The Reaction of Azulene with Nitroethene. A New Route to 2-(1-Azulenyl)ethanamines

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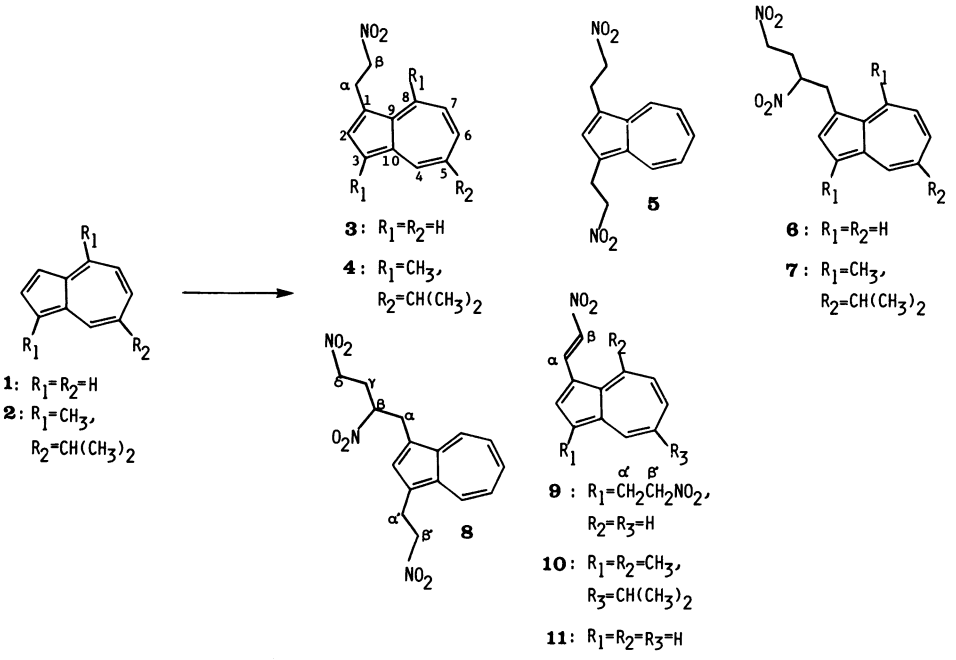
Azulene and guaiazulene react with nitroethene to form substitution products having 2-nitroethyl, 2,4-dinitrobutyl, or 2-nitroethenyl groups at the 1(3)-position in low yields. The presence of formic acid prevented the formation of the dinitrobutyl compound, and increased the yield of the 2-nitroethyl derivative. A reaction course leading to these products is proposed. Reduction of 1-(2-nitroethyl)azulene and 1-(2-nitroethyl)-guaiazulene gave the corresponding amine compounds in good yields. This two-step process provides a new, improved route to 2-(1-azulenyl)ethanamines having a primary amino group. The amine products, like related biogenic amines, inhibited the contraction of smooth muscle.

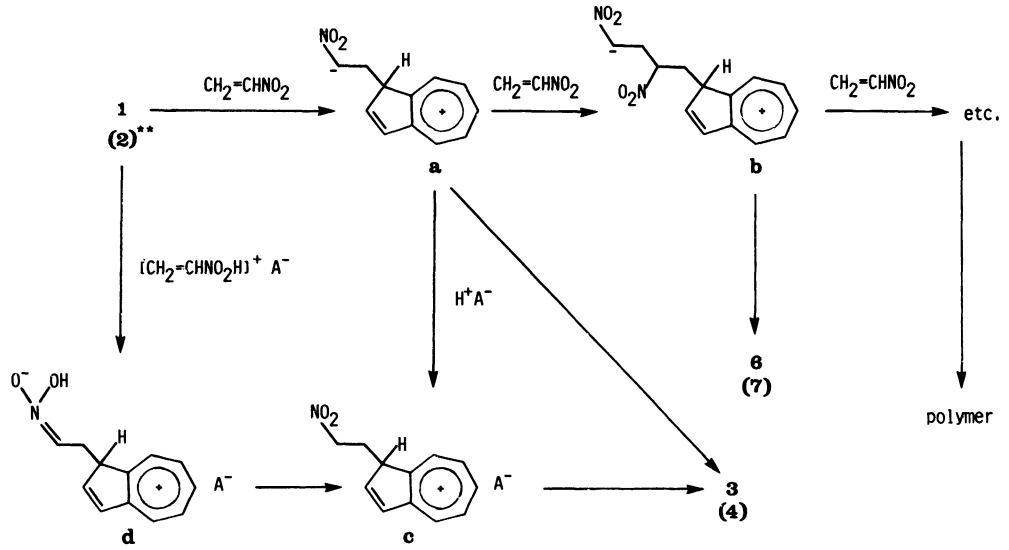
2-Arylethanamine derivatives constitute an important class of physiologically active compounds related to biogenic amines.[1] In studying azulene analogs of biologically active amines, we have previously reported the synthesis of some *N*-alkyl and *N*-acyl derivatives of 2-(1-azulenyl)ethanamines[2] and 2-(4-azulenyl)ethanamine[3,4] compounds by ring aminoethylation and methyl side chain aminomethylation methods, respectively, and the effect of these compounds on specific enzyme activity.[2,4] These methods, however, were not successful for the preparation of azulenylethanamines having a primary amino group as in norepinephrine (noradrenaline), dopamine, serotonin, *etc.* The search for a synthetic route to this type of azulene compound led the investigation of the reaction of azulene and guaiazulene with nitroethene to form the corresponding 1-(2-nitroethyl) derivatives,[5] and the reduction of these to the primary amines.

Results and Discussion

Nitroethene (*ca.* 10% in benzene)[6] reacted with azulene (**1**) at room temperature to yield 1-(2-nitroethyl)azulene (**3**) (8%). Three by-products, **5** (6%), **6** (5%), and **8** (3%), were also formed. The structures of these compounds were determined by spectral analyses.

