Electrophilic Substitution of Some 1,3-Disubstituted Azulenes[1,2,3]

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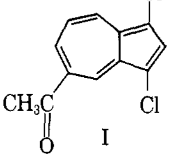
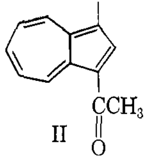
The electrophilic substitution (acetylation, chlorination, or bromination) of some 1,3-disubstituted azulenes has been achieved and shown to occur at the 5-position. The effects of the different groups in the 5-position on the principal maximum in the visible region, and of the 5-halo groups on the absorption in the near-ultraviolet were examined.

In the course of our studies on the chemistry of azulene[6] we had often observed the presence of small amounts of colored by-products from electrophilic substitution reactions which gave mainly 1- and 1,3-substituted derivatives and had considered it likely that these were trisubstitution products. Our interest in investigating the electrophilic introduction of a third group was enhanced by the results of theoretical calculations of the ground state electron densities, which predict the 5-position,[7] or the 2-position[8] to have the highest value after the 1- and 3-positions, and of the localization energies which gave essentially equivalent values to the 2- and 5-positions.[9] These considerations did not include any possible effects of substituents on the 1,3-positions. As such groups might alter the relative reactivity of the unsubstituted positions through both electronic and steric effects, unless it can be shown that this is not the case, experiments on trisubstitution are not a completely definitive test of these predictions.

The first example studied was the acetylation of 1,3-dichloroazulene. From the reaction of this compound with acetyl chloride and stannic chloride in carbon tetrachloride there was obtained 16% (36% net) of 5-acetyl-1,3-dichloroazulene (I). Many different reaction conditions wherein the solvent, temperature, catalyst, and ratios of reactants were varied did not improve the yield. The structure of I was indicated by the wave length (627 mμ) of the principal maximum on the basis of assumed additivity of the spectral shifts due to the substituents.[10] The formation of I in 40% yield from the reaction of 5-acetylazulene and N-chlorosuccinimide confirmed the structure. Crystalline I exhibited unusual melting phenomena in that the green needles of even the analytical sample partially melted at *ca.* 95°, resolidified as the temperature was slowly increased, totally melted at 103–104°, and after cooling and resolidification remelted at 103–104° in a normal manner.


I


II

When aluminum chloride was used as the catalyst, or when *sym*-tetrachloroethane was used as the solvent, a small quantity of dark purple crystals was obtained in addition to I. The identity of the purple compound as 1-chloro-3-acetylazulene (II) was indicated by the position of the principal maximum in the visible spectrum at 576 mμ[11] and verified by the preparation of the same substance by the acetylation of 1-chloroazulene. The formation of II from 1,3-dichloroazulene (in some runs the yield of II exceeded that of I) is the exact reverse of the previously observed displacement of the 1-acetyl group by positive chlorine.[12]

Treatment of 1,3-dichloroazulene with N-chlorosuccinimide in benzene–acetonitrile gave a trichloroazulene in 17% yield. The location of the principal maximum in the visible spectrum of this substance at 667 mμ also pointed to substitution in the 5-position as Parham and Reiff[13] found a shift of +25 mμ for the chloro group in a compound which is most probably 5-chloroazulene. The observed bathochromic shift would seem to preclude substitution at other than the 5-position. A 6-chloro group apparently does not cause any shift as the same value (558 mμ) is reported for both 4,8-dimethylazulene[14] and 6-chloro-4,8-dimethylazulene,[15] and the effect of a 4-chloro group would not be expected to differ greatly from this. The 2-chloro group also apparently does not cause a bathochromic shift[16] and additional evidence against substitution in the 2-position was provided by the presence of a sharp singlet peak at 2.50 τ in the n.m.r. spectrum which was most likely due to the 2-hydrogen.[17] The remainder of the n.m.r. spectrum was also consistent with the proposed structure III.

If the reaction with N-chlorosuccinimide was run in a nonpolar solvent (benzene) only a minute amount of III was formed even after prolonged heating under reflux. However, if the solution was evaporated to dry-

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[1] From the Ph.D. thesis of Lanny L. Replogle.

[2] Supported in part by a grant (G 7397) from the National Science Foundation.

