Chemstrand Research Center, Inc.

Heterocyclic Intermediates for the Preparation of Thermally Stable Polymers (1)

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A number of heterocyclic intermediates useful for the preparation of thermally stable polymers are reported with their physical properties. Most of the intermediates described are new compounds, while others have been reported previously but without physical properties. Improvements in the syntheses of several of the substances reported earlier are given.

In recent years several thermally stable polymers containing heterocycles have been prepared; in the main the heterocycles of these polymers have been formed during the polycondensation reaction. The author (2) has reported ordered heterocycle copolymers in which a heterocycle was preformed prior to polymerization. This paper gives the method of preparation and the properties of a number of heterocyclic intermediates suitable for the preparation of ordered copolymers containing oxadiazole, phenyl triazole, thiazole, and benzimidazole rings. A few comments concerning each of the syntheses used for these compounds follows. (The various syntheses of the dinitro compounds are illustrated by routes A-G; the melting points and analyses of the various nitro and amino materials prepared are given in Tables I, II, III and IV.)

The classical route to 1,3,4-oxadiazoles is the thermal or chemical dehydration of a dihydrazide (3); a variation reported (4) for this route is the *in situ* preparation and chemical dehydration of a dihydrazide in oleum. More recently the preparation of 1,3,4-oxadiazoles by the action of carboxylic acid chlorides or anhydrides on 5-substituted tetrazoles has been reported (5).

Because of the interaction of nitro groups with aniline, the synthesis of dinitrotriazoles from a dinitro hydrazide and aniline in phosphorus pentoxide could not be employed. The reaction of a nitro *N*-phenylbenzimidyl chloride with a nitrobenzhydrazide, however, was found to be effective for the desired dinitro-4-phenyl-1,2,4-triazole; the reaction of *N*-phenylimidyl chlorides on 5-substituted tetrazoles has been reported (6) to lead to the formation of 4-phenyl-1,2,4-triazoles and presumably could be used to prepare the dinitro compounds.

The synthesis of intermediates containing thiazole and bithiazole rings followed the route of the classical Hantzch reaction of an α-haloacetophenone with a thioamide. A great improvement in the yield and the purity of the product resulted from the use of dimethylacetamide (DMAc) as solvent for the reaction. The preparation of the thiazolo[4,5-d]-thiazoles from the reaction of an aromatic aldehyde and dithiooxamide is patterned after the work of Johnson, *et al.* (7); again, the use of DMAc as solvent effected improvements in the yield and the purity of products.

All of the diamines reported here, except for XV and XVI, were prepared from the corresponding dinitro intermediate. However, the classical syntheses of benzimidazoles are of little value in preparing the dinitro intermediates corresponding to XV and XVI; a possible exception might be the reported (8) dehydrogenation and cyclization of a Schiff base effected by lead tetraacetate. In the case of XV and XVI the very convenient synthesis for amino-substituted benzimidazoles using polyphosphoric acid as a condensing agent (9) was available. It was found convenient to use the free tetraamine in this synthesis instead of the hydrochloride used by other workers (10) in their preparation of the unhydrated benzimidazole diamine (XVI).

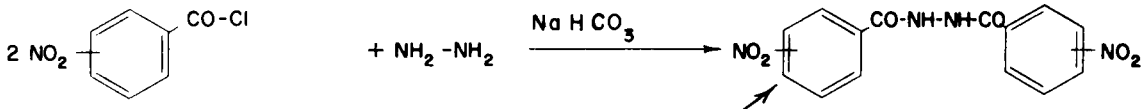
The synthesis of the diacid (XVIII) from isophthalic acid and hydrazine sulfate in oleum was reported (4) but attempts to repeat this work produced only a mixture of XVIII and poly-1,3,4-oxadiazole diacids. These results are not surprising in view of the synthesis of poly-1,3,4-oxadiazoles from equimolar quantities of reactants under similar experimental conditions (11).

Diamines corresponding to the dinitro compounds were obtained in nearly quantitative yields by catalytic hydrogenation or by reduction with stannous chloride and HCl. Route A was used to prepare a tetranitro oxadiazole intermediate (I) by replacing a nitrobenzoyl chloride with 3,4-dinitrobenzoyl chloride; the oxadiazole tetraamine (I') was obtained *via* reduction of I. Route G was used to prepare two diamines (XV and XVI) without resort to a corresponding dinitro intermediate. A diacid and the corresponding diacid chloride were prepared as shown in Route H. (Note: The compounds reported appear to be new except for those cases where literature references are cited.)

