (2 h) or 350 nm (24 h).[18] With this information in hand, the screening of reaction conditions for photoinduced azidation of cyclooctane (**1a**) using TsN_3 as the azide source[19] was conducted in the presence of an aryl ketone irradiating with LED light of 365 nm as shown in Table 1.[20] As expected, benzophenone (Ph_2CO) promoted the C–H azidation to furnish azidocyclooctane (**2a**) in 26% yield (Table 1, entry 1). When 4-benzoylpyridine (4-BzPy)[14i] was applied instead of Ph_2CO, the yield of **2a** was increased to 49% (entry 2). The reaction using a Hg lamp afforded 24% yield of **2a** after 6 hours irradiation with a significant amount of recovered TsN_3, indicating the advantage of monochromatic LED light irradiation (entry 3). Use of other solvents, such as MeCN and *t*-BuOH, and varying the amount of 4-BzPy both diminished the yield of the desired azide **2a** (entries 4–7). The reaction with a reduced amount of the starting alkane **1a** was also detrimental to the yield of **2a** (entry 8). The reaction between cyclooctane (**1a**) (8 equiv) and TsN_3 (1 equiv) in the presence of 4-BzPy (1 equiv) with the irradiating LED light (365 nm) proceeded efficiently in 0.1 M benzene solution and the desired azidocyclooctane (**2a**) was produced in 51% yield (entry 9).

With the optimized reaction conditions in hand, the applicability of various cyclic compounds for photoinduced C–H azidation was examined (Table 2). The azidation of cyclododecane (**1b**) proceeded smoothly with TsN_3 as a limiting agent and cyclododecyl azide (**2b**) was formed in 48% yield (Table 2, entry 1). The azidation of adamantane (**1c**) proceeded chemoselectively at the methine C–H bond to afford 1-azidoadamantane (**2c**) in 40% yield (entry 2). In the case of methine C–H azidation, practically the same yield of **2c** was obtained (37% yield) when adamantane (1 equiv) was treated with a slight excess of TsN_3 (1.2 equiv) and 4-BzPy (1 equiv) in benzene solution (0.1 M), although longer reaction times were required (entry 3). We confirmed the formation of diazidoadamantane starting from 1-azidoadamantane (**2c**) to be very sluggish, indicating mono-azidation took place selectively under the present conditions. The reactivity of the oxygen-containing cycle, ambroxide (**1d**), appeared to be high, and the chemoselective azidation took place at the ethereal C–H bond to provide **2d** in 84% yield in 3 hours (entry 4). Although a decrease in the product yield was observed (33% yield), the reaction could be conducted using ambroxide (**1d**) as a limiting agent (entry 5).[21] The reactivity of the aliphatic azacycle, *N*-(*tert*-butoxycarbonyl)pyrrolidine (**1e**), was even higher to afford the azide **2e** in 90% NMR yield in 40 minutes (entry 6). The azidation occurred chemoselectively at the C–H bond adjacent to the nitrogen atom, although serious decomposition of **2e** was observed during purification by column chromatography. The reaction with **1e** as a limiting agent furnished **2e** in 49% NMR yield in one hour (entry 7).

The derived azides are excellent precursors for a variety of nitrogen-containing molecules and therefore several transformations were conducted to accentuate the utility of the present photoinduced C–H azidation strategy (Scheme 2). Nearly quantitative formation of the *N*-Boc protected cyclododecylamine (**3b**) was obtained by subjecting the purified azide **2b** to Kotsuki conditions (Scheme 2, a).[22] The preparation of cyclododecylamine (**4b**) was achieved by treating azide **2b** with $NaBH_4$ in the presence of a copper catalyst (Scheme 2, b).[12] This reduction could be carried out using the crude adduct **2b** as a starting material without in-

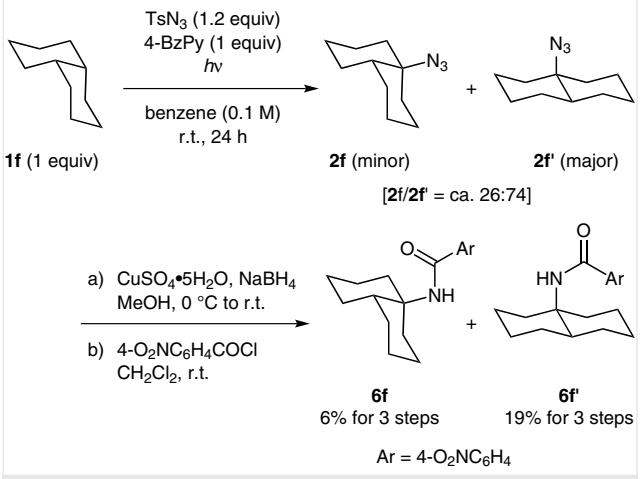


Scheme 2 Transformations of azidocyclododecane (**2b**)

