Versatile Synthesis of Cyclopropanecarboxylic Acid Derivatives by the $Ni(CO)_4$-Induced Reductive Carbonylation Reaction of *gem*-Dibromocyclopropanes

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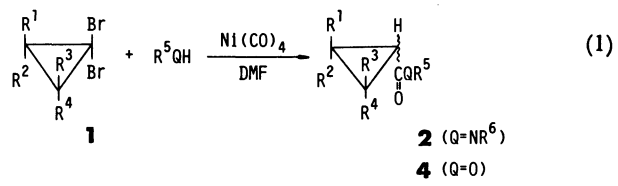
Reductive carbonylation of *gem*-dibromocyclopropanes was achieved by treatment with tetracarbonylnickel in the presence of alcohols, amines, thiols, or imidazole in DMF leading to the corresponding cyclopropanecarboxylic acid derivatives, respectively. Use of disulfides as an initial nucleophile resulted in carbonylation with sulfenylation at the geminal position. This method was applied to the intramolecular reductive carbonylation reaction of 2,2-dibromocyclopropanealkanols into bicyclic lactones. Nickel carbenoid and enolate complexes are assumed to be involved as key intermediates.

Cyclopropane derivatives are versatile synthetic intermediates since ring cleavage permits us to introduce three-carbon unit for selective carbon skeleton construction.[1] The methods for the cyclopropane ring formation have been advanced according to the development of carbene chemistry. On the other hand, the direct introduction of a functional group to a cyclopropane ring is fairly difficult although it diverses the utility of the cyclopropane ring transformation in organic syntheses. We already demonstrated[2] a versatile synthesis of cyclopropanecarboxylic acid derivatives by reductive carbonylation of *gem*-dibromocyclopropanes easily provided by the addition of dibromocarbene to olefinic compounds. The present paper describes a full account for this new method.

Results and Discussion

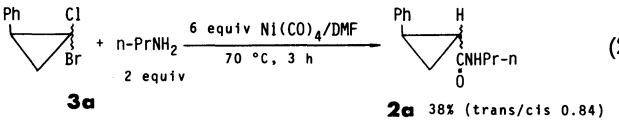
Treatment of the *gem*-dibromocyclopropane **1** with tetracarbonylnickel and amine in DMF gave a mixture of the *cis*- and *trans*-cyclopropanecarboxamides **2** (Eq. 1). This carbonylation reaction is



(1)

characterized by the simultaneous reduction of the geminal C–Br bond (reductive carbonylation). Our results are summarized in Table 1. A variety of *gem*-dibromocyclopropanes underwent reductive carbonylation with functional groups (e.g., methoxycarbonyl and cyano groups) inert under the conditions employed here. Aliphatic and aromatic amines reacted with almost equal ease. Use of excess tetracarbonylnickel increased the yields of **2**. The carbonylation reaction was suppressed substantially under CO flow and completely under 20 kg cm^{-2} of CO. This difference might be due to the occupation of coordination sites with CO.

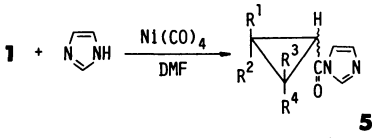
1-Bromo-1-chloro-2-phenylcyclopropane (**3a**) was also converted to the amide **2a** via reductive carbonylation (Eq. 2), this being in sharp contrast to



(2)

no reaction of 1,1-dichloro-2-phenylcyclopropane. The presence of one bromine atom is at least required for the success of the transformation.

Starting from 1-propanol or phenols, a stereoisomeric mixture of the cyclopropanecarboxylates **4** was produced. It is of interest that imidazole behaved as a nucleophile to give the 1-acylimidazoles **5** (Eq. 3). Since 1-acylimidazoles are known to be



(3)

susceptible to nucleophilic attack,[3] this method will permit a facile synthesis of cyclopropyl ketones.

Thiols did not work as a selective nucleophile for reductive carbonylation (Eq. 4). A substantial

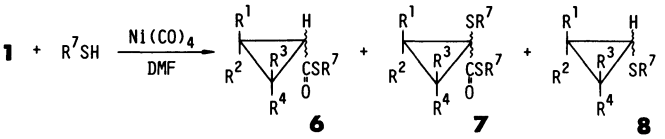


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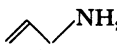
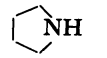
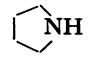
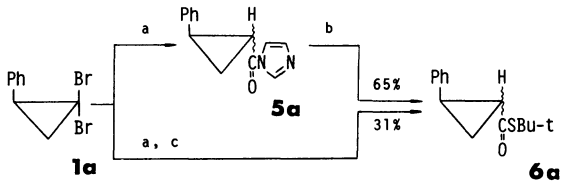
Table 1. Preparation of Cyclopropanecarboxylic Acid Derivatives

