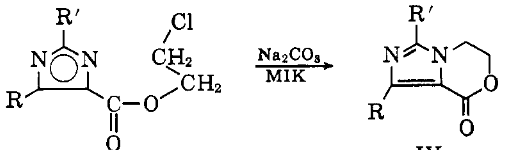
2-Methyl-4-imidazolecarboxylic acid[5] (Ib) was also treated with acetic anhydride, furnishing dimer IIb in 90% yield. The preparation of the latter, initially impeded by the laborious route into Ib, was subsequently simplified by the observation that 2-methyl-4,5-imidazoledicarboxylic acid, when treated with acetic anhydride, afforded IIb directly in 54% yield.

Of interest is the fact that both IIa and b reacted smoothly with ethylene chlorhydrin to give β-chloro esters IIIa and b. Treatment of the latter with sodium carbonate in methyl isobutyl ketone (MIK) brought about cyclization to lactones IVa and b.



III IV

a, R = CH_3; R′ = H
b, R = H; R′ = CH_3

Experimental[6,7]

4,9-Dimethyl-5H,10H-diimidazo[1,5-*a*:1′,5′-*d*]pyrazine (IIa).—A stirred mixture of 20 g. (0.158 mole) of 4-methyl-5-imidazolecarboxylic acid[8,9] and 120 ml. of acetic anhydride was brought to reflux in an apparatus equipped with a distillation take-off. After *ca.* 60 ml. of distillate, b.p. 124–139°, had been collected (this required about 1 hr.), the reaction mixture was cooled. Filtration afforded 15 g. (89% yield) of product, m.p. 230–232°. An analytical sample, m.p. 238–239°, was prepared from DMF–ether.

Anal. Calcd. for $C_{10}H_8N_4O_2$: C, 55.55; H, 3.73. Found: C, 55.50; H, 3.72.

2,7-Dimethyl-5H,10H-diimidazo[1,5-*a*:1′,5′-*d*]pyrazine (IIb). Method A.—Treatment of 76.0 g. (0.60 mole) of 2-methyl-4-imidazolecarboxylic acid[5] with 800 ml. of acetic anhydride, in the fashion described above, furnished 59 g. (90% yield) of dimer IIb, m.p. 269–270°. Recrystallization from dioxane gave yellow leaflets, m.p. 274–275°.

Anal. Calcd. for $C_{10}H_8N_4O_2$: C, 55.55; H, 3.73. Found: C, 55.31; H, 4.03.

Method B.—Dry 2-methyl-4,5-imidazole dicarboxylic acid[5] (200 g., 1.18 moles) was suspended in 3 l. of acetic anhydride and the mixture was refluxed for 72 hr. Upon completion, 2.5 l. of solvent was removed at atmospheric pressure. Cooling of the residue yielded 69 g. (54%) of product, m.p. 274–275°, which was identical with the material prepared by method A.

4-Methyl-5-imidazolecarboxanilide.—To a suspension of 4.32 g. (0.02 mole) of freshly prepared IIa in 15 ml. of DMF was added 5 g. (0.054 mole) of aniline. The mixture was briefly warmed to 100° and was then poured onto ice–water. The anilide, 3.8 g., crystallized immediately and was recrystallized from alcohol, m.p. 259–260°.

Anal. Calcd. for $C_{11}H_{11}N_3O$: C, 65.65; H, 5.51; N, 20.88. Found: C, 65.57; H, 5.46; N, 20.84.

4-Methyl-5-imidazolecarboxylic Acid Chloride, Hydrochloride.—To a suspension of 10 g. (0.079 mole) of Ia in 100 ml. of benzene containing 1 ml. of DMF was added 20 ml. of thionyl chloride. An exothermic reaction ensued, giving a pasty suspension. The mixture was refluxed for 0.5 hr., and the product was isolated by filtration, to give, upon washing and drying, 10.3 g. of acid chloride hydrochloride. The material was not further purified, m.p. 221–223°. Reaction of this material with an excess of aniline gave the **carboxanilide**, m.p. 259–260°, identical with the material obtained from IIa.

