75%, the total reaction time 28 hr. It is apparent that the saturated chloride IV reacted more slowly than the olefinic isomer III and that little skeletal isomerization occurred. It was later found that adjustment of the pH of the diluted acetolysis mixture to just below 7 liberated the saturated acetate VI; basification then liberated the olefinic isomer V, whose infrared spectrum was identical with that of pure V.

Distillation of a mixture of the crude acetates V + VI, b.p. 68–74° (0.25 mm.), was followed by g.l.c. isolation of pure samples of each isomer (silicone grease, 141°; use of Carbowax led to partial formation of the alcohol VII). Compound V, *exo*-2-diethylamino-*syn*-7-acetoxy-5-norbornene, had $n^{25}D$ 1.4726 and infrared bands 5.75 and 8.05 μ (acetate ester) and at 14.10 μ (olefinic *cis*-RCH=CHR); its n.m.r. spectrum is summarized in Table I.

Anal. Calcd. for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27. Found: C, 69.92; H, 9.31; N, 6.28.

Compound VI, 3-acetoxy-5-diethylaminonortricyclene, had $n^{25}D$ 1.4578 and in carbon tetrachloride solution rapidly reverted to a mixture of V and VI. The n.m.r. spectrum of a sample in such a solution containing 85% of VI showed 1 H at 4.90 τ (CHOAc), 10 H at 7.1–8.25 τ (including the hydrogens of NCH_2, R_2CHNR_2, and $OCOCH_3$ [8.05 τ]), 4 H at 8.25–8.85 τ, and 6 H at 9.03 τ (CH_3). The infrared spectrum of VI contained characteristic bands at 5.75 and 8.05 μ (acetate ester) and at 3.26, 12.06, 12.32, and 12.68 μ (substituted nortricyclene).

2-*exo*-Diethylamino-*syn*-7-hydroxy-5-norbornene (VII).—A mixture of 3.9 g. (0.0175 mole) of V and 1.33 g. (0.035 mole) of lithium aluminum hydride was refluxed under nitrogen 2.5 hr. in 200 ml. of ether. The salts and excess hydride were decomposed by the slow addition with rapid stirring of 1.4 ml. of water, 2.0 ml. of 20% sodium hydroxide, and, finally, 4.0 ml. of water. The supernatant ether solution was concentrated to 3.5 g. of a residue C, $n^{24}D$ 1.4846, from which a pure sample of the alcohol VII was obtained by g.l.c., $n^{25}D$ 1.4853. The infrared and n.m.r. spectra of VII were discussed above.

Anal. Calcd. for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.73. Found: C, 72.66; H, 10.31; N, 7.73.

One gram of residue C in 25 ml. of chloroform was converted to the original chloride III by heating it for 1 hr. with 2.3 g. of thionyl chloride and 1.5 ml. of pyridine. Dilution with ice, basification, and a rapid pot-to-pot distillation under reduced pressure afforded a liquid; collection of the material giving the only large peak present in the g.l.c. spectrum of the liquid afforded III, identified from its infrared and n.m.r. spectra. The chlorination did not proceed in the absence of pyridine.

The Reaction between Norbornadiene and N-Chloro-di-*n*-butylamine.—N-Chloro-di-*n*-butylamine was prepared from N-chlorosuccinimide in ether[31]; a solution ~ 0.5 *M* in the undistilled chloramine was then prepared by adding 15.8 g. (0.097 mole) to 190 ml. of 4 *M* sulfuric acid–1.5 *M* water in acetic acid. The reaction with an equivalent amount of norbornadiene was carried out under nitrogen as described above for N-chlorodiethylamine. The work-up afforded 26% of distilled I + II, 27% of the di-*n*-butyl homologs of III and IV, b.p. 82–86° (0.07 mm.), in which the saturated isomer predominated, and 57% of di-*n*-butylamine. The crude aminochloro adducts were boiled 2 hr. in acetic acid–sodium acetate to afford 48% of the corresponding acetates after distillation, b.p. 76.5–82° (0.02 mm.), $n^{25}D$ 1.4755–1.4712. Characteristic infrared bands were obtained of a sample containing 89% of the lower boiling, olefinic isomer (5.75, 8.05, and 14.10 μ) and one containing 67% of the saturated isomer (5.75, 8.05, 12.10, and 12.40 μ). Elemental analyses were obtained for the olefin-rich sample; the pure chlorides and acetates were not isolated.

Anal. Calcd. for $C_{17}H_{29}NO_2$: C, 73.07; H, 10.46; N, 5.01. Found: C, 73.16; H, 10.39; N, 5.07.

(31) E. J. Corey and W. R. Hertler, Jr., *J. Am. Chem. Soc.*, **82**, 1657 (1960).

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY, UNIVERSITY OF WASHINGTON, SEATTLE, WASH., AND SAN JOSE STATE COLLEGE, SAN JOSE, CALIF.]

1H-Cyclohepta[*d*,*e*]-1-pyrindine. A New Conjugate-Unsaturated Heterocyclic System[1,2]

BY LANNY L. REPLOGLE[3]

RECEIVED MARCH 13, 1964

The syntheses of three derivatives (**9a**, **9b**, and **10**) of 1H-cyclohepta[*d*,*e*]-1-pyrindine are described. This new heterocyclic system is iso-π-electronic with the interesting heptalene derivative **5** prepared by Hafner. The ultraviolet and visible spectra of this heterocycle are found to be quite similar to those of Hafner's hydrocarbon; these spectral properties and other data lead to the conclusion that the heterocycle does contain a delocalized π-electron system which involves the "lone pair" electrons of the nitrogen. The n.m.r. spectra of **9a**, **9b**, and **10** are reported and discussed.

