Tetrahedron xxx (2017) 1–6

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Synthesis of 2-azabicyclo[2.1.0]pentanes by the intramolecular nucleophilic substitution of cyclopropylmagnesium carbenoids with magnesium anilide

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ARTICLE INFO

Article history:
Received 4 February 2017
Received in revised form
13 March 2017
Accepted 15 March 2017
Available online xxx

Keywords:
Cyclopropylmagnesium carbenoid
Intramolecular nucleophilic substitution
4-exo-tet cyclization
2-Azabicyclo[2.1.0]pentane
Asymmetric synthesis

ABSTRACT

A variety of 2-azabicyclo[2.1.0]pentanes were synthesized by the intramolecular nucleophilic substitution of cyclopropylmagnesium carbenoids with magnesium anilide. The 1-chlorocyclopropyl *p*-tolyl sulfoxides possessing an *N*-aryl-substituted aminomethyl group were prepared from dichloromethyl *p*-tolyl sulfoxide, α,β-unsaturated carboxylic acid esters, and anilines in four steps. The deprotonation of the amine with *t*-BuMgCl followed by sulfoxide/magnesium exchange of the sulfoxides with *i*-PrMgCl led to the generation of the cyclopropylmagnesium carbenoids possessing a magnesium anilide moiety. Subsequent intramolecular nucleophilic substitution of the cyclopropylmagnesium carbenoids occurred in a *4-exo-tet* manner to give the 2-azabicyclo[2.1.0]pentanes. The optically active 2-azabicyclo[2.1.0]pentane was synthesized using a *p*-tolylsulfinyl group as a chiral auxiliary.

1. Introduction

2-Azabicyclo[2.1.0]pentanes are a class of highly strained bicyclic compounds in which cyclopropane and azetizine are fused across a C–C bond. The 2-azabicyclo[2.1.0]pentane skeleton is found in SF-1836 and attracts attention as a conformationally restricted pyrrolidine analog in the field of drug development.[1,2] 2-Azabicyclo[2.1.0]pentanes are also used as synthetic intermediates in the total synthesis of natural products.[3] Despite their potential utility, the chemistry of 2-azabicyclo[2.1.0]pentanes is scarce mainly due to the lack of efficient synthetic method of 2-azabicyclo[2.1.0]pentanes. One of the most straightforward synthetic methods of 2-azabicyclo[2.1.0]pentanes is the nucleophilic substitution of halocyclopropanes with intramolecular nitrogen nucleophiles in a *4-exo-tet* manner. However, in general, the nucleophilic substitution at the carbon atom of small rings does not proceed efficiently because of the inaccessibility of nucleophiles to the C–X antibonding orbital and a disadvantageous highly strained transition state structure.[4] Nevertheless, cyclopropyl- and cyclobutylmagnesium carbenoids react with nucleophiles such as (α-sulfonylalkyl)lithiums, Grignard reagents, lithium phenolates and naphtholates, and lithium anilides to give multi-substituted cyclopropanes and cyclobutanes.[5,6] If cyclopropylmagnesium carbenoids possessing a nitrogen nucleophile can be generated, intramolecular nucleophilic substitution is expected to occur to give 2-azabicyclo[2.1.0]pentanes. Herein, we report the synthesis of 2-azabicyclo[2.1.0]pentanes by the *4-exo-tet* cyclization of cyclopropylmagnesium carbenoids possessing a magnesium anilide moiety.

2. Results and discussion

2.1. Preparation of cyclization precursors

As cyclization precursors, we designed the 1-chlorocyclopropyl *p*-tolyl sulfoxides **1** possessing *N*-aryl-substituted aminomethyl groups (Scheme 1). Deprotonation and sulfoxide/magnesium exchange of the sulfoxides **1** are expected to generate bifunctional species in which an electrophilic cyclopropylmagnesium carbenoid moiety and a nucleophilic magnesium amide moiety coexist in each molecule. A variety of *N*-aryl-substituted 2-(aminomethyl)-1-chlorocyclopropyl *p*-tolyl sulfoxides **1** were prepared from dichloromethyl *p*-tolyl sulfoxide, α,β-unsaturated carboxylic acid esters, and anilines in four steps.[7] Annulation of α,β-unsaturated carboxylic acid esters with dichloromethyl *p*-tolyl sulfoxide in the

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http://dx.doi.org/10.1016/j.tet.2017.03.045
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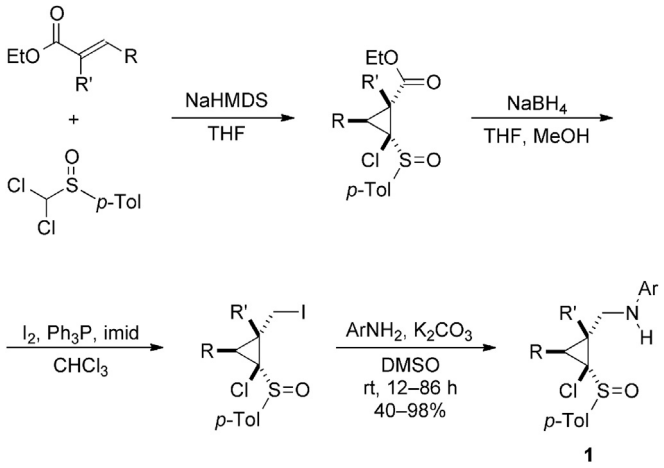
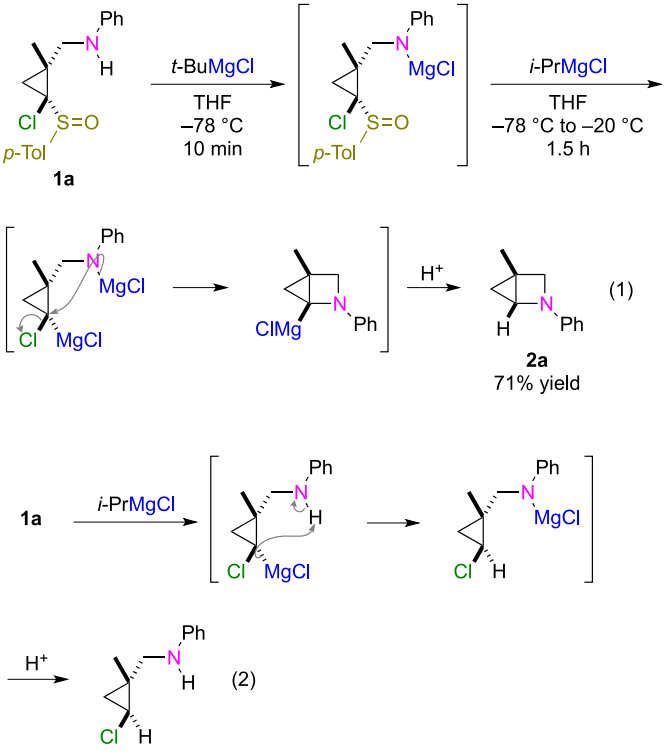


