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Synthesis of Functionalized Chiral Imidazole Derivatives Based on a Bornane Skeleton Bearing a Sterically Crowded Spirocyclic Substituent at the C-3 Position

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Abstract

10-Imidazolylbornane-2-one bearing a sterically crowded spirocyclic substituent at the C-3 position was prepared from *d*-camphor through the procedure involving the formation of 10-bromobornane-2-thiones or 10-iodobornane-2-thiones and the subsequent conversion into the corresponding 10-imidazolylbornane-2-thiones followed by an efficient oxidative S-O exchange *via* thione *S*-oxides.

Keywords

10-halobornane-2-thione, 10-imidazolylbornane-2-thione, thione *S*-oxides, 10-imidazolylbornan-2-one, functionalized imidazolium salt

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d-Camphor and its functionalized derivatives have been widely recognized as the versatile substrates for chiral auxiliaries, ligands, and chiral building blocks for asymmetric syntheses due to the commercial availability with the structural stability and chirality, and therefore, a variety of functionalization of bornane skeletons have been extensively studied within these decades.[1–4] In most cases, preparation of functionalized bornane skeleton bearing functionalities at the C-2 and/or C-3 positions has been carried out *via* commercially available *d*-camphor or camphorquinone. On the other hand, rather limited methods for C-10 functionalization are available to us, and camphor-10-sulfonic acid is usually used as the substrates for the further conversion due to the lack of other convenient methods for functionalization at the C-10 position. Therefore, new synthetic methods involving direct regioselective oxidation or halogenation of the C-10 position of the skeleton are keenly required concerning the current requirements in the expansion of their synthetic diversity of the skeleton to a new type of chiral ligands and organocatalysts. Actually, some limited studies concerning the preparation of 10-halobornane derivatives from *d*-camphor or camphor-10-sulfonic acid have been achieved to date.[5–17]

In the course of our synthetic studies on chiral organosulfur compounds, we have been engaging in the selective halogenation of bornane-2-thiones bearing a highly bulky spirocyclic substituent to afford 10-halobornane-2-thiones **A**.[18] The reaction mechanism of regioselective halogenation of the C-10 position of the skeleton still remains unclear at this time. However, at this time, we have an assumption that the halogenation would proceed through a process involving the formation of some intermediary T-shaped dibromosulfurane-type complexes[19–22] in which one bromine atom is located spatially tightly near to the neighboring C-10 methyl proton of the skeleton to cause dehydrohalogenation. These successful results urged us on the synthesis of new chiral auxiliaries and organocatalysts bearing an imidazole ring at the relatively unconfused C-10 position as a pendant of the camphor derivatives. In this paper, we describe a novel synthesis of chiral imidazole derivatives **B** bearing a sterically crowded camphor substituent as shown in Scheme 1 as well as the attempts toward the synthesis of chiral imidazolium salts having a potentiality of new chiral organocatalysts.

Sterically crowded camphor derivatives **1a-b** bearing a spirocyclic substituent at the C-3 position were at first prepared from *d*-camphor according to the reported method,[23–27 28,29] and ketones **1a-b** were converted into the corresponding thiones **2a-b** by treating with Lawesson's reagent according to our

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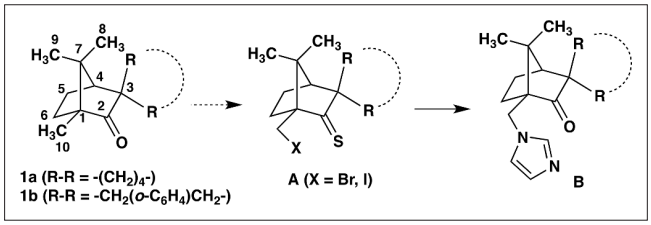


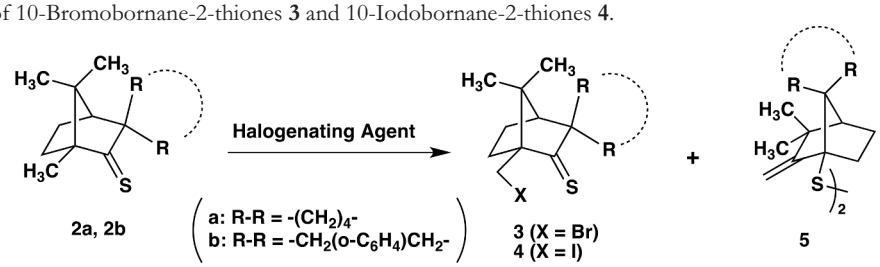
Scheme 1. A new synthetic route for 10-imidazolylbornan-2-ones **B**.

