water. The product (1.25 g.), isolated by benzene extraction, was chromatographed on silica. The unsaturated ketone **12b**, eluted with 10% ethyl acetate in benzene, was recrystallized from acetone–hexane to provide the pure sample: m.p. 156–158°; λ_{max} 2.74, 5.99, 6.18 μ; λ_{max} 239 mμ (log ϵ 4.21); $[\alpha]_D$ +79°.

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79. Found: C, 79.27; H, 9.77.

17α-Hydroxyetiojerv-1-en-3-one (11b).—A solution of 0.10 g. of the benzoate **11a** in 20 ml. of *t*-butyl alcohol and 5 ml. of 5% aqueous potassium hydroxide was stirred at reflux under nitrogen for 7 days. (After 1 day the only material isolated was unchanged starting material.) The butanol was distilled and the remaining mixture was extracted with benzene. The product was crystallized and recrystallized from ether–petroleum ether, yielding 30 mg. of the alcohol **11b**, m.p. 93–96°, λ_{max} 2.72 and 5.96 μ, λ_{max} 230 mμ (log ϵ 3.96).

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79. Found: C, 78.96; H, 9.89.

17β-Methyletiojervane-3β,17-diol (15a).—The ketone **4a** (1.0 g.) in 80 ml. of anhydrous ether was added over a 20-min. period to 20 ml. of 3 *M* methyl magnesium bromide in 50 ml. of anhydrous ether. The reaction mixture was heated at reflux for 20 hr., cooled in an ice bath, treated with 5 ml. of acetone, and acidified with dilute sulfuric acid. The product, 0.79 g. of amorphous material, was isolated by ether extraction and chromatographed on 80 g. of silica. The fractions eluted with 15% ethyl acetate in benzene were combined and recrystallized from acetone–petroleum ether to yield the pure **diol 15a**, m.p. 171–173°, λ_{max} 2.74 μ, $[\alpha]_D$ −36°.

Anal. Calcd. for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.53; H, 11.23.

17α-Hydroxy-17-methyletiojervan-3-one (15b).—The diol **15a** (0.38 g.) in 20 ml. of acetone was oxidized with 0.5 ml. of 4 *N* chromic acid solution[37] at 20°. After 10 min. the solution was diluted with water. The product was filtered and recrystallized twice from acetone–petroleum ether, affording the pure ketone **15b**, m.p. 140–142°, λ_{max} 2.74 and 5.84 μ, $[\alpha]_D$ −12°.

Anal. Calcd. for $C_{20}H_{32}O_2$: C, 78.89; H, 10.59. Found: C, 79.10; H, 10.47.

17α-Hydroxy-17-methyletiojerv-1-en-3-one (11c) and **17α-Hydroxy-17-methyletiojerv-4-en-3-one (12c).**—Bromine (0.84 g.) in 3.0 ml. of methylene chloride was added dropwise over a 10-min. period to the ketone **15b** (1.59 g.) in 24 ml. of tetrahydrofuran at 5°. The solution was stirred for an additional 10 min. and then was neutralized with aqueous potassium bicarbonate. The product, isolated by benzene extraction, was dissolved in 10 ml. of dimethylformamide and added over a 10-min. period to 6 ml. of boiling dimethylformamide containing 0.80 g. of magnesium oxide. The mixture was stirred at reflux for an additional 45 min., cooled, and poured into ice–water. The product (1.57 g. of an oil), isolated by benzene extraction, was chromatographed on 150 g. of silica. The fractions eluted with 10% ethyl acetate in benzene yielded, after recrystallization from acetone–petroleum ether, the pure Δ^1-steroid **11c**: m.p. 139–140°; λ_{max} 2.75, 5.98, 6.25 μ; λ_{max} 229.5 mμ (log ϵ 3.95); $[\alpha]_D$ −30°.

Anal. Calcd. for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.44; H, 10.10.

Continued elution with 10% acetate in benzene afforded a second component, recrystallized from acetone–petroleum ether to give the Δ^4-ketone **12c**, m.p. 121–123°; λ_{max} 2.78, 6.00, 6.20 μ; λ_{max} 236 mμ (log ϵ 4.08).

Anal. Found: C, 79.20; H, 9.86.

17β-Ethynyletiojervane-3β,17-diol (15c).—Potassium hydroxide pellets (21 g.) in 115 ml. of diethylene glycol dimethyl ether and 9.2 ml. of diethylene glycol monoethyl ether were stirred vigorously with a metal stirrer at 135° under an atmosphere of nitrogen. After the pellets had liquified the stirred reaction mixture was cooled slowly to 0° while a fine suspension of potasium hydroxide was formed. The nitrogen atmosphere was replaced by the introduction of a stream of acetylene over the surface of the reaction mixture. (The gas was scrubbed with water and with concentrated sulfuric acid.) Upon saturation of the mixture with acetylene, 3.45 g. of the ketone **4b** in 25 ml. of diethylene glycol dimethyl ether was added. Acetylene passage was continued for 3 more hr. The reaction mixture was diluted with water and the resulting precipitate was separated by filtration, washed with water, dried, and then chromatographed on 120 g. of silica. The fractions eluted with 10% ethyl acetate in benzene were combined and recrystallized from acetone, yielding the pure adduct **15c**, m.p. 176–178°, λ_{max} 2.76 and 3.03 μ, $[\alpha]_D$ −34°.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.40; H, 10.34.

17α-Hydroxy-17-ethynyletiojervan-3-one (15d).—A solution of 2.22 g. of the ethynyl compound **15c** in 200 ml. of acetone was oxidized with 2.0 ml. of 4 *N* chromic acid solution[37] at 20°. After 10 min. the solution was diluted with 3 ml. of 2-propanol and 100 ml. of water. The resulting precipitate was collected on a filter, washed with water, dried, and recrystallized three times from acetone to yield pure ketone **15d**, m.p. 215–221°; λ_{max} 2.74, 3.00, 5.80 μ; $[\alpha]_D$ −12°.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.38; H, 9.43.

The Reaction of Some 1-Trihaloacetyl-8-methylazulenes with Base[1,2]

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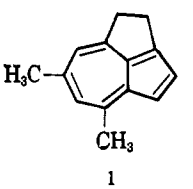
4,6,8-Trimethyl-, 1,4,6,8-tetramethyl-, 2,4,6,8-tetramethyl-, 4,6-diphenyl-8-methyl-, and 3,8-dimethyl-7-isopropylazulene have been acylated with trifluoro- and trichloroacetic anhydrides. Treatment of certain of the 1-trifluoroacetyl derivatives obtained with base has been found to produce a tricyclic alcohol. With certain of the 1-trichloroacetyl compounds, reaction with base resulted in the loss or transformation of the acyl group rather then cyclization. 1-Cyano-4,6,8-trimethylazulene was recovered unchanged after treatment with base.

The achievement of the tricyclic compound (1) by Hafner and Schneider[4] by means of a base-catalyzed cyclization involving the 8-methyl group, plus the discovery of a method for the direct introduction of a trihaloacetyl group into the 1-position,[5] led us to investigate the action of base on 1-trihaloacetyl-8-methylazulenes (*e.g.*, 2) as a possible new route to the ring system of 1.



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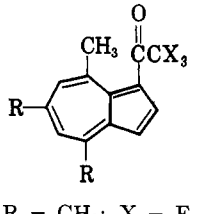


2, R = CH_3; X = F
2a, R = C_6H_5; X = F
2b, R = CH_3; X = Cl

(1) Taken in part from the Ph.D. Thesis of R. G. Anderson, 1961.

(2) Supported in part by grants from the National Science Foundation.

(3) National Science Foundation Predoctoral Fellow, summer 1959; National Institutes of Health Fellow, 1959-1961.

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

(5) A. G. Anderson, Jr., and R. G. Anderson, *J. Org. Chem.*, **27**, 3578 (1962).

