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Synthesis of 2-(4-Azulenyl)ethanamine Derivatives as a Nonbenzenoid Analog of Biogenic Amine

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2-(4-Azulenyl)ethanamine derivatives, nonbenzenoid analogs of the biologically active amine, were synthesized by the action of methyleneammonium salts on sodium 4-methylazulenide, sodium 4,6,8-trimethylazulenide, and sodium guaiazulenide. These compounds, as well as their hydrochlorides, were characterized by UV, IR, ^{1}H NMR, ^{13}C NMR, and MS data. The reaction of sodium guaiazulenide and *N*-ethylidenemethylamine also yielded the corresponding 2-(4-azulenyl)ethanamine derivatives, but the low yield of the product showed that the electrophilicity of azomethine carbon atom to 4-methylene carbanion was insufficient. The enzyme activity for some of those products was investigated. Negligible effect was found on prostaglandin 15-hydroxydehydrogenase, and considerable inhibition to cyclic AMP-phosphodiesterase, *in vitro*.

2-Phenylethanamine derivatives, together with their indole analogs, constitute an important class of biological active compounds related to biogenic amines.[1] In studying azulene analogs of biological active amines, we previously reported the synthesis of some acyl and alkyl derivatives of 2-(1-azulenyl)ethanamine by aminoethylation of azulene or guaiazulene with *N*-acylaziridines or with aziridinium salts, as well as the effect of those compounds on enzyme activity.[2]

Our study on azulene derivatives aminoethylated in the 5-membered ring of the azulene nucleus continued with those having aminoethyl side chains in the 7-membered ring. For this type of compounds we preliminarily reported the synthesis of 2-(4-azulenyl)ethanamine derivatives by the reaction of sodium guaiazulenide and methyleneammonium salts;[3] more details are given in this paper.

The present paper also deals with the synthesis of 2-(4-azulenyl)ethanamine derivatives by the action of *N*-methylenedimethylammonium iodide on sodium 4-methylazulenide or on sodium 4,6,8-trimethylazulenide.

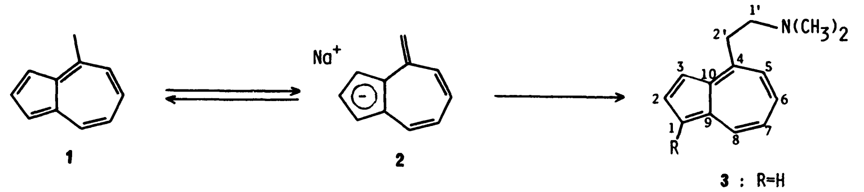
Results and Discussion

Sodium *N*-methylanilinide, used as the reagent, was conveniently prepared from sodium hydride and *N*-methylaniline in THF according to our modification.[4] This reagent reacted smoothly with 4-methylazulene (**1**) to form a reddish-orange solution of sodium 4-methylazulenide (**2**).[5] Next **2** was mixed with *N*-methylenedimethylammonium iodide[6] at *ca.* −80 °C, and left for 5 h to rise to room temperature.

From the hydrochloric acid extract of the reaction mixture, the intended *N*,*N*-dimethyl-2-(4-azulenyl)ethanamine, a major product, was isolated as its hydrochloride (**7**) (44%); this was easily converted to free amine (**3**) (90%) by the usual treatment with alkali. Both compounds (**3** and **7**) were characterized by spectral data.

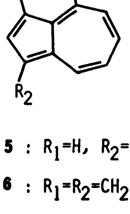
In this reaction, three by-products: **4** (7%), **5** (2%), and **6** (2%), were also obtained. **5** and **6** are already known to occur in the aminomethylation of **1** with *N*,*N*,*N*′,*N*′-tetramethylmethanediamine.[7] The attempted aminomethylation of **1** with *N*-methylenedimethylammonium iodide was also found to yield **5** (7%) and **6** (13%). Consequently, the formation of **5** and **6** as by-products may be reasonably explained by aminomethylation of **1**, which coexists in the solution of **2** at equilibrium and increases in its ratio after the addition of an excess of methyleneammonium salt. Quaternary salt of *N*-methylaniline might act as a proton source.

The assigned position of the dimethylaminomethyl group of the other product, **4**, was indicated by low-field shift of 8-proton (0.15 ppm) of **4** relative to **3** in ^{1}H NMR. This conclusion is consistent with the observation that a dimethylaminomethyl group gives

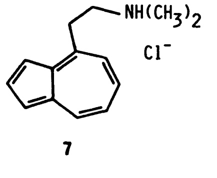


1 **2**

3 : R=H
4 : R=CH$_2$N(CH$_3$)$_2$



5 : R$_1$=H, R$_2$=CH$_2$N(CH$_3$)$_2$
6 : R$_1$=R$_2$=CH$_2$N(CH$_3$)$_2$



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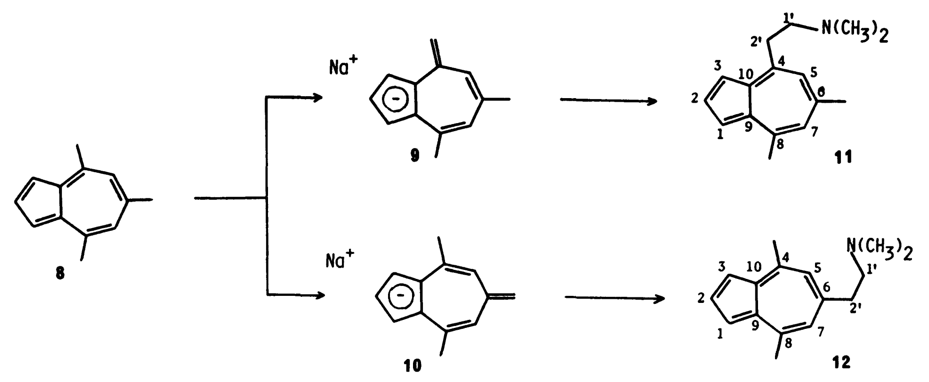

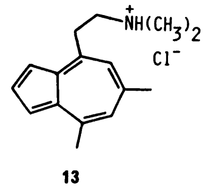

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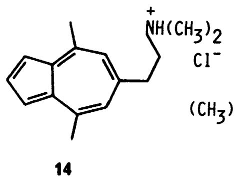

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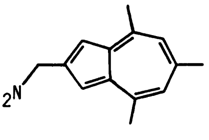

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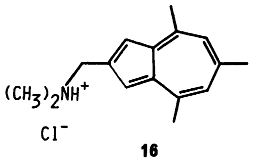

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rise a considerable low-field shift at *peri*-position, as is shown in 8-proton of **5** relative to **1** (0.31 ppm) and in 2′-methylene protons of **22** relative to **21** (0.38 ppm).

Moreover, the structure of **4** was established by the action of sodium *N*-methylanilinide on **5** leading to sodium 1-dimethylaminomethyl-4-methylazulenide, followed by the reaction of it with *N*-methylenedimethylammonium iodide to yield **4** (6%). This process, even if possible, could not be a major course of formation of **4** in the reaction of **2** and methyleneammonium salt, judging from the low yields of **5** from **2** and of **4** from **5**. Thus most of **4** may be formed from the main product **3** by successive aminomethylation after aminoethylation of **2**.

Reaction of 4,6,8-trimethylazulene and sodium *N*-methylanilinide at −15 °C is known to give rise to **9** selectively, though proton abstraction from both 4(8)- and 6-methyl group is possible for this compound at higher temperatures.[5] Sodium 4,6,8-trimethylazulenide was thus prepared at −15 °C and reacted with *N*-methylenedimethylammonium iodide, at first at *ca.* −80 °C, followed by gradual completion at room temperature.

Hydrochloric acid treatment of the reaction products afforded **13** (13%), **14** (15%), and **16** (7%), all of which regenerated the corresponding 2-aminoethyl (**11** and **12**) and aminomethyl derivatives (**15**) almost quantitatively when treated with alkali.