previous reports.[23] Subsequently, thiones **2a-b** were converted into the corresponding 10-bromobornane-2-thiones **3a-b** (X = Br) in almost quantitative yields by treating with bromine (1.1 mol amt.) at room temperature (R.T.). However, the treatment of thiones **2a-b** with iodine (1.1 mol amt.) in a similar manner resulted in the quantitative recovery of substrates. On the other hand, the treatment of thiones **2a-b** with iodine monochloride (ICl, 2.0 mol amt.) under the optimized condition (−30°C for several hours) afforded the corresponding 10-iodobornane-2-thione **4a** or Wagner-Meerwein-type skeletal rearrangement product **5b** in 85% or 74% yield, respectively, without the contamination of 10-chloro derivatives in the crude product,[18] and the treatment of **2a** with *N*-iodosuccinimide just gave a mixture of **4a** and **5a** in 12% and 42%, respectively. A similar treatment of **2a** with iodine monobromide (IBr, 1.1 mol amt.) at R.T. afforded an inseparable mixture of **3a** and **4a** (**3a**:**4a** = ~5:1). Attempts for chlorination of **2a-b** by using a variety of chlorinating agents, such as chlorine (gas, excess), SO_2Cl_2 (1.1 mol amt.), or *t*-butyl hypochlorite (*t*-BuOCl, 1.1 mol amt.), only gave a complex mixture in all cases, and the preparation of 10-chlorobornane-2-thiones in a similar manner to that of 10-bromo and 10-iodo derivatives was not successful at all. It is noteworthy that the reaction of **2a** with a usual acid, such as HCl and HBr, only afforded the recovery of substrate **2a**, and these results suggested that products **5a-b** were formed through a further reaction of **3** or **4** with the halogenating agents. All the results of bromination and iodination of bornane-2-thiones (**2a**, **2b**) are summarized in Table 1.

Alternatively, conversion of **3a-b** into the corresponding 10-iodo derivatives **4a-b** was efficiently carried out in high yields by treating with sodium iodide (NaI, 3.0 mol amt.) in N,N-dimethylformamide (DMF) according to the report of Komarov et al.[30] Therefore, 10-iodobornane-2-thiones (**4a-b**) were easily prepared through a two-step conversion from the starting thiones **2**, and the results urged us on the further functionalization of the bornane skeletons toward chiral imidazolium salts by using S_N2-type reactions to the iodine functionality of the C-10 position of the bornane skeleton with imidazole. Preparative methods for **4a-b** through the reaction of **3a-b** with sodium iodide are summarized in Scheme 2.

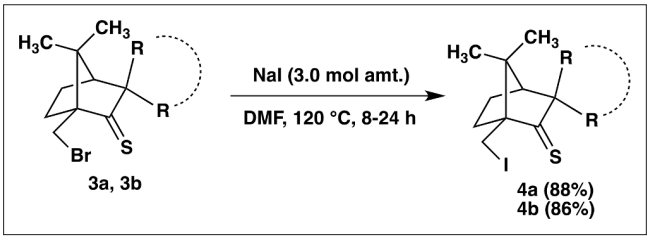
In general, *N*-alkylimidazolium salts are prepared through the reaction of *N*-methylimidazole with an alkylating agent.[8,31,32] However, in our preliminary attempt, reaction of **4b** with *N*-methylimidazole was sluggish to result in the formation of unpurifiable oily matter. Therefore, compounds **3a-b** and **4a-b** were subjected to the treatment with imidazole in place of *N*-methylimidazole to isolate 10-imidazolylbornane-2-thiones **6** as neutral form for the convenience of isolation and characterization of the further reaction products. When a DMF solution of 10-bromobornane-2-thione **3a** or **4a** was treated with sodium hydride (NaH, 1.5 mol amt.) and imidazole (1.5 mol amt.) at 120°C for a prolonged reaction time, each compound was efficiently converted into the corresponding 10-imidazolyl derivative **6a**. On the other hand, unexpectedly, the treatment of **3b** and **4b** with sodium hydride and

Table 1. Preparation of 10-Bromobornane-2-thiones **3** and 10-Iodobornane-2-thiones **4**.



Substrate	Halogenating agent (mol amt.)	Temp (°C)	Time (h)	Yield (%)		
				3, **4**	**5**	Recovery of **2**
2a	Br_2 (1.1)	R.T.	1	86 (**3a**)	0	0
2b	Br_2 (1.1)	0	1	90 (**3b**)	0	0
2a	I_2 (1.1)	R.T.	24	0	0	quant.
2a	ICl (2.0)	−30	5	85 (**4a**)	0	0
2b	ICl (1.1)	−30	3	0	74 (**5b**)	0
2a	IBr (1.1)	R.T.	3	35 (**3a**) + 7 (**4a**)	0	45
2a	NIS (1.2)	0	5	12 (**4a**)	42 (**5a**)	0
2b	NIS (1.2)	0	5	0	53 (**5b**)	0

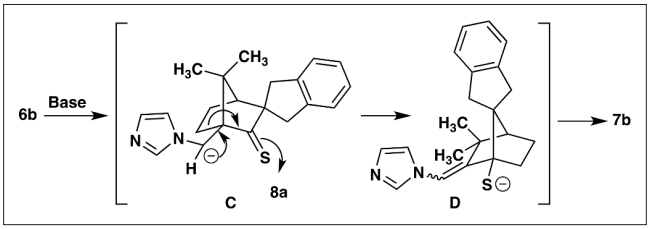
NIS, *N*-iodosuccinimide; R.T., room temperature.



