[CONTRIBUTION FROM THE ROLLIN H. STEVENS MEMORIAL LABORATORY OF THE DETROIT INSTITUTE OF CANCER RESEARCH]

5-Aroyltetrazoles[1]

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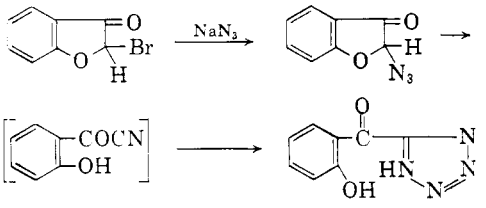
Two synthetic avenues to 5-aryltetrazoles (IV) are described. In the first (Method A) an α-bromo-α-phenoxyacetophenone is converted to IV by treatment with excess sodium azide in glacial acetic acid. A plausible reaction scheme is suggested. In Method B, an aryl-5-tetrazolylcarbinol (VIII), obtained from the interaction of the corresponding mandelonitrile acetate and aluminum azide in tetrahydrofuran, is oxidized to IV with sodium dichromate in aqueous sulfuric acid. The latter method has been extended to the preparation of 5-acetyltetrazole. 5-Benzoyltetrazole (IVa) and its oxime readily undergo the Schmidt reaction and the Beckmann rearrangement, respectively. Wolff-Kishner reduction of IVa affords 5-benzyltetrazole while a photochemical reduction of IVa leads to the corresponding pinacol. The addition of phenylmagnesium bromide to IVa gives diphenyl-5-tetrazolylcarbinol.

The dependence of the acid dissociation constant of a 5-substituted tetrazole on the nature of the substituent and its analogy with the carboxylic acid has recently been reviewed by Herbst.[2] On the basis of a suggestion contained in this same review, several 5-tetrazolyl analogs of physiologically and pharmacologically active carboxylic acids have been synthesized and assayed for analogous or antagonistic activity.[3,4] The results were somewhat disappointing to the extent that no appreciable activity in either sense was detected.

The importance of α-keto acids in the citric acid cycle as well as in a variety of other biochemical transformations stimulated our interest in 5-tetrazolyl analogs of such intermediates as potential growth antagonists. The present communication discloses two approaches to 5-aroyltetrazoles, analogs of arylglyoxylic acids, and the properties of this class of tetrazole derivatives.

The decomposition of 2-azido-3-(2*H*)benzofuranones(2-azidocoumaranones) in glacial acetic acid containing excess sodium azide yields 5-(*o*-hydroxybenzoyl)-tetrazoles.[5] It was suggested that the reaction involves the intermediate formation of *o*-hydroxybenzoylcyanides as direct precursors of the ketones. However, the results of a recent study in this laboratory on the course of the reaction between



aroylcyanides and sodium azide tend to vitiate this hypothesis.[6] Nevertheless, the method constitutes the sole approach to 5-aroyltetrazoles which carry no additional function attached to the heterocycle.[7a,b]

An extension of this method to open chain analogs of 2-azidocoumaranone would circumvent the inherent limitation of simultaneous introduction of an *ortho* hydroxyl function in the 5-aroyltetrazole and, thereby, broaden the scope of the synthesis. Accordingly, it was found that α-bromo-α-phenoxyacetophenone[8] (IIa), on treatment with sodium azide in acetone, affords the corresponding azide (IIIa) in 80% yield. Decomposition of IIIa in glacial acetic acid and in the presence of excess sodium azide gave a solid with properties conforming to 5-benzoyltetrazole (IVa). Alternatively, the entire reaction sequence may be telescoped by simply refluxing IIa with excess sodium azide in glacial acetic acid (Method A). This modification gave IVa in 40% yield, based on α-phenoxyacetophenone, and is applicable to the conversion of α-phenoxy-*p*-bromo- (Ib) and α-phenoxy-*p*-nitroacetophenone (Ic) to the corresponding 5-aroyltetrazole (IVb and c) (*cf.* Table I). However, an attempt to prepare 5-acetyltetrazole from phenoxyacetone by this method was unsuccessful.

Recently, Boyer and Straw demonstrated that the pyrolysis of α-azidocarbonyl compounds leads to the decomposition of the azido group with rearrangement to α-iminocarbonyl compounds.[9] Moreover, in all possible cases hydrogen migration occurred exclusively.