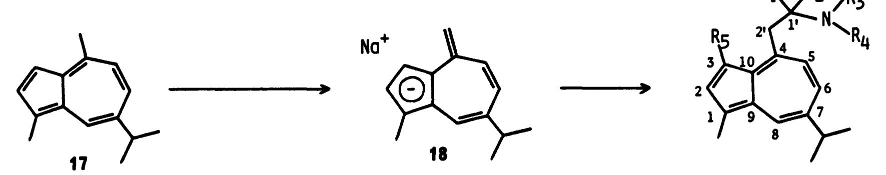
Formation of **12** in this reaction is inconsistent with the observation in Ref. 5, but the same type of product from **10** is also noted in sodium 4,6,8-trimethylazulenide, prepared in THF at −15 °C, when it was successively treated with carbon dioxide at −10 °C.[8] The present reaction, in which the sodium 4,6,8-trimethylazulenide formed is used continuously for the next step, is thought to involve equilibrated species **8**, **9**, and **10** in the reaction mixtures, since *N*-methylaniline coexists also. Thus, **9** formed at first at −15 °C may change into **10** *via* **8** in the following reaction with *N*-methylenedimethylammonium iodide to yield **12**. Another pathway of direct conversion from **9** to **10** would require an ionic-attack of the nucleophile on anion **9** and seems improbable.[8]

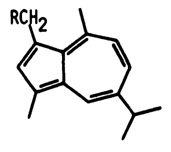
The yield ratio of **11** and **12** (46 : 54) is very close to that (45 : 55) of carbonation products at 4- and 6-methylene positions in sodium 4,6,8-trimethylazulenide prepared at ordinary temperature,[8] indicating that the equilibrium between **9** and **10** is faster than the reaction of those with methyleneammonium salt.

On the other hand, product **15** cannot be formed from **8**, because the electrophilic substitution of azulene is well known to occur at 1(3)-position,[9] and in fact, aminomethylation of **8** was found to yield 1-substituted and 1,3-disubstituted products.[10] Since the substitution at 2-position, along with that at 1(3)-position, is known in carbonation of azulenide anion of Meisenheimer type,[8] this product is though to be formed from **9** and/or **10** by aminomethylation in a similar manner. So far as we know, it is the first case in methyleneazulenide-type anion that the electrophilic substitution was observed in the 5-membered ring of azulenide anion. Moreover, this fact also suggests that **5** and **6** may arise, at least in part, from **2** in the former reaction of **2** and methyleneammonium salt.

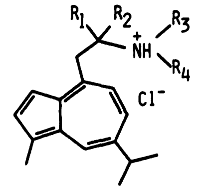
Similarly to the cases of **1** and **8**, **18** was prepared from **17** and allowed to react with some methyleneammonium salts.[3] The reaction of **18** and *N*-methylenedimethylammonium iodide was carried out as described above for **2** to give **21** (50%), **22** (7%), **19** (1%), and **20** (14%). By-products **20** and **22** may be produced by aminomethylation of **17** and/or **18**, or of **21**, as already discussed in cases of **1** and **8**. **19** is thought to be formed by nucleophilic attack of anilinide anion on the 3-methylene position of conjugate acid of **20** ($-CH_2-\overset{+}{N}H(CH_3)_2$), as described before.[3]

By virtually the same procedure as described above, the reaction of **18** with *N*-isopropylidenedimethylammonium perchlorate, *N*-isopropylidenepyrrolidinium perchlorate, or with *N*-(α-methylbenzylidene)pyrrolidinium perchlorate[11] at −20 °C or at room temperature yielded





19 : R=PhNHCH$_3$ (p)
20 : R=N(CH$_3$)$_2$



27: R$_1$=R$_2$=H, R$_3$=R$_4$=CH$_3$
28: R$_1$=R$_2$=CH$_3$, R$_3$=R$_4$=CH$_3$
29: R$_1$=R$_2$=CH$_3$, R$_3$=R$_4$=-(CH$_2$)$_4$-
30: R$_1$=CH$_3$, R$_2$=Ph, R$_3$=R$_4$=-(CH$_2$)$_4$-

21: R$_1$=R$_2$=R$_5$=H, R$_3$=R$_4$=CH$_3$
22: R$_1$=R$_2$=H, R$_3$=R$_4$=CH$_3$, R$_5$=CH$_2$N(CH$_3$)$_2$
23: R$_1$=R$_3$=R$_5$=H, R$_2$=R$_4$=CH$_3$
24: R$_1$=R$_2$=R$_3$=R$_4$=CH$_3$, R$_5$=H
25: R$_1$=R$_2$=CH$_3$, R$_3$=R$_4$=-(CH$_2$)$_4$-, R$_5$=H
26: R$_1$=CH$_3$, R$_2$=Ph, R$_3$=R$_4$=-(CH$_2$)$_4$-, R$_5$=H

TABLE 1. INHIBITION OF CYCLIC AMP-PHOSPHODIESTERASE (a) AND PROSTAGLANDIN 15-HYDROXYDEHYDROGENASE (b) BY 2-(4-AZULENYL)ETHANAMINE DERIVATIVES (ADDITION OF 20 μg cm^{-3} IN EACH)

Compound	Inhibition/%	
	a	b
21	31.7	0
22	39.7	0
24	49.2	4.1
25	45.3	9.2
26	26.4	10.3

the corresponding 2-(4-azulenyl)ethanamine derivatives **24** (64%), **25** (62%), and **26** (54%). No appreciable amount of by-product was found in these cases. Of these 2-aminoethyl derivatives, **21** and **24**—**26** were converted to crystalline hydrochlorides **27** (50%), **28** (65%), **29** (51%), and **30** (28%), respectively. Both free amines and hydrochlorides were characterized by spectral data.

To clarify the reactivity of **18** further, the reaction of **18** and *N*-ethylidenemethylamine[12] was also tried and found to yield the corresponding amine, **23** (8%). However, the low yield of **23** is though to show that the electrophilicity of azomethine carbon atom is rather insufficient to allow a smooth reaction of it with the methylene carbanion of **18**.

An additional investigation was undertaken on the effect of 2-(4-azulenyl)ethanamine derivatives (**21**—**26**) for enzyme activity, *in vitro*.[13] As is observed in Table 1, considerable activities are found in inhibitions of cyclic AMP-phosphodiesterase in all compounds and especially in **24** and **25**, though less active than *N*-butyryl-2-(5-isopropyl-3,8-dimethyl-1-azulenyl)ethanamine (69.9%).[2]

Different from the amide or primary amine derivatives of 2-(1-azulenyl)ethanamine previously reported,[2] these tertiary amine derivatives (**21**—**26**) had almost a negligible effect on prostaglandin 15-hydroxydehydrogenase. This observation well accords with that about tertiary amine derivatives of 2-(1-azulenyl)ethanamine, in which no appreciable effect was found on the inhibition by prostaglandin I$_2$ of ADP-induced aggregation of blood platelets.[14]

Experimental

All the melting points are uncorrected. Spectral data were recorded on the following instruments: UV, Hitachi 624 digital spectrometer with a Hitachi 056 recorder; IR, Hitachi 260-10 spectrometer; ^{1}H NMR, JEOL MH-100; ^{13}C NMR, JNM-FX 100; MS, JEOL-D300 at 70 eV.

