$$nMe_2Si(OCMe_2COOMe)_2 + nHOOC(CH_2)_2COOH \longrightarrow (Me_2SiO)_n + 2nMe_2C(OH)COOMe + nCO(CH_2)_2CO.$$

Methyl α-hydroxyisobutyrate (b.p. 136–17°, $n_D^{20}$ 1.4107–1.4111) was collected in over 90% yield. The non-volatile product (a pasty solid) was digested with two 50 ml. portions of cold *n*-hexane. The insoluble portion (19.8 g., 99% of the theoretical yield) was succinic anhydride [microscopic needles that sublime readily above 100°, m.p. 116° (uncorr.) after crystallization from benzene or toluene]. The *n*-hexane solution was concentrated, filtered from a little more succinic anhydride, and then the remaining solvent was distilled. The limpid oil that remained (12.6 g., 85% of the theoretical amount) was identified as an impure mixture of dimethylsiloxane polymers by refractive index and viscosity characteristics.

Similarly, with bis(α-carbethoxyethoxy)dimethylsilane, nearly quantitative yields of ethyl lactate, succinic anhydride, and polydimethylsiloxane were obtained.

SCHENECTADY, N. Y.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND THE LABORATORY OF PHARMACEUTICAL CHEMISTRY OF THE UNIVERSITY OF NEW MEXICO]

# Imidazo[4,5-*d*]pyridazines. I. Synthesis of 4,7-Disubstituted Derivatives[1]

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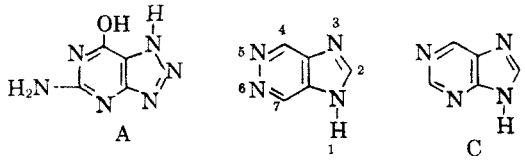
*Received January 6, 1958*

Eleven new imidazo[4,5-*d*]pyridazines were prepared. These include the 4,7-disubstituted compounds: dichloro , monochloromonohydroxy-, diamino-, dimercapto-, and various substituted mercaptans. The adenine analog, 4-aminoimidazo[4,5-*d*]pyridazine has been prepared. In addition, methyl 4(5)-imidazolecarboxylate-5(4)-phenylhydrazide and imidazole-4,5-dicarboxylic acid bismethylhydrazide were prepared. Attempts to prepare 4,5-diamino-3-pyridazone resulted in mixtures of 5-amino-4-chloro-3-pyridazone and 4-amino-5-chloro-3-pyridazone.

The antitumor activity of 8-azaguanine (5-amino-7-hydroxy-*v*-triazolo[*d*]pyrimidine), A[3], encouraged the present authors to prepare the imidazo-[4,5-*d*]pyridazine ring system, B, in which the two nitrogen atoms are adjacent in the six-membered ring with the five-membered imidazole ring remaining the same as in the parent purine ring, C. The work of Robins *et al.*[4] has resulted in additional active compounds.



A B C

After 4,7-dihydroxyimidazo[4,5-*d*]pyridazine, IV, was prepared, the work of Baker,[5] Jones,[6] Gardner, *et al.*,[7] came to our attention. Compound IV is the only imidazo[4,5-*d*]pyridazine reported here that has been previously described. 4,7-Dichloroimidazo-[4,5-*d*]pyridazine, V, was obtained only in low yield by treatment of IV with phosphorus oxychloride in dimethylaniline. Attempts to prepare compound V under a variety of other chlorinating conditions were unsuccessful. Very small amounts of 4(7)-chloro-7(4)-hydroxyimidazo[4,5-*d*]pyridazine, Va, were sometimes obtained.