Scheme 1. Synthesis of cyclization precursors **1**.

presence of NaHMDS gave 1-chlorocyclopropyl *p*-tolyl sulfoxides possessing an ethoxycarbonyl group. Reduction of the ethoxycarbonyl group and iodination of the resulting hydroxy group afforded 1-chloro-2-(iodomethyl)cyclopropyl *p*-tolyl sulfoxides.[8] The reaction of the alkyl iodides with the anilines in the presence of K_2CO_3 gave the cyclization precursors **1** in 40–98% yields.

2.2. Cyclization reaction

With the key precursors **1** in hand, the synthesis of 2-azabicyclo[2.1.0]pentanes was examined (Scheme 2, Eq. 1). Deprotonation of the secondary amine should be carried out in advance of the sulfoxide/magnesium exchange reaction to generate the bifunctional species. Otherwise, the generated cyclopropylmagnesium carbenoids will abstract the proton of the secondary amine to give the undesirable chlorocyclopropanes (Scheme 2, Eq. 2). We chose *t*-BuMgCl, which was unreactive towards the *p*-tolylsulfinyl group, as a base. A solution of *t*-BuMgCl in THF was added to a solution of the sulfoxide **1a** in THF at −78 °C, and then, a solution of *i*-PrMgCl in THF was added to the resulting solution. The reaction mixture was warmed to −20 °C and quenched with aqueous NH_4Cl. As a result, the desired 2-azabicyclo[2.1.0]pentane **2a** was obtained in 71% yield.

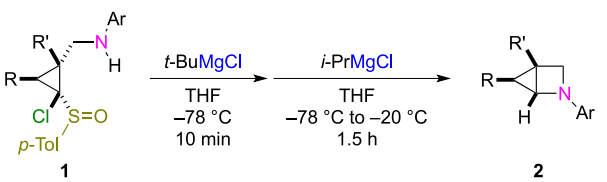


Scheme 2. Synthesis of 2-azabicyclo[2.1.0]pentane **2a**.

The scope of the cyclization was explored with a variety of sulfoxides **1b**–**h** (Table 1). When sulfoxides **1b**, **1c**, and **1e** possessing one or two methoxy groups at the *o*- or *m*-positions were subjected to the reaction with *t*-BuMgCl and *i*-PrMgCl, the corresponding 2-azabicyclo[2.1.0]pentanes **2b**, **2c**, and **2e** were formed in 59–78% yields, whereas 2-azabicyclo[2.1.0]pentane **2d** possessing a *N*-(4-methoxyphenyl) group could not be isolated because of its instability (entries 1–4). The reaction of sulfoxide **1f** possessing an electron-withdrawing trifluoromethyl group at the *m*-position also gave the bicyclic product **2f** in 58% yield (entry 5). The cyclization of the cyclopropylmagnesium carbenoid generated from sulfoxide **1g** possessing a 2-phenylethyl group on the cyclopropane ring occurred to give 2-azabicyclo[2.1.0]pentane **2g** in 74% yield (entry 6). The crude 4,5-dimethyl-2-azabicyclo[2.1.0]pentane **2h** was obtained in 60% yield after short silica gel column purification (entry 7). Further purification of the crude product by column chromatography on silica gel resulted in the decomposition of **2h**. In all cases, small amounts of the chlorocyclopropanes, which originated from the protonation of the cyclopropylmagnesium carbenoids, were formed as by-products. The 2-azabicyclo[2.1.0]pentanes **2**, except the *N*-(4-methoxyphenyl)- and 4,5-dimethyl-substituted derivatives **2d** and **2h**, were sufficiently stable and were purified by column chromatography on silica gel. For instance, neat 2-azabicyclo[2.1.0]pentane **2c** could be stored at −15 °C for several months. When a solution of 2-azabicyclo[2.1.0]pentane **2c** in $CHCl_3$ was left at room temperature for two weeks, a slight amount of decomposition occurred. Approximately half of 2-azabicyclo[2.1.0]pentane **2c** decomposed under reflux in toluene for one week.

To gain insight into the reaction mechanism, the reaction of sulfoxide **1c** with *t*-BuMgCl and *i*-PrMgCl was quenched with CH_3OD (Scheme 3). As a result, 2-azabicyclo[2.1.0]pentane **2c′** possessing a deuterium atom was formed with a high deuterium content. This result indicates the intermediacy of the organomagnesium chloride **3c**. In addition, the reaction of sulfoxide **1c** with *t*-BuMgCl did not afford 1-(*p*-tolylsulfinyl)-2-azabicyclo[2.1.0]pentane. Therefore, we speculate that the nucleophilic substitution

Table 1
Synthesis of 2-azabicyclo[2.1.0]pentanes **2**.



Entry	1	R	R′	Ar	2	Yield of **2** (%)
1	**1b**	H	Me	2-$MeOC_6H_4$	**2b**	59
2	**1c**	H	Me	3-$MeOC_6H_4$	**2c**	76
3	**1d**	H	Me	4-$MeOC_6H_4$	**2d**	0
4	**1e**	H	Me	3,5-$(MeO)_2C_6H_3$	**2e**	78
5	**1f**	H	Me	3-$CF_3C_6H_4$	**2f**	58
6	**1g**	H	$PhCH_2CH_2$	3-$MeOC_6H_4$	**2g**	74
7	**1h**	Me	Me	3-$MeOC_6H_4$	**2h**	60

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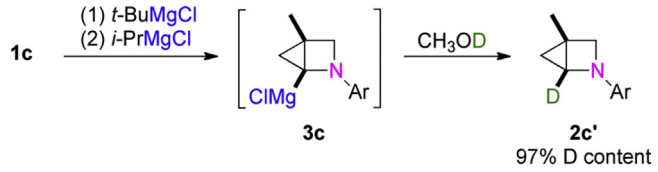


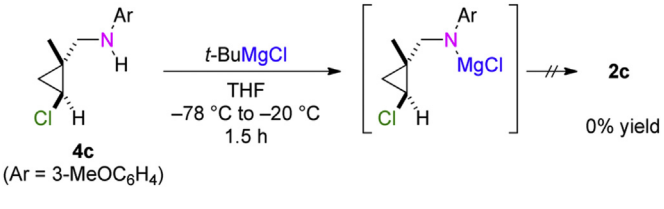
Scheme 3. Deuteration of organomagnesium intermediate **3c**.

of the cyclopropylmagnesium carbenoids with intramolecular magnesium anilide occurs to give the organomagnesium intermediate **3c**.