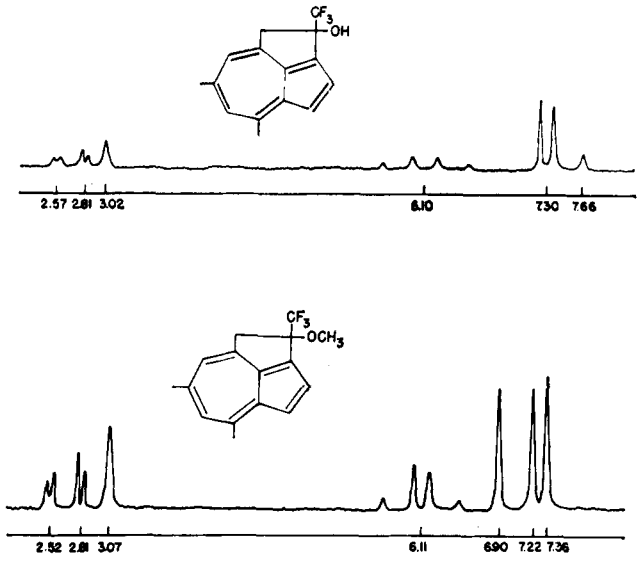
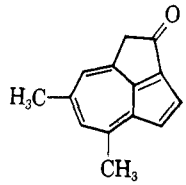


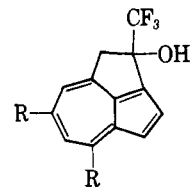
Figure 1.—N.m.r. spectra of 2-trifluoromethyl-2-hydroxy-5,7-dimethyl-1,2-dihydrocyclopent[*cd*]azulene (**4**) and its methyl ether.

4,6,8-Trimethylazulene, the hydrocarbon used by Hafner and Schneider, was chosen for the initial studies. Reaction of this with trifluoroacetic anhydride afforded a good yield of the desired ketone **2**. The presence of the trifluoroacetyl group in **2** caused the expected hypsochromic shift in the visible spectrum (547 to 505 mμ) and the appearance of a band at 6.0 μ in the infrared absorption. Reduction of **2** with lithium aluminum hydride formed the corresponding alcohol.[5] Although unsubstituted 1-trifluoroacetylazulene undergoes hydrolysis with hot alcoholic sodium hydroxide to form the acid in high yield,[5] it was felt that abstraction of a proton from the acidic 8-methyl group and subsequent cyclization through reaction of the carbanion with the carbonyl would be competitive.[6] Loss of the trihalomethyl group coincident with the latter process would result in the formation of the desired ketone **3**.

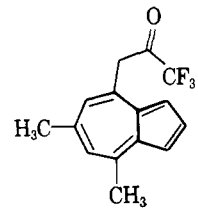


3

The action of alcoholic base on **2** produced a new purple substance which displayed an intense absorption band at 6.2 μ. As previously known 1-acylazulene compounds uniformly exhibit carbonyl absorption in the region near 6.1 μ,[5,7] and, as the peaks of 1-acetyl- and 1-formyl-4,6,8-trimethylazulene, prepared for comparison, were found to occur at 6.1 and 6.15 μ, respectively, it was possible that the new product had a carbonyl function on the 1-position. The presence of a hydroxyl group was shown by a band at 2.77 μ which disappeared and was replaced by a new absorption at 3.76 μ upon exchange with deuterium. That the hydroxyl group did not arise from the incorporation of the hydroxide of the base during the formation of the product from **2** was shown by the formation of the same product from the reaction of **2** with sodium hydride in benzene, or with sodium N-methylanilide in ether. The enol form of **3** (or a mixture of this with **2**) was eliminated as a possibility in that the elementary and molecular weight analyses showed the product to be isomeric with **2**. The two most likely possibilities for the product seemed to be **4** and **5**, but neither appeared to provide an explanation of the spectral data. Structure **5** has a carbonyl group, but one which would be expected to absorb at about the same wave length (5.63 μ)[8] found for 1,1,1-trifluoro-



4, R = CH_3
4a, R = C_6H_5



5

acetone. The existence of **5** in the enol form, however, would allow the assignment of the band at 6.2 μ to the carbon–carbon double bond and, also, explain the hydroxyl absorption. On the other hand, the compound would be expected to show some deuterium exchange at the carbon α to the oxygen even if the enol were considerably more stable than the keto form. No such exchange was found. Structure **4** provided a hydroxyl but no apparent explanation for the 6.2-μ absorption.

It was felt that proton magnetic resonance data would be of value and the spectra of 4,6,8-trimethylazulene, **2**, and the product were analyzed. 4,6,8-Trimethylazulene exhibited peaks of the correct relative intensities at τ 7.48 (6-methyl), 7.23 (4- and 8-methyls), 3.15 (5- and 7-hydrogens), 2.83 (center of doublet for 1- and 3-hydrogens), and 2.50 (center of triplet for 2-hydrogen).[9,10] The spectrum of **2** showed three bands (τ 7.26, 7.35, and 7.53) for the three methyl groups. The azulene ring region had a rather poorly resolved peak of unit area at τ 2.10 which was assigned to the 2-hydrogen, two singlets at τ 2.86 and 2.90 (5- and 7-hydrogens), and a well-defined doublet centered at τ 3.14 (3-hydrogen). These assignments were made with the aid of comparisons with the spectra of several known 1-substituted 4,6,8-trimethylazulenes.[11] The spectrum of the product from the reaction of **2** with base (Figure 1) was quite different. There were but two bands (τ 7.23 and 7.36) corresponding to methyl groups. A new quartet centered at τ 6.10 and a singlet at τ 7.66 were present, and the aromatic region showed two doublets centered at τ 2.57 and 2.81 and a singlet of double intensity at τ 3.02. These data excluded **5** or its enol isomer as either of these would show a triplet in the

(6) Molecular models indicated that the presence of the methyl group in the *peri* position would restrict the free rotation of the trifluoroacetyl group, and would be expected to exert an unfavorable steric effect on the approach of an hydroxide ion to the carbonyl carbon. The orientation of the trifluoromethyl group appeared to be such that ring closure could occur readily.

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

(8) R. N. Hazeldine and K. Leedham, *J. Chem. Soc.*, 3483 (1952).

(9) Values given are chemical shifts in parts per million relative to 10.00 for the absorption of tetramethylsilane as an internal standard.

(10) Subsequent to the completion of our studies, D. Meuche, B. B. Molloy, D. H. Reid, and E. Heilbronner [*Helv. Chim. Acta*, **46**, 2483 (1963)] reported n.m.r. spectra for 4,6,8-trimethylazulene and 4-methyl-6,8-diphenylazulene which agree closely with our results.

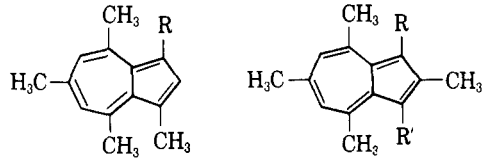
(11) A. G. Anderson, Jr., and L. L. Replogle, unpublished results.

aromatic region (from the coupling of the 2-hydrogen with the 1- and 3-hydrogens).

The observed spectrum was interpreted to fit structure **4** by the following assignments (azulene ring numbering is used for convenience): the singlet at τ 7.66 to the hydroxyl hydrogen, the two doublets in the aromatic region to the 2- and 3-hydrogens, and the singlet of double intensity at τ 3.02 to the hydrogens at the 5- and 7-positions. The quadruplet was attributed to the methylene protons and considered to arise from the spin–spin interaction of the nonequivalent hydrogens with one another. The spacing and relative intensities of the peaks indicated a coupling constant slightly larger than the difference between the chemical shifts of the hydrogens.[12,13] Structure **4**, which would form the oxide anion reversibly provided an explanation for the recovery of the product after further treatment with base. The presence of a hydroxyl group and its conversion to the anion was demonstrated chemically by the formation of a methyl ether from successive reactions with sodium hydride and methyl iodide. In contrast to the broad maximum from 525–565 mμ with a shoulder at *ca.* 610 mμ in the spectrum of the hydroxy compound, that of the methyl ether showed three distinct maxima (527, 547, and 567 mμ) and a lesser peak at 622 mμ. Very similar spectra have been reported for **1** and related 1,4,6,8-substituted azulenes.[5] The n.m.r. spectrum (Figure 1) was very similar to that of **4** except for the absence of the hydroxyl hydrogen peak and the presence of a new peak (τ 6.9) for the methyl ether hydrogens.