Scheme 2. Preparation of 10-iodobornane-2-thiones (**4a-b**) by treating 10-bromobornane-2-thiones (**3a-b**) with NaI.

imidazole in a similar manner mainly afforded an inseparable 1:1 mixture of skeletal rearrangement products assignable to **7b** besides the formation of a trace amount of 10-imidazolyl derivative **6b**. All the physical and spectral data of **6a** and **6b** involving MS, IR, ^{1}H NMR, and ^{13}C NMR spectra, as well as their HRMS data, were fully consistent with the structures of 10-imidazolylbornane-2-thiones, and the structure of **7b** was also supported by the MS spectrum with the parent ion peaks around the m/z 674 region and the base peak at m/z 337 originated by S-S bond fission from the parent ion peak. However, the characterization of **7b** was not finally carried out. The reason for the occurrence of skeletal rearrangement in the cases of **3b** and **4b** under basic conditions still remained unclear. However, it would be assumed that the bulkiness of the spirocyclic substituent at the C-3 position of **3b** and **4b** would accelerate an unusual base-induced Wagner-Meerwein-type rearrangement into the direction to the release of ring strain of the highly sterically crowded bornane skeleton forming intermediate **D** as shown in Scheme 3.[33] All the results on the attempts for the preparation of 10-imidazolylbornane-2-thiones **6a-b** are summarized in Table 2.

Subsequent treatment of **6a** with *m*-chloroperbenzoic acid (*m*CPBA) (2.0 mol amt.) afforded a mixture of thione *S*-oxides (major isomer **8a** and minor isomer **8a′**) in high combined yield.[25,34–39] Both **8a** and **8a′** were the geometrical isomers of thione *S*-oxides and the ratios of formation of **8a: 8a′** were approximately 2:1 in all cases in spite of attempting various reaction conditions. Interestingly, **8a** and **8a′** were chromatographically separable, and the ^{1}H NMR spectra of these compounds indicated a difference in the chemical shifts and splitting patterns of the signals of germinal methylene protons at the C-10 position adjacent to the imidazole ring, *ie*, **8a**: δ = 4.87 (2H, s) vs. **8b**: δ = 4.07 (1H, d, J = 14.8 Hz), 4.19 (1H, d, J = 14.8 Hz). It was assumed that the geometry of the thione *S*-oxide moiety for major-**8a** would be *syn* in which the orientation of the neighboring thione *S*-oxide moiety would cause the characteristic low field shift of the signal of the germinal methylene protons at the C-10 position. However, further structural inspections for **8a** and **8a′** were not carried out. Both geometrical isomers of thione *S*-oxides **8a** and **8a′** were thermally stable enough, and heating of the isomeric mixture of **8** under refluxing temperature in toluene for 24 hours resulted in the recovery of the substrates.[40,41] In addition, both **8a** and **8a′** were unreactive toward further *m*CPBA oxidation even under refluxing temperature in chloroform for 72 hours, and all attempts for the conversion of the mixture of geometrical isomers **8a** and **8a′** into the corresponding ketone **9a** *via* sulfene intermediates were unsuccessful.[42–45] It was assumed that the high thermal and chemical stability of the thione *S*-oxide moiety of **8a** and **8a′** toward heating and further oxidation was attributed to the effect of steric protection of the neighboring spirocyclopentane substituent at the C-3 position.



Scheme 3. Plausible base-induced skeletal rearrangement of sterically crowded 10-imidazolylbornane-2-thione **6b**.

On the other hand, when the isomeric mixture of thione *S*-oxides (**8a** and **8a′**) was subjected to acid-catalyzed hydrolysis by treating with aqueous 35 wt% HCl (excess) in methanol at refluxing temperature for 48 hours, the corresponding ketone **9a** was obtained in 83% yield as a sole product[46] as shown in Scheme 4, and in this case, skeletal rearrangement products were not found at all in the crude products in spite of the possibility to cause Wagner-Meerwein rearrangement of the skeleton. All physical and spectral data for the products involving the IR, ^{1}H NMR, and ^{13}C NMR spectra, as well as the HRMS data, were fully consistent with the structure of 10-imidazolylbornan-2-one **9a**.

Furthermore, a preliminary attempt of conversion of ketone **9a** into imidazolium salt **10a** was carried out successfully by treating with iodomethane (1.1 mol amt.) in THF through a usual manner as shown in Scheme 5.

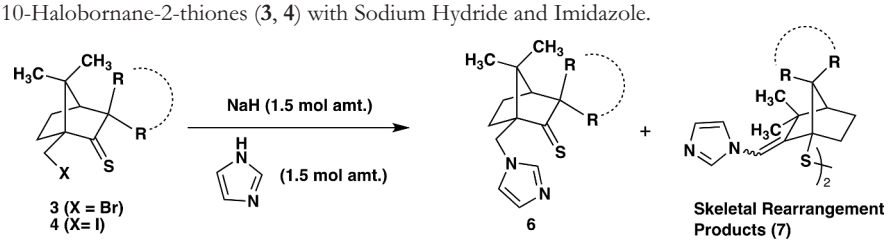
In conclusion, we have achieved a convenient synthesis of 10-imidazolylbornan-2-one (**9a**) bearing a bulky spirocyclic substituent at the C-3 position. These synthetic procedures provide us a new diversity of sterically crowded bornane skeletons for the synthesis of new functionalized imidazolium salts as chiral catalysts and reaction medias for asymmetric synthesis. Further attempts for the conversion of 10-imidazolylbornan-2-one **9a** into various imidazolium salts are in progress in our laboratory.

Experimental

Instruments

Melting points, Barnstead International MEL-TEMP; NMR, Bruker DRX-400P (400 MHz) or Bruker AVANCE III 500 (500 MHz) spectrometer; MS, JEOL JMS-700T mass spectrometer; HRMS, JEOL JMS-700T spectrometer; IR, JASCO

Table 2. Reaction of 10-Halobornane-2-thiones (**3**, **4**) with Sodium Hydride and Imidazole.