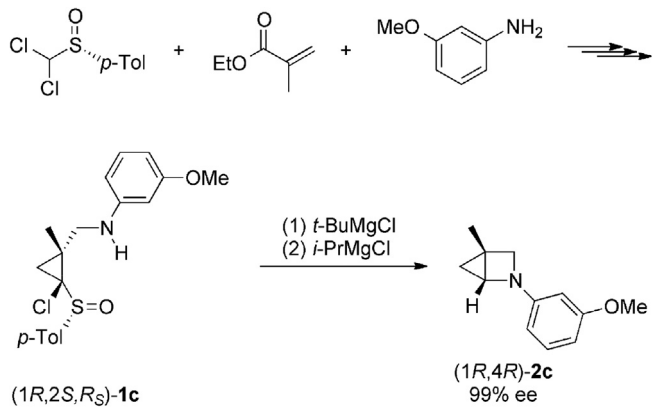
To compare the reactivity of the cyclopropylmagnesium carbenoids towards nucleophiles with that of chlorocyclopropanes, the chlorocyclopropane **4c** was subjected to the reaction conditions similar to those of the cyclization of the cyclopropylmagnesium carbenoids (Scheme 4). The cyclization did not proceed at all, and chlorocyclopropane **4c** was recovered quantitatively. This result suggests that the reactivity of the cyclopropylmagnesium carbenoids is higher than that of chlorocyclopropanes. In our DFT study, we found that 1-chlorocyclopropylmagnesium chloride has a long C—Cl bond and expanded bond angles around the carbenoid carbon atom compared with those of chlorocyclopropane.[6h,9] These structural features seem to mitigate a disadvantage associated with nucleophilic substitution at the carbon atom of small rings to a certain extent.

2.3. Asymmetric synthesis

Previously, we developed an efficient method for the optical resolution of dichloromethyl *p*-tolyl sulfoxide using (−)-menthone as a resolving agent.[10] We performed the asymmetric synthesis of 2-azabicyclo[2.1.0]pentane (1*R*,4*R*)-**2c** using (*R*)-dichloromethyl *p*-tolyl sulfoxide as the starting material (Scheme 5). The cyclization precursor (1*R*,2*S*,R_S)-**1c** was prepared according to the synthetic method described above. The reaction of sulfoxide (1*R*,2*S*,R_S)-**1c** with *t*-BuMgCl followed by *i*-PrMgCl gave (1*R*,4*R*)-2-azabicyclo [2.1.0]pentane (1*R*,4*R*)-**2c** with 99% ee.



Scheme 4. Attempt at cyclization of chlorocyclopropane **4c**.



Scheme 5. Asymmetric synthesis of 2-azabicyclo[2.1.0]pentane (1*R*,4*R*)-**2c**.

3. Conclusion

In summary, we developed an efficient method for the synthesis of 2-azabicyclo[2.1.0]pentanes. The high reactivity of the cyclopropylmagnesium carbenoids enabled the formation of a C—N bond between the carbon atom of the cyclopropane ring and the nitrogen atom by intramolecular nucleophilic substitution. The asymmetric synthesis of azabicyclo[2.1.0]pentane was successfully attained utilizing the *S*-chiral *p*-tolylsulfinyl group as a chiral auxiliary.

4. Experimental section

4.1. General methods

All reactions involving air- or water-sensitive compounds were conducted under an argon atmosphere. Argon gas was dried by passage through P_2O_5. Anhydrous THF was purchased from Kanto Chemical and was used as supplied. The 1-chloro-2-(iodomethyl) cyclopropyl *p*-tolyl sulfoxides and (*R*)-dichloromethyl *p*-tolyl sulfoxide were prepared according to the procedure described in the literature.[7,10a] Silica gel (60 N, Kanto Chemical) containing 0.5% fluorescence reagent 254 and a quartz column were used for column chromatography, and the products that absorbed UV light were detected by UV irradiation.

The melting points were measured using a Yanaco MP-S3 apparatus and are uncorrected. IR spectra were recorded on a Perkin—Elmer Frontier FT IR in ATR mode. NMR spectra were measured in a $CDCl_3$ solution with JEOL JNM-LA 300 and JEOL JNM-LA 500 spectrometers. Mass spectra (MS) were obtained at 70 eV by direct injection with a HITACHI M-80B mass spectrometer. Fast atom bombardment (FAB) mass spectra were obtained with a mixture of *m*-nitrobenzyl alcohol and glycerol as the matrix. Optical rotations were measured on a JASCO DIP-1000 Polarimeter. Enantiomeric excess was determined using HPLC analysis (JASCO Gulliver) with a Chiralcel AD or OD column (ϕ 0.46 cm × 25 cm).

4.2. Typical procedure for the synthesis of sulfoxides *1*

Aniline (4.85 g, 5.21 mmol) was added to a mixture of 1-{[(1*R**,2*R**)-1-chloro-2-(iodomethyl)-2-methylcyclopropyl]sulfinyl}-4-methylbenzene (1.28 g, 3.46 mmol) and K_2CO_3 (1.45 g, 10.5 mmol) in DMSO (7.0 mL) at room temperature, and the mixture was stirred at that temperature for 12 h. Toluene (15 mL) and water (15 mL) were added to the mixture, and the aqueous layer was extracted with toluene (2 × 5 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/EtOAc, 5:1) to give **1a** [813 mg, 2.77 mmol, 70%, R_f = 0.29 (hexane/EtOAc, 2:1)].