1					R^5QH	equiv	$Ni(CO)_4$ equiv	Time/h[a]	2—6	Yield/%	*trans/cis*
R^1	R^2	R^3	R^4								
Ph	H	H	H	**1a**	*n*-$PrNH_2$	2.5	6	3	**2a**	78	45 : 55
	1a				*n*-$PrNH_2$	2.5	2	3	**2a**	66	
	1a				*n*-$PrNH_2$	2.5	1	3	**2a**	52	
	1a				*n*-$PrNH_2$	1	1	3	**2a**	52	
	1a				*n*-$PrNH_2$	1	1[b]	3	**2a**	36	
	1a				*n*-$PrNH_2$	1	1[c]	3	**2a**	0	
	1a				$PhNH_2$	2.5	6	3	**2i**	63	
	1a					2.5	6	3	**2j**	56	
	1a					2.5	6	3	**2k**	66	50 : 50
CO_2Me	Me	H	H	**1b**		2.5	6	3	**2b**	44	
n-BuO	H	H	H	**1c**	*n*-$PrNH_2$	2.5	3	3	**2c**	16	
Me_3SiCH_2	H	H	H	**1d**	*n*-$PrNH_2$	2.5	6	6	**2d**	46	
	1a				*n*-PrOH	2.5	6	3	**4a**	62	34 : 66
	1a				PhOH	2.5	6	3	**4l**	57	
	1a				*m*-ClPhOH	2.5	6	3	**4m**	56	
	1b				*n*-PrOH	2.5	6	3	**4b**	75	
	1d				*n*-PrOH	2.5	6	13	**4d**	27	
CN	Me	H	H	**1e**	*n*-PrOH	2.5	6	3	**4e**	51	
Me_3Si	H	H	Ph	**1f**	*n*-PrOH	2.5	6	6	**4f**	43	
Me_3Si	H	*n*-Bu	H	**1g**	*n*-PrOH	2.5	6	6	**4g**	46	
	1a					2.5	6	6	**5a**	42	
	1d					2.5	6	7	**5d**	73	
	1d					2.5	3	7	**5d**	69	
n-C_6H_{13}	H	H	H	**1h**		2.5	3	7	**5h**	58	
	1a				*t*-BuSH	2.5	6	8	**6a**	13[d]	
	1a				*n*-PrSH	2.5	6	8	**6n**	42[e]	
	1a				PhSH	2.5	6	8	**6o**	33[f]	

a) Reaction temperature, 70 °C. b) CO, flow. c) CO, 20 kg/cm². d) *S*-*t*-Butyl 1-*t*-butylthio-2-phenylcyclopropanecarbothioate (**7a**, 10%) and 1-bromo-2-phenylcyclopropane (33%) were obtained. e) 1-Phenyl-2-propylthiocyclopropane (**8n**, 5%) and 1-bromo-2-phenylcyclopropane (40%) were obtained. f) 1-Phenyl-2-phenylthiocyclopropane (**8o**, 32%) was obtained.

amount of *S*-*t*-butyl 1-*t*-butylthio-2-phenylcyclopropanecarbothioate (**7a**) or the cyclopropyl sulfide **8** was obtained as a by-product together with the desired cyclopropanecarbothioate **6** depending on thiols. For the selective preparation of **6**, the transformation from **5** was examined; 1-(2-phenylcyclopropylcarbonyl)imidazole (**5a**) was converted to **6a** in 65% yield on treatment with 2-methyl-2-propanethiol and a catalytic amount of $Mg(OEt)_2$.[3b] Furthermore, a one-pot transformation was performed only by the addition of 2-methyl-2-propanethiol to the crude resultant mixture of **5a** after removal of excess tetracarbonylnickel leading to **6a** selectively in 31% yield from 1,1-dibromo-2-phenylcyclopropane (**1a**) as shown in Scheme 1.

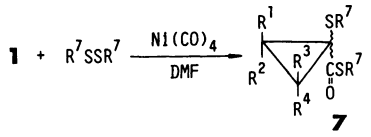
The formation of the 1-alkylthiocyclopropanecarbothioate **7a** is assumed to be explained by the



Reagents and conditions: (a) $Ni(CO)_4$ (6 equiv), Imidazole (2.5 equiv), DMF, 70 °C, 3 h; (b) *t*-BuSH (1.2 equiv), $Mg(OEt)_2$ (cat.), 25 °C, 14 h; (c) *t*-BuSH (1.2 equiv), 25 °C, 14 h.

Scheme 1.

intervention of the disulfide. Actually, the Ni(CO)$_4$-induced reaction of **1a** with dipropyl disulfide gave a mixture of *S*-propyl *cis*- and *trans*-2-phenyl-1-propylthiocyclopropanecarbothioates (**7n**) predominantly. Use of diphenyl or di-*t*-butyl disulfide resulted in the exclusive formation of **7** (Eq. 5, Table 2). This



(5)

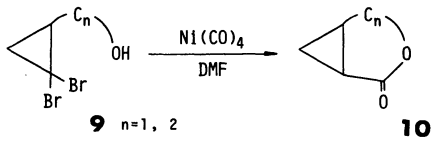
Table 2. Preparation of **7**[a]

1	$R^7_2S_2$	Product, Yield/%			
	R^7	**7**		**6**	
1a	*t*-Bu	**7a**	33	**6a**	2
1a	*n*-Pr	**7n**	34	**6n**	14
1a	Ph	**7o**	40	**6o**	0
1e	*n*-Pr	**7e**	40	**6e**	6

a) The reaction of **1** with Ni(CO)$_4$ (6 equiv) and $R^7_2S_2$ (2.5 equiv) was carried out at 70 °C for 20 h.

carbonylation accompanied by the simultaneous sulfenylation at the geminal position represents one of the scarcely investigated transition metal mediated reactions with disulfides.[4]