For example, the ^{1}H NMR spectrum of **6** showed a complicated splitting pattern for the 2,4-dinitrobutyl moiety. Analysis according to an ABX spin system[7] composed of nonequivalent (adjacent to an asymmetric center) α-methylene protons (3.61 and 3.82 ppm for AB) and a β-methine proton (4.94 ppm for X) afforded reasonable coupling constant of J_{AB}= 14.7, J_{AX}=6.3, J_{BX}=6.8 Hz. A coupling through 4σ-bonds (1.1 Hz)[8] was observed between the β-methine and δ-methylene protons (4.34 ppm) of the dinitro-





Scheme 1.

butyl group. The ^{1}H NMR spectrum of **8** showed the same splitting pattern for the dinitrobutyl group.

Analogously, guaiazulene (**2**) under the same conditions afforded **4** (9%), **7** (3%), and **10** (2%). The 2,4-dinitrobutyl group of **7** exhibited the same ^{1}H NMR splitting pattern as that of **6**. It was further characterized by its ^{13}C NMR spectrum which showed triplet signals for the α-, γ-, and δ-carbons and a doublet for the β-carbon of the assigned structure.

The 2-nitroethenyl product (**10**) had been previously prepared by the reaction of 1-formylguaiazulene with nitromethane,[9] but the configuration of the double bond was not determined. Our data indicate a trans configuration: i) The coupling constant ($J_{\alpha,\beta}$=13.0 Hz) for the olefinic protons in the ^{1}H NMR spectrum has the expected value when the electronegative nitro substituent is taken into account.[10] ii) The chemical shifts for the olefinic protons (7.56 and 8.93 ppm) show full conjugation of the double bond with the azulene ring. Molecular models indicate this to be possible only for the trans geometry. iii) The IR absorption at 956 cm^{-1} corresponds to a trans alkene.

A large amount of insoluble, polymeric material was also observed in these reactions. This was thought to be produced by polymerization of the nitroethene initiated by a nucleophile (*e.g.* **1** or **2**) (*cf.* Scheme 1. **1**→**a**→**b**→polymer). The formation of **6**, **7**, and **8** having a dinitrobutyl side chain provides support for this concept. This polymerization process would be suppresses if an acid was present to react with the intermediate to form **c** (Scheme 1). The effects of trifluoroacetic acid, formic acid, and ether-boron trifluoride (1/1) were examined (Table 1). As expected, the reaction yielding **7** was blocked, but also the yield of **4** was reduced except with formic acid.

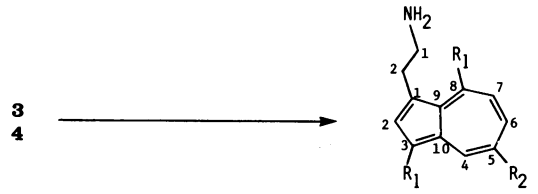
Table 1. Reaction of guaiazulene (**2**) and nitroethene in the presence of acid (nitroethene: acid: **2**=1.5:1.5:1 in mole ratio. Benzene as the solvent)

Acid	Reaction conditions		Yield/%		
	Temp	Time/h	**4**	**7**	**10**
CF_3COOH	0 °C	1.5	5	—	0.2
HCOOH	Ambient	1.5	9	—	2
$BF_3\cdot O(C_2H_5)_2$	Ambient	1.4	0.8	—	10
None	50 °C	3.5	47	9	2
HCOOH	50 °C	5	50	—	2

In another modification, nitroethene was added slowly to a solution of **2** preheated to 50 °C. This minimized the polymerization process and markedly increased the yield of **4** (47%) but also raised the yield of **7** to 9%. This procedure was then used in the presence of formic acid to give 50% of **4** with no detectable amount of **7**. In two runs, the one with the slower addition of nitroethene gave the higher yield of **4**.

Application of the improved method using 1.5 equivalents of nitroethene to **1**, however, gave only 21% of **3** along with 5% of the disubstitution product (**5**). With 3 equivalents of nitroethene at 60 °C the yields of **3** and **5** were 15 and 71%, respectively. A trace amount (≤0.4%) of 1-(2-nitroethenyl)-3-(2-nitroethyl)-azulene (**9**) was also obtained from these reactions. The structures of **9** was assigned by comparison of its spectral characteristics with those of **11**, which was prepared from 1-formylazulene by an established procedure.[11] As described earlier for **10**, the ^{1}H NMR and IR spectra were indicative of a trans double bond in **9** and **11**. Attempted nitroethylation of **11** to form **9** was unsuccessful. This suggests that the nitroethenyl group in **11** is deactivating the

** Corresponding guaiazulene derivatives are shown in parentheses.



12 : $R_1=R_2=H$
13 : $R_1=CH_3$, $R_2=CH(CH_3)_2$

azulene ring and is formed after the nitroethyl group in the formation of **9** from **1**.

Scheme 1 summarizes the proposed reaction process of **1** with nitroethene. Intra- or intermolecular proton migration forms **3** from intermediate **a**. Alternatively, **a** can nucleophilically react with another molecule of nitroethene to form **b**, which can be converted to **6** or, by repetition of the process for **a**→**b** give polymeric material. The reaction of **3** with nitroethene would yield **5** or lead to **8**. The latter may also be formed by the reaction of **6** with nitroethene. Reaction of **a** with a protic acid would form **c** and prevent the process leading to **6** and polymer. The abstraction of a proton from **c** afford **3** if a sufficiently basic species is present. The action of formate ion to form **3** would account for the observation of the 1,3-disubstituted products, as **3** was shown to react further with nitroethene.

When a strong acid is present (*e.g.* trifluoroacetic acid), the conjugate acid of nitroethene could be formed and be the primary electrophilic reagent. If that event, **d** (formed directly from **1**) could tautomerize to give **c**, and **3** would be formed upon neutralization.