There remained unexplained the infrared peak at 6.2 μ. It seemed possible that this could arise from a shift of the aromatic carbon–carbon bond absorption (normally at 6.34 and 6.52 μ) to shorter wave lengths because of the more strained tricyclic structure. As Hafner and Schneider had not recorded the infrared spectra of their compounds, we repeated the synthesis of N,N,5,7-tetramethyl-2-amino-1,2-dihydrocyclopent-[*cd*]azulene.[5] The finding that this substance exhibited absorptions at 6.2 and 6.4 μ corresponding to those of our compound removed the last barrier to the assignment of structure **4** to the latter.

The preparation of 1,4,6,8- and 2,4,6,8-tetramethylazulene (**6** and **8**, respectively) and their trihaloacetyl derivatives was also investigated. It was felt that both hydrocarbons should be formed from the reaction of 2,4,6-trimethylpyrylium perchlorate and sodium methylcyclopentadienide even though Hafner and Kaiser[14] had reported that **8** was produced exclusively. Chromatography of the product mixture did not initially separate two fractions, but two products were obtained after reaction of the mixture with trifluoroacetic anhydride. One analyzed correctly for 1-trifluoroacetyl-3,4,6,8-tetramethylazulene (**7**). The intensities and multiplicities of the peaks in the n.m.r. spectrum fit this structure according to the assignment: τ 2.26 (2-hydrogen), 2.94 (7-hydrogen), 3.05 (5-hydrogen), 7.22 (4-methyl), 7.33 (8-methyl), 7.40 (3-methyl), and 7.54 (6-methyl). The other, at first thought to be the monotrifluoroacetyl derivative of **8**, proved to be the 1,3-bis-



6, R = H **8**, R = R' = H

7, R = $COCF_3$ **9**, R = R' = $COCF_3$

(trifluoroacetyl) derivative (**9**). Further study of the trimethylpyrylium perchlorate–methylcyclopentadienide reaction showed that **6** and **8** could be separated by repeated fractional chromatography. They were obtained in very low yield along with considerable amounts of oxygen-sensitive, higher molecular weight materials. The hydrocarbons were characterized by analysis, and visible and n.m.r. spectra. Compound **6** displayed a maximum at 576 mμ (calcd., 574 mμ) Singlet peaks in the n.m.r. representing three hydrogens each were found at τ 7.20 (4-methyl), 7.26 (8-methyl), 7.35 (1-methyl), and 7.62 (6-methyl). A broad singlet (τ 3.33) of doublet intensity was attributed to unresolved absorptions for the 5- and 7-hydrogens, and an AB quartet (τ 2.62, 2.68, 2.84, 2.93) to the 2- and 3-hydrogens. The isomer **8** exhibited a maximum at 535 mμ (the theoretical is 533 mμ) and other characteristics in agreement with those found by Hafner.[14] N.m.r. absorptions of the expected relative intensity and multiplicity were found at τ 7.36 (4- and 8-methyls), 7.48 (2-methyl), 7.59 (6-methyl), 3.02 (1- and 3-hydrogens), and 3.21 (5- and 7-hydrogens).[15] The obtainment of the pure compounds made it possible to determine the total yield and the isomeric composition from other runs by spectral analysis.[16] The yields realized were low ($\leq$14%) and it was observed that either potassium *t*-butoxide or an excess of sodium cyclopentadienide could serve as the base for the ring-closure step in the reaction. The relative amounts of the two isomers was approximately that expected on a statistical basis (2 parts of **6** to 1 part of **8**), and steric effects were therefore apparently not of importance. Compound **6**, which has a 1-methyl group, was found to decompose on standing more rapidly than the 2-methyl isomer (**8**) and, consequently, mixtures of the two became relatively more rich in **8** with time.

From the reaction of 8 with trifluoroacetic anhydride was obtained only the 1,3-bis(trifluoroacetyl) derivative (**9**), even under conditions favoring monosubstitution. This unexpected result was interpreted to mean that steric crowding prevented the usual planarity of the ring and the carbonyl of the first trifluoroacetyl group to be attached, and deactivation by resonance to further substitution was markedly lessened. The finding that the carbonyl absorption of **9** was at 1719 cm.$^{-1}$ (potassium bromide matrix) compared with the usual

(12) *Cf.* J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, pp. 119-123.

(13) E. F. Kiefer and J. D. Roberts, *J. Am. Chem. Soc.*, **84**, 784 (1962).

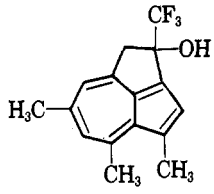
(14) K. Hafner and H. Kaiser, *Ann.*, **618**, 140 (1958); see also A. T. Balaban and C. Nenitzescu, *J. Chem. Soc.*, 3553 (1961); P. F. G. Fraill and A. L. Whitear, *ibid.*, 3573 (1961). The preparation of **6** by a different method was reported while the present paper was being written: K. Hafner and G. Schneider, *Ann.*, **672**, 194 (1964).

(15) These assignments were made with the aid of comparisons with other known compounds[11] and are in agreement with those on similar compounds.[10]

(16) H. H. Jaffe and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy," John Wiley and Sons, Inc., New York, N. Y., 1962, p. 557. The intensities were measured at 558 and 627 mμ since the isobestic point was at 576 mμ. The absorption in this region by possible impurities was shown to be negligible. The accuracy of the method with a mixture of known composition was within ±2%.

range for 1-trifluoroacetylazulenes (1650–1670 cm.$^{-1}$) and with the value for a nonconjugated trifluoroacetyl group (1780 cm.$^{-1}$) indicated an analogous deviation from planarity in the postulated monosubstituted intermediate. It was of interest also that the carbonyl absorption for **9** in carbon tetrachloride was at 1724 cm.$^{-1}$ and, therefore, the structure is less planar in solution than in the crystal matrix.[17]

The fact that all efforts to obtain the monosubstituted compound failed and that unchanged **8** was often obtained along with **9** (even from some runs where an excess of the acylating agent was present) points to a rate for the second substitution process which is faster than that of the first. It may be that the steric effect of the 1-trifluoroacetyl and neighboring methyl groups results in a less crowded transition state for the introduction of the second substituent. The n.m.r. spectrum of **9** had peaks at τ 2.7 (5- and 7-hydrogens), 7.31 (4- and 8-methyls), 7.38 (2-methyl), and 7.59 (6-methyl) in agreement with the structure given. The substance, as has been the case for a number of symmetrical 1,3-substituted azulenes, was obtained in two allotropic crystalline forms. The reaction of a mixture of **6** and **8** with an excess of trifluoroacetic anhydride gave 1-trifluoroacetyl-3,4,6,8-tetramethylazulene (**7**) and **9**. The carbonyl absorption of **7** in the infrared was at 1629 cm.$^{-1}$ in a potassium bromide matrix and at 1678 cm.$^{-1}$ in a carbon tetrachloride solution. The n.m.r. spectrum displayed peaks at τ 2.26 (2-hydrogen), 2.94 (7-hydrogen), 3.05 (5-hydrogen), 7.22 (4-methyl), 7.33 (8-methyl), 7.40 (3-methyl), and 7.54 (6-methyl) such as to correspond with the structure as indicated. Cyclization to form **10** (57%) took place upon reaction of **7** with alcoholic alkali. The infrared spectrum of **10** possessed peaks at 2.8 (hydroxyl) and 6.23 μ in correspondence with those in the spectrum of **4**.



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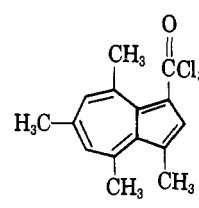
Ring closure to form the tricyclic compound (**4a**) occurred when 1-trifluoroacetyl-4,6-diphenyl-8-methylazulene (**2a**) was treated with base. The infrared spectrum of **4a** had peaks at 2.82 and 6.24 μ, and the n.m.r. spectrum had a singlet for the hydroxyl at τ 6.67 at 23° which shifted to τ 6.98 at 80°, and a quartet centered at τ 6.13. An attempt to eliminate the elements of water from **4a** by heating with anhydrous zinc chloride in benzene gave only unreacted starting material. Curiously, the action of an alcoholic base on 1-trifluoroacetyl-3,8-dimethyl-5-isopropylazulene resulted in decomposition. It was not determined whether or not the cyclic product was formed as an intermediate.

