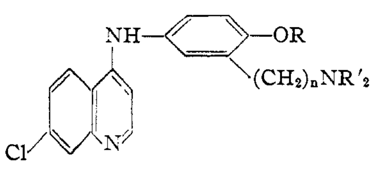
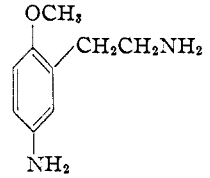


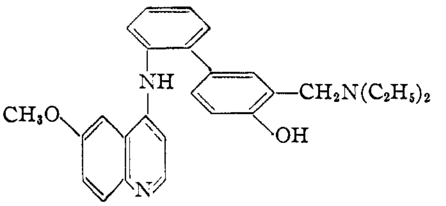
| | *n* | R | R′ |
|---|---|---|---|
| I, | 1 | H | $C_2H_5$ |
| II, | 1 | $CH_3$ | $C_2H_5$ |
| V, | 2 | $CH_3$ | H |



IV

diamine IV, but only in very low yield. Condensation of IV dihydrochloride with 4,7-dichloroquinoline gave V in good yield.

In order to obtain VIII, 2-amino-4′-hydroxybiphenyl was acetylated to its O,N-diacetyl derivative (VI) which was converted to 4-(2-acetamidophenyl)-α-diethylamino-*o*-cresol (VII) by treatment with diethylamine and formaldehyde.[4] VII was then deacetylated with boiling concentrated hydrochloric acid, and after adjustment of the *p*H was condensed with 4-chloro-6-methoxyquinoline to give VIII.



VIII

In may be noted that VIII represents the result of the insertion of an *o*-phenylene group in the side chain of antimalarial SN 10,274,[5] which is eight times as potent as quinine in chicks (*i.e.*, Q8). Compound V is related to both II (Q25) and SN 1,603[6] (Q6) which is the primary amino analog of Camoquin (Q25). Quinine equivalents of 2 for V and 0.8 for VIII against *Plasmodium gallinaceum* in chicks have been assigned by Dr. R. J. Porter, of the University of Michigan, Ann Arbor. These results do not encourage further syntheses in this area.

### Experimental

**2-Methoxy-5-nitrophenylacetonitrile (III).**—A solution of 100 g. of 2-methoxy-5-nitrobenzyl chloride[7] in 300 ml. of absolute alcohol was added slowly to a stirred solution of 32.2 g. of potassium cyanide in 100 ml. of water. Stirring was continued, and the mixture was kept at 75–80° for 2.5 hours while it darkened and potassium chloride separated out. The hot mixture was filtered and cooled whereupon the solid nitrile crystallized. Recrystallization first from benzene and then from alcohol yielded 65 g. (68%) of a yellow product; m.p. 111–113°.

*Anal.* Calcd. for $C_9H_8N_2O_3$: C, 56.25; H, 4.20. Found: C, 56.63; H, 4.25.

**β-(5-Amino-2-methoxyphenyl)-ethylamine (IV) Dihydrochloride.**—A mixture of 32 g. of III and 200 ml. of absolute methanol was subjected to three atmospheres of hydrogen in the presence of Adams catalyst. The solid was kept in solution by means of heat. After two hours, no more hydrogen was being taken up, and the amount consumed corresponded to a complete reduction of the nitro group to amino. After removal of the platinum catalyst, 0.6 g. of sodium hydroxide and Raney nickel was added and the clear brown solution reduced further. After 12 hours, the theoretical amount of hydrogen was consumed. The mixture was filtered through fritted glass and the volume of the filtrate reduced by evaporation. The residue was extracted with ether–benzene solution, and the extract was washed with water before it was dried over potassium carbonate. The desired product IV was precipitated as a yellow dihydrochloride from the filtered solution by means of alcoholic hydrogen chloride; m.p. 238–240° dec. Recrystallization from methanol elevated the melting point to 245–247° dec.; yield 7 g. (17%).

*Anal.* Calcd. for $C_9H_{14}N_2O{\cdot}2HCl$: N, 11.72. Found: N, 11.94.

**4-(3-β-Aminoethyl-4-methoxyanilino)-7-chloroquinoline (V).**—A mixture of 8 g. of IV dihydrochloride, 6.7 g. of 4,7-dichloroquinoline, 50 ml. of water and 25 ml. of dioxane was heated at reflux temperature for 4 hours. A yellow solid separated when the mixture was cooled. After it was collected, washed with water and dried, 11 g. (a theoretical yield) of V was obtained as a light gray colored material; m.p. 185–190°. Recrystallization first from isopropyl alcohol and then from ethanol changed the melting point to 198–200°.

