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SYNTHESIS OF 1-AZAAZULENES USING RING-OPENING CYCLIZATION OF SPIROCYCLOPROPANE WITH AMINE

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Dedicated to Professor Yasuyuki Kita on the occasion of his 77th birthday

Abstract – Synthesis of 1-azaazulenes using ring-opening cyclization of spirocyclopropane with a primary amine was accomplished. The reaction of cycloheptane-1,3-dione-2-spirocyclopropane with 2,4-dimethoxybenzylamine in refluxing acetonitrile resulted in a 94% yield of 1,2,3,6,7,8-hexahydrocyclohepta[*b*]pyrrol-4(5*H*)-one. The obtained product was successfully converted into 1-azaazulenes by deprotecting the amino-protecting group followed by oxidation.

Azaazulenes, aza-analogues of azulene, have intriguing physical and chemical properties and potential biological activities.¹ Of the many azaazulenes, 1-azaazulenes have attracted considerable attention from chemists because of their stabilities and pharmacological activities.²⁻⁴ While many examples of 1-azaazulene syntheses have been reported,⁵⁻¹¹ in most cases, troponoid compounds were used as starting materials. For example, Nitta and co-workers successfully synthesized various 1-azaazulene derivatives **3** from tropones **1** using the aza-Wittig reaction followed by the oxidation of the bicyclic intermediates **2** (Scheme 1, A).⁸ Narasaka and co-workers reported the synthesis of 1-azaazulenes **3** from cycloheptatrienylmethyl ketone *O*-pentafluorobenzoyloximes **4** by palladium(0)-catalyzed cyclization and sequential oxidation (Scheme 1, A).⁹ Although these synthetic methods are direct and efficient, tropone derivatives are expensive and difficult to prepare.

Meanwhile, we have developed a synthetic method of indole employing the ring-opening cyclization of cyclohexane-1,3-dione-2-spirocyclopropanes **5** with primary amines **6** to provide 2,3,6,7-tetrahydro-1*H*-indol-4(5*H*)-ones **7** followed by its oxidation into indole **8** (Scheme 1, B).¹² Based on this approach, we envision that the use of cycloheptane-1,3-dione-derived spirocyclopropane instead of a cyclohexane-1,3-dione derivative can construct a 1-azaazulene skeleton. Herein, we report the synthesis

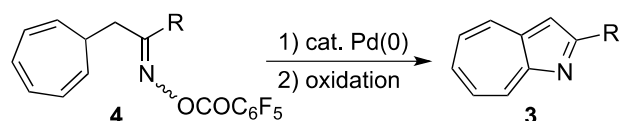
of 1-azaazulenes **3** from a non-troponone starting material using a ring-opening cyclization of cycloheptane-1,3-dione-2-spirocyclopropane **9** with amine **6** followed by the oxidation of the bicyclic intermediate **10** (Scheme 1, C).

A. Syntheses of 1-azaazulenes from troponoid substrates:

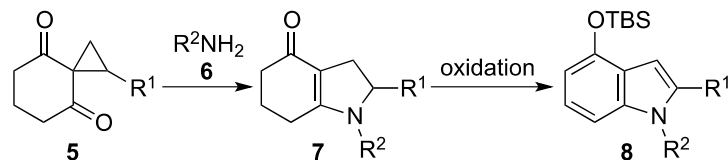
- Aza-Wittig reaction of tropones **1**



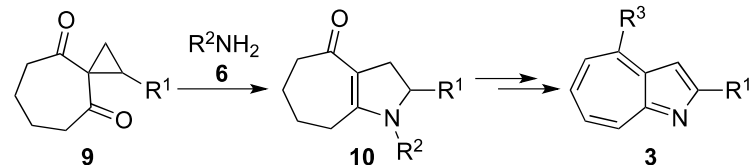
- Pd(0)-catalyzed amino-Heck cyclization of oximes **4**



B. Our previous work: Synthesis of indoles **8** using ring-opening cyclization of spirocyclopropanes **5** with amine **6** followed by oxidation