[3] Reported in part as a communication, *J. Org. Chem.*, **25**, 1275 (1960).

[4] National Science Foundation Senior Postdoctoral Fellow, 1960–1961.

[5] National Science Foundation Predoctoral Fellow, 1959–1960.

[6] A. G. Anderson, Jr., and Robert G. Anderson, *J. Org. Chem.*, **27**, 3578 (1962), and previous papers.

[7] A. Julg, *J. chim. phys.*, **52**, 377 (1955); R. D. Brown and M. L. Heffernan, *Australian J. Chem.*, **13**, 38 (1960); H. Spiesecke and W. G. Schneider, *Tetrahedron Letters*, No. **14**, 468 (1961).

[8] E. Heilbronner, "Non-Benzenoid Aromatic Compounds," D. Ginsburg, Ed., Interscience Publishers, Inc., New York, N. Y., 1959, p. 196.

[9] R. D. Brown, private communication to D. Peters, *J. Chem. Soc.*, 1028 (1958).

[10] Calcd. $\lambda_{\max}$ = 626 mμ = 638 mμ for 1,3-dichloroazulene − 12 mμ for the 5-acetyl group [*cf.* W. Treibs and M. Quarg, *Ann.*, **598**, 38 (1955)].

[11] A. G. Anderson, Jr., C. G. Fritz, and R. Scotoni, Jr., *J. Am. Chem. Soc.*, **79**, 6511 (1957); A. G. Anderson, Jr., R. Scotoni, Jr., and C. G. Fritz, *J. Org. Chem.*, **22**, 1193 (1957).

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

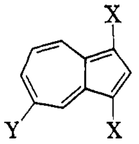
[13] W. E. Parham and H. E. Reiff, *ibid.*, **77**, 1177 (1955).

[14] Pl. A. Plattner and H. Roniger, *Helv. Chim. Acta*, **25**, 1077 (1942).

[15] K. Hafner, H. Patzelt, and H. Kaiser, *Ann.*, **656**, 24 (1962).

[16] The reported violet color of 2-chloroazulene more probably indicates a hypsochromic shift [T. Nozoe, S. Seto, S. Matsumura, and T. Asano, *Proc. Japan Acad.*, **31**, 339 (1956); *Chem. Abstr.*, **51**, 2714 (1957)].

[17] The peak for the 2-hydrogen in 1,3-dichloroazulene is at 249 τ (A. G. Anderson, Jr., and L. L. Replogle, unpublished results). Subsequent to the completion of the present studies, K. Hafner and K. L. Moritz, *Ann.*, **656**, 40 (1962), reported formylation in both the 2- and 5-positions of 1,3-dialkylazulenes.



III. X = Y = Cl
IV. X = Y = Br
V. X = $O_2CC_6H_5$; Y = Cl

ness with heat an appreciable amount of III was formed along with many other products.

An analogous reaction of 1,3-dibromoazulene with N-bromosuccinimide in benzene–acetonitrile afforded 1,3,5-tribromoazulene (IV) in 21% yield. The structure of IV was indicated by the position of the principal maximum in the visible spectrum at 652 mμ (corresponding to a shift of +27 mμ for the 5-bromo group) and the n.m.r. spectrum (which showed a sharp singlet for the 2-hydrogen at 2.33 τ).[17] As with chlorination, the nature of the solvent was important: with dimethylformamide the mixture became brown and no definable products were obtained, while with benzene the reaction was extremely slow. Attempts to effect the bromination with bromine in carbon tetrachloride or dioxane, or with pyridinium bromide perbromide in acetic acid were unsuccessful.

Other efforts to achieve electrophilic substitution of 1,3-dichloroazulene were less successful. Reaction with nitric acid and acetic anhydride gave only yellow material which lacked spectral properties characteristic of the azulene system. Treatment with thiocyanogen gave a small amount of a semicrystalline product which showed a λ_{max} at 600 mμ (a 5-thiocyano group would be expected to give a hypsochromic shift) but which resisted further purification and was not investigated further.

