Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron 64 (2008) 1753–1758
Tetrahedron
www.elsevier.com/locate/tet

Facile synthesis of 2-azaazulenes from thiobenzoyl isocyanates using trimethylsilyldiazomethane

Mikio Morita, Yoshiyuki Hari, Tomoe Iguchi, Toyohiko Aoyama*

Graduate School of Pharmaceutical Sciences, Nagoya City University, 3-1 Tanabe-dori, Mizuho, Nagoya 467-8603, Japan

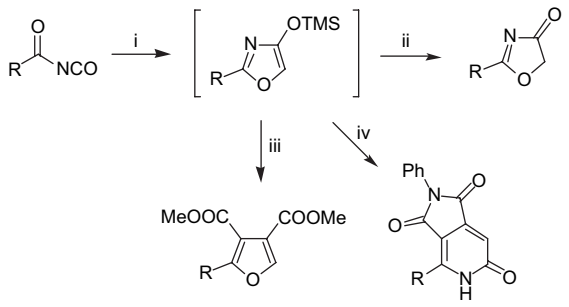
Received 13 November 2007; accepted 30 November 2007
Available online 5 December 2007

Abstract

The reaction of trimethylsilyldiazomethane with thiobenzoyl isocyanates, in situ generated from thiazole-4,5-diones, yielded diazoketones, which were converted into 2-azaazulenes by the intramolecular Buchner reaction.

1. Introduction

Our interest in trimethylsilyldiazomethane ($TMSCHN_2$) as a synthetic reagent originated from the hazardous nature of diazomethane (CH_2N_2), which has been widely used in various organic reactions.[1] $TMSCHN_2$ is stable and safe in contrast to labile and explosive diazomethane. We have already demonstrated that $TMSCHN_2$ can be effectively used not only as a C1-unit introducing reagent and a [C–N–N]azole synthon in place of diazomethane but also as an alkylidene carbene generator from carbonyl compounds.[2] Recently, for example, we have succeeded in the synthesis of multi-substituted furans and bicyclic pyridones by the reaction of $TMSCHN_2$ with acyl isocyanates, followed by Diels–Alder reaction of the resulting 4-trimethylsiloxyoxazoles with dimethyl acetylenedicarboxylate and *N*-phenylmaleimide in one-pot, respectively (Scheme 1).[3] The key point of the one-pot synthesis was the in situ generation of 4-trimethylsiloxyoxazoles, the electron-rich heterodienes, by the reaction of $TMSCHN_2$ with acyl isocyanates. From the results, we thought that thiophenes via 4-trimethylsiloxythiazoles could be synthesized if thioacyl isocyanates in place of acyl isocyanates are used as substrates. However, interestingly, we found that the reaction of $TMSCHN_2$ with thiobenzoyl isocyanates proceeded in a different mode and the *N*-diazoacetylbenzimido derivatives were formed, and almost no 4-trimethylsiloxythiazoles were detected.[4] The *N*-diazoacetylbenzimido derivatives obtained seemed to be good substrates for intramolecular Buchner reaction giving 2-azaazulenes.[5] In this paper, we would like to describe the details of our results for the synthesis of 2-azaazulenes from thiobenzoyl isocyanates using $TMSCHN_2$.



Scheme 1. Reaction of $TMSCHN_2$ with acyl isocyanate. (i) $TMSCHN_2$ (1.2 equiv). (ii) H_2O. (iii) DMAD (2 equiv). (iv) *N*-Phenylmaleimide (1.2 equiv); CSA (0.1 equiv).

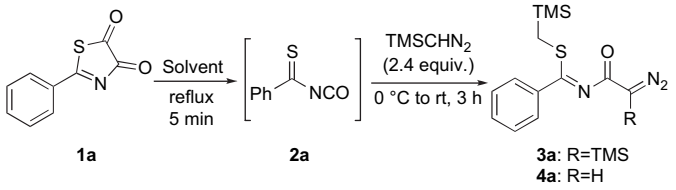
2. Results and discussion

Reaction of $TMSCHN_2$ with thiobenzoyl isocyanate **2a**, in situ generated from the thiazole-4,5-dione **1a** by pyrolysis according to the known procedure,[6] was examined (Table 1). Thiobenzoyl isocyanate **2a** smoothly reacted with 1.2 equiv of $TMSCHN_2$ at 0 °C in *o*-xylene, but the product was the silyldiazoketone **3a** resulting from 2 equiv of $TMSCHN_2$ and

* Corresponding author. Tel./fax: +81 52 836 3439.
E-mail address: aoyama@phar.nagoya-cu.ac.jp (T. Aoyama).

0040-4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.11.107

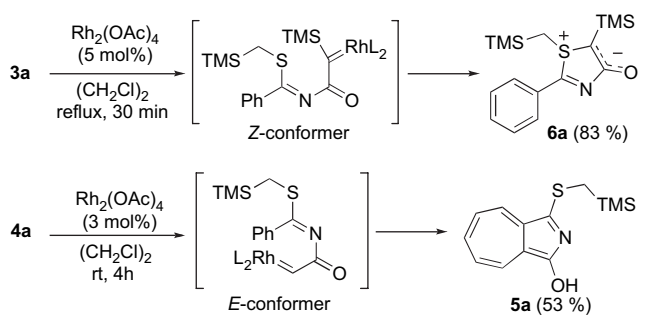
Table 1
Reaction of thiobenzoyl isocyanate with $TMSCHN_2$



Entry	Solvent	Yield (%) of **3a** and **4a**
1[a]	*o*-Xylene	58 (**3a**, 58)
2	*o*-Xylene	76 (**3a**, 56; **4a**, 20)
3	1,4-Dioxane	47 (**4a**, 47)
4	*n*-Heptane	55 (**3a**, 26; **4a**, 29)
5	Toluene	74 (**3a**, 50; **4a**, 24)
6[b]	Toluene	75 (**4a**, 75)

[a] $TMSCHN_2$ (1.2 equiv) was used.
[b] Before work-up, *i*-Pr_2NEt (10 equiv) was added and the mixture was stirred at rt for 1 day.