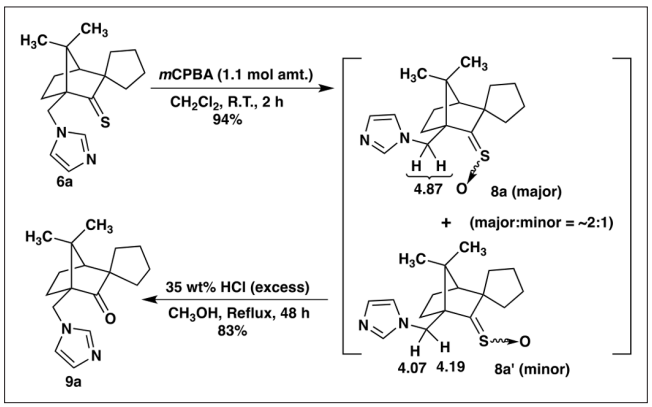
Substrate	Solvent	Temp (°C)	Time (h)	Yield (%) 6	Yield (%) 7
3a	DMF	120	60	63 (**6a**)	0
4a	DMF	120	38	68 (**6a**)	0
3b	DMF	120	168	2 (**6b**)	67 (**7b**)
4b	DMF	120	96	2 (**6b**)	72 (**7b**)
4b	DMF	R.T.	336	6 (**6b**)	76 (**7b**)
3b	THF	Reflux	240	No reaction	
3b	1,4-Dioxane	Reflux	70	No reaction	

R.T., room temperature.

FT/IR-7300 spectrometer; elemental analyses were performed using a Yanagimoto CHN corder MT-5.

*A Typical Procedure for Preparation of 10-Bromobornane-2-thiones (**3a-b**) by Treating Thiones **2** with Bromine*

A 10 mL CH_2Cl_2 solution of thione **2a** (118 mg, 0.53 mmol) was treated with a 5 mL CH_2Cl_2 solution of bromine (Br_2, 89 mg, 0.56 mmol, 1.1 mol amt.) at R.T. for 1 hour, and the reaction was quenched by the addition of an excess amount of saturated aqueous sodium sulfite solution. The reaction mixture was extracted with $CHCl_3$, and the organic layer was washed with saturated sodium bicarbonate solution and then with water, and was dried over anhydrous sodium sulfate powder. After removing the solvent *in vacuo*, the residual crude mixture was subjected to purification using column chromatography on silica gel to afford 10-bromobornane-2-thione **3a** (139 mg, 87% yield) as yellow oil.[18]



Scheme 4. Synthesis of sterically crowded 10-imidazolylbornan-2-one **9a**.

*Physical and Spectral Data for 10-Bromobornane-2-thiones **3***

3a (R-R = -$(CH_2)_4$-)[18]

Orange oil.

$[\alpha]_D^{25}$: +29.2 (*c* 0.1, $CHCl_3$).

IR (neat): 2951, 1455, 1266, 662 cm^{-1}.

^{1}H NMR ($CDCl_3$) δ: 0.92(3H, s), 1.21 (3H, s), 1.44 (1H, ddd, *J* = 14.2, 8.5, 5.5 Hz), 1.49-1.79 (6H, m), 1.81-1.96 (6H, m), 2.00 (1H, d, *J* = 3.6 Hz), 2.21 (1H, ddd, *J* = 11.4, 8.1, 4.4 Hz), 3.49 (1H, d, *J* = 11.0 Hz), 3.87 (1H, d, *J* = 11.0 Hz).

^{13}C NMR ($CDCl_3$) δ: 22.7 (t), 22.8 (t), 26.7 (q), 27.1 (q), 31.3 (dd), 33.6 (dd), 43.2 (t), 45.9 (t), 51.0 (s), 56.9 (d), 67.2 (s), 71.1 (s), 280.0 (s).

MS (*m*/*z*): 300 (M^+; 61%), 221 (bp).

Calcd for $C_{14}H_{21}SBr$: C, 55.81; H, 7.03%. Found: C, 55.81; H, 7.17%.

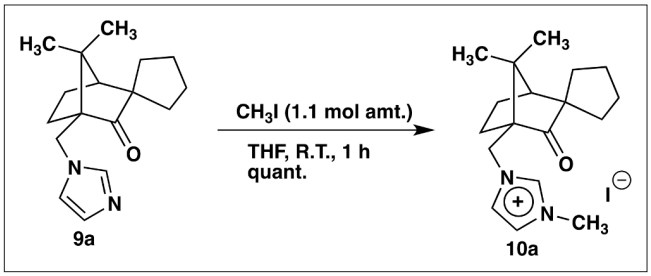
3b (R-R = -CH_2(*o*-C_6H_4)CH_2-)[18] :

Pale red prisms. MP: 92.6-93.2°C.

$[\alpha]_D^{25}$: +8.4 (*c* 0.1, $CHCl_3$).

MS (*m*/*z*): 348 (M^+; 33%), 142 (bp).

IR (KBr): 2938, 2357, 1488, 1371, 1276, 744 cm^{-1}.



Scheme 5. Synthesis of *N*-methylimidazolium salt **10a**.

