[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF ILLINOIS INSTITUTE OF TECHNOLOGY]

III. The Anomalous Behavior of Tetrazolediazonium Chloride toward some Arylhydrazines: The Synthesis of Some 3,5-Diaryl-1-(5'-tetrazolyl)(1H)tetrazolium Betaines[1,2]

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RECEIVED SEPTEMBER 16, 1957

The coupling of tetrazolediazonium chloride with p-X–$C_6H_4NHNH_2$ (X = H, Cl, Br and NO_2) in the presence of hydrochloric acid affords a 1-(5'-tetrazolyl)-3-aryltetrazene (II) and a 1-(5'-tetrazolyl)-3-aryltriazene (VI) instead of the expected mixture of azides and amines. The anomaly is explicable in terms of a cyclic mechanism derived from the coördination of the arylhydrazonium ion with a resonance stabilized zwitterionic form of the diazonium salt. Treatment of II with aromatic aldehydes and then oxidation with nitric acid gives 3,5-diaryl-1-(5'-tetrazolyl)(1H)tetrazolium betaines (X).

The isolable products of coupling a diazonium salt with an arylhydrazine in the presence of mineral acid are an azide and an amine.[4] An unstable 1,4-diaryltetrazene is presumed to be the precursor of these products.[5] By contrast, a relatively stable 1,3-diaryltetrazene is obtained as the major product from the same coupling components in acetic acid.[5] In addition the detection of small amounts of azide and amine indicate the transient formation of the corresponding 1,4-diaryltetrazene.

It appeared of interest to compare the behavior of the tetrazolediazonium ion toward arylhydrazines in the presence of hydrochloric acid. Accordingly, it was found that the interaction of phenylhydrazine hydrochloride and tetrazolediazonium chloride gave a solid, m.p. 142° dec., which afforded a nitrogen analysis consistent with either 1-(5'-tetrazolyl)-(4 or 3)-phenyltetrazene (IIIa or IIa). That a 1,3-disubstituted tetrazene (IIa) had been obtained was established by the isolation of a derivative on treatment with benzaldehyde.

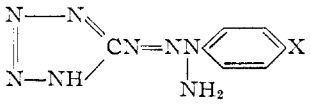
It seems pertinent to point out that, under exactly the same conditions, the coupling of phenylhydrazine hydrochloride with benzenediazonium chloride gave phenyl azide and aniline (isolated as acetanilide) in yields of 29 and 44%, respectively.

Hofmann and Hock had obtained IIa, m.p. 139° dec., from the same coupling components in acetic acid.[6] This structure had been established unequivocally from degradative studies. Repetition of the original procedure provided a sample of IIa, m.p. 138–139° dec., whose infrared spectrum was essentially superimposable with that of the product of coupling in hydrochloric acid. Furthermore, the benzal derivatives were identical.

The use of *para*-negatively substituted phenylhydrazines failed to alter the course of coupling. Thus, p-chloro- (Ib), p-bromo- (Ic) and p-nitrophenylhydrazine (Id) afforded the corresponding 1-(5'-tetrazolyl)-3-aryltetrazene (II) in hydrochloric acid in 31–37% yield. In addition, a 1-(5'-tetrazolyl)-3-aryltriazene (VI) was obtained in approximately 20% yield in each case. The separation of the triazene from the tetrazene was effected with aqueous sodium hydroxide, in which VI is quite soluble while II yields an alkali-insoluble salt.

TABLE I

SOME 1-(5'-TETRAZOLYL)-3-ARYLTETRAZENES



X	M.p., °C. (dec.)	Yield, %	Formula	Nitrogen, % Calcd.	Found
H	142	37	$C_7H_8N_8$	54.88	54.85
Br	159	31	$C_7H_7N_8Br$	39.58	39.30
Cl	165	35	$C_7H_7N_8Cl$	46.96	46.93
NO_2	156	32	$C_7H_7N_9O_2$	50.59	50.50

The isolation of a triazene, VI, requires the following succession of reactions: (a) the formation of a 1-(5'-tetrazolyl)-4-aryltetrazene (III), (b) rapid cleavage of III into the corresponding aniline (IV) and 5-azidotetrazole (V), (c) interaction of IV with excess tetrazolediazonium chloride to produce VI. A parallel exists for "a" and "b" in the reaction of diazonium salts with arylhydrazines in the presence of mineral acid (*vide supra*). However, the final reaction (c) of the sequence is never realized since it is necessary to bind the excess mineral acid in order to effect coupling.[7] Nevertheless, it was found that p-chloroaniline, dissolved in dilute hydrochloric acid, readily coupled with tetrazolediazonium chloride to give 1-(5'-tetrazolyl)-3-(p-chlorophenyl)-triazene (VIa) in 90% yield.

