reflux condenser, dropping funnel with a capillary stem, gas feed tube, and a thermometer. It is important that the capillary of the dropping funnel always remains below the surface of the reaction mixture.

The flask was charged with 250 ml. of 35% hydrochloric acid and cooled to 0°. A 1:2 mixture of chlorine and air (v./v.) was passed through the liquid at a rate of 2 l./min. Forty grams of furfural was added dropwise below 5° from the dropping funnel. After the addition, the reaction mixture was colorless. It was then heated slowly with stirring to 85° over a period of 2 hr. and kept at this temperature for 1.5 hr. The mixture then was cooled to room temperature to yield 14 g. of crystalline mucochloric acid. The mother liquors were extracted with ether, and the ether extract was vacuum distilled to yield 21 g. of a colorless liquid, b.p. 105–115° (4 mm.). This crystallized on standing and had a melting point of 25–27° after recrystallization from water.

Anal. Calcd. for $C_4H_3O_2Cl$: C, 40.50; H, 2.53; Cl, 29.92. Found: C, 40.96; H, 2.55, Cl, 29.94.

Trimorpholino Derivative of VI (VIII).—A mixture of 4 ml. morpholine and 0.8 g. of VI in 40 ml. of dry ether was refluxed for 6 hr. and allowed to stand overnight. The resulting white precipitate was separated and extracted with 50 ml. of dry acetone. Concentration of the acetone extract yielded 500 mg. of white crystals, m.p. 157–158°, after recrystallization from acetone and benzene.

Anal. Calcd. for $C_{16}H_{29}O_5N_3$: C, 55.96; H, 8.51; N, 12.24. Found: C, 55.38; H, 8.58; N, 11.96.

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Some New Reactions and Derivatives of Azulene[1]

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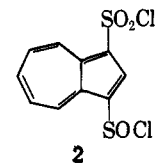
In the course of our studies on the chemistry of azulene[4] a number of new reactions and derivatives of azulene have been found which did not prove pertinent to subsequent papers. These collected results are reported.

The facile reaction of azulene with mercuric chloride to form a bis(chloromercuri)azulene had been observed earlier,[5] but the derivative was very insoluble in organic solvents and attempts to establish the positions occupied by the chloromercuri groups through displacement reactions were unsuccessful (except for the formation of 1-acetylazulene in low yield). The analogous reaction with mercuric acetate has been found to give a diacetoxymercuri derivative (1) in high yield. Treatment of an acetic acid solution of **1** with iodine gave 1,3-diiodoazulene and provided evidence that the dimercuri compounds were, as expected, 1,3 substituted. Reaction of **1** with bromine or nitryl chloride, however, resulted in oxidative decomposition, and treatment with N-bromosuccinimide or N,N-dibromomethylhydantoin gave an unstable red oil which was not characterized. Warming a mixture of acetic anhydride and **1** in acetic acid formed 1-acetylazulene in 34% yield but no 1,3-diacetylazulene. This was unexpected, as no azulene was obtained when **1** was exposed to 85% phosphoric acid for several hours.[6]

Reaction of azulene with sulfur trioxide–dioxane adduct and then basification gave a red solid. That this material, which was not obtained analytically pure, was sodium 1-azulenesulfonate was indicated by the absorptions at 8.5, 8.95, 9.37, and 9.57 μ[7] in its infrared spectrum; its reaction with nitric acid and acetic anhydride to give 1,3-dinitroazulene[8a]; and the formation of azulene-1-sulfonyl-3-sulfinyl dichloride (**2**) from the reaction of the free acid with excess thionyl chloride. Attempts to isolate the free 1-azulenesulfonic acid afforded hygroscopic maroon needles. These results are similar to those obtained by Treibs and Schroth[8b] in the analogous sulfonation of guaiazulene and the preparation of a number of derivatives of the guaiazulenesulfonic acid.



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The direct introduction of a cyano group onto benzenoid aromatic nuclei by Lewis acid-catalyzed reactions with cyanogen bromide is well known.[9] It has been found, however, that uncatalyzed reactions with thiophene[10] and furan[11] gave the α-bromo rather than the cyano substitution products. We have examined the stannic chloride-catalyzed reaction of cyanogen bromide with azulene, and the results obtained differ appreciably from those reported by Treibs[12] while our studies were in progress. The addition of azulene to one equivalent of preformed cyanogen bromide–stannic chloride complex in ether gave a 36% (94% net) yield of 1-cyanoazulene. When the same procedure was used but with a tenfold excess of cyanogen bromide–stannic chloride, there were obtained two different products: 1,3-dibromoazulene (16%) and a new substance which showed absorption at 567 mμ and a sharp band at 4.54

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

(3) National Institutes of Health Fellow, 1961–1963.