It was thought that better results might be obtained with groups less deactivating than chlorine or bromine in the 1,3-positions. In the course of another study[18] a compound of the desired type, 1,3-dibenzoyloxyazulene, had been prepared. Reaction of this derivative with N-chlorosuccinimide was found to occur readily in benzene solution in the cold to give *ca.* 40% of 5-chloro-1,3-dibenzoyloxyazulene (V). The assignment of the structure was based on an absorption maximum at 683 mμ (see Table I) and the analogy of the other trisubstitution products.

TABLE I

PRINCIPAL ABSORPTION MAXIMA (mμ) OF 1,3,5-TRISUBSTITUTED AZULENES

Groups	λ_{max}[a]	$\Delta\lambda_{max}$[c]
5-$COCH_3$	568	−12
1,3-diCl-5-$COCH_3$	627	−11
5-Cl	605[b]	+25
1,3,5-triCl	668	+30
1,3-di$CO_2C_6H_5$-5-Cl	683	+27
1,3,5-triBr	652	+24

[a] All spectra were taken in saturated hydrocarbon solvent. [b] Ref. 13. [c] Based on the values for the corresponding compounds not having the 5-substituent.

The preparation of these 1,3,5-trisubstituted azulenes provided the opportunity to see whether the spectral shifts observed corresponded to the sum of the shifts of the individual groups as has been found to be the case for many 1,3-disubstituted derivatives.[19] In Table I are listed the pertinent spectral data for these compounds. Previously, the carboethoxy,[20] methyl,[20] and acetyl[10] groups in the 5-position had been found to cause a shift in the same direction as in the 1-position but to an appreciably lesser extent. The shift of −11 mμ for the 5-acetyl group in 1,3-dichloro-5-acetylazulene (assuming the additivity of the shifts) is essentially the same as the value for the group alone. These results are in keeping with the calculated values[21] of the electron densities at the 1- and 5-positions in the ground and excited states and the interpretation[19a] of the stabilization of these states by such groups. The calculated electron densities at 1- and 5-positions in the ground and lowest excited states of azulene[21] are shown.

Thus the smaller net change in electron density at the 5-position (0.121) relative to that at the 1-position (0.241) would be expected to result in a smaller shift in the absorption. Neither these considerations nor the additional factor of the relative orientations with respect to the 1- and 5-positions of the ring dipole in the ground and excited states seem to provide an explanation for the observation that the magnitudes of the bathochromic shifts found for the 5-chloro group (*ca.* 27 mμ) and the 5-bromo group (24 mμ) correspond closely to the values of 30 mμ and 25 mμ for a chlorine or a bromine, respectively, on the 1-position.

Examination of the near-ultraviolet (320–400-mμ) spectra of the chloroazulenes revealed that a shift of *ca.* +8 mμ resulted from the introduction of each chlorine as one proceeded from azulene to 1- to 1,3- to 1,3,5-substitution. This was measured most conveniently with the longest wave-length peak where the values found were, respectively, in mμ (log ε): 352 (2.87), 362 (3.69), 369 (3.90), and 377 (4.07). Similar behavior was noted for the corresponding bromoazulenes for which the data were 362 (3.72), 370 (3.95), and 380 (4.08). These spectral characteristics were of value in detecting components of reaction mixtures and in determining the purity of a number of the products.

Experimental[22]

5-Acetylazulene was prepared by the method of Treibs and Quarg.[10] The sweet-smelling purple oil thus obtained was further purified by repeated chromatography on acid-washed alumina

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

(19) (a) A. G. Anderson, Jr., and B. M. Steckler, *J. Am. Chem. Soc.*, **81**, 4941 (1959); (b) A. G. Anderson, Jr., and R. N. McDonald, *ibid.*, **81**, 5669 (1959), and references in these papers.

(20) E. Heilbronner, "Non-Benzenoid Aromatic Compounds," D. Ginsburg, Ed., Interscience Publishers, Inc., New York, N. Y., 1959, pp. 224 and 237. The values for the 1- and 5-positions, respectively, are −36 mμ and −14 mμ for carboethoxy, and +28 mμ and +12 mμ for methyl.

(21) R. Pariser, *J. Chem. Phys.*, **25**, 1112 (1956).

