An enamine method for the synthesis of 1-azaazulene derivatives. Reactions of troponimines with enamines[1]

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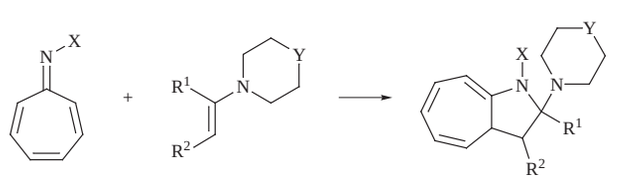
A short new synthesis of 1-azaazulene derivatives consists of the enamine alkylation of troponimines **4**–**7** with pyrrolidino enamines, which are derived from cycloalkanones, aliphatic ketones, and heterocyclic ketones, to lead to formal [8 + 2] cycloadducts and subsequent aromatization under the reaction conditions. The reactions are quite general, and *N*-hydroxy- and *N*-methoxytroponimines, **4** and **5**, are less reactive than *N*-mesyloxy- and *N*-tosyloxytroponimines, **6** and **7**, which react smoothly even at room temperature. In the reaction of the pyrrolidino enamine, which is derived from cyclopentanone, forcing conditions are required, probably because of ring strain in the [8 + 2] cycloadduct **11a**. Furthermore, in the reactions of **4**–**7** with isomeric mixtures of two pyrrolidino enamines, **15/16** and **20/21**, only enamines **15** and **20** can intervene in the cycloaddition reactions, giving 1-azaazulene derivatives. In the context of the reactivity of **4**–**7** and pyrrolidino enamines, and the selectivity observed in the reactions with isomeric mixtures of enamines, minimal neglect of differential overlap (MNDO) calculations on troponimines **4**–**7** and pyrrolidino enamines, as well as isomeric mixtures of two enamines, **15/16** and **20/21**, were performed to gain further insight into the reactions *via* a theoretical interpretation based upon frontier molecular orbital theory (FMO). Troponimines **6** and **7** have lower LUMOs and they are more reactive than troponimines **4** and **5**; the energy level of the HOMO of the pyrrolidino enamine derived from cyclopentanone is relatively higher as compared to those of other pyrrolidino enamines. Enamines **15** and **20** are less stable and energy levels of the HOMOs are higher as compared with those of the corresponding isomers **16** and **21**, respectively.

Introduction

The chemistry of azaazulenes has attracted considerable attention for several decades.[2–8] In a series of studies concerning (vinylimino)phosphoranes,[5] we have demonstrated convenient methodology for synthesizing 1-azaazulenes[6,7] and 5-azaazulenes.[8] Since 1-azaazulenes and 1-azaazulen-2-ones have also attracted much attention from the viewpoint of their pharmacological activities,[9] we have embarked on the exploration of methodology to synthesize versatile 1-azaazulenes. Although cycloaddition of troponimines with electron-deficient acetylene and cumulenes has been studied extensively,[10,11] we have found previously that *N*-diphenylphosphinoyl-,[12] *N*-phenylsulfonyl-,[13] and *N*-methylsulfonyltroponimines,[13] **1a**–**c**, react with enamines **2** leading to 1-azaazulene derivatives in low to modest yields. In the reactions, the yields of 1-azaazulenes would be dependent on the aromatization process of the intermediates **3a**–**c** (Scheme 1). In the search for efficient methodology for the synthesis of 1-azaazulene derivatives, similar to the so-called enamine method for synthesizing azulenoid compounds,[14] we studied the reaction of troponimines **4**–**7**, all of which have a suitable leaving group on the nitrogen atom, with pyrrolidino enamines to give 2,3-ring annulated and 2,3-substituted 1-azaazulenes in good to moderate yields. In the context of the reactivity of compounds **4**–**7** and pyrrolidino enamines, and the selectivity observed in the reaction with isomeric mixtures of two enamines, **15/16** and **20/21**, minimal neglect of differential overlap (MNDO) calculations were also performed. We describe here the results in detail.



1a X = $POPh_2$ **2** (Y = O or electron pair) **3a-c**
1b X = SO_2Ph
1c X = SO_2Me