(4) (a) A. G. Anderson, Jr., and L. L. Replogle, *J. Org. Chem.*, **28**, 262 (1963); (b) A. G. Anderson, Jr., R. G. Anderson, and T. S. Fujita, *ibid.*, **27**, 4535 (1962), and preceding papers.

(5) A. G. Anderson, Jr., E. J. Cowles, J. J. Tazuma, and J. A. Nelson, *J. Am. Chem. Soc.*, **77**, 6321 (1955).

(6) The 1,3-bis(chloromercuri)azulene was readily converted to azulene (66%) by this reagent.[5]

(7) N. B. Colthup, *J. Opt. Soc. Am.*, **40**, 397 (1950).

(8) (a) The electrophilic displacement of groups from the 1-position of azulene is well known [see, for example, A. G. Anderson, Jr., and R. N. McDonald, *J. Am. Chem. Soc.*, **81**, 5669 (1959)]; (b) W. Treibs and W. Schroth, *Ann.*, **586**, 202 (1954).

(9) P. Karrer and E. Zeller, *Helv. Chim. Acta*, **2**, 482 (1919); **3**, 261 (1920).

(10) W. Steinkopf, *Ann.*, **430**, 78 (1923).

(11) A. H. Klopp and G. F. Wright, *J. Org. Chem.*, **4**, 142 (1939).

(12) W. Treibs, *Ber.*, **92**, 606 (1959).

TABLE I

REACTION OF AZULENES WITH CYANOGEN BROMIDE AND STANNIC CHLORIDE

Procedure	Ratio of reactants, moles: Azulene	CNBr	$SnCl_4$	Yield of products, %[a]: Azulene	1-CN	1-Br-3-CN	1,3-DiBr	1-Br
I[b]	1	10	10			49.2	16.1	
I	2	15	15			38.9	17.0	
I	1	1	1	61.7	36 (94)			
I[c]	1	10	10	38.7		21.3	Trace	25.1
II[b]	1	10	10			33.1	5.8	
II	1	1	1	62.5	36 (96)			
II	1	1	4	61.0	36 (93)			
	1-Br							
II	1	1	1					94.6
II	1	10	10			38	42.8	
	1-CN							
I	1	10	10	No reaction				
II	1	10	10	No reaction				
	1,3-DiBr							
I	1	10	10	No reaction				

[a] Figures in parentheses are per cent net yields. [b] See text for description of procedures. [c] Reaction quenched after 1.5 hr.

μ. These data and the elemental analyses corresponded to those of 1-bromo-3-cyanoazulene,[13] and this structure was confirmed by the formation of the same substance from the reaction of 1-bromoazulene with cyanogen bromide–stannic chloride.

The marked difference in the products from the two experiments (no 1-cyanoazulene was formed in the run with excess cyanogen bromide–stannic chloride) led to further investigation. Two procedures were followed and the ratio of reactants was varied in each. In procedure I the cyanogen bromide–stannic chloride complex was preformed and the azulene was added to this. In procedure II the azulene and cyanogen bromide were dissolved in ether and to this was added the stannic chloride. The results obtained are summarized in Table I. It is seen that the use of a large excess of cyanogen bromide and stannic chloride formed only 1,3-dibromo- (6–17%) and 1-bromo-3-cyanoazulene (33–49%) with both procedures. Both procedures, however, gave only 1-cyanoazulene (36%) when the azulene–cyanogen bromide ratio was 1:1. The formation of 1-cyanoazulene and 1,3-dibromoazulene *via* normal electrophilic substitution was expected, but the complete dependence of the nature of the products on the molar ratio of reactants was quite otherwise.

In view of our previous observations that electron-withdrawing groups on the 1-position deactivated the azulene ring to the electrophilic introduction of a second substituent,[4] it seemed likely that the 1-bromo-3-cyano compound was formed *via* 1-bromoazulene. It was demonstrated that the latter was indeed an intermediate by stopping one run after about one-sixth of the usual time. The reaction mixture was found to contain a 25% yield of 1-bromoazulene, 21% of the 1-bromo-3-cyano product, and a trace of the 1,3-dibromo compound. Therefore, it appeared that under these conditions the sole initial reaction was the bromination of the azulene, but that the cyanation of the 1-bromoazulene formed was the preferred mode of the second reaction. The matter is not quite so clear-cut as this, however, since a run starting with 1-bromoazulene gave approximately equal amounts of the cyano and bromo disubstitution products. That the bromocyano compound did not arise from the bromination of 1-cyanoazulene or by a displacement on the dibromoazulene was shown by the finding that the latter compounds were inert to an excess of cyanogen bromide and stannic chloride. The inertness of 1-bromoazulene to a molar equivalent of cyanogen bromide and stannic chloride was also observed and thus the 1-cyanoazulene produced from azulene under these conditions could not have been formed *via* 1-bromoazulene. No satisfactory explanation was found for the change in products caused by the change in molar ratios of reactants.