*Anal.* Calcd. for $C_{18}H_{18}ClN_3O$: C, 65.95; H, 5.53. Found: C, 66.03; H, 5.25.

**2-(4-Acetoxyphenyl)-acetanilide (VI).**—A mixture of 30 g. of 2-amino-4′-hydroxybiphenyl (92.6% purity),[8] 15 g. of acetic anhydride and 100 ml. of glacial acetic acid was heated to boiling for two hours. The liquid was then removed under reduced pressure and the oily residue dissolved in 100 ml. of hot alcohol. Upon cooling the solution, 30 g. (74% yield) of a crystalline product with a purplish tint was obtained; m.p. 183–185°. Recrystallization from isopropyl alcohol effected no change in melting point.

*Anal.* Calcd. for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.62. Found: C, 71.86; H, 5.76.

**4-(2-Acetamidophenyl)-α-diethylamino-*o*-cresol (VII) Hydrochloride.**—A mixture of 8 g. of VI, 1 g. of paraformaldehyde, 5 g. of diethylamine and 75 ml. of isopropyl alcohol was heated to boiling for two hours and then evaporated to an oily consistency. An excess of alcoholic hydrogen chloride was added. After evaporation of the solvent and repeated triturations with mixtures of alcohol, acetone and ether, an off-white crystalline product was finally obtained; m.p. 235–240° dec. After recrystallization from methanol, 5 g. (36% yield) of the desired cresol was obtained; m.p. 245–250° dec.

*Anal.* Calcd. for $C_{19}H_{24}N_2O_2{\cdot}HCl{\cdot}2^1/_2H_2O$: C, 57.93; H, 7.68. Found: C, 57.74; H, 7.20.

**4-[2-(6-Methoxy-4-quinolylamino)-phenyl]-α-diethylamino-*o*-cresol (VIII).**—A mixture of 5 g. of VII hydrochloride and 25 ml. of concentrated hydrochloric acid was heated to boiling for two hours, and then cooled and brought to a *p*H of about 4 by the addition of concentrated ammonium hydroxide. A solution of 2.8 g. of 4-chloro-6-methoxyquinoline in 15 ml. of dioxane was added, and the mixture was heated to boiling for two hours. After cooling the solution, it was treated with an excess of ammonium hydroxide to precipitate an oil which soon solidified. Recrystallized with difficulty first from an ethanol–methanol mixture and then from methanol, the product VIII was obtained in a yield of 3 g. (55%); m.p. 208–210° dec.

*Anal.* Calcd. for $C_{27}H_{29}N_3O_2$: C, 75.85; H, 6.84. Found: C, 75.84; H, 6.86.

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[4] It will be noted that the basic conditions apparently liberated the phenolic group and allowed the Mannich reaction to occur.

[5] Ref. 3a, Table IX.

[6] Ref. 3a, Table XII.

[7] U. S. Patent 2,278,996.

[8] Kindly supplied by General Aniline and Film Corporation.

RESEARCH LABORATORIES
PARKE, DAVIS AND COMPANY
DETROIT 32, MICHIGAN

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## An Interpretation of Bond Lengths in Alkali Halide Gas Molecules

BY R. T. SANDERSON

Alkali halide gas molecules are considered to contain highly polar covalent bonds. The bond lengths in twelve of these compounds have been reported[1] to be generally less than the non-polar covalent radius sums, determined from diatomic gas molecules of the alkali metals and the halogens. They are less also than the internuclear distances in the crystals. Covalent bond "shortening" ascribed to electronegativity differences has been recognized and corrected for empirically,[2] but not clearly understood. The purpose of this note is to suggest a general explanation which for illustration is here applied to the alkali halide gas molecules.