Reaction of Sodium 4-Methylazulenide (2) and N-*Methylenedimethylammonium Iodide.* Under dry nitrogen, a stirred solution of sodium *N*-methylanilinide, prepared from 200 mg (5.1 mmol) of 61% sodium hydride and 1.81 g (16.9 mmol) of *N*-methylaniline in 20 cm^3 of THF according to our modified procedure,[4] was mixed with another solution of 710 mg (4.99 mmol) of 4-methylazulene (**1**)[15] in 5 cm^3 of THF over a period of 15 min, and stirring was continued for 30 min more (violet color changed to reddish orange). To the stirred solution of **3** thus obtained was added, under Dry Ice–acetone cooling, 2.00 g (10.8 mmol) of *N*-methylenedimethylammonium iodide over a period of 20 min (washed in with 5 cm^3 of THF); sitrring was continued for 1 h with Dry Ice -acetone cooling and then for 5 h more, during which period the reaction mixture was gradually brought to room temperature. A facile color change from reddish orange to violet was observed at *ca.* −20 °C. The reaction mixture was taken up into 200 cm^3 of benzene, washed with 50% potassium carbonate solution (100 cm^3×2), dried on sodium sulfate, and concentrated (reduced pressure) to give a violet oil. Successive alumina chromatography (elution with 9 : 1 benzene–ethyl acetate) of the oil gave 2.15 mg (0.3%) of unchanged 4-methylazulene and 637 mg of violet oil, which was again dissolved in 200 cm^3 of benzene, extracted with 1 mol dm^{-3} hydrochloric acid (100 cm^3×3), and the hydrochloric acid solution extracted with chloroform (100 cm^3×10). The chloroform solution was dried (sodium sulfate), concentrated (reduced pressure), and chromatographed on a silica-gel column (elution with 8 : 2 chloroform–methanol) to give 521 mg (44%) of **7** as violet crystals, mp 228—230 °C: UV (C$_2$H$_5$OH) 240 (log ε 4.41), 270 (sh, 4.55), 275 (sh, 4.66), 278 (4.68), 283 (4.67), 298 (3.78), 318 (sh, 3.48), 329 (3.62), 342 (3.72), 354 (3.24), 531 (sh, 2.51), 553 (sh, 2.59), 571 (2.65), 588 (sh, 2.61), 617 (2.57), 644 (sh, 2.33), and 677 nm (2.14); IR (CHCl$_3$) 2545, 2510, 2400, 2310 (NH^+), and 1192 cm^{-1} (C–N); ^1H NMR ($CDCl_3$) $\delta=2.44$ (6H, s, $N(CH_3)_2$), 2.90 (2H, m, 1′-H_2), 3.48 (2H, m, 2′-H_2), 6.96—7.58 (3H, m, 5-, 6-, and 7-H), 7.36 (1H, d, $J=4$ Hz, 1-H), 7.50 (1H, d, $J=4$ Hz, 3-H), 7.82 (1H, t, $J=4$ Hz, 2-H), and 8.28 (1H, d, $J=9$ Hz, 8-H).

The hydrochloric acid solution, after completion of chloroform extraction, was made alkaline by addition of ice-cooled 50% potassium carbonate solution, and extracted with benzene to give 449 mg of violet oil after removal of the solvent. Alumina chromatography of this oil with THF gave 19.6 mg (2%) of **5**, 29.7 mg (2%) of **6**, and 92.0 mg (7%) of **4** as violet oils in each case. **5** and **6** were identical with those in Ref. 7, as well as with authentic specimen obtained by the reaction of **1** and *N*-methylenedimethylammonium iodide, in UV, IR, and ^1H NMR. These compounds were also characterized with MS data. **5**: MS *m/e* (rel intensity) 199 (M^+; 18) and 155 ($M^+ - N(CH_3)_2$; 100). **6**: MS *m/e* (rel intensity) 256 (M^+; 17), 212 ($M^+ - N(CH_3)_2$; 23), and 167 ($M^+ - 2N(CH_3)_2 - H$; 100).

Product **4** was characterized as follows: UV (C_2H_5OH) 242 (log ε 4.28), 278 (sh, 4.49), 282 (4.54), 286 (4.53), 290 (sh, 4.49), 300 (sh, 3.98), 336 (3.55), 345 (3.64), 359 (3.38), 543 (sh, 2.48), 575 (2.76), 617 (2.51), and 677 nm (sh, 2.09); IR (CCl_4) 2870, 2775, 2720 ($N(CH_3)_2$), 2980, 2950, 2860, 1468, 1456, 1440, 1430, 1374 (CH_3 and CH_2), and 1040 cm^{-1} (C–N); ^1H NMR ($CDCl_3$) $\delta=2.25$ (6H, s, $N(CH_3)_2$), 2.35 (6H, s, $N(CH_3)_2$), 2.77 (2H, m, 1′-H_2), 3.39 (2H, m, 2′-H_2), 3.86 (2H, s, 1-CH_2), 7.04 (1H, t, $J=10$ Hz, 7-H), 7.18 (1H, d, $J=10$ Hz, 5-H), 7.43 (1H, d, $J=4$ Hz, 3-H), 7.47 (1H, m, 6-H), 7.78 (1H, d, $J=4$ Hz, 2-H), and 8.47 (1H, d, $J=9.5$ Hz, 8-H); MS *m/e* (rel intensity) 256 (M^+; 37), 212 ($M^+ - N(CH_3)_2$; 7), 198 ($M^+ - CH_2N(CH_3)_2$; 3), 154 ($M^+ - CH_2N(CH_3)_2 - N(CH_3)_2$; 20), and 58 ($(CH_3)_2NCH_2^+$; 100).

Found: C, 79.80; H, 9.35; N, 10.46%. Calcd for $C_{17}H_{24}N_2$: C, 79.64; H, 9.44; N, 10.93%.

In order to obtain **3** from **7**, **7** was dissolved in a mixed solvent of benzene–water (100 cm^3 each) and slowly treated with 200 cm^3 of 50% potassium carbonate solution under ice-cooling and stirring. The benzene layer was separated, the aqueous layer was extracted with benzene (30 $cm^3 \times 2$), and the combined benzene extract, after being dried (sodium sulfate) and concentrated (reduced pressure), was chromatographed over alumina (elution with 98 : 2 benzene–methanol) to give 126 mg (90%) of **3** as a violet oil: UV (C_2H_5OH) 240 (log ε 4.36), 265 (sh, 4.35), 270 (sh, 4.49), 275 (sh, 4.60), 278 (4.62), 283 (4.61), 298 (3.70), 317 (sh, 3.34), 328 (3.51), 342 (3.64), 354 (3.05), 530 (sh, 2.48), 550 (sh, 2.56), 568 (2.61), 587 (sh, 2.58), 615 (2.55), 642 (sh, 2.29), and 675 nm (2.12); IR (CCl_4) 2820, 2770, 2720 (NCH_3), 2980, 2945, 2860, 1456, 1440, 1362 (CH_3 and CH_2), 1045, and 1037 cm^{-1} (C–N); ^1H NMR ($CDCl_3$) $\delta=2.35$ (6H, s, $N(CH_3)_2$), 2.77 (2H, m, 1′-H_2), 3.40 (2H, m, 2′-H_2), 7.06 (1H, t, $J=10.5$ Hz, 7-H), 7.15 (1H, d, $J=10.5$ Hz, 5-H), 7.43 (1H, d, $J=4$ Hz, 1-H), 7.52 (1H, m, 6-H), 7.58 (1H, d, $J=4$ Hz, 3-H), 7.91 (1H, t, $J=4$ Hz, 2-H), and 8.33 (1H, d, $J=9.5$ Hz, 8-H); ^{13}C NMR ($CDCl_3$) $\delta=36.5$ (t, 2′-C), 45.1 (q, $N(CH_3)_2$), 60.6 (t, 1′-C), 115.1 (d, 3-C), 118.8 (d, 1-C), 121.5 (d, 7-C), 125.8 (d, 5-C), 135.3 (d, 2-C), 136.3 (d, 6-C), 136.7 (d, 8-C), 137.4 (s, 10-C), 139.9 (s, 9-C), and 148.8 (s, 4-C) [*cf.* 4-methylazulene in Ref. 16][16)]; MS *m/e* (rel intensity) 199 (M^+; 20), 141 ($M^+ - (CH_3)_2NCH_2$; 3), and 58 ($(CH_3)_2NCH_2^+$; 100).

Found: C, 84.34; H, 8.51; N, 7.07%. Calcd for $C_{14}H_{17}N$: C, 84.37; H, 8.60; N, 7.03%.