No cyclic product was isolated from the treatment of 1-trichloroacetyl-4,6,8-trimethylazulene (**2b**) with hot alcoholic potassium hydroxide. The base effected the removal of the trichloroacetyl group and the formation of 4,6,8-trimethylazuline in 74% yield. A reaction sequence of hydrolysis and then decarboxylation is in keeping with the rapid rate of hydrolysis (relative to that for the trifluoro compound) previously observed with 1-trichloroacetylazulene,[5] and with the steric interaction of the resultant carboxyl with the methyl group on the 8-position. As with the corresponding trifluoroacetyl compound, the action of alcoholic hydroxide on the 1-trichloroacetyl-3,8-dimethyl-5-isopropylazulene gave mainly decomposition.

The reactions of the polyalkylazulenes with trichloroacetic anhydride were in general less clean than those with trifluoroacetic anhydride and the desired products were more difficult to purify. This was especially true for the trichloroacylation of a mixture of **6** and **8**, from which an appreciable amount of **8** was recovered unchanged and the 1-trichloroacetyl-3,4,6,8-tetramethylazulene product (**11**) was not obtained in the usual analytical purity. The similarities of the ultraviolet, visible, infrared, and n.m.r. spectra with those of **7**, however, left no doubt concerning the identity of the substance. Treatment of **11** with methanolic sodium hydroxide gave 1,4,6,8-tetramethylazulene (38%) plus, unexpectedly, a substance indicated (ultraviolet, visible, infrared, and n.m.r. spectra) to be methyl 3,4,6,8-tetramethyl-1-azuloate (**12**)



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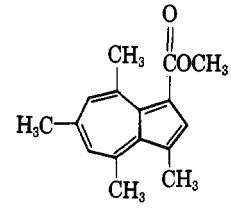

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The ring closure was attempted on two other compounds. 1-Acetyl-4,6,8-trimethylazulene gave only brown decomposition products, and the absence of the color change (red to purple) which had been observed to occur immediately with the trifluoroacetyl compound (**2**) was an indication that the base did not abstract a proton from the 8-methyl group. 1-Cyano-4,6,8-trimethylazulene, prepared *via* the aldehyde oxime, was recovered unchanged after treatment with aqueous hydroxide, alcoholic hydroxide, or sodium hydride. In this case the participation of the cyano group in the stabilization of the anion formed provided an explanation for the observed behavior.

Experimental[18]

1-Trifluoroacetyl-4,6,8-trimethylazulene (**2**).—Under anhydrous conditions 0.5 ml. (*ca.* 3.5 mmoles) of trifluoroacetic anhydride was added to a solution of 0.35 g. (2.06 mmoles) of 4,6,8-trimethylazulene[19] in 10 ml. of dichloromethane and the mixture was allowed to stand for 15 min. The product was isolated in the manner previously described for 1-trifluoroacetylazulene[5] except that neutral alumina was used for chromatographic purification. Elution with benzene removed 33 mg. of unreacted

(17) A. I. Kitaygorodsky, *Tetrahedron*, **9**, 183 (1960).

(18) Melting points are uncorrected and were taken on a Fisher-Johns apparatus. Ultraviolet and visible spectra were recorded on a Model 11S or Model 14 Cary recording spectrophotometer. Infrared spectra were taken on a Perkin-Elmer Model 21 recording spectrophotometer. Nuclear magnetic resonance absorption was recorded by B. J. Nist with a 60-Mc. Varian high resolution spectrophotometer with tetramethylsilane as an internal standard. Microanalyses were performed by G. Weiler and F. B. Strauss, Oxford, England, A. Bernhardt, Max Planck Institute, Mülheim (Ruhr), Germany, and by A. Kuo, L. Ho, and B. J. Nist.

(19) K. Hafner and H. Kaiser, *Ann.*, **618**, 140 (1958); see also A. T. Balban and C. D. Nenitzescu, *J. Chem. Soc.*, 3553 (1961); P. F. G. Praill and A. L. Whitear, *ibid.*, 3573 (1961).

trimethylazulene and 4:1 dichloromethane–ether eluted a bright red fraction which yielded 0.425 g. (77.7%, 85.7% net) of 1-trifluoroacetyl-4,6,8-trimethylazulene as red needles, m.p. 55–56°. A *n*-hexane solution showed maxima in mμ (D_{max}) at 242 (1.07), 283 (0.35), 322 (1.33), 392 (0.27), and 505. The infrared spectrum (chloroform) showed a peak at 6.0 μ.

Anal. Calcd. for $C_{15}H_{13}F_3O$: C, 67.67; H, 4.88. Found: C, 67.81; H, 4.74.

1-(α-Hydroxy-β,β,β-trifluoroethyl)-4,6,8-trimethylazulene.—A solution of 50 mg. (0.188 mmole) of 1-trifluoroacetyl-4,6,8-trimethylazulene in 5 ml. of anhydrous ether was cooled to 0° and 10 mg. of lithium aluminum hydride was added. The solution, the color of which changed rapidly from red to magenta, was maintained at 0° for 10 min., and excess lithium aluminum hydride was then decomposed by the dropwise addition of ice–water followed by a few milliliters of 5% hydrochloric acid. The mixture was thoroughly shaken and the separated organic layer was washed twice with water and then dried over anhydrous sodium sulfate. The solvent was removed and the residue was chromatographed on acid-washed alumina. Ether eluted a magenta band which yielded 44 mg. (88%) of 1-(α-hydroxy-β,β,β-trifluoroethyl)-4,6,8-trimethylazulene as red-purple needles, m.p. 126–128°. A dichloromethane solution displayed maxima in mμ (D_{max}) at 247 (1.24), 289 (2.07), 295 (2.03), 348 (0.29), and 534. The infrared spectrum (chloroform) had a peak at 2.81 μ and no absorption in the carbonyl region.

Anal. Calcd. for $C_{15}H_{15}F_3O$: C, 67.16; H, 5.60. Found: C, 66.91; H, 5.72.

2-Trifluoromethyl-2-hydroxy-5,7-dimethyl-1,2-dihydrocyclopent[*cd*]azulene (4). Method A.—A solution of 0.1 g. (0.376 mmole) of 1-trifluoroacetyl-4,6,8-trimethylazulene in 10 ml. of 10% ethanolic potassium hydroxide was heated under reflux (the color changed from red to purple almost immediately) for 20 min. The mixture was then treated with 50 ml. of water, acidified with 5% hydrochloric acid, and extracted several times with ether; the ether extracts were washed successively with water, 5% sodium bicarbonate solution, and water. The dried (sodium sulfate), concentrated ethereal solution was chromatographed (basic alumina) and a lavender band was eluted with 1:1 dichloromethane–ether which yielded 67 mg. (67%) of **4** as purple needles, m.p. 140–141°. Absorption maxima (dichloromethane) in mμ (D_{max}) were observed at 243 (0.89), 285 (1.35), 292 (1.48), 296 (1.63), 346 (0.24), and 552. The infrared spectrum showed peaks at 2.77 and 6.20 μ.

Anal. Calcd. for $C_{15}H_{13}F_3O$: C, 67.67; H, 4.88; F, 21.43. Found: C, 67.72; H, 5.05; F, 21.00.

Compound **4** was recovered unchanged in 90% yield after heating under reflux with 10% ethanolic potassium hydroxide for 1 hr. and isolation as described above.

Method B.—To a solution of 50 mg. (0.188 mmole) of 1-trifluoroacetyl-4,6,8-trimethylazulene in 20 ml. of anhydrous benzene was added an excess of a 52% oil dispersion of sodium hydride and the mixture (protected from moisture) heated under reflux for 1.5 hr., during which time the color changed from red to purple. After decomposition of excess sodium hydride by the addition of isopropyl alcohol, the mixture was washed three times with water, the solvent was removed from the dried (sodium sulfate) organic layer, and a solution of the residue in the minimal volume of benzene chromatographed over basic alumina. Elution and isolation were performed as described in method A, and 33 mg. (66%) of **4** was obtained as purple needles, m.p. 140–141°, identical in all respects with the material from method A.