Scheme 1

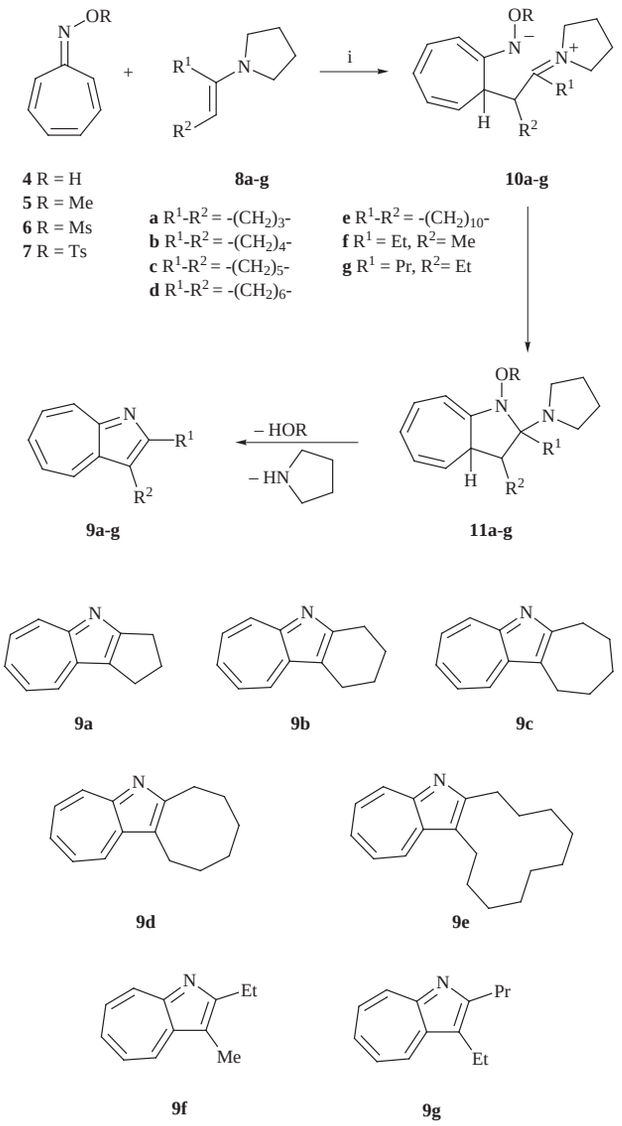
Results and discussion

N-Hydroxytroponimine (tropone oxime) **4**[15] was prepared in 90% yield through the modified reaction of tropone with hydroxylamine hydrochloride in MeOH for 1 week. *N*-Methoxy-,[16] *N*-mesyloxy-[17] and *N*-tosyloxytroponimines,[18] **5**, **6**, and **7**, were prepared by the usual methods. The thermal reaction of **4** and **5** with pyrrolidino enamines **8a**–**g** proceeded in benzene or xylene under reflux to give 1-azaazulenes **9a**–**g**. Attempted reaction of troponimines **4** and **5** with piperidino and/or morpholino enamines afforded 1-azaazulene derivatives in poor to modest yields. On the other hand, troponimines **6** and **7**, reacted with pyrrolidino enamines **8a**–**g** under mild conditions, as compared with those of **4** and **5** to give **9a**–**g** (Scheme 2). The reaction conditions and the yields of the products are summarized in Table 1 (Runs 1–7).

The postulated pathways for the formation of **9a**–**g** are also shown in Scheme 2. The enamine alkylation of **8a**–**g** to C-2 of troponimines **4**–**7** gives the intermediates **10a**–**g**, which undergo cyclization to give **11a**–**g**. The facile aromatization eliminating HOR and pyrrolidine results in the formation of 1-azaazulenes **9a**–**g**. The reddish colour of **9a**–**g** and the formation of the corresponding picrates are characteristic of 1-azaazulenes.[12,13] The structures of **9a**–**c** were confirmed on the basis of comparison of the spectral data with those of the authentic specimens.[12,13] The positions of the alkyl group of compounds, **9f**–**g**, were assigned by the ^{1}H NMR spectra obtained by using $Eu(fod)_3$. On the basis of the spectral data, picrate formations,

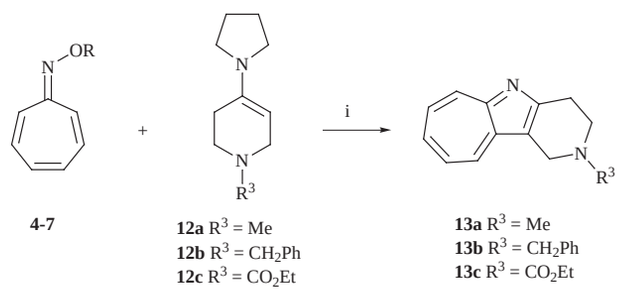
and their elemental analyses, as well as consideration of the structural relationship with enamines **8d**–**g**, the structures of new 1-azaazulenes **9d**–**g** were deduced.

In the cases of the reaction of troponimines **4**–**7** with **8a**, which is derived from cyclopentanone, forcing conditions were required as compared with those of other enamines (Table 1, Run 1). Thus, it is clear that the reaction conditions are sensitive to the ring size of enamines. This feature is presumably ascribed to the ring strain in the cyclization step of the intermediate **10a**, giving **11a**. The ring strain originating from the reaction of **8a** to give **11a** is considered to be larger than that for the others (*vide infra*). The reason for the forcing conditions required for the reaction of troponimines **4** and **5** with **8b** is not explicable at this stage.



Scheme 2 *Reagents and conditions*: i, heat.