Recently there has been considerable interest in heterocyclic analogs of nonbenzenoid aromatic hydrocarbons. The syntheses of several π-excessive[4] heteroanalogs of azulene have been reported. Anderson, Harrison, and Anderson[5] have described the syntheses and some properties of cyclopenta[*c*]thiapyran (**1**) and 2-phenyl-2-pyrindine (**2**). The physical properties of **1** and **2** and the chemical reactivity[6] of **2** appear to be quite similar to those of azulene. Mayer, *et al.*,[7] have briefly described the preparation and some properties of the isomer of **1**, cyclopenta[*b*]-thiapyran (**3**). Reese[8] has provided evidence for the presence of the colored pseudoazulene, 1H-1-pyrindine (**4**), in samples of 5H-1-pyrindine. Both **3** and **4**, which have the heteroatom in the 1-position, are less stable than **1** and **2** which have the heteroatom in the 2-position.[9] All of the data available indicate that these π-excessive heteroanalogs of azulene have properties which correspond more or less to those of azulene.

It seemed desirable to extend studies of heterocyclic analogs of nonbenzenoid aromatic hydrocarbons. Correspondingly, we have prepared three derivatives of the new 1H-cyclohepta[*d*,*e*]-1-pyrindine system. This heterocycle is a π-excessive heteroanalog of the interesting hydrocarbon 2,4-dimethyl[cyclopentadieno-1′,5′,4′:1,11,10-heptalene] (**5**) prepared by Hafner and Schneider.[10]

The general synthetic method involved the intramolecular condensation of an N-methylacetamido group in the 1-position of an azulene with an 8-methyl

(1) Supported in part by grants (G7397 and GP-250) from the National Science Foundation.

(2) Reported in part as a communication: A. G. Anderson, Jr., and L. L. Replogle, *J. Am. Chem. Soc.*, **83**, 3333 (1961).

(3) Chemistry Department, San Jose State College, San Jose, Calif.

(4) A. Albert, "Heterocyclic Chemistry. An Introduction," Essential Books, Fair Lawn, N. J., 1959.

(5) A. G. Anderson, Jr., W. F. Harrison, and R. G. Anderson, *J. Am. Chem. Soc.*, **85**, 3448 (1963).

(6) A. G. Anderson, Jr., and W. F. Harrison, *ibid.*, **86**, 708 (1964).

(7) R. Mayer, J. Franke, V. Horak, I. Hanker, and R. Zharadnik, *Tetrahedron Letters*, **No. 9**, 289 (1961).

(8) C. B. Reese, *J. Am. Chem. Soc.*, **84**, 3979 (1962).

(9) However, it seems that 2-methyl-2-pyrindine was too unstable to characterize; *cf.* ref. 5.

(10) K. Hafner and J. Schneider, *Ann.*, **624**, 37 (1959).

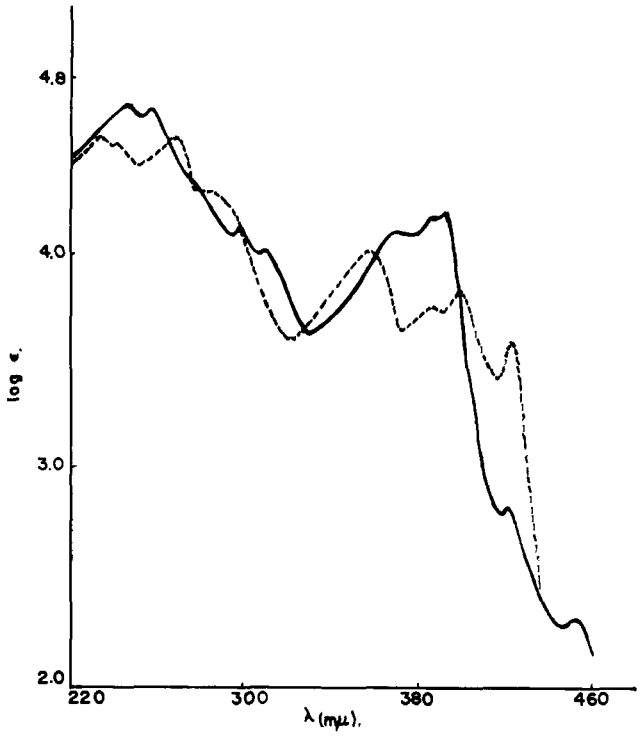


Fig. 1.—The ultraviolet absorption spectra of 1,2,5,7-tetramethylcyclohepta[*d*,*e*]-1-pyridine (- - - - - - - - -) and 2,4-dimethyl-[cyclopentadieno-1′,5′,4′:1,11,10-heptalene] (———) in saturated hydrocarbon solvent.

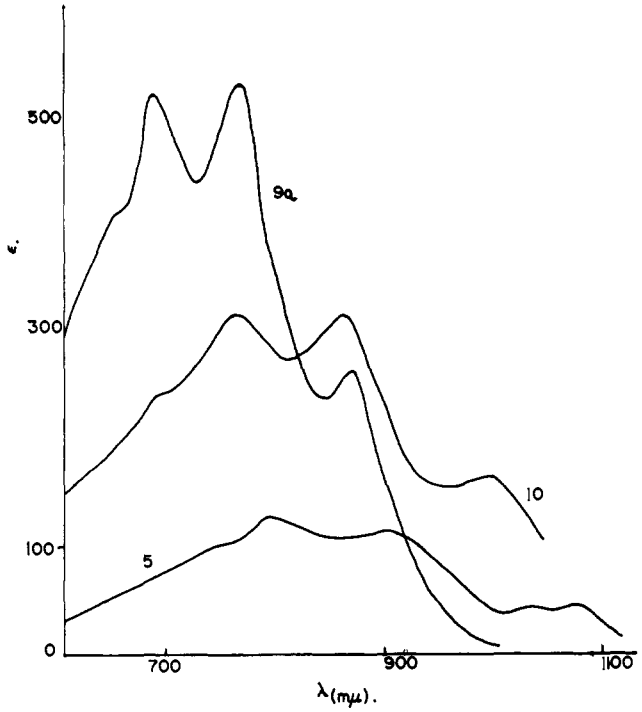
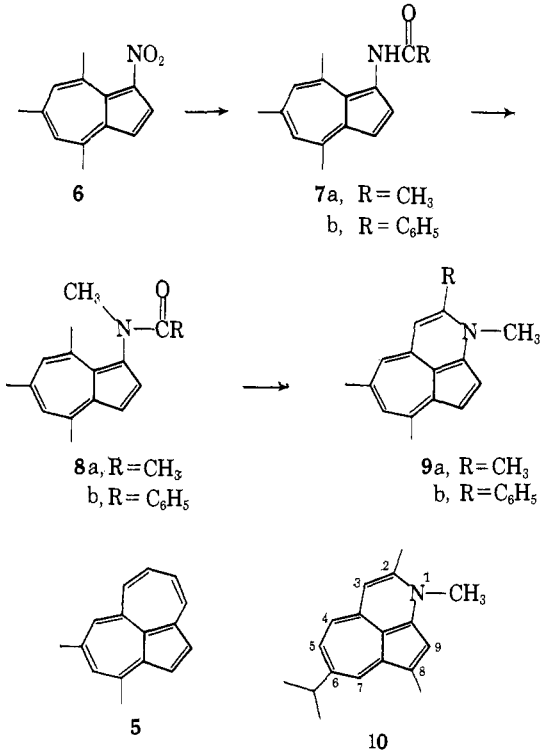