^{1}H NMR ($CDCl_3$) δ: 1.07 (3H, s), 1.26 (3H, s), 1.46 (1H, ddd, *J* = 14.0, 8.7, 5.2 Hz), 1.87 (1H, ddd, *J* = 13.1, 9.3, 3.2 Hz), 1.96-2.05 (1H, m), 2.18 (1H, d, *J* = 3.6 Hz), 2.24 (1H, ddd, *J* = 13.8, 11.1, 3.2 Hz), 3.17 (1H, d, *J* = 16.0 Hz), 3.24 (1H, d, *J* = 16.3 Hz), 3.30 (1H, d, *J* = 16.3 Hz), 3.40 (1H, d, *J* = 16.0 Hz), 3.54 (1H, d, *J* = 11.1 Hz), 3.89 (1H, d, *J* = 11.1 Hz), 7.10-7.16 (4H, m).

^{13}C NMR ($CDCl_3$) δ: 22.9 (q), 23.1 (q), 23.2 (q), 30.7 (dd), 33.2 (dd), 47.7 (t), 50.7 (s), 51.7 (t), 56.3 (d), 67.5 (s), 71.0 (s), 123.5 (d), 123.7 (d), 126.5 (d), 126.6 (d), 140.7 (s), 141.8 (s), 275.8 (s).

Calcd for $C_{18}H_{21}SBr$: C, 61.89; H, 6.06%. Found: C, 61.51; H, 6.22%.

*A Typical Procedure for Preparation of 10-Iodobornane-2-thiones (**4**) by Treating thiones **2** with Iodine Monochloride (ICl)*

To a 10 mL suspended CH_2Cl_2 solution of thione **2a** (108 mg, 0.49 mmol) and sodium bicarbonate powder (97 mg, 1.15 mmol), a 1.00 mol/L CH_2Cl_2 solution of iodine monochloride (ICl, 0.98 mL, 0.98 mmol) at −30°C for 5 hours with stirring, and the reaction was quenched by the addition of an excess amount of saturated aqueous sodium sulfite solution. The reaction mixture was extracted with $CHCl_3$, and the organic layer was washed with saturated sodium bicarbonate solution and then with water, and was dried over anhydrous sodium sulfate powder. After removing the solvent *in vacuo*, the residual crude mixture was subjected to purification using column chromatography on silica gel to afford the 10-iodobornane-2-thione **4a** (144 mg, 85% yield, orange oil). On the other hand, when thione **2b** (54 mg, 0.20 mmol) was treated with a 1.00 mol/L CH_2Cl_2 solution of iodine monochloride (ICl, 0.22 mL, 0.22 mmol) in a similar manner, disulfide **5b** (34 mg, pale brown solid) was obtained in 74% yield.[18]

*General Procedure for the Synthesis of 10-Iodobornane-2-thiones 4 by Treating 10-Bromobornane-2-thiones **3** with Sodium Iodide (NaI)*

A 0.5 mL dry DMF solution of 10-bromobornane-2-thione **3a** or **3b** (0.31 mmol) was treated with sodium iodide (142 mg, 0.95 mmol, 3.0 mol amt.) at 120°C for 8 to 24 hours, and the reaction was quenched by the addition of an excess amount of water. The reaction mixture was extracted with $CHCl_3$, and the organic layer was washed with water and was dried over anhydrous sodium sulfate powder. After removing the solvent *in vacuo*, the residual crude mixture was subjected to column chromatographic separation on silica gel to afford the corresponding 10-iodobornane-2-thione **4a** or **4b**, in 88% and 86% yields, respectively.

Physical and Spectral Data for 10-Iodobornane-2-thiones 4

4a (R-R = -$(CH_2)_4$-)[18] :

Orange oil.

$[\alpha]_D^{25}$: +1.2 (*c* 0.1, $CHCl_3$).

IR (neat): 2922, 2362, 1458, 1075, 774 cm^{-1}.

^{1}H NMR ($CDCl_3$) δ: 0.88 (3H, s), 1.17 (3H, s), 1.50 (1H, ddd, *J* = 13.8, 8.5, 5.7 Hz), 1.55-1.76 (6H, m), 1.83-1.94 (4H, m), 1.98-2.12 (2H, m), 3.26 (1H, d, *J* = 10.4 Hz), 3.50 (1H, d, *J* = 10.4 Hz).

^{13}C NMR ($CDCl_3$) δ: 6.8 (t), 22.5 (q), 22.6 (q), 22.7 (t), 26.5 (t), 27.0 (t), 34.5 (dd), 42.9 (t), 45.9 (t), 50.8 (s), 57.2 (d), 67.0 (s), 69.4 (s), 279.0 (s).

MS (*m*/*z*): 348 (M^+; 46%), 221 (M^+-I; 37%), 163 (bp).

Calcd for $C_{14}H_{21}SI$: C, 48.28; H, 6.08%. Found: C, 48.56; H, 6.06%.

4b (R-R = -CH_2(*o*-C_6H_4)CH_2-):

Pale red needles. MP: 88.1-89.9°C.

IR (KBr): 2941,2356, 1633, 1479, 1412, 1215, 730 cm^{-1}.

^{1}H NMR ($CDCl_3$) δ: 1.03 (3H, s), 1.22 (3H, s), 1.50-1.56 (1H, m), 1.83-1.88 (1H, m), 1.94-2.00 (1H, m), 2.11-2.16 (1H, m), 2.27 (1H, d, *J* = 3.5 Hz), 3.17 (1H, d, *J* = 16.0 Hz), 3.25 (1H, d, *J* = 16.5 Hz), 3.28 (1H, d, *J* = 16.5 Hz), 3.31 (1H, d, *J* = 10.5 Hz), 3.43 (1H, d, *J* = 16.0 Hz), 3.54 (1H, d, *J* = 10.5 Hz), 7.10-7.17 (4H, m).