Hydride abstraction from the intermediate corresponding to **a** by one of the acidic species present would form the nitroethenyl side chains in **9** and **10**. This could have accounted for the increase in the yield of **10** when a Lewis acid was added (*cf.* $BF_3 \cdot O(C_2H_5)_2$ in Table 1). An indication of a possible oxidative dehydrogenation pathway (by air or nitro compounds[12]) to **9** and **10** from **5** and **4**, respectively, was provided by the observation that **4** yielded **10** readily when treated with palladized charcoal at room temperature, and even under reductive conditions.

The conversion of **3** and **4** into the corresponding primary amines (**12** and **13**) in good yields (79 and 77%) was effected by reduction with iron and acetic acid.[13] Other reduction trials with palladized charcoal and sodium borohydride[14] or lithium aluminum hydride were unsatisfactory. The chemical shifts and splittig patterns in the ^1H and ^{13}C NMR spectra of **12** and **13** compounds were in agreement with the assigned structures. Allyl fission of the aminoethyl side chain gave rise to the most abundant ion in the mass spectra, as previously observed for other azulenylethanamines.[2-4]

Compounds **12** and **13**, like related biogenic amines, strongly inhibited the contraction of smooth muscle.[15] Details of these studies will be reported elsewhere.

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; ^1H NMR, JEOL MH-100; ^{13}C NMR, JNM-FX 100; MS, JEOL-D 300 at 70 eV.

Nitroethene. This reagent was prepared from 2-nitroethanol and phthalic anhydride, and made into a *ca.* 10% benzene solution immediately after distillation:[6] ^1H NMR ($CDCl_3$) δ=4.78 (broad d, J=7.0 Hz, anti H), 5.94 (dd, J=15.0 and 2.0 Hz, syn H), and 6.41 (dd, J=7.0 and 15.0 Hz, $=C(NO_2)H$). The solutions of two preparative runs contained 9.7 and 11 wt% (by ^1H NMR) of nitroethene, respectively, and in the former case 3.4% of nitroethane was also noted: ^1H NMR ($CDCl_3$) δ=1.10 (t, J=7.0 Hz, CH_3) and 3.30 (q, J=7.0 Hz, CH_2).

Reaction of Azulene (1) and Nitroethene. A) Without Acid at Room Temperature. To an ice-cooled, stirred solution of 640 mg (4.99 mmol) of azulene in 35 cm^3 of dry dichloromethane was added dropwise, under dry nitrogen, 20 g of 9.7% benzene solution of nitroethene (containing 27 mmol of nitroethene) over a period of 30 min, and stirring was continued for 20 h more at room temperature. Removal of the solvent (reduced pressure) afforded a violet oil (7 spots on TLC over silica gel with benzene), which was chromatographed on a silica-gel column (elution with benzene) to give four products besides 80.2 mg (13%) of unchanged azulene eluted at first and recovered as violet crystals.

From the second eluate, 81.4 mg (8%) of 1-(2-nitroethyl)-azulene (**3**) was obtained as a blue oil: UV (C_2H_5OH) 237 (log ε 4.28), 263 (sh, 4.42), 268 (sh, 4.57), 272 (sh, 4.67), 276 (4.73), 280 (sh, 4.69), 286 (sh, 4.54), 295 (sh, 3.89), 328 (sh, 3.42), 332 (3.64), 342 (3.76), 524 (sh, 2.25), 550 (sh, 2.40), 571 (sh, 2.47), 588 (2.53), 608 (sh, 2.49), 638 (2.45), 668 (sh, 2.20), and 705 nm (2.02); IR (CCl_4) 3060, 3030 (aromatic CH), 2925 (CH_2), 1545, and 1378 cm^{-1} (NO_2); ^1H NMR ($CDCl_3$) δ=3.76 (2H, t, J=7.4 Hz, α-CH_2), 4.54 (2H, t, J=7.4 Hz, β-CH_2), 7.09 (1H, t, J=9.7 Hz, 5-H), 7.12 (1H, t, J=9.7 Hz, 7-H), 7.28 (1H, d, J=4.0 Hz, 3-H), 7.56 (1H, t, J=9.7 Hz, 6-H), 7.71 (1H, d, J=4.0 Hz, 2-H), and 8.22 (2H, dd, J=9.7 and 1.7 Hz, 4- and 8-H); ^{13}C NMR ($CDCl_3$) δ=25.5 (α-CH_2), 76.1 (β-CH_2), 117.3 (3-C), 122.4 (7-C), 123.0 (5-C), 122.9 (1-C), 132.9 (8-C), 136.1 (9-C), 136.7 (4-C), 136.9 (6-C), 137.9 (2-C), and 140.8 (10-C); MS

m/z (rel intensity) 201 (M^+; 80), 155 (M^+-NO_2; 100), and 141 ($M^+-CH_2NO_2$; 55).

Found: C, 71.97; H, 5.72; N, 6.37%. Calcd for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96%.

From the third eluate, 67.5 mg (5%) of 1-(2,4-dinitrobutyl)-azulene (**6**) was obtained as blue crystals, mp 75—76 °C: UV (C_2H_5OH) 237 (log ε 4.47), 268 (sh, 4.69), 273 (sh, 4.79), 276 (4.84), 281 (4.80), 286 (sh, 4.68), 295 (sh, 4.17), 342 (4.01), 357 (3.86), 524 (sh, 2.44), 549 (2.56), 569 (sh, 2.62), 585 (2.66), 606 (sh, 2.62), 635 (2.58), 669 (sh, 2.30), and 701 nm (2.17); IR ($CHCl_3$) 1555 and 1370 cm^{-1} (NO_2); ^1H NMR ($CDCl_3$) δ=2.56 (2H, m, γ-CH_2), 3.61 and 3.82 (2H, symmetrical 8 lines, *J*=14.7, 6.8, and 6.3 Hz, α-CH_2), 4.34 (2H, dt, *J*=6.8 and 1.1 Hz. δ-CH_2), 4.94 (1H, m, β-CH), 7.14 (1H, t, *J*=9.7 Hz, 5-H), 7.16 (2H, t, *J*=9.7 Hz, 7-H), 7.30 (1H, d, *J*=4.0 Hz, 3-H), 7.60 (1H, t, *J*=9.7 Hz, 6-H), 7.70 (1H, d, *J*=4.0 Hz, 2-H), 8.19 (1H, d, *J*=9.7 Hz, 4-H), and 8.27 (1H, d, *J*=9.7 Hz, 8-H); MS *m/z* (rel intensity) 274 (M^+; 24), 180 (M^+-2HNO_2; 11), 167 ($M^+-HNO_2-CH_2NO_2$; 18), and 141 ($M^+-C_3H_5N_2O_4$; 100).

