tended to go to the anhydride VIII. Gradual heating produced a m.p. 287–290° with a change indicated at *ca.* 235–240°. When placed in a preheated bath at 270°, there was an immediate melting with gas evolution, and when the sample was removed thereafter resolidification took place to a material which then did not melt below 300°. Infrared spectra of VII showed only ketone and acid (ester) carbonyl absorption at 5.75, 5.85, whereas an infrared spectra taken on a crude melt of VII indicated the five-membered anhydride carbonyl pattern with bands at 5.40 (w) and 5.60 μ (s).

Anal. Calcd. for $C_{27}H_{38}O_6 \cdot H_2O$: C, 68.20; H, 8.48. Found: C, 68.16, H, 8.44.

Adduct of I with 5(or 6)-*p*-Tolylthiotoluquinone (Product IX).—A solution of I (4 g.) and 2.5 g. 5(or 6)-*p*-tolylthiotoluquinone in 80 ml. of toluene, containing a pinch of hydroquinone was refluxed 48 hr. The toluene was then removed *in vacuo* and the residue was recrystallized from benzene–hexane to afford 2 g. of pale yellowish white crystals (IX), m.p. 300–302°. The infrared absorption of IX indicated ester carbonyls at 5.70–5.73 and ketone bands at 5.88 and 5.96 μ; in addition a band at 6.40 μ (ms) is characteristic of thio-substituted enedione.[11] Also evident were C–OAc stretching bands at 8.05 and 8.23 μ.

Anal. Calcd. for $C_{39}H_{46}O_6S$: C, 72.87; H, 7.21. Found: C, 72.73; H, 7.03.

Zinc–Acetic Acid Reduction of Compound IX (Product X).—A mixture of 1.0 g. of adduct of the acetoxytriene and 5(or 6)-*p*-tolylthiotoluquinone, 80 ml. of 95% acetic acid, and 6.0 g. of zinc dust was refluxed for 14 hr. The filtered solution together with acetic acid washings was evaporated on the steam bath with a rotary evaporator, and the residue was taken up in chloroform, washed with bicarbonate solution and saturated sodium chloride solution, and dried (sodium sulfate). The dark residue remaining after the chloroform removal was recrystallized from dilute ethanol and once again from ethanol to yield X as white needles, m.p. 241–242°.

Anal. Calcd. for $C_{32}H_{42}O_6$: C, 73.50; H, 8.10. Found: C, 73.64; H, 7.92.

Acknowledgment.—We wish to acknowledge with thanks supplies of steroidal starting material from the Julian Laboratories, Inc., and Smith Kline and French Laboratories.

Acridizinium Derivatives from Hydroquinone Dimethyl Ether

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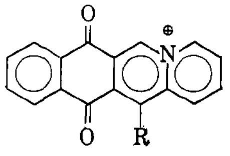
The reaction of an excess of picolinaldoxime with 2,5-bis(bromomethyl)-1,4-dimethoxybenzene affords a salt which can be cyclized (and oxidized) to yield 4a,11a-diazoniapentacene-6,13-quinone dibromide. 2,5-Dimethoxybenzyl bromide, and a quaternary salt prepared therefrom, both undergo bromination in position 6.

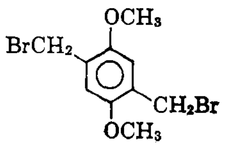
Recently[2] it was shown that 2-bromomethyl-1,4-dimethoxynaphthalene could be converted to quinolizinium derivatives (I), the first examples of quinones in the quinolizinium series. The present communication describes the results of our experiments with bromomethyl derivatives of hydroquinone dimethyl ether.



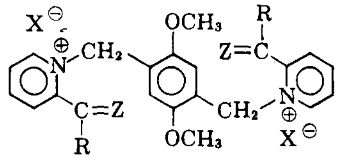
I

2,5-Bis(bromomethyl)-1,4-dimethoxybenzene (II), obtained by bromomethylation of the hydroquinone ether, was diquaternized by reaction with picolinaldoxime. The diquaternary salt (III, X = Br) was made to undergo a double cyclization and air oxidation by heating for 24 hr. at 100° in 48% hydrobromic acid. Similar results were obtained when the bisbromomethyl compound (II) was diquaternized with 2-(1,3-dioxolan-2-yl)pyridine[3] and the salt (IV) cyclized.