*Reaction of 4-Methylazulene (**1**) and* N-*Methylenedimethylammonium Iodide.* To a stirred solution of 300 mg (2.11 mmol) of 4-methylazulene in 5 cm^3 of dry dichloromethane was added 600 mg (3.24 mmol) of *N*-methylenedimethylammonium iodide, and the suspension was stirred for 43 h. The reaction mixture was diluted with 100 cm^3 of water, made alkaline by addition of 50% potassium carbonate solution, and extracted with chloroform (60 $cm^3 \times 3$). The chloroform extract was dried (sodium sulfate), concentrated (reduced pressure), and taken up into 100 cm^3 of benzene. This benzene solution was extracted with 1 mol dm^{-3} hydrochloric acid (35 $cm^3 \times 3$), and the hydrochloric acid solution was extracted with chloroform (50 $cm^3 \times 4$). The chloroform extract, after being dried (sodium sulfate) and concentrated (reduced pressure), was chromatographed over silica gel (elution with 8 : 2 chloroform–methanol) to give 37.0 mg (7%) of hydrochloride of **5** as dark violet crystals, mp 177—179 °C: UV (C_2H_5OH) 241 (log ε 4.42), 271 (sh, 4.47), 277 (sh, 4.62) 281 (4.67), 286 (4.66), 290 (sh, 4.57), 301 (3.98), 318 (sh, 3.45), 332 (3.60), 341 (3.68), 353 (3.40), 550 (2.70), 584 (sh, 2.66), 617 (sh, 2.45), 643 (2.28), and 680 nm (1.72); IR ($CHCl_3$) 2650, 2550, 2500, 2400, 2325 (NH^+), and 1195 cm^{-1} (C–N); ^1H NMR ($CDCl_3$) $\delta=2.74$ (6H, s, $N(CH_3)_2$), 3.02 (3H, s, 4-CH_3), 4.70 (2H, s, CH_2), 6.54 (1H, broad s, NH), 7.48 (1H, t, $J=10$ Hz, 7-H), 7.53 (1H, d, $J=10$ Hz, 5-H), 7.68 (1H, d, $J=4$ Hz, 3-H), 7.92 (1H, t, $J=10$ Hz, 6-H), 8.34 (1H, d, $J=4$ Hz, 2-H), and 8.90 (1H, d, $J=10$ Hz, 8-H).

The hydrochloric acid layer, after completion of chloroform extraction, was made alkaline by addition of 200 cm^3 of 50% potassium carbonate solution, and extracted with benzene (50 $cm^3 \times 3$). Benzene extract, after removal of the solvent (reduced pressure), was submitted to alumina chromatography (elution with 3 : 1 benzene–THF) to afford 68.0 mg (13%) of **6**, identical with that of Ref. 7 and the authentic specimen (described above) in its UV, IR, and ^1H NMR spectra.

In order to obtain **5**, its hydrochloride was suspended in 80 cm^3 of benzene and slowly mixed with 200 cm^3 of ice-cooled 50% potassium carbonate solution. This mixture was worked up as described for **3** from **7** to give, without chromatographic separation, 17.9 mg (90%) of **5**, identical with that of Ref. 7 and the authentic specimen (described above) in its UV, IR, and ^1H NMR spectra.

Reaction of Sodium 1-Dimethylaminomethyl-4-methylazulenide and N-*Methylenedimethylammonium Iodide.* To a stirred solution of 0.114 mmol of sodium *N*-methylanilinide in 4 cm^3 of THF was added, under dry nitrogen, another solution of 21.8 mg (0.110 mmol) of **5** in 1 cm^3 of THF during a period of 15 min, and then, under Dry Ice–acetone cooling, 30 mg (0.162 mmol) of *N*-methylenedimethylammonium iodide (washed in with 1 cm^3 of THF). Stirring was continued at *ca.* −80 °C for 1 h and then 5 h; after the first hour the reaction mixture was gradually brought to room temperature. The reaction mixture was taken up into 20 cm^3 of benzene and extracted with 1 mol dm^{-3} hydrochloric acid (20 $cm^3 \times 3$). The hydrochloric acid extract was washed with benzene (20 $cm^3 \times 3$), made alkaline by addition of 100 cm^3 of ice-cooled 50% potassium carbonate solution, and extracted with benzene (20 $cm^3 \times 3$) to give 19.6 mg of brown oil after removal of the solvent (reduced pressure). Preparative TLC on an alumina sheet (3 : 1 benzene–THF) of the oil afforded 0.56 mg (3%) of unchanged **5** and 1.76 mg (6%) of **4**, identical with authentic specimen in TLC, UV, and IR results.

Reaction of Sodium 4,6,8-Trimethylazulenide and N-*Methylenedimethylammonium Iodide.* Under dry nitrogen, a stirred solution of 5.1 mmol of sodium *N*-methylanilinide in 20 cm^3 of THF was mixed at −15 °C with another solution of 850 mg (4.99 mmol) of **8** in 5 cm^3 of THF (violet color changed to orange), and then, under Dry Ice–acetone cooling, with 2.00 g (10.8 mmol) of *N*-methylenedimethylammonium iodide (washed in with 5 cm^3 of THF). The suspension was stirred for 1 h at *ca.* −80 °C and for 5 h more with a gradual rising of the temperature. The reaction mixture was worked up as described in **2** to give a violet oil, which was taken up into 200 cm^3 of benzene, extracted with 1 mol dm^{-3} hydrochloric acid (100 $cm^3 \times 3$); the hydrochloric acid layer was extracted with chloroform (100 $cm^3 \times 6$). The benzene solution, after being dried (sodium sulfate) and concentrated (reduced pressure), was chromatographed on a silica-gel column with hexane to afford 220 mg (26%) of unchanged **8**. The chloroform extract was also dried (sodium sulfate), concentrated (reduced pressure), and submitted to silica gel chromatography (elution with 8 : 2 chloroform–methanol) to allow separation into three fractions.

From the first eluate, 174 mg (13%) of **13** was obtained as a violet oil; UV (C_2H_5OH) 244 (log ε 4.48), 270 (sh, 4.32), 275 (sh, 4.50), 281 (sh, 4.67), 285 (4.73), 294 (sh, 6.67), 305 (sh, 4.00), 328 (sh, 3.62), 334 (3.70), 343 (3.74), 348 (3.80), 359 (sh, 2.73), 547 (2.78), 565 (sh, 2.76), 580 (sh, 2.73), and 635 nm (sh, 2.31); IR ($CHCl_3$) 2500, 2400, 2360, 2325 (NH^+), and 1195 cm^{-1} (C–N); ^1H NMR ($CDCl_3$) δ=2.40 (6H, s, $N(CH_3)_2$), 2.63 (3H, s, 6-CH_3), 2.84 (2H, m, 1′-H_2), 2.86 (3H, s, 8-CH_3), 3.42 (2H, m, 2′-H_2), 7.13 (1H, s, 7-H), 7.16 (1H, s, 5-H), 7.48 (1H, q, J=4 and 1.8 Hz, 1-H), 7.58 (1H, q, J=4 and 1.8 Hz, 3-H), and 7.80 (1H, t, J=4 Hz, 2-H).

From the second eluate, 201 mg (15%) of **14** was obtained as violet crystals; these showed no certain melting point but decomposed above 200 °C: UV (C_2H_5OH) 245 (log ε 4.43), 270 (sh, 4.26), 275 (sh, 4.46), 281 (sh, 4.63), 285 (4.69), 294 (sh, 4.61), 306 (sh, 3.90), 327 (sh, 3.69), 333 (3.75), 342 (sh, 3.78), 348 (3.84), 520 (sh, 2.53), 555 (2.64), 575 (sh, 2.61), 592 (sh, 2.56), and 650 nm (sh, 2.09); IR ($CHCl_3$) 2550, 2510, 2450, 2390, 2355, 2330, 2280 (NH^+), and 1195 cm^{-1} (C–N); ^1H NMR (CD_3OD) δ=2.88 (6H, s, $N(CH_3)_2$), 2.90 (6H, s, 4- and 8-CH_3), 3.33 (4H, m, 1′- and 2′-H_2), 7.13 (2H, s, 5- and 7-H), 7.36 (2H, d, J=4 Hz, 1- and 3-H), and 7.66 (1H, t, J=4 Hz, 2-H).

From the last fraction, 85.4 mg (7%) of **16** was obtained as violet crystals, mp 41—45 °C: UV (C_2H_5OH) 246 (log ε 4.53), 287 (4.79), 293 (4.79), 335 (4.00), 351 (4.04), 536 (2.72), 560 (sh, 2.70), 615 (sh, 2.33), and 624 nm (sh, 2.27); IR ($CHCl_3$) 2500, 2400, 2350, 2330 (NH^+), and 1190 cm^{-1} (C–N); ^1H NMR ($CDCl_3$) δ=2.17 (6H, s, $N(CH_3)_2$), 2.61 (3H, s, 6-CH_3), 2.86 (6H, s, 4- and 8-CH_3), 3.83 (2H, s, CH_2), 4.48 (1H, broad s, NH^+), 7.08 (2H, s, 5- and 7-H), and 7.33 (2H, s, 1- and 3-H).