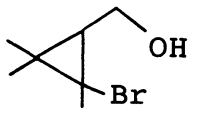
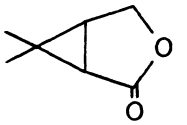
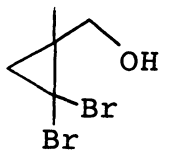
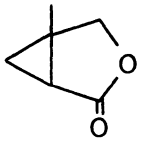
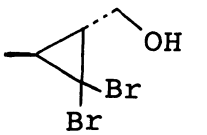
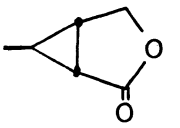
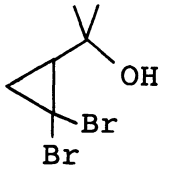
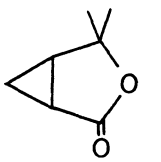
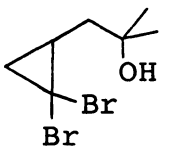
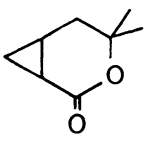
The *gem*-dibromocyclopropanes **9** bearing a hydroxyalkyl group (prepared by the addition of dibromocarbene to allylic or homoallylic alcohols[5]) were subjected to the intramolecular reductive carbonylation reaction giving the bicyclic *γ*- or *δ*-lactones **10**, respectively (Eq. 6, Table 3). It should be



(6)

noted that the intramolecular reaction of **9a** provides a facile preparative method for *cis*-chrysanthemic acid from prenyl alcohol because the bicyclic lactone **10a** has been reported to be its key synthetic intermediate.[6] In the case of *trans*-2,2-dibromo-3-

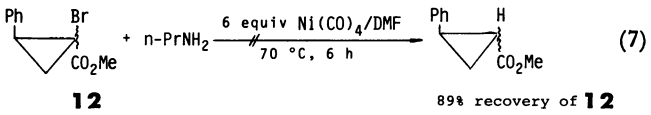
Table 3. Preparation of **10**

9	Ni(CO)$_4$, equiv	Temp/°C	Time/h	**10**, Yield/%	
 **9a**	2.2	80	11	 **10a**	37[a]
	7	75	3		73
	7	80	11[b]		27
	7	75	5[c]		60
	7	66	5[d]		3[e]
 **9b**	7	75	3	 **10b**	82
 **9c**	1.2	80	11	 **10c**	43[f]
 **9d**	7	75	3	 **10d**	70
 **9e**	7	75	3	 **10e**	51

a) *cis*-2-Bromo-3,3-dimethylcyclopropanemethanol (**11a**) was produced as a by-product (10%). b) CO, flow. c) 1-Methyl-2-piperidone was used as a solvent. d) THF was used as a solvent. e) A mixture of *cis*- and *trans*-2-bromo-3,3-dimethylcyclopropanemethanols (18%) was produced as by-products and 72% of **9a** was recovered. f) 6-*endo*-Methyl-3-oxabicyclo[3.1.0]hexan-2-one was not formed and *cis*-2-bromo-*trans*-3-methylcyclopropanemethanol (**11c**, 24%) was produced as a by-product.

methylcyclopropanemethanol (**9c**), 6-*exo*-methyl-3-oxabicyclo[3.1.0]hexan-2-one (**10c**) was produced selectively. Lactonization of tertiary-alcohols (**9d** and **9e**) proceeded well. Decrease in the amount of tetracarbonylnickel led to a small amount of by-product, the *cis*-2-bromocyclopropanemethanol **11**, derived by reduction of the bromine atom *trans* to the hydroxymethyl group of **9**. As observed in the intermolecular reactions, 2,2-dichloro-3,3-dimethylcyclopropanemethanol did not react even at the high reaction temperature (75 °C, 5 h or 120 °C, 7 h).

It is likely that tetracarbonylnickel serves an important role in the reduction step. The carbonylation reaction of **1a** with 1-propanol-*d* gave the corresponding α-deuteriocyclopropanecarboxylate, indicating that the α-proton is derived from the one of the hydroxyl group. No carbonylation of monobromocyclopropanes under the conditions employed above rules out their intervention. Moreover, oxidative addition of **1** to tetracarbonylnickel seems unlikely because the reaction of **1a** with tetracarbonylnickel in the absence of 1-propanol at 70 °C for 3 h resulted in its recovery (94%). Our first proposal refers to the intermediacy of the α-bromocyclopropanecarboxylate which is reduced to **4**.[2] This reaction path was supported by the reduction of α-bromo-β-methyl-γ-butyrolactone to β-methyl-γ-butyrolactone with tetracarbonylnickel and a small amount of water.[7] However, the independently prepared methyl 1-bromo-2-phenylcyclopropanecarboxylate (**12**) was recovered without carbonylation on treatment with tetracarbonylnickel and propylamine (Eq. 7). This finding suggests that an alternative

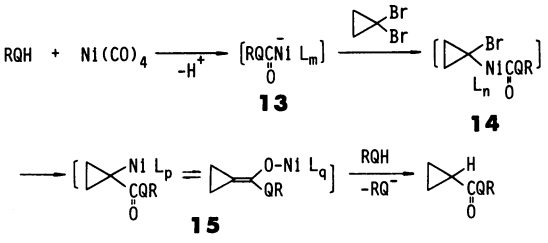


(7)

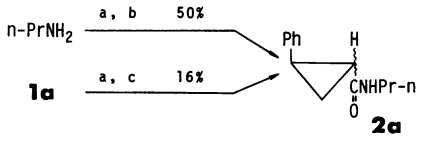
12 89% recovery of **12**

mechanism is operative.