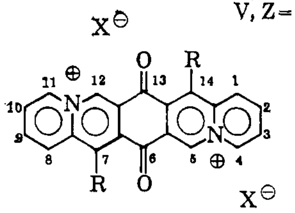
The yellow 4a,11a-diazoniapentacene-6,13-quinone (VI) dibromide is not only extremely insoluble in common solvents, but like the related 6a-azonianaphthacenequinone salts[2] is attacked by most polar solvents to yield a blue solution. The analytical sample was prepared by crystallization from a trifluoroacetic–acetic acid mixture. No method was found for the purification of the perchlorate or picrate.



II



III, Z = NOH; R = H
IV, Z = O(CH₂)₂O; R = H
V, Z = O; R = C₆H₅



VI, R = H
VII, R = C₆H₅

In order to obtain further analytical evidence for the existence of the new quinone system, the diphenyl derivative (VII) was prepared. Quaternization of 2,5-bis(bromomethyl)-1,4-dimethoxybenzene (II) with 2-benzoylpyridine occurred in only 18% yield, but the cyclization–oxidation of the salt (V) occurred in greater than 50% yield.

The ultraviolet absorption spectra (Table I) of the new salts in both neutral and acidified solutions in methanol indicate that the attack of the solvent under neutral conditions upon the aromatic system of the quinone (VI and VII) must be more extensive than was observed with 6a-azonianaphthacenequinone salts.[2]

While 2-bromomethyl-1,4-dimethoxybenzene may be isolated from the reaction products obtained in the

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[1] This research was supported by a research grant (NSF-G 19901) of the National Science Foundation. Taken in part from a thesis submitted in partial fulfillment of the requirements for the Ph.D. degree, Duke University.

[2] C. K. Bradsher and M. W. Barker, *J. Org. Chem.*, **28**, 1669 (1963).

[3] C. K. Bradsher and J. C. Parham, *ibid.*, **28**, 83 (1963).

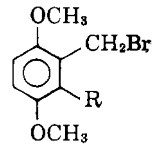
TABLE I

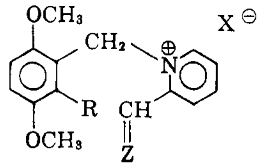
ULTRAVIOLET ABSORPTION MAXIMA (AND LOG EXTINCTION COEFFICIENTS) OF 4a,11a-DIAZONIAPENTACENE-6,13-QUINONE SALTS

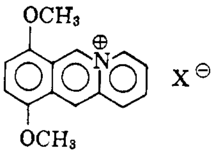
Compound	Acidified,[a] λ_{max} mμ (logϵ)	Neutral, λ_{max} mμ (log s)
VI (dibromide)		227 (4.64)
	251 (4.70)	241[b] (4.57)
	378[b] (4.40)	359[b] (4.34)
	385 (4.41)	372 (4.38)
VII (diperchlorate)	235[b] (4.52)	238 (4.51)
	255 (4.56)	360 (4.02)
	382[b] (4.17)	375 (4.09)
	390 (4.20)	

[a] Approximately 10^{-3} *M* in hydrochloric acid. [b] Shoulder.

bromomethylation of hydroquinone dimethyl ether, the material used in our experiments was obtained by the method of Shulgin and Gal.[4] The bromomethyl compound (VIII) reacted with picolinaldoxime affording a salt (X) which cyclized readily in hydrobromic acid yielding a red compound at first believed to be XIII.[5] The analysis of a recrystallized sample gave results which corresponded to formula XIII *plus one mole of hydroxylamine hydrobromide.* Observation of the red crystals under a microscope revealed only a single type and left the possibilities that the product might be a mixed salt, or the intermediate to be expected if cyclization had occurred, but hydroxylamine had not been eliminated. While the ultraviolet absorption spectrum clearly pointed to the mixed salt explanation, confirmatory experiments were carried out. Fortunately pure 7,10-dimethoxyacridizinium bromide (XIII, X = Br) could be prepared by ion exchange of the picrate obtained from the mixed salt. Crystallization of the bromide (XIII) with hydroxylamine hydrobromide gave a homogenous salt identical in every way with the red cyclization product.[6] Mixed salt formation is not general, for crystallization of the bromide (XIII) with ammonium bromide yielded no evidence of a mixed salt. An alternative synthesis of XIII perchlorate *via* the quaternary salt (XI) from 2-(1,3-dioxolan-2-yl)pyridine avoids the possibility of mixed salt formation.


