Supporting Information

CHLOROAMIDATION OF ALKENES USING SODIUMHYPOCHLORITE PENTAHYDRATE AND ITS APPLICATION TO SYNTHESIS OF AZIRIDINES

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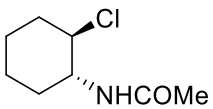
Experimental Details

General

All reagents were purchased from Nacalai Tesque, Wako Pure Chemicals Industries, Kanto Kagaku, Kishida Reagents Chemical Co., Tokyo Chemical Industry (TCI), or Aldrich, and used without further purification. Melting points were measured with a Yanaco micro melting point apparatus (MP-J3) and are uncorrected. NMR spectra were recorded on a JEOL JNM-EX400 spectrometer as solutions in $CDCl_3$ using TMS or the residual solvent peak as an internal standard. The IR spectra were recorded using a Jasco IR-8300 FT-IR spectrophotometer. The mass spectra were recorded on a Shimadzu GCMS-QP1100EX spectrometer (EI), JEOL JMS-T100LC spectrometer (ESI) or JEOL JMS-700 (FAB).

The experimental procedures are provided in the main text as ref. 6, 8, and 11.

trans-N-(2-Chlorocyclohexyl)acetamide (**2aa**)[1)]

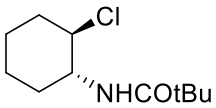


Colorless crystals: mp 128 °C (lit.[1)] 127-130 °C).

^{1}H NMR ($CDCl_3$) δ: 1.20-1.43 (m, 3H), 1.69-1.81 (m, 3H), 2.02 (s, 3H), 2.11-2.28 (m, 2H), 3.72-3.75 (m, 1H), 3.86-3.88 (m, 1H), 5.72 (brs, 1H).

^{13}C NMR ($CDCl_3$) δ: 23.5, 24.1, 25.4, 32.8, 36.0, 55.0, 62.5, 169.7.

trans-*N*-(2-Chlorocyclohexyl)pivalamide (**2ab**)[2)]

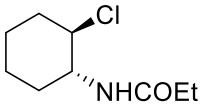


Colorless crystals: mp 149 °C (lit.[2)] 150 °C).

^{1}H NMR ($CDCl_3$) δ: 1.21 (s, 9H), 1.24-1.48 (m, 2H), 1.67-1.82 (m, 2H), 2.14-2.21 (m, 2H), 2.23-2.29 (m, 2H), 3.74-3.86 (m, 2H), 5.64 (brs, 1H).

^{13}C NMR ($CDCl_3$) δ: 24.1, 25.4, 27.5, 32.6, 36.1, 38.7, 55.0, 62.6, 178.0.

trans-*N*-(2-Chlorocyclohexyl)propionamide (**2ac**)[1)]

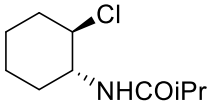


Colorless crystals: mp 120 °C (lit.[1)] 118-119 °C).

^{1}H NMR ($CDCl_3$) δ: 1.19 (t, *J* = 7.2 Hz, 3H), 1.21-1.44 (m, 3H), 1.67-1.79 (m, 3H), 2.17-2.24 (m, 4H), 3.74 (dd, *J* = 10.6, 4.2 Hz, 1H), 3.90-3.82 (m, 1H), 5.44 (brs, 1H).

^{13}C NMR ($CDCl_3$) δ: 9.9, 24.2, 25.4, 29.9, 32.8, 36.1, 54.9, 62.6, 173.4.

trans-*N*-(2-Chlorocyclohexyl)-2-methylpropanamide (**2ad**)



Colorless crystals: mp 117 °C.

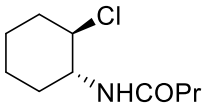
^{1}H NMR ($CDCl_3$) δ: 1.17 (t, 6H, *J* = 6.5 Hz), 1.20-1.46 (m, 2H), 1.69-1.81 (m, 4H), 2.15-2.38 (m, 3H), 3.75-3.85 (m, 2H), 5.53 (brs, 1H).