Fig. 2.—The visible and near-infrared spectra of 1,2,5,7-tetramethylcyclohepta[*d*,*e*]-1-pyridine (**9a**), 1,2,8-trimethyl-6-isopropylcyclohepta[*d*,*e*]-1-pyridine (**10**), and 2,4-dimethyl-[cyclopentadieno-1′,5′,4′:1,11,10-heptalene] (**5**) in saturated hydrocarbon solvent.

group. 1-Nitro-4,6,8-trimethylazulene (**6**) was reductively acetylated[11] to the known[12] 1-acetamido-4,6,8-trimethylazulene (**7a**) in almost quantitative yield. This amide could be alkylated by treatment with sodium hydride dispersion[13] followed by methyl iodide to give the N-methyl derivative **8a** in 89% yield. As anticipated,[14] the intramolecular condensation of **8a** was effected by reaction with sodium N-methylanilide, and an 86% yield of 1,2,5,7-tetramethylcyclohepta[*d*,*e*]-1-pyridine (**9a**) was obtained in the form of green needles. The product slowly decomposed when heated on a melting point block, but a satisfactory melting point, 210–212°, could be determined on a sample in an evacuated capillary tube.

A similar reaction path led to the 2-phenyl derivative **9b**. The benzamide **7b** could be synthesized by treating 1-amino-4,6,8-trimethylazulene, prepared from **6** by the method of Hafner, *et al.*,[12] with benzoyl chloride and pyridine. This amide was converted to the N-methyl derivative **8b** by the same method used for **8a**. Cyclization using sodium N-methylanilide gave **9b** as green needles, m.p. 131–135°,[15] in 64% yield. An analytical sample of **9b**, recrystallized from Skellysolve B, showed m.p. 134–136°.

The other pyrindine derivative, **10**, to be described here was prepared in an analogous manner from guaiazulene. Nitration of guaiazulene with tetranitromethane and subsequent reductive acetylation yielded 3-acetamidoguaiazulene[16] (**11**). Methylation of this amide afforded 3-N-methylacetamidoguaiazulene (**12**) as a blue crystalline solid in 56% yield. Treatment of **12** with sodium N-methylanilide in ether gave 1,2,8-trimethyl-6-isopropylcyclohepta[*d*,*e*]-1-pyridine (**10**) as red-brown needles, m.p. 179–180.5° (evacuated capillary), in 61% yield.



(11) A. G. Anderson, Jr., J. A. Nelson, and J. J. Tazuma, *J. Am. Chem. Soc.*, **75**, 4980 (1953).

(12) K. Hafner, A. Stephan, and C. Bernhard, *Ann.*, **650**, 42 (1962).

(13) W. S. Fones, *J. Org. Chem.*, **14**, 1099 (1949).

(14) The acidic nature of the methyl protons in 4-(8)methylazulenes is well established; *cf.* ref. 10.

(15) The melting point of this derivative **9b** could be obtained in the usual fashion without any apparent decomposition.

(16) K. G. Scheibli, Doctoral Thesis, Eidgenössischen Technischen Hochshule, Zurich, Switzerland, 1952.

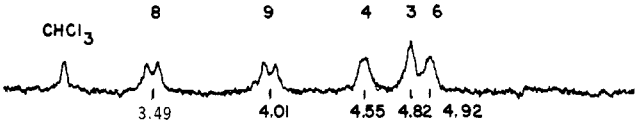


Fig. 3.—The n.m.r. spectrum of 1,2,5,7-tetramethylcyclohepta-[*d*,*e*]-1-pyrindine relative to internal tetramethylsilane (TMS = 10.0).

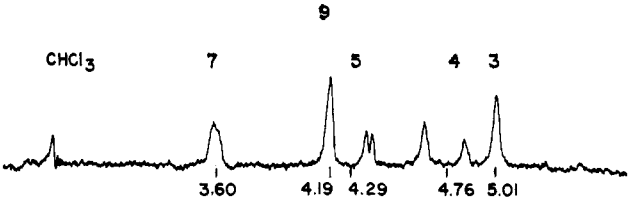


Fig. 4.—The n.m.r. spectrum of 1,2,8-trimethyl-6-isopropyl-cyclohepta[*d*,*e*]-1-pyrindine relative to internal tetramethylsilane (TMS = 10.0).

Absorption Spectra.—The absorption spectra of the 1H-cyclohepta[*d*,*e*]-1-pyrindine system are quite similar to those of its hydrocarbon analog. Comparison of the ultraviolet (Fig. 1) and visible–near-infrared (Fig. 2) spectra of **9a** and **5** shows a close resemblance between the two. Both show a high-intensity band in the ultraviolet and a low-intensity band in the 350–450 mμ region. The general band shapes and intensities are fairly well matched. The long wave length bands of the two are also quite similar, with the maxima for **9a**, which appear about 100 mμ to shorter wave lengths, being about four times as intense. These observations are consistent with Anderson's data[5] which show that the long wave length band of azulene is found at longer wave lengths and has weaker absorption intensities than the corresponding band in its heteroanalogs **1** and **2**. It is interesting to note that while the spectra of **5** show doublets in the tailing regions of all three bands, the spectra of **9a** in the corresponding regions show only single peaks.