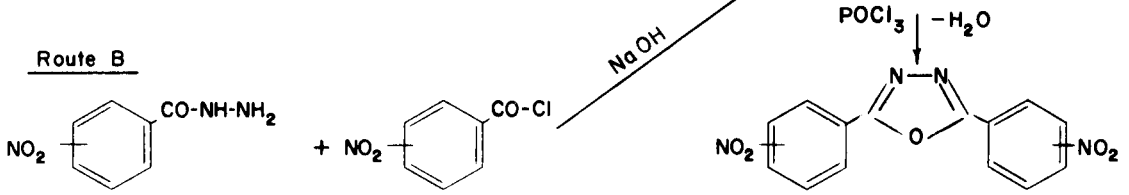
ROUTES TO DI - AND TETRAFUNCTIONAL HETEROCYCLIC INTERMEDIATES

Preparation of 1,3,4 - Oxadiazoles

Route A



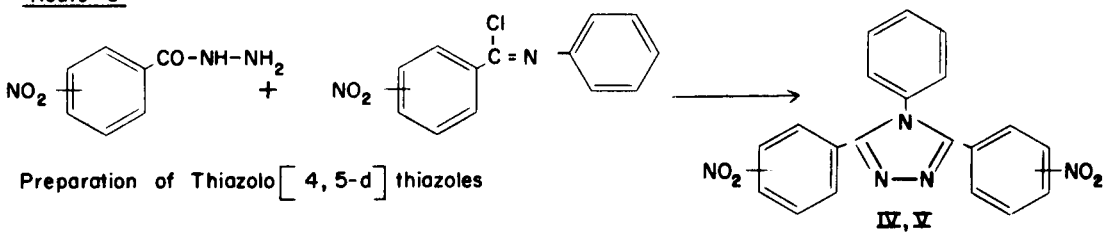
Route B



II , III

Preparation of 4-Phenyl-1,2,4-triazoles

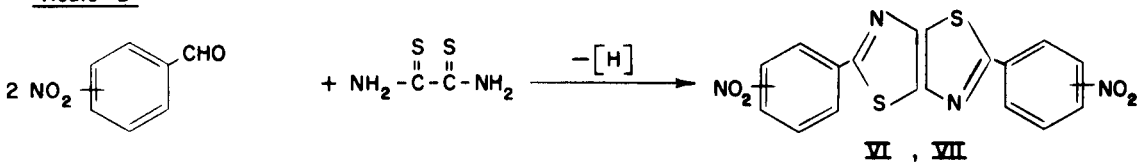
Route C



IV, V

Preparation of Thiazolo[4, 5-d]thiazoles

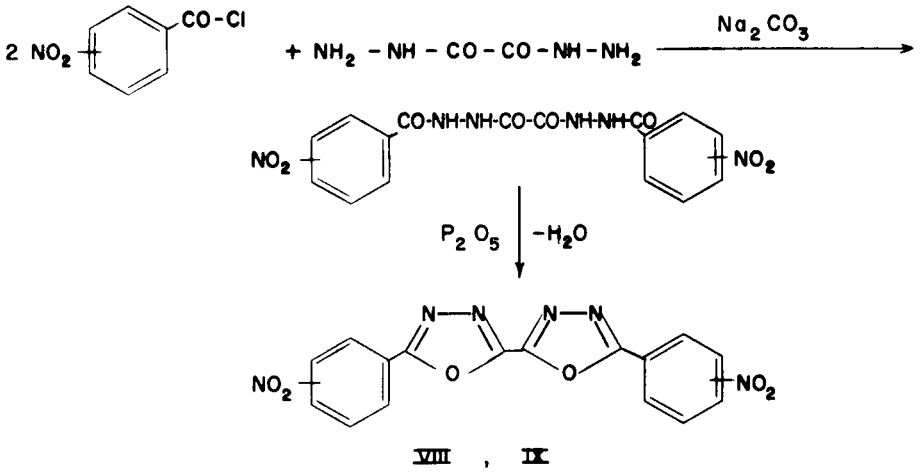
Route D



VI , VII

Preparation of bis-1,3,4-Oxadiazoles

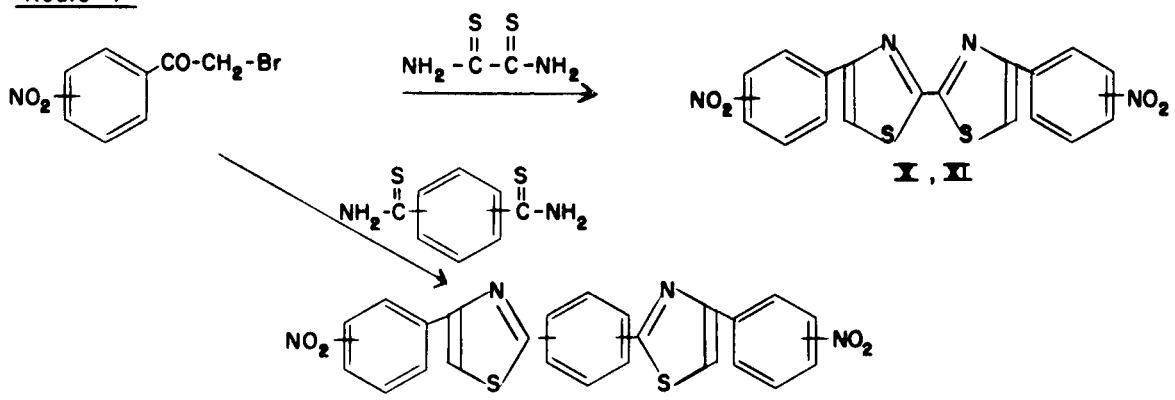
Route E



VIII , IX

Preparation of 2,4 - Thiazoles

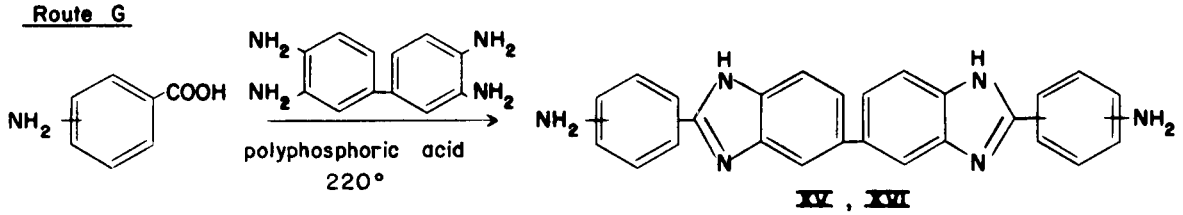
Route F



X , XI

Preparation of 2,2' -5,5' - Bibenzimidazoles XII , XIII , XIV

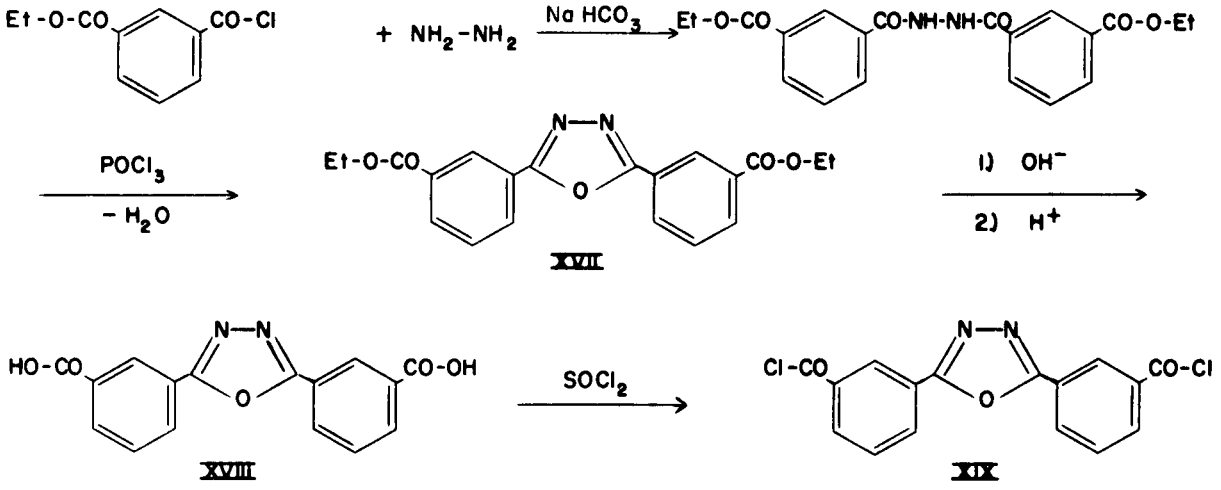
Route G



XV , XVI

Preparation of 1,3,4 - Oxadiazole Diacid and Diacid Chloride

Route H



XVII

XVIII

XIX

TABLE I

Di- and Tetranitro Intermediates Containing A Single Heterocycle

	Compound	M.P.° (Uncor.)	*Anal.* Calcd.	Found
I	2,5-bis(3,4-Dinitrophenyl)-1,3,4-oxadiazole	230-232	C, 41.78 H, 1.50 N, 20.90	C, 41.98, 41.75 H, 2.05, 2.30 N, 20.43, 20.38