In order to obtain **11** from **13**, a solution of 51.6 mg (0.196 mmol) of **13** in 70 cm^3 of benzene–methanol (98 : 2) was mixed dropwise with 200 cm^3 of ice-cooled 50% potassium carbonate solution. After the mixture was worked up in the usual manner as described before, 44.5 mg (100%) of **11** was obtained as a violet oil: UV (C_2H_5OH) 244 (log ε 4.43), 271 (sh, 4.31), 275 (sh, 4.45), 281 (sh, 4.61), 285 (4.67), 290 (4.67), 294 (sh, 4.61), 305 (sh, 3.93), 322 (sh, 3.45), 328 (sh, 3.51), 334 (3.59), 344 (sh, 3.64), 349 (3.71), 359 (sh, 3.06), 547 (2.71), 564 (sh, 2.69), 581 (sh, 2.65), and 637 nm (sh, 2.20); IR (CCl_4) 2825, 2775, 2725 ($N(CH_3)_2$), 2980, 2950, 2860, 1467, 1458, 1438, 1372 (CH_3 and CH_2), 1045, and 1040 cm^{-1} (C–N); ^1H NMR ($CDCl_3$) δ=2.37 (6H, s, $N(CH_3)_2$), 2.60 (3H, s, 6-CH_3), 2.78 (2H, m, 1′-H_2), 2.84 (3H, s, 8-CH_3), 3.38 (2H, m, 2′-H_2), 7.06 (1H, s, 7-H), 7.09 (1H, s, 5-H), 7.40 (1H, q, J=4 and 1.5 Hz, 1-H), 7.50 (1H, q, J=4 and 1.5 Hz, 3-H), and 7.73 (1H, t, J=4 Hz, 2-H); ^{13}C NMR ($CDCl_3$) δ=25.0 (q, 8-CH_3), 28.7 (q, 6-CH_3), 37.3 (t, 2′-C), 45.2 (q, $N(CH_3)_2$), 61.1 (t, 1′-C), 115.5 (d, 3-C), 116.2 (d, 1-C), 126.7 (d, 5-C), 127.0 (d, 7-C), 132.6 (d, 2-C), 136.0 (s, 9- and 10-C), 145.4 (s, 8-C), 146.3 (s, 6-C), and 147.8 (s, 4-C) [*cf.* 4,6,8-trimethylazulene in Ref. 16][16]; MS *m/e* (rel intensity) 227 (M^+; 12), 169 ($M^+-(CH_3)_2NCH_2$; 3), and 58 ($(CH_3)_2NCH_2^+$; 100).

Found: C, 84.23; H, 9.21; N, 6.04%. Calcd for $C_{16}H_{21}N$: C, 84.53; H, 9.31; N, 6.16%.

Similar treatment of 53.4 mg (0.202 mmol) of **14** gave 43.9 mg (0.202 mmol) of **12** as a violet oil: UV (C_2H_5OH) 244 (log ε 4.51), 275 (sh, 4.53), 281 (4.68), 284 (4.74), 289 (4.73), 294 (sh, 4.66), 304 (sh, 4.05), 322 (sh, 3.50), 328 (sh, 3.57), 333 (3.64), 343 (sh, 3.69), 348 (3.75), 548 (2.69), 562 (sh, 2.67), 584 (sh, 2.62), and 638 nm (sh, 2.18); IR (CCl_4) 2825, 2780, 2725 ($N(CH_3)_2$), 2985, 2955, 1470, 1460, 1435, 1375 (CH_3 and CH_2), 1050, and 1042 cm^{-1} (C–N); ^1H NMR ($CDCl_3$) δ=2.32 (6H, s, $N(CH_3)_2$), 2.62 (2H, m, 1′-H_2), 2.88 (6H, s, 4- and 8-CH_3), 2.94 (2H, m, 2′-H_2), 7.08 (2H, s, 5- and 7-H), 7.42 (2H, d, J=4 Hz, 1- and 3-H), and 7.74 (1H, t, J=4 Hz, 2-H); ^{13}C NMR ($CDCl_3$) δ=25.0 (q, 4- and 8-CH_3), 41.2 (t, 2′-C), 45.4 (q, $N(CH_3)_2$), 62.4 (t, 1′-C), 116.0 (d, 1- and 3-C), 126.8 (d, 5- and 7-C), 132.7 (d, 2-C), 136.2 (s, 9- and 10-C), 145.7 (s, 4- and 8-C), and 148.2 (s, 6-C); MS *m/e* (rel intensity) 227 (M^+; 5), 169 ($M^+-(CH_3)_2NCH_2$; 1), and 58 ($(CH_3)_2NCH_2^+$; 100).

Found: C, 84.27; H, 9.03; N, 6.11%. Calcd for $C_{16}H_{21}N$: C, 84.53; H, 9.31; N, 6.16%.

Similar treatment of 37.9 mg (0.144 mmol) of **16** afforded 32.8 mg (100%) of **15** as a violet oil: UV (C_2H_5OH) 246 (log ε 5.40), 287 (5.72), 293 (5.72), 335 (4.55), 351 (4.68), 537 (2.65), 560 (sh, 2.62), and 616 nm (sh, 2.20); IR (CCl_4) 2820, 2775, 2730 ($N(CH_3)_2$), 2980, 2945, 2930, 2860, 1455, 1445, 1376, 1357 (CH_3 and CH_2), 1040, and 1030 cm^{-1} (C–N); ^1H NMR ($CDCl_3$) δ=2.35 (6H, s, $N(CH_3)_2$), 2.61 (3H, s, 6-CH_3), 2.87 (6H, s, 4- and 8-CH_3), 3.82 (2H, s, CH_2), 7.12 (2H, s, 5- and 7-H), and 7.37 (2H, s, 1- and 3-H); MS *m/e* (rel intensity) 227 (M^+; 12), 184 ($M^+ - CH_3NCH_2$; 100), 183 ($M^+-(CH_3)_2N$; 28), 169 ($M^+-(CH_3)_2NCH_2$; 41), and 58 ($(CH_3)_2NCH_2^+$; 13).

Found: C, 84.59; H, 9.30; N, 5.94%. Calcd for $C_{16}H_{21}N$: C, 84.53; H, 9.31; N, 6.16%.

*Reaction of Sodium Guaiazulenide (**18**) with Methyleneammonium Salts or with* N-*Ethylidenemethylamine.* *A) With* N-*Methylenedimethylammonium Iodide*: To a stirred solution of 10 mmol of sodium guaiazulenide (**18**) in 30 cm^3 of THF [from 440 mg (10.2 mmol) of sodium hydride, 3.62 g (33.8 mmol) of *N*-methylaniline, and 1.99 g (10.0 mmol) of guaiazulene, as described in the preparation of **2**], under dry nitrogen and with Dry Ice–acetone cooling, was added 3.70 g (20 mmol) of *N*-methylenedimethylammonium iodide over a period of 20 min (washed with 5 cm^3 of THF), and the suspension was stirred for 1 h at *ca.* −80 °C and for an additional 5 h with a gradual elevation of the temperature. The reaction mixture, after being worked up as described above for **2**, was chromatographed over alumina (elution with 9 : 1 hexane–ethyl acetate) and separated into four fractions. Further elution with ethanol afforded one more fraction.

Rechromatography of the first fraction on a silica-gel column with hexane gave 30.2 mg (2%) of unchanged guaiazulene. Successively the solvent was changed into benzene to give 32.2 mg (1%) of **19** as a blue oil: UV (C_2H_5OH) 248 (log ε 4.44), 283 (sh, 4.54), 290 (4.60), 307 (4.22), 341 (sh, 3.58), 354(3.73), 371 (3.63), 584 (sh, 2.49), 625 (2.58), 676 (sh, 2.49), and 748 (sh, 2.05); IR (CCl_4) 3440 (NH), 1375 and 1360 cm^{-1} (CH_3); ^1H NMR ($CDCl_3$)[18] δ=1.32 (6H, d, J=7 Hz, $CH(C\underline{H}_3)_2$), 2.60 (3H, s, 1-CH_3), 2.70 (3H, s, NCH_3), 2.84 (3H, s, 4-CH_3), 2.98 (1H, m, J=7 Hz, $C\underline{H}(CH_3)_2$), 3.34 (1H, broad s, NH), 4.48 (2H, s, CH_2), 6.48 (2H, d, J=8 Hz, 3″- and 5″-H), 6.76 (1H, d, J=10 Hz, 5-H), 6.88 (2H, d, J=8 Hz, 2″- and 6″-H), 7.22 (1H, q, J=10 and 2 Hz, 6-H), 7.40 (1H, s, 2-H), and 8.08 (1H, d, J=2 Hz, 8-H); MS *m/e* (rel intensity) 317 (M^+; 100), 302 (M^+-CH_3; 57), and 120 ($CH_3NHC_6H_4CH_2^+$; 29).