Though the mechanism of formation of 1,3-diaryltriazenes is not known with certainty, it seems probable that coupling is a two-stage process with rapid proton loss as the second stage.[8] However, such a mechanism is obviously not applicable to the corresponding reaction of tetrazolediazonium chloride.

Aqueous solutions of tetrazolediazonium salts explode at 0° if more concentrated than about 2%.[9,10] However, more dilute solutions may be

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[1] Previous communication on this subject, THIS JOURNAL, **77**, 6711 (1955).

[2] This work was supported by a grant from the Office of Ordnance Research, U. S. Army, Contract DA-11-022-ORD-1276, Project TB-2-0001.

[3] Detroit Institute of Cancer Research, 4811 John R Street, Detroit 1, Mich.

[4] If the coupling components contain different substituents, two azides and two amines are obtained.

[5] For a discussion of this subject see T. W. J. Taylor and W. Baker, "Sidgwick's Organic Chemistry of Nitrogen," Oxford University Press, London, 1949, pp. 383 and 465.

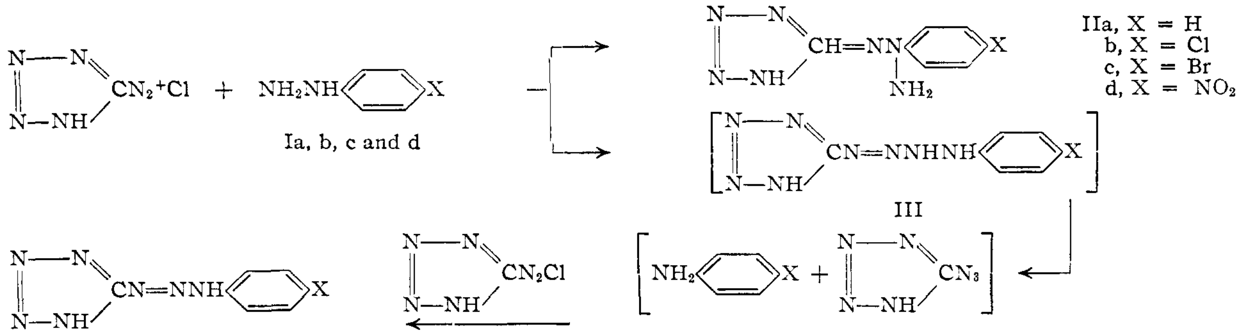
[6] K. A. Hofmann and H. Hock, *Ber.*, **44**, 2946 (1911).

[7] K. H. Saunders, "The Aromatic Diazo Compounds," Edward Arnold and Co., Second Edition, London, 1949, p. 158.

[8] E. R. Alexander, "Principles of Ionic Organic Reaction," John Wiley and Sons, Inc., New York, N. Y., p. 272.

[9] J. Thiele, *Ann.*, **270**, 54 (1892).

[10] J. Thiele and J. T. Marais, *ibid.*, **273**, 144 (1893).


Ia, b, c and d

IIa, X = H
b, X = Cl
c, X = Br
d, X = NO_2

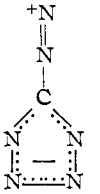
III

IV

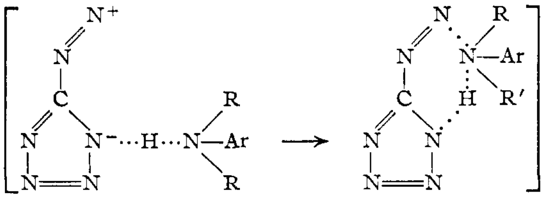
V

VIa, X = Cl; b, X = Br

handled safely with the precautions customarily bestowed upon solutions of diazonium salts. It has been suggested[11] that the enhanced stability in dilute solutions arises from a resonance-stabilized zwitterion form of this diazo compound and it is, furthermore, conceivable that the species involved in coupling is a hybrid derived from VII.


VII

The anomalies observed in the present study are explicable in terms of a cyclic mechanism (VIII) which may develop from the coördination of an amine salt with VII. Thus, the formation of a triazene in mineral acid as depicted by VIIIa involves the synchronous transfer of a proton from the anilinium ion to the tetrazole ring and coupling.


