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Reaction of Olefins with Nitriles under Solvent-Free Conditions Using Molecular Iodine as a Catalyst in the Presence of Water

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Abstract: The reaction of olefins with nitriles using iodine as a catalyst under solvent-free conditions was investigated. The reaction of cycloolefins, such as cyclopentene and cyclohexene, with benzonitrile using iodine as a catalyst produced both amide and heterocyclic compounds. The reaction of chiral (+)-camphene with benzonitrile produced racemic (±)-*N*-isobornylbenzamide (*N*-((1*S*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl)benzamide). This indicated that skeletal rearrangement of camphene as well as amidation occurred. The optimized conditions were determined to be as follows: temperature, 90℃; molar ratio of nitrile:alcohol:iodine:water, 1:5:0.2:1.0; and reaction time, 18 h. The yield was 87% under these conditions. The reaction of (+)-camphene also proceeded with the other aromatic and aliphatic nitriles to produce racemic isobornylamides. However, except for styrene, complex reactions occurred in the reactions of benzonitrile with other terpenic olefins.

Key words: iodine, solvent-free, Ritter reaction, camphene

1 INTRODUCTION

The well-known method for synthesizing amide compounds from alkenes and nitriles is the Ritter reaction[1)]. However, strong acids such as sulfuric acid, compounds which are hard to handle, and structurally complicated compounds have also been used as the efficient catalysts of this reaction[1-6)]. We previously reported that iodine was an efficient catalyst for the amidation of alcohols and nitriles[7)] as well as of esters and nitriles[8)]. On the other hand, iodine is also known to be an efficient catalyst in solvent-free reactions[9-12)]. Solvent-free reactions using iodine as a catalyst have been investigated recently as a part of the "green chemistry" initiative. Thus motivated, the reaction of olefins with nitriles using iodine as a catalyst under solvent-free conditions was investigated in this study.

2 EXPERIMENTAL

2.1 General

NMR spectra were obtained using a 300 MHz FT-NMR spectrometer (Bruker DPX-300) with Me_4Si as an internal standard and $CDCl_3$ as a solvent. IR spectra were recorded on a JASCO FT/IR-230 spectrometer. Mass spectra were recorded on a JEOL JMS-HX110A, a SHIMADZU GCMS-QP5050A, and a Thermo Fischer Exactive type spectrometer. Optical rotations were measured on a JASCO P2000.

2.2 Materials

All nitriles, cyclopentene (**2a**), cyclohexene (**2b**), (+)-camphene (**5**), (±)-α-pinene, (−)-β-pinene, and D-limonene were obtained from Tokyo Chemical Industry Co., Ltd. and Sigma-Aldrich, and used as received. Styrene was obtained from Tokyo Chemical Industry Co., Ltd. and distilled under reduced pressure before use.

2.3 Reaction of benzonitrile (1) with cycloolefin

A typical procedure is as follows:

Iodine (50.0 mg, 0.20 mmol), benzonitrile (**1**) (515 mg, 5.0 mmol), cyclopentene (**2a**) (68.0 mg, 1.0 mmol) and distilled water (18.0 mg, 1.0 mmol) were placed in a reaction tube, which was sealed. The mixture was stirred at 90℃ for 18 h. A 20% aqueous solution of sodium thiosulfate (5 mL) was added to the reaction mixture, which was then ex-

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tracted twice with 10 mL of 6 M HCl and separated into the aqueous layer and the organic layers.

To the aqueous layer, 20 mL of chloroform was added, followed by 6M NaOH aqueous solution until the pH of the mixture was above 7.0. Then the mixture was extracted three times with 20 mL of chloroform, and the combined chloroform solution was dried with anhydrous sodium sulfate. The solution was evaporated, and the product was purified by silica-gel column chromatography and eluted with 4:1 hexane:ethyl acetate. A total of 11.2 mg (6% yield) of 2-phenyl-4,5,6,6a-tetrahydro-3aH-cyclopenta[*d*] oxazole (**4a**) was obtained. GC-MS purities of all products were >98%.

The organic layer was dried with anhydrous sodium sulfate and the solution was evaporated. The product was purified by silica-gel column chromatography eluted with 4:1 hexane:ethyl acetate. A total of 34.0 mg (18% yield) of *N*-(cyclopentylbenzamide) (**3a**) was obtained. GC-MS purities of all products were >98%.