Found: C, 61.11; H, 5.26; N, 9.96%. Calcd for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.15; N, 10.21%.

From the fourth eluate, 76.7 mg (6%) of 1,3-bis(2-nitroethyl)azulene (**5**) was obtained as blue crystals, mp 95—96 °C: UV (C_2H_5OH) 238 (log ε 4.42), 271 (sh, 4.67), 275 (sh, 4.75), 279 (4.80), 283 (4.78), 289 (sh, 4.23), 346 (3.92), 362 (3.83), 560 (sh, 2.52), 600 (2.62), 647 (2.55), and 717 nm (sh, 2.14); IR ($CHCl_3$) 1550 and 1380 cm^{-1} (NO_2); ^1H NMR ($CDCl_3$) δ=3.72 (4H, t, *J*=7.4 Hz, α-CH_2), 4.64 (4H, t, *J*=7.4 Hz, β-CH_2), 7.12 (2H, t, *J*=9.7 Hz, 5- and 7-H), 7.59 (1H, t, *J*=9.7 Hz, 6-H), 7.59 (1H, s, 2-H), and 8.18 (2H, dd, *J*=9.7 and 1.7 Hz, 4- and 8-H); ^{13}C NMR ($CDCl_3$) δ=25.2 (α-CH_2), 76.1 (β-CH_2), 122.1 (1,3-C), 122.8 (5,7-C), 133.2 (4,8-C), 136.6 (9,10-C), 136.9 (6-C), and 138.5 (2-C); MS *m/z* (rel intensity) 274 (M^+; 63), 228 (M^+-NO_2; 47), 227 (M^+-HNO_2; 51), 214 ($M^+-CH_2NO_2$; 28), 182 (M^+-2NO_2; 23), 181 ($M^+-NO_2-HNO_2$; 83), and 167 ($M^+-HNO_2-CH_2NO_2$; 100).

Found: C, 61.83; H, 5.21; N, 10.13%. Calcd for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.15; N, 10.21%.

From the last fraction, 53.1 mg (3%) of 1-(2,4-dinitrobutyl)-3-(2-nitroethyl)azulene (**8**) was obtained as a green oil: UV (C_2H_5OH) 238 (log ε 4.28), 266 (sh, 4.40), 270 (sh, 4.52), 275 (sh, 4.63), 279 (4.70), 284 (sh, 4.57), 298 (sh, 4.08), 345 (3.75), 363 (3.69), 446 (2.79), 562 (sh, 2.49), 585 (sh, 2.54), 596 (2.56), 640 (sh, 2.47), and 711 nm (2.02); IR ($CHCl_3$) 1560 and 1380 cm^{-1} (NO_2); ^1H NMR ($CDCl_3$) δ=2.56 (2H, m, γ-CH_2), 3.70 (2H, symmetrical 8 lines, α-CH_2), 3.73 (2H, t, *J*=6.9 Hz, α'-CH_2), 4.37 (2H, dt, *J*=6.9 and 1.7 Hz, δ-CH_2), 4.65 (2H, t, *J*=6.9 Hz, β'-CH_2), 4.90 (1H, m, β-CH), 7.61 (1H, t, *J*=10.3 Hz, 6-H), 8.16 (1H, d, *J*=10.3 Hz, 4-H), and 8.20 (1H, d, *J*=10.3 Hz, 8-H); MS *m/z* (rel intensity) 347 (M^+; 54), 301 (M^+-NO_2; 52), 300 (M^+-HNO_2; 58), 287 ($M^+-CH_2NO_2$; 12), 254 ($M^+-NO_2-HNO_2$; 21), 253 (M^+-2HNO_2; 33), 227 ($M^+-2CH_2NO_2$; 12), 214 ($M^+-C_3H_5N_2O_4$; 75), 167 ($M^+-HNO_2-C_3H_5N_2O_4$; 100), and 153 ($M^+-CH_2NO_2-C_3H_5N_2O_4-H$; 80).

Found: C, 55.16; H, 4.87; N, 12.08%. Calcd for $C_{16}H_{17}N_3O_6$: C, 55.33; H, 4.93; N, 12.10%.

After the separation of these products, the solvent of the chromatography was changed to chloroform to afford an additional fraction, which was concentrated (reduced pressure) to leave 393 mg of brown solid. This material was insoluble in all organic solvents tested, but was soluble in mineral acid.