1 equiv of **2a** and the expected 4-trimethylsiloxythiazole was hardly detected (entry 1). In this reaction, 2 equiv of $TMSCHN_2$ was required to complete the reaction. Therefore, increase of $TMSCHN_2$ to 2.4 equiv improved the yield (76%) though a separable mixture of **3a** and the desilylated diazoketone **4a** was obtained in 56% and 20% yield (entry 2).[7] Similar result was obtained by the use of toluene as a solvent (entry 5). Other solvent such as 1,4-dioxane and *n*-heptane gave less satisfactory results (entries 3 and 4). We thought that diazoketones **3a** and **4a** could be used as substrates for intramolecular Buchner reaction giving 2-azaazulenes. Thus, the intramolecular Buchner reaction with **3a** and **4a** were individually carried out under typical reaction conditions using $Rh_2(OAc)_4$ as a catalyst (Scheme 2). As expected, the diazoketone **4a** smoothly underwent the Buchner reaction giving the 2-azaazulene **5a** in moderate yield, while the reaction with the silyldiazoketone **3a** proceeded in a different mode and the stable sulfonium ylide **6a** was obtained as a sole isolable product.[8] It is known that there is equilibrium between *E*- and *Z*-configurations in thioimidates,[9] in which the *E*-form might undergo Buchner reaction and the *Z*-form might lead to the sulfonium ylide formation. Although the reason of the difference of the reaction modes between **3a** and **4a** is not clear to date, as one of the possibilities, the steric repulsion between the trimethylsilyl group and the benzene ring might bring **3a** to *Z*-configuration affording **6a**. Thus, reexamination of the reaction conditions was carried out to selectively obtain **4a**. Various additives such as silica gel, AcOH, *p*-TsOH or *i*-Pr_2NEt, etc. were examined to convert **3a** to **4a**. As the result, after the reaction, treatment of the reaction mixture with *i*-Pr_2NEt led to the complete conversion of **3a** to **4a** in one-pot and **4a** was obtained in 75% yield as a sole isolable product (entry 6 in Table 1).

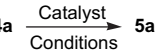


Scheme 2. Decomposition of diazoketones **3a** and **4a** catalyzed by $Rh_2(OAc)_4$.

Next, the reaction conditions of intramolecular Bucher reaction were examined using **4a** as a substrate (Table 2). Several copper catalysts such as CuCl, $Cu(OTf)_2$, and $Cu(hfacac)_2$, often used for Buchner reaction and other diazo-related reactions,[10] were less effective (entries 2–4). Eventually, $Rh_2(OAc)_4$/*o*-xylene system gave the best result (82%) (entry 7).

Under the optimized reaction conditions shown in entry 6 of Table 1 and entry 7 of Table 2, the synthesis of 2-azaazulenes from thiobenzoyl isocyanates was examined (Table 3). Various thiobenzoyl isocyanates smoothly reacted with $TMSCHN_2$ to give the corresponding diazoketones **4b–h** in good yields though in some cases the yields are relatively low. Subsequent conversion of **4** to 2-azaazulenes **5** was examined. Diazoketones **4b** and **4c** bearing substituents at the 4-position on benzene ring smoothly underwent the Buchner reaction to afford the corresponding 2-azaazulenes **5b** and **5c** in moderate to good yields (entries 2 and 3). In these reactions, the effect of substituents was observed. Thus, the methoxy group, an electron-donating group, accelerated the reaction rate and gave the high yield of the product, while the chloro group, an electron-withdrawing group, depressed both the reaction rate and the yield (entries 2 and 3). These results may be explained by the property of carbenoids. Thus, carbenoids are highly electron-deficient species; therefore, the electron-donating group on benzene ring accelerates the insertion reaction of a carbenoid to a C–C double bond of benzene ring. Analogously, the Buchner reaction of other diazoketones **4d** and **4f** afforded the corresponding 2-azaazulenes **5d** and **5f** though the yields were low (entries 4 and 6).[11] In the case of the 3-methyl derivative **4e**, the reaction smoothly proceeded, but the 2-azaazulene (54%) obtained was an unseparable mixture of 5-methyl-2-azaazulene **5e** and its regioisomer (entry 5). Interestingly, in the case of the 3-methoxy derivative **4g**, the ring-expansion reaction proceeded in a different mode,

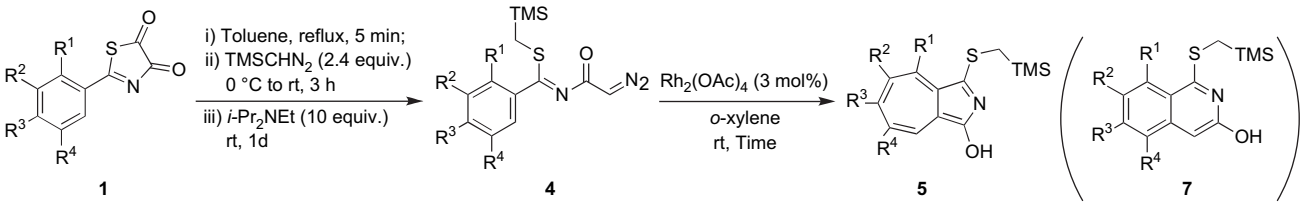
Table 2
Intramolecular Buchner reaction of **4a**



Entry	Catalyst	Conditions	Yield (%) of **5a**
1	$Rh_2(OAc)_4$ (3 mol %)	$(CH_2Cl)_2$, rt	53
2	CuCl (10 mol %)	Toluene, 80 °C	nd[b]
3	$Cu(OTf)_2$ (10 mol %)	$(CH_2Cl)_2$, rt	Trace
4	$Cu(hfacac)_2$[a] (3 mol %)	CH_2Cl_2, rt	10
5	$Rh_2(OAc)_4$ (3 mol %)	CH_2Cl_2, rt	69
6	$Rh_2(OAc)_4$ (3 mol %)	Toluene, rt	55
7	$Rh_2(OAc)_4$ (3 mol %)	*o*-Xylene, rt	82

[a] hfacac, Hexafluoroacetylacetonate.
[b] Not detected.