Azulene derivatives annulated with heterocycles have been synthesized by the reaction of cyclohepta[*b*]furan-2-one with enamines derived from heterocyclic ketones such as 4-piperidone, 3-piperidone **14**, and 3-oxotetrahydrothiophene **19**.[19–21] In extension of the synthetic applicability of the present reaction, synthesis of 1-azaazulenes annulated with heterocycles was accomplished. The reactions of troponimines **4** and **5** with pyrrolidino enamine **12a**,**b**,[21] which are derived from 4-piperidone derivatives, gave *N*-substituted 1,2,3,4-tetrahydrocyclohepta[4,5]pyrrolo[3,2-*c*]pyridines **13a**,**b** in modest to good yields (Scheme 3, Table 1, Run 8 and 9). Furthermore, the



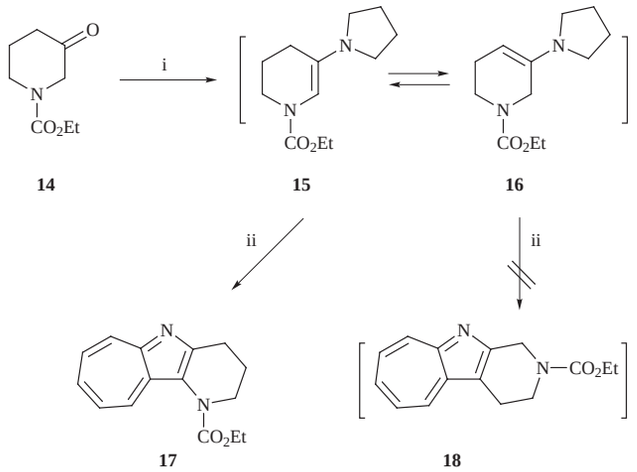
Scheme 3 *Reagents and conditions*: i, heat.

reaction of troponimines **4**, **5**, and **7** with enamine **12c**, which was prepared *in situ*, afforded **13c** in modest yields. (Table 1, Run 10). On the other hand, the condensation of *N*-ethoxycarbonyl-3-piperidone **14**[22] and 3-oxotetrahydrothiophene **19** with pyrrolidine has been clarified to give isomeric mixtures of two enamines **15**/**16**[21] and **20**/**21** (Scheme 4 and 5).[19] Actually, the reactions of the isomeric mixtures of two enamines, **15**/**16** and **20**/**21** with cyclohepta[*b*]furan-2-one gave two isomeric azulenoid compounds, azuleno[2,1-*c*]- and azuleno[1,2-*b*]pyridine derivatives, and azuleno[1,2-*b*]- and azuleno[1,2-*c*]thiophene derivatives, respectively. In these azulene syntheses, the product ratio is not dependent on the composition of enamines but on the reactivities of these enamines.[19,23] However, the reaction of troponimines **4**–**7** with the isomeric mixture of two enamines **15**/**16** gave only *N*-ethoxycarbonyl-1,2,3,4-tetrahydrocyclohepta[4,5]pyrrolo[3,2-*b*]pyridine **17** and did not give **18** (Scheme 4). Similarly, the reaction of troponimines **6** and **7** with an isomeric mixture of two enamines **20**/**21** (in a ratio of 28/72)[19]

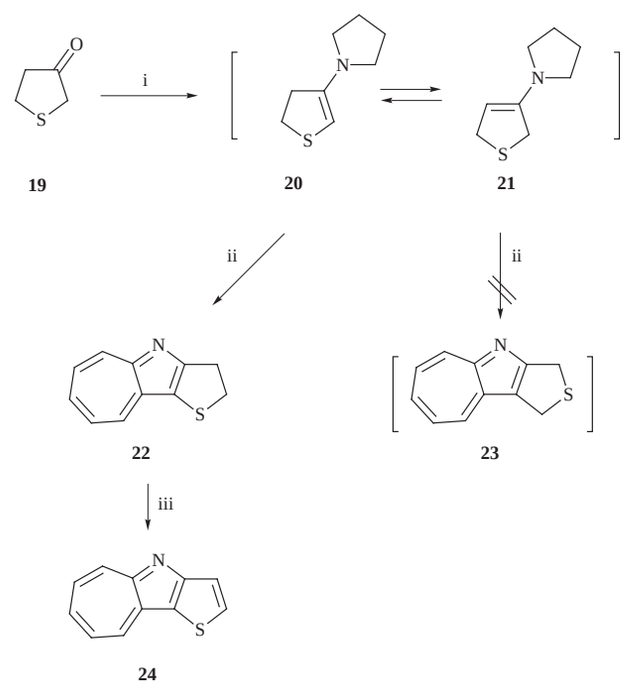
Table 1 Reaction of troponimines **4**–**7** with enamines **8a**–**g**, **12a**–**c**, **15** and **20d**