The reaction of azulene at the 4-position with alkyl and aryl lithium compounds was established by Hafner and co-workers.[14] These reactions gave a dihydroazulene which was readily aromatized to the 4-substituted azulene. Stafford, *et al.*,[15] identified the red oil product from azulene and sodium amide as 4-aminoazulene solely on the basis of the similarity of its absorption spectra with those of 4-methoxyazulene. The direct formation of 4-aminoazulene seemed reasonable,[16] and verification of this result was sought. Heating azulene and sodium amide in tetrahydrofuran afforded an unstable red oil. The shift in the visible region (λ_{max} of principal absorption at 510 mμ) and a peak in the N–H region at 3.0 μ were indicative of a 4-aminoazulene, but the substance could not be obtained analytically pure. However, it formed a crystalline, stable, acetyl derivative which had the expected composition and spectral properties and was thus very probably N-acetyl-4-aminoazulene.

Melville[17] first observed that an azulene and sodium would react to form a substance insoluble in hexane. More recently Weissman and co-workers[18] have studied the reaction of naphthalene and sodium in tetrahydrofuran and found that carbonation of the product formed two isomeric dihydronaphthoic acids. Treatment of a solution of azulene in tetrahydrofuran with sodium caused the color of the solution to change from blue to

(13) The calculated λ_{max} in the visible is 571 mμ based on the additivity of the effects of the two groups in the 1- and 3-positions [see A. G. Anderson, Jr., and B. M. Steckler, *J. Am. Chem. Soc.*, **81**, 4941 (1959), and references therein].

(14) K. Hafner, C. Bernhard, and R. Müller, *Ann.*, **650**, 35 (1961); K. Hafner and H. Weldes, *ibid.*, **606**, 90 (1957).

(15) W. H. Stafford, J. P. Ward, and D. H. Reid, *Chem. Ind.* (London), 1258 (1955).

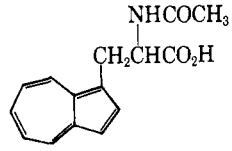
(16) 2-Aminopyridine results directly from the reaction of pyridine and sodium amide, while an alkyl lithium and pyridine form a dihydro addition product.

(17) J. Melville, *J. Am. Chem. Soc.*, **55**, 3288 (1933).

(18) D. E. Paul, D. Lipkin, and S. I. Weissman, *ibid.*, **78**, 116 (1956).

red-brown, and carbonation of the mixture gave a red acidic product from which was obtained methyl 1-azuloate in 7.7% yield and a small yellow fraction. Reaction of the latter with chloranil gave 0.8% of methyl 1-azuloate as the only azulenic product.

1-Bromo-3-acetylazulene was obtained in good yield from the reaction of 1-acetylazulene with N-bromosuccinimide. Treatment of 1-azulylmethyltrimethylammonium iodide with the sodium salt of ethyl acetamidocyanoacetate and hydrolysis of the product gave α-acetamido-β-(1-azulyl)-propionic acid (**3**). Attempts to convert this to the free amino acid were unsuccessful.



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Experimental[19]

1,3-Bis(acetoxymercuri)azulene.—To a stirred solution of 512 mg. (4.0 mmoles) of azulene in 25 ml. of methanol was added 3.828 g. (12.0 mmoles) of mercuric acetate in 75 ml. of methanol. After about 5 min. the solution became light yellow-green and a metallic blue precipitate formed. The precipitate was collected by filtration, washed with methanol (several times) and then with ether, and dried under vacuum for 4 hr. The product (2.36 g., 91%) did not melt at 360° and was soluble only in acetic acid and dimethyl sulfoxide. An acetic acid solution showed λ_{max} in mμ (D^{20a}) at 270 (1.73), 275 (1.85), 280 (1.85), 339 (0.20), and 620 (1.0).

Anal. Calcd. for $C_{14}H_{12}Hg_2O_4$: C, 26.04; H, 1.86; Hg, 62.15. Found: C, 26.02; H, 1.78; Hg, 62.08.