2.4 Reaction of benzonitrile (1) with (+)-camphene (5)

A typical procedure is as follows:

Iodine (50.0 mg, 0.20 mmol), benzonitrile (**1**) (515 mg, 5.0 mmol), (+)-camphene (**5**) (136 mg, 1.0 mmol) and distilled water (18.0 mg, 1.0 mmol) were placed in a reaction tube, which was sealed. The mixture was stirred at 90℃ for 18 h. A 20% aqueous solution of sodium thiosulfate (5 mL) was added to the reaction mixture to remove the iodine. The reaction mixture was then extracted three times with 20 mL of chloroform. The organic layer was dried with anhydrous sodium sulfate and the solution was evaporated. The product was purified by silica-gel column chromatography eluted with 4:1 hexane:ethyl acetate. A total of 231.3 mg (90% yield) of (**6**) was obtained. GC-MS purity of product was >98%.

2.5 Spectroscopic data

N-Cyclopentylbenzamide (3a)

White crystals; m.p. 134-135℃; ^{1}H-NMR ($CDCl_3$) δ: 1.44-1.56 (m, 2H), 1.58-1.77 (m, 4H), 2.02-2.12 (m, 2H), 4.33-4.45 (m, 1H), 6.26 (bs, 1H), 7.37-7.50 (m, 3H), 7.73-7.76 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ: 22.2, 33.9, 34.7, 71.8, 84.8, 127.8, 128.2, 128.2, 131.1, 163.8; IR (KBr): 3294, 2963, 1626 cm^{-1}; EI-MS *m/z* (rel intensity): 189 (M^+, 31)

N-Cyclohexylbenzamide (3b)

White crystals; m.p. 137-138℃; ^{1}H-NMR ($CDCl_3$) δ: 1.13-1.30 (m, 3H), 1.36-1.50 (m, 2H), 1.62-1.79 (m, 3H), 2.01-2.06 (m, 2H), 3.92-4.04 (m, 1H), 6.02 (bs, 1H), 7.39-7.51 (m, 3H), 7.74-7.77 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ: 24.9, 25.5, 33.2, 48.6, 126.8, 128.5, 131.2, 135.1, 166.6; IR (KBr): 3318, 3240, 2929, 2851, 1627 cm^{-1}; EI-MS *m/z* (rel intensity): 203 (M^+, 30)

2-Phenyl-4,5,6,6a-tetrahydro-3a*H*-cyclopenta[*d*] oxazole (4a)

White crystals; m.p. 47-49℃; ^{1}H-NMR ($CDCl_3$) δ: 1.45-2.12 (m, 6H), 4.71-4.76 (m, 1H), 5.10-5.14 (m, 1H), 7.37-7.53 (m, 3H), 7.90-7.94 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ: 22.2, 34.0, 34.7, 71.8, 84.8, 127.7, 128.2, 128.3, 131.1, 163.8; IR (KBr): 2959, 1647, 1065 cm^{-1}; EI-MS *m/z* (rel intensity): 187 (M^+, 59)

2-Phenyl-3a,4,5,6,7,7a-hexahydrobenzo[*d*] oxazole (4b)

White crystals; m.p. 47-48℃; ^{1}H-NMR ($CDCl_3$) δ: 1.38-1.96 (m, 8H), 4.01-4.17 (m, 1H), 4.66-4.72 (m, 1H), 7.38-7.50 (m, 3H), 7.95-7.98 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ: 19.1, 19.8, 26.2, 27.7, 63.5, 78.8, 128.1, 128.3, 128.3, 131.2, 164.2; IR (KBr): 2936, 1638, 1063 cm^{-1}; EI-MS *m/z* (rel intensity): 201 (M^+, 53)

N-((1*S*, 2*S*, 4*S*)-1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl)-benzamide (6)

White crystals; m.p. 125-126℃; ^{1}H-NMR ($CDCl_3$) δ: 0.88 (s, 3H), 0.92 (s, 3H), 1.01 (s, 3H), 1.19-1.25 (m, 1H), 1.33-1.42 (m, 1H), 1.59-1.82 (m, 4H), 1.93-2.00 (m, 1H), 4.08-4.16 (m, 1H), 6.06 (bs, 1H), 7.40-7.52 (m, 3H), 7.70-7.72 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ: 11.8, 20.3, 20.3, 27.0, 35.9, 39.2, 44.9, 47.2, 48.8, 57.1, 126.6, 128.6, 131.2, 135.1, 166.7; IR (KBr): 3335, 2955, 1631, 1526 cm^{-1}; EI-MS *m/z* (rel intensity): 257 (M^+, 21).