4-Methyl-5-imidazolecarboxylic Acid, 2-Chloroethyl Ester (IIIa).—To 228 g. of ethylene chlorohydrin, previously saturated with hydrogen chloride, was added 57 g. (0.264 mole) of IIa. The mixture was refluxed 2 hr., after which sufficient dry ether was added to the cooled solution to precipitate the product **hydrochloride salt.** The filtered material was dissolved in water, brought to pH 8 by addition of solid sodium bicarbonate, and filtered to give 76 g. of ester, m.p. 155–156°, yield 77%. An analytical sample from aqueous alcohol melted at 159–160°.

Anal. Calcd. for $C_7H_9ClN_2O_2$: C, 44.57; H, 4.81; N, 14.85. Found: C, 44.35; H, 4.73; N, 14.68.

2-Methyl-4-imidazolecarboxylic Acid, 2-Chloroethyl Ester (IIIb).—The reaction of 2.36 g. (0.11 mole) of IIb with 15 ml. of ethylene chlorohydrin saturated with hydrogen chloride, according to the method described above, yielded 2.0 g. (49%) of product, m.p. 145–146° (dioxane–isopropyl ether).

Anal. Calcd. for $C_7H_9ClN_2O_2$: C, 44.57; H, 4.81; N, 14.85. Found: C, 44.64; H, 4.91; N, 14.86.

8-Methyl-3,4-dihydro-1-oxo-1H-imidazo[5,1-*c*](1,4)oxazine (IVa).—A suspension of 76 g. (0.40 mole) of IIIa, 1500 ml. of methyl isobutyl ketone, 127 g. of anhydrous sodium carbonate, and 1 g. of potassium iodide was refluxed in an apparatus equipped with a water trap for 2 days. The solids were then removed by filtration, whereupon the filtrate was taken down *in vacuo*. Recrystallization of the residue from isopropyl alcohol gave 18.6 g. of product, m.p. 173–174°, yield 31%. The hydrochloride salt, m.p. 224–225°, was submitted for analysis.

Anal. Calcd. for $C_7H_8N_2O_2 \cdot HCl$: C, 44.57; H, 4.81; N, 14.85. Found: C, 44.46; H, 4.89; N, 14.63.

6-Methyl-3,4-dihydro-1-oxo-1H-imidazo[5,1-*c*](1,4)oxazine (IVb).—This compound, m.p. 175–176° (dioxane-isopropyl ether), was prepared in a fashion analogous to the method offered for IVa. The yield was 38%.

Anal. Calcd. for $C_7H_8N_2O_2$: C, 55.25; H, 5.30; N, 18.41. Found: C, 55.21; H, 5.10; N, 18.75.

Acknowledgment.—The financial support of the IWONL is gratefully acknowledged. Special thanks are due to Dr. P. A. J. Janssen for his helpful advice and continued encouragement.

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(5) R. G. Fargher and F. L. Pyman, *J. Chem. Soc.*, 217 (1919).

(6) Melting points were recorded on a Fisher-Johns block and are uncorrected.

(7) We are indebted to Messrs. F. Sels and W. Verkest for microanalytical data.

(8) H. Böhme and H. Schneider, *Ber.*, **91**, 988 (1959); O. Gerngross, *ibid.*, **45**, 909 (1912).

(9) W. Hubball and F. L. Pyman, *J. Chem. Soc.*, 21 (1928).

Structure *vs.* Reactivity in Azulene Carboxylic Acids and Esters

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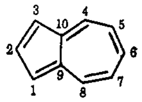
Received June 30, 1964

From simple and also from more sophisticated molecular orbital calculations[1] successful predictions have been made concerning the dipole moment of the azulene nucleus and the relative electron densities on the various carbon atoms. The 1- and 3-positions of azulene (I) are



I

predicted to have a fairly substantial net negative charge, the 4-, 6-, and 8-positions a net positive charge, with the other positions being approximately neutral. Like other aromatic compounds, azulene undergoes electrophilic and nucleophilic substitution reactions. As predicted from a consideration of charge densities

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(1) (a) R. D. Brown, *Trans. Faraday Soc.*, **44**, 984 (1948); (b) A. Julg, *Compt. rend.*, **239**, 1498 (1954).

as well as localization energies, Anderson and co-workers have found that electrophilic substitution takes place virtually exclusively and readily at the 1- and 3-positions.[2] Also in accord with charge-density considerations Hafner and Weldes[3] have found that methide ion attacks the ring at the 4-position (although the conjugation of the ring is destroyed in the process).