^{13}C NMR ($CDCl_3$) δ: 19.5, 19.7, 24.2, 25.5, 32.8, 35.9, 36.1, 54.8, 62.6, 176.6.

IR ($CHCl_3$) cm^{-1}: 672, 751, 1208, 1428, 1516, 1670, 2399, 3010.

HRMS (ESI) $C_{10}H_{18}ClNONa^{+}$ calcd for m/z 226.0969 $(M+Na)^{+}$, found 226.0972.

trans-*N*-(2-Chlorocyclohexyl)butanamide (**2ae**)



Colorless crystals: mp 89 °C.

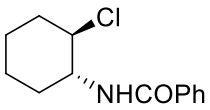
^{1}H NMR ($CDCl_3$) δ: 0.96 (t, 3H, *J* = 7.3 Hz), 1.19-1.47, (m, 4H), 1.63-1.82 (m, 4H), 2.15-2.28 (m, 4H), 3.69-3.76 (m, 1H), 3.83-3.90 (m, 1H), 5.49 (brs, 1H).

^{13}C NMR ($CDCl_3$) δ: 13.6, 19.2, 24.2, 25.4, 32.8, 36.0, 38.9, 54.9, 62.5, 172.6.

IR ($CHCl_3$) cm^{-1}: 664, 747, 1212, 1512, 1661, 2399, 2943, 3010.

HRMS (ESI) $C_{10}H_{18}ClNONa^{+}$ calcd for 226.0969 m/z $(M+Na)^{+}$, found 226.0970.

trans-*N*-(2-Chlorocyclohexyl)benzamide (**2af**)[1)]

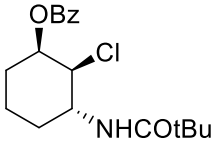


Colorless crystals: mp 140 °C (lit.[1)] 140-141 °C).

^{1}H NMR ($CDCl_3$) δ: 1.30-1.42 (m, 2H), 1.48-1.88 (m, 4H), 2.17-2.37 (m, 2H), 3.85-3.90 (m, 1H), 4.01-4.10 (m, 1H), 6.16 (brs, 1H), 7.42-7.53 (m, 3H), 7.77-7.80 (m, 2H).

^{13}C NMR ($CDCl_3$) δ: 24.2, 25.5, 32.8, 36.2, 55.7, 62.6, 127.0, 128.6, 131.5, 134.8, 167.3.

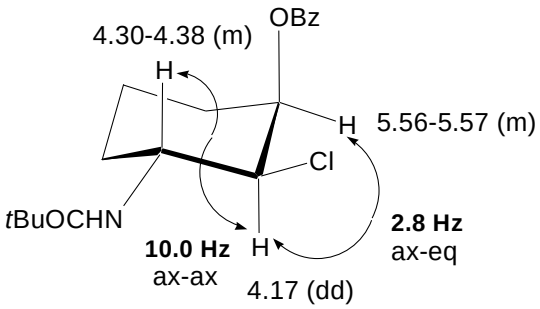
(1*R**,2*S**,3*R**)-2-Chloro-3-pivalamidocyclohexyl benzoate (**2bb**)



Colorless crystals: mp 200-204 °C.

^{1}H NMR ($CDCl_3$) δ: 1.23 (s, 9H), 1.63-1.81 (m, 4H), 2.13-2.21 (m, 1H), 2.23-2.31 (m, 1H), 4.17 (dd, *J* = 10.0, 2.8 Hz, 1H), 4.30-4.38 (m, 1H), 5.56-5.57 (m, 1H), 5.80 (brs, 1H), 7.44-7.48 (m, 2H), 7.56-7.60 (m, 1H), 8.09-8.11 (m, 2H).

Relative stereochemistry of **2bb** was determined by the coupling constants of ^{1}H NMR as shown below.