Found: C, 86.73; H, 8.53; N, 4.30%. Calcd for $C_{23}H_{27}N$:

C, 87.02; H, 8.57; N, 4.41%.

Rechromatography of the second fraction on an alumina column (elution with 98 : 2 hexane–ethyl acetate) gave 346 mg (14%) of **20** as blue crystals, mp 37—38 °C [Ref. 10; blue oil]:[10] UV (cyclohexane) 215 (log ε 4.02), 247 (4.28), 282 (sh, 4.49), 288 (4.56), 292 (4.58), 305 (4.14), 339 (sh, 3.54), 347 (sh, 3.60), 353 (3.73), 371 (3.73), 568 (sh, 2.50), 595 (sh, 2.58), 613 (2.61), 640 (sh, 2.59), 667 (2.53), 708 (sh, 2.22), and 741 nm (2.08) [Ref. 10 (hexane); 613 (2.62), 662 (2.52), 714 (2.18), and 736 nm (2.04)]; IR (CCl_4) 2820, 2775, 2720 ($N(CH_3)_2$), 1460, 1435, and 1420 cm^{-1} $(CH)_2$; ^1H NMR ($CDCl_3$) δ=1.30 (6H, d, *J*=7 Hz, $CH(C\underline{H}_3)_2$), 2.22 (6H, s, $N(CH_3)_2$), 2.60 (3H, s, 1-CH_3), 2.99 (1H, m, *J*=7 Hz, $C\underline{H}(CH_3)_2$) 3.12 (3H, s, 4-CH_3), 3.80 (2H, s, 3-CH_2), 6.90 (1H, d, *J*=11 Hz, 5-H), 7.26 (1H, q, *J*=11 and 2 Hz, 6-H), 7.48 (1H, s, 2-H), and 8.10 (1H, d, *J*=2 Hz, 8-H); MS *m/e* (rel intensity) 255 (M^+; 49) and 211 ($M^+-N(CH_3)_2$; 100).

Rechromatography of the third fraction on an alumina column (elution with 9 : 1 hexane–ethyl acetate) yielded 1.28 g (50%) of **21** as a blue oil: UV (C_2H_5OH) 217 (log ε 4.01), 245 (4.35), 280 (sh, 4.52), 284 (4.57), 288 (4.56), 302 (3.98), 327 (sh, 3.23), 338 (sh, 3.43), 350 (3.60), 367 (3.45), 563 (sh, 2.53), 585 (sh, 2.60), 607 (2.65), 632 (sh, 2.61), 654 (2.58), and 725 nm (2.16); IR (CCl_4) 2820, 2772 (NCH_3), 2964, 2864, 1468, 1445, 1424, 1391, and 1373 cm^{-1} (CH_3 and CH_2); ^1H NMR ($CDCl_3$) δ=1.31 (6H, d, *J*=7 Hz, $CH(C\underline{H}_3)_2$), 2.28 (6H, s, $N(CH_3)_2$), 2.66 (3H, s, 1-CH_3), 2.76 (2H, m, 1′-H_2), 2.98 (1H, m, $C\underline{H}(CH_3)_2$), 3.30 (2H, m, 2′-H_2), 6.98 (1H, d, *J*=10 Hz, 5-H), 7.36 (1H, q, *J*=10 and 1.6 Hz, 6-H), 7.40 (1H, d, *J*=4 Hz, 3-H), 7.68 (1H, d, *J*=4 Hz, 2-H), and 8.26 (1H, d, *J*=1.6 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ=12.9 (q, 1-CH_3), 24.7 (q, $CH(\underline{C}H_3)_2$), 36.3 (t, 2′-C), 38.1 (d, $\underline{C}H(CH_3)_2$), 45.2 (q, $N(\underline{C}H_3)_2$), 60.7 (t, 1′-C), 112.2 (d, 3-C), 124.7 (d, 5-C), 125.0 (s, 1-C), 133.0 (d, 8-C), 135.0 (d, 6-C), 136.0 (s, 10-C), 136.4 (d, 2-C), 137.3 (s, 9-C), 139.6 (s, 7-C), and 146.4 (s, 4-C) [*cf.* *S*-guaiazulene in Ref. 17][17]; MS *m/e* (rel intensity) 255 (M^+; 100), 211 ($M^+-(CH_3)_2N$; 6), and 197 ($M^+-(CH_3)_2NCH_2$; 6).

Found: C, 84.47; H, 9.61; N, 5.61%. Calcd for $C_{18}H_{25}N$: C, 84.65; H, 9.87; N, 5.48%.

The combined fourth and ethanol fractions were chromatographed on an alumina column (elution with 8 : 2 benzene–ethyl acetate) to afford 218 mg (7%) of **22** as dark blue prisms, mp 66—68 °C; UV (C_2H_5OH) 217 (sh, ε 4.09), 247 (4.34), 289 (4.56), 304 (sh, 4.12), 342 (sh, 3.61), 353 (3.72), 372 (3.69), 407 (sh, 2.09), 573 (sh, 2.55), 609 (2.64), 653 (sh, 2.57), and 727 nm (sh, 2.13); IR (CCl_4) 2820, 2770 (NCH_3), 2968, 2865, 1460, 1440, 1430, 1420, 1385, and 1370 cm^{-1} (CH_3 and CH_2); ^1H NMR ($CDCl_3$) δ=1.34 (6H, d, *J*=7 Hz, $CH(C\underline{H}_3)_2$), 2.23 (6H, s, $N(CH_3)_2$), 2.36 (6H, s, $N(CH_3)_2$), 2.61 (3H, s, 1-CH_3), 2.72 (2H, m, 1′-H_2), 3.02 (1H, m, *J*=7 Hz, $C\underline{H}(CH_3)_2$), 3.68 (2H, m, 2′-H_2), 3.84 (2H, s, 3-CH_2), 7.03 (1H, d, *J*=11 Hz, 5-H), 7.38 (1H, q, *J*=11 and 2 Hz, 6-H), 7.56 (1H, s, 2-H), and 8.16 (1H, d, *J*=2 Hz, 8-H); MS *m/e* (rel intensity) 312 (M^+; 3), 254 ($M^+-(CH_3)_2NCH_2$; 9), and 58 ($(CH_3)_2NCH_2^+$; 100).

Found: C, 80.35; H, 10.10; N, 8.81%. Calcd for $C_{21}H_{32}N_2$: C, 80.71; H, 10.32; N, 8.96%.

B) With N-*Isopropylidenedimethylammonium Perchlorate*: Reaction of 10 mmol of **18** and 3.71 g (20.0 mmol) of *N*-isopropylidenedimethylammonium perchlorate[11] was carried out in a manner similar to *A* except that the reagents were reacted at room temperature for 2 h. Chromatography of the reaction mixture on an alumina column (elution with 8 : 2 benzene–chloroform) gave 746 mg of blue oil, which on rechromatography over silica gel with hexane afforded 597 mg (30%) of unchanged **17**. Successive blue eluate gave 2.11 g of blue oil, which was also rechromatographed over alumina (elution with 9 : 1 hexane–ethyl acetate) to give 1.81 g (64%) of **24** as a blue oil: UV (C_2H_5OH) 247 (log ε 4.29), 282 (sh, 4.51), 285 (4.54), 289 (4.53), 305 (sh, 3.94), 340 (sh, 3.55), 351 (3.66), 368 (3.52), 566 (sh, 2.53), 588 (sh, 2.60), 609 (2.66), 634 (sh, 2.61), 659 (2.58), and 728 nm (2.14); IR (CCl_4) 2820, 2780, 2730 (NCH_3), 2960, 2925, 2870, 1460, 1385, 1365 (CH_3 and CH_2), and 1145 cm^{-1} (C–N); ^1H NMR δ=1.01 (6H, s, 1′-$C(CH_3)_2$), 1.29 (6H, d, *J*=7 Hz, $CH(C\underline{H}_3)_2$), 2.44 (6H, s, $N(CH_3)_2$), 2.64 (3H, s, 1-CH_3), 3.05 (1H, m, *J*=7 Hz, $C\underline{H}(CH_3)_2$), 3.30 (2H, s, 2′-H_2), 7.08 (1H, d, *J*=11 Hz, 5-H), 7.40 (1H, d, *J*=4 Hz, 3-H), 7.46 (1H, q, *J*=11 and 2 Hz, 6-H), 7.70 (1H, d, *J*=4 Hz, 2-H), and 8.24 (1H, d, *J*=2.0 Hz, 8-H); MS *m/e* (rel intensity) 283 (M^+; 0.7), 198 ($M^+-C_5H_{11}N$; 15), and 86 ($C_5H_{12}N^+$; 100).