4.2.1. *N*-{[(1*R**,2*S**)-2-Chloro-1-methyl-2-(*p*-tolylsulfinyl) cycropropyl]methyl}aniline (***1a***)

Colorless crystals (hexane/EtOAc); mp 139.1—140.5 °C; IR (ATR) 3350, 3033, 2924, 1600, 1531, 1498, 1261, 1223, 1089, 1059, 1047, 801, 746, 691 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.30 (d, *J* = 7.1 Hz, 1H), 1.49 (s, 3H), 2.08 (d, *J* = 7.1 Hz, 1H), 2.43 (s, 3H), 3.51 (d, *J* = 12.8 Hz, 1H), 3.64 (d, *J* = 12.8 Hz, 1H), 3.78 (br s, 1H), 6.63—6.67 (m, 2H), 6.76 (tt, *J* = 1.1, 7.4 Hz, 1H), 7.19—7.24 (m, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.62 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.7 (CH_3), 21.5 (CH_3), 25.2 (CH_2), 32.5 (C), 48.2 (CH_2), 66.7 (C), 113.1 (CH), 118.1 (CH), 126.1 (CH), 129.4 (CH), 129.6 (CH), 138.8 (C), 142.5 (C), 147.7 (C); MS (FAB^+) *m*/*z* (%) 334 ($[M+H]^+$, 100), 192 (21),

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133 (39), 93 (27); HRMS (FAB$^+$) calcd for $C_{18}H_{21}ClNOS$: 334.1032, found: 334.1031.

4.2.2. N-{[(1R,2S*)-2-Chloro-1-methyl-2-(p-tolylsulfinyl) cyropropyl]methyl}-2-methoxyaniline (**1b**)*

Yield 98% (14 h); brown crystals (hexane/EtOAc); mp 101.8–103.1 °C; IR (ATR) 3393, 3013, 2990, 2962, 2939, 2835, 1600, 1509, 1455, 1250, 1212, 1126, 1084, 1060, 1044, 1019, 810, 748 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (d, J = 7.1 Hz, 1H), 1.50 (s, 3H), 2.10 (d, J = 7.1 Hz, 1H), 2.43 (s, 3H), 3.51 (d, J = 12.6 Hz, 1H), 3.62 (d, J = 12.6 Hz, 1H), 3.88 (s, 3H), 4.36 (br s, 1H), 6.64 (dd, J = 1.4, 8.0 Hz, 1H), 6.72 (dt, J = 1.4, 8.0 Hz, 1H), 6.81 (dd, J = 1.4, 8.0 Hz, 1H), 6.89 (dt, J = 1.4, 8.0 Hz, 1H), 7.31 (d, J = 8.1 Hz, 2H), 7.64 (d, J = 8.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.3 (CH_3), 21.6 (CH_3), 26.0 (C), 32.6 (C), 48.3 (CH_2), 55.4 (CH_3), 67.2 (C), 109.6 (CH), 110.2 (CH), 117.3 (CH), 121.3 (CH), 126.0 (CH), 129.6 (CH), 137.5 (C), 138.7 (C), 142.2 (C), 146.8 (C); MS (FAB$^+$) *m/z* (%) 364 (M$^+$, 100), 163 (45), 136 (28), 93 (30); HRMS (FAB$^+$) calcd for $C_{19}H_{23}ClNO_2S$: 364.1138, found: 364.1136.

4.2.3. N-{[(1R,2S*)-2-Chloro-1-methyl-2-(p-tolylsulfinyl) cyropropyl]methyl}-3-methoxyaniline (**1c**)*

Yield 76% (12 h); brown crystals (hexane/EtOAc); mp 85.6–86.8 °C; IR (ATR) 3349, 2993, 2931, 2834, 1611, 1595, 1513, 1495, 1454, 1207, 1161, 1084, 1039, 809, 751 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.29 (d, J = 7.2 Hz, 1H), 1.48 (s, 3H), 2.07 (d, J = 7.2 Hz, 1H), 2.44 (s, 3H), 3.49 (d, J = 12.9 Hz, 1H), 3.62 (d, J = 12.9 Hz, 1H), 3.79 (s, 3H), 3.81 (br s, 1H), , 6.21 (t, J = 2.3 Hz, 1H), 6.27 (ddd, J = 0.7, 2.3, 8.1 Hz, 1H), 6.32 (ddd, J = 0.7, 2.3, 8.1 Hz, 1H), 7.11 (t, J = 8.1 Hz, 1H), 7.33 (d, J = 8.1 Hz, 2H), 7.62 (d, J = 8.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.7 (CH_3), 21.6 (CH_3), 25.2 (CH_2), 32.4 (C), 48.2 (CH_2), 55.1 (CH_3), 66.7 (C), 99.1 (CH), 103.1 (CH), 106.1 (CH), 126.1 (CH), 129.6 (CH), 130.2 (CH), 138.7 (C), 142.5 (C), 149.1 (C), 160.9 (C); MS (FAB$^+$) *m/z* (%) 364 ([M+H]$^+$, 100), 163 (38), 136 (33), 93 (39); HRMS (FAB$^+$) calcd for $C_{19}H_{23}ClNO_2S$: 364.1138, found: 364.1139.

*4.2.4. N-{[(1R,2S,R_S)-2-Chloro-1-methyl-2-(p-tolylsulfinyl) cyropropyl]methyl}-3-methoxyaniline [(1R,2S,R_S)-**1c**]*

$[\alpha]_D^{24}$ +76.5 (*c* 0.10, EtOH); HPLC, DAICEL CHIRALCEL AD (φ 0.46 cm × 25 cm), *i*-PrOH/hexane/EtOH = 1:9:0.1, flow rate = 0.5 mL/min, detection at 220 nm, retention time = 49.1 min (minor), 51.6 min (major), 99%ee.