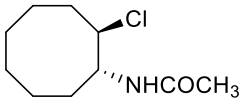
It is not clear why the reaction proceeded regio- and stereoselectively. Corey et al. reported that the similar α-bromoamide was produced from the reaction of **1b** with $CH_3CONHBr$ in CH_3CN.[3)]

^{13}C NMR($CDCl_3$) δ: 19.1, 27.4, 29.4, 31.6, 38.7, 51.9, 62.7, 72.5, 128.4, 129.7, 133.1, 134.0, 165.6, 178.3.

IR ($CHCl_3$) cm^{-1}: 714, 1104, 1269, 1525, 1631, 1718, 2957, 3350.

HRMS (ESI) $C_{18}H_{24}ClNO_3Na^+$ calcd for 360.1337 m/z $(M+Na)^+$, found 360.1336.

trans-*N*-(2-Chlorocyclooctyl)acetamide (**2ca**)



Pale yellow oil.

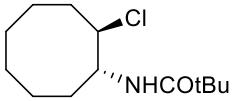
^{1}H NMR ($CDCl_3$) δ: 1.14-1.71 (m, 9H), 1.89-2.01 (m, 3H), 1.87 (s, 3H), 3.85 (m, 1H), 4.12-4.16 (m, 1H), 6.19 (brs, 1H).

^{13}C NMR ($CDCl_3$) δ: 22.8, 22.9, 23.2, 28.3, 30.1, 32.2, 33.7, 49.1, 62.7, 169.0.

IR (neat) cm^{-1}: 746, 1108, 1284, 1372, 1415, 1542, 1646, 2933, 3238.

HRMS (ESI) calcd for $C_{10}H_{18}ClNONa^+$ m/z 226.0969 $(M+Na)^+$, found 226.0970.

trans-*N*-(2-Chlorocyclootyl)pivalamide (**2cb**)



Colorless oil.

^{1}H NMR ($CDCl_3$) δ: 1.17 (s, 9H), 1.47-1.61 (m, 2H), 1.70-1.84 (m, 4H), 1.98-2.27 (m, 6H), 3.90-3.93 (m, 1H), 4.19-4.28 (m, 1H), 5.54 (brs, 1H).

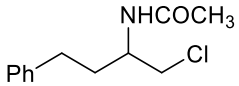
^{13}C NMR ($CDCl_3$) δ: 22.9, 27.5, 28.8, 30.6, 32.4, 33.9, 38.5, 49.0, 62.7, 177.2.

IR (neat) cm^{-1}: 667, 1009, 1202, 1368, 1466, 1525, 1639, 2938, 3343.

HRMS (ESI) $C_{13}H_{24}ClNONa^+$ calcd for m/z 268.1439 $(M+Na)^+$, found 268.1439.

N-[1-(Chloromethyl)-3-phenylpropyl]acetamide (**2da**)

A Markovnikov-type product **2da** was obtained. The chemical shifts of terminal protons (3.63 and 3.72) suggested that the terminal carbon is bonded to chlorine atom.



Colorless crystals: mp 61 °C.

^{1}H NMR ($CDCl_3$) δ: 1.92 (q, 2H, *J* = 7.3 Hz), 1.97 (s, 3H), 2.64-2.68 (m, 2H), 3.63 (dd, *J* =11.5, 3.6 Hz, 1H), 3.72 (dd, *J* = 11.5, 3.6 Hz, 1H), 4.23-4.27 (m ,1H), 5.88 (brs, 1H), 7.17-7.23 (m, 5H).

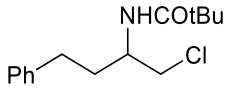
^{13}C NMR ($CDCl_3$) δ: 23.2, 32.1, 33.3, 48.1, 49.0, 126.1, 128.2, 128.4, 140.9, 169.8.

IR ($CHCl_3$) cm^{-1}: 703, 1105, 1281, 1372, 1432, 1543, 1650, 3057, 3279.