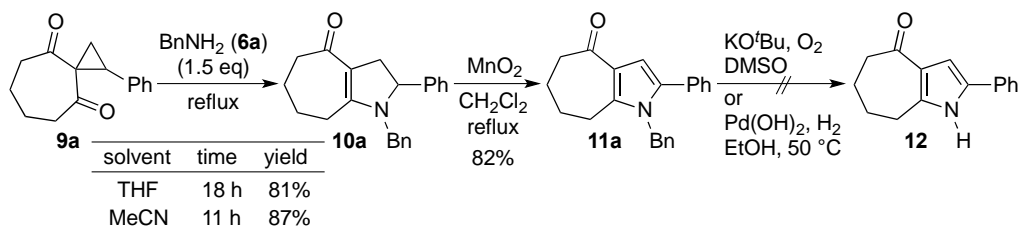
C. This work: Synthesis of 1-azaazulenes **3** using ring-opening cyclization of spirocyclopropanes **9** with amine **6** followed by oxidation



Scheme 1. A: Syntheses of 1-azaazulenes; B: Our previous work; C: Our approach to 1-azaazulenes

Since 2-aryl-1-azaazulene derivatives exhibit interesting biological activities,⁴ 2-phenyl-1-azaazulene was selected as a synthetic target. Furthermore, the use of ammonia as an amine is the most direct method by which to synthesize 1-azaazulene possessing no substituent on the nitrogen atom. However, ammonia was not suitable for the ring-opening cyclization of spirocyclopropane **5** and the reaction yielded low amounts of the corresponding product **7** (Scheme 1, B).^{12a} In the synthesis of unprotected indole, the benzyl group (R² = Bn, Scheme 1, B) worked well as both an effective amino substituent for the ring-opening cyclization of **5** and a stable and easily deprotectable substituent on the nitrogen atom.^{12b} As such, the reaction of 2-phenylspiro[2.6]nonane-4,9-dione (**9a**)¹³ with benzylamine (**6a**) was initially examined under our reported conditions (Scheme 2).^{12a} When the mixture of spirocyclopropane **9a** and 1.5 equivalents (eq) of **6a** in tetrahydrofuran (THF) was stirred at room temperature for several hours, the reaction did not occur. However, the reaction under refluxing conditions was completed within 18 h, affording 1-benzyl-2-phenyl-1,2,3,6,7,8-hexahydrocyclohepta[*b*]pyrrol-4(5*H*)-one (**10a**) in 81% yield.

The use of acetonitrile as a solvent increased the product yield of **10a** to 87%. After the oxidation of **10a** into *N*-benzylpyrrole **11a** with manganese(IV) oxide, we attempted to remove the benzyl-protecting group. Unfortunately, oxidative deprotection with potassium *tert*-butoxide/dimethyl sulfoxide (DMSO) and oxygen did not proceed.¹⁴ Furthermore, hydrogenolysis of **11a** with Pearlman's catalyst (Pd(OH)₂/C) in ethanol was unsuccessful.¹⁵ Therefore, it is necessary to use a protecting group that can be removed more easily than the benzyl one.



Scheme 2. Attempt to synthesize *N*-unprotected product **12**

Next, we examined the ring-opening cyclization of spirocyclopropane **9a** with amines **6** possessing an easily deprotectable group (Table 1). The reaction of **9a** with *p*-methoxybenzylamine (PMBNH₂) (**6b**) in refluxing acetonitrile was completed in 12 h, providing a 91% yield of the corresponding product **10b** (entry 1). The use of 2,4-dimethoxybenzylamine (2,4-DMBNH₂) (**6c**) afforded the corresponding product **10c** in 94% yield (entry 2). Since amino (NH₂) and methoxy (OMe) groups can sometimes be used as a removable amino substituent, the reactions using phenylhydrazine (**6d**) and methoxyamine (**6e**) were investigated. When **6d** was used, instead of the corresponding cyclization product, hydrazone **13** was obtained in 42% yield (entry 3). In the reaction with **6e**, the corresponding cyclization product could not be detected (entry 4). To be certain, we examined the use of ammonia (**6f**) in 1,4-dioxane solution (entry 5), but the reaction with 10 eq of **6f** at room temperature did not proceed even after 48 h.