^{13}C NMR ($CDCl_3$) δ: 6.5 (t), 23.0 (q), 23.1 (q), 23.4 (t), 34.1 (dd), 47.6 (t), 50.7 (t), 52.0 (s), 56.7 (d), 67.7 (s), 69.6 (d), 123.7 (d), 123.9 (d), 126.7 (d), 126.8 (d), 140.1 (s), 142.0 (s), 275.2 (s).

MS (*m*/*z*): 396 (M^+; 82%), 363 (M^+-SH; bp), 269 (M^+-I; 32%), 235 (M^+-HI-S; 56%).

HRMS Calcd for $C_{18}H_{21}SI$: *m*/*z* 396.0409. Found: *m*/*z* 396.0409.

*Physical and Spectral Data for Rearrangement Products **5***

5a (R-R = -$(CH_2)_4$-):

Colorless oil.

IR (neat): 2938, 2357, 1488, 1371, 1276, 744 cm^{-1}.

^{1}H NMR ($CDCl_3$) δ: 1.09 (6H, s), 1.19 (6H, s), 1.28-1.32 (2H, m), 1.47-1.77 (20H, m), 2.01-2.09 (2H, m), 2.38-2.45 (2H, m), 4.79 (2H, s), 5.09 (2H, s).

^{13}C NMR ($CDCl_3$) δ: 24.5 (t), 25.0 (t), 27.3 (t), 29.9 (q), 30.5 (q), 31.5 (t), 31.6 (t), 33.8 (t), 41.6 (s), 55.0 (d), 63.7 (s), 65.2 (s), 102.5 (br. t), 166.1 (s).

MS (*m*/*z*): 442 (M^+; 28%), 253 (M^+-$C_{14}H_{21}$; 8%), 221 (M^+/2; 68%), 95 (bp).

Calcd for $C_{28}H_{42}S_2$: C, 75.95; H, 9.56%. Found: C, 75.51; H, 9.80%.

5b (R-R = -CH_2(*o*-C_6H_4)CH_2-):

Yellow oil.

IR (neat): 2927, 1716, 1659, 1462, 1384, 1284, 1221, 1140, 1090, 891, 745 cm^{-1}.

^{1}H NMR ($CDCl_3$) δ: 1.16 (6H, s), 1.28 (6H, s), 1.81-1.85 (8H, m), 2.07 (2H, s), 2.25-2.34 (4H, m), 2.93 (2H, d, *J* = 15.8 Hz), 3.00 (2H, d, *J* = 16.2 Hz), 3.06 (2H, d, *J* = 15.8 Hz), 3.11 (2H, d, *J* = 16.2 Hz), 4.95 (2H, s), 5.30 (4H, d, *J* = 7.4 Hz), 7.14-7.17 (8H, m).

^{13}C NMR ($CDCl_3$) δ: 25.0 (q), 29.5 (q), 33.8 (t), 38.8 (t), 39.8 (t), 56.2 (t), 63.6 (s), 63.8 (s), 104.4 (t), 124.0 (d), 124.2 (d), 126.6 (d), 126.7 (d), 141.6 (s), 142.9 (s), 163.1 (s).

MS (*m/z*): 538 (M^+; 9%), 269 (M^+/2; bp), 237 (M^+/2-S; 11%).

HRMS Calcd for $C_{36}H_{42}S_2$: *m/z* 538.2728. Found: *m/z* 538.2826.

*A Typical Procedure for the Synthesis of 10-Imidazolylbornane-2-thiones **6** by Treating 10-Bromobornane-2-thiones (**3a-b**) with Imidazole*

A dry hexane solution of imidazole (200 mg, 2.94 mmol, 1.5 mol amt.) was treated with commercial NaH (50 wt% in mineral oil, 140 mg, 2.94 mmol, 1.5 mol amt.) at R.T. for 5 minutes, and then, the reaction mixture was treated with a 2 mL dry DMF solution of 10-bromobornane-2-thione **3a** (442 mg, 1.47 mmol) at 120°C for 60 hours. The reaction was then quenched by the addition of ethanol and water, and the reaction mixture was extracted with chloroform. The organic layer was washed with water and was dried over anhydrous Na_2SO_4 powder, and then the organic solvent was evaporated *in vacuo*. The crude products were purified by column chromatography on silica gel to obtain 10-imidazolylbornane-2-thiones **6a** (267 mg, 63% yield) as pale yellow oil.

*A Typical Procedure for the Synthesis of 10-Imidazolylbornane-2-thiones **6** by Treating 10-Iodobornane-2-thione (**4a-b**) with Imidazole*

A dry hexane solution of imidazole (259 mg, 3.81 mmol, 1.5 mol amt.) was treated with commercial NaH (50 wt% in mineral oil, 187 mg, 3.81 mmol, 1.5 mol amt.) at R.T. for 5 minutes, and then, the reaction mixture was treated with a 5 mL dry DMF solution of 10-iodobornane-2-thione **4a** (660 mg, 1.89 mmol) at 120°C for 38 hours. The reaction was then quenched by the addition of ethanol and water, and the reaction mixture was extracted with chloroform. The organic layer was washed with water and was dried over anhydrous Na_2SO_4 powder, and then the organic solvent was evaporated in vacuo. The crude products were purified by column chromatography on silica gel to obtain 10-imidazolylbornane-2-thiones **6a** (373 mg, 68% yield) as pale yellow oil. On the other hand, when 10-iodobornane-2-thione **4b** (1.698 g, 4.28 mmol) was treated with sodium hydride and imidazole in a similar manner, 10-imidazolylbornane-2-thione **6b** was obtained only in trace amount (86 mg, 7% yield) as brown oil besides the predominant formation of a mixture of skeletal rearrangement product **7b**.