Found: C, 84.64; H, 10.24; N, 4.41%. Calcd for $C_{20}H_{29}N$: C, 84.75; H, 10.31; N, 4.94%.

C) With N-*Isopropylidenepyrrolidinium Perchlorate*: Reaction of 10 mmol of **18** and 4.25 g (20.1 mmol) of *N*-isopropylidenepyrrolidinium perchlorate[11] was carried out in a manner similar to *A*, except that the reaction mixture was stirred for 3 h at −20 °C (ice salt mixture) and an additional 1 h at room temperature. Elution of the reaction mixture on an alumina column with hexane gave 156 mg (8%) of unchanged **17**. Then the solvent was changed into hexane–ethyl acetate (9 : 1) to give 1.93 g (62%) of **25** as a blue oil: UV (C_2H_5OH) 218 (sh, log ε 4.00), 246 (4.31), 275 (sh, 4.37), 281 (sh, 4.47), 285 (4.50), 289 (4.48), 304 (sh, 3.92), 568 (sh, 2.49), 592 (2.57), 611 (2.61), 634 (sh, 2.58), 661 (2.55), and 729 nm (2.11); IR (CCl_4) 2968, 2940, 2916, 2875, 2814, 1468, 1453, 1440, 1423, 1390, and 1370 cm^{-1} (CH_3 and CH_2); ^1H NMR ($CDCl_3$)[18] δ=1.06 (6H, s, 1′-$C(CH_3)_2$), 1.31 (6H, d, *J*=7 Hz, $CH(C\underline{H}_3)_2$), 1.75 (4H, m, *J*=6 Hz, β- and γ-H_2), 2.64 (3H, s, 1-CH_3), 2.79 (4H, m, *J*=6 Hz, α- and δ-H_2), 3.00 (1H, m, *J*=7 Hz, $C\underline{H}(CH_3)_2$), 3.32 (2H, s, 2′-H_2), 7.01 (1H, d, *J*=11 Hz, 5-H), 7.32 (1H, q, *J*=11 and 2 Hz, 6-H), 7.36 (1H, d, *J*=4 Hz, 3-H), 7.60 (1H, d, *J*=4 Hz, 2-H), and 8.16 (1H, d, *J*=2 Hz, 8-H); MS *m/e* (rel intensity) 309 (M^+; 3), 197 ($M^+-(CH_3)_2CNC_4H_8$; 4), 112 ($C_4H_8NC(CH_3)_2^+$; 100), and 70 ($C_4H_8N^+$; 37).

Found: C, 85.56; H, 10.09; N, 4.24%. Calcd for $C_{22}H_{31}N$: C, 85.38; H, 10.10; N, 4.53%.

D) With N-*(α-Methylbenzylidene)pyrrolidinium Perchlorate*: Reaction of 10 mmol of **18** and 5.00 g (18.3 mmol) of *N*-(α-methylbenzylidene)pyrrolidinium perchlorate was carried out in a manner similar to *C*. Elution of the reaction mixture on a silica-gel column with hexane afforded 399 mg (20%) of unchanged **17**. Then the solvent was changed into benzene–methanol (98 : 2) to give 2.02 g (54%) of **26** as a blue oil: UV (C_2H_5OH) 247 (log ε 4.32), 286 (4.51), 290 (sh, 4.49), 304 (sh, 3.93), 327 (sh, 3.40), 341 (sh, 3.51), 351 (3.61), 368 (3.50), 415 (2.27), 435 (2.26), 566 (sh, 2.49), 529 (sh, 2.62), 633 (sh, 2.58), 658 (2.55), and 730 nm (2.13); IR (CCl_4) 3110, 3090, 3070, 3035 (aromatic CH), 2975, 2880, 1465, 1450, 1440, 1423, 1390, 1380, 1370, and 1368 cm^{-1} (CH_3 and CH_2); ^1H NMR ($CDCl_3$)[18] δ=1.23 (6H, d, *J*=7 Hz, $CH(C\underline{H}_3)_2$), 1.24 (3H, s, 1′-$C(CH_3)$), 1.74 (4H, m, β- and γ-H_2), 2.60 (3H, s, 1-CH_3), 2.70 (4H, t, *J*=6 Hz, α- and δ-H_2), 2.90 (1H, m, *J*=7 Hz, $C\underline{H}(CH_3)_2$), 3.31 (1H, d, *J*=12.5 Hz, 2′-H), 4.01 (1H, d, *J*=12.5 Hz, 2′-H), 6.03 (1H, d, *J*=11 Hz, 5-H), 6.85 (1H, q, *J*=11 and 2 Hz, 6-H), 7.10—7.38 (6H, m, 3-H and Ph), 7.52 (1H, d, *J*=4 Hz, 2-H), and 8.04 (1H, d, *J*=2 Hz, 8-H); ^{13}C NMR ($CDCl_3$)[18] δ=13.0 (1-CH_3), 14.3 (1′-$C(\underline{C}H_3)$), 24.1 (β- and γ-C), 24.6 ($CH(\underline{C}H_3)_2$), 37.9 ($\underline{C}H(CH_3)_2$), 46.1 (α- and δ-C), 49.7 (2′-C), 63.3 (1′-C), 113.1 (3-C), 124.4 (5-C), 126.2 (1-C), 126.7 (4″-C), 127.5 (2″-, 3″-, 5″-, and 6″-C), 132.3 (8-C), 133.5 (6-C), 135.6 (2-C), 136.1 (10-C), 139.0 (9-C), 139.7 (7-C), 144.9 (1″-C), and 146.2 (4-C); MS *m/e* (rel intensity) 371 (M^+; 2), 174 ($C_6H_5C(CH_3)NC_4H_8^+$; 100), and 70 ($C_4H_8N^+$; 4).

Found: C, 87.17; H, 8.67; N, 3.35%. Calcd for $C_{27}H_{33}N$: C, 87.28; H, 8.95; N, 3.77%.

E) With N-*Ethylidenemethylamine*: Reaction of 10 mmol of **18** and 3.0 cm^3 (40 mmol) of *N*-ethylidenemethylamine was carried out as described in *B*. Chromatography of the reaction mixture on an alumina column (elution with 8 : 2 benzene–methanol) yielded 4.08 g of blue oil, which on rechromatography (hexane–silica gel) afforded 1.74 g (88%) of unchanged **17**. The second blue eluate was rechromatographed on an alumina column (elution with 8 : 2 benzene–methanol) to afford 210 mg (8%) of **23** as a blue oil: UV (C_2H_5OH) 219 (log ε 4.02), 246 (4.36), 285 (4.58), 289 (4.58), 303 (3.99), 349 (3.62), 367 (3.49), 565 (sh, 2.55), 607 (2.66), 656 (2.59), and 725 nm (sh, 2.15); IR (CCl_4) 3330 (NH), 2790 (NCH_3), 2960, 2925, 2870, 1470, 1460, 1445, 1438, 1420, 1390, and 1370 cm^{-1} (CH_3 and CH_2); ^{1}H NMR ($CDCl_3$) $\delta=1.12$ (3H, d, $J=6.3$ Hz, 1′-C(CH_3)), 1.35 (6H, d, $J=6.9$ Hz, $CH(C\underline{H}_3)_2$), 1.71 (1H, broad s, NH), 2.39 (3H, s, NCH_3), 2.64 (3H, s, 1-CH_3), 2.88—3.40 (4H, m; 1′-H, 2′-H_2, and $C\underline{H}(CH_3)_2$), 6.96 (1H, d, $J=10.3$ Hz, 5-H), 7.28 (1H, d, $J=3.4$ Hz, 3-H), 7.36 (1H, q, $J=10.3$ and 1.7 Hz, 6-H), 7.59 (1H, d, $J=3.4$ Hz, 2-H), and 8.14 (1H, d, $J=1.7$ Hz, 8-H;) MS *m/e* (rel intensity) 255 (M^+; 7), 198 ($M^+-C_3H_7N$; 32), and 58 ($C_3H_8N^+$; 100).