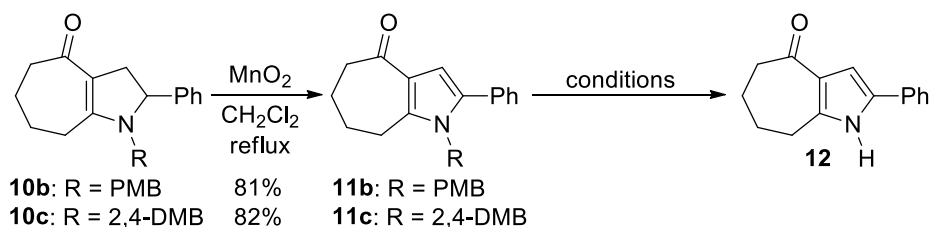
Table 1. Ring opening cyclization of spirocyclopropane **9a** with various amines **6**

entry	RNH ₂ 6	time (h)	product	yield (%)
1	PMBNH ₂ (6b)	12	10b	91
2	2,4-DMBNH ₂ (6c)	12	10c	94
3	PhNHNH ₂ (6d)	10	13	42
4	NH ₂ OMe (6e)	12	not detected	
5	NH ₃ (6f)/1,4-dioxane ^a	48	no reaction	

^a 10 eq of NH₃ was used in 1,4-dioxane at room temperature.

With PMB- and 2,4-DMB-protected products **10b** and **10c** (respectively) in hand, we investigated the removal of amino-protecting groups in **11b** and **11c**, which were prepared by oxidizing **10b** and **10c** with manganese(IV) oxide in refluxing dichloromethane (Table 2). The reaction of PMB-protected pyrrole **11b** with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) produced several unidentifiable products (entry 1). The acid-promoted deprotection of **11b** in refluxing trifluoroacetic acid (TFA) did not occur (entry 2).¹⁶ The reaction of 2,4-DMB-protected pyrrole **11c** with DDQ also did not provide the desired product **12** (entry 3). However, we found that the reaction of **11c** in refluxing TFA for 1 h afforded a less than 85% yield of the deprotected product **12** containing a small amount of inseparable impurity (entry 4). Moreover, the addition of anisole, which can trap cationic intermediates,¹⁷ in the reaction mixture produced an 87% yield of **12** in its pure form (entry 5).

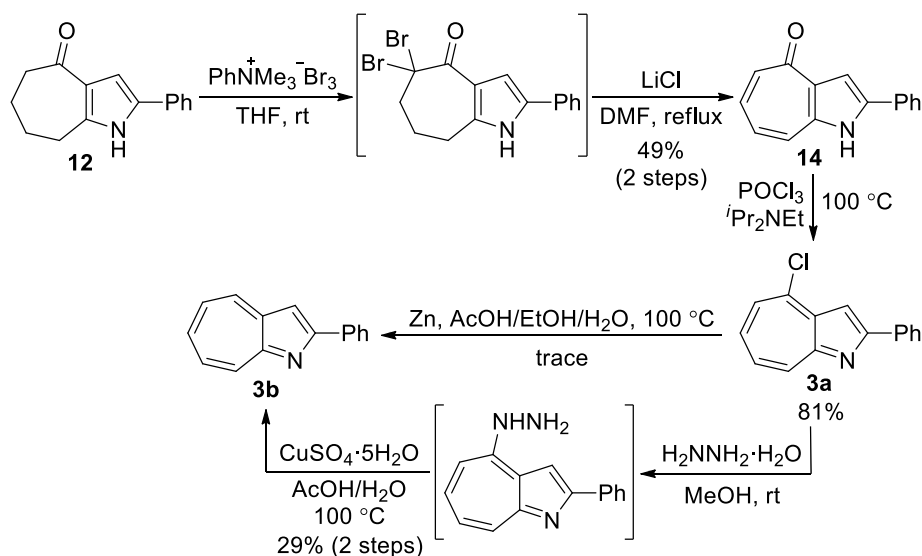
Table 2. Removal of *N*-protecting group in **11** prepared from **10**



entry	11	conditions	time (h)	yield of 12
1	11b	DDQ, CH ₂ Cl ₂ /H ₂ O, rt	24	not detected
2	11b	TFA, reflux	24	no reaction
3	11c	DDQ, CH ₂ Cl ₂ /H ₂ O, rt	24	not detected
4	11c	TFA, reflux	1	<85% ^a
5	11c	anisole, TFA, reflux	5	87%

^a A small amount of inseparable impurity was contained in the obtained product **12**.