(22) 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 spectrophotometer. Infrared spectra were taken on a Perkin-Elmer Model 21 spectrophotometer. Nuclear magnetic resonance absorption was recorded by Mr. B. J. Nist with a 60-Mc. Varian high resolution spectrometer with tetramethylsilane or hexamethyldisiloxane as an internal standard. Gas–liquid chromatographic analyses were carried out at *ca.* 200° on an Aerograph Model A-90-C with a silicone 710 column. Microanalyses were performed by Dr. A. Bernhardt, Max-Planck Institute, Mulheim (Ruhr), Germany, Drs. G. Weiler and F. B. Strauss, Oxford, England, or by A. Kuo, L. Ho, and B. J. Nist.

with 1:1 petroleum ether–methylene chloride and then 1:1 petroleum ether–benzene as the eluents. The oil was finally crystallized from petroleum ether and afforded 219 mg. (7.1%) of violet needles, m.p. 35–38°.[10] A petroleum ether solution exhibited λ_{max} in mμ at 514 (shoulder), 529, 548, 569, 593, 621, 648, and 684.[10] The infrared spectrum (neat) had a peak at 5.98 μ. The n.m.r. spectrum was recorded.

A semicarbazone, prepared as described for the derivative of 1-acetylazulene,[12] crystallized from ethanol as lavender plates, m.p. 213–220° dec.[10]

Oxidation with sodium hypoiodite as described for this reaction on 1-acetylazulene[12] gave 5-azuloic acid, m.p. 203–205°, λ_{max} (methylene chloride) 564 mμ.[23]

In addition to the 5-acetylazulene there was obtained a lesser amount of a blue oil which showed peaks in the infrared at 5.85 and 5.93 μ, and in the visible at *ca.* 650 mμ and thus possibly contained the isomeric 4-acetyl- and 6-acetylazulenes which would be expected to be produced. The material yielded a crystalline semicarbazone, m.p. 151.5–153°, and a green crystalline fraction, m.p. 72–75°, but was not further investigated.

1,3-Dichloro-5-acetylazulene (I). **A. From 1,3-Dichloroazulene.**—To a solution of 50 mg. (0.25 mmole) of 1,3-dichloroazulene in 10 ml. of dry carbon tetrachloride was added 5 ml. (0.07 mole) of acetyl chloride and 0.5 ml. (4.2 mmoles) of stannic chloride. The green solution was heated under reflux for 1 hr. and then cooled and shaken thoroughly with dilute hydrochloric acid containing ice. The mixture was extracted with ether and the solvent was removed from the separated organic layer. The residue was chromatographed on acid-washed alumina (basic alumina caused extensive decomposition), and petroleum ether removed a blue band which yielded 28 mg. of unchanged dichloroazulene. Elution with 1:1 petroleum ether–methylene chloride gave a pale yellow eluate and developed a green band which was removed with methylene chloride. Rechromatography of the solid from the green fraction afforded 9.5 mg. (16% actual, 36% net) of green needles which partially melted at 92–95° and totally melted at 101–103°. The resolidified sample melted at 101–103°. The analytical sample partially melted at *ca.* 95°, resolidified as the temperature was increased, and melted at 103–104°. A cyclohexane solution exhibited maxima in mμ (log ε) in the ultraviolet at 227 (4.19), 242 (4.38), 296 (4.50), 306 (4.53), 322 (4.04), 379 (3.97), and 400 (3.21), and in the visible (ε) with a shoulder at 578 (323), shoulder at 606 (410), 627 (467), 655 (410), 644 (420), 687 (428), and shoulders at 738 (180) and 769 (170). The infrared spectrum (potassium bromide pellet) showed a peak at 5.97 μ. The n.m.r. spectrum was recorded.

Anal. Calcd. for $C_{12}H_8OCl_2$: C, 60.28; H, 3.37. Found: C, 60.55; H, 3.29.

B. From 5-Acetylazulene.—A mixture of 15 mg. (0.088 mmole) of 5-acetylazulene, 25 mg. (0.19 mmole) of N-chlorosuccinimide, and 10 ml. of redistilled N,N-dimethylformamide was allowed to stand at room temperature for 21 hr. (a starch iodide test for halogen was still positive) and was then heated on a steam bath for 25 min. (a test for positive halogen was negative). The solution, which had become green, was poured into water and the whole was extracted with ether. The combined ether extracts were repeatedly extracted with water (to remove the dimethylformamide) and then dried. Removal of the solvent and chromatography of the green oil which remained on acid-washed alumina with 1:1 benzene–methylene chloride as the eluent gave a green fraction which afforded 9 mg. (43%) of 1,3-dichloro-5-acetylazulene as green needles which were identical (melting point, ultraviolet, visible, and infrared spectra) with the material obtained in method A.