tensive purification after azidation. The conversion to the triazole **5b** was attained by the [3+2] cycloaddition of azide **2b** with phenylacetylene in the presence of the cationic copper complex (Scheme 2, c).[23] The triazole formation proceeded in high yield even when the crude azide **2b** was applied as a starting material, although a longer reaction time was required.

We further examined the azidation of *cis*-decalin (**1f**) to obtain some information on the reaction mechanism (Scheme 3).[24] Monitoring the azidation by gas chromatography indicated the generation of both *cis*- and *trans*-fused azide adducts, **2f** and **2f'** (ca. 26:74). The mixture of crude azides was subjected to the reduction conditions and the derived amines were benzoylated before isolation. The formation of both *cis*- and *trans*-fused amides, **6f** (6.2% in 3 steps) and **6f'** (19% in 3 steps), respectively, was confirmed. This configurational change explains an intermediacy of radical species caused by hydrogen abstraction effected by the photoexcited ketone as we have proposed in our series of investigations on photoinduced C–H functionalizations.[14]

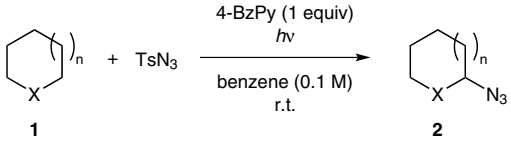
In conclusion, we have developed a new preparative method of aliphatic azides via a photoinduced azidation of C(sp^3)–H bonds. The chemoselective cleavage of C–H bonds was effected by photoexcited 4-benzoylpyridine with tosyl azide as an azide source. The present transformation was optimized to proceed under the irradiation of a monochromatic LED lamp (365 nm) to avoid the degradation of potentially photolabile azide compounds, including the azide source (TsN_3) and generated azide products. The newly developed protocol allows direct conversion of cyclic alkanes as well as tetrahydrofuran and pyrrolidine derivatives into the corresponding azides in a single step under mild reaction conditions.



Scheme 3 One-pot amidation of *cis*-decalin (**1f**)

All reactions sensitive to air or moisture were carried out under an argon atmosphere under anhydrous conditions, unless otherwise noted. Analytical TLC was performed on E. Merck silica gel 60 F254 precoated plates. Column chromatography was performed using 40–50 μm Silica Gel 60N (Kanto) or with a Biotage Isolera using a prepacked column. Recycling HPLC was carried out using a LC-9210II

Table 2 Photoinduced C–H Azidation of Cyclic Compounds **1**[a]



1 **2**

Entry	**1**	Conditions	Time (h)	**2**	Yield (%)[b]
1	**1b**	A	9	**2b**	48
2	**1c**	A	7	**2c**	40
3		B	12		37
4	**1d**	A	3	**2d**	84 (51:49)[c]
5		B	3		33 (53:47)[c]
6	**1e**	A	0.67	**2e**	(90)[d]
7		B	1		(49)[d]

[a] Conditions A: cyclic compound **1** (8 equiv), TsN_3 (1 equiv), 4-BzPy (1 equiv), benzene (0.1 M), photoirradiation using a LED lamp (365 nm) at r.t. Conditions B: cyclic compound **1** (1 equiv), TsN_3 (1.2 equiv), 4-BzPy (1 equiv), benzene (0.1 M), photoirradiation using a LED lamp (365 nm) at r.t.
[b] Isolated yield unless otherwise noted.
[c] Ratio of diastereomers is shown in parentheses.
[d] NMR yield is shown in parentheses.

NEXT instrument equipped with a GPC column (20 mm × 600 mm, JAI) with $CHCl_3$ as an eluent. The ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance III-400 (400 MHz) or Bruker DRX500 (500 MHz) spectrometer. Chemical shifts are reported in δ (ppm) relative to residual solvent signals [^1H NMR: $CHCl_3$ (7.26); ^{13}C NMR: $CDCl_3$ (77.0)]. Standard abbreviations were used to denote signal patterns. IR spectra were recorded on a Jasco FT/IR-4100 spectrometer. HRMS were recorded on a Bruker Daltonics micrOTOF II (APCI) instrument. Melting points were measured on a Cornes MPA100 micro melting point apparatus. The reactions were conducted in a Pyrex test tube (18 × 130 mm), and the photoirradiation was carried out by using a Keyence UV-400 with UV-50A LED lamp and a Riko 100 W medium-pressure mercury lamp.