Table 3
Synthesis of 2-azaazulenes



Entry	Substrate	Yield (%) of **4**	Time	Yield (%) of **5** (or **7**)
1	**1a** (R^1=R^2=R^3=R^4=H)	75 (**4a**)	1 h	82 (**5a**)
2	**1b** (R^1=R^2=H, R^3=Cl, R^4=H)	73 (**4b**)	12 h	47 (**5b**)
3	**1c** (R^1=R^2=H, R^3=MeO, R^4=H)	30 (**4c**)	30 min	88 (**5c**)
4	**1d** (R^1=Me, R^2=R^3=R^4=H)	32 (**4d**)	3 h	26 (**5d**)
5	**1e** (R^1=H, R^2=Me, R^3=R^4=H)	70 (**4e**)	2 h	54[a] (**5e**)
6	**1f** (R^1=H, R^2=Me, R^3=H, R^4=Me)	60 (**4f**)	3 h	12 (**5f**)
7	**1g** (R^1=H, R^2=MeO, R^3=R^4=H)	39 (**4g**)	15 min	11 (**7g**)
8	**1h** (R^1=H, R^2=MeO, R^3=H, R^4=MeO)	65 (**4h**)	2 h	44 (**7h**)

[a] A mixture of 5-methyl-2-azaazulene **5e** and its regioisomer (R^1=R^2=R^3=H, R^4=Me) was obtained (major/minor=ca. 2.5:1).

and the isoquinoline **7g** was obtained as a sole isolable product though the yield was low (entry 7). Another 3-methoxy derivative **4h** also gave **7h** in moderate yield (entry 8). These results are similar to those of the intramolecular Buchner reaction of the carbon analogues, 1-diazo-4-(3-methoxyphenyl)butan-2-ones, giving 2-tetralones.[12]

The reaction mechanism for the formation of **5** and **7** may be as follows (Scheme 3). Initially, insertion of the carbenoid to the C–C double bond of benzene ring affords the norcaradiene intermediate, which is then isomerized to **5**. In the case of the 3-methoxy derivatives, the electron-donating methoxy group remarkably affects the isomerization mode and **7** is formed.[12a]

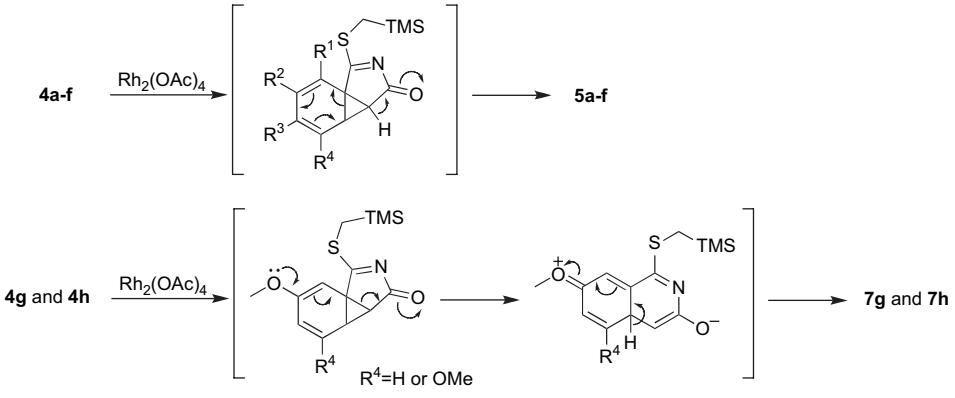
3. Conclusion

In summary, we found that the reaction of $TMSCHN_2$ with thiobenzoyl isocyanates generated from thiazole-4,5-diones and followed by intramolecular Buchner reaction of the resulting diazoketones gave 2-azaazulenes. 2-Azaazulenes, one of the aza analogues of azulenes, will be fascinating targets[13] because they may have attractive biological activities such as anti-inflammatory and anti-allergic activity of azulenes.[14] To our knowledge, there are only several reports for the synthesis of 2-azaazulenes.[15] Therefore, our present method using $TMSCHN_2$ will provide a new approach to the synthesis of 2-azaazulenes.

4. Experimental

4.1. General

IR spectra were measured on a SHIMADZU FTIR-8100 diffraction grating IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were measured on a JEOL JNM-EX-270 NMR spectrometer, operating at 270 MHz for ^{1}H NMR and at 68 MHz for ^{13}C NMR. ^{1}H and ^{13}C NMR spectra were reported in δ units, parts per million (ppm) downfield from tetramethylsilane (δ=0). EIMS and FABMS spectra were measured on a JEOL JMS-SX-102A instrument. All reactions were performed under an argon atmosphere. H_2O was used without purification. Toluene, *o*-xylene, CH_2Cl_2, and 1,2-dichloroethane were distilled from CaH_2. Silica gel column chromatography was performed on Fuji Silysia BW200 or BW820MH silica gel. Thiobenzamides were purchased from commercial suppliers or synthesized from the corresponding benzamides



Scheme 3. Possible reaction mechanism.

by Lawesson's reagent. 2-Phenylthiazole-4,5-dione **1a**,[16] 2-(4-chlorophenyl)thiazole-4,5-dione **1b**,[16] 2-(4-methoxyphenyl)thiazole-4,5-dione **1c**,[16] and 2-(3-methoxyphenyl)thiazole-4,5-dione **1h**[17] were already reported.