A plausible reaction path is explained as depicted in Scheme 2. Tetracarbonylnickel is considered to contact with a nucleophile, e.g., alcohol to generate the complex **13**. A similar kind of intermediate has been reported to be present in carbonylation of vinyl halides.[8] This initial step is also ascertained by the following observations. Addition of **1a** to the DMF solution of tetracarbonylnickel pretreated with propylamine gave 50% yield of **2a**, but the reverse operation as shown in scheme 3 resulted in a poor yield of **2a** (16%). The interaction of amine with tetracarbonylnickel should be important to achieve the present transformation. The next step might be explained by invoking the attack of the complex **13** on **1** to form the nickel carbenoid complex **14**.[9] The migration of the alkoxycarbonyl group leads to the stable enolate complex **15**. Protonation with alcohol



Scheme 2.



Reagents and conditions: (a) $Ni(CO)_4$ (1 equiv), DMF, 70 °C, 3 h; (b) **1a** (1 equiv), 70 °C, 3 h; (c) *n*-$PrNH_2$ (1 equiv), 70 °C, 3 h.

Scheme 3.

completes the debromination process giving the reductive carbonylation product together with the generation of **13** from tetracarbonylnickel. Checking a crude mixture of the intermolecular reaction, a small amount of the reduced monobromocyclopropane was detected. The formation of this monobromocyclopropane and **11** is assumed to be derived by the degradation of the carbenoid complexes **14**. The present scheme also accounts for the reaction with disulfides which play both roles of a nucleophile and an electrophile. Reductive carbonylation of *gem*-dibromocyclopropanes is considered to depend on the intermediacy of the novel nickel carbenoid and enolate complexes.

Experimental

IR spectra were taken on a JASCO IRA-1 spectrometer. NMR spectra were obtained on JEOL JNM PMX-60 and JEOL JNM FX-90Q spectrometers in $CDCl_3$ solutions with tetramethylsilane as an internal standard. Mass spectrometry was performed with Hitachi RMU-6E and JEOL JMS-DX 300 (high resolution) spectrometers. The *gem*-dibromocyclopropanes **1**[10] and **9**,[5] 1-bromo-1-chloro-2-phenylcyclopropane (**3a**),[10] and methyl 1-bromo-2-phenylcyclopropanecarboxylate (**12**)[11] were prepared according to the reported methods.

General Procedure for the Preparation of Cyclopropanecarboxylic Acid Derivatives. To a stirred solution of the *gem*-dibromocyclopropane **1** (5.0 mmol) and a nucleophile (11 mmol) in freshly distilled DMF (12 mL) was added dry tetracarbonylnickel (30 mmol) at room temperature. The mixture was stirred at 70 °C for 3 h unless otherwise stated in Table 1. Excess of tetracarbonylnickel was removed under the reduced pressure. Ether (15 mL) and 5% aq HCl (15 mL) were added to the resultant mixture, which was

stirred at room temperature for 1 h and extracted with ether (3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. The residue was flash chromatographed to give a mixture of *cis*- and *trans*-cyclopropanecarboxylic acid derivatives. To purify **5**, chromatography on normal silica-gel column was done eluting with 20% EtOAc-hexane.

2a (*cis*): Mp 71—72 °C (uncorrected); IR (neat) 1620 cm^{-1}; ^{1}H NMR (90 MHz) δ=0.67 (t, 3H, J=5.0 Hz), 1.0—1.5 (m, 2H), 1.22 (ddd, 1H, J=9.5, 8.6, 7.0 Hz), 1.67 (ddd, 1H, J=9.5, 8.5, 5.8 Hz), 1.89 (ddd, 1H, J=7.0, 5.8, 5.0 Hz), 2.40 (ddd, 1H, J=8.6, 8.5, 5.0 Hz), 2.99 (q, 2H, J=5.1 Hz), 5.5—5.9 (m, 1H), 7.22 (broad s, 5H); MS m/z 203 (M$^+$). (***trans***): Mp 107—112 °C (uncorrected); IR (neat) 1620 cm^{-1}; ^{1}H NMR (90 MHz) δ=0.90 (t, 3H, J=5.0 Hz), 1.0—1.7 (m, 5H), 2.3—2.6 (m, 1H), 3.0—3.4 (m, 2H), 5.0—6.2 (m, 1H), 6.9—7.4 (m, 5H); MS m/z 203 (M$^+$). Found (mixture): C, 76.90; H, 8.35; N, 7.01%. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89%.

2b: Oil; IR (neat) 1720, 1630 cm^{-1}; ^{1}H NMR (60 MHz) δ=1.27 (s, 3H), 1.43 (d, 2H, J=7.4 Hz), 1.7—2.1 (m, 4H), 2.32 (t, 1H, J=7.4 Hz), 3.3—3.6 (m, 4H), 3.70 (s, 3H). MS m/z 179 (M$^+$). Found: C, 62.10; H, 8.19; N, 6.49%. Calcd for $C_{11}H_{17}NO$: C, 62.54; H, 8.11; N, 6.63%. The other isomer was obtained in a small amount.

2c (*cis* and *trans*): Oil; IR (neat) 1620 cm^{-1}; ^{1}H NMR (60 MHz) δ=0.7—1.9 (m, 15H), 3.0—3.7 (m, 5H), 6.1—6.6 (broad, 1H); MS, Found 199.1572, Calcd for $C_{11}H_{21}NO_2$ 199.1571.