4-Methoxy-*N*-((1*S*, 2*S*, 4*S*)-1,7,7-trimethylbicyclo[2.2.1]-hept-2-yl) benzamide (7a)

White crystals; m.p. 94-96℃; ^{1}H-NMR ($CDCl_3$) δ: 0.87 (s, 3H), 0.91 (s, 3H), 1.01 (s, 3H), 1.11-1.25 (m, 1H), 1.34-1.41 (m, 1H), 1.58-1.80 (m, 4H), 1.92-2.05 (m, 1H), 3.84 (s, 3H), 4.06-4.14 (m, 1H), 5.99 (bs, 1H), 5.99-6.01 (m, 2H), 7.66-7.69 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ: 11.8, 20.3, 20.3, 27.0, 35.9, 39.3, 44.9, 47.1, 48.8, 55.4, 57.0, 113.7, 127.4, 128.4, 162.0, 166.2; IR (KBr): 3397, 2945, 1637 cm^{-1}; EI-MS *m/z* (rel intensity): 287 (M^+, 14)

4-Chloro-*N*-((1*S*, 2*S*, 4*S*)-1,7,7-trimethylbicyclo[2.2.1]-hept-2-yl) benzamide (7b)

White crystals; m.p. 102-103℃; ^{1}H-NMR ($CDCl_3$) δ: 0.87 (s, 3H), 0.91 (s, 3H), 0.97 (s, 3H), 1.00-1.25 (m, 1H), 1.32-1.40 (m, 1H), 1.37-1.82 (m, 4H), 1.92-2.00 (m, 1H), 4.06-4.13 (m, 1H), 6.00 (bs, 1H), 7.39-7.42 (m, 2H), 7.62-7.66 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ: 11.8, 20.2, 20.3, 27.0, 35.9, 39.2, 44.9, 47.2, 48.8, 57.2, 128.1, 128.8, 133.5, 137.4, 165.6; IR (KBr): 3318, 2952, 2874, 1633 cm^{-1}; EI-MS *m/z* (rel intensity): 291 (M^+, 22)

2-Chloro-*N*-((1*S*, 2*S*, 4*S*)-1,7,7-trimethylbicyclo[2.2.1]-hept-2-yl) benzamide (7c)

White crystals; m.p. 90-91℃; ^{1}H-NMR ($CDCl_3$) δ: 0.86 (s, 3H), 0.95 (s, 3H), 0.96 (s, 3H), 1.18-1.28 (m, 1H), 1.32-1.39

(m, 1H), 1.58-1.80 (m, 4H), 1.93-2.00 (m, 1H), 4.10-4.17 (m, 1H), 6.24 (bs, 1H), 7.30-7.41 (m, 3H), 7.69-7.72 (m, 1H); ^{13}C-NMR ($CDCl_3$) δ: 12.0, 20.2, 20.4, 27.0, 36.0, 39.0, 44.8, 47.1, 48.8, 57.5, 127.1, 130.2, 130.4, 130.6, 131.2, 135.2, 165.5; IR (KBr): 3333, 2936, 1632 cm^{-1}; EI-MS *m/z* (rel intensity): 291 (M^+, 19); HRMS (FAB-MS) *m/z* calcd for $C_{17}H_{22}ONCl$ + H: 292.1463, found 292.1463

N-((1*S*, 2*S*, 4*S*)-1,7,7-Trimethylbicyclo [2.2.1] hept-2-yl)-1-naphthamide (7d)

White crystals; m.p. 145-146℃; ^{1}H-NMR ($CDCl_3$) δ: 0.87 (s, 3H), 0.91 (s, 3H), 1.02 (s, 3H), 1.20-1.28 (m, 1H), 1.40-1.48 (m, 1H), 1.61-1.81 (m, 4H), 2.00-2.07 (m, 1H), 4.21-4.29 (m, 1H), 5.92 (bs, 1H), 7.43-7.59 (m, 4H), 7.85-7.92 (m, 2H), 8.29-8.32 (m, 1H); ^{13}C-NMR ($CDCl_3$) δ: 12.0, 20.2, 20.3, 27.0, 35.9, 39.1, 44.9, 47.1, 48.9, 57.1, 124.4, 124.7, 125.4, 126.4, 127.0, 128.2, 130.1, 130.3, 133.6, 135.1, 168.8; IR (KBr): 3334, 2948, 1636 cm^{-1}; EI-MS *m/z* (rel intensity): 307 (M^+, 11); HRMS (FAB-MS) m/z calcd for $C_{21}H_{25}ON$ + Na: 330.1828, found 330.1816

