ULTRAVIOLET SPECTRA OF SOME RIBITYL PURINES AND PYRIMIDINES

Compound	0.1N HCl			H_2O			0.1N NaOH		
	λ_{min}	λ_{max}	$\epsilon^a \times 10^{-4}$	λ_{min}	λ_{max}	$\epsilon^a \times 10^{-4}$	λ_{min}	λ_{max}	$\epsilon^a \times 10^{-4}$
2-Amino-6-hydroxy-4-ribitylaminopyrimidine, II	232	267	1.89	242	268	1.69	240	264	1.67
2-Amino-6-hydroxy-5-nitroso-4-ribitylaminopyrimidine, III	231	265	1.39	265	318	1.86	237	318	2.27
9-Ribitylguanine, V	227	254	1.17	225	252	1.12	232	268	1.05
8-Aza-9-ribitylguanine, VI	229	253	1.24	229	253	1.17	—[b]	—[b]	—[b]

[a] $\epsilon = \frac{\text{absorbance}}{\text{moles/liter}}$, calculated at λ_{max}. [b] Compound decomposes in alkaline solution.

17.8 g. of ribitylamine in 200 ml. of water was heated at 130–145° for 7 hr. in a sealed glass pressure bottle. The resulting clear yellow neutral solution was cooled to 0–5°, and the unchanged pyrimidine which precipitated was filtered and washed with a small portion of cold water. After the combined filtrates were decolorized with Darco, the solution was evaporated *in vacuo* to about one-third the original volume, ethanol was added to induce turbidity, and the solution was cooled overnight at 0–5°. The pale yellow solid which precipitated was filtered, washed with ethanol and dried. The addition of ethanol produced a second batch of product from the mother liquor. The combined crude material was then recrystallized from water giving 8.8 g. of product., m.p. 189-190°.

Anal. Calcd. for $C_9H_{16}N_4O_5$: C, 41.53; H, 6.20; N, 21.53. Found: C, 41.58; H, 6.28; N, 21.37.

2-Amino-6-hydroxy-5-nitroso-4-ribitylaminopyrimidine (III). To a stirred cold solution of 6.8 g. of 2-amino-6-hydroxy-4-ribitylaminopyrimidine and 6.8 g. of sodium nitrite in 300 ml. of water was added sufficient 4N acetic acid to make the solution about *pH* 4. After standing in the cold for 5–10 min., an orange product began to precipitate. After further cooling, the resulting product was filtered, washed with cold water and dried to yield 6.7 g. of material; which, after recrystallization from water melted between 219–220° dec.

Anal. Calcd. for $C_9H_{15}N_5O_6$: C, 37.37; H, 5.23; N, 24.21. Found: C, 37.07; H, 5.30; N, 23.61.

Reduction of 2-amino-6-hydroxy-5-nitroso-4-ribitylaminopyrimidine (IV). A suspension of 1.5 g. of 2-amino-6-hydroxy-5-nitroso-4-ribitylaminopyrimidine in 30 ml. of water was heated over a steam bath, and to the hot stirred solution 2.5 g. of sodium hydrosulfite was added in small portions. When the clear red solution turned pale yellow it was cooled immediately in an ice bath, and the solution was adjusted to *p*H 3 with formic acid. After evaporation to dryness *in vacuo*, the residue was suspended in ethanol, and the ethanol was removed *in vacuo* to yield a yellow residue which was used directly in the subsequent condensation reactions.

2-Amino-6-hydroxy-9-ribitylpurine (*9-Ribitylguanine*) (V). The dry yellow residue from the reduction of 1.5 g. of 2-amino-6-hydroxy-5-nitroso-4-ribitylaminopyrimidine was suspended in 30 ml. of 98% formic acid, and the mixture was heated under reflux for about 8 hr. After cooling, some insoluble material precipitated which was removed and the filtrate was evaporated to dryness *in vacuo*. The resulting residue was dissolved in water and again evaporated to dryness *in vacuo* to remove the excess formic acid. The residue was crystallized twice from water to yield 0.9 g. of product, m.p. 290–291° dec.