2d (*cis* and *trans*): Oil; IR (neat) 1640 cm^{-1}; ^{1}H NMR (60 MHz) δ=0.05 (s, 9H), 0.4—1.8 (m, 11H), 3.20 (dt, 2H, J=6.8, 6.0 Hz), 5.8—6.4 (broad, 1H); MS, Found 213.1547, Calcd for $C_{11}H_{23}NOSi$ 213.1547.

2i (*cis*): Mp 159—160 °C (uncorrected); IR (neat) 1640 cm^{-1}; ^{1}H NMR (90 MHz) δ=1.29 (ddd, 1H, J=8.6, 7.9, 5.0 Hz), 1.75 (ddd, 1H, J=7.1, 5.7, 5.0 Hz), 1.98 (ddd, 1H, J=8.9, 8.6, 7.1 Hz), 2.48 (ddd, 1H, J=8.9, 7.9, 5.7 Hz), 6.8—7.4 (m, 10H), 7.4—7.6 (broad, 1H); MS, Found 237.1154, Calcd for $C_{16}H_{15}NO$ 237.1153. (*trans*): Mp 162—163 °C (uncorrected); IR (neat) 1640 cm^{-1}; ^{1}H NMR (90 MHz) δ=1.1—1.4 (m, 1H), 1.5—1.9 (m, 2H), 1.4—2.7 (m, 1H), 6.8—7.6 (m, 10H), 7.6—8.0 (broad, 1H); MS, Found 237.1155, Calcd for $C_{16}H_{15}NO$ 237.1153.

2j: Oil; IR (neat) 1635 cm^{-1}; ^{1}H NMR (60 MHz) δ=1.0—2.7 (m, 4H), 3.5—3.9 (m, 2H), 4.6—5.1 (m, 2H), 5.3—5.9 (m, 2H), 7.30 (broad s, 5H); MS, Found 201.1153, Calcd for $C_{13}H_{15}NO$ 201.1153. **The Other Isomer**: Oil; IR (neat) 1635 cm^{-1}; ^{1}H NMR (60 MHz) δ=0.9—2.0 (m, 3H), 2.3—2.7 (m, 1H), 3.7—4.1 (m, 2H), 4.9—5.4 (m, 2H), 5.5—6.2 (m, 2H), 6.7—7.5 (m, 5H); MS, Found 201.1155, Calcd for $C_{13}H_{15}NO$ 201.1153.

2k (*cis* and *trans*): Oil; IR ($CHCl_3$) 1620 cm^{-1}; ^{1}H NMR (60 MHz) δ=1.1—3.7 (m, 12H), 7.14 (broad s, 5H); MS, Found 215.1309, Calcd for $C_{14}H_{17}NO$ 215.1309.

4a: IR (neat) 1735 cm^{-1}; ^{1}H NMR (90 MHz) δ=0.75 (t, 3H, J=6.6 Hz), 1.0—2.8 (m, 6H), 3.73 (t, 2H, J=6.6 Hz), 7.0—7.3 (m, 5H); MS, Found 204.1147, Calcd for $C_{13}H_{16}O_2$ 204.1149. **The Other Isomer:** IR (neat) 1735 cm^{-1}; ^{1}H NMR (90 MHz) δ=0.93 (t, 3H, J=6.4 Hz), 1.1—2.1 (m, 5H), 2.3—2.7 (m, 1H), 4.03 (t, 2H, J=6.4 Hz), 6.8—7.4 (m, 5H); MS, Found 204.1150, Calcd for $C_{13}H_{16}O_2$ 204.1149. Bp (mixture, Kugelrohr) 78—80 °C/0.25 mmHg (1 mmHg= 133.322 Pa).

4b: IR (neat) 1720 cm^{-1}; ^{1}H NMR (60 MHz) δ=0.97 (t, 3H, J=6.6 Hz), 1.2—1.9 (m, 7H), 2.40 (dd, 1H, J=6.6, 6.4 Hz), 3.70 (s, 3H), 4.10 (t, 2H, J=6.6 Hz); MS m/z 200 (M$^+$). **The Other Isomer:** IR (neat) 1720 cm^{-1}; ^{1}H NMR (60 MHz) δ=0.97 (t, 3H, J=6.6 Hz), 1.2—2.0 (m, 8H), 3.67 (s, 3H), 4.10 (t, 2H, J=6.6 Hz); MS m/z 200 (M$^+$). Bp (mixture, Kugelrohr) 78 °C/0.2 mmHg. Found (mixture): C, 59.91; H, 8.26%. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05%.

4d: IR (neat) 1720 cm^{-1}; ^{1}H NMR (60 MHz) δ=0.05 (s, 9H), 0.6—2.0 (m, 11H), 4.03 (t, 2H, J=6.4 Hz); MS m/z 214 (M$^+$). **The Other Isomer:** IR (neat) 1720 cm^{-1}; ^{1}H NMR (60 MHz) δ=0.10 (s, 9H), 0.5—2.0 (m, 11H), 4.07 (t, 2H, J=6.4 Hz); MS m/z 214 (M$^+$). Bp (mixture, Kugelrohr) 102 °C/0.2 mmHg. Found (mixture). C, 61.59; H, 10.49%. Calcd for $C_{11}H_{22}O_2Si$: C, 61.63; H, 10.34%.