4.2.5. N-{[(1R,2S*)-2-Chloro-1-methyl-2-(p-tolylsulfinyl) cyropropyl]methyl}-4-methoxyaniline (**1d**)*

Yield 95% (48 h); brown crystals (hexane/EtOAc); mp 94.0–94.9 °C; IR (ATR) 3326, 3057, 3030, 2996, 2949, 2815, 1621, 1524, 1506, 1451, 1441, 1254, 1230, 1211, 1080, 1051, 1037, 816, 784 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (d, J = 7.1 Hz, 1H), 1.48 (s, 3H), 2.07 (d, J = 7.1 Hz, 1H), 2.43 (s, 3H), 3.46 (d, J = 12.6 Hz, 1H), 3.51 (br s, 1H), 3.57 (d, J = 12.6 Hz, 1H), 3.76 (s, 3H), 6.63 (d, J = 9.0 Hz, 2H), 6.81 (d, J = 9.0 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.63 (d, J = 8.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.6, 21.5, 25.4, 32.5, 49.5, 55.8, 66.9, 114.6, 115.0, 126.1, 129.6, 138.8, 141.8, 142.4, 152.6; MS (FAB$^+$) *m/z* (%) 364 ([M+H]$^+$, 100), 222 (50), 163 (42), 136 (35); HRMS (FAB$^+$) calcd for $C_{19}H_{23}ClNO_2S$: 364.1138, found: 364.1138.

4.2.6. N-{[(1R,2S*)-2-Chloro-1-methyl-2-(p-tolylsulfinyl) cyropropyl]methyl}-3,5-dimethoxyaniline (**1e**)*

Yield 64% (14 h); brown crystals (hexane/EtOAc); mp 83.5–84.2 °C; IR (ATR) 3345, 3328, 3000, 2962, 2935, 2844, 2815, 1596, 1471, 1458, 1200, 1175, 1149, 1062, 1038, 815, 747 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.28 (d, J = 7.2 Hz, 1H), 1.48 (s, 3H), 2.06 (d, J = 7.2 Hz, 1H), 2.44 (s, 3H), 3.48 (d, J = 12.8 Hz, 1H), 3.61 (d, J = 12.8 Hz, 1H), 3.77 (s, 6H), 3.83 (br s, 1H), 5.83 (d, J = 2.2 Hz, 2H), 5.92 (t, J = 2.2 Hz, 1H), 7.33 (d, J = 8.1 Hz, 2H), 7.61 (d, J = 8.1 Hz, 2H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 20.9, 21.6, 25.1, 32.4, 48.1, 55.2, 66.7, 90.3, 91.9, 126.1, 129.6, 138.8, 142.6, 149.6, 161.8; MS (FAB$^+$) *m/z* (%) 394 ([M+H]$^+$, 100), 193 (48), 166 (28), 137 (28), 93 (35); HRMS (FAB$^+$) calcd for $C_{20}H_{25}ClNO_3S$: 394.1244, found: 394.1238.

4.2.7. N-{[(1R,2S*)-2-Chloro-1-methyl-2-(p-tolylsulfinyl) cyropropyl]methyl}-3-(trifluoromethyl)aniline (**1f**)*

Yield 44% (86 h); yellow crystals (hexane/EtOAc); mp 81.4–82.8 °C; IR (ATR) 3351, 3313, 3063, 2937, 2923, 2889, 2846, 1616, 1597, 1539, 1498, 1476, 1347, 1316, 1304, 1164, 1122, 1090, 1062, 1039, 808, 784, 701 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24 (d, J = 7.2 Hz, 1H), 1.51 (s, 3H), 2.07 (d, J = 7.2 Hz, 1H), 2.44 (s, 3H), 3.54 (dd, J = 6.3, 12.9 Hz, 1H), 3.65–3.70 (dd, J = 5.1, 12.9 Hz, 1H), 4.04 (br t, 1H), 6.80 (d, J = 7.9 Hz, 1H), 6.84 (s, 1H), 6.98 (d, J = 7.9 Hz, 1H), 7.29 (t, J = 7.9 Hz, 1H), 7.33 (d, J = 8.1 Hz, 2H), 7.61 (d, J = 8.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.2, 21.6, 23.9, 32.2, 47.5, 65.9, 109.4 (q, $^3J_{C-F}$ = 3.9 Hz), 114.3 (q, $^3J_{C-F}$ = 3.9 Hz), 115.8, 124.3 (q, $^1J_{C-F}$ = 272.3 Hz), 126.2, 129.7, 129.8, 131.7 (q, $^2J_{C-F}$ = 31.8 Hz), 138.9, 142.8, 148.0; MS (FAB$^+$) *m/z* (%) 402 ([M+H]$^+$, 100), 262 (21), 201 (45), 185 (33), 154 (27), 93 (47); HRMS (FAB$^+$) calcd for $C_{19}H_{20}ClF_3NOS$: 402.0906, found: 402.0903.

4.2.8. N-{[(1R,2S*)-2-Chloro-1-phenethyl-2-(p-tolylsulfinyl) cyropropyl]methyl}-3-methoxyaniline (**1g**)*

Yield 40% (14 h); colorless crystal (hexane/EtOAc); mp 72.4–73.5 °C; IR (ATR) 3347, 3026, 3001, 2956, 2932, 2862, 2835, 1612, 1597, 1495, 1453, 1208, 1162, 1087, 1042, 752, 730, 699, 688 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (d, J = 7.0 Hz, 1H), 1.90 (ddd, J = 5.0, 11.2, 14.5 Hz, 1H), 2.06 (d, J = 7.0 Hz, 1H), 2.22 (ddd, J = 6.2, 11.0, 14.5 Hz, 1H), 2.44 (s, 3H), 2.59–2.70 (m, 2H), 3.64 (br s, 2H), 3.77 (s, 1H), 3.80 (s, 3H), 6.22 (t, J = 2.1 Hz, 1H), 6.28 (dd, J = 2.1, 8.1 Hz, 1H), 6.35 (dd, J = 2.1, 8.1 Hz, 1H), 7.11 (d, J = 7.3 Hz, 2H), 7.12–7.18 (m, 2H), 7.24 (t, J = 7.3 Hz, 2H), 7.35 (d, J = 8.2 Hz, 2H), 7.62 (d, J = 8.2 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 21.6 (CH_3), 25.5 (CH_2), 32.4 (CH_2), 35.4 (CH_2), 35.8 (C), 45.3 (CH_2), 55.2 (CH_3), 67.5 (C), 99.3 (CH), 103.2 (CH), 106.2 (CH), 125.9 (CH), 126.2 (CH), 128.3 (CH), 128.5 (CH), 129.7 (CH), 130.3 (CH), 138.5 (C), 141.0 (C), 142.7 (C), 149.0 (C), 161.0 (C); MS (FAB$^+$) *m/z* (%) 454 ([M+H]$^+$, 100), 312 (25), 162 (33), 136 (35), 91 (22); HRMS (FAB$^+$) calcd for $C_{26}H_{29}ClNO_2S$: 454.1608, found: 454.1609.