Anal. Calcd. for $C_{10}H_{15}N_5O_5$: C, 42.10; H, 5.30; N, 24.55. Found: C, 41.70; H, 5.33; N, 23.79.

5-Amino-7-hydroxy-3-ribityl-v-triazolo[d]pyrimidine (*8-aza-9-ribitylguanine* (VI). The reduction of 1 g. of 2-amino-6-hydroxy-5-nitroso-4-ribitylaminopyrimidine was carried out in the manner previously described. After the addition of sodium hydrosulfite, the reaction mixture was cooled in an ice bath, the solution was adjusted to *p*H 3 with acetic acid, and 0.5 g. of sodium nitrite dissolved in 5 ml. of cold water was added dropwise while the reaction mixture was stirred at 0–5°. The addition required about 15 min., and stirring was continued for an additional hour at room temperature. The volume of the reaction mixture was reduced *in vacuo* to about 25 ml., ethanol was added to induce turbidity, and the solution was cooled overnight in a refrigerator. The inorganic precipitate was removed, the filtrate was further reduced in volume, ethanol was added, and the solution was placed in the refrigerator overnight. There was obtained 0.6 g. of crude product which was recrystallized repeatedly from water and ethanol, m.p. 268–269° dec.

Anal. Calcd. for $C_9H_{14}N_6O_5$· C, 37.76; H, 4.93; N, 29.36. Found: C, 37.55; H, 5.39; N, 28.62.

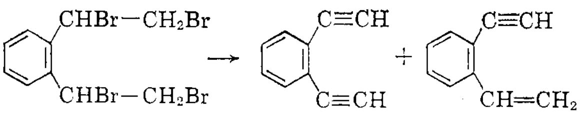
CLAYTON FOUNDATION BIOCHEMICAL INSTITUTE AND
THE DEPARTMENT OF CHEMISTRY
THE UNIVERSITY OF TEXAS
AUSTIN 12, TEX.

1-Ethynyl-2-vinylbenzene[1a]

JOHN J. MILLER[1b]

Received February 3, 1961

The recent report[2] of the isolation of a mixture of *o*-diethynylbenzene (II) and 1-ethynyl-2-vinylbenzene (III) from the reaction of *o*-bis(1,2-dibromoethyl)benzene (I) with sodium amide in liquid ammonia prompted the publication of an independent study of this reaction.



I II III

Treatment of the bromo compound I with commercial sodium amide[3] in liquid ammonia provided an inseparable mixture of II and III; however, use of sodium amide prepared *in situ* gave only III. That this product was pure was demonstrated

---

[1] (a) This work was conducted under Army Ordnance Contract DA-01-021-ORD-5135. (1)(b) Present address: Rohm & Haas Co., Research Laboratories, P. O. Box 219, Bristol, Pa.

[2] O. M. Behr, G. Eglinton, A. R. Galbraith and R. A. Raphael, *J. Chem. Soc.*, 3614 (1960).

[3] Obtained from Farchan Research Laboratories, Cleveland, Ohio.

by infrared and NMR spectroscopy, elemental analysis and gas phase chromatography.

The infrared spectrum of III, which exhibits bands attributable to an acetylenic hydrogen (3310 cm.$^{-1}$), a triple bond (2110 cm.$^{-1}$), a double bond (1640 cm.$^{-1}$), and to vinyl type CH$_2$ and CH out-of-plane deformations (920 and 995 cm.$^{-1}$), is completely consistent with the structure proposed. Analytical data also supported this structure.

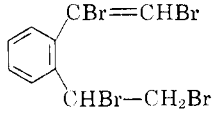
Gas phase chromatograms of II (prepared by the method of Hay[4]) and of III indicate that the materials are pure. Although the retention times are too close to allow physical separation of a mixture into its components, small amounts of either material in the presence of the other are detectable; chromatograms of known mixtures have demonstrated this. The product of the reaction employing commercial sodium amide has been shown by this method to be a mixture of approximately two parts of II to one part of III.