VIII, R = H
IV, R = Br


X, R = H; Z = NOH
XI, R = H; Z = O(CH$_2$)$_2$O
XII, R = Br; Z = O(CH$_2$)$_2$O


XIII

Since it was found that 2-bromomethyl-1,4-dimethoxybenzene readily undergoes monobromination, it was thought that the bromination product would form a useful starting material in the synthesis of a bromo-7,10-dimethoxyacridizinium bromide. When the quaternary salt (XII) failed to cyclize it was suspected that bromination of the 2-bromomethyl-1,4-dimethoxybenzene had occurred *ortho* rather than *para* to the bromomethyl group, and the product was IX. This was confirmed by oxidation with 2-nitropropane and sodium methoxide to the known[7] 2,5-dimethoxy-6-bromobenzaldehyde. It is of interest that, when quaternary salt XI was brominated, the orientation was again *ortho* since the only product isolated was XII.

Experimental

All analyses were by Dr. Ing. A. Schoeller, Mikroanalytisches Laboratorium, Kronach, West Germany. Melting points were determined using a Laboratory Devices Mel-Temp block and are uncorrected. Infrared spectra were measured in potassium bromide pellets using the Perkin-Elmer Model 21 spectrophotometer. The ultraviolet absorption spectra were recorded using a Cary Model 14 recording spectrophotometer with methanol as the solvent. Wave lengths are recorded in millimicrons (mμ) and shoulders are indicated by an asterisk (*).

2,5-Bis(bromomethyl)-1,4-dimethoxybenzene (II).—A stirred suspension of 1,4-dimethoxybenzene (69 g.) and paraformaldehyde (33 g.) in glacial acetic acid (100 ml.) and carbon tetrachloride (600 ml.) was saturated with hydrogen bromide at room temperature. The solid was collected and recrystallized from chloroform as colorless needles; yield, 31.4 g. (19%); m.p. 196–198°. The analytical sample melted at 203–203.5°. Concentration of the acetic acid–chloroform mother liquor yielded impure 2-bromomethyl-1,4-dimethoxybenzene.

Anal. Calcd. for $C_{10}H_{12}Br_2O_2$: C, 37.06; H, 3.73; Br, 49.33. Found: C, 37.29; H, 3.45; Br, 49.78.

2,5-Bis(1-methylene-2-aldoximinomethylpyridinium bromide)-1,4-dimethoxybenzene (**III, X = Br**).—A solution of the bisbromomethyl compound (II, 13 g.) and picolinaldoxime (12.2 g.) in dimethylformamide (400 ml.) was allowed to stand for 30 days at room temperature. Ether was then added to assure complete precipitation, and the yellow powder, 11.6 g. (51%), was collected. This material gave evidence of decomposition starting at 220° and did not melt below 350°. The analytical sample which formed pale yellow needles from methanol showed similar behavior on heating.

Anal. Calcd. for $C_{22}H_{24}Br_2N_4O_4$: C, 46.49; H, 4.26; N, 9.86. Found: C, 46.67; H, 4.40; N, 9.73.

The **diperchlorate** (III, X = ClO_4) was recrystallized from methanol solution as colorless needles, m.p. 224–225°.

Anal. Calcd. for $C_{22}H_{24}Cl_2N_4O_{12}$: C, 43.50; H, 3.98; N, 9.23. Found: C, 43.68; H, 3.97; N, 9.22.

2,5-Bis[1-methylene-2-(1,3-dioxolan-2-yl)pyridinium bromide]-1,4-dimethoxybenzene (IV).—A solution of the bisbromomethylcompound (II, 10 g.) and 2-(1,3-dioxolan-2-yl)pyridine[3] (11.8 g.) in dimethylformamide (200 ml.) was allowed to stand at room temperature for 11 days. Ether was added to precipitate the salt, 13.3 g. (69%), m.p. 197–198°. Recrystallization from methanol–ethyl acetate gave colorless needles, m.p. 198.5–199°.