Finally, the conversion of the bicyclic unprotected pyrrole **12** into 1-azaazulene derivatives **3a** and **3b** was investigated (Scheme 3). After several attempts, we found that two step-conversion from **12** was suitable for the formation of 1-azaazulene. Bromination of **12** with trimethylphenylammonium tribromide in THF afforded α -dibrominated cycloheptanone, which was subsequently converted into a 49% yield of 2-phenylpyrrolo[2,3-*b*]tropone (**14**) using lithium chloride in refluxing *N,N*-dimethylformamide (DMF).¹⁸ The reaction of the bicyclic tropone **14** with phosphoryl chloride and *N,N*-diisopropylethylamine resulted in an 81% yield of 4-chloro-2-phenyl-1-azaazulene (**3a**) as a red solid.¹⁹ Furthermore, we examined the synthesis of 2-phenyl-1-azaazulene (**3b**) from **3a**. The dechlorination of **3a** with zinc in acetic acid at 100 °C only produced a trace amount of the desired product **3b**. Eventually, we found that, by transforming **3a** into the corresponding hydrazine and then treating the resulting product with copper(II) sulfate pentahydrate in aqueous acetic acid,¹⁹ red-colored **3b**^{6,8b,9b} was obtained in 29% yield from **3a**.



Scheme 3. Conversion of **12** into 1-azaazulene derivatives **3a** and **3b**

In conclusion, we achieved the synthesis of 1-azaazulenes from a non-tropone starting material using the ring-opening cyclization of spirocyclopropane with amine. The reaction of cycloheptane-1,3-dione-2-spirocyclopropane with 2,4-dimethoxybenzylamine afforded 1,2,3,6,7,8-hexahydrocyclohepta[*b*]pyrrol-4(5*H*)-one in high yield. We converted the obtained product into 1-azaazulenes by deprotecting the amino-protecting group followed by oxidation. Currently, we are in the progress of synthesizing a variety of 1-azaazulene derivatives using the present protocol.

EXPERIMENTAL

General. Melting points are uncorrected. IR spectra were recorded on a JASCO FT/IR-460 Plus spectrophotometer and absorbance bands are reported in wavenumber (cm^{-1}). ^1H NMR spectra were recorded on JEOL JNM-ECX400P (400 MHz) and JEOL JNM-ECA500II (500 MHz) spectrometers. Chemical shifts are reported relative to internal standard (tetramethylsilane at δ_{H} 0.00, CDCl_3 at δ_{H} 7.26, or CD_3OD at δ_{H} 3.31). Data are presented as follows: chemical shift (δ , ppm), multiplicity (s = singlet, d = doublet, t = triplet, quint = quintet, m = multiplet, br = broad), coupling constant and integration. ^{13}C NMR spectra were recorded on JEOL JNM-ECX400P (100 MHz) spectrometer. The following internal reference was used (CDCl_3 at δ_{C} 77.0 or CD_3OD at δ_{C} 49.0). All ^{13}C NMR spectra were determined with complete proton decoupling. High-resolution mass spectra (HRMS) were determined with Thermo Scientific LTQ Orbitrap XL ETD [electrospray ionization (ESI)]. Column chromatography was performed on Kanto silica gel 60 N (63–210 mesh) under pressure. Analytical thin layer chromatography (TLC) was carried out on Merck Kieselgel 60 F₂₅₄ plates. Visualization was accomplished with UV light and phosphomolybdic acid stain solution followed by heating.

Unless otherwise noted, reagents were obtained from commercial suppliers and used without further purification. Dehydrated THF, MeCN, CH₂Cl₂, DMSO, EtOH, and DMF were purchased from Kanto Chemical Co., Inc. 2-Phenylspiro[2.6]nonane-4,9-dione (**9a**) was prepared according to our reported procedure.¹³

1-(2,4-Dimethoxyphenyl)methyl-2-phenyl-2,3,5,6,7,8-hexahydrocyclohepta[*b*]pyrrol-4(1*H*)-one (10c).