II	2,5-bis(*m*-Nitrophenyl)-1,3,4-oxadiazole	234-236	C, 53.85 H, 2.58 N, 17.95	C, 53.75, 53.58 H, 2.76, 2.37 N, 17.74, 17.70
III	2,5-bis(*p*-Nitrophenyl)-1,3,4-oxadiazole	319-321 (a)	C, 53.85 H, 2.58 N, 17.95	C, 53.80, 53.38 H, 2.70, 2.50 N, 18.19, 17.89
IV	3,5-bis(*m*-Nitrophenyl)-4-phenyl-1,2,4-triazole	283-286	C, 62.02 H, 3.36 N, 18.09	C, 62.30, 62.08 H, 3.60, 3.56 N, 17.80, 18.07
V	3,5-bis(*p*-Nitrophenyl)-4-phenyl-1,2,4-triazole	272-274 (b)	C, 62.02 H, 3.36 N, 18.09	C, 62.22, 62.28 H, 3.35, 3.37 N, 18.01, 17.95
VI	2,5-bis(3-Nitrophenyl)thiazolo[4,5-d]thiazole	320-322 (c)	C, 50.00 H, 2.10 N, 14.58	C, 50.13, 50.05 H, 2.40, 2.35 N, 14.27, 14.01
VII	2,5-bis(4-Nitrophenyl)thiazolo[4,5-d]thiazole	413 (dec.) (d)	C, 50.00 H, 2.10 N, 14.58	C, 50.12, 50.38 H, 2.35, 2.23 N, 14.53, 14.51

(a) The reported melting points are: (4), 301-302°; (5), 309-310°; (12), 302°. The color of III was reported (5) to be yellow-brown, although in this work it was found to be a clear bright yellow. (b) Lit. (12) m.p. 270°. (c) Lit. (7) m.p. 317-321°. (d) Lit. (7) m.p. 400-405° dec.