By analogy, a rearrangement accompanying the decomposition of IIIa would lead to phenyl benzoylformimidate (V). Moreover, the conversion of

(1) This work was supported in part by research grant CY-2903 from the National Cancer Institute, Public Health Service and in part by an institutional grant from the American Cancer Society, Southeastern Michigan Division.

(2) R. M. Herbst in Graff's "*Essays in Biochemistry*," Wiley and Sons, New York, 1956, p. 141.

(3) C. van de Westeringh and H. Veldstra, *Rec. trav. chim.*, **77**, 1107 (1958).

(4) B. Brouwer-van Straaten, D. Solinger, C. van de Westeringh, and H. Veldstra, *Rec. trav. chim.*, **77**, 1129 (1958).

(5) K. Fries and K. Saftien, *Ber.*, **59**, 1246 (1926).

(6) J. P. Horwitz, B. E. Fisher, and A. J. Tomasewski, *J. Am. Chem. Soc.*, **81**, 3076 (1959).

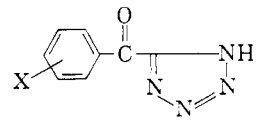
(7) Indirect syntheses of 1-phenyl-5-tetrazolylmethyl ketone have been described by (a) E. K. Harvill, R. M. Herbst, and E. G. Schreiner, *J. Org. Chem.*, **17**, 1597 (1952) and (b) C. R. Jacobson and E. D. Amstutz, *J. Org. Chem.* **19**, 1652 (1954).

(8) E. B. Knott, *J. Chem. Soc.*, 4099 (1952).

(9) J. H. Boyer and D. Straw, *J. Am. Chem. Soc.*, **75**, 1642 (1953).