VIIIa, R = R′ = H, Ar = C_6H_5
b, R = H, R′ = NH_2, Ar = C_6H_5
c, R = R′ = H, Ar = C_6H_5NH

The mechanism of coupling an arylhydrazine with a classical diazonium ion, as indicated above, has never been established. However, it would appear that the two observed modes of coupling are related to the relative concentration of the free arylhydrazine and its salts. Thus, in solutions buffered with sodium acetate the relatively weak

$$\mathrm{ArNHNH_2} \rightleftharpoons \underset{a}{\mathrm{ArNHNH_3^+}} + \underset{b}{\mathrm{ArNH_2^+NH_2}} \qquad (1)$$

base, *e.g.*, phenylhydrazine, K_b 1.6 × 10^{-9},[12] should predominate and coupling may (and apparently does) occur at both nitrogen atoms. However, in mineral acid little or no free base is anticipated. Instead, the medium should favor a significant concentration of two conjugate acids ("a" and "b" in eq. 1) of the hydrazine. The possibility of species "a" being involved in the coupling reaction seems remote. Thus, an inductive effect (+I), generated by the adjacent ammonium residue, should lead to a state of electron impoverishment at the imino nitrogen atom and preclude the possibility of attack by the weakly electrophilic benzenediazonium ion.[13,14] A positive charge residing in the imino nitrogen atom (b) should exert a comparatively smaller effect on the terminal amino group since the effectiveness of the charge is partially reduced by the availability of electrons from an adjacent sink. Consequently, coupling may occur at the terminal amino group of "b." The incipient 1,4-diaryltetrazene, bearing a positive charge, then cleaves to an azide and an aniline salt.

In contradistinction, the zwitterion VII may coordinate with either protonated form of the arylhydrazine, and the products are consistent with the corresponding cyclic mechanism (VIIIb and c).

The characterization of II through benzal derivatives IX presented some difficulty, as the common organic solvents effected what appeared to be some decomposition of the derivative. Thus, the crystallization of a sample of the yellow, solid 1-(5′-tetrazolyl)-3-phenyl-4-benzaltetrazene (IXa), m.p. 114–117°, from an ether–petroleum ether mixture yielded a small amount of a white solid, m.p. 300° dec. A somewhat larger sample of the high melting material was detected on recrystallization of IXa from ethyl acetate.

Elementary analysis indicated that the white solid contained approximately the same percentage of carbon and nitrogen as found for IXa. The hydrogen content, however, was somewhat lower than that of the benzal derivative. The fact that the empirical formula of the oxidation product differed from IXa by only two less hydrogen atoms suggested the possibility of oxidative ring closure. On the basis of this interpretation the structure 3,5-diphenyl-1-(5′-tetrazolyl)(1H)tetrazolium betaine[15a,b] (Xa) was tentatively assigned.

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[11] R. Kuhn and H. Kainer, *Angew. Chem.*, **65**, 442 (1953).

[12] V. H. Verley *J. Chem. Soc.*, **88**, 2122 (1908).

[13] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 298.

[14] While the reactivity of benzenediazonium ion may be increased by the introduction of electronegative substituents, the large amounts of mineral acid required in the diazotization of the precursory amine inhibit coupling. Attempts to neutralize the excess acid prior to coupling frequently result in the precipitation of the diazonium hydroxide.

[15] (a) The designation "(1H)" indicates that the betaine is formed by the quaternation of a 1-substituted tetrazole. (b) It is recognized that additional resonance contributors may be written but, for convenience, the structure is represented as shown.

In an effort to explain the observed phenomenon, consideration was given to the possibility of autoxidation of the benzal derivative IXa. Confirmatory evidence for this hypothesis was obtained from the oxidation of a sample of IXa with potassium permanganate. The solid that remained after removal of the inorganic salts proved to be identical with that detected in the recrystallization.