Spirocyclopropane **9a** (68 mg, 0.30 mmol) was added to a solution of 2,4-dimethoxybenzylamine (**6c**) (75 mg, 0.45 mmol) in MeCN (1.5 mL). After stirring at reflux for 12 h, the reaction mixture was cooled to room temperature and concentrated in vacuo, and the residue was purified by column chromatography (silica gel, 5% MeOH in EtOAc) to provide **10c** (106 mg, 94%) as a pale yellow amorphous: IR (film, cm⁻¹) ν 2934, 1613, 1550, 1507, 1462, 1436, 1293, 1233, 1209, 1157, 1035, 755; ¹H NMR (400 MHz, CDCl₃) δ 7.33 (t, *J* = 7.3 Hz, 2H), 7.27 (t, *J* = 6.0 Hz, 1H), 7.18 (d, *J* = 6.9 Hz, 2H), 6.84 (d, *J* = 9.2 Hz, 1H), 6.45–6.42 (m, 2H), 4.59 (dd, *J* = 11.9, 7.3 Hz, 1H), 4.44 (d, *J* = 16.5 Hz, 1H), 3.88 (d, *J* = 16.5 Hz, 1H), 3.80 (s, 3H), 3.73 (s, 3H), 3.31 (dd, *J* = 15.1, 11.9 Hz, 1H), 2.79 (dd, *J* = 15.1, 6.9 Hz, 1H), 2.68–2.62 (m, 4H), 1.94–1.82 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 193.9, 164.0, 160.4, 158.1, 142.6, 128.6, 128.5, 127.6, 126.7, 116.6, 109.9, 103.7, 98.5, 64.5, 55.3, 55.1, 43.2, 42.5, 37.7, 28.2, 24.6, 23.1; HRMS (ESI) *m/z* calcd for C₂₄H₂₈NO₃ (M+H)⁺ 378.2064, found 378.2061.

1-(2,4-Dimethoxyphenyl)methyl-2-phenyl-5,6,7,8-tetrahydrocyclohepta[*b*]pyrrol-4(1*H*)-one (11c).

MnO₂ (190 mg, 500 wt%) was added to a solution of **10c** (38 mg, 0.10 mmol) in CH₂Cl₂ (2.0 mL). After stirring at reflux for 1.5 h, the reaction mixture was cooled to room temperature and filtered through a pad of Celite. The filter cake was rinsed with CH₂Cl₂ (20 mL), and the combined filtrates were evaporated in vacuo. The residue was purified by column chromatography (silica gel, 40% EtOAc in hexane) to provide **11c** (31 mg, 82%), as a white solid: mp 125.5–126.0 °C; IR (KBr, cm⁻¹) ν 2936, 2838, 1634, 1607, 1592, 1509, 1440, 1414, 1304, 1212, 1151, 1105, 1033, 937, 827, 765, 702; ¹H NMR (400 MHz, CDCl₃) δ 7.32–7.25 (m, 5H), 6.78 (s, 1H), 6.46–6.38 (m, 3H), 5.00 (s, 2H), 3.79 (s, 6H), 2.75 (quint, *J* = 3.2 Hz, 4H), 1.88 (quint, *J* = 3.2 Hz, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 197.7, 160.2, 156.7, 140.3, 135.6, 132.5, 128.8, 128.4, 127.5, 126.5, 123.9, 118.2, 109.1, 104.1, 98.3, 55.3, 55.2, 43.3, 43.2, 26.7, 25.4, 22.5; HRMS (ESI) *m/z* calcd for C₂₄H₂₆NO₃ (M+H)⁺ 376.1907, found 376.1906.

2-Phenyl-5,6,7,8-tetrahydrocyclohepta[*b*]pyrrol-4(1*H*)-one (12).