B) With Formic Acid at 50 °C. To a stirred solution of 130 mg (1.01 mmol) of azulene in 2 cm^3 of benzene, kept at 50 °C under dry nitrogen, was added dropwise a mixed reagent of 1.00 g (1.51 mmol) of 11% nitroethene solution and 69.4 mg (1.51 mmol) of formic acid during a period of 1 h, and stirring was continued for an additional 2 h at 50 °C. The reaction mixture was taken up in 100 cm^3 of benzene, washed with 10% potassium carbonate solution (50 cm^3×2), then with water (50 cm^3×3), dried on sodium sulfate, and concentrated (reduced pressure) to give a blue oil. Chromatography of the blue oil over silica gel (elution with benzene) gave 65.3 mg (50%) of unchanged **1**, 43.1 mg (21%) of **3**, 14.4 mg (5%) of **5**, and a small amount of brown crystalline material as the last fraction. The last fraction was rechromatographed over silica gel (benzene) to give 0.13 mg (0.5%) of 1-(2-nitroethenyl)-3-(2-nitroethyl)azulene (**9**) as dark brown crystals, mp 187—189 °C: UV (C_2H_5OH) 230 (log ε 4.20), 275 (sh, 4.22), 283 (4.26), 289 (sh, 4.24), 307 (sh, 3.95), 337 (3.88), 436 (sh, 4.11), and 448 nm (4.13); IR (KBr) 1550, 1318 (NO_2), and 950 cm^{-1} (trans CH); ^1H NMR ($CDCl_3$) δ=3.78 (2H, t, *J*=7.0 Hz, α'-CH_2), 4.73 (2H, t, *J*=7.0 Hz, β'-CH_2), 7.43 (1H, t, *J*=10.0 Hz, 5-H), 7.45 (1H, t, *J*=10.0 Hz, 7-H), 7.67 (1H, d, *J*=13.0 Hz, β-H), 7.81 (1H, t, *J*=10.0 Hz, 6-H), 7.96 (1H, s, 2-H), 8.31 (1H, d, *J*=10.0 Hz, 4-H), 8.58 (1H, d, *J*=13.0 Hz, α-H), and 8.55 (1H, d, *J*=10.0 Hz, 8-H); MS *m/z* (rel intensity) 272 (M^+; 72), 226 (M^+-NO_2; 42), 225 (M^+-HNO_2; 69); 178 (M^+-2HNO_2; 100), and 165 ($M^+-HNO_2-CH_2NO_2$; 98).

Found: N, 10.13%. Calcd for $C_{14}H_{12}N_2O_4$: N, 10.29%.

C) With Formic Acid at 60 °C. To a stirred solution of 64.0 mg (0.499 mmol) of azulene in 2 cm^3 of benzene, kept at 60 °C, was added dropwise a mixed reagent of nitroethene and formic acid (1.51 mmol in each) over a period of 1 h, and stirring was continued for an additional 2 h at 60 °C. The reaction mixture was worked up as described in *B* to give 1.50 mg (2%) of unchanged **1**, 14.8 mg (15%) of **3**, 97.1 mg (71%) of **5**, and 0.54 mg (0.4%) of **9**.

Synthesis of 1-(2-Nitroethenyl)azulene (11). To a stirred solution of 320 mg (1.47 mmol) of 1-formylazulene, which was prepared in a 76% yield according to Ref. 11, in 5 cm^3 of ethanol was added a mixed reagent of 100 mg (1.64 mmol) of nitromethane and 130 mg (1.55 mmol) of piperidine over a period of 10 min, and stirring was continued for 4 h more. Chromatography of the reaction mixture on a silica-gel column (dichloromethane) gave 31.4 mg (11%) of **11** as reddish-brown solid, besides 63 mg of reddish brown oil. After recrystallization from methanol containing a trace amount of acetone, **11** was obtained as dark brown crystals, mp 149—150 °C: UV (C_2H_5OH) 231 (log ε 4.22), 272 (sh, 4.28), 278 (4.32), 282 (4.32), 285 (4.31), 295 (sh, 4.19), 327 (sh, 3.82), 337 (3.85), 350 (sh, 3.81), 422 (sh, 4.05), 428 (sh, 4.08), and 443 nm (4.11); IR ($CHCl_3$), 1560, 1330 (NO_2), and 960 cm^{-1} (trans CH); ^1H NMR ($CDCl_3$) δ=7.20—7.68 (2H, m, 5- and 7-H), 7.56 (1H, d, *J*=4.0 Hz, 3-H), 7.85 (1H, d, *J*=13.0 Hz, β-H), 7.94 (1H, t, *J*=10.0 Hz, 6-H), 8.24 (1H, d, *J*=4.0 Hz, 2-H), 8.52 (1H, d, *J*=10.0 Hz, 4-H), 8.74 (1H, d, *J*=10.0 Hz, 8-H), and 8.78 (1H, d, *J*=13.0 Hz, α-H); MS *m/z* (rel intensity) 199 (M^+; 43) and 152 (M^+-HNO_2; 100).

Found: C, 72.31; H, 4.45; N, 6.97%. Calcd for $C_{12}H_9NO_2$: C, 72.35; H, 4.55; N, 7.03%.

In the attempted synthesis of **9** from **11**, **11** was treated at first with a 2 molar equivalent of the mixed reagent of nitroethene and formic acid at 50 °C, followed by treatment with an additional 2 molar equivalent of nitroethene at 80 °C. The recovery of **11** from each process was indicated by TLC (benzene–silica gel).

*Reaction of Guaiazulene (**2**) and Nitroethene. A) Without Acid at Room Temperature.* To an ice-cooled, stirred solution of 1.72 g (8.67 mmol) of guaiazulene in 35 cm^3 of dry dichloromethane was added dropwise 35 g (47 mmol) of 9.7% nitroethene solution during a period of 30 min, and stirring was continued for an additional 20 h at room temperature. Removal of the solvent (reduced pressure) and chromatography of the residue over silica gel (benzene) gave 2.38 g of blue oil, which was taken up in a mixed solvent of petroleum ether–benzene (220 cm^3) and extracted with 85% phosphoric acid (100 cm^3, then 50 cm^3×3). The acid layer was washed with petroleum ether (100 cm^3×3), diluted with ice-water (500 cm^3), and extracted with petroleum ether (100 cm^3, then 50 cm^3×3). The organic extract, after being washed with water (100 cm^3, then 50 cm^3×3), dried (sodium sulfate), and concentrated (reduced pressure), was chromatographed on a silica-gel column (benzene) to give three products.