That the oxidation product Xa is indeed a tetrazolium betaine, was established from the degradation of Xa with concentrated hydrochloric acid, which gave a mixture of 5-hydroxytetrazole (XI) (60% yield) and 2,5-diphenyltetrazole (XII) (98% yield). However, the degradative evidence did not permit the unequivocal assignment of the relative positions of the tetrazolyl and N-phenyl substituents. Furthermore, it seems pertinent to point out that all of the tetrazolium salts, which have previously been reported, have been prepared, directly or indirectly, by the oxidation of C,N,N′-trisubstituted formazans.[16] However, the method affords derivatives of (2H)tetrazole.[17]

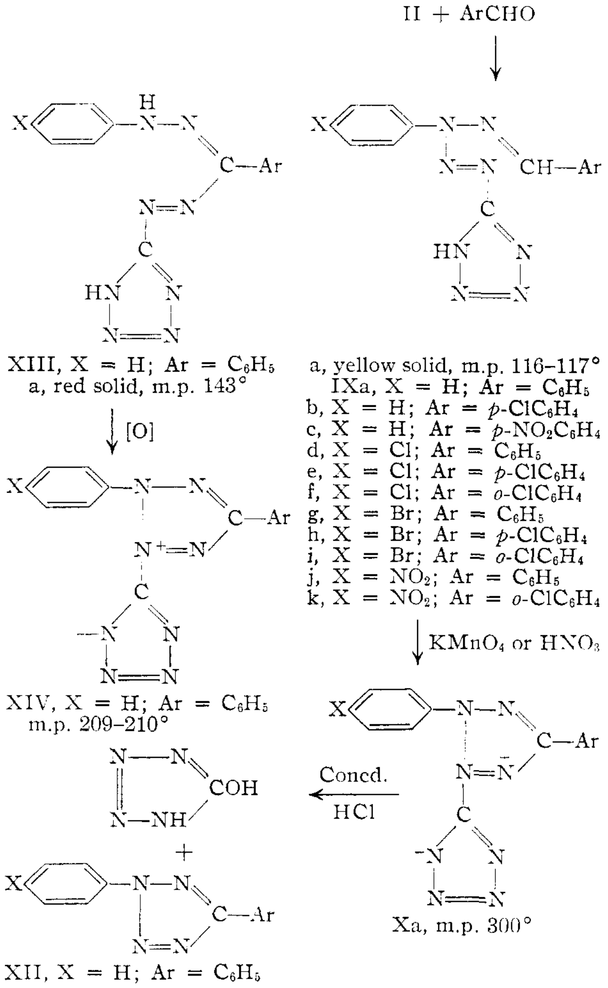
It was demonstrated by Busch and Pfeiffer that the condensation of a 1,3-diaryltetrazene with an aromatic aldehyde yields a triarylformazan instead of the expected tetrazene derivative.[18] This phenomenon was explained in terms of a tetrazene–formazan rearrangement. A recent study has confirmed this hypothesis and suggests that the transformation is intramolecular.[19]

The occurrence of a tetrazene–formazan rearrangement (IX → XIII) in the present work would lead to the isomeric 2,5-diphenyl-3-(5′-tetrazolyl)-(2H)tetrazolium betaine (XIV) as the product of oxidative cyclization. Furthermore, it is conceivable that the same degradation products (XI and XII) could be derived from XIV. Quite fortunately, Kuhn and Kainer had earlier described the synthesis of XIV, which was obtained by the oxidation of C,N-diphenyl-N′-(5′-tetrazolyl)-formazan (XIII) with N-bromosuccinimide.[11] Compound XIIIa, m.p. 143°, possesses the characteristic red color of a formazan[14] and was obtained by the action of benzenediazonium chloride on benzal-5-tetrazolylhydrazone.

The differences noted (*cf.* Chart I) between IXa and XIIIa and Xa and XIVa preclude the possibility of a tetrazene–formazan rearrangement in the present study and hence lend credence to the tetrazolium structure assigned to Xa.

It subsequently was found that the oxidative ring closure of IX may be effected in 70% yield with cold concentrated nitric acid in contrast to the 12% yield of this same product obtained with potassium permanganate. A number of other 1-(5′-tetrazolyl)-3-aryl-4-benzaltetrazenes (IX) were subjected to nitric acid oxidation and the corresponding tetrazolium betaines X were obtained in yields of 30–90% (*cf.* Table I).

CHART I



Experimental[20]

Coupling of Phenylhydrazine Hydrochloride and Benzenediazonium Chloride.—A solution of benzenediazonium chloride was prepared in the usual manner by the addition of 7.0 g. of sodium nitrite (0.1 mole) dissolved in 100 ml. of water to a solution of 9.3 g. of aniline (0.1 mole) in a mixture of 25 ml. of concentrated hydrochloric acid and 300 ml. of water. The diazonium salt solution was added all at once with vigorous stirring to an ice-cold solution of 14.5 g. of phenylhydrazine hydrochloride (0.1 mole). Following an additional period of stirring for 0.5 hours, the turbid reaction mixture was saturated with sodium chloride and extracted with ether. The combined ether extracts were dried over magnesium sulfate and distilled to give 3.5 g. (29% yield) of phenyl azide, b.p. 29–31° (1.5 mm.). The identity of this product was established from infrared measurements.