Found: C, 84.70; H, 9.56; N, 5.62%. Calcd for $C_{18}H_{25}N$: C, 84.65; H, 9.87; N, 5.48%.

Preparation of Hydrochlorides from 2-(7-Isopropyl-1-methyl-4-azulenyl)ethanamine Derivatives. *A) From **21***: A solution of 209 mg (0.818 mmol) of **21** in 100 cm^3 of benzene was extracted with 1 mol dm^{-3} hydrochloric acid (50 cm^3 × 3); the hydrochloric acid layer was then extracted with chloroform (50 cm^3 × 3). The chloroform solution was dried (sodium sulfate) and concentrated (reduced pressure) to leave a blue crystalline mass, which was washed with hexane (20 cm^3 × 5) and chromatographed on a silica-gel column (elution with 9 : 1 chloroform–methanol) to give 120 mg (50%) of **27** as blue crystals, mp 200—204 °C: UV (C_2H_5OH) 218 (sh, log ε 4.05), 245 (4.29), 280 (sh, 4.46), 285 (4.52), 289 (4.51), 303 (3.95), 350 (3.58), 367 (3.41), 565 (sh, 2.51), 588 (sh, 2.57), 605 (2.61), 633 (sh, 2.56), 658 (2.53), and 730 nm (2.09); IR ($CHCl_3$) 2500, 2400, 2350, 2328 (NH^+), and 1097 cm^{-1} (C–N); ^{1}H NMR ($CDCl_3$) $\delta=1.28$ (6H, d, $J=7$ Hz, $CH(C\underline{H}_3)_2$), 2.32 (6H, s, $N(CH_3)_2$), 2.61 (3H, s, 1-CH_3), 2.74 (2H, m, 1′-H_2), 3.02 (1H, m, $J=7$ Hz, $C\underline{H}(CH_3)_2$), 3.31 (2H, m, 2′-H_2), 7.00 (1H, d, $J=11$ Hz, 5-H), 7.32 (1H, d, $J=4$ Hz, 3-H), 7.38 (1H, q, $J=11$ and 2 Hz, 6-H), 7.64 (1H, d, $J=4$ Hz, 2-H), and 8.18 (1H, d, $J=2$ Hz, 8-H).

*B) From **24***: By treating 210 mg (0.741 mmol) of **24** as described above in *A*, 153 mg (65%) of **28** was obtained as blue crystals, mp 200—204 °C: UV (C_2H_5OH) 215 (log ε 4.64), 246 (5.00), 285 (5.28), 290 (5.27), 303 (sh, 4.65), 330 (sh, 2.52), 351 (3.19), 368 (2.90), 440 (sh, 2.43), 565 (sh, 2.35), 614 (2.45), 666 (2.36), and 740 nm (1.89); IR ($CHCl_3$) 2615, 2540, 2510, 2440, 2350, 2340 (NH^+), and 1144 cm^{-1} (C–N); ^{1}H NMR ($CDCl_3$) $\delta=1.34$ (6H, s, 1′-$C(CH_3)_2$), 1.40 (6H, d, $J=7$ Hz, $CH(C\underline{H}_3)_2$), 2.72 (3H, s, 1-CH_3), 2.82 (6H, s, $N(CH_3)_2{}^+$), 3.16 (1H, m, $J=7.0$ Hz, $C\underline{H}(CH_3)_2$), 3.68 (2H, s, 2′-H_2), 7.12 (1H, d, $J=11$ Hz, 5-H), 7.54 (1H, q, $J=11$ and 4 Hz, 6-H), 7.60 (1H, d, $J=4$ Hz, 3-H), 7.84 (1H, d, $J=4$ Hz, 2-H), and 8.38 (1H, d, $J=2$ Hz, 8-H).

*C) From **25***: By treating 321 mg (1.04 mmol) of **25** as described in *A*, except that 6 mol dm^{-3} hydrochloric acid and a mixed solvent of chloroform–methanol (7 : 3) were used for extraction and for chromatographic separation respectively, 183 mg (51%) of **29** was obtained as blue crystals, mp 82—84 °C: UV (C_2H_5OH) 216 (log ε 3.21), 245 (3.69), 284 (4.03), 290 (4.02), 304 (sh, 2.54), 338 (sh, 3.38), 352 (3.46), 368 (3.38), 608 (2.59), 660 (2.49), and 730 nm (2.02); IR ($CHCl_3$) 2690, 2645, 2560, 2500—2400, 2360, 2340 (NH^+), and 1194 cm^{-1} (C–N); ^{1}H NMR ($CDCl_3$)[18] $\delta=1.32$ (6H, s, $C(CH_3)_2$), 1.43 (6H, d, $J=7$ Hz, $CH(C\underline{H}_3)_2$), 2.08 (4H, m, β- and γ-H_2), 2.24 (1H, s, NH^+), 2.76 (3H, s, 1-CH_3), 3.18 (1H, m, $J=7$ Hz, $C\underline{H}(CH_3)_2$), 3.32 (4H, t, $J=6$ Hz, α- and δ-H_2), 3.68 (2H, s, 2′-H_2), 7.19 (1H, d, $J=11$ Hz, 5-H), 7.58 (1H, q, $J=11$ and 2 Hz, 6-H), 7.64 (1H, d, $J=4$ Hz, 3-H), 7.84 (1H, d, $J=4$ Hz, 2-H), and 8.36 (1H, d, $J=2$ Hz, 8-H).

*D) From **26***: By treating 415 mg (1.12 mmol) of **26** as described in *C*, 128 mg (28%) of **30** was obtained as blue crystals, mp 80—85 °C: UV (C_2H_5OH) 246 (log ε 4.03), 286 (4.34), 291 (4.31), 303 (3.52), 329 (sh, 3.46), 335 (sh, 3.54), 351 (3.66), 368 (3.54), 416 (2.90), 436 (2.89), 560 (sh, 2.50), 602 (sh, 2.59), 611 (2.60), 660 (2.52), and 730 nm (2.08); IR ($CHCl_3$) 2670, 2560, 2490—2430, 2400, 2360, 2340 (NH^+), and 1192 cm^{-1} (C–N); ^{1}H NMR ($CDCl_3$)[18] $\delta=1.23$ (3H, s, 1′-$C(CH_3)$), 1.32 (6H, d, $J=7$ Hz, $CH(C\underline{H}_3)_2$), 1.88 (4H, m, β- and γ-H_2), 2.64 (3H, s, 1-CH_3), 3.02 (4H, m, α- and δ-H_2), 3.70 (1H, d, $J=12.5$ Hz, 2′-H), 4.15 (1H, d, $J=12.5$ Hz, 2′-H), 6.10 (1H, d, $J=11$ Hz, 5-H), 6.96 (1H, q, $J=11$ and 2 Hz, 6-H), 7.30 (3H, m, 3″-, 4″-, and 5″-H), 7.34 (1H, d, $J=4$ Hz, 3-H), 7.64 (2H, m, 2″- and 6″-H), 7.62 (1H, d, $J=4$ Hz, 2-H), and 8.16 (1H, d, $J=2$ Hz, 8-H).

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$$\begin{array}{ccccccccc} \mathrm{N-} & \mathrm{CH_2} & - & \mathrm{CH_2} & - & \mathrm{CH_2} & - & \mathrm{CH_2} \\ & \alpha & & \beta & & \gamma & & \delta \end{array} \qquad \begin{array}{cccccc} \mathrm{C-} & \mathrm{C=} & \mathrm{CH-} & \mathrm{CH=} & \mathrm{C-CH=} & \mathrm{CH} \\ 1'' & 2'' & 3'' & 4'' & 5'' & 6'' \end{array}$$