4.2. Preparation of thiazoline-4,5-diones *1a–h*: general procedure

To a solution of thiobenzamide (1.0 mmol) in acetone (10 mL) was added dropwise oxalyl chloride (1.0 mmol) at 0 °C, and the mixture was stirred for 5 min at the same temperature. The formed precipitate was collected by filtration and washed with acetone to give the following products.

4.2.1. 2-(2-Methylphenyl)thiazole-4,5-dione (*1d*)

Yield 30%. A yellow solid. Mp 104–106 °C (decomposed, acetone). IR (Nujol): ν=1734 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=2.81 (s, 3H), 7.42–7.49 (m, 2H), 7.60–7.68 (m, 1H), 7.95 (d, 1H, J=9.2 Hz). ^{13}C NMR ($CDCl_3$): δ=23.55, 126.71, 130.77, 131.85, 133.17, 135.70, 142.54, 171.53, 184.91, 190.57. FABMS: m/z=206 (M^++1). Anal. Calcd for $C_{10}H_7NO_2S$: C, 58.52; H, 3.44; N, 6.82. Found: C, 58.70; H, 3.57; N, 6.98.

4.2.2. 2-(3-Methylphenyl)thiazole-4,5-dione (*1e*)

Yield 46%. A yellow solid. Mp 108–109 °C (decomposed, acetone). IR (Nujol): ν=1734 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=2.50 (s, 3H), 7.52 (t, 1H, J=7.6 Hz), 7.65 (d, 1H, J=7.8 Hz), 8.02 (d, 1H, J=7.8 Hz), 8.05 (s, 1H). ^{13}C NMR ($CDCl_3$): δ=21.31, 127.34, 129.38, 130.11, 131.85, 138.78, 139.72, 171.25, 173.54, 190.90. FABMS: m/z=206 (MH^+). Anal. Calcd for $C_{10}H_7NO_2S$: C, 58.52; H, 3.44; N, 6.82. Found: C, 58.30; H, 3.50; N, 7.01.

4.2.3. 2-(3,5-Dimethylphenyl)thiazole-4,5-dione (*1f*)

Yield 79%. A yellow solid. Mp 126–127 °C (decomposed, acetone). IR (Nujol): ν=1732 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=2.45 (s, 6H), 7.46 (s, 1H), 7.85 (s, 2H). ^{13}C NMR ($CDCl_3$): δ=21.21, 127.67, 131.77, 139.49, 139.94, 171.35, 184.23, 190.98. FABMS: m/z=220 (MH^+). Anal. Calcd for $C_{11}H_9NO_2S$: C, 60.26; H, 4.14; N, 6.39. Found: C, 59.97; H, 4.38; N, 6.27.

4.2.4. 2-(3,5-Dimethoxyphenyl)thiazole-4,5-dione (*1g*)

Yield 34%. A yellow solid. Mp 121–125 °C (decomposed, acetone). IR (Nujol): ν=1755 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=3.89 (s, 6H), 6.88 (t, 1H, J=2.2 Hz), 7.36 (d, 2H, J=2.2 Hz). ^{13}C NMR ($CDCl_3$): δ=55.95, 104.94, 107.32, 110.39, 133.58, 161.10, 171.30, 190.86. FABMS: m/z=252 (MH^+). Anal. Calcd for $C_{11}H_9NO_4S$: C, 52.58; H, 3.61; N, 5.57. Found: C, 52.69; H, 3.64; N, 5.57.

4.3. Reaction of thiobenzoyl isocyanate *2a* with $TMSCHN_2$

A solution of **1a** (100 mg, 0.52 mmol) in *o*-xylene (8 mL) was refluxed with stirring for 5 min. After cooling to 0 °C, a solution of $TMSCHN_2$ in hexane (1.5 M, 0.86 mL, 1.3 mmol) was added, and the mixture was stirred at rt for 3 h. Then, the mixture was poured into water (30 mL), and the mixture was extracted with EtOAc (50 mL×3). The combined organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane/EtOAc=15:1 to 5:1) to give **3a** (56%) and **4a** (20%).

4.3.1. (Trimethylsilyl)methyl N-2-diazo-2-(trimethylsilyl)-ethanoylbenzimidothioate (*3a*)

A yellow solid. Mp 58–60 °C (EtOAc). IR (neat): ν=2924, 2105, 1626, 1600 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=0.15 (s, 9H), 0.19 (s, 9H), 2.27 (s, 2H), 7.31–7.49 (m, 3H), 7.53–7.58 (m, 2H). ^{13}C NMR ($CDCl_3$): δ=−1.60, −1.57, 17.26, 126.98, 128.25, 130.78, 136.27, 172.81, 179.37. FABMS: m/z=364 (MH^+). Anal. Calcd for $C_{16}H_{25}N_3OSSi_2$: C, 52.85; H, 6.93; N, 11.56. Found: C, 53.07; H, 6.66; N, 11.64.

4.3.2. (Trimethylsilyl)methyl N-2-diazoethanoyl-benzimidothioate (*4a*)

An orange oil. IR (neat): ν=2954, 2104, 1637 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=0.16 (s, 9H), 2.26 (s, 2H), 4.77 (s, 1H), 7.35–7.50 (m, 3H), 7.52–7.57 (m, 2H). ^{13}C NMR ($CDCl_3$): δ=−1.56, 17.38, 51.09, 126.98, 128.46, 130.97, 136.04, 176.49. EIMS: m/z=263 (M^+-N_2). FABMS: m/z=292 (MH^+). HRMS (M^+-N_2): calcd for $C_{13}H_{17}NOSSi$: 263.0800; found: 263.0798.