N-((1*S*,2*S*, 4*S*)-1,7,7-Trimethylbicyclo [2.2.1] hept-2-yl)-furan-2-carboxamide (7e)

White crystals; m.p. 70-71℃; ^{1}H-NMR ($CDCl_3$) δ: 0.87 (s, 3H), 0.89 (s, 3H), 1.00 (s, 3H), 1.16-1.25 (m, 1H), 1.31-1.39 (m, 1H), 1.56-1.81 (m, 4H), 1.89-1.97 (m, 1H), 4.02-4.10 (m, 1H), 6.33 (bs, 1H), 6.48-6.50 (m, 1H), 7.08-7.09 (m, 1H), 7.42-7.43 (m, 1H); ^{13}C-NMR ($CDCl_3$) δ: 11.8, 20.1, 20.3, 27.0, 35.9, 39.1, 44.9, 47.1, 48.8, 56.2, 112.1, 113.9, 143.6, 148.2, 157.7; IR (KBr): 3343, 3130, 2948, 1632 cm^{-1}; EI-MS *m/z* (rel intensity): 247 (M^+, 19); HRMS (FAB-MS) m/z calcd for $C_{21}H_{25}ON$ + H: 248.1645, found 248.1640

N-((1*S*, 2*S*, 4*S*)-1,7,7-Trimethylbicyclo [2.2.1] hept-2-yl)-propanamide (8a)

White crystals; m.p. 106-107℃; ^{1}H-NMR ($CDCl_3$) δ: 0.83 (s, 6H), 0.91 (s, 3H), 1.15 (m, 4H), 1.25-1.34 (m, 1H), 1.52-1.60 (m, 2H), 1.66-1.74 (m, 2H), 1.82-1.90 (m, 1H), 2.19 (q, *J* = 7.6 Hz, 2H), 3.88-3.95 (m, 1H), 5.39 (bs, 1H); ^{13}C-NMR ($CDCl_3$) δ: 10.0, 11.6, 20.2, 26.9, 30.0, 30.9, 35.8, 39.1, 44.8, 47.0, 48.3, 56.4, 172.8; IR (KBr): 3343, 2953, 2879, 1640 cm^{-1}; EI-MS *m/z* (rel intensity): 209 (M^+, 38)

N-((1*S*, 2*S*, 4*S*)-1,7,7-Trimethylbicyclo [2.2.1] hept-2-yl)-2-methylpropionamide (8b)

White crystals; m.p. 104-105℃; ^{1}H-NMR ($CDCl_3$) δ: 0.83 (s, 3H), 0.83 (s, 3H), 0.91 (s, 3H), 1.13-1.61 (m, 6H), 1.26-1.34 (m, 1H), 1.49-1.61 (m, 2H), 1.65-1.74 (m, 3H), 1.82-1.90 (m, 1H), 2.27-2.36 (m, 1H), 3.86-3.94 (m, 1H), 5.38 (bs, 1H); ^{13}C-NMR ($CDCl_3$) δ: 11.6, 19.5, 19.9, 20.2, 27.0, 35.9, 35.9, 39.1, 44.8, 47.0, 48.4, 56.2, 176.0; IR (KBr): 3333, 2955, 1638 cm^{-1}; EI-MS *m/z* (rel intensity): 223 (M^+, 47)

2,2-Dimethyl-*N*-((1*S*, 2*S*, 4*S*)-1,7,7-trimethylbicyclo [2.2.1] hept-2-yl)-propanamide (8c)

White crystals; m.p. 54-56℃; ^{1}H-NMR ($CDCl_3$) δ: 0.82 (s, 3H), 0.84 (s, 3H), 0.92 (s, 3H), 1.12-1.18 (m, 1H), 1.18 (s, 9H), 1.26-1.33 (m, 1H), 1.49-1.61 (m, 2H), 1.66-1.75 (m, 2H), 1.82-1.90 (m, 1H), 3.84-3.91 (m, 1H), 5.62 (bs, 1H); ^{13}C-NMR ($CDCl_3$) δ: 11.6, 20.1, 20.2, 27.0, 27.6, 35.8, 38.6, 39.2, 44.8, 47.0, 48.4, 56.2, 177.3; IR (KBr): 3399, 2953, 2876, 1647 cm^{-1}; EI-MS *m/z* (rel intensity): 237 (M^+, 29)

N-((1*S*, 2*S*, 4*S*)-1,7,7-Trimethylbicyclo [2.2.1] hept-2-yl)-2-propenamide (8d)