The effect of the position of alkyl groups on the cyclohepta[*d*,*e*]-1-pyrindine ring with respect to shifting the long wave length band is quite similar to that in azulene. Changing the alkyl substitution pattern from 4,6,8-trimethylazulene to 1,4-dimethyl-7-isopropylazulene (guaiazulene) causes a bathochromic shift, *viz.*, 547 to 605 mμ[17] ($\Delta\nu_{max} \simeq 1700$ cm.$^{-1}$); there is a corresponding bathochromic shift ($\Delta\nu_{max} \simeq 1400$ cm.$^{-1}$) observed in going from **9a** to **10** where there is a similar change in alkyl substitution.

N.m.r. Spectra.—An interpretation of the n.m.r. spectra of the pyrindines would be desirable since, in addition to providing proof of structure, it may be valuable in helping to determine the position(s) of attack in substitution reactions. Comparison of the proton magnetic spectra of **9a** (Fig. 3) and **10** (Fig. 4) allows a reasonable interpretation to be made. Examining the spectrum of **10** first, one observes a broad peak with some unresolved splitting at 3.60 τ. This is assigned to the 7-proton since the corresponding 4(8)-proton in azulene is also found at lowest field.[18] The 4- and 5-proton resonances should be doublets, and the doublet centered at 4.76 τ is assigned to the former. The doublet corresponding to the 5-proton is believed to be centered at 4.29 τ with a sharp singlet at 4.19 τ obscuring the left-hand member of the doublet.[19] The right-hand member of this doublet shows a small additional splitting ($J \simeq 1.8$ c.p.s.) which is probably due to cross-ring coupling with the 7-proton.[20] This leaves only the sharp singlets at 4.19 and 5.01 τ to be assigned. Evidence that the former is due to the 9-proton is provided by the spectrum of **9a** which shows doublets ($J \simeq 3.5$ c.p.s.)[21] centered at 3.49 and 4.01 τ which must correspond to the 8- and 9-protons. The different alkyl substitution in **9a** and **10** would not be expected to cause much difference in the chemical shift values for a given proton in the two structures. Thus it seems reasonable that the doublet centered at 4.01 τ in the spectrum of **9a** and the singlet at 4.19 τ in the spectrum of **10** are due to the 9-proton. The 3.49 τ doublet must be the resonance of the 8-proton of **9a**, and the remaining three peaks in this spectrum at 4.55, 4.82, and 4.92 τ are tentatively assigned to the 4-, 3-, and 6-protons, respectively. The assignment of these latter three peaks is based on their chemical shifts being close to the corresponding resonances for the same protons in **10**, and the observation that the peaks at 4.55 and 4.92 τ are broader (possibly due to some weak cross-ring coupling between the 4- and 6-protons). If these assignments are accepted, one observes that the proton resonances for **10** are shifted *ca.* 0.2 p.p.m. to higher fields from the corresponding peaks in the spectrum of **9a**.

At higher fields (not shown in Fig. 3 and 4) in the spectrum of **9a**, the N-methyl group resonance is observed at 6.80 τ while the ring methyl signals are observed around 8 τ with the highest field peak being assigned to the 5-methyl group. The intense peak at 6.92 τ in the spectrum of **10** is assigned to the N-methyl group, and the resonances at 7.72 and 8.00 τ are assigned to the 8-methyl and 2-methyl groups, respectively; the doublet due to the methyl groups of the isopropyl group is centered at 8.98 τ.

The proton magnetic resonance spectrum of **9b** is consistent with its proposed structure, showing a broad phenyl peak at 2.80 τ, the same ring proton spectrum as **9a**, and only two aromatic methyl groups at 7.98 and 8.17 τ.

Comparison of the n.m.r. spectrum[22] of Hafner's hydrocarbon (**5**) with the spectra of the pyrindines shows that, in general, the resonances of the ring protons in the heterocyclic system are found at higher fields. This is to be expected because of the greater electron density on the ring carbon atoms, which should cause greater shielding of the protons, for this π-excessive heterocyclic system; this observation is also consistent with Anderson's data.[5]

Other Properties.—The 1H-cyclohepta[*d*,*e*]-1-pyrindine ring system is quite basic. Both **9a** and **10** are completely protonated in 5% hydrochloric acid giving orange-red solutions. As expected, the absorption spectrum of protonated **9a** (in 10% sulfuric acid) is

(17) M. Scholz and W. Treibs, *Z. Elektrochem.*, **65**, 120 (1961).

(18) W. G. Schneider, H. J. Bernstein, and J. A. Pople, *J. Am. Chem. Soc.*, **80**, 3497 (1958).

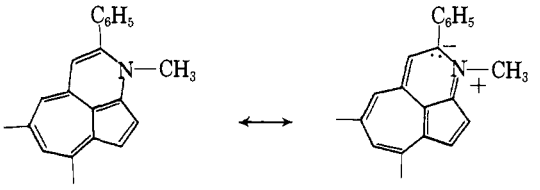
(19) A spectrum of **10** in carbon tetrachloride shows the singlet shifted from the doublet.

(20) Such cross-ring coupling between the corresponding protons (6- and 8-) of guaiazulene has been observed (unpublished data).

(21) The observed coupling constants for protons in the 5-membered ring, 3.5 c.p.s., and for protons in the 7-membered ring, 11 c.p.s., are consistent with those found for azulene; *cf.* ref. 18.

(22) E. G. Hoffman, *Ann.*, **624**, 47 (1959).

quite different from the unprotonated species, and the long wave length band now appears in the 450–510 mμ region. In contrast to the behavior of **9a** and **10**, **9b** is much less basic. Even repeated extractions of an ethereal solution of this derivative with 10% hydrochloric acid left some of the pyrindine in the ether layer. It is not understood why there should be such a difference in basicity caused by the replacement of a methyl group by a phenyl group in the 2-position. Possibly it is due to stabilization of the neutral base by the phenyl group involving a charge-separated resonance structure. The pronounced basicity of this heterocyclic system is in agreement with observations for 1-methyl-1-pyrindine[8] and 2-phenyl-2-pyrindine.[6]



The 1H-cyclohepta[*d*,*e*]-1-pyrindine heterocycle appears to be more stable than its parent ring system 1-pyrindine. Thus **9a**, **9b**, and **10** are all fairly stable in crystalline form and can be handled in the usual manner while 1-methyl-1-pyrindine is too unstable to be isolated.[8] All of the tricyclic pyrindines can be chromatographed successfully on deactivated (Grade IV or V) neutral alumina, but they decompose if active neutral alumina or Merck alumina is used as the adsorbent.