Anal. Calcd. for $C_{26}H_{30}Br_2N_2O_6$: C, 49.85; H, 4.83; N, 4.47. Found: C, 49.68; H, 5.05; N, 4.63.

The **diperchlorate** (IV, X = ClO_4) crystallized from methanol as colorless needles, m.p. >350°.

Anal. Calcd. for $C_{26}H_{30}Cl_2N_2O_{14}$: C, 46.93; H, 4.55; N, 4.21. Found: C, 47.34; H, 4.32; N, 4.55.

4a,11a-Diazoniapentacene-6,13-quinone Dibromide (**VI, X = Br**). **A. From the Oximino Salt** (III).—A mixture of the crude oximino diquaternary salt (III, 0.5 g.) and 48% hydrobromic acid (10 ml.) was heated for 17 hr. on the steam bath. Heating for shorter periods gave material which could not be purified. The solution was diluted with water and cooled giving 0.3 g. (71%) of a dark solid, m.p. >350°. The infrared spectrum exhibited a strong band at 5.94 μ in the carbonyl region. The compound was very sensitive to attack by polar solvents, and even distilled water afforded blue solutions. The solution became yellow on addition of acid. Recrystallization of the

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(4) A. T. Shulgin and E. M. Gal, *J. Chem. Soc.*, 1316 (1953).

(5) The preliminary work on this problem was done by Dr. T. W. G. Solomons.

(6) For another example of mixed salt formation in the benzoquinolizinium series, see C. K. Bradsher and N. L. Yarrington, *J. Org. Chem.*, **26**, 78 (1963).

(7) L. Rubenstein, *J. Chem. Soc.*, 1998 (1925).

product from trifluoroacetic acid–acetic acid afforded a yellow powder, m.p. >350°.

B. **From the Bisdioxolanylpyridinium Salt (IV).**—Cyclization of the bisdioxolanylpyridinium salt (IV, X = Br, 0.5 g.) under the conditions used with III afforded 0.2 g. (52%) of the quinone (VI).

Anal. Calcd. for $C_{20}H_{12}Br_2N_2O_2$: C, 50.87; H, 2.56; N, 5.93. Found: C, 50.88; H, 2.92; N, 5.89.

The **diperchlorate** (VI, X = ClO_4), m.p. >350°, was practically insoluble in organic solvents (including trifluoroacetic acid and N-methylpyrrolidone) and was not obtained in pure form.

2,5-Bis(1-methylene-2-benzoylpyridinium bromide)-1,4-dimethoxybenzene (V).—A solution of the bisbromomethyl compound (II, 10 g.) and 2-benzoylpyridine (11.9 g.) in dimethylformamide (300 ml.) was allowed to stand at room temperature for 18 days. Addition of ether precipitated the product as a hygroscopic yellow powder, m.p. 200–201°; yield, 3.95 g. (18%). Recrystallization of the product from methanol–ethyl acetate afforded short yellow needles, m.p. 194–195°, which appeared on analysis to be hydrated.

Anal. Calcd. for $C_{34}H_{30}Br_2N_2O_4 \cdot {}^3/_2H_2O$: C, 56.91; H, 4.63; N, 3.90. Found: C, 57.10; H, 4.46; N, 4.25.

7,14-Diphenyl-4a,11a-diazoniapentacene-6,13-quinone Dibromide (VII).—The quaternary salt (V, 2 g.) was heated in 48% hydrobromic acid (20 ml.) on the steam bath for 24 hr. while air was passed through. The acid was removed under reduced pressure (aspirator) at 100° and the yellow residue crystallized from methanol to yield 1.02 g. (53%); m.p. >350°. The infrared spectrum exhibited a strong absorption at 5.95 μ. Like its congener (VI) the new salt was sensitive to attack by water and polar solvents. Recrystallization from an acidified water solution gave yellow needles, m.p. >350°.

Anal. Calcd. for $C_{32}H_{20}Br_2N_2O_2$: C, 61.56; H, 3.23; N, 4.49. Found: C, 61.32; H, 3.32; N, 4.60.

The **perchlorate** crystallized from water as yellow needles, m.p. >350°.

Anal. Calcd. for $C_{32}H_{20}Cl_2N_2O_{10} \cdot {}^1/_2H_2O$: C, 57.15; H, 3.15; N, 4.16. Found: C, 57.36; H, 3.41; N, 4.14.