1-Chloro-3-acetylazulene (II). **A. From 1-Chloroazulene.**—To a solution of 79 mg. (0.49 mmole) of 1-chloroazulene[12] and 2 ml. (28 mmoles) of acetyl chloride in 10 ml. of dry carbon tetrachloride was added 0.5 ml. (4.2 mmoles) of stannic chloride, whereupon the solution immediately turned green. The reaction mixture was heated under reflux on a steam bath for 10 min. and then poured into dilute hydrochloric acid. The whole was extracted with ether and the purple ether extracts were washed with water and then dried. The solid which remained after removal of the solvent was chromatographed on acid-washed alumina. Elution with petroleum ether removed a blue band and a light blue band. A small green fraction was then eluted with 5:1 benzene–methylene chloride and a purple band was removed with methylene chloride. The blue fraction yielded 11 mg. of 1-chloroazulene (which contained some 1,3-dichloroazulene presumably present as an impurity in the starting material) and the purple fraction afforded 71 mg. (71%) of 1-chloro-3-acetylazulene as dark purple needles, m.p. 86–89.5°. The analytical sample was recrystallized from ligroin and melted at 89.5–90.5°. A cyclohexane solution showed maxima in mμ in the ultraviolet (log ε) at 240 (4.0), 268 (3.68), shoulder at 286 (3.89), 291 (4.04), 298 (4.11), 303 (4.08), 310 (4.23), 378 (3.51), and 3.95 (3.52), and in the visible (ε) at 576 (510), 601 (440), 620 (410), shoulder at 660 (180), shoulder at 678 (140), and 693 (150). The infrared spectrum (Nujol) had a peak at 6.09 μ. The n.m.r. spectrum was recorded.

Anal. Calcd. for $C_{12}H_9OCl$: C, 70.42; H, 4.43. Found: C, 69.77; H, 4.65.

B. From 1,3-Dichloroazulene.—To a solution of 50 mg. (0.25 mmole) of 1,3-dichloroazulene[12] in 10 ml. of dry carbon tetrachloride was added 5 ml. (0.07 mole) of acetyl chloride and then 139 mg. (1.04 mmoles) of aluminum chloride, whereupon the blue solution became green and a brown precipitate formed. The mixture was heated under reflux for 1.5 hr. and then poured into cold, dilute hydrochloric acid. The whole was extracted with methylene chloride and the solvent was removed from the separated, dried organic extracts. The residue which remained was chromatographed on acid-washed alumina. Petroleum ether eluted a blue band from which was recovered 18 mg. of 1,3-dichloroazulene. Elution with benzene developed a yellow band which gave a yellow-green eluate, and a green band which was removed with methylene chloride. This process also developed a violet band which was eluted with 4:1 methylene chloride–ether. The green fraction yielded 5 mg. (8%, 13% net) of 1,3-dichloro-5-acetylazulene (identified by its absorption spectra) and the violet fraction afforded 6 mg. (11%, 18% net) of 1-chloro-3-acetylazulene which was identical (melting point, mixture melting point, ultraviolet, visible, and infrared spectra) with the material obtained in method A.

1,3,5-Trichloroazulene (III).—A solution of 197 mg. (1 mmole) of 1,3-dichloroazulene, 135 mg. (1.01 mmoles) of N-chlorosuccinimide, 5 ml. of benzene, and 5 ml. of acetonitrile under a nitrogen atmosphere was heated under reflux for 1 hr. Petroleum ether was then added to the green mixture and the whole was extracted with water. The solvent was removed from the dried organic layer and the green, crystalline material (117 mg.) obtained from this was fractionally sublimed at 60–70° and 8 mm. The ultraviolet spectra of the fractions were taken and the later fractions which contained predominantly the desired product were combined and recrystallized from *n*-hexane. There was obtained 39 mg. (17%) of green needles, m.p. 96–99°, which gave only one peak upon gas–liquid chromatography. The analytical sample melted at 98–100°. A cyclohexane solution exhibited maxima in mμ in the ultraviolet (log ε) at 225 (4.06), 246 (4.16), 284 (4.58), 342 (3.54), 352 (3.60), 359 (3.89), 3.71 (4.68), and 377 (4.07) with shoulders at 306 (4.12) and 335 (3.32), and in the visible (ε) at 667 (394), 697 (349), 712 (344), 753 (349), 798 (142), and 828 (156) with shoulders at 610 (273), 642 (349), and 779 (157). The n.m.r. spectrum had a strong singlet at 2.5 τ attributed to the 2-hydrogen and was otherwise consistent with structure III.