Method C.—To 0.266 g. (1.0 mmole) of 1-trifluoroacetyl-4,6,8-trimethylazulene dissolved in 10 ml. of anhydrous ether and protected from moisture was added 5 ml. of sodium N-methylanilide (*ca.* 0.5 *M*) in ether and the mixture was stirred at room temperature. Almost immediately a red material separated from the solution. After 20 min. the mixture was heated (steam bath) for 20 min. and then treated as described in method A for the isolation of the product. There was obtained 0.181 g. (68%) of purple needles, m.p. 140–141°, identical in every respect with the material from methods A and B.

Treatment of 2-Trifluoromethyl-2-hydroxy-5,7-dimethyl-1,2-dihydrocyclopent[*cd*]azulene (4) with Deuterium Oxide.—A solution of 35 mg. (0.124 mmole) of **4** and 1 ml. of 95% deuterium oxide in 5 ml. of anhydrous tetrahydrofuran was allowed to stand at room temperature for 10 min. and the solvent then was removed under reduced pressure. Pure, dry nitrogen was admitted and the infrared spectrum of the material was recorded at once. The peak at 2.77 μ exhibited by **4** was almost completely absent and a new band at 3.76 μ was present.

2-Trifluoromethyl-2-methoxy-5,7-dimethyl-1,2-dihydrocyclopent[*cd*]azulene.—A mixture of 0.3 g. (1.13 mmoles) of 1-trifluoroacetyl-4,6,8-trimethylazulene, 25 ml. of anhydrous tetrahydrofuran, and 0.5 g. of a 52% oil dispersion of sodium hydride (10.8 mmoles) was protected from moisture and heated under reflux for 30 min. The solution was cooled, an excess of methyl iodide was added, and heating under reflux was resumed for 10 min. The reaction mixture was then treated as described for the isolation of **4** (method B) and the crude product so obtained was chromatographed over basic alumina with pentane–dichloromethane (5:1) as the eluent. The purple fraction yielded 0.174 g. (55%) of the desired product as purple needles, m.p. 67–68°. A cyclohexane solution showed maxima in mμ (D_{max}) at 243 (0.52), 285 (1.16), 292 (1.31), 296 (1.17), 346 (0.17), 527 (1.07), 547 (1.09), and 567 (1.16). The infrared spectrum was very similar to that of **4** but had no band in the hydroxyl region.

Anal. Calcd. for $C_{16}H_{15}F_3O$: C, 68.57; H, 5.36. Found: C, 68.42; H, 5.62.

2-Trifluoromethyl-2-hydroxy-5,7-diphenyl-1,2-dihydrocyclopent[*cd*]azulene (4a).—To a solution of 149 mg. (0.51 mmole) of 4,6-diphenyl-8-methylazulene[19] in 10 ml. of dichloromethane was added 0.5 ml. of trifluoroacetic anhydride and the mixture was allowed to stand at room temperature for 15 min. The crude product was isolated in the manner previously described for 1-trifluoroacetylazulene[5] and chromatographed over basic alumina. The red fraction eluted with dichloromethane afforded 165 mg. (83.5%) of material which hardened to a glass. This was presumed to consist principally of 1-trifluoroacetyl-4,6-diphenyl-8-methylazulene (plus perhaps some of the isomeric 3-trifluoroacetyl compound) and was not obtained analytically pure.

Method A.—The above product (0.317 g., 0.985 mmole) was dissolved in 10 ml. of 10% ethanolic potassium hydroxide, and the solution was heated under reflux for 30 min. The mixture was then flooded with water and extracted three times with ether. The combined organic extracts were washed three times with water and dried over sodium sulfate. The solvent was removed, and the residue was chromatographed on acid-washed alumina. Dichloromethane removed a purple fraction which yielded 235 mg. (60%) of 2-trifluoromethyl-2-hydroxy-5,7-diphenyl-1,2-dihydrocyclopent[*cd*]azulene as a purple glass. A cyclohexane solution exhibited absorption maxima in mμ (D_{max}) at 242 (0.83), 309 (1.60), a broad peak at 347 (0.16), and 373 (0.14). The visible spectrum showed maxima in mμ at 570, 604, and 660 (shoulder). The infrared spectrum (chloroform) had peaks at 2.82 and 6.24 μ. The proton magnetic resonance spectrum (carbon tetrachloride at 80°) displayed a quartet centered at 6.13 p.p.m. (assigned to the methylene hydrogens) and a singlet at 6.98 p.p.m. (attributed to the hydroxyl).

Anal. Calcd. for $C_{25}H_{17}OF_3$: C, 76.91; H, 4.39. Found: C, 76.88; H, 4.40.

Method B.—To a solution of the material presumed to be 1-trifluoroacetyl-4,6-diphenyl-8-methylazulene (0.246 g., 0.63 mmole) in 20 ml. of anhydrous benzene was added an excess of a 52% oil dispersion of sodium hydride, and the mixture was heated under reflux for 1 hr. Excess sodium hydride was decomposed by the addition of absolute ethanol, and the mixture was then neutralized with 5% hydrochloric acid. The separated organic layer was washed three times with water and dried over sodium sulfate. The product was isolated as described in method A and there was obtained 154 mg. (62.5%) of a purple glass identical (ultraviolet, visible, and infrared spectrum) with the substance from method A.

1,4,6,8-Tetramethylazulene (6) and 2,4,6,8-Tetramethylazulene (8).—To a cold (−30 to −20°), stirred suspension of 22.2 g. (0.1 mole) of 2,4,6-trimethylpyrylium perchlorate (m.p. 248–250° dec.) in 75 ml. of dry, freshly distilled tetrahydrofuran (contained under a nitrogen atmosphere in a three-necked flask equipped with a condenser and a Claisen distillation head fitted with a pentane thermometer, which extended into the suspension, and a pressure-equalized dropping funnel) was added dropwise a solution prepared by the reaction of 2.4 g. (0.1 mole) of sodium hydride (as a 53.4% dispersion in mineral oil) and 9 g. (0.11 mole) of freshly distilled (b.p. 73°) methylcyclopentadiene in 50 ml. of the purified tetrahydrofuran. The temperature was maintained at *ca.* −20° during the addition. The orange-yellow mixture which resulted was cooled to −50° and 250 ml. of a 1 *M* solution of potassium *t*-butoxide in *t*-butyl alcohol was

added dropwise with stirring and cooling such that the temperature did not exceed −20°. The flask and contents were then allowed to come to room temperature and stirring was continued for 12 hr. After about 150 ml. of the solvent had been removed by distillation, the semisolid residue was poured into 2.5 l. of water and the mixture was extracted several times with 300-ml. portions of ether. The solvent was removed under reduced pressure from the dried (sodium sulfate) extracts and the violet residue was chromatographed over basic alumina with *n*-pentane as the eluent. The first yellow band was discarded and the magenta and blue bands which followed, and which partially overlapped, were collected as two impure fractions. A second yellow band remained on the column. The concentrate from the magenta fraction was rechromatographed with 20–40° petroleum ether as the eluent and with the best possible separation of the magenta and blue components. The material from the magenta fraction was crystallized from absolute ethanol and the chromatography was then repeated. There was obtained 0.278 g. (1.5%) of 2,4,6,8-tetramethylazulene as magenta needles, m.p. 100–101°.[14] A cyclohexane solution displayed λ_{max} in mμ (log ε) at 247 (4.24), 287 (4.56), 296 (4.72), 314 (4.02), inflection at 330 (3.53), inflection at 337 (3.58), 339 (3.65), inflection at 354 (3.77), 355 (3.79), 535 (2.57), 564 (2.54), inflection at 580 (2.48), shoulder at 613 (2.16), and shoulder at 634 (1.99). Infrared spectra were recorded on a potassium bromide matrix and a carbon tetrachloride solution.

Anal. Calcd. for $C_{14}H_{16}$: C, 91.25; H, 8.75. Found: C, 90.95; H, 8.76.

The combined concentrates from the blue fractions were chromatographed over basic alumina with cyclohexane as the eluent and the blue material from this was purified by chromatography five additional times with 20–40° petroleum ether as the eluent. There was finally obtained 0.286 g. (1.6%) of 1,4,6,8-tetramethylazulene as blue crystals, m.p. 41–42°. A cyclohexane solution exhibited λ_{max} in mμ (log ε) at 247 (4.07), 287 (4.36), 294 (4.40), inflection at 330 (3.23), 340 (3.32), shoulder at 348 (3.29), shoulder at 355 (3.36), 357 (3.37), 369 (2.62), inflection at 550 (2.43), 5.76 (2.50), inflection at 600 (2.44), 627 (2.38), inflection at 664 (2.04), and 692 (1.92). Infrared spectra were recorded on a potassium bromide matrix and a carbon tetrachloride solution.