The well-recognized tendency for the electronic sphere of an atom or ion to expand when it gains electrons and contract when it loses electrons need not be thought of as confined to complete electron transfer but may reasonably be expected of any atoms forming polar covalent bonds. From bond energies, Pauling[3] has derived "electronegativity" values which represent the relative attractions of atoms in a covalent bond for the valence electrons. It seems entirely reasonable to consider the electronegativities to become equalized in the process of covalent bond formation. If the atoms after combination have equal attraction for the valence electrons although before combination the attraction was unequal, then an adjustment must have occurred during the combining. Such an adjustment is easily visualized. Polarity of the bond results because the valence electrons spend more than half-time more closely associated with the atom initially attracting them more. In effect, this gives this atom a partial negative charge and results in expansion of its electronic sphere. Expansion of its electronic sphere diminishes the attraction of the nucleus for these valence electrons. Similarly, the atom initially having less attraction for the valence electrons gains a partial positive charge which results in contraction of its electronic sphere. This contraction results in increased attraction of its nucleus for the valence electrons. In combining to form a covalent bond, then, the more electronegative atom expands, thereby lessening its attraction for the valence electrons, and the less electronegative atom contracts, thereby increasing its attraction for the valence electrons, until the attractions of the two atoms are equal. The bond length is then the sum of the *adjusted radii*. If a relation between electronegativity and radius were known, the length of a bond between two atoms initially different in electronegativity could be calculated.

A relationship between electronegativity and radius has been found, by inquiring into the origin of the chemical differences between inert element atoms and isoelectronic ions. Such ions differ from the atoms of the inert elements not only in nuclear charge but also in the average packing of electrons. The degree of packing may be simply expressed as the "*average* electronic density (*ED*)," in number of electrons per cu. Å.

$$ED = Z/4.19r^3 \qquad (1)$$

where $Z$ is the electronic number and $r$ the ionic or non-polar covalent radius. *ED*'s of atoms of the inert elements, calculated from radii suggested by Pauling,[4] are: He 0.61, Ne 1.70, A 1.18, Kr 1.78, Xe 1.87, Rn 1.93. The electronic spheres of cations are more compact and of anions less compact than those of the isoelectronic inert atoms. The *ED*'s of all the active atoms are likewise different from those of the inert atoms, only the most active metals having less dense electronic spheres and the most active non-metals having spheres of much greater average density.

If it is assumed that the great chemical stability of the inert elements is associated not only with their atomic number but also with their *ED*, then the relative attraction for electrons, or in a sense the electronegativity, of an atom or ion of an active element may be expressed as the ratio of its *ED* to that of an isoelectronic inert atom (real, or determined by linear interpolation between real values). This ratio is called the "stability ratio (*SR*)." The *SR* values for some of the elements are compared with electronegativity values in Table I. The numerical similarity is of course fortuitous but the comparison indicates that *SR* values may be used for determining bond lengths as suggested above.

TABLE I

STABILITY RATIOS AND ELECTRONEGATIVITIES

| | *EN* | *SR* | | *EN* | *SR* | | *EN* | *SR* |
|---|---|---|---|---|---|---|---|---|
| Li | 1.0 | 0.39 | Na | 0.9 | 0.44 | K | 0.8 | 0.50 |
| Be | 1.5 | 1.45 | Mg | 1.2 | 0.82 | Rb | 0.8 | 0.53 |
| B | 2.0 | 2.10 | Al | 1.5 | 1.24 | Br | 2.8 | 3.22 |
| C | 2.5 | 2.68 | Si | 1.8 | 1.70 | Cs | 0.7 | 0.62 |
| N | 3.0 | 3.04 | P | 2.1 | 2.20 | I | 2.4 | 2.89 |
| O | 3.5 | 3.42 | S | 2.5 | 2.74 | | | |
| F | 4.0 | 3.66 | Cl | 3.0 | 3.35 | | | |

The adjusted radius, $r$, of each atom in a molecule may be determined by use of the equation

$$r = \sqrt[3]{\frac{Z}{4.19SR_{\mathrm{m}}ED_{\mathrm{i}}}} \qquad (2)$$

where $SR_{\mathrm{m}}$, the stability ratio of the molecule, is the geometric mean of the SR's of all the atoms of the molecule before combination, and $ED_{\mathrm{i}}$ is the *ED* corresponding to inert atom stability for electronic number $Z$.

Application of this method to the alkali halide gas molecules is illustrated in Table II. For these particular molecules, the bonds were considered to be so polar that slightly greater accuracy would result from substituting the ionic rather than covalent values of $Z$. The difference is slight and such a correction is unnecessary for most molecules. It may be observed from a careful study of these data that if it is reasonable to expect fairly uniform differences among bond lengths of such similar molecules, then such discrepancies as shown for CsBr and RbI are more likely to be the result of errors in measurement rather than in calculation.

According to the ideas presented herein, bond

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(1) S. B. Hendricks and V. M. Mosley, *Phys. Rev.*, **51**, 1000 (1937); L. R. Maxwell, S. B. Hendricks and V. M. Mosley, *ibid.*, **52**, 968 (1937).