4e (*cis* and *trans*): Bp (Kugelrohr) 85 °C/0.2 mmHg; IR (neat) 2220, 1720 cm^{-1}; ^{1}H NMR (60 MHz) δ=0.8—1.1 (m, 3H), 1.1—2.2 (m, 7H), 2.4—3.0 (m, 1H), 3.9—4.3 (m, 2H); MS m/z 167 (M$^+$). Found: C, 64.84; H, 8.10; N, 8.31%. Calcd for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.38%. One Isomer was Separated: IR (neat) 1720 cm^{-1}; ^{1}H NMR (60 MHz) δ=1.00 (t, 3H, J=6.6 Hz), 1.50 (s, 3H), 1.2—2.0 (m, 4H), 2.30 (dd, 1H, J=8.6, 6.8 Hz), 4.10 (t, 2H, J=6.6 Hz).

4f (R^1=Me_3Si, R^2=R^3=H, R^4=Ph, CO_2Pr-*n* *cis* to Ph): IR (neat) 1720 cm^{-1}; ^{1}H NMR (60 MHz) δ=0.07 (s, 9H), 0.70 (t, 3H, J=6.6 Hz), 1.07 (dd, 1H, J=8.8, 7.0 Hz), 1.1—1.5 (m, 2H), 1.90 (dd, 1H, J=8.4, 7.0 Hz), 2.37 (dd, 1H, J=8.8, 8.4 Hz), 3.72 (t, 2H, J=6.6 Hz), 6.9—7.4 (m, 5H); MS m/z 276 (M$^+$). (R^1=Me_3Si, R^2=R^3=H, R^4=Ph, CO_2Pr-*n* *trans* to Ph): IR (neat) 1720 cm^{-1}; ^{1}H NMR (60 MHz) δ=0.17 (s, 9H), 0.50 (dd, 1H, J=10.0, 8.6 Hz), 0.82 (t, 3H, J=6.8 Hz), 1.2—1.8 (m, 2H), 1.95 (dd, 1H, J=10.0, 4.4 Hz) 2.43 (dd, 1H, J=8.6, 4.4 Hz), 3.90 (t, 2H, J=6.8 Hz), 6.8—7.3 (m, 5H); MS m/z 276 (M$^+$). Bp (mixture, Kugelrohr) 117 °C/0.09 mmHg. Found (mixture): C, 69.71; H, 9.02%. Calcd for $C_{16}H_{24}O_2Si$: C, 69.52; H, 8.75%.

4g (*cis* and *trans*): IR (neat) 1720 cm^{-1}; ^{1}H NMR (60 MHz) δ=0.02 (s, 3.5 H), 0.07 (s, 5.5 H), 0.6—2.0 (m, 17H), 3.8—4.1 (m, 2H); MS, Found 256.1856, Calcd for $C_{14}H_{28}O_2Si$ 256.1857.

4m (*cis*): IR (neat) 1650 cm^{-1}; ^{1}H NMR (90 MHz) δ=1.39 (ddd, 1H, J=8.1, 7.8, 5.1 Hz), 1.84 (ddd, 1H, J=7.5, 5.6, 5.1 Hz), 2.24 (ddd, 1H, J=9.0, 7.8, 5.6 Hz), 2.71 (ddd, 1H, J=9.0, 8.1, 7.5 Hz), 6.3—7.4 (m, 9H). (***trans***): IR (neat) 1650 cm^{-1}; ^{1}H NMR (90 MHz) 1.45 (ddd, 1H, J=9.0, 7.0, 4.9 Hz), 1.73 (ddd, 1H, J=9.6, 5.0, 4.9 Hz), 2.08 (ddd, 1H, J=9.0, 5.0, 4.9 Hz), 2.65 (ddd, 1H, J=9.6, 7.0, 4.9 Hz), 6.8—7.4 (m, 9H); MS (mixture), Found 272.0603, Calcd for $C_{16}H_{13}O_2Cl$ 272.0604.

5a: Mp 85—87 °C (uncorrected); IR (neat) 1710 cm^{-1}; ^{1}H NMR (90 MHz) δ=1.59 (ddd, 1H, J=8.7, 8.5, 5.3 Hz), 2.10 (ddd, 1H, J=7.6, 5.6, 5.3 Hz), 2.64 (ddd, 1H, J=8.8, 8.7, 5.6 Hz), 2.91 (ddd, 1H, J=8.8, 8.5, 7.6 Hz), 7.04 (broad s, 1H), 7.20 (broad s, 5H), 7.42 (broad s, 1H), 8.17 (broad s, 1H); MS m/z 212 (M$^+$). Found: C, 73.47; H, 5.81; N, 13.32%. Calcd for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70; N, 13.20%. The other isomer was obtained in a small amount.

5d: Oil; IR (neat) 1720 cm^{-1}; ^{1}H NMR (90 MHz) δ=0.04 (s, 9H), 0.1—2.0 (m, 6H), 7.12 (broad s, 1H), 7.53 (broad s, 1H), 8.28 (broad s, 1H); MS m/z 222 (M$^+$). **The Other**

Isomer: Oil; IR (neat) 1720 cm^{-1}; ^1H NMR (90 MHz) δ=−0.07 (s, 9H), 0.7—0.8 (m, 2H), 1.2—2.0 (m, 3H), 2.2—2.5 (m, 1H), 7.11 (broad s, 1H), 7.56 (broad s, 1H), 8.23 (broad s, 1H); MS *m/z* 222 (M^+). Found (mixture): C, 59.31; H, 7.99; N, 12.91%. Calcd for $C_{11}H_{18}N_2OSi$: C, 59.42; H, 8.16; N, 12.60%.