Anal. Calcd. for $C_{14}H_{16}$: C, 91.25; H, 8.75. Found: C, 91.48; H, 8.66.

In subsequent runs where the effects of changes in the temperature, solvent, dilution, base, reaction time, work-up procedure, etc., were observed, the magenta and blue portions from the initial chromatography were collected as one fraction and rechromatographed using 30–60° petroleum ether to develop the column and petroleum ether–dichloromethane (9:1) to elute the mixture of tetramethylazulenes. The crystalline material obtained by removal of the solvent under reduced pressure at room temperature was used for the determination of the relative and total yields of the two azulenes by spectral analysis.[16] The total yield varied from essentially 0 to 14% and several factors seemed to be of importance: the temperature should not be allowed to exceed 25° at any time after the addition process, and acid-washed glassware should be made neutral before use. A reaction time of 2 hr. at room temperature following the addition of the methylcyclopentadienide was sufficient. The ratio of the 1-methyl (**6**) to the 2-methyl (**8**) isomer was 66:34 (11% yield) and 64:36 (8% yield) in two runs which were worked up promptly. A run in which the work-up was allowed to extend over a period of about a week gave a corresponding product ratio of 52:48 (14% yield), and a run with a 3-week work-up period gave a 43:57 ratio of isomers (10% yield).

1,3-Bis(trifluoroacetyl)-2,4,6,8-tetramethylazulene (9).—To a stirred solution of 0.1 g. (0.545 mmole) of 2,4,6,8-tetramethylazulene (m.p. 100–101° in 12 ml. of dichloromethane was added 2 ml. (*ca.* 14 mmoles) of trifluoroacetic anhydride over a period of 3 min. The stirred reaction mixture, which turned red during the addition, was cooled in an ice–water bath and then a saturated sodium bicarbonate solution (30 ml.) was added dropwise (30 min.). Stirring was continued for an additional 30 min. and the layers which had formed were separated. The aqueous layer was tinted violet by the presence of small amounts of azulene carboxylic acid salts. The dichloromethane solution was washed with a mixture of 10 ml. of saturated sodium bicarbonate solution and 10 ml. of water, and then with two 70-ml. portions of water. The solvent was removed from the dried (sodium sulfate) solution under reduced pressure and the red-orange residue (0.187 g.), dissolved in 30 ml. of 20–40° petroleum ether and 1 ml. of dichloromethane, was chromatographed on acid-washed alumina. Development with 20–40° petroleum ether gave a rapidly moving magenta band which was removed with the petroleum ether, and then an orange band which was eluted with 1:1 petroleum ether–dichloromethane. From the magenta fraction was obtained 18 mg. of unchanged starting material (**8**), m.p. 100–101°, and the red-orange fraction yielded 0.14 g. (73%) of crystalline product (**9**), m.p. 122–125°, which appeared to be a mixture of crystalline forms. Rechromatography separated a trace of magenta material and left a small light orange band on the column. A third chromatograph of the red-orange fraction with 1:1 petroleum ether–dichloromethane as the only solvent separated the main fraction from a smal blue leading band and a small light orange trailing band. A fourth chromatography in the same manner gave only a single red-orange band and from this was obtained 0.112 g. (58%, 66% net) of red-orange needles, m.p. 107–109°. The analytical sample, m.p. 111–112°, was obtained by recrystallization from the petroleum ether. The material was also obtained in a red crystalline form, m.p. 137–138°, which was otherwise identical (infrared spectra) with the lower melting form, from some recrystallizations or by carefully heating the lower melting form at its melting point. A cyclohexane solution exhibited λ_{max} in mμ (log ε) at 233 (4.54), inflection at 237 (4.55), 244 (4.59), 286 (4.58), 318 (4.55), inflection at 334 (4.53), 387 (2.98), and 500 (2.88). Infrared spectra were taken on a potassium bromide matrix and on a carbon tetrachloride solution.

Anal. Calcd. for $C_{18}H_{14}F_6O_2$: C, 57.45; H, 3.75; mol. wt., 376. Found: C, 57.57; H, 3.69; mol. wt. (Rast), 389.

1-Trifluoroacetyl-3,4,6,8-tetramethylazulene (7).—To a stirred solution of a mixture of 0.097 g. (0.53 mmole) of 1,4,6,8-tetramethylazulene and 0.033 g. (0.18 mmole) of 2,4,6,8-tetramethylazulene (determined by spectral analysis) in 10 ml. of dichloromethane under anhydrous conditions was added dropwise over a period of 5 min. 2 ml. (*ca.* 3 g., 14 mmoles) of trifluoroacetic anhydride. The mixture, which turned red during the addition, was stirred for an additional 15 min. at room temperature and then cooled in an ice bath. Saturated sodium bicarbonate (15 ml.) was added dropwise over a 1-hr. period and stirring of the cold mixture was continued for 1 hr. An additional 10 ml. of bicarbonate solution was then added (the evolution of carbon dioxide was vigorous) and stirring and cooling were continued for 6 hr. The layers were separated and the dichloromethane solution, which had been washed with two 125-ml. portions of water and dried over sodium sulfate, was evaporated to dryness under reduced pressure. A solution of the red crystalline residue in a few milliliters of 1:1 dichloromethane–petroleum ether (20–40°) was placed on a column of acid-washed alumina. Elution with the petroleum ether developed violet, orange-yellow, and red-orange bands and left a small green fraction at the top of the column. The violet band was removed with the same solvent and gave 19 mg. of magenta crystals, m.p. 52–80°, which were suspected to be impure **8**. Elution with 1:1 dichloromethane–petroleum ether removed the yellow-orange and red-orange fractions, which were combined, and then a small yellow band which was discarded. The concentrate from the orange-red eluate was rechromatographed using the same solvent mixture, and afforded a separation of a red band from smaller preceding orange and following yellow bands. The crystalline residue from the red fraction was rechromatographed in the same manner and thus separated into small magenta and larger orange and red fractions. From the orange eluate was obtained 29 mg. of red-orange crystals, m.p. 96–99°, which were identified by their ultraviolet, visible, and infrared spectra as 1,3-bis(trifluoroacetyl)2,4,6,8-tetramethylazulene (**9**).

The red eluate afforded 40 mg. (77%) of crystalline 1-trifluoroacetyl-3,4,6,8-tetramethylazulene (**8**), m.p. 98.5–100°. A cyclohexane solution showed λ_{max} in mμ (log ε) at 245 (4.46), 288 (4.04), 332 (4.41), 413 (3.02), 533 (2.96), with inflections at 235 (4.37), 285 (4.03), 400 (3.0), 575 (2.8), 588 (2.69), and 603 (2.52). Infrared spectra were taken on a potassium bromide matrix and a carbon tetrachloride solution.

Anal. Calcd. for $C_{16}H_{15}F_3O$: C, 68.56; H, 5.40. Found: C, 68.18; H, 5.32.

2-Trifluoromethyl-2-hydroxy-4,5,7-trimethyl-1,2-dihydrocyclopent[*cd*]azulene (10).—A mixture of 0.4 g. (1.43 mmoles) of 1-trifluoroacetyl-3,4,6,8-tetramethylazulene (**8**) and 15 ml. of 10% ethanolic potassium hydroxide was heated under reflux for 20 min. and then treated as described in method A for the preparation of **4**. The crude product so obtained was chromatographed over

acid-washed alumina with ether as the eluent and afforded 0.227 g. (57%) of **10** as violet needles, m.p. 96–97°. A cyclohexane solution displayed λ_{max} in mμ (D) in the ultraviolet at 243 (0.67), 280 (1.31), 286 (1.38), 300 (1.22), 345 (0.15), with shoulders at 285 (1.08), 328 (0.11), 335 (0.12), and 352 (0.12). The visible region had a λ_{max} at 553 mμ. The infrared spectrum of a carbon tetrachloride solution was recorded.