Anisole (108 mg, 1.0 mmol) was added to a solution of **11c** (38 mg, 0.10 mmol) in TFA (0.50 mL) at room temperature. After stirring at reflux for 5.5 h, the reaction mixture was cooled to 0 °C and quenched by addition of saturated aqueous NaHCO₃ (5 mL), and the resulting mixture was extracted with EtOAc (3 \times 5 mL). The combined organic layers were washed with water (5 mL) and brine (5 mL), and dried over anhydrous MgSO₄. Filtration was concentrated in vacuo, and the residue was purified by column

chromatography (silica gel, 40% EtOAc in hexane) to provide **12** (20 mg, 87%) as a white solid: mp 221.0–222.0 °C; IR (KBr, cm^{-1}) ν 3212, 2925, 2812, 1599, 1462, 1429, 1224, 929, 829, 755, 688; ^1H NMR (400 MHz, CDCl_3) δ 8.91 (br s, 1H), 7.47 (d, $J = 7.3$ Hz, 2H), 7.35 (t, $J = 7.8$ Hz, 2H), 7.22 (t, $J = 7.3$ Hz, 1H), 6.91 (d, $J = 3.2$ Hz, 1H), 3.02 (t, $J = 6.4$ Hz, 2H), 2.74 (t, $J = 6.4$ Hz, 2H), 2.00 (quint, $J = 6.4$ Hz, 2H), 1.92 (quint, $J = 6.4$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 197.6, 139.8, 131.5, 131.3, 128.9, 126.8, 124.5, 123.9, 106.7, 43.4, 28.5, 25.4, 22.9; HRMS (ESI) m/z calcd for $\text{C}_{15}\text{H}_{16}\text{NO}$ ($\text{M}+\text{H}$) $^+$ 226.1226, found 226.1226.

2-Phenylcyclohepta[*b*]pyrrol-4(1*H*)-one (**14**).

Trimethylphenylammonium tribromide (83 mg, 0.22 mmol) was added to a solution of **12** (23 mg, 0.10 mmol) in THF (2.0 mL). After stirring at room temperature for 12 h, the reaction mixture was cooled to room temperature and quenched by addition of water (5 mL), and the resulting mixture was extracted with EtOAc (3×5 mL). The combined organic layers were washed with brine (5 mL), and dried over anhydrous MgSO_4 . Filtration and evaporation in vacuo furnished the crude product (73 mg), which was used in the next step without further purification.

LiCl (9.3 mg, 0.22 mmol) was added to a solution of crude product in DMF (1.0 mL). The mixture was stirred at reflux for 1.5 h, and then LiCl (2.1 mg, 0.05 mmol) was further added. After stirring at reflux for 1 h, the reaction was cooled to room temperature and quenched by addition of water (5 mL), and the resulting mixture was extracted with EtOAc (3×5 mL). The combined organic layers were washed with brine (5 mL), and dried over anhydrous MgSO_4 . Filtration was concentrated in vacuo, and the residue was purified by column chromatography (silica gel, 90% EtOAc in hexane) to provide **14** (11 mg, 49%) as a yellow solid: mp 260.5–261.0 °C; IR (KBr, cm^{-1}) ν 3367, 3123, 2969, 1619, 1557, 1523, 1497, 1479, 1412, 1330, 1232, 761; ^1H NMR (400 MHz, CD_3OD) δ 7.82 (dt, $J = 7.3, 1.4$ Hz, 2H), 7.70 (d, $J = 10.5$ Hz, 1H), 7.47 (td, $J = 7.3, 1.4$ Hz, 2H), 7.40 (s, 1H), 7.37 (td, $J = 7.3, 1.4$ Hz, 1H), 7.35 (dd, $J = 12.4, 8.8$ Hz, 1H), 7.06 (d, $J = 11.9$ Hz, 1H), 6.93 (dd, $J = 10.5, 8.7$ Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 183.9, 141.4, 139.8, 137.0, 135.7, 135.1, 131.8, 130.3, 129.9, 128.0, 126.7, 125.5, 107.5; HRMS (ESI) m/z calcd for $\text{C}_{15}\text{H}_{12}\text{NO}$ ($\text{M}+\text{H}$) $^+$ 222.0913, found 222.0914.

4-Chloro-2-phenyl-1-azaazulene (**3a**).