From the first eluate, 203 mg (9%) of 1-(2-nitroethyl)-guaiazulene (**4**) was obtained as blue crystals, mp 85—89 °C: UV (C_2H_5OH) 246 (log ε 4.40), 287 (4.65), 291 (sh, 4.63), 305 (4.20), 336 (sh, 3.63), 346 (sh, 3.70), 352 (3.79), 369 (3.75), 544 (sh, 2.48), 614 (2.70), 668 (sh, 2.60), and 734 nm (sh, 2.23); IR (CCl_4) 1542 and 1378 cm^{-1} (NO_2); ^1H NMR ($CDCl_3$) δ=1.30 (6H, d, J=7.0 Hz, $CH(CH_3)_2$), 2.58 (3H, s, 3-CH_3), 2.82 (3H, s, 8-CH_3), 2.99 (1H, m, J=7.0 Hz, $CH(CH_3)_2$), 3.76 (2H, t, J=8.0 Hz, α-CH_2), 4.44 (2H, t, J=8.0 Hz, β-CH_2), 6.84 (1H, d, J=10.0 Hz, 7-H), 7.29 (1H, dd, J=10.0 and 2.0 Hz, 6-H), 7.37 (1H, s, 2-H), and 8.16 (1H, d, J=2.0 Hz, 4-H); ^{13}C NMR ($CDCl_3$) δ=12.8 (q, 3-CH_3), 24.6 (q, $CH(CH_3)_2$, 26.8 (q, 8-CH_3), 29.4 (t, α-CH_2), 37.7 (d, $CH(CH_3)_2$), 77.2 (t, β-CH_2), 120.1 (s, 1-C), 124.7 (s, 3-C), 127.1 (d, 7-C), 132.8 (s, 9-C), 133.8 (d, 4-C), 135.1 (d, 6-C), 138.1 (s, 10-C), 138.9 (d, 2-C), 139.9 (s, 5-C), and 144.6 (s, 8-C); MS m/z (rel intensity) 271 (M^+; 85), 225 (M^+-NO_2; 100), 224 (M^+-HNO_2; 44), and 211 ($M^+-CH_2NO_2$; 80).

Found: C, 75.52; H, 7.86; N, 5.12%. Calcd for $C_{17}H_{21}NO_2$: C, 75.25; H, 7.80; N, 5.16%.

From the second eluate, 89.2 mg (3%) of 1-(2,4-dinitrobutyl)guaiazulene (**7**) was obtained as a blue oil: UV (C_2H_5OH) 246 (log ε 4.29), 287 (4.50), 290 (sh, 4.49), 305 (4.08), 340 (sh, 3.54), 352 (3.64), 369 (3.62), 524 (sh, 2.31), 572 (sh, 2.50), 609 (2.57), 658 (sh, 2.48), and 731 nm (sh, 2.01); IR (CCl_4) 1540 and 1380 cm^{-1} (NO_2); ^1H NMR ($CDCl_3$) δ=1.31 (6H, d, J=7.0 Hz, $CH(CH_3)_2$), 2.54 (2H, m, γ-CH_2), 2.56 (3H, s, 3-CH_3), 2.90 (3H, s, 8-CH_3), 3.01 (1H, m, J=7.0 Hz, $CH(CH_3)_2$), 3.64 and 3.96 (2H, symmetrical 8 lines, J=14.9, 7.2, and 7.2 Hz, α-CH_2), 4.26 (2H, t, J=7.0 Hz, δ-CH_2), 4.88 (1H, m, β-CH), 6.91 (1H, d, J=11.0 Hz, 7-H), 7.32 (1H, dd, J=11.0 and 2.0 Hz, 6-H), 7.37 (1H, s, 2-H), and 8.13 (1H, d, J=2.0 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ=12.8 (q, 3-CH_3), 24.5 (q, $CH(CH_3)_2$), 26.9 (q, 8-CH_3), 29.7 (t, α-CH_2), 35.6 (t, γ-CH_2), 37.6 (d, $CH(CH_3)_2$), 71.0 (t, δ-CH_2), 87.1 (d, β-CH), 118.8 (s, 1-C), 124.8 (s, 3-C), 127.5 (d, 7-C), 133.0 (s, 9-C), 234.0 (d, 4-C), 135.2 (d, 6-C), 138.3 (s, 10-C), 139.8 (d, 2-C), 140.3 (d, 5-C), and 144.4 (s, 8-C); MS m/z (rel intensity) 344 (M^+; 48), 298 (M^+-NO_2; 15), 297 (M^+-HNO_2; 7), and 211 ($M^+-C_3H_5NO_2$; 100).

Found: C, 66.45; H, 6.96; N, 8.44%. Calcd for $C_{19}H_{24}N_2O_4$: C, 66.26; H, 7.02; N, 8.13%.

From the last fraction, 5.00 mg (2%) of 1-(2-nitroethenyl)-guaiazulene (**10**) was obtained as reddish-brown crystals, mp 154—155 °C. It was identical with that of Ref. 9 in its mp, IR, and ^1H NMR: UV (C_2H_5OH) 227 (log ε 4.02), 241 (4.06), 281 (sh, 4.01), 291 (4.07) 305 (sh, 3.91), 313 (sh, 3.77), 341 (3.77), 354 (3.76), 367 (sh, 3.44), 424 (sh, 3.88), 442 (4.06), and 466 nm (4.05); IR (CCl_4) 1540, 1310 (NO_2), and 956 cm^{-1} (trans CH); ^1H NMR ($CDCl_3$) δ=1.36 (6H, d, J=7.0 Hz, $CH(CH_3)_2$), 2.57 (3H, s, 3-CH_3), 3.11 (3H, s, 8-CH_3), 3.14 (3H, m, J=7.0 Hz, $CH(CH_3)_2$), 7.24 (1H, d J=10.5 Hz, 7-H), 7.48 (1H, dd, J=10.5 and 2.0 Hz, 6-H), 7.56 (1H, d, J=13.0 Hz, β-H), 7.75 (1H, s, 2-H), 8.12 (1H, d, J=2.0 Hz, 4-H), and 8.98 (1H, d, J=13.0 Hz, α-H); MS m/z (rel intensity) 269 (M^+; 59), 254 (M^+-CH_3; 11), 223 (M^+-NO_2; 27), 222 (M^+-HNO_2; 45), and 211 (M^+-CNO_2 100).