In an attempt to determine whether any correlation exists between electron densities in unperturbed azulene and reactivity of some of its derivatives, we have studied the pK_A values of the 1-, 5-, and 6-azuloic acids and 3-chloro-1-azuloic acid, and have measured the rates of saponification of the ethyl 1-, 5-, and 6-azuloates.

A. The Azuloic Acids.—The electron density at various positions on the azulene nucleus should have an effect on the electron density in the immediate vicinity of the carboxyl group in the corresponding position, thereby affecting the acid strength. The electron densities at the various positions on the unsubstituted azulene nucleus might serve as a reasonable model to predict the reactivity of the carboxylic acids if the cross conjugation of the carboxylate group with the aromatic ring does not significantly alter the electron densities on the ring.

Table I lists the π-electron densities in the unperturbed azulene nucleus calculated by the simple Hückel MO method and by the self-consistent field method. Table II lists the measured pK_A values of the azuloic acids as well as those of benzoic and naphthoic acids, all in 50% aqueous ethanol at 25°. In all cases the effect on acid strength predicted by electron densities was found to hold. Electron density at the 1-position in azulene is greatest, and one finds that 1-azuloic acid is the weakest. The 3-chloro-1-azuloic acid has the electron density at the 1-position slightly reduced by the electron-withdrawing chlorine atom thus giving a smaller pK_A. 6-Azuloic acid, with the carboxyl adjacent to a presumably electron-poor carbon, is nearly an order of magnitude stronger than the 1-acid. The 5-acid is intermediate as anticipated.

TABLE I[a]

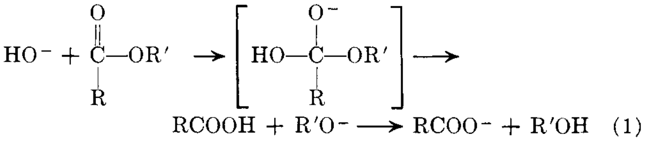
Atom	q_i (H.M.O.)[b]	q_i (S.C.F.)[c]
1 and 3	−0.173	−0.049
2	−0.047	+0.003
4 and 8	+0.145	+0.092
5 and 7	+0.014	−0.034
6	+0.130	+0.062
9 and 10	−0.027	−0.042

[a] E. Heilbronner, "Non-benzenoid Aromatic Compounds," D. Ginsberg, Ed., Interscience Publishers, Inc., New York, N. Y., 1959, p. 196. [b] Hückel MO method. [c] Self-consistent field method.

TABLE II

Acid	pK_A
6-Azuloic	5.75
5-Azuloic	5.91
1-Azuloic	6.67
3-Chloro-1-azuloic	6.07
Benzoic	5.46
1-Naphthoic	5.54

B. The Ethyl Azuloates.—In the mechanism for the base-catalyzed hydrolysis of an ester (eq. 1), it is reasonable to assume that the bracketed intermediate resembles the transition state of the rate-determining



$$\mathrm{HO^-} + \underset{\mathrm{R}}{\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}}\mathrm{-OR'} \rightarrow \left[\mathrm{HO-}\underset{\mathrm{R}}{\overset{\mathrm{O^-}}{\mathrm{C}}}\mathrm{-OR'}\right] \longrightarrow$$

$$\mathrm{RCOOH} + \mathrm{R'O^-} \longrightarrow \mathrm{RCOO^-} + \mathrm{R'OH} \qquad (1)$$

step.[4] Groups, then, which decrease electron density at the reaction center in the intermediate should facilitate the reaction. In the intermediate the carbonyl carbon has become sp^3 and thus in the case of the azuloic esters not conjugated with the ring and might not significantly perturb the ring molecular orbitals.

The electron densities at the various positions on the azulene nucleus should affect the electron density at the reaction center in the intermediate and therefore have an effect on the rate of hydrolysis of the ester. *If* the localized charge on the intermediate does not significantly perturb the ring electron densities, one would predict that the 4-ester would hydrolyze the most rapidly, followed by the 6-, 5-, 2-, and 1-esters, respectively.