White crystals; m.p. 126-127℃; ^{1}H-NMR ($CDCl_3$) δ: 0.84 (s, 3H), 0.85 (s, 3H), 0.93 (s, 3H), 1.13-1.21 (m, 1H), 1.28-1.36 (m, 1H), 1.54-1.64 (m, 2H), 1.68-1.76 (m, 2H), 1.86-1.93 (m, 1H), 3.96-4.03 (m, 1H), 5.56 (bs, 1H), 5.62 (dd, *J* = 1.6 and 10.0 Hz, 1H), 6.06 (dd, *J* = 10.1 and 17.0 Hz, 1H), 6.25 (dd, *J* = 1.6 and 16.9 Hz, 1H); ^{13}C-NMR (δ, $CDCl_3$): 11.7, 20.2, 20.3, 27.0, 35.9, 39.1, 44.8, 47.1, 48.7, 56.7, 126.0, 131.2, 164.8; IR (KBr): 3330, 2957, 2879, 1655 cm^{-1}; EI-MS *m/z* (rel intensity): 207 (M^+, 17)

2-Methyl-*N*-((1*S*, 2*S*, 4*S*)-1,7,7-trimethylbicyclo [2.2.1]-hept-2-yl)-2-propenamide (8e)

White crystals; m.p. 74-75℃; ^{1}H-NMR ($CDCl_3$) δ: 0.85 (s, 3H), 0.86 (s, 3H), 0.94 (s, 3H), 1.13-1.22 (m, 1H), 1.28-1.36 (m, 1H), 1.54-1.62 (m, 2H), 1.66-1.77 (m, 2H), 1.86-1.91 (m, 1H), 1.94-1.96 (m, 3H), 3.91-3.98 (m, 1H), 5.29 (t, *J* = 1.4 Hz, 1H), 5.63 (s, 1H), 5.76 (bs, 1H); ^{13}C-NMR ($CDCl_3$) δ: 11.7, 18.7, 20.2, 20.2, 27.0, 35.9, 39.2, 44.9, 47.1, 48.6, 56.6, 118.7, 140.6, 167.6; IR (KBr): 3328, 2952, 2877, 1653, 1618 cm^{-1}; EI-MS *m/z* (rel intensity): 221 (M^+, 18)

2-Methyl-*N*-((1*S*, 2*S*, 4*S*)-1,7,7-trimethylbicyclo [2.2.1]-hept-2-yl)-2-propenamide (9a)

White crystals; m.p. 74-75℃; ^{1}H-NMR ($CDCl_3$) δ: 0.85 (s, 3H), 0.86 (s, 3H), 0.94 (s, 3H), 1.13-1.22 (m, 1H), 1.28-1.36 (m, 1H), 1.54-1.62 (m, 2H), 1.66-1.77 (m, 2H), 1.86-1.91 (m, 1H), 1.94-1.96 (m, 3H), 3.91-3.98 (m, 1H), 5.29 (t, *J* = 1.4 Hz, 1H), 5.63 (s, 1H), 5.76 (bs, 1H); ^{13}C-NMR ($CDCl_3$) δ: 11.7, 18.7, 20.2, 20.2, 27.0, 35.9, 39.2, 44.9, 47.1, 48.6, 56.6, 118.7, 140.6, 167.6; IR (KBr): 3328, 2952, 2877, 1653, 1618 cm^{-1}; EI-MS *m/z* (rel intensity): 221 (M^+, 18)

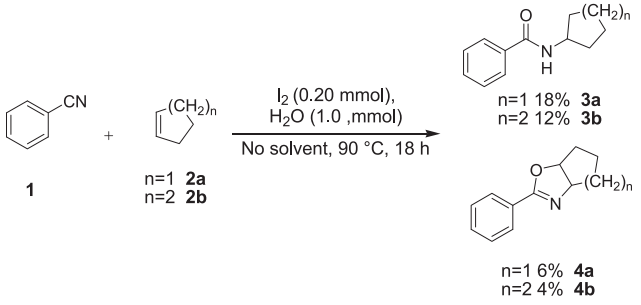
3 RESULTS AND DISCUSSION

The reaction was performed as follows: Benzonitrile (**1**), cyclopentene (**2a**), iodine, and a small amount of water were placed in a reaction tube, which was sealed, and then the mixture was stirred with heating. After the reaction, an aqueous solution of sodium thiosulfate was added in order to remove the iodine. The product was isolated and found to consist of two compounds. After purification, the major product was confirmed by spectroscopic analysis to be the

