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CYCLOADDITION REACTIONS OF TRIMETHYLSILYL-KETENE WITH 8-AZAHEPTAFULVENES AND 6-AMINO-1-AZAFULVENES†

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Abstract- Trimethylsilylketene smoothly reacts with 8-azaheptafulvenes to give 3,3a-dihydro-3-trimethylsilyl-1-azaazulen-2(1*H*)-ones, the [8+2] cycloadducts, in excellent yields. Furthermore, trimethylsilylketene also undergoes the [6+2] cycloaddition reaction with 6-amino-1-azafulvenes to afford 1*H*-pyrrolizin-3(2*H*)-ones.

Heterocumulenes have been reported to react with 8-azaheptafulvenes[1] and 6-amino-1-azafulvenes[2] to give the corresponding [8+2]- and [6+2] cycloadducts, respectively. For example, ketenes such as phenylketene, diphenylketene, and chloroketene react with 8-azaheptafulvenes to give 3,3a-dihydro-1-azaazulen-2(1*H*)-ones.[1a,e] Reaction of ketenes with 6-amino-1-azafulvenes also proceeds to afford 2,3-dihydro-1*H*-pyrrolizin-3-ones.[2b] To our knowledge, however, there is no report dealing with reaction of silylketenes, an electron-rich ketene, with azafulvene derivatives.

We have already revealed that silylketenes can be effectively used as heterodienophiles for the [4+2] cycloaddition reaction with electron-rich 1,3-dienes or *o*-quinodimethanes[3] and as dienophiles for the [4+2] cycloaddition reaction with acyl isocyanates.[4] Our continued interest in the reactivities of silylketenes[5] has led us to investigate the reaction of trimethylsilylketene (TMSCH=C=O) with 8-azaheptafulvenes and 6-amino-1-azafulvenes.

We have found that TMSCH=C=O smoothly reacts with 8-(*p*-methylphenyl)-8-azaheptafulvene (**1a**) in refluxing chloroform to give 3,3a-dihydro-3-trimethylsilyl-1-azaazulen-2(1*H*)-one (**2a**), the [8+2] cycloadduct, in high yield together with a small amount of the desilylated product (**3a**), as shown in Table (Run 1). The stereochemistry of C-3 and C-3a positions of **2a** was determined to be *trans* by Noe experiments and coupling constants (J = 4 Hz)[1a] between C-3 and C-3a protons on its ^{1}H NMR spectra. Under similar reaction conditions, 8-(*p*-bromophenyl)- (**1b**) and 8-(*p*-methoxyphenyl)-8-azaheptafulvene (**1c**) also gave the corresponding 1-azaazulen-2(1*H*)-ones (**2b,c**) in excellent yields, respectively (Runs 4,5). Both benzene and ethyl acetate can be used as a reaction solvent (Runs 2,3). In contrast to the results with 8-azaheptafulvenes, the reaction of TMSCH=C=O with tropones was completely inactive.[6]

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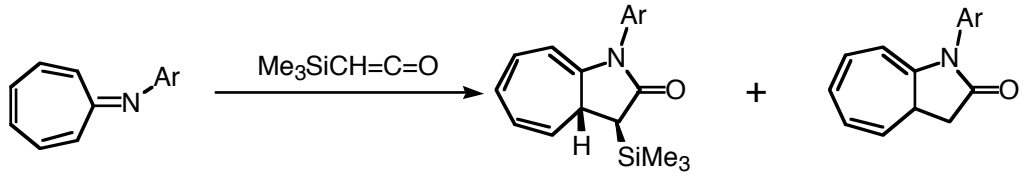
†Dedicated to Prof. Shô Itô on the occasion of his 77th birthday.