4.2.9. N-([(1R,2S*,3S*)-2-chloro-1,3-dimethyl-2-(p-tolylsulfinyl) cyclopropyl]methyl)-3-methoxyaniline (**1h**)*

Yield 67% (73 h); colorless crystals (hexane/EtOAc); mp 117.2–118.0 °C; IR (ATR) 3353, 2931, 1596, 1538, 1491, 1463, 1311, 1211, 1157, 1086, 1053, 809, 764 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.15 (d, J = 6.4 Hz, 3H), 1.27 (s, 3H), 2.13 (q, J = 6.4 Hz, 1H), 2.43 (s, 3H), 3.46 (d, J = 13.0 Hz, 1H), 3.61 (d, J = 13.0 Hz, 1H), 3.81 (s, 3H), 3.85 (br s, 1H), 6.20 (t, J = 2.2 Hz, 1H), 6.26 (dd, J = 2.2, 8.0 Hz, 1H), 6.31 (dd, J = 2.2, 8.0 Hz, 1H),7.11 (t, J = 8.0 Hz, 1H), 7.31 (d, J = 8.1 Hz, 2H), 7.60 (d, J = 8.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 8.9, 15.1, 21.6, 24.7, 33.9, 49.5, 55.1, 70.7, 99.1, 103.0, 106.1, 126.1, 129.6, 130.1, 139.0, 142.4, 149.2, 160.9; MS (FAB$^+$) *m/z* (%) 378 ([M+H]$^+$, 100), 238 (38), 163 (42), 93 (27); HRMS (FAB$^+$) calcd for $C_{20}H_{25}ClNO_2S$: 378.1295, found: 378.1294.

*4.3. Typical procedure for the synthesis of 2-azabicyclo[2.1.0] pentanes **2***

A 1.0 mol/L solution of *t*-BuMgCl in THF (0.38 mL, 0.38 mmol) was added to a solution of **1a** (107 mg, 0.320 mmol) in THF (21.0 mL) at −78 °C, and the mixture was stirred at that temperature for 10 min. A 2.0 mol/L solution of *i*-PrMgCl in THF (0.48 mL,

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0.96 mmol) was added to the mixture at −78 °C, and the mixture was allowed to warm to −20 °C over a period of 1.5 h. The reaction was quenched with saturated aqueous NH_4Cl (3 mL). $CHCl_3$ (15 mL) and water (10 mL) were added to the mixture, and the aqueous layer was extracted with $CHCl_3$ (2 × 10 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/AcOEt, 200:1) to give **2a** [36.0 mg, 0.226 mmol, 71%, $R_f = 0.62$ (hexane/AcOEt, 2:1)].

4.3.1. (1R*,4R*)-2-phenyl-4-methyl-2-azabicyclo[2.1.0]pentane (**2a**)

Yellow oil; IR (ATR) 3055, 3034, 2943, 2924, 2863, 1598, 1495, 1321, 752, 693 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.54 (dd, J = 3.5, 5.3 Hz, 1H), 0.86 (d, J = 5.3 Hz, 1H), 1.42 (s, 3H), 3.25 (dd, J = 2.3, 7.6 Hz, 1H), 3.54 (dd, J = 2.3, 3.5 Hz, 1H), 3.99 (d, J = 7.6 Hz, 1H), 6.59 (dd, J = 1.1, 8.5 Hz, 2H), 6.74 (tt, J = 1.1, 7.3 Hz, 1H), 7.19 (dd, J = 7.3, 8.5 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 15.9, 16.5, 20.5, 44.7, 61.0, 114.0, 118.1, 128.7, 151.2; MS (EI) *m/z* (%) 159 (M^+, 51), 158 (51), 144 (100), 104 (95), 77 (89); HRMS (EI) calcd for $C_{11}H_{13}N$: 159.1048, found: 159.1047.

4.3.2. (1R*,4R*)-2-(2-methoxyphenyl)-4-methyl-2-azabicyclo[2.1.0]pentane (**2b**)

Yellow oil; IR (ATR) 3057, 2943, 2869, 2833, 1594, 1498, 1454, 1305, 1228, 1131, 1027, 736 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.57 (dd, J = 3.5, 5.4 Hz, 1H), 0.91 (d, J = 5.4 Hz, 1H), 1.42 (s, 3H), 3.21 (dd, J = 2.2, 8.4 Hz, 1H), 3.48 (dd, J = 2.2, 3.5 Hz, 1H), 3.78 (s, 3H), 4.03 (d, J = 8.4 Hz, 1H), 6.75–6.88 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 16.5, 17.4, 20.2, 43.8, 55.3, 62.0, 111.0, 115.6, 120.0, 120.7, 140.0, 150.2; MS (EI) *m/z* (%) 189 (M^+, 78), 174 (100), 134 (100), 92 (22), 77 (42); HRMS (EI) calcd for $C_{12}H_{15}NO$: 189.1154, found: 189.1151.

4.3.3. (1R*,4R*)-2-(3-methoxyphenyl)-4-methyl-2-azabicyclo[2.1.0]pentane (**2c**)

Yellow oil; IR (ATR) 2942, 2924, 2863, 1611, 1596, 1587, 1579, 1491, 1455, 1336, 1318, 1286, 1256, 1205, 1175, 1162, 1107, 1045, 757, 688 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.53 (dd, J = 3.0, 5.4 Hz, 1H), 0.87 (d, J = 5.4 Hz, 1H), 1.42 (s, 3H), 3.24 (dd, J = 3.0, 7.5 Hz, 1H), 3.51 (t, J = 3.0 Hz, 1H), 3.77 (s, 3H), 3.96 (d, J = 7.5 Hz, 1H), 6.13 (d, J = 2.2 Hz, 1H), 6.20 (dd, J = 2.2, 8.1 Hz, 1H), 6.31 (dd, J = 2.2, 8.1 Hz, 1H), 7.09 (t, J = 8.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 15.7 (C), 16.4 (CH_3), 20.5 (CH_2), 44.6 (CH), 55.1 (CH_3), 60.9 (CH_2), 100.1 (CH), 103.3 (CH), 106.9 (CH), 129.5 (CH), 152.7 (C), 160.4 (C); MS (EI) *m/z* (%) 189 (M^+, 76), 174 (100), 134 (85), 107 (55), 77 (27); HRMS (EI) calcd for $C_{12}H_{15}NO$: 189.1154, found: 189.1156.