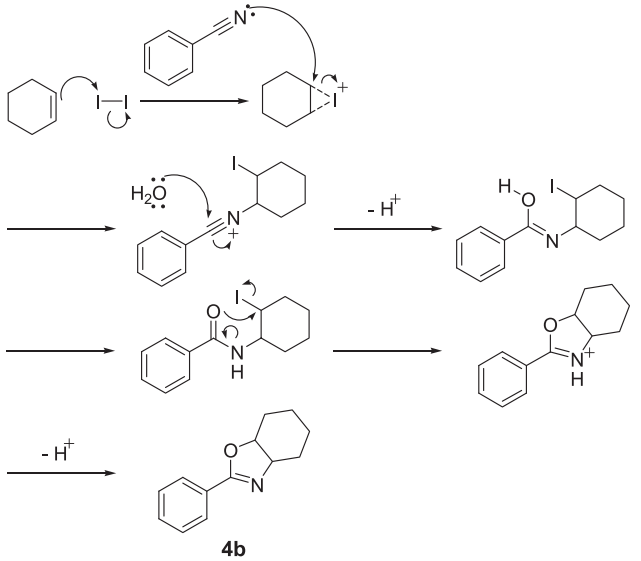
amide compound *N*-cyclopentylbenzamide (**3a**). The structure of the minor product was confirmed to be 2-phenyl-4,5,6,6a-tetrahydro-3a*H*-cyclopenta[*d*]oxazole (**4a**). These results indicated that the Ritter reaction proceeded to form an amide linkage between the cycloolefin and the nitrile, but it was accompanied by a side reaction. A similar side reaction also proceeded in the reaction of benzonitrile with cyclohexene (**2b**), as shown in Scheme 1. A proposed reaction mechanism of the side reaction is shown in Scheme 2.

A π-electron from the double bond in cyclohexene attacks iodine to form a cation intermediate with a three-membered ring. An electron pair from the nitrogen atom in the nitrile attacks this cation intermediate. A water molecule then adds to the cation intermediate, and deprotonation proceeds to form an amide compound with a six-membered ring and an iodide group. An electron pair on the oxygen atom of the amide attacks the carbon atom adjacent to the iodide, resulting in elimination of an iodine atom. Deprotonation subsequently occurs to form (**4b**). The proposed reaction mechanism suggested that addition of iodine to the cycloolefin proceeded easily, accompanying the amidation.

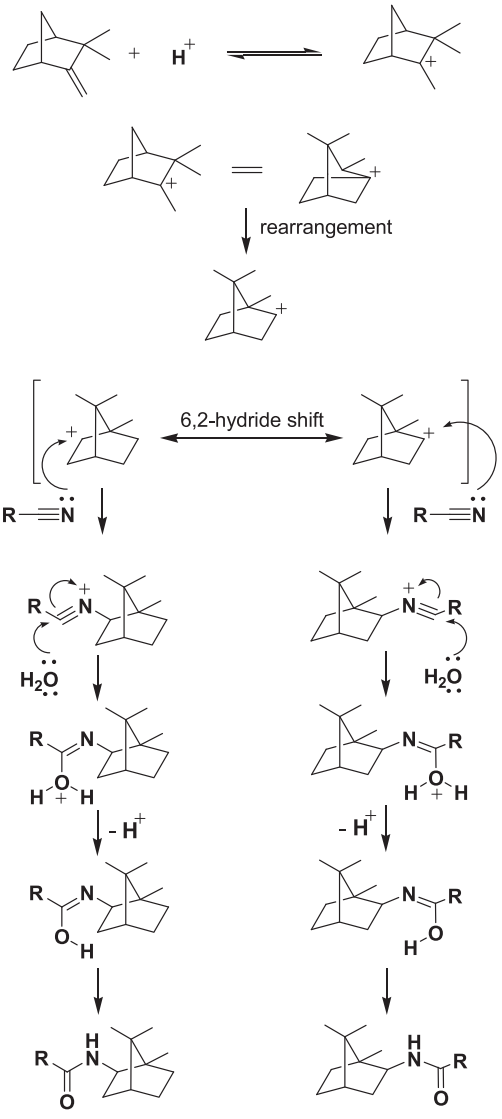
Therefore, (+)-camphene (**5**) was selected as the substrate because addition of iodine to the di-substituted olefin is difficult because of steric hindrance. In addition, formation of a stable tertiary cation intermediate was expected. The reaction was carried out as follows. (+)-Camphene (**5**) (1.0 mmol), benzonitrile (3.0 mmol), iodine (0.20 mmol) and water (1.0 mmol) were reacted at 90℃ for 18 h. After isolation and purification, the product was identified by spectroscopic analysis and measurement of optical rotation as (±)-exo-*N*-isobornylbenzamide (*N*-(1*S*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl)benzamide) (**6**). Although chiral (+)-camphene was used as the substrate, the product was racemic (±)-exo-*N*-isobornylbenzamide. A proposed reaction mechanism of the reaction is shown in Scheme 3. Iodine reacts with water to form hydrogen iodide, which acts as an acidic catalyst. (+)-Camphene