HRMS (ESI) $C_{12}H_{16}ClNONa^+$ calcd for 248.0813 m/z $(M+Na)^+$, found 248.0805.

N-[1-(Chloromethyl)-3-phenylpropyl)pivalamide (**2db**)

A Markovnikov-type product **2db** was obtained. The chemical shifts of terminal protons (3.60-3.73) suggested that the terminal carbon is bonded to chlorine atom.



Colorless crystals: mp 55-61 °C

^{1}H NMR ($CDCl_3$) δ: 1.17 (s, 9H), 1.92-194 (m, 2H), 2.63-2.71 (m, 2H), 3.60-3.73 (m, 2H), 4.23-4.28 (m, 1H), 5.76 (brs, 1H), 7.18-7.33 (m, 5H).

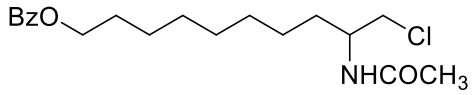
^{13}C NMR ($CDCl_3$) δ: 27.4, 33.4, 38.7, 48.2, 66.9, 70.5, 126.1, 128.2, 128.5, 141.0, 178.1.

IR ($CHCl_3$) cm^{-1}: 746, 1033, 1206, 1525, 1639, 2961, 3339.

HRMS (ESI) $C_{15}H_{22}ClONa^+$ calcd for m/z 290.1288 $(M+Na)^+$, found 290.1274.

9-Acetylamino-10-chlorodecyl benzoate (**2ea**)

A Markovnikov-type product **2ea** was obtained. The chemical shifts of terminal protons (3.58-3.70) suggested that the terminal carbon is bonded to chlorine atom.



Colorless oil.

^{1}H NMR ($CDCl_3$) δ: 1.32-1.75 (m, 15H), 2.01 (s, 3H), 3.58-3.70 (m, 2H), 4.29-4.32 (m, 2H), 6.17 (brs, 1H), 7.41-7.45 (m, 2H), 7.52-7.74 (m, 1H), 8.03-8.04 (m, 2H).

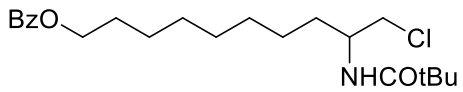
^{13}C NMR ($CDCl_3$) δ: 23.0, 25.5, 28.4, 28.7, 28.9, 29.0, 31.4, 47.8, 49.2, 60.1, 64.8, 128.1, 129.3, 130.2, 132.6, 166.5, 169.7.

IR (neat) cm^{-1}: 757, 1115, 1281, 1379, 1446, 1536, 1646, 1714, 2930, 3276.

HRMS (ESI) $C_{19}H_{28}ClNO_3Na^+$ calcd for m/z 376.1650 $(M+Na)^+$, found 376.1637.

10-Chloro-9-pivalaminodecyl benzoate (**2eb**)

A Markovnikov-type product **2eb** was obtained. The chemical shifts of terminal protons (3.61 and 3.71) suggested that the terminal carbon is bonded to chlorine atom.



Colorless oil.

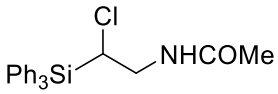
^{1}H NMR ($CDCl_3$) δ: 1.20 (s, 9H), 1.32-1.42 (m, 12H), 1.52-1.63 (m, 2H), 1.69-1.79 (m, 3H), 3.61 (d, *J* = 3.7 Hz, 1H), 3.71 (d, *J* = 3.7 Hz, 1H), 5.70 (brs, 1H), 7.42-7.46 (m, 2H), 7.53-7.55 (m, 1H), 8.03-8.05 (m, 2H).

^{13}C NMR ($CDCl_3$) δ: 25.8, 25.9, 27.4, 28.6, 29.1, 31.6, 38.7, 48.3, 48.8, 65.0, 65.3, 66.9, 128.2, 129.4, 130.4, 132.7, 166.6, 178.0.