1,3-Diiodoazulene from 1,3-Bis(acetoxymercuri)azulene.—To a solution of 1.215 g. (1.6 mmoles) of 1,3-bis(acetoxymercuri)azulene in 300 ml. of acetic acid was added 1.219 g. (4.8 mmoles) of iodine in 100 ml. of acetic acid. The mixture was stirred for 4 hr. and poured into 1.6 l. of water; the blue material was extracted with 300-, 100-, 100-, and then 50-ml. portions of dichloromethane. The combined extracts were washed with two 500-ml. portions of water, dried over calcium chloride, and evaporated to dryness in an air stream. The residue was chromatographed on an alumina column and elution with petroleum ether (b.p. 30–60°) separated most of the excess iodine from the blue fraction. The residue from the latter was rechromatographed with 1:1 petroleum ether–dichloromethane as the eluent and yielded 130 mg. (21.3%) of green needles which were identical (ultraviolet, visible, and infrared spectra) with an authentic sample.[20b]

Anal. Calcd. for $C_{10}H_6I_2$: C, 31.61; H, 1.59. Found: C, 31.67; H, 1.61.

1-Acetylazulene from 1,3-Bis(acetoxymercuri)azulene.—A solution of 200 mg. (0.305 mmole) of 1,3-bis(acetoxymercuri)-azulene in 10 ml. of acetic acid and 5 ml. of acetic anhydride was heated on a steam bath for 2.5 hr., then cooled, and added to 150 ml. of water. The aqueous mixture was extracted with 100- and 50-ml. portions of dichloromethane, and the combined extracts were washed with 200 ml. of water and dried over calcium sulfate. The solvent was removed, and the residue was chromatographed on an alumina column. Petroleum ether was used as the eluent until the reaction of acetic anhydride with the alumina ceased, and thereafter petroleum ether–dichloromethane (2:1) was used. A small blue band was followed by a lavender band, and several small colored bands remained near the top of the column: Removal of the solvent from the lavender eluate left 18 mg. (34.4%) of a maroon oil which was identified (visible and infrared spectra) as 1-acetylazulene.[5]

Reaction of Azulene with Sulfur Trioxide–Dioxane Adduct.—A solution of 50 mg. (0.39 mmole) of azulene in 5 ml. of dry 1,2-dichloroethane was added dropwise to a cooled (ice bath), stirred suspension of sulfur trioxide–dioxane adduct prepared by passing sulfur trioxide (generated by warming an excess of Sulfan B) into 5 ml. of dry 1,2-dichloroethane and 2 ml. of dry dioxane until a small amount of the white complex was visible. The orange-red mixture was stirred for 15 min. and then poured into water. The mixture was made alkaline with sodium carbonate, and the aqueous layer then was separated and filtered. Evaporation of the filtrate to dryness, extraction of the red residue with hot ethanol, and removal of the solvent from the violet alcoholic solution left 40 mg. of red solid which did not melt up to 300°. The peaks in the infrared spectrum (8.5, 8.95, 9.37, and 9.57 μ) were those expected for sodium 1-azulenesulfonate.[7]

The salt was treated with 10 ml. of a solution prepared by adding 1 ml. of concentrated nitric acid to 25 ml. of acetic anhydride at 0° and an emulsion formed. One drop of concentrated nitric acid was added, and the emulsion broke as the color of the solution changed to orange. After 5 min., the mixture was poured into water, the whole was extracted with dichloromethane, and the organic extracts were dried over sodium sulfate. Removal of the solvent left orange needles, m.p. 262–263°, which were identical (mixture melting point, ultraviolet and visible spectra) with an authentic sample of 1,3-dinitroazulene.[5]

Azulene-1-sulfonyl-3-sulfinyl Dichloride.—Azulene (100 mg., 0.78 mmole) and sulfur trioxide–dioxane adduct were allowed to react as described above and then were filtered to remove excess adduct. (The isolation of hygroscopic maroon neeldes, which were presumed to be 1-azulenesulfonic acid, could be accomplished by concentration of the filtrate). To the filtrate was added 3 ml. of thionyl chloride, and the mixture was heated under reflux for 40 min. The solution, the color of which had become green, was cooled and poured into water; the whole was extracted with dichloromethane. The combined organic extracts were washed with water and saturated salt water, dried over sodium sulfate, and evaporated to dryness. Crystallization of the residue from petroleum ether–dichloromethane gave yellow-brown crystals, m.p. 115–129° dec., which on recrystallization amounted to 112 mg. (46%) of golden needles, m.p. 117–125° dec. A chloroform solution showed λ_{max} in mμ (D^{20a}) at 238 (0.69), 297 (1.62), 321 (0.29), 365 (0.38), and 466 (1.5).

Anal. Calcd. for $C_{10}H_6Cl_2O_3S_2$: C, 38.84; H, 1.96; Cl, 22.93. Found: C, 38.90; H, 2.34; Cl, 23.10.

Reaction of Azulene with Cyanogen Bromide. Procedure I.—Anhydrous stannic chloride was added dropwise with cooling and stirring to cyanogen bromide in dry ether under a dry nitrogen atmosphere. A white precipitate separated, and the mixture was stirred at room temperature for 10 min. Azulene then was added, and the mixture was stirred overnight and then worked up as described below for the preparation of 1-bromo-3-cyanozulene.