The aqueous phase remaining from the ether extraction was concentrated to a small volume, made alkaline with 10% sodium hydroxide and treated with 12.0 g. of acetic anhydride. The crude product was collected, and then purified by dissolving in hot water and treating with Norit. Acetanilide separated on cooling and was collected, wt. 6.0 g. (44% yield), m.p. 111–113° (lit.[21] 114°).

1-(5′-Tetrazolyl)-3-aryltetrazenes (II).—The preparation of this group of compounds was accomplished in all cases by the addition of a solution of tetrazolediazonium chloride to a solution of the arylhydrazine hydrochloride. The preparation of 1-(5′-tetrazolyl)-3-(p-chlorophenyl)-tetrazene

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[16] For an excellent discussion of this subject see A. W. Nineham, *Chem. Revs.*, **55**, 385 (1955).

[17] The preparation of a (1H)tetrazolium betaine has been reported by S. Hunig and O. Boes, *Ann.*, **579**, 28 (1953). However, the structure is not known with certainty.

[18] M. Busch and H. Pfeiffer, *Ber.*, **59**, 1162 (1926).

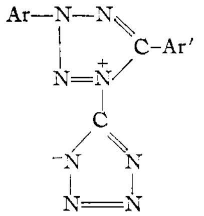
[19] H. Hauptmann and A. C. de M. Périsse, *Experientia*, **10**, 60 (1954).

[20] All melting points are uncorrected. Analyses by Micro-Tech Laboratories, Skokie, Ill.

[21] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," Third Edition, John Wiley and Sons, Inc., New York, N. Y., p. 234.

TABLE II

SOME 3,5-DIARYL-1-(5′-TETRAZOLYL)-TETRAZOLIUM BETAINES



Ar	Ar′	M.p., °C. (dec.)	Yield, %	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
C_6H_5	C_6H_5	300	70	$C_{14}H_{10}N_8$	57.92	58.12	3.47	3.76	38.61	38.50
C_6H_5	*p*-ClC_6H_4	280–282	70	$C_{14}H_9N_8Cl$	51.78	51.70	2.79	3.10	34.51	34.50
C_6H_5	*p*-$NO_2C_6H_4$	277–279	30	$C_{14}H_9N_9O_2$	50.15	50.02	2.71	2.97	37.60	37.64
p-BrC_6H_4	C_6H_5	308–310	80	$C_{14}H_9N_8Br$	45.54	45.53	2.46	2.62	30.35	30.37
p-BrC_6H_4	*p*-ClC_6H_4	302–304	76	$C_{14}H_8N_8ClBr$	41.66	41.11	2.00	2.11	27.76	27.49
p-BrC_6H_4	*o*-ClC_6H_4	259–260	42	$C_{14}H_8N_8ClBr$	41.66	41.67	2.00	2.11	27.76	27.60
p-ClC_6H_4	C_6H_5	312–315	90	$C_{14}H_9N_8Cl$	51.78	51.28	2.79	3.09	34.51	34.72
p-ClC_6H_4	*p*-ClC_6H_4	306–307	93	$C_{14}H_8N_8Cl_2$	46.81	46.79	2.24	2.47	31.20	30.90
p-ClC_6H_4	*o*-ClC_6H_4	262–263	66	$C_{14}H_8N_8Cl_2$	46.81	46.93	2.24	2.43	31.20	31.47
p-$NO_2C_6H_4$	C_6H_5	308–309	74	$C_{14}H_9N_9O_2$	50.15	50.10	2.71	2.98	37.60	37.30
p-$NO_2C_6H_4$	*o*-ClC_6H_4	269–271	34	$C_{14}H_8N_9ClO_2$	45.48	45.07	2.18	2.36	34.10	34.11

(IIb) along with the isolation of 1-(5′-tetrazolyl)-3-(*p*-chlorophenyl)-triazene (VIa) is presented as a typical example.