$i\text{Pr}_2\text{NEt}$ (280 mg, 2.2 mmol) was added to a solution of **14** (96 mg, 0.43 mmol) in POCl_3 (4.3 mL) at 0 °C. After stirring at 100 °C for 2 h, the reaction mixture was cooled to 0 °C and poured into saturated aqueous NaHCO_3 (30 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×30 mL). The combined organic layers were washed with saturated aqueous NaHCO_3 (2×20 mL), water (20 mL) and brine (20 mL), and dried over anhydrous MgSO_4 . Filtration was concentrated in vacuo, and the residue was purified by column chromatography (silica gel, 70% EtOAc in hexane) to provide **3a** (84 mg, 81%)

as a red solid: mp 106.5–107.5 °C; IR (KBr, cm^{-1}) ν 3062, 2925, 1603, 1509, 1461, 1441, 1361, 1325, 1228, 1200, 1069, 1046, 909, 807, 760, 687; ^1H NMR (500 MHz, CDCl_3) δ 8.60 (d, $J = 9.7$ Hz, 1H), 8.33 (dd, $J = 8.0, 1.7$ Hz, 2H), 7.90 (s, 1H), 7.73 (d, $J = 10.9$ Hz, 1H), 7.64 (t, $J = 9.7$ Hz, 1H), 7.56 (t, $J = 10.3$ Hz, 1H), 7.51 (td, $J = 6.9, 1.7$ Hz, 2H), 7.46 (tt, $J = 6.9, 1.7$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.2, 156.3, 144.8, 142.2, 135.6, 134.7, 133.9, 130.5, 130.3, 129.0, 128.9, 128.2, 111.6; HRMS (ESI) m/z calcd for $\text{C}_{15}\text{H}_{11}\text{NCl}$ ($\text{M}+\text{H}$) $^+$ 240.0575, found 240.0574.

2-Phenyl-1-azaazulene (**3b**).^{6,8b,9b}

$\text{H}_2\text{NNH}_2 \cdot \text{H}_2\text{O}$ (38 mg, 0.75 mmol) was added to a solution of **3a** (28 mg, 0.12 mmol) in MeOH (2.3 mL). After stirring at room temperature for 3 h, the reaction mixture was concentrated in vacuo, and the residue was purified by column chromatography (silica gel, 8:1 $\text{CH}_2\text{Cl}_2/\text{MeOH}$) to provide crude product containing a small amount of impurity (16 mg) as a yellow oil.

$\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (350 mg, 1.4 mmol) was added to a solution of the crude product in AcOH/ H_2O (1:3, 2.8 mL). The mixture was stirred at 100 °C for 0.5 h, the reaction was cooled to 0 °C and quenched by addition of 2 M aqueous NaOH (10 mL), and the resulting mixture was extracted with EtOAc (3×5 mL). The combined organic layers were washed with water (5 mL) and brine (5 mL), and dried over anhydrous MgSO_4 . Filtration was concentrated in vacuo, and the residue was purified by column chromatography (silica gel, 60% EtOAc in hexane) to provide **3b** (6.9 mg, 29% from **3a**) as a red powder: mp 156.5–157.5 °C [lit.,^{9b} mp 158–159 °C]; IR (KBr, cm^{-1}) ν 2925, 2853, 1577, 1510, 1464, 1441, 1406, 1332, 1217, 1027, 772, 754, 690; ^1H NMR (500 MHz, CDCl_3) δ 8.68 (d, $J = 9.7$ Hz, 1H), 8.52 (d, $J = 9.7$ Hz, 1H), 8.33 (dd, $J = 8.0, 1.1$ Hz, 2H), 7.79 (t, $J = 9.7$ Hz, 1H), 7.76 (s, 1H), 7.74 (t, $J = 9.7$ Hz, 1H), 7.61 (t, $J = 9.7$ Hz, 1H), 7.52 (td, $J = 7.4, 1.1$ Hz, 2H), 7.46 (tt, $J = 7.4, 1.1$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.2, 158.7, 148.0, 136.6, 135.3, 135.2, 134.7, 129.9, 129.7, 128.9, 128.8, 128.1, 110.7.