4.4. One-pot preparation of diazoketones *4a–g*: general procedure

A solution of 1,3-thiazole-4,5-diones **1** (0.50 mmol) in toluene (8 mL) was refluxed with stirring for 5 min. After cooling to 0 °C, a solution of $TMSCHN_2$ in hexane (1.2 mmol) was added, and the mixture was stirred at 0 °C for 1 h and at rt for 2 h. Then, *i*-Pr_2NEt (5.0 mmol) was added, and the mixture was stirred at rt for 1 day. The resulting mixture was poured into water (30 mL), and the aqueous layer was extracted with EtOAc (50 mL×3). The combined extracts were dried over Na_2SO_4 and concentrated in vacuo. Purification by silica gel chromatography using hexane–EtOAc system gave the following products.

4.4.1. (Trimethylsilyl)methyl 4-chloro-N-2-diazoethanoyl-benzimidothioate (*4b*)

Yield 47%. A brown oil. IR (neat): ν=2956, 2106, 1601 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=0.16 (s, 9H), 2.25 (s, 2H), 4.80 (s, 1H), 7.37 (d, 2H, J=8.6 Hz), 7.50 (d, 2H, J=8.9 Hz). ^{13}C NMR ($CDCl_3$): δ=−1.54, 17.50, 51.26, 128.44, 128.78, 134.40, 137.21, 176.20. EIMS: m/z=297 and 299 (M^+-N_2). FABMS: m/z=326 and 328 (MH^+). HRMS (M^+-N_2): calcd for $C_{13}H_{16}^{35}ClNOSSi$: 297.0410; found: 297.0402.

4.4.2. (Trimethylsilyl)methyl N-2-diazoethanoyl-4-methoxy-benzimidothioate (*4c*)

Yield 30%. A yellow oil. IR (neat): ν=2954, 2104, 1605 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=0.15 (s, 9H), 2.24 (s, 2H), 3.83 (s, 3H), 4.76 (s, 1H), 6.89 (d, 2H, J=8.6 Hz), 7.56 (d, 2H, J=8.9 Hz). ^{13}C NMR ($CDCl_3$): δ=−1.46, 17.50, 51.10, 55.43, 113.89, 128.46, 129.06, 161.83, 176.84.

EIMS: *m*/*z*=293 (M^+-N_2). FABMS: *m*/*z*=322 (MH^+). HRMS ($M-N_2^+$): calcd for $C_{14}H_{19}NO_2SSi$: 293.0906; found: 293.0903.

4.4.3. (Trimethylsilyl)methyl N-2-diazoethanoyl-2-methylbenzimidothioate (**4d**)

Yield 32%. A yellow oil. IR (neat): ν=2956, 2105, 1644 cm^{-1}. ^1H NMR ($CDCl_3$): δ=0.14 (s, 9H), 2.25 (s, 2H), 2.37 (s, 3H), 4.79 (br s, 1H), 7.13–7.35 (m, 4H). ^{13}C NMR ($CDCl_3$): δ=−1.52, 17.13, 19.59, 51.19, 125.30, 126.58, 129.63, 130.31, 134.44, 136.28, 176.22. EIMS: *m*/*z*=277 (M^+-N_2). FABMS: *m*/*z*=306 (MH^+). HRMS (M^+-N_2): calcd for $C_{14}H_{19}NOSSi$: 277.0966; found: 277.0966.

4.4.4. (Trimethylsilyl)methyl N-2-diazoethanoyl-3-methylbenzimidothioate (**4e**)

Yield 70%. A brown oil. IR (neat): ν=2955, 2104, 1597 cm^{-1}. ^1H NMR ($CDCl_3$): δ=0.16 (s, 9H), 2.25 (s, 2H), 2.37 (s, 3H), 4.76 (s, 1H), 7.25–7.35 (m, 4H). ^{13}C NMR ($CDCl_3$): δ=−1.49, 17.46, 21.46, 51.11, 124.18, 127.49, 128.41, 131.83, 136.14, 138.39, 176.54. EIMS: *m*/*z*=277 (M^+-N_2). FABMS: *m*/*z*=306 (MH^+). HRMS (M^+-N_2): calcd for $C_{14}H_{19}NOSSi$: 277.0966; found: 277.0957.

4.4.5. (Trimethylsilyl)methyl N-2-diazoethanoyl-3,5-dimethylbenzimidothioate (**4f**)

Yield 60%. A yellow oil. IR (neat): ν=2955, 2104, 1591 cm^{-1}. ^1H NMR ($CDCl_3$): δ=0.15 (s, 9H), 2.24 (s, 2H), 2.33 (s, 3H×2), 4.76 (s, 1H), 7.08 (s, 1H), 7.13 (s, 2H). ^{13}C NMR ($CDCl_3$): δ=−1.46, 17.44, 21.39, 51.17, 124.64, 132.82, 136.12, 138.29, 176.69. EIMS: *m*/*z*=291 (M^+-N_2). FABMS: *m*/*z*=320 (MH^+). HRMS (M^+-N_2): calcd for $C_{15}H_{21}NOSSi$: 291.1113; found: 291.1114.

4.4.6. (Trimethylsilyl)methyl N-2-diazoethanoyl-3-methoxybenzimidothioate (**4g**)

Yield 39%. A yellow oil. IR (neat): ν=2956, 2105, 1622 cm^{-1}. ^1H NMR ($CDCl_3$): δ=0.13 (s, 9H), 2.24 (s, 2H), 3.81 (s, 3H), 4.78 (s, 1H), 6.95–7.02 (m, 1H), 7.05–7.13 (m, 2H), 7.30 (t, 1H, *J*=8.1 Hz). ^{13}C NMR ($CDCl_3$): δ=−1.38, 17.40, 51.07, 55.32, 112.31, 116.91, 119.32, 129.62, 137.28, 159.28, 176.53. EIMS: *m*/*z*=293 (M^+-N_2). FABMS: *m*/*z*=322 (MH^+). HRMS (M^+-N_2): calcd for $C_{14}H_{19}NO_2SSi$: 293.0906; found: 293.0898.