Photoinduced C(sp^3)–H Azidation; Azidocyclooctane (2a); Typical Procedure

[CAS Reg. No. 33794-96-6]

Cyclooctane (**1a**; 0.54 mL, 4 mmol, 8 equiv), TsN_3 (98.6 mg, 0.5 mmol), and 4-benzoylpyridine (91.6 mg, 0.5 mmol, 1 equiv) in benzene (5 mL, 0.1 M) were added to a Pyrex test tube under an argon atmosphere. The test tube was placed at ca. 1 cm distance from a Keyence LED lamp and was irradiated at 365 nm for 6 h. After consumption of TsN_3, the solution was passed through a short silica gel column using pentane. The eluent was evaporated and the residue was purified by column chromatography (silica gel, pentane) to afford azidocyclooctane (**2a**); yield: 38.7 mg (51%); colorless oil.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.43–1.63 (m, 8 H), 1.64–1.79 (m, 4 H), 1.81–1.94 (m, 2 H), 3.56 (tt, *J* = 8.4, 4.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.1, 25.1, 27.2, 30.8, 62.2.

Azidocyclododecane (2b)

[CAS Reg. No. 153757-18-7]

Yield: 47% (48.9 mg); colorless oil.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.23–1.61 (m, 20 H), 1.62–1.76 (m, 2 H), 3.48 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3, 23.2, 23.3, 23.7, 23.9, 29.0, 59.2.

1-Azidoadamantane (2c)

[CAS Reg. No. 24886-73-5]

Yield: 37% (33.0 mg); colorless solid; mp 77.6–79.1 °C.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.55–1.75 (m, 6 H), 1.78–1.82 (m, 6 H), 2.14 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.8, 35.9, 41.5, 58.9.

Azidoambroxide 2d

This azide was obtained as an inseparable mixture of two diastereomers (51:49); yield: 77% (47.5 mg); colorless oil.

IR (ATR, neat): 2995, 2928, 2868, 2115, 1457, 1380, 1240 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.83 (s, 447/100 H), 0.85 (s, 153/100 H), 0.87 (s, 147/100 H), 0.88 (s, 153/100 H), 0.92–1.12 (m, 2 H), 1.15–1.25 (m, 1 H), 1.13 (s, 147/100 H), 1.27 (s, 153/100 H), 1.29–1.73 (m, 8 H), 1.74–1.85 (m, 1 H), 1.94–2.09 (m, 2 H), 5.32 (d, *J* = 6.4 Hz, 49/100 H), 5.45 (dd, *J* = 6.4 Hz, 51/100 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (detectable signals) = 15.1, 15.3, 18.2, 18.3, 20.5, 20.7, 21.0, 22.6, 22.9, 30.5, 30.8, 33.0, 33.4, 36.1, 36.2, 39.6, 39.7, 39.86, 39.89, 42.35, 42.48, 57.0, 57.4, 60.5, 82.6, 84.1, 89.5, 91.5.

HRMS (APCI): *m*/*z* [M – N_2 + H]$^+$ calcd for $C_{16}H_{28}NO$: 250.2165; found: 250.2176.

***tert*-Butyl 2-Azidopyrrolidine-1-carboxylate (2e)**[19e]

[CAS Reg. No. 156268-09-6]

The product was intensively purified by silica gel column chromatography to collect compound data. The compound was obtained as a mixture of rotamers (64:36). The isolated yield was not determined due to the serious decomposition of **2e** during the purification process; colorless oil.

IR (ATR, neat): 2982, 2892, 2114, 1711, 1394, 1168 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.47 (br s, 576/100 H), 1.50 (br s, 324/100 H), 1.77–2.10 (m, 4 H), 3.29 (m, 1 H), 3.50 (m, 1 H), 5.44 (br d, *J* = 3.6 Hz, 64/100 H), 5.52 (br d, *J* = 3.3 Hz, 36/100 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.0, 22.9, 28.0, 28.2, 28.4, 32.3, 33.3, 45.8, 46.2, 74.4, 80.4, 81.1, 153.6, 154.6.