From the limited data available it seems that this new heterocycle contains a delocalized π-electron system which involves the "lone pair" on the nitrogen. It certainly shows a closer similarity to Hafner's hydrocarbon (**5**) than to a 1-aminoazulene. For example, the absorption spectra of **9a** closely resemble those of its hydrocarbon analog **5** and are unlike those of 1-amino-4,6,8-trimethylazulene.[12] Also, **9a** is much more stable than this amine.

Visible Spectra of 1-Acylamidoazulene Derivatives.—Schulze and Heilbronner[23] have discussed steric hindrance in 1-acetamidoazulene derivatives which have a methyl group in the 2- or 8-positions. For these compounds the adjacent methyl group interferes with conjugation of the "lone pair" electrons of the nitrogen atom with the ring. Electron-donating conjugation in the 1-position should cause a bathochromic shift.[24] As a result of the steric hindrance by a 2- or 8-methyl group, the bathochromic shift due to a 1-acetamido group in these compounds is greatly diminished. This effect is also observed (Table I) for the analogous amides prepared in this study. A 1-acetamido group on 4,6,8-trimethylazulene causes a bathochromic shift of only +16 mμ as compared to +57 mμ when substituted on azulene. The greater bathochromic shift observed for the 1-benzamido group (+35 mμ) relative to that of the 1-acetamido group is probably due to the lesser electron-withdrawing power of the benzoyl group. Since there will be conjugation between the carbonyl group and the benzene ring, there will be less amide resonance in the benzamido group; a decrease in amide resonance will make the "lone pair" electrons of the nitrogen more available for conjugation with the ring.

(23) J. Schulze and E. Heilbronner, *Helv. Chim. Acta*, **41**, 1492 (1958).

(24) A. G. Anderson, Jr., and B. M. Steckler, *J. Am. Chem. Soc.*, **81**, 4941 (1959).

TABLE I

PRINCIPAL MAXIMA (mμ) IN THE VISIBLE REGION FOR 1-(3)-ACYLAMIDOAZULENE DERIVATIVES[a]

Compound[b]	λ_{max}, mμ	$\Delta\lambda_{max}$,[c] mμ
1-NHAc–TMA (**7a**)	563	+16
1-N(CH_3)Ac–TMA (**8a**)	553	+ 6
1-NHBz–TMA (**7b**)	582	+35
1-N(CH_3)Bz–TMA (**8b**)	560	+13
3-NHAc–Gz (11)	616	+11
3-N(CH_3)Ac–Gz (12)	610	+ 5
1-NHAc–Az	637[d]	+57
1-N(CH_3)Ac–Az (**14**)	590	+10

[a] Cyclohexane solution. [b] TMA = 4,6,8-trimethylazulene, Gz = guaiazulene, Az = azulene. [c] Shift measured relative to corresponding hydrocarbon, *viz.*, 4,6,8-trimethylazulene, guaiazulene, or azulene. [d] Ref. 23 reports 630 mμ; ref. 11, 625 mμ (ethanol solution).

Replacement of the hydrogen attached to the nitrogen in the 1-acetamido group by a methyl group apparently causes more steric hindrance as a further hypsochromic shift is observed. Thus the shift due to a 1-(3)-N-methylacetamido group on 4,6,8-trimethylazulene or guaiazulene is only +5 or 6 mμ. One would have expected the inductive effect of the methyl group to aid the nitrogen in releasing electrons to the azulene ring, thus causing a greater bathochromic shift. In order to determine the effect of the 1-N-methylacetamido group in the absence of an 8-methyl group, 1-N-methylacetamidoazulene (**14**) was prepared from 1-acetamidoazulene (**13**). Rather surprisingly, the introduction of the N-methyl group caused a strong hypsochromic shift from 637 mμ, the principal maximum of **13**, to 590 mμ, the principal maximum of **14**. Apparently there must be considerable steric interference between the N-methyl group and the 8-proton.

Experimental[25]

The petroleum ether used was reagent grade, b.p. 30–60°. Dry ether and tetrahydrofuran (THF) were distilled from lithium aluminum hydride just prior to use.

1-Acetamido-4,6,8-trimethylazulene (**7a**).—To a stirred mixture of 546 mg. of 1-nitro-4,6,8-trimethylazulene,[26] 600 mg. of sodium acetate, 10 ml. of acetic acid, and 10 ml. of acetic anhydride was added 1.5 g. of zinc dust, in portions, over a period of 5 min. During this addition the solution changed from a red to a purple color. After being stirred for 10 more minutes, the reaction mixture was poured into water and extracted with dichloromethane. The combined extracts were washed with water, dilute ammonium hydroxide, and then water again, and dried over sodium sulfate. Removal of solvent left a purple, crystalline solid which was chromatographed over alumina; the single purple band was eluted with dichloromethane. Removal of solvent from the purple eluate left 562 mg. of purple crystals, m.p. 178–181°. The position of the principal maximum in the visible, λ_{max} (cyclohexane) 563 mμ (ε 524), and the m.p. corre-

(25) Melting points were taken on a calibrated Fisher–Johns apparatus or, where indicated, in sealed evacuated capillaries using a Hershberg-type apparatus. Infrared spectra were recorded using a Perkin–Elmer Model 21 or a Beckman IR-5. Ultraviolet, visible, and near-infrared spectra were taken on a Cary Model 14. Nuclear magnetic resonance spectra were taken in deuteriochloroform solution with an internal tetramethylsilane marker, and were recorded by Mr. B. J. Nist on a 60 Mc. Varian Associates spectrometer, Model V-K3507, or by the author on a Model A-60. Microanalyses were performed by Dr. A. Bernhardt, Max Planck Institute, Mülheim, Germany, or by Berkeley Analytical Labs, Berkeley, Calif.