The ethyl 1-, 5-, and 6-azuloates were synthesized and saponified in 50% aqueous dioxane at 70°. The rate constants, along with those for saponification of ethyl benzoate and ethyl 1-naphthoate for comparison, are given in Table III. As can be seen, the 6-ester did indeed hydrolyze the most rapidly, but the most salient feature is that the difference in rates between the azuloates is not great, and that the 1-ester saponifies *faster* than the 5-ester. The latter difference, however, is quite small, and, if one notes the self-consistent field electron density calculations (Table I), one sees that the calculated charges on C-1 and -5 of azulene are actually quite similar in magnitude.

TABLE III

Ester	$k \times 10^3$ l. mole^{-1} sec.$^{-1}$
Ethyl 6-azuloate	14.8 ± 0.1
Ethyl 5-azuloate	9.4 ± 0.1
Ethyl 1-azuloate	10.7 ± 0.3
Ethyl benzoate	9.0 ± 0.2
Ethyl 1-naphthoate	9.2 ± 0.1

Conclusions.—It is clear that even to a first approximation the electron densities on azulene will not be a good or even a fair model for the ring densities of any of the compounds and intermediates studied. In addition, charge-density considerations are not so valid as localization energies in predicting reactivity. Steric effects play an important role in determining chemical reactivity.

However, one finds that, in fact, the relative pK_A values of the azulene carboxylic acids are indeed predictable (perhaps fortuitously) from electron densities of unsubstituted azulene. Thus, although the carboxyl and, more importantly, the carboxylate anionic groups surely perturb the ring densities, this effect is apparently not enough to reverse the relative densities at the positions studied. Steric effects alone could not account

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[2] (a) A. G. Anderson, Jr., and R. G. Anderson, *J. Org. Chem.*, **27**, 3578 (1962); (b) A. G. Anderson, Jr., and J. J. Tazuma, *J. Am. Chem. Soc.*, **75**, 4979 (1953); (c) *ibid.*, **74**, 3455 (1952); (d) A. G. Anderson and J. A. Nelson, *ibid.* **72**, 3824 (1950), and other papers in the series.

[3] (a) K. Hafner and H. Weldes, *Angew Chem.*, **67**, 302 (1955); (b) K. Hafner and H. Weldes, *Ann.*, **606**, 90 (1957).

[4] E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Reinhart, and Winston, New York, N. Y., 1959, p. 316.

for the order of magnitude difference in the pK_A values of the 1- and 6-acids.

In the ester saponification kinetics there was found extremely little effect of ring position on reactivity. This insensitivity probably has nothing to do with differences in electron densities and lack thereof at various positions on the ring, but rather is probably inherent in the nature of the reaction itself. Four of the five compounds studied (including the benzoate and naphthoate esters) reacted at rates within 10% of each other. This alone is of more than casual interest and warrants further investigation.[5]

Experimental

Materials.—Azulene was obtained from Aldrich Chemical Co. Dioxane was Baker reagent grade and was distilled from sodium prior to use. All other organic and inorganic chemicals were reagent grade and were used without further purification.

Acid pK_A Values.—The method used to determine the relative strengths of the azuloic acids was based on the Henderson–Hasselbalch equation.

$$\mathrm{pH} = \mathrm{p}K_\mathrm{A} + \log \frac{\text{neutralized acid}}{\text{residual acid}}$$

This equation relates pH of a partially neutralized aqueous solution of a weak acid with degree of neutralization. In a dilute aqueous organic system a similar relation may be assumed and, if such a solution is 50% neutralized, the apparent pH will be a measure of the acid strength in that solvent.

The acids were dissolved in 50% ethanol–water and titrated with 0.050 N sodium hydroxide. A potentiometric titration using a combination glass and saturated calomel electrode system was used to determine the pH at various points during the titration. The readings at the calculated half-neutralization point of a solution of acid on the pH scale of a Beckman Zeromatic pH meter were therefore taken as the acid strengths or pK_A values. The meter was calibrated with aqueous buffers before and after the titration and no correction was made for liquid junction potentials.

Saponification Rates.—The hydrolysis of esters in alkaline media is a bimolecular reaction and has been shown to be first order in both ester and hydroxyl ion concentrations.[6] The rate constants were determined graphically by plotting $1/C$ *vs.* time (in sec.), where C is the concentration in moles/l. of either reagent.