1-(2,5-Dimethoxybenzyl)-2-aldoximinomethylpyridinium Bromide (X, X = Br).—A solution containing 14.4 g. of 2,5-dimethoxybenzylbromide[5] (VIII) and 12.2 g. of picolinaldoxime in 55 ml. of dimethylformamide was allowed to stand at room temperature for 7 days. After addition of ethyl acetate the yellow solid was collected; yield, 18.5 g. (48%); m.p. 185–187°. Recrystallization from methanol gave yellow prisms, m.p. 184.5–185°.

Anal. Calcd. for $C_{15}H_{17}BrN_2O_3$: C, 50.99; H, 4.82; N, 7.93. Found: C, 51.09; H, 4.76; N, 7.78.

Mixed Salt of 7,10-Dimethoxyacridizinium Bromide (XIII, X = Br) with Hydroxylamine Hydrobromide.—A solution of 1 g. of the oximino salt (X) and 7.5 ml. of 48% hydrobromic acid was heated and stirred for 10 min. on the steam bath. The acid was removed under reduced pressure (aspirator) and the residue crystallized from methanol–ethyl acetate as red needles; yield, 0.84 g. (65%); m.p. 227–229° dec.; λ_{max}, 251 mμ (log ε 4.36), and 396 (4.08); λ_{min} 331 (3.46).

Anal. Calcd. for $C_{15}H_{18}Br_2N_2O_3$: C, 41.49; H, 4.17; N: 6.45. Found: C, 41.62; H, 4.16; N, 6.62.

7,10-Dimethoxyacridizinium Picrate (XIII, X = OC_6H_2-$(NO_2)_3$).—A small sample of the mixed salt was dissolved in ethanol and precipitated as the picrate by addition of a saturated solution of picric acid in ethanol. The picrate formed irregular orange crystals, m.p. 276–278°, and was free from hydroxylamine.

Anal. Calcd. for $C_{21}H_{16}N_4O_9$: C, 53.85; H, 3.44; N, 11.96. Found[8]: C, 53.90; H, 3.73; N, 11.96.

7,10-Dimethoxyacridizinium Bromide (XIII, X = Br).—A methanolic solution of the picrate was passed through an anion exchange column (Amberlite IRA-401) loaded with bromide ion. From the concentrated solution red-orange needles, m.p. 270° dec., were obtained by addition of ethyl acetate.

Anal. Calcd. for $C_{15}H_{14}BrNO_2$: C, 56.25; H, 4.41; N, 4.38. Found: C, 56.49; H, 4.57; N, 4.60.

Crystallization of 0.10 g. of the bromide (XIII, X = Br) from methanol–ethyl acetate containing an excess of hydroxylamine hydrobromide afforded 0.11 g. of orange needles, m.p. 227–227.5° dec. This material appeared uniform under the microscope. The material was identical with the mixed salt obtained by cyclization of the oxime (X, X = Br) as evidenced by infrared spectrum and mixture melting point determinations. No mixed salt was obtained when the bromide (XIII, X = Br) was crystallized in the presence of ammonium bromide.

Refluxing the bromide (XIII, X = Br) with 48% hydrobromic acid (ether-cleaving conditions) failed to yield a pure product. The crude ether-cleavage products gave no infrared spectral evidence of the formation of a carbonyl group when oxidation was attempted using air, ferric chloride, or potassium periodate.

1-(2,5-Dimethoxybenzyl)-2-(1,3-dioxolan-2-yl)pyridinium Bromide (XI, X = Br).—A solution of 2,5-dimethoxybenzyl bromide (VIII, 6.9 g.) and 2-(1,3-dioxolan-2-yl)pyridine (5 g.) in dimethylformamide (15 ml.) was allowed to stand for 7 days at room temperature. On addition of ethyl acetate, 11 g. (100%) of yellow solid was obtained, m.p. 161–163°. Recrystallization from methanol–ethyl acetate afforded yellow plates, m.p. 167.5–169°.

Anal. Calcd. for $C_{17}H_{20}BrNO_4$: C, 53.41; H, 5.27; N, 3.66. Found: C, 53.61; H, 5.17; N, 3.87.

The **perchlorate** crystallized from methanol–ethyl acetate as yellow plates with an unusual melting point behavior, m.p. 111°, resolidifying at 160° and finally decomposing at 210°.