4.4.7. (Trimethylsilyl)methyl N-2-diazoethanoyl-3,5-dimethoxybenzimidothioate (**4h**)

Yield 65%. An orange oil. IR (neat): ν=2957, 2105, 1593 cm^{-1}. ^1H NMR ($CDCl_3$): δ=0.15 (s, 9H), 2.23 (s, 2H), 3.79 (s, 6H), 4.79 (s, 1H), 6.53 (s, 1H), 6.67 (s, 2H). ^{13}C NMR ($CDCl_3$): δ=−1.57, 17.28, 51.00, 55.42, 102.96, 105.00, 137.74, 160.44, 176.54. EIMS: *m*/*z*=323 (M^+-N_2). FABMS: *m*/*z*=352 (MH^+). HRMS (M^+-N_2): calcd for $C_{15}H_{21}NO_3SSi$: 323.1013; found: 323.1012.

4.4.8. S-Ylide (**6a**)

A mixture of **3a** (63 mg, 0.17 mmol) and $Rh_2(OAc)_4$ (3 mg, 0.007 mmol) in 1,2-dichloroethane was refluxed with stirring for 30 min. After cooling to rt, the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel using hexane/EtOAc (30:1) to give the title compound (48.5 mg, 83%) as a yellow oil. IR (neat): ν=2956 cm^{-1}. ^1H NMR ($CDCl_3$): δ=0.16 (s, 9H), 0.38 (s, 9H), 2.25 (s, 2H), 7.38–7.50 (m, 3H), 8.02–8.10 (m, 2H). ^{13}C NMR ($CDCl_3$): δ=−1.70, −1.01, 22.90, 126.38, 127.56, 128.51, 130.00, 143.04, 152.51, 163.37. EIMS: *m*/*z*=335 (M^+). HRMS (M^+): calcd for $C_{16}H_{25}NOSSi_2$: 335.1196; found: 335.1199.

4.5. Intramolecular Buchner reaction of diazoketones 4a–h: general procedure

A mixture of **4** (0.5 mmol) and $Rh_2(OAc)_4$ (3 mol %) in *o*-xylene (5 mL) was stirred at rt for 3 h. Then, the solvent was removed in vacuo, and the residue was purified by silica gel chromatography using hexane–EtOAc system to give the following products.

4.5.1. 3-[(Trimethylsilyl)methylthio]cyclohepta[c]pyrrol-1-ol (**5a**)

Yield 82%. Black amorphous. IR (Nujol): ν=1685, 1633 cm^{-1}. ^1H NMR ($CDCl_3$): δ=0.10 (s, 9H), 2.14 (s, 2H), 5.58 (dd, 1H, *J*=8.4, 11.1 Hz), 5.85 (dd, 1H, *J*=7.6, 11.1 Hz), 6.16 (dd, 1H, *J*=8.4, 11.3 Hz), 6.79 (d, 1H, *J*=11.3 Hz), 6.91 (d, 1H, *J*=7.6 Hz), 10.66 (br, 1H). ^{13}C NMR ($CDCl_3$): δ=−1.76, 20.62, 120.81, 121.96, 122.61, 126.27, 135.61, 135.75, 135.97, 140.48, 165.91. EIMS: *m*/*z*=263 (M^+). HRMS (M^+): calcd for $C_{13}H_{17}NOSSi$: 263.0800; found: 263.0805.

4.5.2. 6-Chloro-3-[(trimethylsilyl)methylthio]cyclohepta[c]pyrrol-1-ol (**5b**)

Yield 47%. A dark green solid. Mp 149–152 °C (EtOAc). IR (Nujol): ν=1683, 1634 cm^{-1}. ^1H NMR ($CDCl_3$): δ=0.13 (s, 9H), 2.07 (s, 2H), 5.64 (d, 1H, *J*=12.2 Hz), 6.08 (d, 1H, *J*=8.6 Hz), 6.65–6.70 (m, 2H), 8.51 (br, 1H). ^{13}C NMR ($CDCl_3$): δ=−1.76, 20.14, 119.41, 124.36, 124.57, 124.61, 131.94, 134.54, 135.01, 147.24, 166.05. EIMS: *m*/*z*=297 and 299 (M^+). HRMS (M^+): calcd for $C_{13}H_{16}ClNOSSi$: 297.0410; found: 297.0404.

4.5.3. 6-Methoxy-3-[(trimethylsilyl)methylthio]cyclohepta[c]pyrrol-1-ol (**5c**)

Yield 88%. A dark green solid. Mp 174–176 °C (EtOAc). IR (Nujol): ν=1674 cm^{-1}. ^1H NMR ($CDCl_3$): δ=0.12 (s, 9H), 2.08 (s, 2H), 3.71 (s, 3H), 5.75 (d, 1H, *J*=9.2 Hz), 5.65 (d, 1H, *J*=11.9 Hz), 7.00 (d, 1H, *J*=12.2 Hz), 7.14 (d, 1H, *J*=8.1 Hz), 8.59 (br, 1H). ^{13}C NMR ($CDCl_3$): δ=−1.71, 21.65, 55.62, 99.92, 120.06, 121.04, 121.42, 127.03, 135.01, 135.44, 165.72, 169.33. EIMS: *m*/*z*=293 (M^+). HRMS (M^+): calcd for $C_{14}H_{19}NO_2SSi$: 293.0906; found: 293.0903.