4.3.4. (1R*,4R*)-2-(3-methoxyphenyl)-4-methyl-2-aza[1-^{2}H]bicyclo[2.1.0]pentane (**2c'**)

Yield 76%; 97% deuterium content; yellow oil; IR (ATR) 2924, 2863, 1597, 1491, 1455, 1333, 1286, 1242, 1208, 1177, 1165, 1141, 1040, 837, 757, 688 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.53 (d, J = 5.4 Hz, 1H), 0.86 (d, J = 5.4 Hz, 1H), 1.41 (s, 3H), 3.23 (d, J = 7.5 Hz, 1H), 3.77 (s, 3H), 3.96 (d, J = 7.5 Hz, 1H), 6.13 (t, J = 2.2 Hz, 1H), 6.19 (dd, J = 2.2, 8.0 Hz, 1H), 6.31 (dd, J = 2.2, 8.0 Hz,1H), 7.08 (t, J = 8.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 15.6, 16.4, 20.4, 44.3 (t, $^1J_{C-D}$ = 29.4 Hz), 55.1, 61.0, 100.1, 103.4, 106.9, 129.5, 152.7, 160.4; MS (EI) *m/z* (%) 190 (M^+, 78), 175 (100), 135 (74), 107 (52), 92 (18); HRMS (EI) calcd for $C_{12}H_{14}DNO$: 190.1216, found: 190.1218.

4.3.5. (1R,4R)-2-(3-methoxyphenyl)-4-methyl-2-azabicyclo[2.1.0]pentane ((1R,4R)-**2c**)

$[\alpha]_D^{25}$ −260 (*c* 0.10, EtOH); HPLC, DAICEL CHIRALCEL OD (φ 0.46 cm × 25 cm), *i*-PrOH/hexane = 1:9, flow rate = 0.5 mL/min, detection at 254 nm, retention time = 13.4 min (major), 14.6 min (minor), 99%ee.

4.3.6. (1R*,4R*)-2-(3,5-dimethoxyphenyl)-4-methyl-2-azabicyclo[2.1.0]pentane (**2e**)

Yellow oil; IR (ATR) 2941, 2863, 1586, 1459, 1264, 1201, 1178, 1147, 1058, 814 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.54 (dd, J = 3.5, 5.3 Hz, 1H), 0.88 (d, J = 5.3 Hz, 1H), 1.41 (s, 3H), 3.23 (dd, J = 2.2, 7.5 Hz, 1H), 3.49 (dd, J = 2.2, 3.5 Hz, 1H), 3.75 (s, 6H), 3.94 (d, J = 7.5 Hz, 1H), 5.75 (d, J = 2.2 Hz, 2H), 5.91 (t, J = 2.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 15.6, 16.4, 20.7 ($^1J_{CH}$ = 160 Hz), 44.6 ($^1J_{CH}$ = 195 Hz), 55.2, 60.9, 90.5, 92.7, 153.3, 161.4; MS (EI) *m/z* (%) 219 (M^+, 85), 204 (100), 164 (48), 137 (59), 122 (38); HRMS (EI) calcd for $C_{13}H_{17}NO_2$: 219.1259, found: 219.1263.

4.3.7. (1R*,4R*)-2-[3-(trifluoromethyl)phenyl]-4-methyl-2-azabicyclo[2.1.0]pentane (**2f**)

Yellow oil; IR (ATR) 2929, 2868, 1609, 1492, 1455, 1345, 1313, 1282, 1160, 1115, 1065, 785, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.60 (dd, J = 2.6, 5.4 Hz, 1H), 0.84 (d, J = 5.4 Hz, 1H), 1.44 (s, 3H), 3.27 (dd, J = 2.6, 7.5 Hz, 1H), 3.56 (t, J = 2.6 Hz, 1H), 4.01 (d, J = 7.5 Hz, 1H), 6.71 (d, J = 7.9 Hz, 1H), 6.77 (s, 1H), 6.97 (d, J = 7.9 Hz, 1H), 7.26 (t, J = 7.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 16.1, 16.3, 20.7, 44.7, 61.1, 110.2 (q, $^3J_{C-F}$ = 3.9 Hz), 114.5 (q, $^3J_{C-F}$ = 3.9 Hz), 116.9 (q, $^4J_{C-F}$ = 1.4 Hz), 124.4 (q, $^1J_{C-F}$ = 272.4 Hz), 129.1, 131.1 (q, $^2J_{C-F}$ = 31.7 Hz), 151.5; MS (EI) *m/z* (%) 227 (M^+, 35), 226 (40), 212 (100), 172 (80), 145 (90); HRMS (EI) calcd for $C_{12}H_{12}F_3N$: 227.9022, found: 227.0919.

4.3.8. (1R*,4R*)-2-(3-methoxyphenyl)-4-phenethyl-2-azabicyclo[2.1.0]pentane (**2g**)

Yellow oil; IR (ATR) 3026, 3001, 2925, 2858, 1597, 1579, 1491, 1454, 1337, 1285, 1250, 1205, 1162, 1108, 1041, 837, 751, 689 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.57 (dd, J = 3.5, 5.5 Hz, 1H), 0.86 (d, J = 5.5 Hz, 1H), 1.86 (ddd, J = 6.2, 8.7, 14.7 Hz, 1H), 2.14–2.21 (ddd, J = 7.2, 8.6, 14.7 Hz, 1H), 2.67–2.74 (m, 2H), 3.10 (dd, J = 2.2, 7.6 Hz, 1H), 3.52 (dd, J = 2.2, 3.5 Hz, 1H), 3.76 (s, 3H), 3.91 (d, J = 7.6 Hz, 1H), 6.10 (t, J = 2.2 Hz, 1H), 6.17 (dd, J = 2.2, 8.1 Hz, 1H), 6.31 (dd, J = 2.2, 8.1 Hz,1H), 7.08 (t, J = 8.1 Hz, 1H), 7.17–7.29 (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 19.5 (CH_2), 20.1 (C), 32.5 (CH_2), 33.9 (CH_2), 44.0 (CH), 55.1 (CH_3), 59.7 (CH_2), 100.1 (CH), 103.4 (CH), 106.9 (CH), 126.0 (CH), 128.39 (CH), 128.42 (CH), 129.5 (CH), 141.7 (C), 152.6 (C), 160.4 (C); MS (EI) *m/z* (%) 279 (M^+, 10), 188 (100); HRMS (EI) calcd for $C_{19}H_{21}NO$: 279.1623, found: 279.1621.