IR (neat) cm^{-1}: 718, 1120, 1277, 14.54, 1525, 1650, 1718, 2934, 3390.

HRMS (ESI) $C_{22}H_{34}NO_3Na^+$ calcd for m/z 418.2119 $(M+Na)^+$, found 418.2111.

N-[2-Chloro-2-(triphenylsilyl)ethyl]acetamide (**2fa**)[1)]

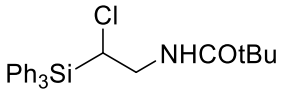


Colorless crystals: mp 154 °C (lit.[1)] 152-153 °C).

^{1}H NMR ($CDCl_3$) δ: 1.84 (s, 3H), 3.31-3.23 (m, 2H), 4.31 (dd, *J* = 3.2, 10.6 Hz, 1H), 6.09 (brs, 1H), 7.46-7.35 (m, 9H), 7.66-7.63 (m, 6H).

^{13}C NMR ($CDCl_3$) δ: 22.3, 43.3, 47.8, 128.0, 130.2, 131.4, 136.0, 170.2.

N-[2-Chloro-2-(triphenylsilyl)ethyl]pivalamide (**2fb**)



Colorless crystals: mp 155-160 °C.

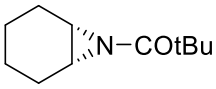
^{1}H NMR ($CDCl_3$) δ: 1.12 (s, 9H), 3.17-3.23 (m, 2H), 4.39 (dd, *J* = 3.0, 11.4 Hz,1H), 6.19 (brs, 1H), 7.35-7.46 (m, 9H), 7.60-7.66 (m, 6H).

^{13}C NMR ($CDCl_3$) δ: 24.4, 28.4, 57.2, 64.7, 127.9, 128.1, 130.1, 136.0, 178.7.

IR ($CHCl_3$) cm^{-1}: 702, 1111, 1206, 1304, 1427, 1517, 1646, 2965, 3059.

HRMS (ESI) $C_{25}H_{28}ClNOSiNa^+$ calcd for m/z 444.1521 $(M+Na)^+$, found 444.1517.

N-Pivaloyl-7-azabicyclo[4.1.0]heptane (**3ab**)[3)]



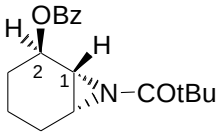
Colorless oil.

^{1}H NMR ($CDCl_3$) δ: 1.23 (s, 9H), 1.28-1.29 (m, 2H), 1.42-1.49 (m, 2H), 1.81-1.83 (m, 2H), 1.87-1.96 (m, 2H), 2.63-2.64 (m, 2H).

^{13}C NMR ($CDCl_3$) δ: 20.0, 23.7, 28.0, 35.9, 41.1, 192.3.

(1*R**,2*R**,6*R**)-*N*-Pivaloyl-7-azabicyclo[4.1.0]heptan-2-yl benzoate (**3bb**)

Relative stereochemistry of **3bb** was determined by NOE-experiment of ^{1}H-NMR. H^1 and H^2 are *trans* because NOE was not observed between them.



Colorless oil.

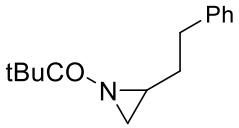
^{1}H NMR ($CDCl_3$) δ: 1.19 (s, 9H), 1.35-1.59 (m, 3H), 1.78-1.92 (m, 3H), 2.72-2.73 (m, 1H), 2.58-2.77 (m, 1H), 5.31 (t, *J* = 5.8 Hz, 1H), 7.36-7.39 (m, 2H), 7.48-7.51 (m, 1H), 7.98-8.01 (m, 2H).

^{13}C NMR ($CDCl_3$) δ: 15.3, 23.0, 26.2, 27.9, 36.4, 38.2, 41.3, 68.6, 128.4, 129.6, 130.2, 133.0, 165.8, 191.8.

IR (neat) cm^{-1}: 1096, 1151, 1269, 1450, 1710, 2953.