Scheme 1



Scheme 2



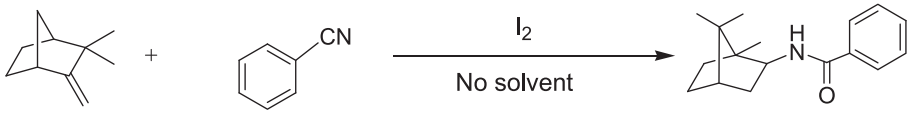
Scheme 3

then reacts with hydrogen iodide to form a cation intermediate, which rearranges to an isobornyl cation. The isobornyl cation undergoes a 6,2-hydride shift to form another cation[11, 12]. These two cations react similarly, and thus, the lone electron pair of the nitrile group attacks these cations to form another pair of cation intermediates. A lone electron pair of water then attacks the resulting cation intermediates. Proton elimination occurs, followed by tautomerization to form the amide linkage. As a result, two optical isomeric exo-*N*-isobornylbenzamides are formed.

The optimized conditions for the formation of (**6**) were investigated, and the results are tabulated in **Table 1**. The molar ratio of (**5**):(**1**) was studied (entries 1-4). When the molar ratio of (**5**):(**1**) was changed from 1:3 to 1:6, the yield remained nearly constant (81-87%). Reaction temperature was also investigated (entries 3, 5-8) at a 1:5 molar ratio. The highest yield (87%) was obtained at a temperature of 90℃ (entry 3). However, when the temperature was raised to 100-110℃, the yield did not increase any further (86%, entries 7 and 8). The amount of iodine was also varied (entries 3, 9, and 10). When iodine was not used, amide (**6**) was not obtained (entry 9). When the molar ratio of benzonitrile:iodine was 1:0.2, the highest yield was obtained at 87% (entry 3). Next, the amount of water was varied (entries 3, 11 and 12). Amide (**6**) was still obtained in 14% yield even when no water was added (entry 11). In this case, moisture in the air may have reacted with the iodine in the reaction system. For a 0.2:1 molar ratio of iodine:water (entry 3), amide (**6**) was obtained in 87% yield. However, further increasing the ratio of water to 0.2:2 produced a slightly decreased yield (75%, entry 12). Thus, the optimized molar ratio of iodine:water was determined to be 0.2:1. Finally, the reaction time was investigated (entries 3 and 11-14). The highest yield (87%) was obtained after a reaction time of 18 h (entry 3). When the reaction time was increased to 24 h, the yield decreased slightly to 85% (entry 16). From these results, the optimized conditions were determined to be as follows: molar ratio of nitrile:iodine:water, 1:0.2:1.0; molar ratio of nitrile:ester, 1:5; temperature, 90℃; and reaction time, 18 h.

The results of the reaction of (+)-camphene (**5**) carried out using these conditions with other aromatic nitriles are summarized in **Table 2**. When 4-methoxybenzonitrile, having an electron-donating methoxy group, was used in place of benzonitrile (entry 1), the yields increased slightly

Table 1 Reactions of benzonitrile (**1**) with (+)-camphene (**5**).

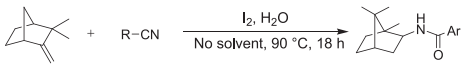


5 **6**

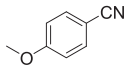
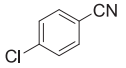
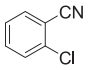
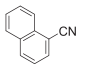
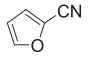
Entry	Molar ratio of (**5**):(**1**)	I_2 (mmol)	H_2O (mmol)	Temp. (℃)	Time (h)	Yield (%)
1	1:3	0.20	1.0	90	18	81
2	1:4	0.20	1.0	90	18	80
3	1:5	0.20	1.0	90	18	87
4	1:6	0.20	1.0	90	18	86
5	1:5	0.20	1.0	70	18	74
6	1:5	0.20	1.0	80	18	84
7	1:5	0.20	1.0	100	18	86
8	1:5	0.20	1.0	110	18	86
9	1:5	0	1.0	90	18	0
10	1:5	0.10	1.0	90	18	75
11	1:5	0.20	0	90	18	14
12	1:5	0.20	2.0	90	18	75
13	1:5	0.20	1.0	90	6	78
14	1:5	0.20	1.0	90	7	80
15	1:5	0.20	1.0	90	8	81
16	1:5	0.20	1.0	90	24	85

All reactions were carried out using 1.0 mmol of (**1**).