HRMS (APCI): *m*/*z* [M – N_2 + H]$^+$ calcd for $C_9H_{17}N_2O_2$: 185.1285; found: 185.1278.

Reductive Transformation of Azidocyclododecane (2b) under Kotsuki Conditions; *tert*-Butyl Cyclododecylcarbamate (3b)

[CAS Reg. No. 308288-44-0]

A mixture of purified azidocyclododecane (**2b**; 20.9 mg, 0.1 mmol), Boc_2O (34.4 μL, 0.15 mmol), Et_3SiH (48 μL, 0.3 mmol), and $Pd(OH)_2/C$ (1 mg; 20 wt%, Aldrich) in EtOH (1 mL, 0.1 M) was stirred at r.t. for 0.5 h. After the consumption of the starting azide **2b**, the mixture was filtered through a Celite pad and concentrated. The residue was purified by using a recycling HPLC (GPC column, $CHCl_3$) to afford **3b**; yield: 27.8 mg (98%); colorless solid; mp 115.1–116.3 °C.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.22–1.65 (m, 31 H), 3.69 (br m, 1 H), 4.33 (br m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4, 23.4, 23.5, 23.7, 24.0, 28.4, 30.5, 47.3, 78.8, 155.4.

Reduction of Azidocyclododecane (2b) with $NaBH_4$ in the Presence of a Copper Catalyst; Cyclododecylamine (4b)

[CAS Reg. No. 1502-03-0]

Crude azidocyclododecane (**2b**) was prepared by following the typical procedure starting from cyclododecane (**1b**; 672 mg, 4 mmol) and TsN_3 (98.6 mg, 0.5 mmol). To the MeOH–THF solution (1:1, 10 mL) of the crude azide **2b**, mainly contaminated with **1b**, were added $CuSO_4{\cdot}5H_2O$ (5.2 mg, 10 mol%) and $NaBH_4$ (31.8 mg, 4 equiv) at 0 °C and the mixture was stirred at r.t .for 18 h. Next, additional $CuSO_4{\cdot}5H_2O$ (5.2 mg, 10 mol%) and $NaBH_4$ (31.8 mg, 4 equiv) were introduced and the mixture was further stirred at r.t. for 21 h. The reaction was quenched with H_2O and the mixture was extracted with $CHCl_3$. The residue was purified by column chromatography [YMC-Dispo-PackAT NH2-25 12 g, hexane–EtOAc (100:0 → 0:100)] to afford **4b**; yield over two steps: 34.1 mg (37%) colorless oil.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.23–1.45 (m, 22 H), 1.51–1.60 (m, 2 H), 2.89 (br tt, *J* = 5.7, 5.7 Hz, 1 H).

Copper-Promoted [3+2] Cycloaddition of Azidocyclododecane (2b) with Phenylacetylene; 1-Cyclododecyl-4-phenyltriazole (5b)

*Triazole Formation Using the Pure Azide **2b***: $[(MeCN)_4Cu]PF_6$ (74.5 mg, 1 equiv) and phenylacetylene (44 μL, 2 equiv) were added to the 1,2-dichloroethane solution (2 mL) of the purified azide **2b** (41.9 mg, 0.2 mmol) under an argon atmosphere, and the mixture was stirred at r.t. for 1 h and 60 °C for 1 h. The mixture was cooled to r.t. and the residue was purified by column chromatography (silica gel, $CHCl_3$) to afford cyclododecyl triazole **5b**; yield: 62.6 mg (quant.).

*Triazole Formation Using the Crude Azide **2b***: Crude azidocyclododecane (**2b**) was prepared by following the typical procedure starting from cyclododecane (**1b**; 672 mg, 4 mmol) and TsN_3 (98.6 mg, 0.5 mmol). $[(MeCN)_4Cu]PF_6$ (89.5 mg, 1 equiv) and phenylacetylene (52.7 μL, 2 equiv) were added to the 1,2-dichloroethane solution (4.8 mL) of the crude azide **2b**, mainly contaminated with **1b**, under an argon atmosphere, and the mixture was stirred at 60 °C for 24 h. The mixture was cooled to r.t. and extracted with $CHCl_3$. The residue was purified by column chromatography (silica gel, $CHCl_3$) to afford **5b**; yield over two steps: 54.8 mg (35%); colorless solid; mp 166.0–167.5 °C.