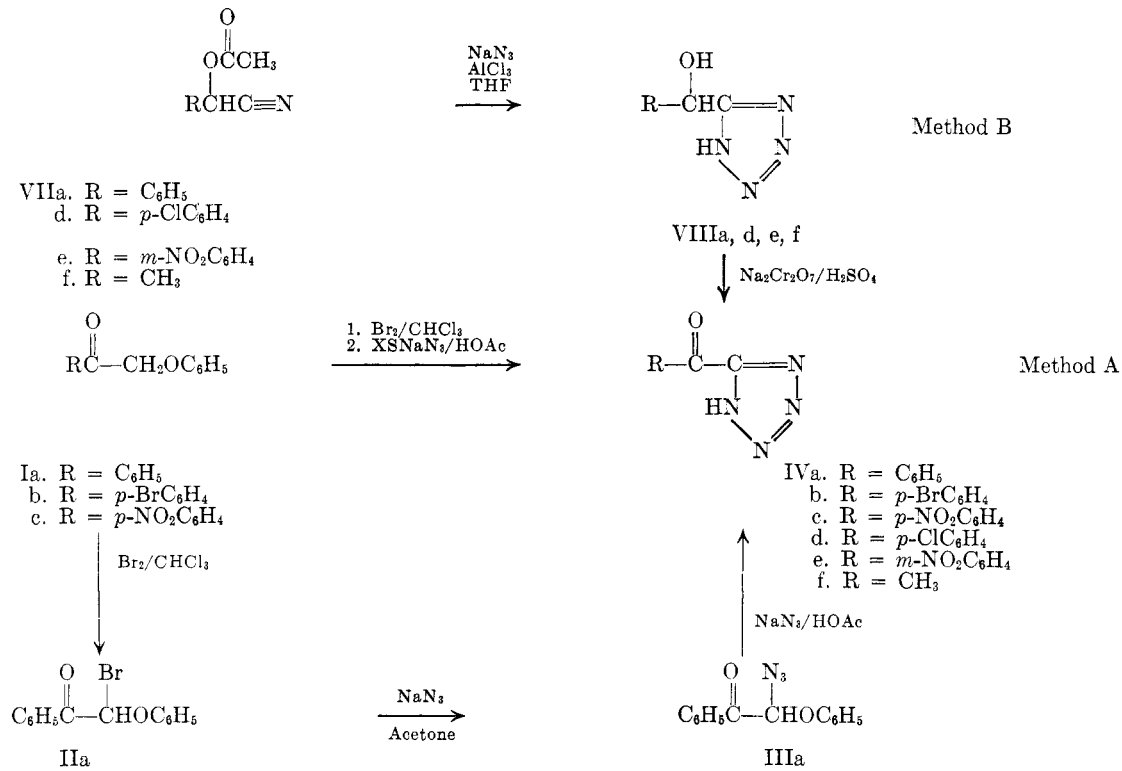
TABLE I

5-AROYLTETRAZOLES



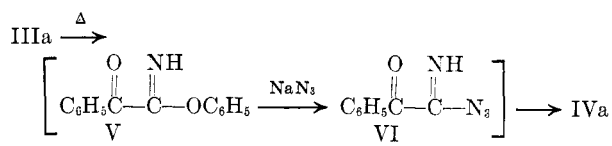
X	M.P.[a]	Method of Synthesis	Yield,[b,c] %	$\lambda_{max.}$,[d] Mμ	Log ε	Formula	Analyses Calcd. C	H	N	Found C	H	N
H	140–141	A	40	261	4.10	$C_8H_6N_4O$	55.17	3.47	32.17	55.34	3.48	32.10
		B	78									
p-Cl	174–175	B	75	270	4.14	$C_8H_5N_4OCl$	46.05	2.42	26.87	46.29	2.43	27.16
p-Br	176–177	A	50	272	4.12	$C_8H_5N_4OBr$	37.97	1.99	22.14	38.15	2.22	22.44
p-NO_2	161–163[d]	A		271	4.18	$C_8H_5N_5O_3$	43.84	2.30	31.96	43.91	2.46	32.14
m-NO_2	131–132	B	75	245	4.29	$C_8H_5N_5O_3$	43.84	2.30	31.96	44.13	2.45	31.83

[a] All of the tetrazoles were recrystallized from benzene. [b] Yield by Method A is based on the phenoxyacetophenone. [c] Yield by Method B is based on the aryl-5-tetrazolylcarbinol. [d] Spectra determined in 95% ethanol with a Cary Model 11 recording spectrophotometer.



this ester to the corresponding imidyl azide (VI) by sodium azide followed by cyclization would account for the formation of IVa by a plausible reaction scheme.[10]

The oxidation of aryl-5-tetrazolylcarbinol aryl-5-tetrazolylcarbinols (VIII) with sodium dichromate in aqueous sulfuric acid provided an alternative route to IV. Thus, mandelonitrile acetate (VIIa), on



treatment with aluminum azide in anhydrous tetrahydrofuran, affords phenyl-5-tetrazolylcarbinol (VIIIa).[11]

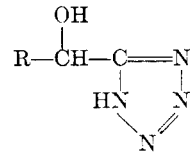
Oxidation of VIIIa with sodium dichromate gave 5-benzoyltetrazole (IVa) in 77% yield. This method (B) was successfully extended to the preparation of

(10) Syntheses of 5-substituted tetrazoles from imino esters and sodium azide are relatively uncommon since the same transformation may be accomplished with the more readily accessible nitrile or cyanamide. However, all such reactions involve the intermediate formation of an imidyl azide which readily undergo ring closure in acetic acid, *cf.* F. Benson, *Chem. Rev.*, **41**, 1 (1947).

(11) H. Behringer and K. Kohl, *Chem. Ber.*, **89**, 2648 (1956) report an 80% yield for this transformation. In our hands, the yield of reasonably pure VIIIa never exceeded 50%.

TABLE II

SUBSTITUTED-5-TETRAZOLYLCARBINOLS



R	M.P.	Yield, %	Analyses					
			Calcd.			Found		
			C	H	N	C	H	N
C_6H_5	159–160[a]	48	...	...	...	...	...	...
p-ClC_6H_4	188–189[b]	38	45.62	3.35	26.60	45.83	3.52	27.12
m-$NO_2C_6H_4$	171–172[c]	31	43.44	3.19	31.82	43.47	3.49	32.03
CH_3	133–134[c]	39	31.57	5.30	49.10	31.72	5.37	49.57