Procedure II.—Anhydrous stannic chloride was added dropwise with stirring and cooling under a dry nitrogen atmosphere to a solution of azulene and cyanogen bromide in dry ether. The mixture was stirred overnight at room temperature and worked up as described below for the preparation of 1-bromo-3-cyanoazulene.

1-Bromo-3-cyanozulene. A. From Azulene by Procedure I.—Azulene (0.256 g., 2 mmoles) was treated with cyanogen bromide (2.12 g., 20 mmoles) and stannic chloride (5.2 g., 20 mmoles) according to procedure I. After 24 hr., 10 ml. of 5% hydrochloric acid was added and the separated organic layer was washed with water, 5% sodium bicarbonate, and then water. The residue from the dried (sodium sulfate) solution was chromatographed on a column of acid-washed alumina. Elution with *n*-hexane gave a blue fraction from which was obtained 92 mg. (16.1%) of green needles, m.p. 89–90°, which were identical (mixture melting point, absorption spectra) with an authentic sample of 1,3-dibromoazulene. A very small green band was eluted next with 2:5 dichloromethane–*n*-hexane, and the main product was removed as a purple fraction by a 1:1 mixture of these solvents. The residue from the purple solution formed purple needles, m.p. 162–165°, which after recrystallization from *n*-hexane amounted to 0.228 g. (49.2%) and melted at 167–168.5°. A dichloromethane solution showed λ_{max} in mμ (D^{20a}) at 236 (0.70), 285 (0.79), 291 (1.07), 297 (1.01), 303 (1.38), 373 (0.22),

(19) Melting points were taken on a calibrated Fisher-Johns apparatus and are uncorrected. Visible and ultraviolet absorption spectra were recorded with a Cary Model 11S or 14 spectrophotometer. Infrared spectra were recorded with a Perkin-Elmer Model 21 spectrophotometer. Elementary analyses were performed by Dr. G. Weiler and Dr. F. B. Strauss, Oxford, England; Dr. Alfred Bernhardt, Mulheim (Ruhr), Germany; Elek Microanalytical Laboratory, Los Angeles, Calif.; or Mr. B. J. Nist and Mr. C. H. Ludwig and Miss K. Schwarz, Miss A. Kuo, and Miss L. Ho.

(20) (a) *D* represents optical density. (b) A. G. Anderson, Jr., and B. M. Steckler, *J. Am. Chem. Soc.*, **81**, 4941 (1959).

and 567 (1.24) with a shoulder at 598 (1.12). The infrared spectrum showed a peak attributed to the nitrile group at 4.54 μ.

Anal. Calcd. for $C_{11}H_6BrN$: C, 56.71; H, 2.60; N, 6.06. Found: C, 56.88; H, 2.81; N, 5.78.

B. From Azulene by Procedure II.—Azulene (0.256 g., 2 mmoles), cyanogen bromide (2.12 g., 20 mmoles), and stannic chloride (5.2 g., 20 mmoles) were allowed to react according to procedure II, and the reaction mixture was worked up as described in A. There was obtained 33 mg. (5.8%) of 1,3-dibromoazulene and 0.153 g. (33.1%) of 1-bromo-3-cyanoazulene which were identical to the products in A.

C. From 1-Bromoazulene by Procedure I.—1-Bromoazulene (0.16 g., 0.77 mmole) was treated with cyanogen bromide (0.82 g., 7.7 mmoles) and stannic chloride (2.02 g., 7.7 mmoles) according to procedure I. After 24 hr., the reaction mixture was worked up as described in A. From the *n*-hexane eluate was obtained 94 mg. (42.7%) of 1,3-dibromoazulene, and from the 1:1 dichloromethane–*n*-hexane eluate was isolated 68 mg. (38%) of 1-bromo-3-cyanoazulene which were identical with the products in A.

1-Cyanoazulene. Procedure I.—Azulene (0.256 g., 2 mmoles), cyanogen bromide (0.212 g., 2 mmoles), and stannic chloride (0.522 g., 2 mmoles) were allowed to react according to procedure I, and the reaction mixture was worked up as described for 1-bromo-3-cyanoazulene. The crude product was chromatographed on an acid-washed alumina column. Elution with *n*-pentane removed 0.158 g. (61.7%) of unchanged azulene, and then dichloromethane removed a reddish fraction from which was obtained 0.11 g. (36%, 94% net) of 1-cyanoazulene as maroon needles, m.p. 50–51°, which were identical (mixture melting point, absorption spectra) with an authentic sample.