In view of the difficulties in obtaining V it appeared desirable to obtain 4,7-diaminoimidazo[4,5-*d*]pyridazine from the 4,7-bismethylmercaptoimidazo[4,5-*d*]pyridazine. Compound VII was obtained from 4,7-dimercaptoimidazo[4,5-*d*]pyridazine, VI, by methylation in alkali. Compound VI was obtained from compound IV by thiation with phosphorus pentasulfide in dry pyridine in good yield. When compound VI was treated with one mole of methyl iodide in alkaline solution 4(7)-methylmercapto-7(4)-mercaptoimidazo[4,5-*d*]pyridazine, IX, was obtained in good yield. Compound IX when dethiated with Raney nickel gave 4-methylmercaptoimidazo[4,5-*d*]pyridazine, X. Compound X was converted to the adenine analog, 4-aminoimidazo[4,5-*d*]pyridazine, XXIV, with ethanolic ammonia in a bomb at 200°. 4(7)-Ethylmercapto-7(4)-mercaptoimidazo[4,5-*d*]pyridazine, XI, was obtained from VI by treatment with equal molar proportions of ethyl iodide in alkaline solution. However, when VI was treated with excess ethyl iodide in limited alkaline solution 4,7-bisethylmercapto-1-ethylimidazo[4,5-*d*]pyridazine hydrogen iodide, XII, was obtained. Compound XII upon treatment with sodium hydroxide solution produced the free base, XIII.

(1) Supported in part by the National Institutes of Health, grant number C-2653.

(2) In partial fulfillment of the requirements of the Master of Science degree in chemistry at the University of New Mexico.

(3) G. W. Kidder, V. C. Dewey, R. E. Parks, Jr., and G. L. Woodside, *Science*, **109**, 511 (1949).

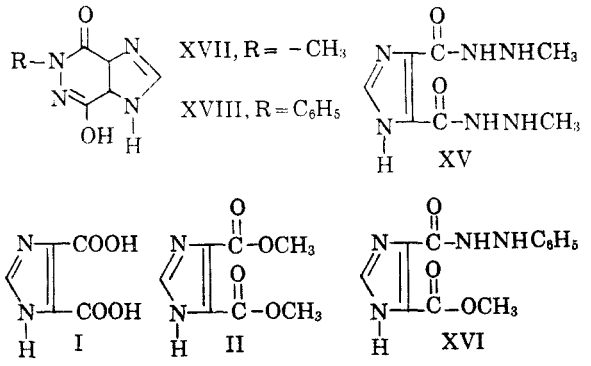
(4) R. K. Robins and G. H. Hitchings, *J. Am. Chem. Soc.*, **77**, 2256 (1956); **78**, 973 (1956); R. K. Robins, F. W. Furcht, A. D. Grauer, and J. W. Jones, *J. Am. Chem. Soc.*, **78**, 2418 (1956); R. K. Robins, J. W. Jones, and H. H. Lin, *J. Org. Chem.*, **21**, 695 (1956); R. K. Robins, *J. Am. Chem. Soc.*, **78**, 784 (1956).

(5) B. R. Baker, private communications.

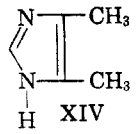
(6) R. G. Jones, *J. Am. Chem. Soc.*, **78**, 159 (1956).

(7) T. S. Gardner, F. A. Smith, E. Wenis, and J. Lee, *J. Org. Chem.*, **21**, 530 (1956).

Attempts to prepare 5-methyl-7-hydroxyimidazo-[4,5-*d*]-4-pyridazone, XVII, from the imidazole-4,5-dicarboxylic acid bismethylhydrazide, XV, by refluxing with 10% hydrochloric acid were unsuccessful. Instead the hydrazide was cleaved into the imidazole-4,5-dicarboxylic acid, I. When dimethyl imidazole-4,5-dicarboxylate, II, was treated with phenylhydrazine, methyl 4(5)-imidazolecarboxylate-5(4)-phenylhydrazide, XVI, was obtained. This compound when heated with 10% hydrochloric acid was cleaved to I, instead of cyclization to XVIII.

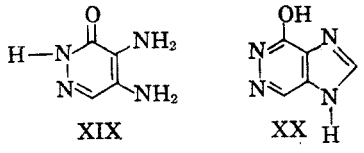



Attempts to prepare the 4,5-bishydroxymethylimidazole from the diester, II, by lithium aluminum hydride reduction in boiling diglyme[8] produced 4,5-dimethylimidazole, XIV. Micovic and