To a solution of 8.24 g. of 5-aminotetrazole hydrate (0.08 mole), in 23 ml. of concentrated hydrochloric acid and 240 ml. of water, cooled to 0° was added, dropwise with stirring, a solution of 5.6 g. of sodium nitrite (0.08 mole) in 50 ml. of water. After the addition was completed, the cold solution was stirred for ten minutes and then added slowly to a solution of 14.4 g. of *p*-chlorophenylhydrazine hydrochloride (0.08 mole) in 500 ml. of water. A tan solid appeared almost immediately and after approximately 15 minutes of continued stirring, the product was collected. The moist filter cake was dissolved in 200 ml. of cold 1% sodium hydroxide. The addition of 150 ml. of 6 *N* sodium hydroxide precipitated the sodium salt of IIb which was collected and washed with additional 6 *N* sodium hydroxide until the washings were light yellow in color.

The yellow filter cake was dissolved in 200 ml. of cold water and the solution acidified with dilute hydrochloric acid. The yellow solid was collected, washed with water and dried *in vacuo*, wt. 6.6 g. (35% yield) of IIb, m.p. 165° dec. (*cf.* Table I for analysis).

The initial alkaline filtrate was acidified with dilute hydrochloric acid and the product collected, wt. 3.2 g. (18% yield) of crude VIa, m.p. 106–114°. A sample of VIa was purified by several precipitations from dilute alkali and finally by recrystallization from ether to give a yellow amorphous solid, m.p. 132–134° dec.

An authentic sample of VIa was prepared in the following manner. *p*-Chloroaniline (5.1 g., 0.04 mole) dissolved in 20 ml. of hot 6 *N* hydrochloric acid was first diluted with water to 300 ml. and cooled by the addition of *ca.* 100 g. of crushed ice.

A solution of tetrazolediazonium chloride prepared from 4.12 g. of 5-aminotetrazole hydrate (0.04 mole) slowly was added with mechanical stirring to the solution of *p*-chloroaniline hydrochloride. A yellow solid appeared immediately. After stirring the mixture for 15–20 minutes, the product was collected, washed with several portions of water and sucked dry, wt. 8.0 g. (90% yield), m.p. 131–134° dec. An analytical sample was obtained by recrystallization from a mixture of ether-petroleum ether (30–60°), m.p. 133–134° dec. A mixture melting point with the product obtained above showed no depression.

Anal. Calcd. for $C_7H_6N_7Cl$: N, 43.85. Found: N, 43.56.

1-(5′-Tetrazolyl)-3-aryl-4-benzaltetrazenes (IX).—The benzal derivatives of II are difficult to purify because of the ease with which they autoxidize to tetrazolium betaines (X). Consequently, an effort was made to purify only IXa for elementary analysis. In all other cases the crude benzal derivative was employed directly in the oxidation reaction. The examples presented below are considered typical of the methods used to obtain these derivatives.

(IXa).—To a suspension of 5.0 g. of 1-(5′-tetrazolyl)-3-phenyltetrazene IIa (0.025 mole) in *ca.* 50 ml. of benzaldehyde, cooled externally with an ice–water-bath, was added with mechanical stirring 5 drops of concentrated hydrochloric acid. The tetrazene dissolved readily on addition of acid to yield a greenish-brown solution which was filtered to remove a small amount (0.1 g.) of dark solid, m.p. 270–300° dec. The addition of 400 ml. of ether gave an additional 30 mg. of the same dark material, m.p. 280–300° dec., which is presumed to be an impure form of the corresponding tetrazolium betaine (Xa) (*vide infra*). The filtrate was then heated, treated with Norit and filtered. To the clear yellow filtrate was added 400 ml. of petroleum ether (60–90°), and a small amount of solid (0.2 g.), m.p. 120–190°, was collected. To the filtrate was added 800 ml. of petroleum ether (60–90°) and the mixture then cooled externally with a Dry Ice–acetone-bath whereupon a light yellow solid was deposited, wt. 6.0 g. (84% yield), m.p. 114–117° dec.

An analytical sample was obtained by dissolving 0.5 g. of the crude material in 10 ml. of benzaldehyde followed by the addition of 100 ml. of benzene. On cooling, a yellow amorphous solid separated which was collected, washed several times with benzene and finally with ether, m.p. 116–117° dec.

Anal. Calcd. for $C_{14}H_{12}N_8$: C, 57.52; H, 4.14; N, 38.34. Found: C, 57.30; H, 4.33; N, 38.04.