Anal. Calcd. for $C_{16}N_{15}F_3O$: C, 68.56; H, 5.40. Found: C, 68.77; H, 5.64.

1-Trifluoroacetyl-3,8-dimethyl-5-isopropylazulene.—To a solution of 0.5 g. (2.52 mmoles) of 1,4-dimethyl-7-isopropylazulene in 10 ml. of dichloromethane protected from moisture was added 2 ml. (*ca.* 14 mmoles) of trifluoroacetic anhydride. The mixture was allowed to stand for 10 min. and then treated as previously described for the preparation of 1-trifluoroacetylazulene.[5] The crude product thus obtained was chromatographed on neutral alumina with 1:1 dichloromethane–petroleum ether (40–60°) as the eluate. The concentrate from the red fraction was rechromatographed with 3:2 *n*-pentane–benzene as the solvent and the red eluate yielded 0.548 g. (74.6%) of product as red needles, m.p. 50–51.5°. The ultraviolet spectrum of a dichloromethane solution showed λ_{max} in mμ (D) at 242 (2.44), 286 (1.51), 332 (2.08), and 422 (1.52). The visible spectrum had a maximum at 530 mμ.

Anal. Calcd. for $C_{17}H_{17}F_3O$: C, 69.39; H, 5.78. Found: C, 69.37; H, 5.63.

1-Trichloroacetyl-4,6,8-trimethylazulene (2b).—To 0.17 g. (1.0 mmole) of 4,6,8-trimethylazulene dissolved in 5 ml. of dichloromethane was added 0.5 ml. (*ca.* 3.5 mmoles) of trichloroacetic anhydride. The mixture was allowed to stand overnight at room temperature under anhydrous conditions and was then washed four times with water. The combined aqueous extracts were washed with ether, the combined, dried (sodium sulfate) organic solutions were concentrated, and the residue was chromatographed on neutral alumina. A 3:2 pentane–benzene mixture removed 24 mg. of unreacted trimethylazulene. Ether eluted a red band which afforded 0.16 g. (50.8%, 59% net) of 1-trichloroacetyl-4,6,8-trimethylazulene as red needles, m.p. 106–107°. Absorption maxima in mμ (log ε) of a cyclohexane solution were observed at 243 (4.38), 289 (4.29), 324 (4.30), 388 (3.94), and 515 (2.92). The infrared spectrum (chloroform) showed a peak at 6.0 μ.

Anal. Calcd. for $C_{15}H_{13}Cl_3O$: C, 57.05; H, 4.12. Found: C, 57.03; H, 4.22.

Reaction of 1-Trichloroacetyl-4,6,8-trimethylazulene with Base.—A solution of 0.1 g. (0.32 mmole) of 1-trichloroacetyl-4,6,8-trimethylazulene in 10 ml. of 10% ethanolic potassium hydroxide was heated under reflux for 75 min. The mixture was then flooded with water, acidified with 5% hydrochloric acid, and extracted with ether. The ether phase was washed three times with water and dried (sodium sulfate); the solvent was then removed. The residue was chromatographed on acid-washed alumina. Dichloromethane separated a purple band from some dark material which remained at the top of the column. Removal of the solvent from the purple eluate gave 40 mg. (74.2%) of purple crystals, m.p. 80–82°, which were identical (mixture melting point and ultraviolet and infrared spectra) with an authentic sample of 4,6,8-trimethylazulene.

1-Acetyl- and 1,3-Diacetyl-4,6,8-trimethylazulene.—4,6,8-Trimethylazulene[14] (0.3 g., 1.77 mmoles) was treated with a solution of 5 ml. (53.5 mmoles) of redistilled acetic anhydride and 0.5 ml. (*ca.* 4.3 mmoles) of anhydrous stannic chloride, and the whole was protected from moisture. The color of the mixture changed immediately from blue to red-brown and deepened with time. After 2 hr. the stannic chloride complex was decomposed by the addition of 20 ml. of 5% hydrochloric acid. The two phases were thoroughly shaken, then separated, and the aqueous layer was extracted with two 25-ml. portions of dichloromethane. The combined organic layers were washed with five 50-ml. portions of water and dried (sodium sulfate). The solvent was removed (steam bath) and the residue was chromatographed on acid-washed alumina. A purple band eluted with benzene yielded 0.118 g. of unreacted trimethylazulene. Dichloromethane eluted a slowly moving red band and a partially overlapping, following, red-orange band. Rechromatography of the material from the colored eluate fraction and elution with ether separated the two substances. Removal of the solvent from the red fraction gave 37 mg. (9.9%, 16.3% net) of 1-acetyl-4,6,8-trimethylazulene as a red oil which crystallized on standing as red needles, m.p. 67–69°. A sample, sublimed at 90° and 0.5 mm., melted at 69–70°. A cyclohexane solution exhibited maxima in mμ (log ε) at 229 (4.27), 247 (4.37), 310 (4.52), and 528 (2.81). The infrared spectrum (chloroform) had a peak at 6.1 μ.

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.90; H, 7.55. Found: C, 85.54; H, 7.37.

The red-orange fraction yielded 0.215 g. (47.8%, 79.1% net) of 1,3-diacetyl-4,6,8-trimethylazulene as red needles, m.p. 170–173°. The analytical sample after recrystallization from benzene melted at 173–174°. A dichloromethane solution showed λ_{max} in mμ (log ε) at 257 (4.44), 300 (4.34), 319 (4.40), 387 (3.93), and 503 (2.99). The infrared spectrum (chloroform) had a peak at 6.08 μ.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.31; H, 7.09. Found: C, 80.22; H, 7.09.

1,4-Dimethyl-3-trichloroacetyl-7-isopropylazulene.—To a solution of 1,4-dimethyl-7-isopropylazulene (0.198 g., 1.0 mmole) in 10 ml. of dichloromethane was added 1.0 ml. (*ca.* 7 mmoles) of trichloroacetic anhydride and the whole was allowed to stand protected from moisture for 1 hr. The mixture was washed four times with water and dried (sodium sulfate). The solvent was removed and the residue was chromatographed on neutral alumina. A 3:2 pentane–benzene solvent removed 0.108 g. of unreacted guaiazulene and ether eluted the remaining red band which yielded 0.16 g. (46.7%; 100% net) of 1,4-dimethyl-3-trichloroacetyl-7-isopropylazulene as dark red needles, m.p. 86–89°. Sublimation at 100° and 1 mm. afforded an analytical sample, m.p. 86–87.5°. Absorption maxima in mμ (log ε) of a cyclohexane solution were recorded at 238 (4.37), 288 (4.32), 325 (4.21), 462 (4.03), and 582 (2.80).

Anal. Calcd. for $C_{17}H_{17}Cl_3O$: C, 59.39; H, 4.95. Found: C, 59.30; H, 5.24.

1-Trichloroacetyl-3,4,6,8-tetramethylazulene (11).—To a stirred solution of a mixture of 75 mg. (0.41 mmole) of 2,4,6,8-tetramethylazulene and 134 mg. (0.73 mmole) of 1,4,6,8-tetramethylazulene (determined by spectral analysis) in 10 ml. of dichloromethane under a nitrogen atmosphere was added 1 ml. (*ca.* 1.7 g., 5.5 mmoles) of redistilled trichloroacetic anhydride. The color of the mixture became a very dark red and after 10 min. it was washed with four 100-ml. portions of water. The combined aqueous layers were extracted with 100 ml. of ether and the ether extract was combined with the dichloromethane solution. The residue (1.14 g.) obtained by removal of the solvent (reduced pressure) from the dried (sodium sulfate) organic solution was treated with a 1:1 dichloromethane–petroleum ether (30–60°) solvent and the solution plus some insoluble material which resulted was placed on a column of acidic alumina. Development with petroleum ether formed magenta and yellow-brown bands which were not well resolved and left a wide, dark band at the top of the column. Elution with the 1:1 dichloromethane–petroleum ether mixture removed the yellow-brown and magenta material and the residue (0.26 g.) obtained by removal of the solvent under reduced pressure as rechromatographed. Part of the magenta fraction was removed with petroleum ether and the remaining portion with 3:1 petroleum ether–dichloromethane. The latter solvent also developed a brown band with a diffuse yellow front and a separate yellow band. Continued elution removed the former as a red-brown eluate.