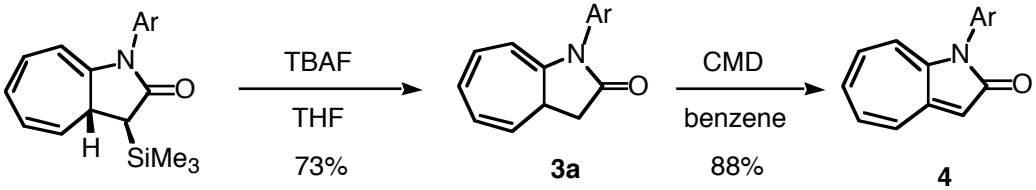
Table. Reaction of Trimethylsilylketene with 8-Azaheptafulvenes (**1**)



1 **2** **3**

Run	Ar	Solvent	Yield(%) **2**	**3**
1	*p*-MeC_6H_4 (**a**)	$CHCl_3$	86	10
2	*p*-MeC_6H_4 (**a**)	benzene	86	6
3	*p*-MeC_6H_4 (**a**)	AcOEt	85	8
4	*p*-BrC_6H_4 (**b**)	$CHCl_3$	85	5
5	*p*-$MeOC_6H_4$ (**c**)	$CHCl_3$	72	7

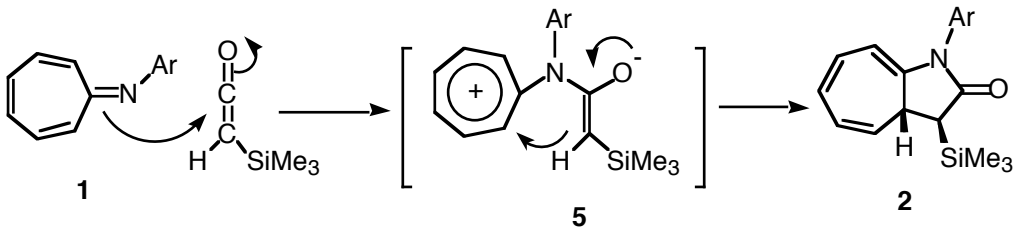
The trimethylsilyl group of **2a** was easily removed by treatment with tetrabutylammonium fluoride (TBAF) to give the compound (**3a**) which was dehydrogenated with chemical manganese dioxide (CMD)[7] to afford 1-(*p*-methylphenyl)-1-azaazulen-2(1*H*)-one (**4**), as shown in Scheme 1.



2a Ar = *p*-MeC_6H_4

Scheme 1

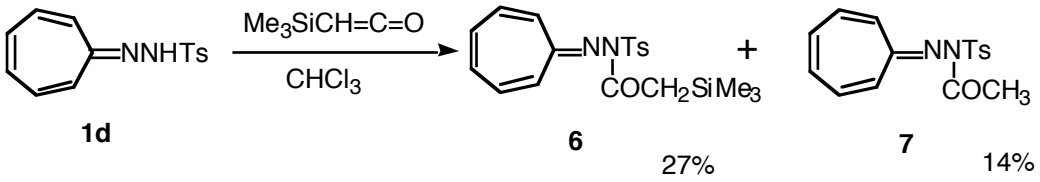
The mechanism of the formation of **2** may be as shown in Scheme 2. In analogy with the reaction of ketenes with **1**,[1e] nucleophilic attack of the nitrogen atom of **1** to the central carbon of TMSCH=C=O gives the betaine intermediate (**5**) which cyclizes to give the [8+2] cycloadduct (**2**).