IR (ATR, neat): 3122, 3056, 2924, 2859, 2847, 1612, 1469, 1223, 765, 694 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.29–1.60 (m, 18 H), 1.76–1.90 (m, 2 H), 2.05–2.18 (m, 2 H), 4.79 (tt, *J* = 6.4, 6.4 Hz, 1 H), 7.32 (br t, *J* = 7.6 Hz, 1 H), 7.42 (br t, *J* = 7.6 Hz, 2 H), 7.74 (s, 1 H), 7.84 (br d, *J* = 7.6 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (detectable signals) = 21.7, 23.2 (2 ×), 23.5, 23.6, 30.9, 57.9, 117.6, 125.6, 127.9, 128.7, 130.9, 147.4.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{30}N_3$: 312.2434; found: 312.2435.

Photoinduced Azidation of *cis*-Decalin (1f) and Derivatization of the Derived Azides 2f, 2f′; 4-Nitro-*N*-[(4a*R*,8a*R*)-octahydronaphthalen-4a(2*H*)-yl]benzamide (6f) and 4-Nitro-*N*-[(4a*S*,8a*S*)-octahydronaphthalen-4a(2*H*)-yl]benzamide (6f′)

A mixture of crude azidodecalins **2f** and **2f′** was prepared by following the typical procedure, starting from *cis*-decalin (**1f**; 69 mg, 0.5 mmol) and TsN_3 (118 mg, 0.6 mmol). The combined yield of azides **2f** and **2f′** was estimated to be <64% based on the total weight of the crude mixture. $CuSO_4{\cdot}5H_2O$ (8.1 mg, >10 mol%) and $NaBH_4$ (49.0 mg, >4 equiv) were added at 0 °C to the MeOH solution (3 mL) of the crude azides **2f** and **2f′** (58.0 mg, <0.32 mmol), mainly contaminated with *cis*-decalin (**1f**), and the mixture was stirred at r.t. for 18 h. Next, additional $CuSO_4{\cdot}5H_2O$ (8.1 mg, >10 mol%) and $NaBH_4$ (49.0 mg, >4 equiv) were introduced and the mixture was further stirred at r.t. for 27 h. The reaction was quenched with H_2O and the mixture was extracted with Et_2O. The residue was dissolved in CH_2Cl_2 (5 mL) and treated with 4-nitrobenzoyl chloride (120.1 mg, >2 equiv) at r.t. for 18 h. The mixture was extracted with CH_2Cl_2 and the residue was purified by preparative TLC (silica gel, hexane–EtOAc, 5:1) to afford **6f** in 6% yield (9.3 mg) and **6f′** in 19% yield (28.4 mg) for three steps.

6f

Colorless solid; mp 160.8–161.6 °C.

IR (ATR, neat): 3420, 3102, 3069, 2950, 2919, 2866, 1664, 1515, 1348, 851, 714 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.41 (m, 2 H), 1.48–1.75 (m, 11 H), 1.96 (m, 2 H), 2.02–2.20 (m, 2 H), 5.88 (br s, 1 H), 7.87 (d, *J* = 8.7 Hz, 2 H), 8.27 (d, *J* = 8.7 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ (detectable signals) = 22.3, 27.5, 38.8, 57.8, 123.7, 127.7, 141.9, 149.2, 164.5; two signals in the cyclohexane ring are probably missing due to the rapid ring-flip of the *cis*-decalin core.

HRMS (APCI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{23}N_2O_3$: 303.1703; found: 303.1716.

6f′[12]

[CAS Reg. No. 1654756-89-4]

Colorless solid; mp 191.1–192.6 °C.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.10–1.28 (m, 4 H), 1.31–1.48 (m, 4 H), 1.49–1.62 (m, 5 H), 1.72–1.78 (m, 2 H), 2.76–2.83 (m, 2 H), 5.74 (br s, 1 H), 7.90 (d, *J* = 8.8 Hz, 2 H), 8.30 (d, *J* = 8.8 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.6, 25.9, 28.8, 34.3, 45.3, 56.9, 123.9, 127.7, 141.9, 149.3, 164.4.

HRMS (APCI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{23}N_2O_3$: 303.1703; found: 303.1701.

Acknowledgment

This research was supported by a Grant-in-Aid for Scientific Research on Innovative Areas 'Advanced Molecular Transformations by Organocatalysts' (MEXT, Japan) and a Program to Disseminate Tenure Tracking System (MEXT, Japan) to S.K.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1560705.

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