TABLE II

Di- and Tetraamines Containing A Single Heterocycle

	Compound	M.P.° (Uncor.)	*Anal.* Calcd.	Found
I'	2,5-bis(3,4-Diaminophenyl)-1,3,4-oxadiazole	277-281	C, 59.54 H, 5.00 N, 29.77	C, 59.63, 59.55 H, 5.31, 5.15 N, 29.82, 29.62
II'	2,5-bis(*m*-Aminophenyl)-1,3,4-oxadiazole	257-258	C, 66.69 H, 4.80 N, 22.22	C, 66.16, 66.15 H, 4.99, 5.11 N, 22.10, 22.09
III'	2,5-bis(*p*-Aminophenyl)-1,3,4-oxadiazole	260-262 (a)	C, 66.69 H, 4.80 N, 22.22	C, 66.63, 66.39 H, 4.82, 4.83 N, 22.29, 22.10
IV'	3,5-bis(*m*-Aminophenyl)-4-phenyl-1,2,4-triazole	343-346	C, 73.37 H, 5.24 N, 21.39	C, 73.17, 72.83 H, 5.58, 5.41 N, 21.48, 21.40
VI'	2,5-bis(3-Aminophenyl)-thiazolo[4,5-d]thiazole	287-289	C, 59.25 H, 3.73 N, 17.27	C, 59.04, 59.04 H, 3.99, 3.82 N, 16.79, 16.74
VII'	2,5-bis(4-Aminophenyl)-thiazolo[4,5-d]thiazole	302-305 (b)	C, 59.25 H, 3.73 N, 17.27	C, 59.17, 59.00 H, 3.96, 3.83 N, 16.84, 16.82

(a) Reported (4) but no m.p. or analysis given. (b) Lit. (7) m.p. 301-303°.