Proton NMR spectra of neat samples of II and III were measured employing cyclohexane as an external standard by the capillary method. The values obtained were referred to benzene using a value of +212 cps from benzene to cyclohexane. A single sharp peak at +138 cps was exhibited in the spectrum of the diacetylene (II) along with the benzene peaks which centered at −11 cps. The spectrum of 1-ethynyl-2-vinylbenzene (III) contained three peaks other than those assigned to the ring protons (centered at −3 cps) and the acetylenic proton (+154 cps). These were observed at +49, +69, and +80 cps. A striking similarity between this portion of the spectrum and that of *o*-divinylbenzene is apparent. Absence of a peak in the region +138 to +150 cps confirms the fact that no diacetylene is present in III.

The mechanism of formation of III is not understood. That II is not an intermediate in the reaction was shown by subjecting it to the reaction conditions. Unchanged *o*-diethynylbenzene was recovered. Reduction of II by sodium in liquid ammonia is not responsible for the formation of III since both II and III were isolated from a reaction employing sodium free sodium amide. An unusual debromination, which may be successful because of the hindrance in the molecule, may be the first step in the sequence. An interesting possibility is the removal of an alpha bromine from I to give a quinodimethane derivative[5] as an intermediate.

The different courses of reactions with sodium amide and other bases[6] might be explained by the strength of the base; however, the differences observed in various sodium amide reactions are more puzzling. These could possibly be due to the physical state of the sodium amide. Certainly the amide prepared *in situ* is more reactive than the commercial material.

Bromination of III has provided a tetrabromo derivative; apparently the addition of another mole of bromine is sterically hindered. Structure IV is proposed for this material on the basis of spectral and analytical data. The proton NMR spectrum of *o*-bis(1,2-dibromoethyl)benzene (I) in carbon disulfide solution contains a high field doublet due to the protons of the terminal bromomethyl groups. A triplet at lower field can be assigned to the benzyl —CHBr— protons. The spectrum of IV in carbon disulfide shows a pattern which is almost identical except for an additional peak due to a vinyl proton and splitting of the peak due to the ring protons.



IV

EXPERIMENTAL[7]

Instruments. An Aerograph model A-100-C vapor fractometer with a five foot by one-quarter inch column of Dow Corning 710 silicone oil supported on Chromosorb was employed for gas chromatography at 129° with a helium pressure of 12 p.s.i. The NMR spectra were obtained on a Varian Associates Model V-4300-B operating at 40 mc.

o-Bis(1,2-dibromoethyl)benzene (I). This material was prepared by bromination of *o*-divinylbenzene in ether at 0° Removal of the ether and recrystallization of the product from an ether-petroleum ether (b.p. 30–60°) mixture provided white plates, m.p. 71–73° in 85% yield. (Reported melting points are 72–74°[2] and 71–74°[6].) *o*-Divinylbenzene was synthesized from *o*-di(bromomethyl)benzene by the method of Halford and Weissman.[8]

o-Diethynylbenzene (II). The method of Hay[4] for dehydrobromination of the corresponding *meta* and *para* isomers was applied to I. The product, a clear liquid, b.p. 80° (14–15 mm.), n_D^{20} 1.5897 (reported n_D^{20} 1.5900[2] and $n_D^{17.5}$ 1.5915[6]), was isolated in 36% yield. Bromine-containing unsaturated materials were also obtained, but were not purified.