Anal. Calcd. for $C_{10}H_5Cl_3$: C, 51.88; H, 2.18; Cl, 45.95. Found: C, 51.47; H, 2.43; Cl, 45.59.

1,3,5-Tribromoazulene (IV).—A solution of 143 mg. (0.5 mmole) of 1,3-dibromoazulene, 90 mg. (0.51 mmole) of N-bromosuccinimide, 8 ml. of benzene, and 4 ml. of acetonitrile under a nitrogen atmosphere was heated under reflux for 2 hr. Petroleum ether was added to the green reaction mixture and the whole was shaken with an aqueous solution of sodium thiosulfate and then extracted with ether. Removal of the solvent from the combined, dried (sodium sulfate) green ether extracts left a residue which was chromatographed on alumina. Petroleum ether removed a blue fraction, and the green residue (112 mg.) from this was fractionally sublimed. The first fraction, collected at 70–80° and 8 mm., was unchanged 1,3-dibromoazulene. The second fraction, collected at 80–100° and 1 mm., was recrystallized from *n*-hexane and gave 48 mg. of 1,3,5-tribromoazulene as green needles, m.p. 103–108°. An additional 9 mg. of material (31% total) of like purity was obtained from the mother liquor. Recrystallization from the same solvent afforded 39 mg. (21%) of purer product, m.p. 110–112°. A cyclohexane solution showed maxima in mμ in the ultraviolet (log ε) at 230 (4.12), 249 (4.18), 295 (4.56), 2.98 (4.56), 346 (3.55), 353 (3.60), 362 (3.89), 370 (3.69), 375 (3.72), and 380 (4.08) with shoulders at

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(23) P. A. Plattner, A. Fürst, A. Müller, and A. R. Somerville, *Helv. Chim. Acta*, **34**, 971 (1951).

267(4.21), 303(4.46), 309(4.27), and 339(3.33), and in the visible (ε) at 652(3.81), 684(333), 718(339), and 807(130) with shoulders at 602(270), 670(342), and 763(147). The n.m.r. spectrum had a sharp singlet at 2.33 τ attributed to the 2-hydrogen and was otherwise consistent with structure IV.

Anal. Calcd. for $C_{10}H_5Br_3$: C, 32.91; H, 1.38; Br, 65.70. Found: C, 33.00; H, 1.23; Br, 66.12.

1,3-Dibenzoyloxy-5-chloroazulene (V).—To a solution of 70 mg. (0.19 mmole) of 1,3-dibenzoyloxyazulene[18] and 10 ml. of methylene chloride was added 26 mg. (0.2 mmole) of N-chlorosuccinimide and the mixture was allowed to stand overnight in a refrigerator. Ether was then added and the whole was washed with water. The residue from the dried organic solution was chromatographed on Florisil. Benzene eluted a pale yellow fraction and a band which was originally green changed to blue-green. The latter material was removed with methylene chloride and removal of the solvent left a green residue which crystallized when triturated with ether and afforded 55 mg. (72%) of green needles, m.p. 122–129°. Recrystallization from ether gave 24 mg. of chartreuse needles, m.p. 132–133°. A second crop amounted to 10 mg., m.p. 126–129.5° (total yield, 44%). A cyclohexane solution exhibited maxima in mμ in the ultraviolet (log ε) at 237 (4.58), 281 (4.69), and 379 (3.93), and in the visible (ε) a broad peak at 683 (380) with a broad shoulder at 728 (340).

Anal. Calcd. for $C_{24}H_{15}O_4Cl$: C, 71.56; H, 3.75. Found: C, 71.63; H, 3.73.