*Physical and Spectral Data for 10-Imidazolylbornane-2-thiones **6***

6a (R-R = -$(CH_2)_4$-):

Colorless needles. MP: 103.7-104.6°C.

$[\alpha]_D^{25}$: +293.4 (*c* 0.1, C_2H_5OH)

IR (KBr): 3088, 2945, 1700, 1501, 1244, 740 cm^{-1}.

^{1}H NMR ($CDCl_3$) δ: 0.86 (3H, s), 1.13 (3H, s), 1.23-1.26 (1H, m),

1.60-1.98 (13H, m), 4.07 (1H, d, *J* = 15.2 Hz), 4.52 (1H, d, *J* = 15.2 Hz), 7.00 (1H, s), 7.04 (1H, br. s), 7.56 (1H, br. s).

^{13}C NMR ($CDCl_3$) δ: 21.0 (t), 22.2 (q), 22.4 (q), 26.5 (t), 27.0 (t), 29.6 (t), 43.4 (d), 45.9 (t), 46.2 (t), 49.8 (s), 56.5 (d), 67.1 (s), 72.4 (s), 129.8 (d), 128.5 (d), 138.4 (d), 281.8 (s).

MS (*m/z*): 288 (M^+; bp), 255 (M^+-SH; 32%). 150 (32%).

HRMS Calcd for $C_{17}H_{24}N_2S$: *m/z* 288.1660. Found: *m/z* 288.1663.

Calcd for $C_{17}H_{24}N_2S$: C, 70.79; H, 8.39; N, 9.71%. Found: 70.54. H, 8.11, N, 9.51%.

6b (R-R = -CH_2(*o*-C_6H_4)CH_2-):

Pale brown oil.

MS (*m/z*): 336 (M^+; 62%), 303 (M^+-SH; bp), 179 (26%).

IR (neat): 2935, 1496, 1276, 749, 667 cm^{-1}.

^{1}H NMR ($CDCl_3$) δ: 1.00 (3H, s), 1.09 (3H, s), 1.24-1.29 (3H, m), 1.83-1.94 (4H, m), 1.95-2.17 (1H, br. s), 3.18-3.40 (4H, m), 4.15 (1H, d, *J* = 15.2 Hz), 4.55 (1H, d, *J* = 15.2 Hz), 7.00 (1H, s), 7.06 (1H, s), 7.11-7.18 (4H, m), 7.62 (1H, s).

^{13}C NMR ($CDCl_3$) δ: 21.2, 22.4, 23.0, 29.2, 29.6, 46.4, 47.9, 49.6, 51.5, 56.0, 67.4, 72.6, 121.1, 123.4, 123.7, 126.5, 127.9, 138.4, 140.4, 141.6, 277.0.

HRMS Calcd for $C_{21}H_{24}N_2S$: *m/z* 336.1660. Found: *m/z* 336.1648.

7b (R-R = -CH_2(*o*-C_6H_4)CH_2-), an approximately 1:1 mixture:

Pale brown oil.

^{1}H NMR ($CDCl_3$) δ (partially listed data): 1.12 (6H, s), 1.24 (3H, s), 1.40 (3H, s), 2.61 (1H, d, *J* = 12.0 Hz), 2.80 (1H, d, *J* = 12.0 Hz), 3.30 (1H, d, *J* = 13.5 Hz), 3.90 (1H, s), 4.11 (1H, s), 5.793 (1H, s), 5.797 (1H, s), 6.728 (1H, s), 6.731 (1H, s).

MS (*m/z*): 674 (M^+; 1%), 673 (M^+-1; 2%), 337 (M^+/2; bp).

*Synthesis of a Geometrical Mixture of 10-Imidazolylbornane-2-thione S-Oxides **8** by Treating 10-Imidazolylbornane-2-thione **7a** with mCPBA*

A 25 mL CH_2Cl_2 solution of 10-imidazolylbornane-2-thione **6a** (783 mg, 2.70 mmol) was treated with *m*CPBA (855 mg, 2.97 mmol, 1.1 mol amt.) at R.T. for 2 hours, and the reaction was quenched by the addition of an excess amount of saturated aqueous sodium sulfite solution. The reaction mixture was extracted with ethyl acetate, and the organic layer was washed with saturated sodium bicarbonate solution and then with water, and was dried over anhydrous sodium sulfate powder. After removing the solvent *in vacuo*, the residual crude mixture was subjected to separation using column chromatography on silica gel to afford 10-imidazolylbornane-2-thione *S*-oxide **8a** (544 mg, 63% yield, yellow needles) and its geometrical isomer **8a′** (272 mg, 31% yield, yellow needles).

*Physical and Spectral Data for 10-Imidazolylbornane-2-thione S-Oxides **8a** and **8a′***

8a (R-R = -$(CH_2)_4$-, major isomer):

Yellow needles.

MP: 135.1-136.1°C.