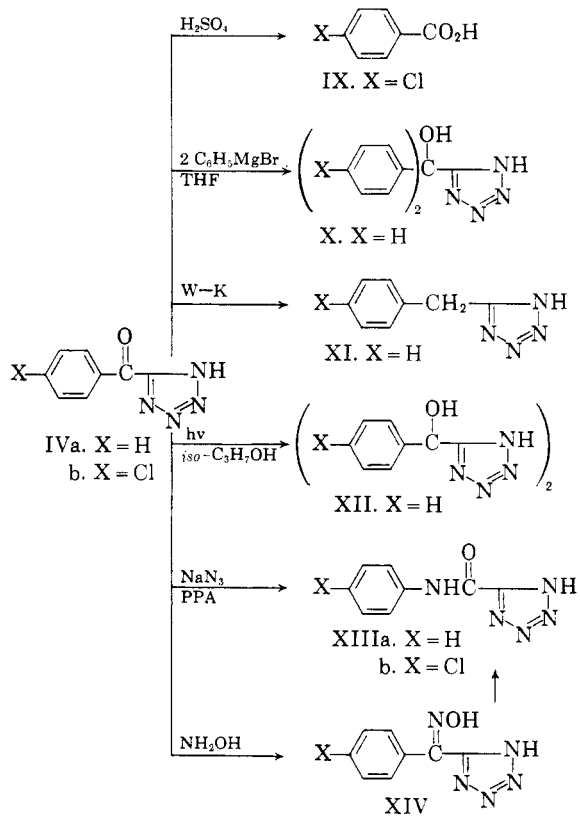
[a] Lit. m.p. 159. See ref. 11. [b] Recrystallized from a mixture of ethyl acetate and petroleum ether (65–110°). [c] Recrystallized from ethyl acetate.

5-(p-chlorobenzoyl)- (IVd) and 5-(m-nitrobenzoyl)-tetrazole (IVe) (Table II). Similarly the interaction of lactonitrile acetate (VIIf) and aluminum azide gave methyl-5-tetrazolylcarbinol (VIIIf), the analog of lactic acid. Oxidation of VIIIf in the usual manner provided the corresponding analog of pyruvic acid, 5-acetyltetrazole (IVf), though in relatively low yield (20%). On the other hand reagents such as potassium permanganate, manganese dioxide, and chromic anhydride all failed to accomplish this oxidation.

The 5-aroyltetrazoles are colorless acidic solids which are soluble in aqueous alkali, alkali carbonates, and bicarbonates. They dissolve in warm (60–70°) polyphosphoric acid and are recovered unchanged on dilution with water. However, they are degraded to benzoic acids (IX) by the action of hot, 70% sulfuric acid. All of the 5-aroyltetrazoles exhibit prominent absorption maxima in the region of 245 mμ – 272 mμ (*cf.* Table I).

The interaction of IVa and excess phenylmagnesium bromide gave diphenyl-5-tetrazolylcarbinol (X) in 64% yield. A Wolff-Kishner reduction of IVa afforded 5-benzyltetrazole (XI) in 76% yield whereas a photochemical reduction of IVa in isopropyl alcohol produced 1,2-bis(5-tetrazolyl)-1,2-diphenyl-1,2-ethanediol (XII) in 70% yield. The correctness of structure XII is indicated by elementary analysis and infrared data (no carbonyl absorption, strong hydroxyl absorption at 2.93μ and 3.03μ).

The principal product of a Schmidt reaction on IVd in polyphosphoric acid proved to be 5-tetrazolecarbox(p-chloroanilide) (XIIIb). The course and extent of migration was established from the observation that hydrolysis of the crude reaction product with concentrated hydrochloric acid followed by acetylation gave p-chloroacetanilide in 75% yield. The reaction mixture yielded, in addition, a small quantity (*ca.* 7%) of p-chlorobenzoic acid which might be attributed to the migration of the 5-tetrazolyl group. However, in view of the ease with which IVd is degraded by mineral acid it is highly probable that the formation of IX stems from the presence of unreacted IVd in the crude amide.



A Schmidt reaction on IVa was observed to pursue a similar course. Thus, successive hydrolysis and acetylation of the initial reaction product gave acetanilide in 66% yield. However, no benzoic acid was detected in this case. Moreover, recrystallization of the crude reaction product in a subsequent experiment gave 5-tetrazolecarboxanilide (XIIIa) in 51% yield.