The saponification-rate measurements were carried out in the following manner. The solvent used was aqueous dioxane, prepared by diluting 50 ml. of water with 50 ml. of dioxane. The rate measurements were carried out by mixing equal volumes of 0.02 M sodium hydroxide and 0.02 M ester solutions at the desired temperature and then withdrawing samples at intervals by means of volumetric pipets. The sample was titrated with standard hydrochloric acid solutions with the end point determined potentiometrically.

Preparation of Compounds. 1-Azuloic Acid.[2a]—A solution of azulene (2.5 g., 20 mmoles) in 100 ml. of dry carbon tetrachloride was treated with 10 ml. (70 mmoles) of trifluoroacetic anhydride and protected from moisture. The color changed from blue to red. The mixture was swirled intermittently for 10 min. at room temperature and the excess trifluoroacetic anhydride was decomposed by careful addition of 50 ml. of 10% sodium bicarbonate solution followed by thorough shaking. The separated red organic phase was washed three times with water (20-ml. portions) and dried over anhydrous magnesium sulfate. The solvent was removed on a steam bath and the residue was chromatographed on silica gel. The column was eluted with benzene and the intense red band was collected. The solvent was evaporated and 2.3 g. of 1-trifluoroacetylazulene was obtained as red needles, m.p. 62–63°, which agreed with m.p. 62.5–63.5° reported by Anderson.[2a]

1-Trifluoroacetylazulene (2.3 g., 1.03 mmoles) was dissolved in 100 ml. of 0.6 M sodium hydroxide in 50% aqueous ethanol and refluxed for 2 hr., during which time the bright red solution turned to purple. The crude azuloic acid was precipitated from the aqueous layer by acidification with 2 N hydrochloric acid and extracted into ether. The ether solution was washed twice with water, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*, and the residue was chromatographed on silica gel. Eluents less polar than ether did not affect the tightly adsorbed purple band. This band was removed with ether and removal of the solvent gave 1.8 g. of 1-azuloic acid as lavender plates, m.p. 161–162°, lit.[2a] 181–182°. The visible and ultraviolet spectrum recorded on a Cary Model 14 spectrophotometer showed absorptions at 237, 289, 294, 300, 368, and 531 $m\mu$ in perfect agreement with the literature.[2a] The infrared spectrum showed carbonyl absorption at 6.08 μ. The neutralization equivalent was 171 compared with the calculated value of 172.

3-Chloro-1-azuloic Acid.—To 1.55 g. (12 mmoles) of dry benzene was added dropwise a solution of 1.63 g. (12 mmoles) of N-chlorosuccinimide in 75 ml. of dry benzene.[2b] The reaction was stirred for 15 hr. at room temperature. When the reaction was allowed to proceed longer than 15 hr., only 1,2-dichloroazulene was obtained. The reaction mixture was filtered through a short alumina column. The column was washed with petroleum ether (b.p. 60–90°) and the total filtrate was concentrated *in vacuo*. The filtrate was then placed on a 3-ft. alumina column and the column was eluted with petroleum ether. Two fractions were obtained, first a dark blue band followed by a light blue band. The second band was 1-chloroazulene and the first band was azulene. From the second band 0.5 g. of 1-chloroazulene was obtained.

1-Trifluoroacetyl-3-chloroazulene was prepared from 1-chloroazulene in the same manner as 1-trifluoroacetylazulene mentioned above.

The 3-chloro-1-azuloic acid was prepared from 3-chloro-1-trifluoroacetylazulene in the same manner as the 1-azuloic acid. The blue needles of 3-chloro-1-azuloic acid were recrystallized from methylene chloride and decomposed at about 220° compared with 230° reported by Anderson.[2a] The infrared spectrum showed absorption for a carbonyl group at 5.9 μ. The neutralization equivalent was 207 compared with the calculated value of 208.