(2) V. Schomaker and D. P. Stevenson, THIS JOURNAL, **63**, 37 (1941).

(3) L. Pauling, "Nature of the Chemical Bond," 2nd Ed., Cornell University Press, Ithaca, N. Y., 1940.

(4) L. Pauling, "General Chemistry," W. H. Freeman and Co., San Francisco, Calif., 1948, p. 145.

TABLE II

BOND LENGTHS (Å.) IN ALKALI HALIDE GAS MOLECULES

| Compound | Non-polar covalent radius[5] $r_m$ | $r_x$ | Sum | Adjusted covalent radius $r_m$ | $r_x$ | Sum | Reported bond length[1] |
|---|---|---|---|---|---|---|---|
| NaCl | 1.54 | 0.99 | 2.53 | 1.05 | 1.44 | 2.49 | 2.51 ± 0.03 |
| KCl | 1.96 | .99 | 2.95 | 1.41 | 1.41 | 2.82 | 2.79 ± 0.02 |
| RbCl | 2.11 | .99 | 3.10 | 1.54 | 1.40 | 2.94 | 2.89 ± 0.01 |
| CsCl | 2.25 | .99 | 3.24 | 1.69 | 1.36 | 3.05 | 3.06 ± 0.03 |
| NaBr | 1.54 | 1.14 | 2.68 | 1.06 | 1.59 | 2.65 | 2.64 ± 0.01 |
| KBr | 1.96 | 1.14 | 3.10 | 1.42 | 1.56 | 2.98 | 2.94 ± 0.03 |
| RbBr | 2.11 | 1.14 | 3.25 | 1.55 | 1.55 | 3.10 | 3.06 ± 0.02 |
| CsBr | 2.25 | 1.14 | 3.39 | 1.70 | 1.51 | 3.21 | 3.14 ± 0.03 |
| NaI | 1.54 | 1.33 | 2.87 | 1.08 | 1.83 | 2.91 | 2.90 ± 0.02 |
| KI | 1.96 | 1.33 | 3.29 | 1.45 | 1.79 | 3.24 | 3.23 ± 0.04 |
| RbI | 2.11 | 1.33 | 3.44 | 1.58 | 1.77 | 3.35 | 3.26 ± 0.02 |
| CsI | 2.25 | 1.33 | 3.58 | 1.73 | 1.73 | 3.46 | 3.41 ± 0.03 |

"shortening" results when the contraction of the less electronegative atom of a covalent bond exceeds the expansion of the more electronegative atom.

[5] G. Herzberg, "Molecular Spectra and Molecular Structure. I. Spectra of Diatomic Molecules," 2nd Ed., D. Van Nostrand Co., Inc., New York, N. Y.

DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING
STATE UNIVERSITY OF IOWA
IOWA CITY, IOWA
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## An Improved Synthesis of 3-Acetimido-5-methyltetronic Acid[1]

BY THEODORE L. REBSTOCK AND HAROLD M. SELL

3-Acetimido-5-methyltetronic acid has recently become of added interest because of its chlorophyll inhibition and herbicidal action on several plants.[2] Since this publication numerous inquiries have been made concerning its preparation as several investigators[3] have often failed to realize the desired product. The method of synthesis described by Lecocq[4] in most cases leads to a sirup and other crystalline by-products or produces the substance in very low yields. The reason for these failures may be use of too high temperatures during the condensation, too rapid addition of α-bromopropionyl bromide, moist solvents and reagents, and not using the proper ratio of ethyl β-aminocrotonate and α-bromopropionyl bromide. Low temperature condensation may also aid in yielding the correct product by preventing internal heating and causing the ethyl β-aminocrotonate to react in the imino[5] form with the acid bromide.

The purpose of this report is to present a modification of Lecocq's method which will consistently give 3-acetimido-5-methyltetronic acid in better yields.