1

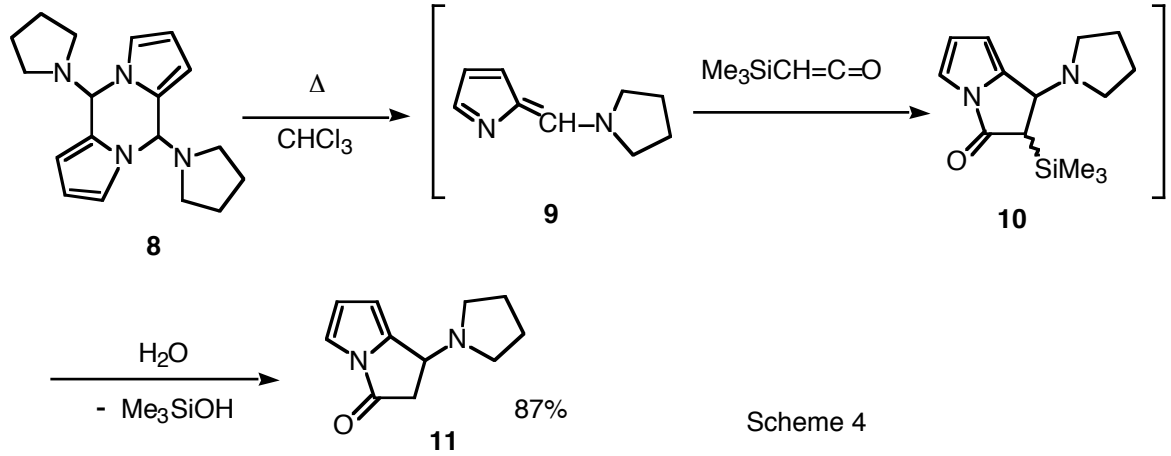
Scheme 2

Tropone tosylhydrazone (**1d**) has also been reported to undergo [8+2] cycloaddition reaction with ketenes,[1e,8] but the reaction with TMSCH=C=O afforded a mixture of *N*-trimethylsilylacetylhydrazone (**6**) and its desilylated product (**7**), and no cycloadduct was obtained (Scheme 3).



Scheme 3

Next, the reaction of TMSCH=C=O with 6-amino-1-azafulvenes was investigated. TMSCH=C=O also reacted with 6-pyrrolidino-1-azafulvene (**9**) generated by thermal decomposition of dipyrrolo[1,2-a:1',2'-d]pyrazine (**8**) to give 1-pyrrolidino-1*H*-pyrrolizin-3(2*H*)-one (**11**) in excellent yield which was formed by desilylation of the first produced [6+2] cycloadduct (**10**) with water (Scheme 4). Although the reaction of ketenes with 1-azafulvenes giving 1*H*-pyrrolizin-3(2*H*)-ones has been reported, the yields are low to moderate.[2b]



Scheme 4

In conclusion, trimethylsilylketene (TMSCH=C=O) smoothly reacts with 8-azaheptafulvenes and 6-amino-1-azafulvenes to give the corresponding 3,3a-dihydro-1-azaazulen-2(1*H*)-one and 2,3-dihydro-1*H*-pyrrolizin-3-ones in excellent yields, respectively. The synthetic reactions developed here will open a new possibility for the use of trimethylsilylketene as a building block for heterocycles.

EXPERIMENTAL

General : Melting points were determined on a YAMATO MP-21 apparatus and a YAMATO micro melting point apparatus (hot plate). All melting points were uncorrected. IR spectra were measured on a SHIMADZU FTIR-8100 spectrophotometer. NMR spectra were measured on a JEOL EX-270 spectrometer referred to tetramethylsilane (TMS) or $CHCl_3$ as an internal standard in $CDCl_3$. MS spectra

were obtained on a JEOL JMS-SX 102A spectrometer. Flash column chromatography was performed on silica gel (Silica Gel 60 particle size 40-63 μm, MERCK).

Preparation of 1-azaazulen-2(1*H*)-ones (2 and 3)

General procedure : A mixture of **1**[9] (0.5 mmol) and TMSCH=C=O in $CHCl_3$ (5 mL) was stirred at reflux for 12 h under argon. After concentration *in vacuo,* the residue was purified by flash column chromatography on silica gel to give **2** and **3**.