Run	Enamine	Product	Yield (%) (Reaction time/h)			
			Method A[a] for **4**	Method B[a] for **5**	Method C[b] for **6**	Method D[b] for **7**
1	**8a**	**9a**	64 (6)[c]	64 (6)[c]	40 (0.5)[a]	40 (0.5)[a]
2	**8b**	**9b**	89 (2)[c]	76 (6)[c]	76 (1)	61 (1)
3	**8c**	**9c**	100 (2)	77 (3)	99 (0.2)	100 (0.2)
4	**8d**	**9d**	83 (4)	100 (12)	90 (0.5)	66 (0.5)
5	**8e**	**9e**	98 (4)	100 (12)	90 (0.5)	79 (0.5)
6	**8f**	**9f**	65 (6)	59 (12)	50 (1)	50 (1)
7	**8g**	**9g**	42 (6)	55 (10)	85 (1)	85 (1)
8	**12a**	**13b**	24 (24)	78 (24)	—	—
9	**12b**	**13c**	20 (24)	47 (24)	—	—
10	**12c**[d]	**13a**	33 (24)	60 (24)	—	42 (24)
11	**15**	**17**	33 (24)	4 (24)	45 (6)	19 (6)
12	**20d**	**22**	none (24)	none (24)	45 (6)	58 (6)

[a] Heated under reflux in benzene. [b] Stirred at room temp. in benzene. [c] Heated under reflux in xylene. [d] Prepared *in situ*.



Scheme 4 *Reagents and conditions*: i, pyrrolidine, TsOH, PhH, reflux; ii, troponimine, PhH, heat.



Scheme 5 *Reagents and conditions*: i, pyrrolidine, TsOH, PhH, reflux; ii, troponimine, PhH, heat; iii, MnO_2, PhH, room temp.

at room temp. gave only 2,3-dihydrocyclohepta[*b*]thieno[2,3-*d*]-pyrrole **22**, and isomeric cyclohepta[*b*]thieno[3,4-*d*]pyrrole **23** was not obtained (Scheme 5). Since the reaction of troponimine **4** and **5** with a mixture of **20/21** under reflux in benzene did not give any product such as **22** but produced only intractable tarry materials, compound **22**, which contains an electron-donating substituent at the 3-position of the 1-azaazulene skeleton, seems to be labile and it may decompose gradually under the reaction conditions of refluxing benzene. Actually, compound **22** as well as its picrate seemed to be labile and decomposed gradually even at room temp. Thus, on dehydrogenation by activated MnO_2, compound **22** was converted to stable cyclohepta[*b*]thieno[2,3-*d*]pyrrole **24** in good yield. The structures of new 1-azaazulene derivatives, **13a**–**c**, **17**, **22**, and **24** were confirmed on the basis of the spectral data and picrate formation, and elemental analyses, as well as consideration of the structural relationship with enamines **12a**–**c**, **15**, and **20**.

The reactions of troponimines, **6** and **7**, with enamines proceeded under very mild conditions as compared with those of troponimines, **4** and **5** (Table 1). One useful aspect of the principle of hard and soft acids and bases is the way in which it classifies our idea of reactivity.[24] The site where most of the

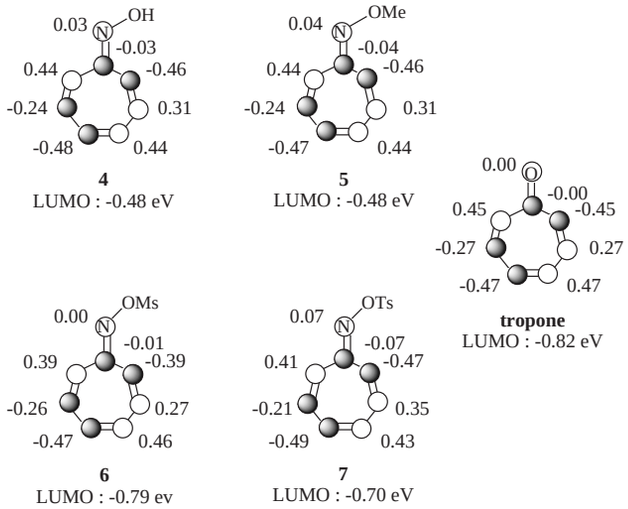


Fig. 1 Coefficients and energy level of the LUMO.

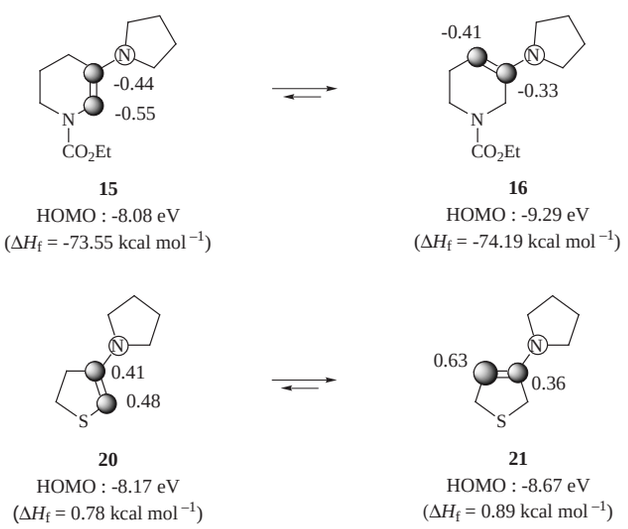


Fig. 2 Coefficients, energy level of the HOMO, and heat of formation (ΔH_r).