(26) K. Hafner and C. Bernhard, *Ann.*, **625**, 108 (1959).

responded well with the m.p. (181–182°), and λ_{max} (benzene) 560 mμ, reported[12] in the literature. An infrared spectrum taken in carbon tetrachloride solution displayed carbonyl absorption at 5.93 μ and N–H absorption at 2.94 μ.

1-N-Methylacetamido-4,6,8-trimethylazulene (8a).—A mixture of 500 mg. (2.20 mmoles) of 1-acetamido-4,6,8-trimethylazulene, 121 mg. of 51.5% sodium hydride–oil dispersion (62 mg., 2.6 mmoles), and 30 ml. of dry tetrahydrofuran was heated to reflux with stirring for 1 hr. The solution, originally purple, turned bluish green. To the cooled mixture was added, with stirring, 1 ml. of methyl iodide, whereupon the mixture became purple. After being stirred for 15 min., the reaction mixture was treated with water and extracted with ether. The ether extract was washed with water, dried over sodium sulfate, and the solvent removed. Chromatography of the purple residue gave a broad purple band followed by a small blue band and then a purple band. Removal of solvent from the eluate of the main purple band gave 474 mg. (89%) of purple crystals, m.p. 162–164° (softening at *ca.* 155°). A cyclohexane solution of **8a** showed maxima in mμ (log ε) in the ultraviolet at 246 (4.46), 291 (4.65), 337 (3.63), 347 (3.70), and 352 (3.75). There was a single maximum in the visible at 553 mμ (ε 525) with shoulders at 592 mμ (ε 442) and 650 mμ (ε 160). A carbon tetrachloride solution showed carbonyl absorption in the infrared at 6.01 μ.

Anal. Calcd. for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.81. Found: C, 79.70; H, 7.89; N, 5.82.

1,2,5,7-Tetramethylcyclohepta[*d*,*e*]-1-pyridine (9a).—In a dry flask 482 mg. (2.00 mmoles) of 1-N-methylacetamido-4,6,8-trimethylazulene in 30 ml. of dry ether was treated under nitrogen with 3.0 ml. of a 0.72 *N* sodium N-methylanilide solution; the stirred reaction mixture immediately became yellow-brown and then began to turn green. After being refluxed and stirred (under nitrogen) for 2 hr., the green mixture was treated with water containing ammonium chloride and then extracted with ether. The combined ether extracts were washed well with water and then successively with one 200-ml. portion of 0.1 *N* hydrochloric acid, two 100-ml. portions of 0.1 *N* hydrochloric acid, and a 100-ml. and a 50-ml. portion of 0.3 *N* hydrochloric acid. The last acid extract was almost colorless. Chromatography of the residue from the ether extracts yielded 44 mg. of starting material (**8a**).

The combined orange-red acid extracts were neutralized with solid sodium carbonate (cooling). The resultant green precipitate was collected over a layer of filter-aid and taken up in dichloromethane. This solution was dried over sodium sulfate, and solvent was removed under diminished pressure. The residue consisted of 385 mg. of green needles, m.p. 210–212° (evacuated capillary), a yield of 86% (95% net). The pyrindine **9a** in cyclohexane solution showed maxima in mμ (log ε) in the ultraviolet at 236 (4.52), shoulder at 243 (4.47), 270 (4.51), 290 (4.26), 358 (3.99), 387 (3.74), 399 (3.81), 423 (3.56), and in the visible (ε) with a shoulder at 630 (365), 688 (519), 766 (529), and 869 (267). An infrared spectrum showed no absorption corresponding to NH or carbonyl bands. A solution of **9a** in 10% sulfuric acid showed maxima in mμ (log ε) at 238 (4.33), shoulder at 253 (4.20), 278 (4.06), 292 (4.04), 301 (4.02), shoulder at 323 (3.87), 456 (3.10), 481 (3.10), and a shoulder at 510 (3.03).

Anal. Calcd. for $C_{16}H_{17}N$: C, 86.05; H, 7.68; N, 6.27. Found: C, 85.96; H, 7.43; N, 6.31.

1-Benzamido-4,6,8-trimethylazulene (7b).—1-Nitro-4,6,8-trimethylazulene (432 mg., 2.00 mmoles) was reduced to the amine, using the procedure of Hafner, *et al.*,[12] with 20 ml. of 5% hydrochloric acid, 15 ml. of acetone, and 0.8 g. of zinc dust. Considerable difficulty with emulsions was encountered during benzene extraction. The green benzene extracts (containing emulsion) were dried over magnesium sulfate, filtered, and treated with a mixture of 8 ml. of pyridine and 4 ml. of benzoyl chloride. This reaction mixture, which was becoming purple in color, was allowed to stand for 0.5 hr. with occasional swirling. After extraction with 5% hydrochloric acid and then 5% sodium hydrogen carbonate, the purple benzene solution was concentrated and cooled. The resulting crystalline solid was collected and washed with ether; 324 mg. of **7b**, as small blue crystals, m.p. 253–256°, was obtained. The mother liquor was concentrated and chromatographed over acid-washed alumina. Dichloromethane eluted an orange-red band and then a purple band which had a brown tailing region. The residue from the purple eluate was recrystallized from benzene, yielding another 47 mg. of product, m.p. 251–257°. The combined yield was 64%. An analytical sample, recrystallized from carbon tetrachloride, showed m.p. 256–258°. A chloroform solution of **7b** showed maxima in mμ (log ε) in the ultraviolet at 244 (4.45), 296 (4.56), shoulder at 350 (3.90), and 385 (3.68); there was a single broad maximum in the visible at 563 mμ (ε 452). The maximum in the visible region for a cyclohexane solution (10-cm. cells) was at 582 mμ. An infrared spectrum (Nujol mull) showed an NH band at 3.06 μ and a carbonyl band at 6.07 μ.

Anal. Calcd. for $C_{20}H_{19}NO$: C, 83.01; H, 6.62; N, 4.84. Found: C, 82.59; H, 6.73; N, 5.02.