1-Ethynyl-2-vinylbenzene (III). To 250 ml. of liquid ammonia in a three necked, round-bottom flask equipped with a mechanical stirrer, solid carbon dioxide-acetone condenser, and pressure equalizing dropping funnel was added 0.32 g. of ferric nitrate nonahydrate. After 10.59 g. (0.461 g. atom) of sodium was added in small pieces, the mixture was cooled in a solid carbon dioxide–acetone bath and 25.95 g. (0.058 mole) of *o*-bis(1,2-dibromoethyl)benzene (I) in 100 ml. of absolute ether was introduced over a 15-min. period. The mixture was kept at −80° for 1 hr. and allowed to warm to room temperature overnight. Decomposition of the brown residue which remained was accomplished by cautious addition to water. Extraction with ether followed by drying with magnesium sulfate and evaporation of the ether gave a dark oil. Distillation in vacuum gave 3.5 g. of a clear liquid which was redistilled through a Holzman column. 1-Ethynyl-2-vinylbenzene, b.p. 80–82° (14 mm.), n_D^{20} 1.5852, was obtained in 42.3% yield (3.14 g.).

---

[4] A. S. Hay, *J. Org. Chem.*, **25**, 637 (1960).

[5] M. P. Cava, A. A. Deana, and K. Muth, *J. Am. Chem. Soc.*, **81**, 6458 (1959).

[6] M. Deluchat, *Compt. rend.*, **192**, 1387 (1931).

[7] All melting and boiling points are uncorrected.

[8] J. O. Halford and B. Weissman, *J. Org. Chem.*, **17**, 1646 (1952).

Anal. Calcd. for $C_{10}H_8$: C, 93.71; H, 6.29. Found: C, 93.84; H, 6.34.

Repeated experiments gave essentially the same results. Use of commercial sodium amide in this procedure gave a mixture of II and III in about a two to one ratio. The yield was 46%.

o-(1,2-Dibromoethyl)-(1,2-dibromovinyl)benzene (IV). Excess bromine was added to an ethereal solution of 0.5 g. (3.9×10^{-3} mole) of 1-ethynyl-2-vinylbenzene cooled in an ice bath. The red solution was allowed to warm to room temperature and after 1 hr. was poured into an aqueous sodium thiosulfate solution. Separation of the layers and washing of the colorless ether layer with water was followed by drying over magnesium sulfate. Removal of the ether provided an oil which crystallized on standing. Recrystallization from an ether-petroleum ether (b.p. 30–60°) mixture gave 0.7 g. (40% yield) of the tetrabromo derivative (IV), m.p. 84–86°.

Anal. Calcd. for $C_{10}H_8Br_4$: C, 26.82; H, 1.80; Br, 71.38. Found: C, 26.91; H, 1.98; Br, 71.89.

ROHM & HAAS CO.
REDSTONE ARSENAL RESEARCH DIVISION
HUNTSVILLE, ALA.

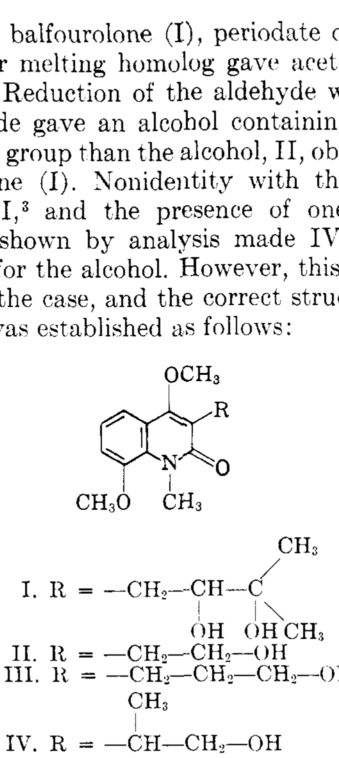
Alkaloids of *Balfourodendron riedelianum*. The O^4-Ethyl Analog of Balfourolone

HENRY RAPOPORT AND KENNETH G. HOLDEN[1]