Anal. Calcd. for $C_{17}H_{20}ClNO_8$: C, 50.81; H, 5.02; N, 3.49. Found: C, 50.90; H, 4.85; N, 3.59.

2,5-Dimethoxy-6-bromobenzyl Bromide (IX).—To a solution of 2,5-dimethoxybenzyl bromide (VIII, 11.55 g.) in 200 ml. of carbon tetrachloride cooled in an ice bath, a solution containing 8 g. of bromine in 30 ml. of carbon tetrachloride was added dropwise. After 24 hr. the carbon tetrachloride was washed with water until neutral, and then dried over anhydrous magnesium sulfate. Evaporation of the solvent afforded an oil, which crystallized from ethyl acetate as colorless needles, m.p. 87.5–89°; yield, 9.7 g. (62%). Recrystallization afforded colorless needles, m.p. 102.5–103.5°.

Anal. Calcd. for $C_9H_{10}Br_2O_2$: C, 34.87; H, 3.25; Br, 51.56. Found[8]: C, 35.00; H, 3.07; Br, 51.66.

Oxidation of 2,5-Dimethoxy-6-bromobenzyl Bromide (IX).—A solution of the bromination product (IX, 0.92 g.) with 0.36 g. of 2-nitropropane in 20 ml. of methanol was added to a solution of 0.22 g. of sodium methoxide in 30 ml. of methanol. The mixture was allowed to stand at room temperature for 5 hr., and then concentrated on the steam bath. Water was added to the residue, and the mixture extracted with ether. The ethereal extract was washed with bicarbonate and dried. Evaporation of the ether afforded a yellow residue which crystallized from ethanol; yield, 0.15 g.; m.p. 130–131°; lit.[7] m.p. 125–126°. This was identical with an authentic sample, m.p. 129.5–130.5°, prepared by the method of Rubenstein[7] and gave no depression of mixture melting point.

1-(2,5-Dimethoxy-6-bromobenzyl)-2-(1,3-dioxolan-2-yl)pyridinium Bromide (XII, X = Br).—A solution of 2,5-dimethoxy-6-bromobenzyl bromide (IX, 3.8 g.) and 2-(1,3-dioxolan-2-yl)-pyridine (2 g.) in 35 ml. of dimethylformamide was allowed to stand for 7 days at room temperature. Ethyl acetate precipitated 2.9 g. (52%) of solid, m.p. 146–148°. Recrystallization from methanol–ethyl acetate gave colorless plates, m.p. 147–148.5°.

Anal. Calcd. for $C_{17}H_{19}Br_2NO_4$: C, 44.27; H, 4.15; N, 3.04. Found[8]: C, 44.18; H, 4.14; N, 3.24.

1-(2,5-Dimethoxy-6-bromomethyl)-2-(1,3-dioxolan-2-yl)pyridinium Perchlorate (XII, X = ClO_4). A. From the Bromide (XII, X = Br).—Addition of perchloric acid to an aqueous solution of the bromide followed by recrystallization of the product from methanol–ethyl acetate afforded colorless plates, m.p. 144.5–145°.

B. **By Bromination of the Salt (XI).**—To a solution of the quaternary salt (XI, X = Br, 1.4 g.) in 15 ml. of glacial acetic acid, 1.28 g. of bromine in 5 ml. of glacial acetic acid was added, and the precipitate which first formed (probably the tribromide) was dissolved by addition of 50 ml. of acetic acid. After the mixture had stood for 2 hr., the precipitate which had formed during this period was collected. The solid was dissolved in aqueous ethanol (100 ml.), silver chloride added, and the mixture stirred in the dark for 2 hr. to give the chloride anion. The silver salts were filtered off and the solution concentrated. Addition of perchloric acid to the solution afforded 0.22 g. of solid which crystallized from methanol–ethyl acetate as colorless needles, m.p. 144–144.5°. This was identical (mixture melting point) with the material obtained by procedure A.

Anal. Calcd. for $C_{17}H_{19}BrClNO_8$: C, 42.47; H, 3.98; N, 2.91. Found[8]: C, 42.45; H, 3.74; N, 3.11.

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[8] Analysis were by A. Daessle, Montreal, Quebec, Canada.