charge exists (the hard center) will be the site of attack by a charged or relatively charged electrophile (hard electrophile) and the site of the highest coefficient in the highest occupied molecular orbital (HOMO) of the nucleophile (soft center) will be the site of attack by an electrophile with a relatively low-energy lowest unoccupied molecular orbital (LUMO) (soft electrophile). Thus, the reaction of troponimines with enamines is now explicable in terms of the Frontier Molecular Orbital theory (FMO).[25] The energy levels and coefficient of LUMO of troponimines **4**–**7** and tropone, and the heat of formation (ΔH_f), the energy levels of HOMO of isomeric mixtures of two isomers, **15/16** and **20/21**, are presented in Fig. 1 and Fig. 2, respectively, as obtained by the MNDO method.[26] The energy levels of the LUMO of **4** (−0.48 eV) and **5** (−0.48 eV) are higher than those of **6** (−0.79 eV) and **7** (−0.70 eV) (Fig. 1). The energy level of LUMO of tropone (−0.82 eV), which is known to react with enamines to give an [8 + 2] cycloadduct,[27] is slightly lower than those of **6** and **7**. Energy levels of the HOMO are obtained as **4** (−8.57 eV); **5** (−8.57 eV); **6** (−9.21 eV), **7** (−8.75 eV), and tropone (−9.25 eV). The charge densities on the nitrogen and imine-carbon atoms are also obtained as **4** (−1.2 and +0.04), **5** (−1.2 and +0.05), **6** (−1.2 and +0.11) and **7** (−1.6 and +0.09), and they are lower than those on the oxygen and carbonyl-carbon atoms of tropone (−0.31 and +0.29), respectively, suggesting the less polarized nature of **4**–**7** compared with tropone. Generally, the coefficient of the HOMO on the β-carbon atom of enamines **8a**–**g** is larger

Table 2 Calculated energy levels of the LUMO and HOMO of enamines

Compound	**8a**	**8b**	**8c**	**8d**	**8e**	**8f**	**8g**	**12a**	**12b**	**12c**
HOMO/eV	−8.43	−9.44	−9.47	−9.33	−9.30	−9.34	−9.33	−9.19	−9.26	−8.61
LUMO/eV	+1.16	+0.79	+0.78	+0.80	+0.87	+0.87	+0.89	+0.70	+0.29	+0.91

than that on the nitrogen atom (*cf.* Fig. 2), Thus, the enamine alkylation of **8a**–**g** occurs on the C-2 position of the low-lying LUMO of troponimines **6** and **7**, under mild conditions, as compared with that of **4** and **5** possessing a relatively higher LUMO. Regarding the energy level of the HOMO of **8a**, it is higher as compared with those of enamines **8b**–**g**, but forcing conditions are required for the reaction of troponimines with **8a** (Table 1, Run 1). This feature would be ascribed to the ring strain originating from the reaction of **8a** to give the intermediate **11a** (Scheme 2). On the other hand, in the reaction of troponimines with isomeric mixtures of two enamines, **15/16** and **20/21**, enamines **15** and **20** could intervene in the reaction to give 1-azaazulenes, **17** and **22**, respectively. Regarding enamines **15** and **20**, they are suggested to be less stable (heat of formation: ΔH_f in Fig. 2), and they have higher HOMOs as compared to those of the corresponding isomers **16** and **21**, respectively (Fig. 2). Thus, enamines **15** and **20** could react with troponimines more rapidly than the corresponding isomers **16** and **21**, respectively (Table 1, Run 12 and 13). Thus, the present reactions are rationalized on the basis of the FMO theory.

In conclusion, the present method using troponimines **4**–**7** and pyrrolidino enamines provides an efficient route to the synthesis of 2,3-annulated and 2,3-disubstituted 1-azaazulenes. This methodology establishes the experimental framework for a new approach to 2,3-annulated and 2,3-disubstituted 1-azaazulenes, similar to the so-called enamine method synthesizing azulenoid compounds established by Takase, Yasunami and co-workers.[14] Further studies are underway to explore the scope and limitations of the enamine method to construct the 1-azaazulene skeleton and to find further useful applications of the method for the preparation of compounds involving 1-azaazulene of theoretical interest and demonstrated utility.

Experimental

IR spectra were recorded on a Shimadzu IR-400 spectrometer. The mass spectral and high-resolution mass spectral studies were run on JEOL Automass 150 and DX-300 spectrometers, respectively. ^{1}H and ^{13}C NMR spectra were recorded on Hitachi R-90, JEOL JNM-EX270, and JEOL GSX-400 spectrometers using $CDCl_3$ as a solvent, and chemical shifts are given relative to internal Me_4Si standard: *J*-values are given in Hz. Mps were recorded on a Yamato MP-21 apparatus and are uncorrected. *N*-Hydroxytroponimine (tropone oxime) **4** was prepared by a modification (*vide infra*) of the literature method.[12] Troponimines, **5**,[16] **6**,[17] and **7**[18] were prepared by the usual methods described in the literature. Almost all of the enamines, **8a**–**g**, **12a**,**b**, and **15/16** were prepared by the usual method and purified by distillation under reduced pressure. Enamines **12c** and the isomeric mixture of two enamines, **20/21** were prepared *in situ* and used for the further reaction with troponimines. All the thermal reactions were carried out under anhydrous conditions and dry nitrogen atmosphere.