1-N-Methylbenzamido-4,6,8-trimethylazulene (8b).—About 50 ml. of dry tetrahydrofuran was distilled into a dry flask containing 289 mg. (1.00 mmole) of 1-benzamido-4,6,8-trimethylazulene and 59 mg. of a 51.5% sodium hydride–oil dispersion (26 mg., 1.1 mmoles). Bubbles of gas were evolved and the solution turned green. The reaction mixture was refluxed for 1 hr., and, after cooling, was treated with 2 ml. of methyl iodide. The resulting purple mixture was stirred for 20 min., poured into water, and extracted with dichloromethane. The combined dichloromethane extracts were washed with water, dried over sodium sulfate, and the solvent was removed. The residue was chromatographed over acid-washed alumina. A small yellow band was eluted with chloroform. The broad purple band was eluted with dichloromethane, with the tailing portion which contained a brown band being collected separately. Removal of solvent from the main purple eluate left 273 mg. (90%) of a purple, crystalline solid, m.p. 139.5–142°. An analytical sample was recrystallized twice from Skellysolve B to give purple plates, m.p. 143.5–144.5°. A cyclohexane solution of **8b** showed maxima in mμ (log ε) in the ultraviolet at 246 (4.44), 299 (4.56), shoulder at 340 (3.66), and 354 (3.76); there was a single broad maximum in the visible at 560 mμ (ε 481). The infrared spectrum of a carbon tetrachloride solution showed a carbonyl peak at 6.1 μ.

Anal. Calcd. for $C_{21}H_{21}NO$: C, 83.13; H, 6.98; N, 4.62. Found: C, 83.08; H, 6.97; N, 4.69.

1,5,7-Trimethyl-2-phenylcyclohepta[*d*,*e*]-1-pyridine (9b).—Approximately 10 ml. of dry ether was distilled into a dry 50-ml. flask containing 152.5 mg. (0.500 mmole) of 1-N-methylbenzamido-4,6,8-trimethylazulene and the mixture was treated with 0.8-ml. of an ethereal solution of sodium N-methylanilide (0.72 *N*) (dry nitrogen atmosphere). The brown-green reaction mixture was stirred for 7.5 hr.; water was added and the mixture extracted with ether. The combined blue-green ethereal extracts were washed with water and saturated salt solution, and dried over sodium sulfate. Removal of solvent left a semicrystalline solid which was chromatographed over Grade IV Woelm alumina. Benzene eluted a green band, dichloromethane a purple band. From the purple eluate was obtained 12 mg. of the starting amide **8b**. Removal of solvent (rotary evaporator) from the green eluate left a green crystalline solid which was triturated with two 3-ml. portions of petroleum ether. A yield of 91 mg. (64%) of **9b** as green needles, m.p. 131–135° (softening at about 120°), was obtained. An analytical sample, recrystallized from Skellysolve B, showed m.p. 134–136°. A cyclohexane solution of **9b** showed maxima in the ultraviolet in mμ (log ε) at 230 (4.40), 244 (4.45), 274 (4.56), shoulder at 285 (4.45), shoulder at 350 (3.95), 361 (4.09), 387 (3.66), 404 (3.74), and 425 (3.54), and in the visible (ε) with a shoulder at 645 (345), 702 (472), 783 (468), and 887 (233).

Anal. Calcd. for $C_{21}H_{19}N$: C, 88.38; H, 6.71; N, 4.91. Found: C, 88.09; H, 6.55; N, 4.96.

3-Nitroguaiazulene.—Guaiazulene was allowed to react with tetranitromethane in ethanol and pyridine according to the procedure of Scheibli.[16] A 46% yield was obtained.

3-Acetamidoguaiazulene (11).—3-Nitroguaiazulene was reductively acetylated[11] with zinc dust, acetic acid, and acetic anhydride. The product was isolated as green needles, m.p. 168–170° (lit.[16] 163.5–164°). The principal maximum in the visible region of a cyclohexane solution was at 616 mμ.

3-N-Methylacetamidoguaiazulene (12).—Dry THF (50 ml.) was distilled into a dry flask containing 409 mg (1.60 mmoles) of 3-acetamidoguaiazulene, and 140 mg. of a 51.5% sodium hydride–oil dispersion (72 mg., 3.0 mmoles) was added. The reaction mixture was stirred and refluxed for 4 hr. and, after cooling, was treated with 1.0 ml. of methyl iodide and stirred for an additional 15 min. Some water as added and the mixture extracted with ether. The ethereal extract was dried over sodium sulfate and the solvent removed. Chromatography of the residue gave a single, blue band. Removal of solvent from the blue eluate left

346 mg. (80%) of a blue oil that slowly crystallized, m.p. 62–68°. A portion of this, 95 mg., was rechromatographed and recrystallized from hexane giving 67 mg. (70% recovery, 56% net yield) of blue crystals, m.p. 75–77.5°.

A cyclohexane solution of **12** showed maxima in mμ (log ε) in the ultraviolet at 246 (4.38), 288 (4.57), 304 (4.25), 351 (3.76), and 368 (3.73). There was a single broad maximum in the visible at 610 mμ (ε 490) with shoulders at 660 mμ (ε 403) and 731 mμ (ε 144). The infrared spectrum of a carbon tetrachloride solution showed carbonyl absorption at 6.00 μ.

Anal. Calcd. for $C_{15}H_{23}NO$: C, 80.25; H, 8.61; N, 5.20. Found: C, 80.31; H, 8.67; N, 5.22.

1,2,8-Trimethyl-6-isopropylcyclohepta[*d,e*]-1-pyrindine (10).—A dry flask containing 120 mg. (0.447 mmole) of 3-N-methylacetamidoguaiazulene was flushed with dry nitrogen, and 2.0 ml. of a 0.36 *N* sodium N-methylanilide–ether solution was injected with stirring. The blue reaction mixture immediately turned brown-green. After being refluxed and stirred for 4 hr., the mixture was treated with ammonium chloride solution and extracted with ether. The green ether phase was extracted with 5% hydrochloric acid giving a purple acid layer and a faint yellow-green ether layer. The combined acid extracts were washed well with ether (yellow ethereal extracts), and neutralized with solid sodium carbonate. Ether dissolved the precipitated green solid. The green ethereal extract was washed with water and dried over sodium sulfate. A rotary evaporator was used, first to remove the solvent at reduced pressure (water pump), and then all volatile material by heating the flask at a lower pressure (*ca.* 2 mm.) for several hours. The crystalline residue, after trituration with three 5-ml. portions of petroleum ether, yielded 68 mg. (61%) of red-brown needles, m.p. 179–180.5° (evacuated capillary). The analytical sample after recrystallization from ether melted at 180.5–182°. A cyclohexane solution of **10** showed maxima in mμ (log ε) in the ultraviolet at 238 (4.47), 253 (4.43), 270 (4.49), shoulder at 300 (3.84), 361 (4.12), 398 (3.69), 422 (3.62), 449 (3.43); the far wave length band had maxima μ (ε) at 763 (317), 862 (315), and 996 (166) with a shoulder at 690 (241). The infrared spectrum showed no absorption corresponding to NH or carbonyl groups.