When a sample of IIa as obtained by the procedure of Hofmann and Hock[6] was treated with benzaldehyde, in the manner described above, IXa was obtained in 50% yield, m.p. 116–117° dec. alone or when admixed with a sample of the product obtained by the present method.

(IXf).—To a stirred suspension of 4.0 g. of finely powdered 1-(5′-tetrazolyl)-3-(*p*-chlorophenyl)-tetrazene (IIb) (0.017 mole) in 25 ml. of *o*-chlorobenzaldehyde was added 5 drops of concentrated hydrochloric acid. The tetrazene readily dissolved on addition of acid, and a small amount of yellow solid began to appear in a few minutes. The reaction mixture was stirred for an additional 15–20 minutes, then 100 ml. of ether and *ca.* 400 ml. of petroleum ether (60–90°) was successively added. The yellow solid was collected and washed with 50–70 ml. of petroleum ether, wt. 6.7 g. (90% yield), m.p. 100–110° dec. This procedure was also used to prepared IXd, g, i, j and h. The crude solids were oxidized directly to the corresponding tetrazolium betaine.

(IXe).—A suspension of 2.0 g. of finely powdered IIb (0.008 mole) in 10 g. of molten (45–50°) *p*-chlorobenzaldehyde was treated with 5 drops of concentrated hydrochloric acid. The reaction mixture turned to a paste which was stirred manually for 10–15 minutes allowing the temperature of the mixture to drop slowly to 20–25°. The yellow solid was triturated with 80 ml. of ether followed by the addition of *ca.* 300 ml. of petroleum ether (60–90°) and the yellow product collected. The filter cake was washed with additional petroleum ether and sucked dry; wt. 3.0 g. (80% yield), m.p. 115–120° dec. The same procedure was employed to prepare IXh, m.p. 119–125°.

(**IXc**).—To a solution of 1.7 g. of *p*-nitrobenzaldehyde (0.011 mole) in 40 ml. of absolute ethanol was added 2.0 g. of IIa (0.01 mole). The addition of 5 drops of concentrated hydrochloric acid provided a homogeneous mixture from which a brown solid was deposited on cooling. The product was collected and sucked dry (wt. 1.4 g.), and oxidized to a tetrazolium betaine.

3,5-Diaryl-1-(5′-tetrazolyl)(1H)tetrazolium Betaines (X).—The oxidative ring closure of the benzaltetrazenes (IX) was accomplished in all cases with concentrated nitric acid. The yields reported in Table II are based on the corresponding 1-(5′-tetrazolyl)-3-aryltetrazene (II), rather than IX, since the degree of purity of the benzal derivatives was uncertain. The preparation of Xe is presented as a typical example.

Crude 1-(5′-tetrazolyl)-3-(*p*-chlorophenyl)-4-(*p*-chlorobenzal)-tetrazene (IXe) (3.0 g.), obtained from 2.0 g. of 1-(5′-tetrazolyl)-3-(*p*-chlorophenyl)tetrazene (IIb) (0.008 mole) was added portionwise to 30 ml. of cold concentrated nitric acid. The solid dissolved readily with a slight evolution of gas with the temperature rising to 20°. The yellow solution was poured onto ice, the off-white colored solid collected, washed with water and sucked dry; wt. 2.8 g. (93% yield), m.p. 304–307° dec. An analytical sample was obtained by recrystallization from glacial acetic acid, m.p. 306–307° dec. (*cf.* Table I for analysis). It was convenient to recrystallize Xa, c, f, j and k from ethanol. On the other hand Xd, e, g and h are best recrystallized from glacial acetic acid.

Acid Degradation of 3,5-Diphenyl-1-(5′-tetrazolyl)(1H)-tetrazolium Betaine (Xa).—A suspension of 4.0 g. of Xa (0.014 mole) was suspended in 130 ml. of concentrated hydrochloric acid and the mixture refluxed for 48 hours. During this period the solid slowly disappeared and a yellow oil was deposited at the bottom of the flask. In addition a small amount of solid crystallized in the condenser. To the cooled reaction mixture was added 20 ml. of water and the yellow oil, which solidified, was collected; wt. 1.8 g., m.p. 91–98°. This material was combined with the solid which was deposited in the condenser and the solid crystallized from ethanol in the form of white needles, wt. 2.55 g., m.p. 101–102°.

Anal. Calcd. for $C_{13}H_{10}N_4$: C, 70.27; H, 4.50; N, 25.22. Found: C, 70.21; H, 4.51; N, 24.90.