4.5.4. 4-Methyl-3-[(trimethylsilyl)methylthio]cyclohepta[c]pyrrol-1-ol (**5d**)

Yield 26%. Black amorphous. IR (Nujol): ν=2955, 1674, 1626 cm^{-1}. ^1H NMR ($CDCl_3$): δ=0.13 (s, 9H), 2.23 (s, 2H),

2.38 (s, 3H), 5.64 (d, 1H, J=8.6 Hz), 5.91 (dd, 1H, J=7.8, 10.8 Hz), 6.22 (t, 1H, J=10.3 Hz), 7.07 (d, 1H, J=7.6 Hz), 9.74 (br, 1H). ^{13}C NMR ($CDCl_3$): δ=−1.66, 22.69, 26.96, 120.61, 120.68, 124.54, 125.81, 134.77, 135.42, 139.96, 148.14, 165.61. EIMS: m/z=277 (M^+). HRMS (M^+): calcd for $C_{14}H_{19}NOSSi$: 277.0957; found: 277.0956.

*4.5.5. A mixture of 5-methyl-3-[(trimethylsilyl)methylthio]-cyclohepta[c]pyrrol-1-ol (**5e**) and 7-methyl-3-[(trimethylsilyl)methylthio]cyclohepta[c]pyrrol-1-ol*

Yield 54% (major/minor=ca. 2.5:1). Brown amorphous. IR (Nujol): ν=1681, 1634 cm^{-1}. ^{1}H NMR ($CDCl_3$): major: δ=0.13 (s, 9H), 1.91 (s, 3H), 2.09 (s, 2H), 5.89 (dd, 1H, J=7.8, 11.9 Hz), 6.05−6.14 (m, 1H), 6.67−6.75 (m, 1H), 6.90 (d, 1H, J=1.1 Hz), 9.32 (br, 1H). Minor: δ=0.12 (s, 3H), 1.96 (s, 3H), 2.08 (s, 2H), 5.60 (dd, 1H, J=8.4, 11.3 Hz), 6.05−6.14 (m, 1H), 6.67−6.75 (m, 1H), 6.88 (d, 1H, J=1.1 Hz), 9.32 (br, 1H). EIMS: m/z=277 (M^+). HRMS (M^+): calcd for $C_{14}H_{19}NOSSi$: 277.0957; found: 277.0955.

*4.5.6. 5,7-Dimethyl-3-[(trimethylsilyl)methylthio]cyclohepta-[c]pyrrol-1-ol (**5f**)*

Yield 12%. Black amorphous. IR (Nujol): ν=3221, 1715 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=0.12 (s, 9H), 1.91 (s, 3H), 1.98 (s, 3H), 2.09 (s, 2H), 6.03 (s, 1H), 6.64 (s, 1H), 6.90 (s, 1H), 9.45 (s, 1H). ^{13}C NMR ($CDCl_3$): δ=−1.70, 21.06, 26.08, 26.80, 118.25, 121.08, 129.45, 131.01, 134.46, 134.77, 137.05, 140.16, 165.73. EIMS: m/z=291 (M^+). HRMS (M^+): calcd for $C_{15}H_{21}NOSSi$: 291.1113; found: 291.1123.

*4.5.7. 7-Methoxy-1-[(trimethylsilyl)methylthio]isoquinolin-3-ol (**7g**)*

Yield 11%. A yellow oil. IR (neat): ν=2956, 1636 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=0.18 (s, 9H), 2.47 (s, 2H), 3.93 (s, 3H), 6.47 (s, 1H), 7.22 (dd, 1H, J=2.2, 8.9 Hz), 7.33 (d, 1H, J=2.2 Hz), 7.52 (d, 1H, J=8.9 Hz). ^{13}C NMR ($CDCl_3$): δ=−1.36, 15.19, 55.52, 96.24, 102.38, 123.74, 124.42, 127.47, 134.73, 155.95, 156.48, 157.57. EIMS: m/z=293 (M^+). HRMS (M^+): calcd for $C_{14}H_{19}NO_2SSi$: 293.0906; found: 293.0909.

*4.5.8. 5,7-Dimethoxy-1-[(trimethylsilyl)methylthio]-isoquinolin-3-ol (**7h**)*

Yield 44%. A yellow solid. Mp 103−106 °C (EtOAc). IR (Nujol): ν=1641 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ=0.19 (s, 9H), 2.46 (s, 2H), 3.83 (s, 3H×2), 6.56 (d, 1H, J=1.6 Hz), 6.89 (d, 1H, J=1.6 Hz), 6.98 (s, 1H). ^{13}C NMR ($CDCl_3$): δ=−1.46, 15.37, 55.49, 55.63, 92.43, 93.92, 101.40, 123.56, 128.60, 154.98, 156.22, 156.55, 156.91. EIMS: m/z=323 (M^+). HRMS (M^+): calcd for $C_{15}H_{21}NO_3SSi$: 323.1012; found: 323.1014.

Acknowledgements

This work was financially supported by a Grant-in-Aid for Scientific Research (KAKENHI). M.M. was financially supported by Pfizer Japan Inc.