IR (KBr): 3102, 2940, 1726, 1504, 1444, 1369, 1235, 1044, 753, 662 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 0.89 (3H, s), 0.94 (3H, s), 1.18-1.88 (13H, m), 2.04-2.17 (1H, m), 4.87 (2H, s), 7.15 (1H, s), 7.16 (1H, s), 7.62 (1H, s).

^{13}C NMR ($CDCl_3$) δ: 19.5 (t), 22.6 (q), 22.8 (q), 26.2 (t), 26.3 (t), 31.1 (t), 44.3 (d), 45.2 (t), 46.9 (t), 51.1 (s), 56.8 (s), 59.0 (s), 67.2 (s), 120.8 (d), 128.9 (d), 138.4 (d), 215.1 (s).

MS (*m*/*z*): 304 (M^+; bp), 288 (M^+-O; 39%), 255 (M^+-O-SH; 60%).

HRMS Calcd for $C_{17}H_{24}N_2OS$: *m*/*z* 304.1609. Found: *m*/*z* 304.1612.

8a′ (R-R = -$(CH_2)_4$-, minor isomer):

Yellow needles. MP: 138.0-139.0°C.

IR (KBr): 3096, 2946, 1725, 1507, 1450, 1366, 1233, 1038, 739, 656 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 0.97 (3H, s), 1.13 (3H, s), 1.68-2.28 (13H, m), 2.52-2.57 (1H, m), 4.07 (1H, d, *J* = 14.8 Hz), 4.19 (1H, d, *J* = 14.8 Hz), 6.96 (1H, s), 7.06 (1H, s), 7.50 (1H, s).

^{13}C NMR ($CDCl_3$) δ: 20.7 (t), 22.5 (q), 22.6 (q), 26.8 (t), 27.3 (t), 32.2 (t), 38.0 (d), 39.8 (t), 46.1 (t), 51.2 (s), 56.5 (s), 59.1 (s), 61.2 (s), 120.4 (d), 129.5 (d), 138.3 (t), 215.6 (s).

MS (*m*/*z*): 304 (M^+; bp), 288 (M^+-O; 94%), 255 (M^+-O-SH; 70%).

HRMS Calcd for $C_{17}H_{24}N_2OS$: *m*/*z* 304.1609. Found: *m*/*z* 304.1607.

*General Procedure for the Conversion of an Isomeric Mixture of 10-Imidazolylbornane-2-thione S-Oxides (**8a, 8a′**) into 10-Imidazolylbornan-2-one **9a***

A 3 mL methanolic solution of an isomeric mixture of thione *S*-oxides (**8a** and **8a′**, 62 mg, 2.04 mmol) was treated with concentrated hydrochloric acid (3 mL, excess) at refluxing temperature for 48 hours, and the reaction was quenched by the addition of an excess amount of 1 M aqueous sodium hydroxide solution. The reaction mixture was extracted with ethyl acetate, and the organic layer was washed with saturated sodium bicarbonate solution and then with water, and was dried over anhydrous sodium sulfate powder. After removing the solvent *in vacuo*, the residual crude mixture was subjected to purification using column chromatography on silica gel to afford 10-imidazolylbornan-2-one **9a** (46 mg, 83% yield) as pale brown solids.

*Physical and Spectral Data for 10-Imidazolylbornan-2-one **9a***

9a (R-R = -$(CH_2)_4$-):

Pale brown solids.

MS (*m*/*z*): 272 (M^+; bp), 244 (M^+-C_2H_4; 15%), 150 (31%).

IR (neat): 2958, 1731, 1499, 1267, 1076, 803, 666 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 0.86 (3H, s), 1.06 (3H, s), 1.24-1.29 (1H, m), 1.55-1.89 (13H, m), 3.87 (1H, d, *J* = 12.0 Hz), 4.14 (1H, d, *J* = 12.0 Hz), 6.99 (1H, s), 7.06 (1H, s), 7.53 (1H, s).

^{13}C NMR ($CDCl_3$) δ: 20.6 (t), 22.2 (q), 22.6 (q), 26.7 (t), 26.8 (t), 27.0 (t), 38.3 (d), 39.5 (t), 43.9 (t), 47.2 (s), 55.0 (d), 56.4 (s), 62.4 (s), 120.9 (d), 128.9 (d), 138.5 (d), 223.8 (s).

HRMS Calcd for $C_{17}H_{24}N_2O$: *m*/*z* 272.1889. Found: *m*/*z* 272.1890.

*Conversion of Ketone **9a** into N-Methylimidazolium Salt **10a***

A 5 mL THF solution of ketone **9a** (83 mg, 0.30 mmol) was treated with iodomethane (41 mg, 1.1 mol amt.) at R.T. for 1 hour, and the reaction was quenched by evaporation of the solvent. The crude product was washed with ethyl acetate for several times and was subjected to the removing of the solvent *in vacuo* to afford *N*-methylimidazolium salt **10a** (122 mg, quantitative yield) as pale brown solids.

*Physical and Spectral Data for N-Methylimidazolium Salt **10a***

10a (R-R = -$(CH_2)_4$-):

Pale brown solids.

MP: 132.0-134.5°C.

^1H NMR ($CDCl_3$) δ: 0.92 (3H, s), 1.24 (3H, s), 1.58-2.04 (19H, m), 2.05-2.16 (1H, m), 4.10 (3H, s), 4.35 (1H, d, *J* = 16.0 Hz), 4.46 (1H, d, *J* = 16.0 Hz), 7.44 (1H, s), 7.83 (1H, s), 10.13 (1H, s).

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