This product proved to be 2,5-diphenyltetrazole (XII), m.p. (lit.[22] 101–101.5°).

The acid filtrate was evaporated to dryness on a steam-bath in a stream of air and the residue heated to boiling with 40 ml. of water. The insoluble material, 0.6 g., m.p. 296–300°, was identified as starting material. The aqueous filtrate was treated with Norit, filtered and the filtrate concentrated to *ca.* 5 ml. A white solid was deposited on cooling, wt. 0.5 g., m.p. 253–255°. A second crop of the same solid was obtained on further concentration of the mother liquor, wt. 0.1 g., m.p. 249–253°. This material failed to depress the melting point of an authentic sample of 5-hydroxytetrazole (XI).

The conversion of Xa to 2,5-diphenyltetrazole and 5-hydroxytetrazole was 98 and 60%, respectively.

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[22] O. Dimroth and S. Merzbacher, *Ber.*, **40**, 2402 (1907).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

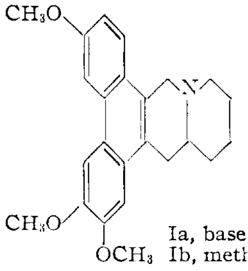
Aromatic Cyclodehydration. XXXVI.[1,2] The Synthesis of (±)-Cryptopleurine

BY C. K. BRADSHER AND H. BERGER

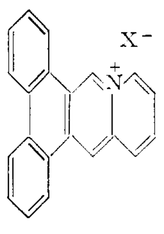
RECEIVED AUGUST 15, 1957

The correctness of the structural formula proposed by Fridrichsons and Mathieson for (±)-cryptopleurine methiodide has been demonstrated by synthesis. The first steps involved preparation of 2,3,6-trimethoxy-9-phenanthroic acid (VI) *via* the Pschorr synthesis. The carboxyl group of acid VI was converted in three steps to the bromomethyl group and the resulting compound IX used as the halide component in an acridizinium ion synthesis. The crude X thus obtained was reduced to yield (±)-cryptopleurine (Ia).

The alkaloid cryptopleurine, isolated[3] from the bark of an Australian laurel *Cryptocarya pleurosperma* (White and Francis), is a vesicant[3,4] which has been reported to stimulate the growth of nerve tissue[5] and to be highly toxic to animals.[3] To date there are no reports to indicate that the alkaloid has been synthesized, or degraded to compounds of known structure. In arriving at the unusual formula (Ia) shown, Fridrichsons and Mathieson[6] had available chemical evidence concerning the composition[7] and the presence of three methoxyl groups,[3,7] as well as spectral evidence for the presence of a phenanthrene or triphenylene nucleus,[7] but relied almost completely upon their own X-ray crystallographic studies on what is now[8] known to be the methiodide (Ib) of (±)-cryptopleurine.



Ia, base
Ib, methiodide



II

Since cryptopleurine (Ia) is closely related in structure to the dibenzo[h,j]acridizinium ion (II) which has been prepared earlier[9] by the aromatic cyclodehydration method, it seemed probable that the alkaloid could be synthesized. The 2,3,6-trimethoxy-9-phenanthroic acid needed was pre-

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[1] For the preceding communication of this series see THIS JOURNAL, **79**, 6033 (1957).

[2] This work was supported by a research grant (H-2170) from the National Heart Institute of the National Institutes of Health, Public Health Service. This paper was presented at the 132nd National Meeting of the American Chemical Society in New York, N. Y., September 10, 1957. A preliminary report appeared as a Communication to the Editor, THIS JOURNAL, **79**, 3287 (1957).

[3] I. S. de la Lande, *Australian J. Exp. Biol. Med. Sci.*, **26**, 181 (1948).

[4] L. J. Webb, *Australian J. Sci.*, **11**, 26 (1948).

[5] H. Hofmann, *Australian J. Exp. Biol. Med. Sci.*, **30**, 541 (1952).

[6] J. Fridrichsons and A. Mathieson, *Acta Cryst.*, **8**, 761 (1955); *cf. Nature*, **173**, 732 (1954).

[7] E. Gellert and N. V. Riggs, *Australian J. Chem.*, **7**, 113 (1954).

[8] E. Gellert, *ibid.*, **9**, 489 (1956).

[9] C. K. Bradsher and L. E. Beavers, THIS JOURNAL, **78**, 2459 (1956).