The oximation of IVa yielded a single isomer (XIV) which was subjected to a Beckmann rearrangement. The product, obtained in 50% yield, was identical with XIIIa. Apparently, the more stable of the two possible oximes is that in which the hydroxyl group is *syn* to the tetrazole ring.

A more efficacious route to 5-acetyltetrazole (IVf) and its homologs is currently under investigation. Accordingly, a discussion of the properties of IVf is deferred until a broader spectrum of 5-acyltetrazoles has been examined. However, it seems pertinent to report at this time that methyl-5-tetrazolyl-carbinol (VIIIf) is an acceptable substrate for lactic dehydrogenase, as determined by histochemical methods.

EXPERIMENTAL[12]

Phenoxyacetophenones (I). The procedure used for the preparation of Ia is that described by Yates *et al.*[13] The extension of this method to the synthesis of Ib and c required only the substitution of benzene for ether as the solvent.

α-Phenoxy-4-bromoacetophenone (Ib). Off-white plates from methanol (50% yield), m.p. 92–93°.

Anal. Calcd. for $C_{14}H_{11}O_2Br$: C, 57.75; H, 3.81; Br, 27.45. Found: C, 57.80; H, 3.82; Br, 27.48.

α-Phenoxy-4-nitroacetophenone (Ic). Yellow plates from 95% ethanol (35% yield), m.p. 114–115°.

Anal. Calcd. for $C_{14}H_{11}NO_4$: C, 65.36; H, 4.31; N, 5.45. Found: C, 65.48; H, 4.44; N, 5.49.

α-Bromo-α-phenoxyacetophenones (II). The bromoethers were prepared according to the method of Knott.[8] In accord with the prior report, it was observed that IIa, m.p. 68–70° (lit. m.p. 72°), is an unstable solid and recrystallization leads to a considerable loss of product. Therefore, upon completion of the bromination of Ib and c in chloroform, the solvent was removed under reduced pressure and the residue, IIb or IIc, was used directly in the synthesis of the ketone (IV) (*vide infra*).

α-Azido-α-phenoxyacetophenone (IIIa). To a solution of 5.8 g. of IIa (0.02 mole) in 40 ml. of acetone diluted with 15 ml. of water was added 1.3 g. of sodium azide (0.02 mole) and the mixture heated to boiling and held at this temperature for 3 min. The clear solution was quickly cooled to room temperature and poured on ice. The product was collected and recrystallized from aqueous ethanol to give 3.3 g. of a white solid, m.p. 79–81°. An additional 0.7 g. of material, m.p. 75–80°, was deposited from the filtrate on standing; total yield 80%. Two recrystallizations from 95% ethanol provided an analytical sample in the form of white needles, m.p. 83–84°.

Anal. Calcd. for $C_{14}H_{11}N_3O_2$: C, 66.39; H, 4.38; N, 16.59. Found: C, 66.51; H, 4.35; N, 16.71.

5-Aroyltetrazoles (IV) *Method A.* The conversion of Ib to 5-(*p*-bromobenzoyl)-tetrazole (IVb) without isolation of the corresponding intermediates, IIb and IIIb, is presented as an example typical of the method. To a solution of 8.7 g. of Ib (0.03 mole) in 40 ml. of chloroform, cooled to 0° by an external salt-ice mixture, was added, dropwise with stirring, a solution of 5.3 g. of bromine (0.033 mole) in 12 ml. of chloroform. The temperature of the reaction mixture was maintained at 5–8° during the course of bromination. The solvent was next removed *in vacuo* and the residue dissolved in 50 ml. of glacial acetic acid to which 6.0 g. of sodium azide (0.092 mole) was added. The mixture was slowly brought to reflux and maintained at this temperature for 1.5 hr. The inorganic salts were removed by filtration, and the filtrate was evaporated in a stream of air to a thick paste. To this dark residue was added 50 ml. of water, followed by sufficient 10% sodium hydroxide to render the oily mixture alkaline. The tarry alkali-insoluble material was removed by filtration through Celite and the filtrate acidified with concentrated hydrochloric acid. The mixture was then placed in a refrigerator for 24 hr. and the product collected, wt. 3.8 g. (50% yield), m.p. 167–171°. Two recrystallizations from a mixture of benzene and ethyl acetate gave colorless plates, m.p. 176–177° (*cf.* Table I for analysis).