TABLE III

Dinitro Intermediates Containing Two Heterocycles

	Compound	M.P.° (Uncor.)	*Anal.* Calcd.	Found
VIII	5,5'-Di(3-nitrophenyl)-bis-1,3,4-oxadiazolyl-(2,2')	275-278	C, 50.53 H, 2.10 N, 22.11	C, 50.59, 50.47 H, 2.25, 2.22 N, 22.17, 22:16
IX	5,5'-Di(4-nitrophenyl)-bis-1,3,4-oxadiazol-(2,2')	359-361	C, 50.53 H, 2.10 N, 22.11	C, 50.58, 50.75 H, 2.26, 2.29 N, 22.16, 22.30
X	4,4'-bis(*m*-Nitrophenyl)-2,2'-bithiazole	349-351	C, 52.68 H, 2.45 N, 13.65	C, 52.68, 52.79 H, 2.57, 2.62 N, 13.51, 13.44
XI	4,4'-bis(*p*-Nitrophenyl)-2,2'-bithiazole	327-329 (a)	C, 52.68 H, 2.45 N, 13.65	C, 53.24, 53.27 H, 2.48, 2.32 N, 13.35, 13.35
XII	*m*-bis(4-*p*-Nitrophenyl-thiazol-2-yl)benzene	271-272	C, 59.25 H, 2.90 N, 11.52	C, 59.07, 59.04 H, 2.89, 3.14 N, 11.07, 11.29
XIII	*p*-bis(4-*m*-Nitrophenyl-thiazol-2-yl)benzene	309-311	C, 59.25 H, 2.90 N, 11.52	C, 59.09, 59.07 H, 2.99, 3.11 N, 11.05, 11.32
XIV	*p*-bis(4-*p*-Nitrophenyl-thiazol-2-yl)benzene	339-341	C, 59.25 H, 2.90 N, 11.52	C, 59.28, 59.21 H, 2.99, 3.00 N, 11.35, 11.24

(a) Lit. (13) m.p. 310-312° dec.

TABLE IV

Diamines Containing Two Heterocycles

	Compound	M.P.° (Uncor.)	*Anal.* Calcd.	Found
VIII'	5,5'-Di(3-Aminophenyl)-bis-[1,3,4-oxadiazolyl]-(2,2')	339-341	C, 60.00 H, 3.77 N, 26.23	C, 59.27 H, 3.74, 3.58 N, 25.76
IX'	5,5'-Di(4-Aminophenyl)-bis-[1,3,4-oxadiazolyl]-(2,2')	400 (dec.)	C, 60.00 H, 3.77 N, 26.23	C, 59.14 H, 3.89, 3.83 N, 25.28
X'	4,4'-bis(*m*-Aminophenyl)-2,2'-bithiazole	243-245	H, 4.02 N, 15.98	H, 4.11, 3.66 N, 15.92, 15.65
XI'	4,4'-bis(*p*-Aminophenyl)-2,2'-bithiazole	284-286 (a)	C, 61.67 H, 4.02 N, 15.98	C, 61.55, 61.24 H, 4.07, 4.09 N, 15.92, 15.82
XII'	*m*-bis(4-*p*-Aminophenyl)thiazol-2-yl benzene	230-232	C, 67.58 H, 4.25 N, 13.14	C, 67.98, 67.75 H, 4.37, 4.40 N, 12.80, 12.60
XIV'	*p*-bis(4-*p*-Aminophenylthiazol-2-yl)benzene	280-282	H, 4.25 N, 13.14	H, 4.54 N, 12.70, 12.52
XV	2,2'-bis(*m*-Aminophenyl)-5,5'bibenzimidazole	297-299 (b)	C, 74.98 H, 4.84 N, 20.18	C, 74.61, 74.39 H, 4.85, 4.82 N, 20.08, 20.02
XVI	2,2'-bis(*p*-Aminophenyl)-5,5'-bibenzimidazole EtOH	407-411 (c)	C, 72.70 H, 5.67 N, 18.17	C, 73.07, 73.37 H, 5.50, 5.72 N, 18.10, 18.91

(a) Lit. (13) m.p. 272-275°. (b) Sublimed sample. The recrystallized sample had m.p. 308-311°. (c) Lit. (10) m.p. 321-322° for a sample heated at 290-300° in a vacuum below 1 mm. Hg for 1.5 hours. The sample whose m.p. and analysis are given was recrystallized from ethanol; the analysis corresponds to one molecule of ethanol of crystallization.