B) With Trifluoroacetic Acid at 0 °C. To an ice-cooled, stirred solution of 11% nitroethene in benzene (5.00 g; 7.53 mmol) was added dropwise 860 mg (7.54 mmol) of trifluoroacetic acid. This reagent was mixed dropwise with an ice-cooled, stirred solution of 1.00 g (5.04 mmol) of guaiazulene in 5 cm^3 of benzene over a period of 20 min; stirring was continued for a further 1 h under ice-cooling. The reaction mixture was poured into 100 cm^3 of ice-water, extracted with ether (500 cm^3×4), organic extract washed with 10% potassium carbonate solution (50 cm^3×2), then with water (50 cm^3×3), dried (sodium sulfate), and concentrated (reduced pressure) leaving a green oil. Chromatography of the oil on a silica-gel column (benzene) gave 226 mg (23%) of unchanged **2**, 64.0 mg (5%) of **4**, and 2.99 mg (0.2%) of **10**.

C) With Formic Acid at Room Temperature. A mixed reagent of nitroethene (7.53 mmol) and formic acid (7.54 mmol) was prepared in the same manner as described in *B*. This reagent was mixed dropwise with a stirred solution of 1.00 g (5.04 mmol) of guaiazulene in 6 cm^3 of benzene during a period of 20 min and stirring was continued for 1 h more at room temperature. After being extracted with ether (50 cm^3, then 25 cm^3×2), dried (sodium sulfate), and concentrated (reduced pressure), the reaction mixture was chromatographed over silica gel (benzene) to give a blue oil. This oil was taken up in 100 cm^3 of petroleum ether and extracted with 85% phosphoric acid (100 cm^3×3). The acid extract was diluted with 1 dm^3 of ice-water, and extracted with benzene (100 cm^3×3). Removal of the solvent and subsequent chromatography over silica gel (benzene) gave 157 mg (16%) of unchanged **2**, 129 mg (9%) of **4**, and 46.0 mg (2%) of **10**.

D) With Ether-Boron Trifluoride (1/1) at Room Temperature. To an ice-cooled, stirred solution of 1.00 g (5.04 mmol) of guaiazulene in 5 cm^3 of benzene was added dropwise 1.00 g (7.05 mmol) of ether–boron trifluoride (1/1) over a period of 5 min, and stirring was continued for an additional 20 min at room temperature. This solution was mixed dropwise with 5.00 g (7.53 mmol) of 11% nitroethene solution during a period of 30 min and stirring was continued for 3.5 h more. The reaction mixture was taken up into 100 cm^3 of petroleum

ether and extracted with 85% phosphoric acid (50 cm^3×3). Similar work up as described in *C* and subsequent chromatography over silica gel (benzene) gave 50.8 mg (5%) of unchanged **2**, 11.0 mg (0.8%) of **4**, and 134 mg (10%) of **10**.

E) Without Acid at 50 °C. To a stirred solution of 1.00 g (5.04 mmol) of guaiazulene in 5 cm^3 of benzene, kept at 50 °C, was added 5.00 g (7.53 mmol) of 11% nitroethene solution over a period of 1 h, and stirring was continued for additional 2 h at room temperature. The reaction mixture, after the usual work up as described in *D*, gave 162 mg (16%) of unchanged **2**, 637 mg (47%) of **4**, 163 mg (9%) of **7**, and 31.6 mg (2%) of **10**.

F) With Formic Acid at 50 °C. To a stirred solution of 2.00 g (10.1 mmol) of guaiazulene in 10 cm^3 of benzene was added a mixed reagent of 10.0 g (15.1 mmol) of 11% nitroethene solution and 700 mg (15.2 mmol) of formic acid during a period of 2 h, and stirring was continued for additional 3 h at 50 °C. The reaction mixture, after being worked up as in *D*, gave 44.0 mg (2%) of unchanged **2**, 1.36 g (50%) of **4**, and 61.2 mg (2%) of **10**.

A small scale experiment with the use of 200 mg (1.01 mmol) of **2**, accompanied with changes of the reaction time (1 h for addition of the mixed reagent, followed by 4 h for additional stirring), gave 10.0 mg (5%) of unchanged **2**, 133 mg (49%) of **4**, and 20.1 mg (7%) of **10**.

Reduction of 1-(2-Nitroethyl)azulene (3) with Iron and Acetic Acid. Ninety milligrams (1.61 mmol) of fine iron powder (200 meshes) was mixed with 1 cm^3 of 5% hydrochloric acid, rinsed with acetic acid (1 cm^3×2), and transferred to the reaction vessel with 2 cm^3 of acetic acid. To the stirred suspension of iron in acetic acid was added dropwise, under dry nitrogen, a solution of 38.6 mg (0.192 mmol) of **3** in 1 cm^3 of acetic acid over a period of 30 min (washed in with additional 1 cm^3 of acetic acid), and stirring was continued for 38 h more at room temperature. The progress of the reaction was checked by TLC (silica gel-benzene). The reaction mixture was poured into 30 cm^3 of ice-water. The precipitated iron powder was collected by decantation, washed throughly with 20 cm^3 of water and then with 50 cm^3 of chloroform, and the combined organic and aqueous solution was made alkaline by the addition of 50 cm^3 of 30% sodium hydroxide solution under ice-cooling. The chloroform layer was separated, and the aqueous solution was extracted with chloroform (50 cm^3, then 30 cm^3×2). The combined, dried (sodium sulfate), and concentrated (reduced pressure) organic extracts were chromatographed on a silica-gel column (7:3 chloroform–methanol) to give 0.75 mg (2%) of unchanged **3** and 25.8 mg (79%) of 2-(1-azulenyl)ethanamine (**12**) as blue prisms, mp 104—105 °C: UV (C_2H_5OH) 237 (log ε 4.22), 268 (sh, 4.52), 273 (sh, 4.64), 277 (4.71), 282 (4.66), 287 (sh, 4.52), 296 (sh, 3.79), 331 (sh, 3.55), 343 (3.68), 358 (3.38), 556 (sh, 2.41), 578 (sh, 2.47), 597 (2.52), 620 (sh, 2.46), 650 (2.43), 682 (sh, 2.15), and 720 nm (1.97); IR (CCl_4) 3390 and 1625 cm^{-1} (NH); ^1H NMR ($CDCl_3$) δ=1.36 (2H, s, NH_2), 3.21 (4H, 8 lines, CH_2-CH_2), 7.15 (1H, t, *J*=10.0 Hz, 5-H), 7.18 (1H, t, *J*=10.0 Hz, 7-H), 7.45 (1H, d, *J*=4.0 Hz, 3-H), 7.65 (1H, t, *J*=10.0 Hz, 6-H), 7.91 (1H, d, *J*=4.0 Hz, 2-H), 8.37 (1H, d, *J*=10.0 Hz, 4-H), and 8.42 (1H, d, *J*=10.0 Hz, 8-H); ^{13}C NMR ($CDCl_3$) δ=30.8 ($2\text{-}CH_2$), 53.3 ($1\text{-}CH_2$), 116.8 (3-C), 121.5 (7-C), 122.1 (5-C), 127.9 (1-C), 133.5 (8-C), 136.3 (4- and 9-C), 137.1 (6-C), 137.3 (2-C), and 140.6 (10-C); MS *m/z* (rel intensity) 171 (M^+; 14) and 141 ($M^+-CH_2NH_2$; 100).