Preparation of *N*-hydroxytroponimine (tropone oxime) 4

A solution of tropone (21.3 g, 0.2 mol) and hydroxylamine hydrochloride (69.5 g, 1 mol) in MeOH (100 cm^3) was stirred at room temp. for 1 week. After the reaction mixture was filtered, the filtrate was neutralized with aq. $NaHCO_3$ solution, extracted with CH_2Cl_2, and the extract was dried over Na_2SO_4. After evaporation of the solvent, the residual solid was recrystallized from CCl_4 to give **4** (21.9 g, 90%): purple needles; mp 76–77 °C (lit.,[15] mp 76–77 °C).

General procedure for the reaction of troponimines 4 and 5 with enamines 8a–g, 12a,b, and 15

Method A or B (Table 1): A solution of **4** (122 mg, 1 mmol), enamine (2 mmol), and 0.4 nm molecular sieves (100 mg) or a solution of **5** (135 mg, 1 mmol) and enamine (2 mmol) in anhydrous PhH or xylene (1 cm^3) was heated under reflux for the period indicated in Table 1. After the reaction was completed, the reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The resulting residue was purified by TLC on alumina (hexane–AcOEt 1:1) to give 1-azaazulenes **9a**–**g**, **13a**,**b**, and **17**. The reaction conditions and the yields of the products are summarized in Table 1.

7,8,9,10,11,12-Hexahydrocyclohepta[*b*]cycloocta[*d*]pyrrole 9d. Red oil; δ_H (400 MHz) 1.35–1.40 (2H, m), 1.42–1.47 (2H, m), 1.73–1.79 (2H, m), 1.83–2.00 (2H, m), 3.11 (2H, t, *J* 6.4), 3.25 (2H, t, *J* 6.4), 7.51 (1H, dd, *J* 9.5, 10.1), 7.61 (1H, dd, *J* 9.4, 10.5), 7.71 (1H, dd, *J* 9.5, 10.5), 8.26 (1H, d, *J* 10.1), 8.49 (1H, d, *J* 9.4). Picrate: mp 202–205 °C (from MeOH) (Found: C, 57.1; H, 4.5; N, 12.4. $C_{21}H_{20}N_4O_7$ requires C, 57.27; H, 4.58; N, 12.72%).

7,8,9,10,11,12,13,14,15,16-Decahydrocyclododeca[*b*]cyclohepta[*d*]pyrrole 9e. Red oil; δ_H (400 MHz) 1.26–1.60 (12H, m), 1.80–2.10 (4H, m), 3.02 (2H, t, *J* 7.0), 3.07 (2H, t, *J* 7.5), 7.54 (1H, dd, *J* 9.5, 9.9), 7.63 (1H, dd, *J* 9.7, 9.9), 7.73 (1H, dd, *J* 9.7, 9.9), 8.33 (1H, d, *J* 9.9), 8.51 (1H, d, *J* 9.5). Picrate: mp 177–178 °C (from MeOH) (Found: C, 60.3; H, 5.8; N, 11.0. $C_{25}H_{28}N_4O_7$ requires C, 60.48; H, 5.68; N, 11.28%).

2-Ethyl-3-methylcyclohepta[*b*]pyrrole 9f. Reddish orange oil; δ_H (400 MHz) 1.42 (3H, t, *J* 7.7), 2.50 (3H, s), 3.11 (2H, q, *J* 7.7), 7.52 (1H, dd, *J* 9.2, 9.9), 7.60 (1H, dd, *J* 9.5, 9.9), 7.71 (1H, dd, *J* 9.5, 9.9), 8.25 (1H, d, *J* 9.9), 8.49 (1H, d, *J* 9.2). Picrate: mp 188–190 °C (from MeOH) (Found: C, 53.8; H, 3.8; N, 14.0. $C_{18}H_{16}N_4O_7$ requires C, 54.00; H, 4.03; N, 13.99%).

3-Ethyl-2-propylcyclohepta[*b*]pyrrole 9g. Reddish orange oil; δ_H (400 MHz) 1.05 (3H, t, *J* 7.3), 1.25 (3H, t, *J* 7.3), 1.92 (2H, tq, *J* 7.3, 7.7), 2.97 (2H, q, *J* 7.3), 3.05 (2H, t, *J* 7.7), 7.51 (1H, dd, *J* 9.5, 9.9), 7.60 (1H, dd, *J* 9.5, 9.9), 7.71 (1H, dd, *J* 9.5, 10.3), 8.28 (1H, d, *J* 10.3), 8.48 (1H, d, *J* 9.5). Picrate: mp 190–191 °C (from MeOH) (Found: C, 56.2; H, 4.6; N, 13.2. $C_{20}H_{20}N_4O_7$ requires C, 56.07; H, 4.71; N, 13.08%).