3,3a-Dihydro-1-(*p*-methylphenyl)-3-trimethylsilyl-1-azaazulen-2(1*H*)-one (2a) and 3,3a-dihydro-1-(*p*-methylphenyl)-1-azaazulen-2(1*H*)-one (3a)

Prepared from **1a** (98 mg, 0.5 mmol) and TMSCH=C=O (77 mg, 0.68 mmol). Pale yellow crystals **2a** (133 mg, 86%) and pale yellow crystals **3a** (12 mg, 10%), purified by flash column chromatography on silica gel (hexane : AcOEt = 5:1 to 3:1).

Compound (2a) : mp 128-130℃ (hexane). IR ν_{max}^{nujol} cm^{-1}: 1705, 1634, 1250, 860, 843. ^1H NMR ($CDCl_3$) δ : 0.20 (9H, s), 2.37 (3H, s), 2.39 (1H, d, J = 3.96 Hz), 2.77-2.79 (1H, m), 5.09 (1H, dd, J = 3.96, 9.23 Hz), 5.34 (1H, d, J = 5.94 Hz), 6.12-6.26 (2H, m), 6.39-6.45 (1H, m), 7.08 (2H, d, J = 8.25 Hz), 7.24 (2H, d, J = 8.25 Hz). *Anal.* Calcd for $C_{19}H_{23}NOSi$: C ; 73.74, H ; 7.49, N ; 4.53. Found : C ; 73.58, H ; 7.48, N ; 4.42.

Compound (3a) : mp 134-136℃ . IR ν_{max}^{nujol} cm^{-1}: 1723, 1632, 1516, 1370, 1252. ^1H NMR ($CDCl_3$) δ : 2.38 (1H, s), 2.77 (1H, dd, J = 4.29, 17.82 Hz), 3.00-3.04 (1H, m), 3.23 (1H, dd, J = 10.55, 17.82 Hz), 5.18 (1H, dd, J = 3.63, 8.91 Hz), 5.35 (1H, d, J = 5.61 Hz), 6.15-6.27 (2H, m), 6.35-6.42 (1H, m), 7.13 (2H, d, J = 8.25 Hz), 7.27 (2H, d, J = 8.25 Hz). *Anal.* Calcd for $C_{16}H_{15}NO$: C ; 80.98, H ; 6.37, N ; 5.93. Found : C ; 81.21, H ; 6.43, N ; 5.93.

3,3a-Dihydro-1-(*p*-bromophenyl)-3-trimethylsilyl-1-azaazulen-2(1*H*)-one (2b) and 3,3a-dihydro-1-(*p*-bromophenyl)-1-azaazulen-2(1*H*)-one (3b)

Prepared from **1b** (130 mg, 0.5 mmol) and TMSCH=C=O (83 mg, 0.73 mmol). Orange crystals **2b** (158 mg, 85%) and orange crystals **3b** (8 mg, 5%), purified by flash column chromatography on silica gel (hexane : AcOEt = 5:1 to 3:1).

Compound (2b) : mp 118 - 120℃ (hexane). IR ν_{max}^{nujol} cm^{-1}: 1705, 1628, 1611, 1538, 1250, 843. ^1H NMR ($CDCl_3$) δ : 0.20 (9H, s), 2.40 (1H, d, J = 3.96 Hz), 2.75-2.78 (1H, m), 5.09 (1H, dd, J = 3.96, 9.24 Hz), 5.39 (1H, d, J = 5.61 Hz), 6.13-6.18 (1H, m), 6.23-6.29 (1H, m), 6.40-6.46 (1H, m), 7.11 (2H, d, J = 8.58 Hz), 7.57 (2H, d, J = 8.58 Hz). *Anal.* Calcd for $C_{18}H_{20}NOBrSi$: C ; 53.75, H ; 5.38, N ; 3.74. Found : C ; 53.73, H ; 5.46, N ; 3.48.