### Experimental

A mixture containing 96 g. (0.74 mole) of ethyl β-aminocrotonate, 65.5 g. (0.83 mole) of anhydrous pyridine and 320 ml. of anhydrous ethyl ether was placed in a 1-liter three-necked round-bottom flask fitted with an efficient mercury-sealed mechanical stirrer, reflux condenser with a calcium chloride tube and a dropping funnel. The flask and contents were cooled in a Dry Ice–ethanol mixture to -60°; 180 g. (0.83 mole) of freshly distilled α-bromopropionyl bromide was added dropwise to the cooled solution over a period of two hours. The solution was stirred vigorously during the entire addition of the acid bromide and the temperature was maintained between -50 to -60°. After adding the α-bromopropionyl bromide, the stirring was continued and the solution was permitted to come to room temperature which required approximately two hours. To this mixture was added 160 ml. of chloroform and 400 ml. of water. The ether-chloroform phase (upper layer) was separated from the aqueous phase in a 2-l. separatory funnel and the organic layer dried over 20 g. of anhydrous sodium sulfate for two hours. The drying agent was removed by filtration upon a buchner funnel, the cake washed with ether, and the filtrate was concentrated under reduced pressure to a volume of 175 ml. The amorphous material which separated from the mixture was dissolved upon the addition of 50 ml. of absolute ethanol. The clear solution was placed in the refrigerator overnight for crystallization. Occasionally it was necessary to scratch the side of the flask containing the cooled mixture in order to induce crystallization. The product was collected on a dry filter paper in a buchner funnel. It was recrystallized by dissolving the material in 100 ml. of hot 30% methanol, decanting the supernatant liquid from the insoluble oil and permitting the solution to crystallize in the refrigerator overnight. The yield of white rectangular crystals was 28 g., m.p. 160–161°.[4] Upon further concentration of the mother liquor and crystallization by the method previously described, an additional 7 g., m.p. 160–161° is obtained. The total yield is 35 g. (30.2%).

*Anal.*[6] Calcd. for $C_7H_9O_3N$: N, 9.02. Found: N, 8.99.

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[1] Published as Journal Article No. 1275 of the Michigan Agricultural Experiment Station. This research was supported in part by a grant from the Rockefeller Foundation.

[2] Hamner and Tukey, *Bot. Gaz.*, **112**, 525 (1951).

[3] Personal communications to H. M. S. and T. L. R.

[4] Lecocq, *Compt. rend. acad. sci.*, **222**, 183 (1946).

[5] Knoevenagel, *Ber.*, **32**, 853 (1899).

[6] No analysis was given on this compound by Lecocq.[4]

DEPARTMENT OF AGRICULTURAL CHEMISTRY
MICHIGAN STATE COLLEGE
EAST LANSING, MICHIGAN
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## Stable Bromonium and Chloronium Salts

BY REUBEN B. SANDIN AND ALLAN S. HAY

Mascarelli and Benati[1] prepared diphenyleneiodonium iodide[2] by the addition of potassium iodide to tetrazotized 2,2'-diaminobiphenyl. More recently this reaction has been used, without any apparent difficulty, by various workers[3] for the preparation of derivatives of diphenyleneiodonium iodide. However, as far as the authors of this paper are aware no bromonium or chloronium compounds have been isolated as such. Nevertheless the concept of a three-membered positively charged cylic halonium ion has been proposed by Roberts and Kimball.[4] This concept has been used with much success by Winstein and Lucas and co-workers.[5] In their work, there is ample evidence for the existence of cyclic bromonium and chloronium intermediates. Bartlett and Tarbell[6] have demonstrated the existence of intermediate positive ions containing halogen atoms in the re-

[1] L. Mascarelli and Benati, *Gazz. chim. ital.*, [II] **38**, 624 (1908).

[2] This compound is also called dibenziodolium iodide. For nomenclature see *C. A.*, **39**, 5938 (1945).

[3] N. E. Searle and R. Adams, THIS JOURNAL, **55**, 1649 (1933); W. C. Lothrop, *ibid.*, **63**, 1187 (1941); M. Rieger and F. H. Westheimer, *ibid.*, **72**, 28 (1950).

[4] I. Roberts and G. E. Kimball, *ibid.*, **59**, 947 (1937).

[5] S. Winstein and H. J. Lucas, *ibid.*, **61**, 1576, 2845 (1939); H. J. Lucas and C. W. Gould, *ibid.*, **63**, 2541 (1941); S. Winstein, *ibid.*, **64**, 2791, 2792 (1942); S. Winstein, E. Grunwald, R. E. Buckles and C. Hanson, *ibid.*, **70**, 816 (1948); S. Winstein and E. Grunwald, *ibid.*, **68**, 536 (1946); S. Winstein, E. Grunwald and L. L. Ingraham, *ibid.*, **70**, 812 (1948); H. J. Lucas and H. K. Garner, *ibid.*, **72**, 2145 (1950).

[6] P. D. Bartlett and D. S. Tarbell, *ibid.*, **58**, 466 (1936); **59**, 407 (1937).