2-Methyl-1,2,3,4-tetrahydrocyclohepta[4,5]pyrrolo[3,2-*c*]-pyridine 13a. Red oil; δ_H (90 MHz) 2.35 (2H, s, H-1), 2.58 (3H, s, CH_3), 2.80–3.92 (4H, m, H-3, 4), 7.56 (1H, dd, *J* 9.5, 10.3, H-8), 7.68 (1H, dd, *J* 9.9, 10.3, H-9), 7.77 (1H, dd, *J* 9.5, 9.9, H-7), 8.18 (1H, d, *J* 9.9, H-10), 8.35 (1H, d, *J* 9.5, H-6); ν_{max} ($CHCl_3$)/cm^{-1} 2930, 2800, 1720; *m*/*z* (rel. int.) 198 (M^+, 22), 110 (100%). Picrate: mp 138-144 °C (from CH_3CN) (decomp.) (Found: C, 53.3; H, 3.8; N, 16.5. $C_{19}H_{17}N_5O_7$ requires C, 53.40; H, 4.01; N, 16.39%).

2-Benzyl-1,2,3,4-tetrahydrocyclohepta[4,5]pyrrolo[3,2-*c*]-pyridine 13b. Red oil; δ_H (400 MHz) 3.03–4.32 (8H, m, H-1, 3, 4, CH_2), 7.31–7.50 (5H, m, Ph-H), 7.52 (1H, dd, *J* 9.5, 9.9, H-9),

7.66 (1H, dd, *J* 9.9, 9.9, H-8), 7.75 (1H, dd, *J* 9.9, 9.6, H-7), 8.13 (1H, d, *J* 9.9, H-10), 8.51 (1H, d, *J* 9.5, H-6); *m*/*z* (rel. int.) 274 (M^+, 5), 157 (100%). Picrate: mp 156–160 °C (from CH_3CN) (decomp.) (Found: C, 59.3; H, 4.2; N, 14.1. $C_{21}H_{19}N_5O_9$ requires C, 59.64; H, 4.20; N, 13.91%).

Ethyl 1,2,3,4-tetrahydrocyclohepta[4,5]pyrrolo[3,2-*b*]pyridine-1-carboxylate 17. Purple oil; δ_H (90 MHz) 1.42 (3H, t, *J* 7.2, CH_3), 2.12–2.40 (2H, m, H-2 , 3, or 4), 3.40 (2H, t, H-2 , 3, or 4), 3.96–4.10 (2H, m, H-2 , 3, or 4), 4.36 (2H, q, *J* 7.2, CH_2), 7.52–7.86 (3H, m, H-7, 8, 9), 8.52 (2H, br d, *J* 9.2, H-6, 10); *m*/*z* (rel. int.) 256 (M^+, 93), 181 (100%). Picrate: mp 113–118 °C (from CH_3CN) (decomp.) (Found: C, 52.2; H, 3.8; N, 14.6. $C_{21}H_{19}N_5O_9$ requires C, 51.96; H, 3.95; N, 14.43%).

General procedure for the reaction of troponimines 6 and 7 with enamines 8a–g and 15

Methods C and D (Table 1): A solution of **6** (199 mg, 1 mmol) or **7** (275 mg, 1 mmol), enamine (2 mmol) and Et_3N (101 mg, 1 mmol) in anhydrous PhH (1 cm^3) was stirred at room temperature or under heating for the periods indicated in Table 1. After the reaction was completed, the solvent was removed *in vacuo*, the residue was separated by TLC on alumina (hexane–AcOEt 1 : 1) to give 1-azaazulenes **9a**–**g** and **17**. The reaction conditions and the yields of the products are summarized in Table 1. The structures of **9a**–**g** and **17** were identical with the authentic specimens (*vide supra*).

General procedure for the reaction of troponimines 4, 5 and 7 with enamine 12c prepared *in situ*

A solution of *N*-ethoxycarbonyl-4-piperidone (511 mg, 3 mmol), pyrrolidine (456 mg, 6.5 mmol) and TsOH (52 mg, 0.3 mmol) in PhH (10 cm^3) was placed in a 20 cm^3 round-bottomed flask fitted with a Dean–Stark apparatus, and the mixture was heated under reflux for 20 h. After the solvent and excess pyrrolidine were removed *in vacuo*, the residual yellow oil of enamine **12c** was used for further reactions with troponimines.

Methods A and B (Table 1): A solution of **4** (183 mg, 1.5 mmol), **12c** prepared as described above, and 0.4 nm molecular sieves (150 mg) in PhH (9 cm^3), or a solution of **5** (203 mg, 1.5 mmol) and **12c** in PhH (9 cm^3) was heated under reflux for the period indicated in Table 1.