Procedure II.—Azulene (0.256 g., 2 mmoles), cyanogen bromide (0.25 g., 2.36 mmoles), and stannic chloride (0.67 g., 2.56 mmoles) were allowed to react according to procedure II, and the reaction mixture was worked up as described above for 1-bromo-3-cyanoazulene. Chromatography of the crude product on an acid-washed alumina column gave 0.16 g. (62.5%) of unchanged azulene and 0.11 g. (36%, 96% net) of 1-cyanoazulene, m.p. 50–51°, which was identical with an authentic sample.

Incomplete Reaction of Azulene and Cyanogen Bromide–Stannic Chloride.—Azulene (0.256 g., 2 mmoles), cyanogen bromide (2.12 g., 20 mmoles), and stannic chloride (5.2 g., 20 mmoles) were allowed to react according to procedure I, except that the reaction was quenched by the addition of water after 1.5 hr. The reaction mixture was worked up as described for 1-bromo-3-cyanoazulene, and the crude product was chromatographed on a column of acid-washed alumina. Elution with *n*-pentane removed a blue fraction and from the fractional sublimation (room temperature and 0.2-mm. pressure) of the residue from this were obtained azulene (99 mg., 38.7%), 1-bromoazulene (0.104 g., 25.1%), and a trace of 1,3-dibromoazulene which were identical with authentic samples of these compounds. A 1:1 *n*-pentane–dichloromethane solvent eluted a purple band from which was obtained 99 mg. (21.3%) of 1-bromo-3-cyanoazulene which was identical with an authentic sample.

N-Acetyl-4-aminoazulene.—A solution of 512 mg. (4 mmoles) of azulene and 200 mg. (5 mmoles) of sodium amide in 200 ml. of pure, dry tetrahydrofuran was heated under reflux for 24 hr. under anhydrous conditions. The mixture was cooled, treated with 2 ml. of water, and the solvent was removed under reduced pressure. Nitrogen was admitted to the flask, then 200 ml. of ether, and 100 ml. of water. The mixture was shaken and filtered. The separated ethereal solution was washed with two 200-ml. portions of water. The solvent was removed (nitrogen atmosphere, room temperature) from the dried (calcium sulfate) solution, and the residue was chromatographed on a basic alumina column. Petroleum ether eluted unchanged azulene, and dichloromethane removed a green band and then a red fraction. The red fraction was rechromatographed and afforded an unstable red oil (probably 4-aminoazulene in *ca.* 10% yield) which was not obtained analytically pure. A dichloromethane solution showed λ_{max} in mμ (D^{20a}) at 262 (2.15), 294 (1.55), 318 (0.80), and 510 (1.0). The infrared spectrum showed a sharp peak in the N–H region at 3.0 μ. A sample of the red oil was dissolved in 5 ml. of dichloromethane and to the solution was added 3 ml. of freshly distilled acetic anhydride. The mixture was warmed on a steam bath for 15 min. and then allowed to stand overnight. Careful chromatography on alumina (the unreacted acetic anhydride reacted exothermically) with 1:1 dichloromethane–chloroform as the eluent separated a blue band which was collected, concentrated, and rechromatographed. Removal of the solvent left a blue solid which was recrystallized from *n*-hexane–dichloromethane and afforded blue needles, m.p. 170–171°. A dichloromethane solution showed λ_{max} in mμ (D^{20a}) at 266 (0.5), 294 (2.19), 305 (1.87), 374 (0.27), and 560 (1.0). The infrared spectrum showed N–H (3.0) and carbonyl (5.9 μ) absorption.

Anal. Calcd. for $C_{12}H_{11}NO$: C, 77.81; H, 5.99. Found: C, 78.11; H, 6.05.

Methyl 1-Azuloate. A. From 1-Cyanoazulene.—A solution of 158.5 mg. (1 mmole) of 1-cyanoazulene in 15 ml. of methanol and 15 ml. of 50% aqueous potassium hydroxide was heated under reflux for 24 hr., and the alcohol then was removed by distillation. The aqueous residue was diluted with 150 ml. of water, extracted with 150 ml. of dichloromethane, and then acidified with hydrochloric acid. The red precipitate which formed was extracted into ether, and the concentrate (25 ml.) of the combined extracts was treated with a large excess of an ethereal solution of diazomethane. The solvent was removed, and the residue was chromatographed on a column of neutral alumina. Elution with 1:1 petroleum ether–dichloromethane removed a lavender band which yielded 179 mg. (96%) of methyl 1-azuloate as lavender needles, m.p. 56–57°, which were identical with an authentic sample.[21]