Found: C, 84.06; H, 7.05; N, 8.20%. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18%.

Reduction of 1-(2-Nitroethyl)guaiazulene (4). A) With Iron and Acetic Acid. To a suspension of 500 mg (8.95 mmol) of iron powder (200 meshes), treated as above with hydrochloric acid and acetic acid, in 12 cm^3 of acetic acid was added a solution of 270 mg (0.995 mmol) of **4** in 10 cm^3 of acetic acid over a period of 30 min (washed in with additional 5 cm^3 of acetic acid), and stirring was continued for 16 h more at room temperature. The reaction mixture, after being worked up as described in **3**, gave 60.2 mg (22%) of unchanged **4** and 184 mg (77%) of 5-isopropyl-3,8-dimethyl-2-(1-azulenyl)ethanamine (**13**) as a greenish blue oil: UV (log ε 4.02), 248 (4.19), 282 (sh, 4.40), 288 (4.47), 293 (4.46), 307 (4.02), 338 (sh, 3.45), 353 (3.62), 371 (3.58), 546 (sh, 2.33), 576 (sh, 2.52), 600 (sh, 2.57), 623 (2.59), and 673 nm (2.51); IR (CCl_4) 3390 and 1610 cm^{-1} (NH); ^1H NMR (CCl_4) δ=1.29 (6H, d, *J*=7.0 Hz, $CH(CH_3)_2$), 2.59 (3H, s, $3\text{-}CH_3$), 2.87 (3H, s, $8\text{-}CH_3$), 2.81—3.07 (1H, m, $CH(CH_3)_2$), 2.95 (2H, t, *J*=6.0 Hz, $1\text{-}CH_2$), 3.32 (2H, t, *J*=6.0 Hz, $2\text{-}CH_2$), 3.63 (2H, broad s, NH_2), 6.73 (1H, d, *J*=11.0 Hz, 7-H), 7.20 (1H, dd, *J*=11.0 and 2.0 Hz, 6-H), 7.49 (1H, s, 2-H), and 8.11 (1H, d, *J*=2.0 Hz, 4-H); ^{13}C NMR ($CDCl_3$) δ=12.8 (q, $3\text{-}CH_3$), 24.5 (q, $CH(CH_3)_2$), 26.9 (q, $8\text{-}CH_3$), 30.8 (t, $2\text{-}CH_2$), 37.6 (d, $CH(CH_3)_2$), 52.9 (t, $1\text{-}CH_2$), 124.2 (s, 3-C), 125.4 (s, 1-C), 126.2 (d, 7-C), 132.5 (s, 9-C), 133.2 (d, 4-C), 134.5 (d, 6-C), 137.7 (s, 10-C), 138.9 (d, 5-C), and 145.0 (s, 8-C); MS *m/z* (rel intensity) 241 (M^+; 14) and 211 ($M^+-CH_2NH_2$; 100).

Found: C, 84.21; H, 9.90; N, 5.32%. Calcd for $C_{17}H_{23}N$: C, 84.59; H, 9.60; N, 5.80%.

B) With Palladized Charcoal and Sodium Borohydride. To a stirred suspension of 5.0 mg (0.0047 mmol) of 10% palladized charcoal in 3 cm^3 of methanol, with bubbling of nitrogen below the surface, was added dropwise a solution of 10 mg (0.26 mmol) of sodium borohydride in 2 cm^3 of water, and then another solution of 27.0 mg (0.0995 mmol) of **4** in 5 cm^3 of 2 mol dm^{-3} methanolic sodium hydroxide. The mixture was refluxed for 1.5 h and cooled to room temperature. After the addition of 10 cm^3 of 1 mol dm^{-3} hydrochloric acid, the mixture was filtered to remove the catalyst, and the catalyst was washed with chloroform (30 cm^3×2). The combined organic and aqueous solution was worked up as described in *A* to give 7.06 mg (36%) of unchanged **4** and 5.10 mg (21%) of **13**.

Similar treatment of **4** with palladized charcoal in water and at low reaction temperature (30 min at room temperature) yielded 0.93 mg (5%) of **2**, 17.5 mg (65%) of unchanged **4**, and 1.23 mg (5%) of **10**.

C) With Lithium Aluminum Hydride. To a cooled (−50 °C), stirred solution of 10 mg (0.26 mmol) of lithium aluminum hydride in 0.5 cm^3 of THF was added dropwise another solution of 18.4 mg (0.0678 mmol) of **4** in 1 cm^3 of THF over a period of 5 min. This mixture was gradually brought to −4 °C, and kept for 20 min at −4 to −3 °C, during which period the color of the solution changed from blue to green. The reaction mixture was again cooled to −50 °C, mixed slowly with 2 cm^3 of 10% sodium hydroxide solution, and extracted with ether (5 cm^3×4). The usual work up of the organic extract gave 15.4 mg of dark resinous material and 1.34 mg (8%) of **13**.

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