Alternate synthesis of IVa *from* IIIa. A solution of 2.5 g. of IIIa (0.01 mole) in 25 ml. of glacial acetic acid, containing 2.5 g. of sodium azide (0.039 mole) was carefully brought to boiling and then gently refluxed for 2 hr. Using the same procedure described above for the isolation of IVb, there was obtained 1.0 g. (58% yield) of 5-benzoyltetrazole, m.p. 138–140°. A single recrystallization from benzene gave white plates, m.p. 140–141°.

Mandelonitrile acetates (VIId and e). Of the α-acetoxypropionitriles employed in this work, only VIId and e, to our knowledge, have not, previously, been described.

To a cold solution of 42.3 g. of *p*-chlorobenzaldehyde (0.3 mole) in 150 ml. of glacial acetic acid was added, with stirring and intermittent cooling to maintain a temperature of approximately 25° C., 27.3 g. of potassium cyanide. The solution was, then, treated with 66.0 g. of acetic anhydride (0.65 mole) and the mixture heated to 60° with stirring for 0.5 hr. The dark solution was poured on ice and the resulting oil extracted with ether. The extract was washed successively with a saturated solution of sodium bicarbonate and water, then dried over magnesium sulfate. Distillation gave 49.0 g. (78%) yield of product, b.p. 104–107°/0.5 mm (m.p. 31–32°). Redistillation gave a water-white product, b.p. 121–122°/0.6 mm.

Anal. Calcd. for $C_{10}H_8NClO_2$: C, 57.29; H, 3.86. Found: C, 57.49; H, 3.98.

The same procedure applied to *m*-nitrobenzaldehyde affords a solid product when the reaction mixture is poured on ice. The crude material was dissolved in 95% ethanol, treated with Norit, and on cooling, VIIIe was deposited in the form of white needles, yield 82%, m.p. 75–76°.

Anal. Calcd. for $C_{10}H_8N_2O_4$: C, 54.55; H, 3.66. Found: C, 54.47; H, 3.64.

Methyl- and aryl-5-tetrazolylcarbinols (VIII). The procedure described by Behringer and Kohl[11] for the preparation of VIIIa from mandelonitrile acetate was extended to the present study. The conversion of VIId to VIIId is presented as a typical example of this transformation.

A solution of 13.5 g. of anhydrous aluminum chloride in 150 ml. of dry tetrahydrofuran was added, all at once, to a suspension of 19.5 g. of sodium azide (0.3 mole) in 50 ml. of tetrahydrofuran. The mixture was stirred at room temperature for 1 hr., then, a solution of 21.0 g. of *p*-chloromandelonitrile acetate (0.1 mole) in 50 ml. of tetrahydrofuran was introduced, and the yellow suspension stirred under gentle reflux for 20 hr. The reaction vessel was cooled externally with an ice-salt bath, acidified with 75 ml. of 6*N* hydrochloric acid, and, then, evaporated to dryness *in vacuo*. The dry residue was triturated with three-250 ml. portions of hot acetone and the filtered extract evaporated to dryness *in vacuo*. The light tan residue crystallized from a mixture of ethyl acetate and petroleum ether (65–110°), wt. 8.0 g. (38% yield), m.p. 183–188°. Two recrystallizations from this same solvent provided an analytical sample, m.p. 188–189°.

5-Aroyltetrazoles IV. *Method B.* The oxidation of VIII was effected in each case with a solution of sodium dichromate in dilute sulfuric acid. The conversion of VIIIa to IVa is considered typical. A suspension of 9.0 g. of finely divided VIIIa (0.05 mole) in 55 ml. of 2*N* sulfuric acid containing 9.0 g. of sodium dichromate dihydrate (0.03 mole) was carefully heated to 80–85° with vigorous stirring and held at this

(12) All melting points are uncorrected. Analyses were performed by Micro-Tech Laboratories, Skokie, Ill.