Compound (3b) : mp 137 - 140℃ . IR ν_{max}^{nujol} cm^{-1}: 1717, 1634, 1487, 1252, 1067. ^1H NMR ($CDCl_3$) δ : 2.78 (1H, dd, J = 4.63, 18.16 Hz), 2.99-3.03 (1H, m), 3.23 (1H, dd, J = 10.89, 18.16 Hz), 5.18 (1H, dd, J = 3.96, 9.24 Hz), 5.38 (1H, d, J = 6.27 Hz), 6.17-6.27 (2H, m), 6.29-6.44 (1H, m), 7.16 (2H, d, J = 8.58 Hz), 7.60 (2H, d, J = 8.58 Hz). HRMS Calcd for $C_{15}H_{12}NO^{79}Br$: 301.0103. Found : 301.0080. HRMS Calcd for $C_{15}H_{12}NO^{81}Br$: 303.0083. Found : 303.0082.

3,3a-Dihydro-1-(*p*-methoxyphenyl)-3-trimethylsilyl-1-azaazulen-2(1*H*)-one (2c) and 3,3a-dihydro-1-(*p*-methoxyphenyl)-1-azaazulen-2(1*H*)-one (3c)

Prepared from crude **1c** (87 mg, 0.41 mmol) and TMSCH=C=O (70 mg, 0.61 mmol). A pale yellow oil **2c** (96 mg, 72%) and pale orange crystals **3c** (7 mg, 7%), purified by flash column chromatography on silica gel (hexane : AcOEt = 5:1 to 3:1).

Compound (2c) : IR ν_{max}^{neat} cm^{-1}:1713, 1632, 1514, 1248, 848. ^1H NMR ($CDCl_3$) δ : 0.20 (9H, s), 2.39 (1H, d, J = 3.96 Hz), 2.77-2.79 (1H, m), 3.82 (3H, s), 5.09 (1H, dd, J = 3.96, 9.24 Hz), 5.31 (1H, d, J = 6.59 Hz), 6.11-6.26 (2H, m), 6.39-6.45 (1H, m), 6.96 (2H, d, J = 8.91 Hz), 7.12 (2H, d, J = 8.91 Hz). HRMS Calcd for $C_{19}H_{23}NO_2Si$: 325.1499. Found : 325.1498.

Compound (3c) : IR ν_{max}^{nujol} cm^{-1}: 1717, 1636, 1538, 1250, 1034. ^1H NMR ($CDCl_3$) δ : 2.77 (1H, dd, J = 4.29, 18.15 Hz), 3.01-3.05 (1H, m), 3.22 (1H, dd, J = 10.55, 17.81 Hz), 3.83 (3H, s), 5.17 (1H, dd, J = 3.63, 8.90 Hz), 5.34 (1H, d, J = 5.61 Hz), 6.15-6.27 (2H, m), 6.36-6.42 (1H, m), 6.98 (2H, d, J = 8.91 Hz), 7.17 (2H, d, J = 8.91 Hz). HRMS Calcd for $C_{16}H_{15}NO_2$: 253.1104. Found : 253.1103.

3,3a-Dihydro-1-(*p*-methylphenyl)-1-azaazulen-2(1*H*)-one (3a)

The azaazulene (**2a**) (91 mg, 0.29 mmol) was dissolved in THF (1 mL) and tetrabutylammonium fluoride (184 mg, 0.58 mmol) was added. After being stirred at rt for 30 min, the mixture diluted with ether (50 mL) was washed with saturated brine (30 mL×3), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane : AcOEt = 4 : 1) to give **3a** (50 mg, 73%) as pale yellow crystals, which was identified by spectroscopic comparison with the authentic sample.