REFERENCES AND NOTES

1. For recent reviews, see: (a) N. Abe and T. Gunji, *Heterocycles*, 2010, **82**, 201; (b) N. Abe, *Heterocycles*, 2018, **97**, 43; (c) N. Abe, *Heterocycles*, 2020, **101**, 33.
2. M. Nagahara, J. Nakano, M. Miura, T. Nakamura, and K. Uchida, *Chem. Pharm. Bull.*, 1994, **42**, 2491.
3. N. Abe, M. Nabeshima, H. Fujii, A. Kakehi, Y. Kageura, and T. Konakahara, *Heterocycles*, 2001, **54**, 329.
4. R. J. Sciotti and R. Wagner, PCT Int. Appl., US01/02944, 2001; Pub., WO 01/57018 A1, 2001.
5. (a) T. Nozoe, S. Seto, S. Matsumura, and T. Terasawa, *Chem. Ind.*, 1954, 1357; (b) T. Nozoe, Y. Kitahara, and T. Arai, *Proc. Jpn. Acad.*, 1954, **30**, 478; (c) T. Nozoe, S. Seto, and S. Nozoe, *Proc. Jpn. Acad.*, 1956, **32**, 472.

6. Y. Sugimura, N. Soma, and Y. Kishida, [Bull. Chem. Soc. Jpn., 1972, 45, 3174.](#)
7. C. Wentrup and J. Becker, [J. Am. Chem. Soc., 1984, 106, 3705.](#)
8. (a) M. Nitta and T. Kobayashi, [Chem. Lett., 1986, 15, 463](#); (b) M. Nitta, Y. Iino, E. Hara, and T. Kobayashi, [J. Chem. Soc., Perkin Trans. 1, 1989, 51](#); (c) Y. Iino, E. Hara, and M. Nitta, [Bull. Chem. Soc. Jpn., 1989, 62, 1913](#); (d) M. Nitta, Y. Iino, E. Hara, and T. Kobayashi, *Heterocycles*, 1997, **48**, 3150; (e) T. Takayasu, H. Katayama, and M. Nitta, [Heterocycles, 1997, 45, 567](#); (f) T. Takayasu and M. Nitta, [J. Chem. Soc., Perkin Trans. 1, 1999, 687.](#)
9. (a) M. Kitamura, S. Chiba, O. Saku, and K. Narasaka, [Chem. Lett., 2002, 31, 606](#); (b) S. Chiba, M. Kitamura, O. Saku, and K. Narasaka, [Bull. Chem. Soc. Jpn., 2004, 77, 785.](#)
10. S. Carret, A. Blanc, Y. Coquerel, M. Berthod, A. E. Greene, and J.-P. Deprés, [Angew. Chem. Int. Ed., 2005, 44, 5130.](#)
11. M. Oda, A. Sugiyama, R. Takeuchi, Y. Fujiwara, R. Miyatake, T. Abe, and S. Kuroda, [Eur. J. Org. Chem., 2012, 2231.](#)
12. (a) H. Nambu, M. Fukumoto, W. Hirota, and T. Yakura, [Org. Lett., 2014, 16, 4012](#); (b) H. Nambu, W. Hirota, M. Fukumoto, T. Tamura, and T. Yakura, [Chem. Eur. J., 2017, 23, 16799](#); (c) H. Nambu, T. Tamura, and T. Yakura, [J. Org. Chem., 2019, 84, 15990.](#)
13. Y. Onuki, H. Nambu, and T. Yakura, [Chem. Pharm. Bull., 2020, 68, 479.](#)
14. A. A. Haddach, A. Kelleman, and M. V. Deaton-Rewolinski, [Tetrahedron Lett., 2002, 43, 399.](#)
15. After oxidizing **11a** into *N*-benzyl-protected tropone derivative, we also examined the deprotection of the oxidized product. However, the *N*-unprotected compound could not be obtained.
16. T. J. Donohoe, D. J. Johnson, L. H. Mace, M. J. Bamford, and O. Ichihara, [Org. Lett., 2005, 7, 435.](#)
17. (a) T. Watanabe, A. Kobayashi, M. Nishiura, H. Takahashi, T. Usui, I. Kamiyama, N. Mochizuki, K. Noritake, Y. Yokoyama, and Y. Murakami, [Chem. Pharm. Bull., 1991, 39, 1152](#); (b) Y. Lu and B. A. Arndtsen, [Org. Lett., 2009, 11, 1369.](#)
18. K. Yamane and K. Fujimori, [Bull. Chem. Soc. Jpn., 1976, 49, 1101.](#)
19. K. Yamane, K. Fujimori, J.-K. Sin, and T. Nozoe, [Bull. Chem. Soc. Jpn., 1977, 50, 1184.](#)