From the magenta fraction, following purification by chromatography twice more with petroleum ether as the eluate, was obtained 61 mg. of magenta needles which were indicated by spectrophotometric and n.m.r. analysis to consist of unchanged **6** and **8** in a ratio of 2:23. A 5:1 petroleum ether–dichloromethane solvent was used to develop a subsequent chromatogram of the residue from the red-brown eluate and produced light brown, dark brown, yellow, and green bands. The first was eluted with 10:1 petroleum ether–dichloromethane and discarded. The second was removed with a 5:1 mixture of the same solvents and yielded 0.132 g. (57%) of **11** as red-brown needles, m.p. 145–146°. The analytical sample was crystallized from petroleum ether. A cyclohexane solution showed λ_{max} in mμ (log ε) at 245 (4.14), 295 (3.39), 330 (4.02), 408 (3.92), and 540 (2.93). The infrared spectrum was recorded on a potassium bromide matrix. The n.m.r. spectrum of a saturated carbon tetrachloride had absorptions at τ 2.0 (2-hydrogen), 2.91 (7-hydrogen), 2.95 (5-hydrogen), 7.04 (8-methyl), 7.22 (4-methyl), 7.32 (3-methyl), and 7.42 (6-methyl) in agreement with structure **11**.

Anal. Calcd. for $C_{16}H_{15}Cl_3O$: C, 58.29; H, 4.59. Found: C, 58.89; H, 4.79.

Reaction of 1-Trichloroacetyl-3,4,6,8-tetramethylazulene with Base.—A mixture of 99 mg. (0.3 mmole) of 1-trichloroacetyl-3,4,6,8-tetramethylazulene and 5 ml. of a 1:1 solution of 0.6 *M* sodium hydroxide–methanol was heated at just below the boiling point for 2 hr. and then under reflux for 30 min. during which time the azulene derivative slowly dissolved, and the solution became dark violet in color. The reaction mixture was then extracted with 50 ml. of 5:1 petroleum ether (30–60°)–dichloromethane and the separated, purple aqueous layer was washed with 100- and then 50-ml. portions of the same solvent.

The aqueous layer was made just acid to litmus with 5% hydrochloric acid; it became cloudy and turned from purple to pink and then to blue. This solution was extracted with 50- and then 25-ml. portions of the above solvent mixture, and the combined extracts were washed with three 25-ml. portions of saturated sodium bicarbonate solution and then dried over sodium sulfate. Removal of the solvent under reduced pressure left 16 mg. (38%) of a blue oil which was indicated to be 1,4,6,8-tetramethylazulene by its visible spectrum (λ_{max} 576 in cyclohexane).

The solvent was removed under reduced pressure from the combined, dried (sodium sulfate) organic layers from the initial extraction and the red-brown, partially crystalline residue (58 mg.) was chromatographed on acidic alumina with 5:1 petroleum ether–dichloromethane as the solvent. Brown, violet, orange, and red-brown bands developed, and the first was collected in two portions. From these were obtained, respectively, 3 mg., m.p. 130–135°, and 20 mg., m.p. 139–140°, of unchanged starting material as red-brown crystals (a mixture melting point showed no depression). Continued elution with a 3:1 mixture of the same solvents removed the violet band which yielded 21 mg. of reddish oil which slowly formed rosettes of blue needles, m.p. 50–55°. The violet fraction from the rechromatography of this solid gave 17 mg. (30%) of methyl 3,4,6,8-tetramethyl-1-azuloate (12) as blue needles, m.p. 51–53°. Sublimation at 40–50° and 10^{-4} mm. separated a trace of maroon oil and raised the melting point to 68–69°. A sodium fusion test for chlorine was negative. A cyclohexane solution showed λ_{max} in mμ (log ε) at 250 (3.43), 308 (4.47), 355 (3.58), 376 (3.56), 557 (2.64), and a shoulder at 562 (2.63). The infrared spectrum (carbon tetrachloride) had peaks at 5.85 (carbonyl) and 8.25 μ (carboxylic ester). The n.m.r. spectrum (carbon tetrachloride) had absorptions at τ 2.46 (2-hydrogen), 3.07 (7-hydrogen), 3.27 (5-hydrogen), 6.09 (methoxy), 7.22 (8-methyl), 7.24 (4-methyl), 7.35 (3-methyl), and 7.58 (6-methyl) in agreement with the assigned structure.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 80.03; H, 7.55.

1-Formyl-4,6,8-trimethylazulene.—To 5 ml. of redistilled dimethylformamide was added, under anhydrous conditions and with cooling in ice, 0.5 ml. of phosphorus oxychloride. This solution was added dropwise with cooling and vigorous stirring to 0.34 g. (2.0 mmoles) of 4,6,8-trimethylazulene dissolved in 20 ml. of dimethylformamide, whereupon the color changed immediately from purple to red. The mixture was allowed to stand at 0° for 30 min. and was then poured into a solution of 2 g. of sodium acetate in 30 ml. of ice–water. The solution was then made alkaline with 10% sodium hydroxide solution and extracted four times with ether. The combined ether extracts were washed three times with water and dried over anhydrous sodium sulfate. The solvent was then removed (steam bath) and the residue was chromatographed on acid-washed alumina. Benzene was used to remove a trace of unreacted trimethylazulene. Ether eluted a red band which yielded 0.348 g. (87.5%) of 1-formyl-4,6,8-trimethylazulene, m.p. 103–106°. A sample recrystallized from cyclohexane melted at 106–107°. A solution in dichloromethane showed absorption maxima in mμ (D_{max}) at 246 (0.63), 320 (1.24), 382 (0.35), and 505. The infrared spectrum (chloroform) had a peak at 6.15 μ.

Anal. Calcd. for $C_{14}H_{14}O$: C, 84.85; H, 7.07. Found: C, 84.92; H, 7.10.

1-Formyl-4,6,8-trimethylazulene Oxime.—A solution of 0.1 g. (0.505 mmole) of 1-formyl-4,6,8-trimethylazulene, 0.378 g. (5.52 mmoles) of hydroxylammonium chloride, 0.441 g. (5.5 mmoles) of sodium acetate, in 4 ml. of water and 15 ml. of 95% aqueous ethanol was heated under reflux for 1.5 hr. To the warm alcoholic solution was added 25 ml. of warm water, and the mixture was allowed to stand overnight. More water (100 ml.) was then added and the suspension which formed was extracted with ether until the aqueous phase was colorless. The combined organic extracts were washed once with water and dried over anhydrous sodium sulfate. The solvent was then removed and recrystallization of the residue from benzene gave 97 mg. (90.2%) of 1-formyl-4,6,8-trimethylazulene oxime as purple needles, m.p. 160–161°. A dichloromethane solution showed absorption maxima in mμ (D_{max}) at 249 (1.20), 310 (2.00), 357 (0.34), 374 (0.35), and 555. The infrared spectrum (chloroform) had peaks at 3.13 (attributed to >C=N—) and at 2.81 μ (attributed to the oxime O—H).

Anal. Calcd. for $C_{14}H_{15}NO$: C, 78.87; H, 7.04; N, 6.57. Found: C, 79.17; H, 6.82; N, 6.68.

1-Cyano-4,6,8-trimethylazulene.—1-Formyl-4,6,8-trimethylazulene oxime (0.1 g., 0.47 mmole) was dissolved in 5 ml. of redistilled acetic anhydride and 4 drops of glacial acetic acid were added. The mixture was heated on a steam bath for 3 hr. and then flooded with water and the whole was extracted twice with ether. The combined ethereal extracts were washed four times with water and dried over anhydrous sodium sulfate. The solvent was then removed and the residue was chromatographed on basic alumina. A mixture of 5:1 dichloromethane–ether eluted a red band which yielded 54 mg. (59%) of 1-cyano-4,6,8-trimethylazulene as red needles, m.p. 121–122°. A dichloromethane solution showed absorption maxima in mμ (D_{max}) at 234 (0.91), 296 (1.25), 308 (1.44), 347 (0.23), 364 (0.17), and 513. The infrared spectrum (chloroform) had a peak at 4.55 μ attributed to the cyano group.

Anal. Calcd. for $C_{14}H_{13}N$: C, 86.15; H, 6.67. Found: C, 86.19; H, 6.47.