The Synthesis and Chemistry of Certain 2-Substituted 5,6-Dihydroimidazo-, -oxazolo-, and -thiazolo[*ij*]quinolines

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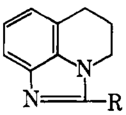
Isosteric 2-substituted 5,6-dihydroimidazo-, -oxazolo-, and -thiazolo[*ij*]quinolines were synthesized and examined for their chemical and physical properties. The 2-oxo and 2-thioxo derivatives are neutral compounds, but the 2-imino derivatives are of sufficient basic character to form salts and otherwise to become involved in reactions with acidic reagents. The infrared absorption peaks due to the substituents were determined. On the basis of infrared and ultraviolet spectral studies, the imidazoquinolines were assigned the tautomeric *exo* double bond structure (II). The ultraviolet studies also allowed a determination of important chromophores in these systems.

In a previous publication,[1] the synthesis and chemistry of 2-substituted 5,6-dihydro-4*H*-imidazo[4,5,1-*ij*]quinolines (I) was discussed. Included as part of that work was an investigation of the ultraviolet spectra of the title compounds. On the basis of certain chemical and spectral characteristics, the authors concluded that the 2-hydroxy and the 2-mercapto derivatives existed in the cyclic urea form (II), which is tautomeric with the structure usually assigned to the 5,6-dihydroimidazo[4,5,1-*ij*]quinolines (I). As an extension of that work, it was necessary to prepare those compounds (III) where X and Y are the same or different and are chosen from O, S, or NH in order to observe the chemical and spectra similarities and differences in the three (III, X = O, S, NH) isosteric families under consideration. As will be seen later, this work confirms the cyclic urea structure (II) reported[1] earlier for the 2-hydroxy and 2-mercapto derivatives. Furthermore, the data obtained in this work indicate an exo-imino structure for the 2-amino derivative. The imidazo[*ij*]quinolines, therefore, will hereafter be referred to in light of structure II.



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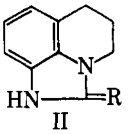

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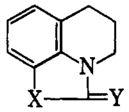

III

The 2-imino-5,6-dihydro-1*H*,4*H*-imidazo[4,5,1-*ij*]quinoline (IV) was prepared by condensing 8-amino-1,2,3,4-tetrahydroquinoline with cyanogen bromide in an aqueous medium. No difficulties were encountered during this procedure. Although the product was first isolated as a hydrobromide salt, the base was readily obtained by treatment of the salt with aqueous sodium hydroxide solution. The corresponding 2-oxo (V) and 2-thioxo (VI) derivatives were described earlier.[1]

The 2-imino-5,6-dihydro-4*H*-oxazolo[5,4,3-*ij*]quinoline (VII) was prepared by condensing 8-hydroxy-1,2,3,4-tetrahydroquinoline with cyanogen bromide in an aqueous medium. The product separated as the hydrobromide salt, and the base, an oil, was obtained by treatment of this salt with aqueous sodium hydroxide solution. The corresponding 2-oxo (VIII) and 2-thioxo (IX) derivatives were prepared by treating 8-hydroxy-1,2,3,4-tetrahydroquinoline with phosgene and thiophosgene, respectively.

The basic character of the imino group of VII was exemplified by the reactions of that compound with certain other reagents. The imino compound reacted with *p*-acetamidobenzenesulfonyl chloride to yield the corresponding sulfonimido derivative (XIII). Compound XIII was subsequently hydrolyzed to form 2-(*p*-aminobenzenesulfonimido)-5,6-dihydro-4*H*-oxazolo[5,4,3-*ij*]quinoline (XIV). In another reaction, the imine (VII) was condensed with benzoyl isothiocyanate to yield 2-[(N-benzoylthiocarbamyl)imino]-5,6-dihydro-4*H*-oxazolo[5,4,3-*ij*]quinoline (XV) which was deep yellow in color. Attempts to N-nitrosate VII in aqueous media failed.

The 2-imino-5,6-dihydro-4*H*-thiazolo[5,4,3-*ij*]quinoline (X) was prepared *via* an adaptation of the

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[1] A. Richardson, Jr., and E. D. Amstutz, *J. Org. Chem.*, **25**, 1138 (1960).