(13) P. Yates, D. G. Farnum, and G. H. Stout, *J. Am. Chem. Soc.*, **80**, 196 (1956).

temperature for 0.5 hr. The reaction mixture was cooled, the product was collected and crystallized from benzene, wt. 6.5 g. (77% yield), m.p. 137–138°, alone or when admixed with a sample of IVa prepared by Method A.

5-Acetyltetrazole (IVf). To a solution of 4.5 g. of sodium dichromate dihydrate (0.015 mole) in 27 ml. of 3*N* sulfuric acid was added 5.0 g. of the carbinol (VIIIf) (0.044 mole). The mixture was vigorously stirred while the temperature was carefully raised to 75–80° and maintained for 0.5 hr. The solution was evaporated to dryness *in vacuo* and the residue triturated with three 50-ml. portions of hot acetone. Evaporation of the acetone left a colorless sirup which was subjected to vacuum sublimation. The sublimate was recrystallized from a mixture of ether–petroleum ether (60–110°) to give 1.0 g. (20% yield) of product in the form of small white needles, m.p. 89–90°.

Anal. Calcd. for $C_3H_4N_4O$: C, 32.14; H, 3.60; N, 50.00. Found: C, 32.25; H, 3.67; N, 50.64.

Acid degradation of IVd. A solution of 250 mg. of IVd (1.2 mmoles) was suspended in 10 ml. of 70% sulfuric acid and the mixture refluxed for 0.5 hr. The cooled solution was diluted with 30 ml. of water, extracted with ether, and the extract dried over magnesium sulfate. Evaporation of the ether left a residue which crystallized from aqueous ethanol, wt. 160 mg. (85% yield), m.p. 240–241° alone or when admixed with an authentic sample of *p*-chlorobenzoic acid.

Diphenyl-5-tetrazoylcarbinol (X). A solution of 7.5 g. of IVa (0.043 mole) in 50 ml. of dry tetrahydrofuran was added, dropwise with stirring, to a solution of phenylmagnesium bromide, prepared from 33.8 g. of bromobenzene (0.22 mole) and 5.3 g. of magnesium (0.22 g. atom) in 200 ml. of anhydrous ether. The reaction mixture was stirred under reflux for 1 hr. and, then, poured on a mixture of ice and sulfuric acid. The ether phase was drawn off and the aqueous layer extracted with three portions of ether. The combined extracts were dried over magnesium sulfate, then, concentrated to a crystalline mass under reduced pressure. Crystallization from a mixture of ether–petroleum ether (65–110°) gave 7.0 g. (64% yield) of product, in the form of colorless needles, m.p. 172–174° dec.

Anal. Calcd. for $C_{14}H_{12}N_4O$: C, 66.65; H, 4.80; N, 22.21. Found: C, 66.83; H, 5.14; N, 22.78.

5-Benzyltetrazole (XI). A solution of 3.48 g. of IVa (0.02 mole) in 50 ml. of diethylene glycol containing 1.68 g. of potassium hydroxide (0.03 mol.) and 5 ml. of 85% hydrazine hydrate was refluxed for 2 hr., the water being removed by a take-off condenser. The reflux period was continued until the evolution of nitrogen subsided (*ca.* 1.5). The glycol was removed *in vacuo*, the residue dissolved in water and acidified with concentrated hydrochloric acid. The reaction mixture was chilled and the product collected, wt. 2.12 g., m.p. 122–124°. A second crop, wt. 0.35 g., m.p. 122–123°, was deposited from the filtrate on standing. The combined solids, amounting to 2.47 g. (76% yield), were crystallized from benzene to give colorless needles, m.p. 125–126° (lit.[14] 125.5–126°).

1,2-Bis(5-tetrazolyl)-1,2-diphenyl-1,2-ethanediol (XII). A solution of 3.48 g. of IVa (0.02 mole) in 200 ml. of isopropyl alcohol, contained in a quartz flask, was placed in a window of the laboratory. After two weeks the solid, which began to appear after the third day, was collected, wt. 1.5 g., m.p. 181–182° dec. The filtrate was returned to the window for a total elapsed time of 30 days and a second crop of material, wt. 1.0 g., m.p. 181–182° dec., was obtained; total yield 2.5 g. (71%).