4.3.9. (1R*,4R*,5S*)-2-(3-methoxyphenyl)-4,5-dimethyl-2-azabicyclo[2.1.0]pentane (**2h**)

Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.94 (d, J = 6.4 Hz, 3H), 1.11 (q, J = 6.4 Hz, 1H), 1.35 (s, 3H), 3.11 (d, J = 2.0 Hz, 1H), 3.24 (dd, J = 2.0, 7.5 Hz, 1H), 3.77 (s, 3H), 3.97 (d, J = 7.5 Hz, 1H), 6.13 (t, J = 2.2 Hz, 1H), 6.18 (dd, J = 2.2, 8.0 Hz, 1H), 6.31 (dd, J = 2.2, 8.0 Hz, 1H), 7.09 (t, J = 8.0 Hz, 1H).

4.3.10. N-{[(1R*,2S*)2-Chloro-1-methylcyclopropyl]methyl}-3-methoxyaniline (**4c**)

Yellow oil. IR (ATR) 3410, 2932, 2835, 1614, 1588, 1510, 1496, 1461, 1207, 1160, 1037, 825, 755, 686 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.66 (dd, J = 4.1, 6.3 Hz, 1H), 1.06 (dd, J = 6.3, 7.6 Hz, 1H), 1.34 (s, 3H), 2.98 (d, J = 12.6 Hz, 1H), 3.05 (dd, J = 4.1, 7.6 Hz, 1H), 3.06 (d, J = 12.6 Hz, 1H), 3.68 (br s, 1H), , 3.77 (s, 3H), 6.13 (t, J = 2.1 Hz, 1H), 6.20 (dd, J = 2.1, 8.1 Hz, 1H), 6.28 (dd, J = 2.1, 8.1 Hz, 1H), 7.07 (t, J = 8.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 17.3, 20.5, 22.2, 38.1, 51.4, 55.1, 98.7, 102.8, 105.8, 130.0, 149.7, 160.9; MS (EI) *m/z* (%) 225 (M^+, 78), 190 (36), 162 (22), 148 (12), 136 (100); HRMS (EI) calcd for $C_{12}H_{16}ClNO$: 225.0920, found: 225.0922.

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Acknowledgements

This work was supported by the JSPS KAKENHI Grant Number 25810030, which is gratefully acknowledged.

References

1. (a) Shimura M, Iwata M, Omoto S, Sekizawa Y. *Agric Biol Chem*. 1979;43:2279;
(b) Iwata M, Suzuki Y, Kondo Y, Inohara T, Watanabe T, Sekizawa Y. *Ann Phytopath Soc Jpn*. 1979;45:192;
(c) Kodama Y, Ito T. *Agric Biol Chem*. 1980;44:73.
2. Artamonov OS, Slobodyanyuk EY, Volochnyuk DM, Komarov IV, Tolmachev AA, Mykhailiuk PK. *Eur J Org Chem*. 2014;2014:3592.
3. (a) Espejo VR, Li X-B, Rainier JD. *J Am Chem Soc*. 2010;132:8282;
(b) Wang M, Feng X, Cai L, Xu Z, Ye T. *Chem Commun*. 2012;48:4344.
4. (a) Roberts JD, Chambers VC. *J Am Chem Soc*. 1951;73:5034;
(b) Masson E, Leroux F. *Helv Chim Acta*. 2005;88:1375;
(c) Brown HC, Fletcher RS, Johannesen RB. *J Am Chem Soc*. 1951;73:212.
5. (a) Satoh T. *Heterocycles*. 2012;85:1;
(b) Satoh T, Kimura T. *J Synth Org Chem Jpn*. 2013;71:1033.
6. (a) Satoh T, Saito S. *Tetrahedron Lett*. 2004;45:347;
(b) Satoh T, Miura M, Sakai K, Yokoyama Y. *Tetrahedron*. 2006;62:4253;
(c) Yajima M, Nonaka R, Yamashita H, Satoh T. *Tetrahedron Lett*. 2009;50:4754;
(d) Yamada Y, Mizuno M, Nagamoto S, Satoh T. *Tetrahedron*. 2009;65:10025;
(e) Satoh T, Kasuya T, Ishigaki M, et al. *Synthesis*. 2011:397;
(f) Satoh T, Kashiwamura G, Nagamoto S, Sasaki Y, Sugiyama S. *Tetrahedron Lett*. 2011;52:4468;
(g) Satoh T, Kimura T, Sasaki Y, Nagamoto S. *Synthesis*. 2012;44:2091;
(h) Kimura T, Inumaru M, Migimatsu T, Ishigaki M, Satoh T. *Tetrahedron*. 2013;69:3961.
7. (a) Miyagawa T, Tatenuma T, Tadokoro M, Satoh T. *Tetrahedron*. 2008;64:5279;
(b) Satoh T, Tsuru T, Ikeda S, Miyagawa T, Momochi H, Kimura T. *Tetrahedron*. 2012;68:1071;
(c) Kimura T, Wada N, Tsuru T, Sampei T, Satoh T. *Tetrahedron*. 2015;71:5952.
8. Soai K, Oyamada H, Takase M, Ookawa A. *Bull Chem Soc Jpn*. 1984;57:1948.
9. (a) Kimura T. In: Morin J, Pelletier JM, eds. *Density Functional Theory: Principles, Applications and Analysis*. Hauppauge, NY: Nova Science Publishers, Inc; 2013:p 59;
(b) Kimura T, Satoh T. *J Organomet Chem*. 2012;715:1;
(c) Kimura T, Satoh T. *Tetrahedron Lett*. 2013;54:5072.
10. (a) Noguchi T, Miyagawa T, Satoh T. *Tetrahedron Asymmetry*. 2009;20:2073;
(b) Satoh T, Momochi H, Noguchi T. *Tetrahedron Asymmetry*. 2010;21:382;
(c) Kimura T, Tsuru T, Momochi H, Satoh T. *Heteroat Chem*. 2013;24:131.

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