Received February 6, 1961

In previous publications[2,3] the isolation of alkaloids from *Balfourodendron riedelianum*, a Rutaceous plant indigenous to Brazil and Argentina, was described, and the structures of seven alkaloids were assigned. Balfourolone, m.p. 99–100°, the compound isolated in largest amount, was shown to have structure I. In a subsequent large scale isolation of alkaloids, the balfourolone fraction melted over a wide range, 88–108°. Repeated crystallization gave material whose melting point, 137°, did not change on further recrystallization. The ultraviolet spectrum of this higher melting material was identical with that of balfourolone (I), but its infrared spectrum showed some minor differences, and analysis established the presence of an additional methylene group. The identity of the ultraviolet spectra showed that the aromatic nucleus was the same as in balfourolone (I) and indicated that the additional carbon atom was probably contained in the side chain. An *O*- or *N*-ethyl group would also satisfy the data but seemed unlikely since all the other alkaloids from this plant source, and from Rutaceous plants in general,[4] have only *O*- and *N*-methyl groups.

As with balfourolone (I), periodate oxidation of this higher melting homolog gave acetone and an aldehyde. Reduction of the aldehyde with sodium borohydride gave an alcohol containing one more methylene group than the alcohol, II, obtained from balfourolone (I). Nonidentity with the synthetic alcohol III,[3] and the presence of one C-methyl group as shown by analysis made IV a possible structure for the alcohol. However, this was shown not to be the case, and the correct structure of the homolog was established as follows:



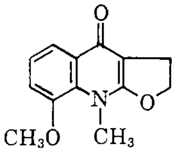
$\text{I. } R = -CH_2-\underset{OH}{CH}-\underset{OH}{C}(CH_3)_2$

$\text{II. } R = -CH_2-CH_2-OH$

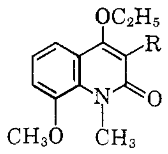
$\text{III. } R = -CH_2-CH_2-CH_2-OH$

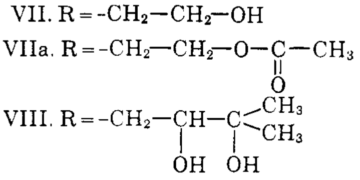
$\text{IV. } R = -\overset{CH_3}{CH}-CH_2-OH$

Acid catalyzed ring closure of the alcohol, II, obtained from balfourolone (I) has been shown[2] to give a mixture of the linear and angular dihydrofuroquinolines, V and VI. Refluxing the acetyl derivative of the alcohol obtained from the balfourolone homolog with 6*N* hydrochloric acid gave the same two products, identical in all respects with authentic samples of V and VI. From this it must be concluded that the alcohol obtained from the homolog of balfourolone has structure VII, and the homolog is then VIII.



V

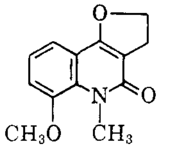




$\text{VII. } R = -CH_2-CH_2-OH$

$\text{VIIa. } R = -CH_2-CH_2-O-\underset{\underset{O}{\|}}{C}-CH_3$

$\text{VIII. } R = -CH_2-\underset{OH}{CH}-\underset{OH}{C}\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}$



VI

Synthesis of the homolog VIII, the O^4-ethyl analog of balfourolone, was easily accomplished by a route similar to that previously[1] used for balfourolone (I). Treatment of balfourodine (IX)[1,2] with ethyl iodide gave O^4-ethylbalfourodinium iodide (X) which, on treatment with alkali, was converted to VIII. The ultraviolet and infrared spectra, and melting point of VIII were identical with those of the high melting component isolated from the balfourolone fraction of plant extract.

---

(1) Public Health Service Predoctoral Research Fellow of the National Heart Institute.

(2) H. Rapoport and K. G. Holden, *J. Am. Chem. Soc.*, **81**, 3738 (1959).

(3) H. Rapoport and K. G. Holden, *J. Am. Chem. Soc.*, **82**, 4395 (1960).

(4) J. R. Price in *Progress in the Chemistry of Organic Natural Products*, Vol. XIII, Springer-Verlag, Vienna, 1956, pp. 317–320.