Ethyl 5-Azuloate.[7]—A 500-ml. three-necked flask was fitted with an equal-pressure dropping funnel, a condenser, and a thermometer. To this flask was added 96 g. of indan and 3 g. of powdered copper metal. The solution was heated to 130° and stirred with a magnetic stirrer. To this solution 50 g. of diazoacetic ester was added dropwise over a period of 2 hr. Upon completion of the addition of diazoacetic ester, the solution was heated to 160–165° for 3 hr. The copper metal was filtered from the reaction mixture, and the mixture was vacuum distilled. A blue distillate was collected at 110° (1 mm.) followed by a red-brown fraction at 130–160° (1 mm.). The two fractions were combined to give a total of 25 ml. of reaction product. The combined fractions were put through a dehydrogenation column which contained 5% palladium–charcoal on asbestos. The column was heated to 300° and purged with a stream of nitrogen. After all the distillate had passed through, the column was washed with benzene to remove any product remaining on the asbestos. The solution was dried over magnesium sulfate and the solvent was evaporated on a steam bath. The blue oil was chromatographed on silica gel and petroleum ether removed a yellow-brown band. Benzene removed a deep blue band which gave a blue oil when the solvent was removed. The blue oil proved to be ethyl 5-azuloate showing a carbonyl peak at 5.8 μ in the infrared spectrum. The visible spectrum showed peaks at 680, 644, 618, 588, 566, and 544 $m\mu$ in cyclohexane. This spectrum agrees both in position and relative intensity with that reported by Müller.[8] The spectrum recorded in the literature was 680, 644, 618, 588, 566, 543, and 522 $m\mu$.

Ethyl 6-Azuloate.—After removal of the blue band from the silica gel column in the above synthesis of ethyl 5-azuloate, the column was eluted with benzene–ether. This removed a blue-green band which on removal of the solvent gave a blue-green oil. This oil proved to be 6-ethyl azuloate showing a carbonyl

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(5) Saponification of methyl benzoates certainly is a sensitive function of substituents, as manifested by a ρ-value (at 0°, 70% aqueous acetone) of 2.46 (*cf.* ref. 4, p. 222). However, the effect of small charge differences in the azulene esters, and the effect of varying the aromatic nucleus seem minimal.

(6) R. B. Warder, *Ber.*, **14**, 1361 (1881).

(7) P. A. Plattner, A. Furst, A. Müller, and A. R. Sommerville, *Helv. Chim. Acta*, **34**, 971 (1951).

(8) A. Müller, Ph.D. Thesis, Eidgenossischen Technischen Hochschule, 1951.

group absorption at 5.8 μ in the infrared spectrum. The visible spectrum showed peaks at 740, 697, 660, 630, 606, and 579 $m\mu$ in cyclohexane. This spectrum agrees both in position and relative intensity with the spectrum of 6-methyl azuloate reported by Müller[8] to possess maxima at 743, 697, 666, 636, 606, and and 578 $m\mu$. The spectrum of ethyl 6-azuloate is not in the literature, but the visible spectra of the methyl and ethyl esters of 5 azuloic acid are identical, and we assume this to be the case for the 6-esters as well.

5-Azuloic Acid.—A solution of ethyl 5-azuloate and 3 *N* sodium hydroxide in 50% ethanol was refluxed for 5 hr. The solution was then flooded with water and extracted with ether to remove any remaining ester. The water layer was then acidified and extracted with ether. The ether layer was dried over magnesium sulfate and the solvent was removed yielding a viscous blue oil. The oil was chromatographed on silica gel. Benzene removed a blue band which yielded a blue oil on removal of the solvent. This blue oil proved to be 5-azuloic acid. The infrared spectrum showed a carbonyl group absorption at 5.85 μ. The visible spectrum showed peaks at 679, 645, 617, 588, 566, 542, and 523 $m\mu$ in ethanol. The spectrum agrees both in position and relative intensity with that reported by Müller[8] with maxima at 679, 645, 617, 588, 566, 542, and 523 $m\mu$. The neutralization equivalent was 180 compared with the calculated value of 172.

6-Azuloic Acid.—This acid was prepared in a manner analogous to the 5-azuloic acid. The crude acid was a blue-green oil which was chromatographed on silica gel. The column was eluted with benzene which removed a blue band and then eluted with benzene ether which removed a green band. The solvent was removed from the green portion and the 6-azuloic acid was obtained as a green oil. The infrared spectrum showed a carbonyl group absorption at 5.85 μ. The visible spectrum shows peaks at 750 698, 660, and 580 $m\mu$ in ethanol. This spectrum agrees both in position and relative intensity with that in the literature[8] with peaks at 750, 698, 665, 633, and 580 $m\mu$. The neutralization equivalent was 171 compared with the calculated value of 172.