5h (*cis* and *trans*): IR (neat) 1720 cm^{-1}; ^1H NMR (60 MHz) δ=0.5—2.4 (m, 17H), 7.12 (broad s, 1H), 7.42 (broad s, 1H), 8.15 (broad s, 1H); MS *m/z* 220 (M^+). Found: C, 71.02; H, 9.17; N, 12.65%. Calcd for $C_{13}H_{20}N_2O$: C, 70.87; H, 9.15; N, 12.72%.

6a: Bp (Kugelrohr) 162—163 °C/0.45 mmHg; IR (neat) 1680 cm^{-1}; ^1H NMR (90 MHz) δ=1.26 (s, 9H), 1.1—1.5 (m, 1H), 1.7—2.0 (m, 1H), 2.2—2.8 (m, 2H), 7.21 (broad s, 5H); MS, Found 234.1075, Calcd for $C_{14}H_{18}OS$ 234.1078. The other isomer was obtained in a small amount.

6n (*cis*): IR (neat) 1680 cm^{-1}; ^1H NMR (90 MHz) δ=0.81 (t, 3H, *J*=7.0 Hz), 1.2—1.6 (m, 4H), 1.90 (ddd, 1H, *J*=7.3, 5.6, 5.1 Hz), 2.3—2.8 (m, 1H), 2.69 (t, 2H, *J*=7.0 Hz), 7.25 (broad s, 5H); MS, Found 220.0921, Calcd for $C_{13}H_{16}OS$ 220.0921. **(*trans*):** IR (neat) 1680 cm^{-1}; ^1H NMR (90 MHz) δ=0.98 (t, 3H, *J*=7.1 Hz); 1.48 (ddd, 1H, *J*=8.2, 6.5, 4.4 Hz), 1.4—1.8 (m, 2H), 1.75 (ddd, 1H, *J*=8.6, 4.7, 4.4 Hz), 2.27 (ddd, 1H, *J*=8.2, 4.7, 3.8 Hz), 2.67 (ddd, 1H, *J*=8.6, 6.5, 3.8 Hz), 2.90 (t, 2H, *J*=7.1 Hz), 7.0—7.4 (m, 5H); MS, Found 220.0920, Calcd for $C_{13}H_{16}OS$ 220.0921. Bp (mixture, Kugelrohr) 114—118 °C/0.2 mmHg.

6o (*cis* and *trans*): White solid; IR (neat) 1680 cm^{-1}; ^1H NMR (60 MHz) δ=1.1—1.6 (m, 1H), 1.7—2.1 (m, 1H), 2.4—3.0 (m, 2H), 7.24 (broad s, 10H); MS, Found 254.0765, Calcd for $C_{16}H_{14}OS$ 254.0765.

Conversion of 5a to 6a. According to the reported method,[3b] treatment of **5a** with 1.2 equiv of 2-methyl-2-propanethiol and a catalytic amount of $Mg(OEt)_2$ at 25 °C for 14 h gave **6a** in 65% yield.

One-Pot Synthesis of 6a. After treatment of **1a** with tetracarbonylnickel and imidazole, excess tetracarbonylnickel was removed under the reduced pressure. Then, 1.2 equiv of 2-methyl-2-propanethiol was added to the resultant mixture, which was stirred at 25 °C for 14 h. Workup was done in the similar manner as mentioned above to give **6a** in 31% yield.

Preparation of 7. The reaction of **1** with disulfides was carried out in the similar manner as mentioned above. The conditions are shown in footnotes of Table 2.

7a: IR (neat) 1660 cm^{-1}; ^1H NMR (90 MHz) δ=1.06 (s, 9H), 1.2—1.6 (m, 1H), 1.40 (s, 9H), 1.68 (dd, 1H, *J*=5.2, 2.7 Hz), 2.71 (dd, 1H, *J*=13.0, 5.2 Hz), 7.18 (broad s, 5H); MS *m/z* 322 (M^+). **The Other Isomer:** IR (neat) 1660 cm^{-1}; ^1H NMR (90 MHz) δ=1.19 (s, 9H), 1.50 (s, 9H), 1.71 (dd, 1H, *J*=9.4, 5.6 Hz), 2.27 (dd, 1H, *J*=8.1, 5.6 Hz), 3.23 (dd, 1H, *J*=9.4, 8.1 Hz), 7.17 (broad s, 5H); MS *m/z* 322 (M^+). Found (mixture): C, 66.98; H, 8.20; S, 20.01%. Calcd for $C_{18}H_{26}OS_2$: C, 67.03; H, 8.13; S, 19.88%.

7e (*cis* and *trans*): Oil; IR (neat) 2250, 1665 cm^{-1}; ^1H NMR (90 MHz) δ=1.00 (broad t, 6H), 1.2—2.6 (m, 9H), 2.6—3.1 (m,4H); MS *m/z* 257 (M^+). Found: C, 56.08; H, 7.69; N, 5.51; S, 24.60%. Calcd for $C_{12}H_{19}NOS_2$: C, 55.99; H, 7.44; N, 5.44; S, 24.91%.

7n (*cis* and *trans*): Oil; IR (neat) 1680 cm^{-1}; ^1H NMR (90 MHz) δ=0.7—1.1 (m, 6H), 1.2—1.8 (m, 6H), 2.1—2.8 (m, 5H), 7.1—7.5 (m, 5H); MS *m/z* 294 (M^+). Found: C, 65.41; H, 7.47; S, 21.65%. Calcd for $C_{16}H_{22}NOS_2$: C, 65.26; H, 7.53; S, 21.78%.