EXPERIMENTAL (14)

The preparation of the nitro intermediates is illustrated with a single example taken from Routes A-F. The reduction of all of the nitro intermediates to the corresponding diamines or tetraamine is illustrated by an example of a catalytic reduction and an example of a reduction with stannous chloride.

Preparation of Nitro Intermediates.

Route A.

(I). A solution of 32 g. of 3,4-dinitrobenzoyl chloride in 30 ml. of tetrahydrofuran (THF) was added to a rapidly stirred solution of 8.5 g. of hydrazine sulfate in 200 ml. of water; 25 g. of sodium bicarbonate was added and the mixture was stirred for ten minutes. The product, *N,N'*-bis(3,4-dinitrobenzoyl)hydrazine, had a m.p. of 278-280°, yield 30 g., 89%.

Anal. Calcd. for $C_{14}H_8N_6O_{10}$: C, 39.99; H, 1.92; N, 19.99. Found: C, 39.87, 40.12; H, 2.20; N, 19.63, 19.40.

A portion of the above hydrazide (25.3 g.) was refluxed with 250 ml. of phosphorus oxychloride for 3 hours; excess phosphorus oxychloride was removed and the product (I) was washed with water and dried, yield, 19.0 g., 78%.

Route B.

(II). A solution of 8.4 g. of *m*-nitrobenzoyl chloride in 25 ml. of THF was added to a rapidly stirred mixture of 8.1 g. of *m*-nitrobenzhydrazide (Eastman), 150 ml. of water, and 1.9 g. of sodium hydroxide contained in a Blendor jar. The mixture was stirred for 15 minutes, filtered, and the product, *N,N'*-bis(*m*-nitrobenzoyl)hydrazine, dried, yield; 9.59 g., (65%), m.p. 244-246°.

Anal. Calcd. for $C_{14}H_{10}N_4O_6$: N, 16.95. Found: N, 16.76, 16.97.

The above hydrazide was refluxed with 360 ml. of phosphorus oxychloride for 16 hours; the excess phosphorus oxychloride was stripped off and the residue was washed with water and dried. A pure product (II) was obtained after recrystallization from 2-methoxyethanol, yield, 8.5 g., 93%.

Route C.

(IV). *N*-Phenyl-*m*-nitrobenzimidyl chloride was prepared by refluxing 43 g. of *N*-*m*-nitrobenzanilide (m.p. 153-154°) with 300 ml. of thionyl chloride for 3.5 hours. The excess thionyl chloride was distilled and the residue distilled at 190-195°/1 mm; 17.1 g. of imidyl chloride was collected.

A solution of 17.1 g. *N*-phenyl-*m*-nitrobenzimidyl chloride in 95 ml. of dimethylacetamide (DMAc) was refluxed with 11.7 g. of *m*-nitrobenzhydrazide (Eastman) for 2.5 hours; 14.3 g. of IV separated upon cooling, (57%).

Route D.

(VI). A solution of 61 g. of *m*-nitrobenzaldehyde, 24 g. of dithioxamide, and 100 ml. DMAc was refluxed for thirty minutes; the solution was cooled to 70° and filtered. The crude product, 36.9 g. m.p. 314-317°, was recrystallized from 800 ml. of nitrobenzene to yield 28.9 g. of VI (38%).

Route E.

(VIII). To a suspension of 5 g. of oxalic dihydrazide, and 11 g. of sodium carbonate in 150 ml. of water contained in a Blendor jar was added 19 g. of *m*-nitrobenzoyl chloride in 25 ml. of THF. The mixture was stirred for 10 minutes and the product was collected and dried, yield, 16.9 g., 98%. The m.p. of the hydrazide intermediate after recrystallization from DMAc was 312-314°.

A mixture of 9 g. of the above hydrazide and 9 g. of phosphorus pentoxide was heated to 250°, cooled, and poured into water (yield, 6.7 g.). The crude product, m.p. 235-238°, was recrystallized from 60 ml. of dimethylformamide (DMF) to yield 4.5 g. of pure VIII, (51%).