HRMS (ESI) $C_{18}H_{23}NO_3Na^+$ calcd for m/z 324.1570 $(M+Na)^+$, found 324.1565.

2,2-Dimethyl-1-[2-(2-phenethyl)aziridin-1-yl)propan-1-one (**3db**)



Pale yellow oil.

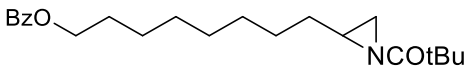
^{1}H NMR ($CDCl_3$) δ: 1.23 (s, 9H), 1.66 (m, 1H), 1.93 (d, *J* = 4.5 Hz, 1H), 2.10-2.13 (m, 1H), 2.35 (d, *J* = 4.5 Hz, 1H), 2.46-2.27 (m, 1H), 2.72-2.76 (m, 2H), 7.17-7.21 (m, 3H), 7.27-7.30 (m, 2H).

^{13}C NMR ($CDCl_3$) δ: 27.9, 30.6, 32.7, 33.7, 36.9, 41.2, 126.0, 128.4, 128.4, 141.2, 191.8.

IR (neat) cm^{-1}: 1115, 1162, 1300, 1402, 1466, 1682, 2866, 2965.

HRMS (ESI) $C_{15}H_{21}NONa^+$ calcd for m/z 254.1515 $(M+Na)^+$, found 254.1508.

8-[1-Pivaloylaziridin-2-yl]octyl benzoate (**3eb**)



Colorless oil.

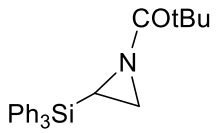
^{1}H NMR ($CDCl_3$) δ: 1.24 (s, 9H), 1.29-1.42 (m, 14H), 1.73-1.84 (m, 2H), 1.92 (d, *J* = 4.8 Hz, 1H), 2.35 (d, *J* = 4.8 Hz, 1H), 2.38-2.43 (m, 1H), 7.42-7.45 (m, 2H), 7.53-7.57 (m, 1H), 8.03-8.05 (m, 2H).

^{13}C NMR ($CDCl_3$) δ: 26.0, 26.3, 38.0, 28.7, 29.2, 29.2, 29.4, 30.4, 32.0, 37.7, 41.2, 65.1, 128,3, 129.5, 130.5, 132.8, 166.7, 191.9.

IR (neat) cm^{-1}: 1111, 1273, 1457, 1682, 1718, 2858, 2930.

HRMS (ESI) $C_{22}H_{33}NO_3$ calcd for m/z 382.2353 $(M+Na)^+$, found 382.2341.

2,2-Dimethyl-1-[2-(triphenylsilyl)azairidin-1-yl]propan-1-one (**3fb**)



Pale yellow oil.

^{1}H NMR ($CDCl_3$) δ: 1.25 (s, 9H), 2.12-2.14 (m, 1H), 2.47 (dd, *J* = 8.2, 4.4 Hz, 1H), 2.58 (dd, *J* = 8.2, 4.4 Hz, 1H), 7.34-7.42 (m, 9H), 7.58-7.63 (m, 6H).

^{13}C NMR ($CDCl_3$) δ: 22.0, 27.8, 30.2, 41.3, 127.8, 129.8, 132.7, 135.9, 192.1.

IR (neat) cm^{-1}: 1022, 1107, 1293, 1430, 1678, 2957.

HRMS (ESI) calcd for $C_{25}H_{27}NOSiNa^{+}$ m/z 408.1754 $(M+Na)^{+}$, found 408.1751.

References

1) D. W. Tay, I. T. Tsoi, J. C. Er, G. Y. C. Leung, and Y. Yeung, *Org. Lett.*, 2013, **15**, 1310.

2) J. Lessad, M. Mondon, and D. Tochard, *Can. J. Chem.*, 1981, **59**, 431.

3) Y. Yeung, X. Gao, and E. J. Corey, *J. Am. Chem. Soc.*, 2006, 128, **30**, 9644.