Method D (Table 1): A solution of **7** (413 mg, 1.5 mmol) and **12c** in PhH (9cm^3) was stirred at room temp. for the period indicated in Table 1.

After the reaction was completed, the reaction mixture was filtered, and the filtrate was concentrated *in vacuo*. The resulting residue was separated by TLC on alumina (hexane–AcOEt 1 : 1) to give **13c**. The reaction conditions and the yields of the products are summarized in Table 1.

Ethyl 1,2,3,4-tetrahydrocyclohepta[4,5]pyrrolo[3,2-*c*]pyridine-2-carboxylate 13c. Red oil; δ_H (90 MHz) 1.31 (3H, t, *J* 7.0, CH_3), 1.83–4.30 (8H, m, H-1, 3, 4, CH_2), 7.56–7.82 (3H, m, H-7, 8, 9), 8.19 (1H, d, *J* 9.2, H-10), 8.51 (1H, d, *J* 9.1, H-6); *m*/*z* (rel. int.) 256 (M^+, 29), 227 (100%). Picrate: mp 113–118 °C (from CH_3CN) (decomp.) (Found: C, 51.7; H, 3.7; N, 14.6. $C_{21}H_{19}N_5O_9$ requires C, 51.96; H, 3.95; N, 14.43%).

General procedure for the reaction of troponimines 4–7 with the isomeric mixture of two enamines 20/21 prepared *in situ*

A solution of tetrahydrothiophen-3-one **19** (306 mg, 3 mmol), pyrrolidine (456 mg, 6.5 mmol) and TsOH (52 mg, 0.3 mmol) in PhH (10 cm^3) was placed in a round-bottomed flask (20 cm^3) fitted with a Dean–Stark apparatus, and heated under reflux for 20 h. After the solvent and excess pyrrolidine were removed *in vacuo*, the residual yellow oil contained an isomeric mixture of two enamines **20/21**.

Method A and B (Table 1): A solution of **4** (183 mg, 1.5 mmol), **20/21**, and 0.4 nm molecular sieves (150 mg) in PhH (9 cm^3) or a solution of troponimine **5** (203 mg, 1.5 mmol) and **20/21** was heated under reflux for the period indicated in Table 1. After the reaction was completed, the reaction mixture was concentrated, and the residual oil was purified by TLC on alumina (hexane–AcOEt 1 : 1) to give only tarry materials and the expected product was not obtained.

Method C and D (Table 1): A solution of **6** (299 mg, 1.5 mmol) or **7** (414 mg, 1.5 mmol), **20/21**, and Et_3N (202 mg, 2 mmol) in PhH (9 cm^3) was stirred at room temp. for the period indicated in Table 1. After the reaction was completed, the reaction mixture was concentrated and the residual oils were separated by TLC on alumina (hexane–AcOEt 1 : 1) to give **22**. The reaction conditions and the yields of the products are summarized in Table 1.

2,3-Dihydrocyclohepta[*b*]thieno[2,3-*d*]pyrrole 22. Purple oil; δ_H (90 MHz) 3.42 (2H, t, *J* 7.0, H-3), 3.85 (2H, t, *J* 7.0, H-2), 7.21–7.52 (3H, m, H, 6, 7, 8), 7.89 (1H, d, *J* 9.2, H-9), 8.18 (1H, d, *J* 8.8, H-5); *m*/*z* (rel. int.) 187 (M^+, 95), 149 (100%). Picrate: mp 183–185 °C (from CH_3CN) (decomp.) (Found: C, 49.7; H, 3.2; N, 12.6. $C_{17}H_{12}N_4O_7S$ requires C, 49.04; H, 2.91; N, 13.46%).

Dehydrogenation of 22

To a solution of **22** (400 mg, 2.1 mmol) in PhH (50 cm^3) was added activated MnO_2 (1.86 g, 21 mmol), and the mixture was stirred at room temp. for 24 h. After the reaction was completed, the reaction mixture was filtered and the filtrate was concentrated *in vacuo*, and the residual oil was purified by TLC on alumina (hexane–AcOEt 1 : 1) to give cyclohepta[*b*]-thieno[3,2-*d*]pyrrole **24** (324 mg, 82%): purple oil; δ_H (500 MHz) 7.59 (1H, d, *J* 5.2, H-3), 7.71 (1H, dd, *J* 9.5, 9.8, H-8), 7.83 (1H, dd, *J* 9.8, 9.8, H-7), 7.90 (1H, dd, *J* 9.8, 10.4, H-6), 7.95 (1H, d, *J* 5.2, H-2), 8.66 (1H, d, *J* 9.5, H-9), 8.76 (1H, d, *J* 10.4, H-5); *m*/*z* (rel. int.) 185 (M^+, 100%). Picrate: mp 93–97 °C (from CH_3CN) (decomp.) (Found: C, 49.3; H, 2.3; N, 13.2. $C_{17}H_{10}N_4O_7S$ requires C, 49.28; H, 2.43; N, 13.52%).

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