Route F.

(XII). A solution of 225 g. of *p*-nitrophenacyl bromide in 250 ml. DMAc was added dropwise to a solution of 94.4 g. of dithioisophthalamide (Penisular Chem. Research, Inc.) in 320 ml. of DMAc. Crystals precipitated from solution during the mildly exothermic reaction. The mixture was stirred on a steam bath for one hour, cooled and the product collected. Two recrystallizations from 1.5 liters of DMAc gave 151 g. of XII, (65%).

Preparation of Amine Intermediates.

(I'). A mixture of 4.2 g. of I, 30 g. of stannous chloride hydrate, 50 ml. of concentrated hydrochloric acid, and 50 ml. of ethanol was refluxed for one hour. The mixture was cooled and the precipitated hydrochloride was collected and washed with ethanol. The precipitate was dissolved in hot water and the solution was filtered. Upon addition of dilute sodium hydroxide solution, the free base (I') was obtained; this was washed and dried to yield 2 g. of I'.

(II'). A mixture of 6.24 g. of II, 190 ml. of 2-methoxyethanol, and 0.1 g. of Adam's catalyst was placed in a 300 ml. heavy-walled bottle. The bottle was attached to a hydrogeneration apparatus (Parr Instrument Co.) and the system was pressurized with hydrogen to 48 psi. The contents of the flask was heated to 60° and was shaken for 3 hours. The reaction mixture was filtered hot to remove the catalyst; 3.1 g. of II' crystallized from solution upon cooling. A small additional crop of crystals was obtained upon addition of water to the mother liquor.

Route G.

(XIV). A mixture of 10.7 g. of 3,3'-diaminobenzidine (Koppers, recrystallized from water-methanol), m.p. 176-177°, 13.7 g. of *m*-aminobenzoic acid (Eastman), and 150 ml. of polyphosphoric acid (Matheson) was stirred and heated at 220° for 3.5 hours under a nitrogen atmosphere. The solution was cooled and poured into water and stirred rapidly in a Blendor jar; the product was collected on a filter, then soaked in 10% sodium carbonate solution overnight. The crude product, after washing and drying, had a m.p. of 292-300°. Recrystallization from ethanol afforded 15 g. of material, m.p. 306-309°; recrystallization from 2-methoxyethanol gave XV, m.p. 308-311° (72%).

Preparation of Diacid Intermediates.

Route H.

(XVII-XIX). A solution of 9 g. of *m*-carbethoxybenzoyl chloride b.p. 134-134°/5.6 mm., prepared according to the procedure of Cohen *et al.* (15), in 20 ml. THF was added with rapid stirring to 2.6 g. hydrazine sulfate in 100 ml. of water; 8 g. of sodium bicarbonate was added and the mixture was stirred for 10 minutes. The product, *N,N'*-bis(*m*-carbethoxybenzoyl) hydrazide, m.p. 185-187°, was obtained in 7.7 g. yield, (100%).

Anal. Calcd. for $C_{20}H_{20}O_6N_2$: C, 62.47; H, 5.25; N, 7.29. Found: C, 62.81; H, 5.42; N, 7.15, 7.33.

The hydrazide, 19.2 g., was converted to the corresponding oxadiazole by the action of refluxing phosphorus oxychloride. Excess phosphorus oxychloride was distilled and the residue was recrystallized from ethanol to give XVII, m.p. 133-134°.

Anal. Calcd. for $C_{20}H_{18}O_5N_2$: C, 65.55; H, 4.96; N, 7.65. Found: C, 65.76, 65.60; H, 5.05; N, 7.69, 7.54.

A mixture of 17.8 g. of XVII, 6 g. of potassium hydroxide and 100 ml. of water was refluxed for one hour. The resulting solution was cooled, filtered, and made acid with hydrochloric acid; 12.7 g. of product, m.p. 368-371° (lit. (4), > 300°), was collected, (85%).

Anal. Calcd. for $C_{16}H_{10}O_5N_2$: N, 9.03. Found: N, 8.60.

A mixture of 12.4 g. of XVIII and 300 ml. of thionyl chloride (Eastman) was refluxed for 8 hours. The thionyl chloride was distilled and the residue was recrystallized from 100 ml. dry toluene to yield 9.3 g. of XIX, m.p. 173-175° (67%).

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