B. From Azulene.—Small pieces of sodium (1 g.) were added to a stirred solution of 512 mg. (4 mmoles) of azulene in 100 ml. of pure, dry tetrahydrofuran, and the mixture was stirred for 24 hr. under anhydrous conditions. The maroon suspension was poured onto 500 g. of powdered Dry Ice, the mixture was allowed to come to room temperature, and the unchanged sodium was removed. The solution was acidified with hydrochloric acid and extracted with chloroform. The combined extracts were washed three times with water and then extracted twice with 75-ml. of 10% sodium carbonate solution. The combined extracts were acidified with hydrochloric acid and extracted with two 75-ml. portions of ether. The ethereal extracts were concentrated to a volume of 25 ml. and treated with an excess of diazomethane in ether. The solvent was removed, and the residue was chromatographed on alumina. Petroleum ether–dichloromethane eluted a lavender fraction and methanol removed a small yellow fraction. The residue from the lavender eluate was rechromatographed three times and yielded 50.8 mg. (6.8%) of methyl 1-azuloate as lavender needles which were identical with an authentic sample.[21] Treatment of the residue from the yellow fraction with chloranil in the usual manner afforded an additional 6 mg. (0.8%) of the same ester as the only azulenic product.

1-Bromo-3-acetylazulene.—N-Bromosuccinimide (229 mg., 1.29 mmoles) was added to a solution of 1-acetylazulene (219 mg., 1.29 mmoles) in 27 ml. of purified dichloromethane. An immediate color change from lavender to violet occurred and a starch–iodide test was negative. An additional 5 mg. of N-bromosuccinimide was consumed at once, but a second 5-mg. portion produced a faint test for positive halogen. The mixture was concentrated and chromatographed on a column of activated, acid-washed alumina. Elution with dichloromethane separated the major purple-brown band from small yellow-brown and purple-red zones. The latter fractions were discarded. The eluate then was changed to 1:1 petroleum ether–dichloromethane, and elution continued until the purple-brown band was completely removed (the column remained a pale pink). The residue from this fraction was chromatographed. Removal of the solvent and drying under reduced pressure in the presence of Drierite gave 302 mg. of crystalline material which yielded 270 mg. (84%) of 1-bromo-3-acetylazulene as deep green needles, m.p. 99–100° after recrystallization from *n*-hexane. An *n*-hexane solution showed λ_{max} in mμ (D^{20a}) at 268 (0.62), 291 (0.98), 297 (1.19), 303 (1.11), 309 (1.43), 376 (0.28), and 393 (0.3). The maximum in the visible region was at 570 mμ with shoulders at 524, 597, 618, and 683 mμ. The infrared spectrum was recorded.

Anal. Calcd. for $C_{12}H_9BrO$: C, 57.85; H, 3.64. Found: C, 57.82; H, 3.75.

α-Acetamido-β-(1-azulyl)propionic Acid.—To a stirred suspension of 0.6 g. of sodium hydride (in mineral oil) in 20 ml. of anhydrous, redistilled N,N-dimethylformamide was added carefully 1.3 g. (7.73 mmoles) of dry ethyl acetamidocyanoacetate.[22] After the evolution of hydrogen had ceased, a nitrogen atmos-

(21) A. G. Anderson, Jr., and J. J. Tazuma, *J. Am. Chem. Soc.*, **75**, 4979 (1953).

(22) J. D. Carbon and S. Brehm, *J. Org. Chem.*, **26**, 3376 (1961).

phere was introduced, 900 mg. (2.75 mmoles) of 1-azulylmethyltrimethylammonium iodide[4b] was added, and the solution was heated at 100–110° for 3.5 hr. The solvent was removed under reduced pressure and the residue was chromatographed on an alumina column. The blue fraction eluted by 3:1 dichloromethane–petroleum ether gave 836 mg. of a blue oil presumed to be ethyl α-acetamido-α-cyano-β-(1-azulyl)propionate.

A solution of 340 mg. (1:1 mmoles) of the blue oil in 20 ml. of a 10% solution of potassium hydroxide in 50% ethanol was heated under reflux for 2 hr. Water (50 ml.) was added and the whole was extracted with 100 ml. of ether. The separated aqueous layer was acidified with 6 *N* hydrochloric acid and then extracted with ether. The residue from the dried (sodium sulfate) ethereal solution was chromatographed on a column of silica gel. Removal of the solvent from the blue fraction eluted by ether and recrystallization of the blue solid from water gave 171 mg. (64%) of α-acetamido-β-(1-azulyl)propionic acid as blue crystals, m.p. 126–128°.

Anal. Calcd. for $C_{15}H_{15}NO_3$: C, 69.99; H, 5.85; N, 5.44. Found: C, 69.66; H, 6.12; N, 5.20.