Ethyl 1-Azuloate.—To 1.1 g. of 1-azuloic acid dissolved in 75 ml. of anhydrous ether was added 2 ml. of thionyl chloride. The solution was then refluxed for 12 hr. after which 25 ml. of absolute ethanol was added and allowed to reflux overnight. The ether and ethanol were then distilled off, and the residue was dissolved in ether. The ether was washed twice with sodium carbonate and then dried over magnesium sulfate. The ether was removed on a steam bath and the dark blue oil was chromatographed on silica gel. The column was eluted with petroleum ether and then benzene. A red band developed first and was discarded. This was followed by a deep purple band which gave a purple oil in approximately 30% yield on removal of the solvent. This purple oil proved to be ethyl 1-azuloate and showed a carbonyl group absorption at 5.85 μ. The visible spectrum showed peaks at 686, 645, 620, 588, and 545 $m\mu$. This spectrum agrees with the spectrum of methyl 1-azuloate, reported by Anderson,[2b] with maxima at 686, 650, 590, and 544 $m\mu$.

Acknowledgment.—We are indebted to Professor E. Heilbronner for furnishing us with spectral data from the thesis of A. Müller. Financial support of this work by the American Academy of Arts and Sciences is gratefully acknowledged.

The Synthesis of Bicyclic Esters of Phosphorus Acids

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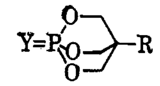
Received November 6, 1963

Recently Verkade and Reynolds,[1] Neunhoffer and Maiwald,[2] and Wadsworth and Emmons[3] published the synthesis of bicyclic esters of phosphorus acids. We wish to report our own independent study.



I, Y = none; R = CH_3
II, Y = O; R = CH_3
III, Y = S; R = CH_3
IV, Y = none; R = C_2H_5
V, Y = O; R = C_2H_5
VI, Y = S; R = C_2H_5
VII, Y = Se; R = C_2H_5
VIII, Y = O; R = C_6H_5
IX, Y = S; R = C_6H_5
X, Y = O; R = $CH_2O—C_6Cl_5$
XI, Y = S; R = $CH_2O—C_6Cl_5$
XII, Y = S; R = $CH_2O—C_6Br_5$
XIII, Y = O; R = NO_2

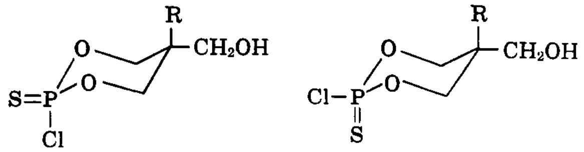
In this laboratory, the previously unknown compounds VII to XII have been synthesized, and the compounds I to VI also have been independently synthesized. Most of the compounds were prepared by a procedure modified from that of Zetzsche and Zurbrugy.[4] Thus, I was prepared in 50% yield by the reaction of phosphorus trichloride and 2-ethyl-2-(hydroxymethyl)-1,3-propanediol in the presence of ether. The product was thermally stable permitting purification by distillation. When phosphorus oxychloride or phosphorus thiotrichloride were used instead of phosphorus trichloride, the products were the bicyclic phosphate and thiophosphates derived from the corresponding triol. The phosphates and thiophosphates were not distillable, but they were stable in water and were high-melting solids. Thus, they could be isolated from aqueous or organic solution without difficulties.

The bicyclic phosphites have been reported to be converted by hydrogen peroxide[1,2,5] and by peracetic acid[3] to the corresponding phosphate, and by sulfur[1,2] and by a mercaptan[3] to the corresponding thiophosphates. We further found that I behaved like triphenyl phosphite in being stable to pure oxygen at room temperatures,[6] but it was instantly oxidized by ozone to yield V. Analogous to the conversion of phosphine to phosphine selenide,[7] I was converted to VII by selenium in the presence of sodium selenide.

A particularly interesting feature of this reaction is that the triols react with the phosphorus trihalides without forming cross-linked polymers as the main products, and satisfactory results can be obtained without using high-dilution technique and lowest possible temperatures.

The formation of the bicyclic esters may involve either one or both of the two intermediates[8] (Chart I), which will further close by either a front or a back-side attack of the OH group on P–Cl to give bicyclic products. However, a study of the formation of 1-phospha-

CHART I



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[8] Compounds of this type, such as *cis*- and *trans*-2-chloromethyl-2-ethyl-1,3-propylene benzylphosphonates, were actually isolated.[3]