Table 2 Iodine-catalyzed amidation of (5) with aromatic nitriles.

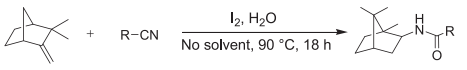


5 7

Entry	Nitrile	Yield (%)
1		91 (7a)
2		98 (7b)
3		87 (7c)
4		73 (7d)
5		77 (7e)

Reaction conditions: (5) 1.0 mmol, nitriles 5.0 mmol, iodine 0.20 mmol, and water 1.0 mmol.

Table 3 Iodine-catalyzed amidation of (5) with aliphatic nitriles.



5 8

Entry	Nitrile	Yield (%)
1		68 (8a)
2		59 (8b)
3		93 (8c)
4		83 (8d)
5		89 (8e)

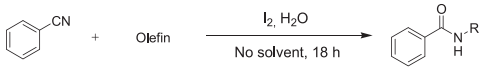
Reaction conditions: (5) 1.0 mmol, nitriles 5.0 mmol, iodine 0.20 mmol, and water 1.0 mmol.

to 91%. When 4-chlorobenzonitrile containing a chloro group as an electron-withdrawing group was used (entry 2), the yield of the corresponding amide increased to 98%. However, when 2-chlorobenzonitrile was used (entry 3), the yield remained virtually the same (87%). This was attributed to the steric hindrance of the 2-chloro group. When 2-cyanonaphthalene (entry 4) or 2-cyanofuran (entry 5) was used, the yield decreased.

The results of the reaction of aliphatic nitriles with (+)-camphene (5) are shown in Table 3. The yield in the reaction with 2,2-dimethylpropanenitrile (entry 3) was higher compared to those of propanenitrile (entry 1) and 2-methylpropanenitrile (entry 2). This was due to the higher electron density on the nitrogen atom from the three electron-donating methyl groups in 2,2-dimethylpropanenitrile. We previously reported that, in the reactions of aliphatic nitriles with 1-phenylethyl acetate, higher yield is obtained with saturated rather than unsaturated nitriles[8]. However, when (+)-camphene was used instead of 1-phenylethyl acetate, there was no difference in the yield of the corresponding amide compounds.

The reactions of several terpenic olefins with benzonitrile were attempted, and the results are shown in Table 4. (±)-α-Pinene (entry 1) and (−)-β-pinene (entry 3) were reacted with benzonitrile under the optimized conditions obtained from the reaction of (+)-camphene with benzonitrile. However, neither reaction proceeded. The reaction temperature was subsequently raised to 125℃ (entries 2 and 4), affording a complex mixture of products. These results were attributed to the unstable four-membered ring in pinenes. D-Limonene was reacted with benzonitrile at 90℃ (entry 5), but again a complex mixture of products was obtained, possibly because D-limonene has two double bonds. Styrene was reacted at a lower temperature, 70℃ (entry 6), to prevent polymerization. The amide compound (9a) was obtained at a low yield of 11%.

Table 4 Iodine-catalyzed amidation of (1) with terpenic olefins.



1 9

Entry	Olefin	Temp. (℃)	Yield (%)
1		90	No reaction
2		125	Complex mixture
3		90	No reaction
4		125	Complex mixture
5		90	Complex mixture
6		70	11 (9a)

Reaction conditions: olefin 1.0 mmol, benzonitriles 5.0 mmol, iodine 0.20 mmol, and water 1.0 mmol.

In conclusion, the reaction of cycloolefins, such as cyclopentene and cyclohexene, with benzonitrile using iodine as a catalyst under solvent-free conditions gave two products: an amide compound and a heterocyclic compound. The reaction of chiral (+)-camphene with benzonitrile using

iodine as a catalyst under solvent-free conditions caused skeletal rearrangement of camphene, i.e., a 6,2-hydride shift of the isobornyl cation and amidation, resulting in racemic(±)-*N*-isobornylbenzamide. Similar amidation also proceeded in the reaction of(+)-camphene with several aromatic and aliphatic nitriles.

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