Anal. Calcd. for $C_{18}H_{21}N$: C, 86.00; H, 8.42; N, 5.57. Found: C, 85.77; H, 8.51; N, 5.73.

1-Acetamidoazulene (13) was prepared from 1-nitroazulene by the method of Anderson, *et al.*[11] A cyclohexane solution exhibited the principal maximum in the visible at 637 mμ (5-cm. cells).

1-N-Methylacetamidoazulene (14).—About 5 ml. of dry tetrahydrofuran was distilled into a dry 10-ml. flask containing 37 mg. (0.20 mmole) of 1-acetamidoazulene and 12 mg. of a 51.5% sodium hydride–oil dispersion (6.2 mg., 0.26 mmole). The reaction mixture, which began to bubble and turn green, was stirred for 0.5 hr. Methyl iodide (1.0 ml., 16 mmoles) was added, and the mixture stirred for 45 min. Ether was added, and the blue ethereal solution was washed with water and dried. The blue oil left after removal of solvent was chromatographed over alumina. The single blue band was eluted with a 1:1 ether–dichloromethane mixture. Removal of solvent from the blue eluate left a blue oil that crystallized when triturated with petroleum ether giving 40 mg. (100%) of **14**, m.p. 71–73°. A cyclohexane solution exhibited maxima in the ultraviolet in mμ (log ε) at 237 (4.28), 277 (4.61), 282 (4.61), shoulder at 286 (4.51), 333 (3.51), shoulder at 342 (3.61), 344 (3.63), and 357 (3.40), and in the visible (ε) with a shoulder at 572 (291), 590 (341), 613 (319,) 642 (306), shoulders at 669 (177) and 710 (124). An infrared spectrum (carbon tetrachloride solution) showed carbonyl absorption at 6.0 μ.

Anal. Calcd. for $C_{13}H_{13}NO$: C, 78.36; H, 6.57; N, 7.03. Found: C, 77.93; H, 6.87; N, 6.94.

Acknowledgment.—The author is greatly indebted to Dr. A. G. Anderson, Jr., for providing a postdoctoral appointment, which enabled some of this work to be done, and for valuable discussions. Financial support by the National Science Foundation is gratefully acknowledged.

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE STATE UNIVERSITY OF IOWA, IOWA CITY, IOWA]

Benzopyrylium Salts. VIII. The Synthesis and Properties of 7-Dimethylaminoflavylium Salts[1]

BY WILLIAM C. BAIRD, JR.,[2,3] AND R. L. SHRINER

RECEIVED FEBRUARY 29, 1964

The synthesis of 7-dimethylaminoflavylium salts has been realized according to the reaction series: 4-dimethylaminosalicyaldehyde → 2-hydroxy-4-dimethylaminochalcone → 7-dimethylaminoflavylium salt. Flavylium salts have been prepared where the anion is represented by chloride, ferrichloride, and perchlorate ions. The ultraviolet and visible spectra of these compounds have been measured and compared to those of the parent compound, flavylium perchlorate. The effect of pH on 7-dimethylaminoflavylium chloride has been observed by noting the changes induced in the spectrum of this salt as the pH was varied.

The introduction of various auxochromes, notably hydroxy, methoxy, and amino groups, into the chromophoric flavylium cation has been the subject of several investigations designed to study the effects of structure and substitution on the spectra of flavylium salts.[1-9] The effect of a benzo-substituted dimethylamino group has not previously been observed; in fact only a single flavylium salt containing such an amino group, 2′,4′-dimethoxy-4-methyl-7-dimethylaminoflavylium perchlorate, has been reported.[8b] In this case the presence of the auxochromic methoxy groups in the 2-phenyl ring precludes a definite conclusion regarding the influence of the dimethylamino group on the spectrum of this salt.

The synthesis of 7-dimethylaminoflavylium salts has been achieved according to three general synthetic routes. These are summarized in Chart I, which illustrates the synthesis of 7-dimethylaminoflavylium perchlorate (I). The required intermediate, 4-dimethylaminosalicylaldehyde (II), was prepared by the reaction of *m*-dimethylaminophenol with dimethylformamide in the presence of phosphorus oxychloride. Subjecting this aminoaldehyde to an aldol condensation with acetophenone in the presence of ethanolic potassium hydroxide led to the formation of 2-hydroxy-4-dimethylaminochalcone (III). Cyclization of the chalcone with anhydrous hydrogen chloride gave 7-

(1) Preceding paper in this series: R. L. Shriner and R. Sutton, *J. Am. Chem. Soc.*, **85**, 3989 (1963).

(2) du Pont Predoctoral Fellow. Abstracted in part from a thesis submitted to the Graduate School of the State University of Iowa in partial fulfillment for the Ph.D. Degree.

(3) Central Basic Research Laboratory, Esso Research Center, Linden, N. J.

(4) E. H. Charlesworth and R. Robinson, *J. Chem. Soc.*, 1619 (1934).

(5) H. Healey and R. Robinson, *ibid.*, 1625 (1934).

(6) K. Hayashi, *Acta Phytochim.*, **7**, 117 (1933).

(7) A. M. Robinson and R. Robinson, *J. Chem. Soc.*, 1439 (1932); 25 (1933).

(8) (a) C. Michaelidis and R. Wizinger, *Helv. Chim. Acta*, **34**, 1761 (1951); (b) *ibid.*, **34**, 1770 (1951); (c) *ibid.*, **34**, 1776 (1951).

(9) R. Wizinger and A. Luthiger, *ibid.*, **36**, 526 (1953).