References and notes

1. For reviews on TMSCHN2, see: (a) Hodnett, N. S. *Synlett* **2003**, 2095−2096; (b) Shioiri, T.; Aoyama, T. *Science of Synthesis*; Fleming, I., Ed.; Georg Thieme: Stuttgart, 2002; Vol. 4, p 569; (c) Shioiri, T.; Aoyama, T. *J. Synth. Org. Chem., Jpn.* **1996**, *54*, 918−928; (d) Shioiri, T.; Aoyama, T. *Advances in the Use of Synthons in Organic Chemistry*; Dondoni, A., Ed.; JAI: London, 1993; Vol. 1, p 51.
2. For our recent application of $TMSCHN_2$, see: (a) Hari, Y.; Kanie, T.; Aoyama, T. *Tetrahedron Lett.* **2006**, *47*, 1137−1139; (b) Hari, Y.; Kanie, T.; Miyagi, T.; Aoyama, T. *Synthesis* **2006**, 1249−1252; (c) Hari, Y.; Tsuchida, S.; Aoyama, T. *Tetrahedron Lett.* **2006**, *47*, 1977−1980; (d) Tsuchida, S.; Hari, Y.; Aoyama, T. *Heterocycles* **2005**, *65*, 2667−2674; (e) Miyagi, T.; Hari, Y.; Aoyama, T. *Tetrahedron Lett.* **2004**, *45*, 6303−6305.
3. (a) Hari, Y.; Iguchi, T.; Aoyama, T. *Synthesis* **2004**, 1359−1362; (b) Hari, Y.; Iguchi, T.; Aoyama, T. *Synthesis* **2005**, 2147−2150.
4. The synthesis of thiazolones from diazo compounds and thiobenzoyl isocyanate was reported. See: (a) Tsuge, O.; Shinaki, I.; Koga, M. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 3657−3660; (b) Goerdeler, J.; Schimpf, R. *Chem. Ber.* **1973**, *106*, 1496−1500.
5. Buchner, E. *Chem. Ber.* **1896**, *29*, 106−109.
6. (a) Goerdeler, J.; Weiss, R. *Chem. Ber.* **1967**, *100*, 1627−1632; (b) Weiss, R. *Chem. Ber.* **1967**, *100*, 685−689; (c) Tsuge, O.; Kanemasa, S.; Tashiro, M. *Tetrahedron* **1968**, *24*, 5205−5214.
7. The diazoketone **4a** seemed to be formed by protodesilylation of **3a** with water during the purification by silica gel column chromatography.
8. For a review on the *S*-ylide formation, see: Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263−309.
9. (a) Walter, W.; Meese, C. O. *Chem. Ber.* **1976**, *109*, 922−946; (b) Walter, W.; Meese, C. O. *Chem. Ber.* **1977**, *110*, 2463−2479.
10. (a) CuCl: Constantino, A.; Linstrumelle, G.; Julia, S. *Bull. Soc. Chim. Fr.* **1970**, 907−912; Scott, L. T.; Minton, M. A.; Kirms, M. A. *J. Am. Chem. Soc.* **1980**, *102*, 6311−6314; (b) $Cu(hfacac)_2$: Pusino, A.; Saba, A. *Tetrahedron* **1986**, *42*, 4319−4324; (c) $Cu(OTf)_2$: Yadav, J. S.; Reddy, B. V. S.; Gupta, M. K.; Prabhakar, A.; Jagadeesh, B. *Chem. Commun.* **2004**, 2124−2125.
11. The low yields were presumably due to decomposition of the resulting **5d** and **5f** during the purification by silica gel column chromatography because of their relative lability.
12. (a) Marguire, A. R.; O'Leary, P.; Harrington, F.; Lawrence, S. E.; Blake, A. J. *J. Org. Chem.* **2001**, *66*, 7166−7177; (b) Kennedy, M.; Mckervey, M. A.; Maguire, A. R.; Tuladhar, S. M.; Twohig, M. F. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1047−1054.
13. Many researches about drug discovery of azaazulenes were reported. For example: (a) 1-Azaazulenes:*Chem. Pharm. Bull.* **1994**, *42*, 2491−2499; (b) 1,3-Diaazaazulenes: Satake, N.; Zhou, Q.; Kosakai, K.; Nimura, M.; Shibata, S. *Eur. J. Pharmacol.* **1994**, *251*, 1−7; (c) 1,2-Diazaazulenes: Imafuku, K.; Aradono, K.; Uono, T.; Ogawa, K.; Matsushita, Y. *Chem. Pharm. Bull.* **1992**, *40*, 1606−1609.
14. Many studies about synthesis of biologically active azulenes were reported. For example: (a) Fujio, K.; Kobayashi, H.; Ozeki, S.; Fujimori, K. *Chem. Lett.* **2006**, *35*, 1272−1273; (b) Rekka, E.; Chrysselis, M.; Siskou, I.; Kourounakis, A. *Chem. Pharm. Bull.* **2002**, *50*, 904−907; (c) Noguchi, K.; Kase, J.; Saitoh, M.; Masumiya, H.; Saitoh, M.; Nakazawa, T.; Tanaka, Y.; Tanaka, H.; Hashimoto, K.; Shigenobu, K. *Pharmacology* **2002**, *64*, 36−42; (d) Hong, B.-C.; Jiang, Y.-F.; Kumar, E. S. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1981−1984; (e) Yokota, M.; Uchibori, S.; Hayashi, H.; Koyama, R.; Kosakai, K.; Wakabayashi, S.; Tomiyama, T. *Bioorg. Med. Chem.* **1996**, *4*, 575−591; (f) Asato, A. E.; Peng, A.; Hossain, M. Z.; Mirzadegan, T.; Bertram, J. S. *J. Med. Chem.* **1993**, *36*, 3137−3147; (g) Tomiyama, T.; Yokota, M.; Wakabayashi, S.; Kosakai, K.; Yanagisawa, T. *J. Med. Chem.* **1993**, *36*, 791−800.
15. (a) Kreher, R.; Vogt, G.; Schultz, M. L. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 821; (b) Jones, R. A.; Singh, S. *Heterocycles* **1976**, *4*, 969−972; (c) Seitz, G.; The, H. S. *Synthesis* **1984**, 119−121.
16. Goerdeler, J.; Schenk, H. *Chem. Ber.* **1965**, *98*, 2954−2965.
17. Kehrbach, W.; Mlinaric, M.; Ziegler, D.; Brueckner, R.; Bielenberg, W. U.S. Patent 5,547,967, 1996.