1-(*p*-Methylphenyl)-1-azaazulene-2(1*H*)-one (4)

A mixture of **3a** (71 mg, 0.3 mmol) and CMD (261 mg, 3 mmol) in benzene (3 mL) was stirred at rt for 12 h. The insoluble materials were filtered through the pad of celite, and washed with AcOEt. The combined organic solvent was concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane : AcOEt = 1 : 2) to give **4** (62 mg, 88%) as red crystals, mp 117-119℃ (AcOEt) (lit.,[1e] 116-117℃). IR ν_{max}^{nujol} cm^{-1}: 1682, 1588, 1532, 1514, 1483, 1256, 1205. ^1H NMR ($CDCl_3$) δ : 2.44 (3H, s), 6.17 (1H, s), 6.74 (1H, d, J = 9.11 Hz), 6.81-7.06 (3H, m), 7.23 (2H, d, J = 8.24 Hz), 7.36 (2H, d, J = 8.24 Hz), 7.43 (1H, d, J = 11.21 Hz). *Anal.* Calcd for $C_{16}H_{13}NO$: C ; 81.68, H ; 5.57, N ; 5.95. Found : C ; 81.56, H ; 5.61, N ; 5.75.

Tropone *N*-trimethylsilylacetyl-*p*-tosylhydrazone (6) and tropone *N*-acetyl-*p*-tosylhydrazone (7)

A mixture of **1d**[10](137 mg, 0.5 mmol) and TMSCH=C=O (79 mg, 0.69 mmol) in $CHCl_3$ (3 mL) was stirred at reflux for 12 h under argon. After concentration *in vacuo*, the residue was purified by flash column chromatography on silica gel (hexane : AcOEt = 3:1 to 2:1 to 1:1) to give **6** as a pale yellow oil (53 mg, 27%) and **7** as pale yellow crystals (22 mg, 14%).

Compound (6) : IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1680, 1639, 1360, 1252, 1169, 1086, 854. ^1H NMR ($CDCl_3$) δ : -0.04 (9H, s), 2.04 (2H, s), 2.41 (3H, s), 6.62-6.84 (5H, m), 7.00-7.05 (1H, m), 7.29 (2H, d, J = 8.24 Hz), 7.91 (2H, d, J = 8.24 Hz). HRMS Calcd for $C_{18}H_{21}N_2O_3SSi$: 373.1042. Found : 373.1044.

Compound (7) : mp 147-149℃ (AcOEt-hexane). IR ν_{max}^{nujol} cm^{-1}: 1690, 1640, 1223, 1088, 1001. ^1H NMR ($CDCl_3$) δ : 2.07 (3H, s), 2.43 (3H, s), 6.66-6.88 (4H, m), 7.05-7.10 (1H, m), 7.23-7.29 (1H, m), 7.32 (2H, d, J = 8.58 Hz), 7.93 (2H, d, J = 8.58 Hz). HRMS Calcd for $C_{16}H_{16}N_2O_3S$: 316.0883. Found : 316.0883.

1-Pyrrolidino-1*H*-pyrrolizin-3(2*H*)-one (11).

A mixture of dipyrrolo[1,2-a: 1', 2'-d]pyrazine (**8**)[2a] (74 mg, 0.25 mmol) and TMSCH=C=O (85 mg, 0.74 mmol) in $CHCl_3$ (5 mL) was stirred at reflux for 4 h. After concentration *in vacuo,* the residue was purified by flash column chromatography on silica gel (AcOEt) to give **11** (83 mg, 87%) as an orange oil. IR ν_{max}^{neat} cm^{-1}: 1759, 1624, 1566, 1464, 1397, 1294, 1277, 1088. ^1H NMR ($CDCl_3$): 1.79-1.93 (4H, m), 2.55-2.59 (2H, m), 2.70-2.73 (2H, m), 2.99 (1H, dd, J = 2.97, 18.47 Hz), 3.21 (1H, dd, J = 7.26, 18.48 Hz), 4.20 (1H, dd, J = 2.97, 7.26 Hz), 6.14 (1H, d, J = 3.3 Hz), 6.47-6.57 (1H, m), 7.05 (1H, d, J = 2.31 Hz). *Anal.* Calcd for $C_{11}H_{14}N_2O$: C ; 69.45, H ; 7.42, N ; 14.72. Found: C; 69.32, H; 7.60, N; 14.48.

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