Proton Nuclear Magnetic Resonance Spectra of 1-Acyl Pyrazoles

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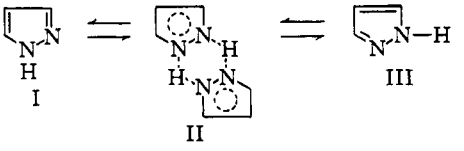
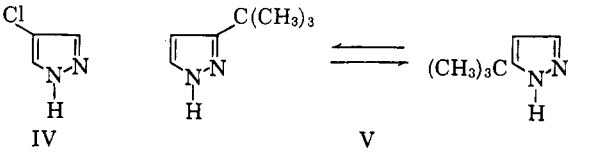
The n.m.r. spectra of the annular protons of 1-acyl pyrazoles are useful in determining the structures of isomers formed by acylation of unsymmetrically substituted pyrazoles. The spin–spin coupling constants of the annular protons fall into narrow ranges that are characteristic of the position of the protons on the pyrazole ring. The relative chemical shifts of these protons are also dependent upon their location on the ring. A 1-acyl pyrazole with an unambiguous structure has been prepared to aid in these correlations.

When the 1-position of a pyrazole is unsubstituted, the 3- and 5-positions are equivalent in the sense that tautomers of unsymmetrically substituted pyrazoles cannot be separated. It has been suggested that pyrazoles exist in solution largely as hydrogen-bonded dimers[1,2] (II), and that the equivalency of the 3- and 5-positions results from delocalization of electrons in the dimer.[3] No available evidence precludes the existence of monomeric species (I and III) in dilute solution, but in any event, if present, they would be in rapid equilibrium with each other *via* the dimeric, hydrogen-bonded species.



I II III

Evidence for the equivalency of the 3- and 5-positions of pyrazoles unsubstituted in the 1-position can be found by examining their proton n.m.r. spectra.[4] For 4-chloropyrazole (IV) only two resonances in the ratio of 1:2 are observed: a single low-field resonance at τ −3.27 corresponding to the N–H, and a single unsplit resonance at τ 2.32 corresponding to the protons on the 3- and 5-positions. If unassociated forms such as I and III were present, they would not be detectable by n.m.r. if the frequency at which they are interconverted, *via* II, is higher than that used in making the observation.[5] Because of the equivalency of the 3- and 5-protons, no spin–spin splitting is observed. Similarly, for 3(5)-*t*-butylpyrazole (V), a single, sharp resonance is observed for the protons of the *t*-butyl group at τ 8.63, and a single resonance at τ −2.96 for



IV V

the N–H. The two annular protons split each other into doublets appearing at τ 2.49 and 3.91 with a coupling constant, *J*, of 2.0 c.p.s. This coupling constant must be an average of the coupling constants J_{34} and J_{45} weighted by the population of each tautomer in the equilibrium mixture. Comparison of the spectrum of IV with that of V suggests that the higher field doublet at τ 3.91 is the 4-proton, since it is missing in the spectrum of IV.

The most complicated spectrum is produced by pyrazole itself. The N–H appears as a single resonance at τ −3.60. The 4-proton appears as a triplet at τ 3.60, split by the equivalent 3- and 5-protons, while the 3- and 5-protons appear as a single doublet at τ 2.26. The coupling constant for this A_2B system is 2.1 c.p.s.

When pyrazole is acetylated on the 1-nitrogen the 3- and 5-positions become nonequivalent. As a result the three annular protons of 1-acetylpyrazole (VI) appear as three separate quadruplets at τ 1.78, 2.36, and 3.60. Analysis of the splitting in these quadruplets shows that all three protons are coupled to each other and that the coupling constants have values of 0.6, 1.5, and 2.9 c.p.s. Examination of the spectrum of 1-acetyl-4-chloropyrazole (VII) reveals that the 3- and 5-protons are split by 0.7 c.p.s. into doublets that appear at τ 1.81 and 2.44. Clearly the coupling constant across the ring between the 3- and 5-protons (J_{35}) must be 0.6–0.7 c.p.s. The remaining two coupling constants of 1.5 and 2.9 c.p.s. observed in the spectrum of VI must be J_{34} and J_{45}. The problem remains of deciding which corresponds to J_{34} and which to J_{45}.

When the unsymmetrically substituted *t*-butylpyrazole (V) is acetylated, two isomeric 1-acetyl compounds, VIII and IX, could be formed. Actually, acetylation of V leads to a single product having a pair of doublets in its spectrum at τ 1.88 and 3.71 with a coupling con-

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(2) H. Hayes and L. Hunter, *J. Chem. Soc.*, 1 (1941).

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(4) All spectra were measured with a Varian A60 n.m.r. spectrometer at room temperature on 0.5 *M* solutions in carbon tetrachloride containing 0.05 *M* tetramethylsilane as an internal standard.

(5) 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.