(14) J. S. Mihina and R. M. Herbst, *J. Org. Chem.*, **15**, 1082 (1950).

Anal. Calcd. for $C_{16}H_{14}N_8O_2$: C, 54.85; H, 4.03; N, 31.99. Found: C, 54.65; H, 4.02; N, 31.99.

5-Tetrazolecarboxanilide (XIIIa). To a suspension of 1.80 g. of IVa (0.01 mol.) in 25 g. of polyphosphoric acid was added, all at once, 2.0 g. of sodium azide (0.03 mol.) and the mixture heated to 55–60° for 2.5 hr. The semisolid mass was diluted with a mixture of ice and water and the solid collected. The crude product was twice recrystallized from aqueous ethanol to give 1.0 g. (51% yield) of anilide in the form of pale yellow needles, m.p. 219–220° dec. The product was dissolved in 10% sodium hydroxide, treated with Norit and reprecipitated by the addition of concentrated hydrochloric acid. The solid was collected and recrystallized from aqueous ethanol to give colorless needles, m.p. 220–221° dec.

Anal. Calcd. for $C_8H_7N_5O$: C, 50.79; H, 3.73; N, 37.02. Found: C, 50.96; H, 3.95; N, 36.70.

A sample of the crude amide (0.7 g.), obtained according to the procedure described above was refluxed for 1 hr. with 20 ml. of 70% sulfuric acid. The solution was extracted with three portions of ether. No solid remained on evaporation of the dried extract. The aqueous phase was made alkaline with 50% sodium hydroxide and extracted with three portions of benzene. Evaporation of the dried extract left an oily residue which was suspended in 10% sodium hydroxide and treated with 1.0 ml. of acetic anhydride. The mixture was chilled and the product collected, wt. 0.33 g. (2.45 mmoles), m.p. 110–112°, alone or when admixed with acetanilide. The crude reaction product, therefore, contained, at least, 66% XIIIa.

Beckmann rearrangement of 5-benzoyltetrazole oxime (XIV). The preparation of the oxime (87% yield, m.p. 219–220°) was carried out in the usual way.

Anal. Calcd. for $C_8H_7N_5O$: C, 50.78; H, 3.73; N, 37.02. Found: C, 50.80; H, 3.98; N, 37.59.

A mixture of 700 mg. of the oxime (3.7 mmoles) in polyphosphoric acid, prepared from 20 g. of phosphorus pentoxide and 12 ml. of 85% *ortho* phosphoric acid, was heated at 100° for 4 hr. Ice was then added to the cooled mixture and the product collected. The filter cake was dissolved in aqueous sodium carbonate, treated with Norit, and the filtrate was acidified. The product was collected, wt. 250 mg., m.p. 214–216°. The filtrate was extracted with three portions of chloroform and the dried extract was evaporated to dryness *in vacuo* to give an additional 110 mg. of product (total yield 51%), m.p. 215–216°. A mixed melting point with the product of the Schmidt reaction showed no depression.

Schmidt reaction on IVd. To a suspension of 2.09 g. of ketone (IVd) (0.01 mol.) in 25 g. of polyphosphoric was added, portionwise over a period of 6 hr., 2.0 g. of sodium azide (3.01 mmoles) at a temperature of 55–60°. The mixture was diluted with ice and the product collected, wt. 1.93 g. The crude amide (1.93 g.) was suspended in 100 ml. of concentrated hydrochloric acid and the mixture refluxed for 24 hr. A solid was deposited, on cooling, which was combined with a small amount of material which had sublimed into the condenser, wt. 180 mg., m.p. 230–240° (with sublimation). Two recrystallizations from aqueous alcohol gave shiny plates, m.p. 240–241° which failed to depress the melting point of *p*-chlorobenzoic acid.

The original acid filtrate was evaporated to dryness, the residue made alkaline with 10% sodium hydroxide and treated with 3 ml. of acetic anhydride. The solid was collected and sucked dry, wt. 1.16 g., m.p. 174–177° (lit., *p*-chloroacetanilide, 176–177°). Accordingly, it is concluded that the crude product of rearrangement contains at least 75% 5-tetrazolecarbox(*p*-chloroanilide) (XIIIb).

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