7o: Oil; IR (neat) 1690 cm^{-1}; ^1H NMR (90 MHz) δ=1.71 (dd, 1H, *J*=9.1, 8.0 Hz), 2.71 (dd, 1H, *J*=8.0, 5.1 Hz), 3.21 (dd, 1H, *J*=9.1, 5.1 Hz), 7.1—7.6 (m, 15H); MS *m/z* 362 (M^+). Found: C, 72.76; H, 5.05; S, 17.80%. Calcd for $C_{22}H_{18}OS_2$: C, 72.89; H, 5.01; S, 17.69%. The other isomer was not isolated.

6e (*cis* and *trans*): Oil; IR (neat) 2250, 1670 cm^{-1}; ^1H NMR (90 MHz) δ=1.00 (broad t, 3H), 1.2—2.7 (m, 8H), 2.7—3.1 (m, 2H); MS, Found 183.0717, Calcd for $C_9H_{13}NOS$ 183.0717.

Preparation of 10. The reaction was carried out in the similar manner as mentioned above by mixing **9** and tetracarbonylnickel in DMF. The conditions are shown in Table 3.

10a: Bp (Kugelrohr) 90—94 °C/2.8 mmHg; IR (neat) 1760 cm^{-1}; ^1H NMR (60 MHz) δ=1.16 (s, 6H), 1.8—2.3 (m, 2H), 4.0—4.6 (m, 2H); ^{13}C NMR δ=14.4 (q), 23.0 (s), 25.2 (q), 30.1 (d), 30.6 (d), 66.5 (t), 174.8 (s); MS *m/z* 126 (M^+). Found: C, 66.68; H, 8.21%. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99%.

10b: Bp (Kugelrohr) 107—110 °C/4.0 mmHg; IR (neat) 1765 cm^{-1}; ^1H NMR (90 MHz) δ=1.01 (dd, 1H, *J*=4.6, 3.2 Hz), 1.20 (dd, 1H, *J*=8.8, 4.6 Hz), 1.40 (s, 3H), 1.84 (dd, 1H, *J*=8.8, 3.2 Hz), 4.06 (d, 1H, *J*=9.0 Hz), 4.14 (d, 1H, *J*=9.0 Hz); ^{13}C NMR δ=16.9 (q), 19.0 (t), 23.7 (d), 25.4 (s), 73.5 (t), 176.7 (s); MS *m/z* 112 (M^+). Found: C, 64.04; H, 7.32%. Calcd for $C_6H_8O_2$: C, 64.27; H, 7.19%.

10c: Bp (Kugelrohr) 80—82 °C/0.9 mmHg; IR (neat) 1765 cm^{-1}; ^1H NMR (90 MHz) δ=1.19 (s, 3H), 1.0—1.4 (m, 1H), 1.79 (dd, 1H, *J*=5.9, 2.8 Hz), 1.9—2.1 (m, 1H), 4.1—4.4 (m, 2H); ^{13}C NMR δ=16.0 (q), 21.0 (d), 25.1 (d), 25.2 (d), 69.5 (t), 175.9 (s); MS *m/z* 112 (M^+). Found: C, 64.33; H, 7.08%. Calcd for $C_6H_8O_2$: C, 64.27; H, 7.19%.

10d: Bp (Kugelrohr) 69—70 °C/0.4 mmHg; IR (neat) 1765 cm^{-1}; ^1H NMR (90 MHz) δ=0.8—1.4 (m, 3H), 1.36 (s, 3H), 1.48 (s, 3H), 2.0—2.2 (m, 1H); ^{13}C NMR δ=11.1 (t), 19.2 (d), 24.1 (q), 27.6 (d), 29.1 (q), 82.7 (s), 175.7 (s); MS *m/z* 126 (M^+). Found: 66.55; H, 7.63%. Calcd for $C_7H_{10}O_2$: C, 66.64; H, 7.99%.

10e: Bp (Kugelrohr) 85—87 °C/0.5 mmHg; IR (neat) 1725 cm^{-1}; ^1H NMR (90 MHz) δ=0.7—0.9 (m, 1H), 1.1—2.3 (m, 5H), 1.34 (s, 3H), 1.47 (s, 3H); ^{13}C NMR δ=11.9 (d), 12.5 (d), 18.8 (t), 27.5 (q), 29.1 (q), 35.8 (t), 83.1 (s), 172.4 (s); MS *m/z* 140 (M^+). Found: C, 68.32; H, 8.51%. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63%.

11a: Oil; IR (neat) 3300, 1250 cm^{-1}; ^1H NMR (60 MHz) δ=1.08 (dt, 1H, *J*=7.5, 7.4 Hz), 1.17 (s, 6H), 1.56 (broad s, 1H), 3.00 (d, 1H, *J*=7.4 Hz), 3.75 (d, 2H, *J*=7.5 Hz); MS, Found 160.9966, Calcd for $C_6H_{11}OBr$–OH 160.9965.

11c: Oil; IR (neat) 3480, 1250 cm^{-1}; ^1H NMR (90 MHz) δ=0.92 (ddt, 1H, *J*=7.7, 6.1, 4.0 Hz), 1.17 (ddq, 1H, *J*=5.7, 4.0, 3.6 Hz), 1.27 (d, 3H, *J*=5.7 Hz), 1.62 (broad s, 1H), 2.97 (dd, 1H, *J*=7.7, 3.6 Hz), 3.59 (d, 2H, *J*=6.1 Hz); MS, Found 163.9835, Calcd for C_5H_9OBr 163.9837.

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