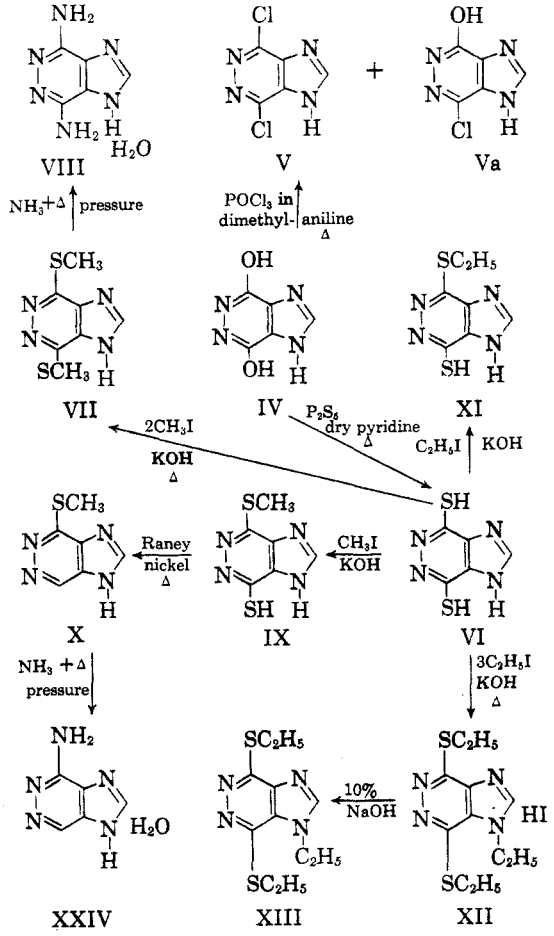



Mihailovic[9] cited several instances of an ester group being reduced to a methyl group under forcing conditions.

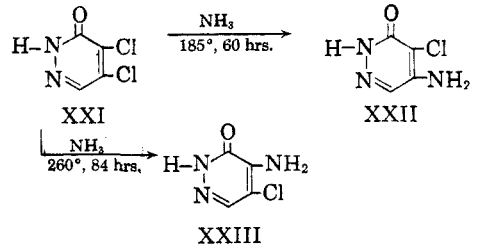
In order to prepare monosubstituted imidazo[4,5-*d*]pyridazines, it appeared advisable to close the five-membered ring last. This necessitated the preparation of appropriately substituted pyridazines. It was thought 4,5-diamino-3-pyridazone, XIX, could be readily cyclized to 4-hydroxyimidazo[4,5-*d*]pyridazine, XX. 4,5-Dichloro-3-pyridazone was




prepared by the method of Mowry.[10] Compound XXI upon treatment with a large excess of ammonia in absolute ethanol at temperatures of 185–260° produced a mixture of two isomeric compounds, XXII and XXIII. An unequivocal assignment of structure has not been made. However the difficulty of replacing a chlorine atom on the pyridazine ring is indicated by Kuraishi.[11]




Reaction Scheme I: Imidazo[4,5-*d*]pyridazines




Reaction Scheme II: Pyridazines

## EXPERIMENTAL

Carbon and hydrogen analyses are by Weiler and Strauss, Oxford, or Department of Chemistry, New Mexico Highlands University. Nitrogen analyses are by Weiler and Strauss and this laboratory. All melting points were determined in a copper melting point block and are uncorrected.

*Imidazole-4,5-dicarboxylic acid* (I).[12] This compound was

(8) H. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **78**, 2582 (1956).

(9) V. M. Micovic and M. L. Mihailovic, *Lithium Aluminum Hydride in Organic Chemistry*, Serbian Academy of Science, Monographs Vol. **237**, Izdavacko Preduzece, Beograd, 1955, p. 37.

(10) D. T. Mowry, *J. Am. Chem. Soc.*, **75**, 1909 (1953).

(11) T. Kuraishi, *Pharm. Bull.*, **4**, 497 (1956).

(12) This compound was later purchased from Eastman Organic Chemical, compound number 5988.

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA OF IMIDAZO[4,5-*d*]PYRIDAZINES AND RELATED COMPOUNDS

| Compound | No. | 0.1*N* HCl | | Distilled Water | | *N* NaOH | | Absolute Ethanol | |
|---|---|---|---|---|---|---|---|---|---|
| | | $\lambda_{max}$ | $\epsilon\times10^{-3}$ | $\lambda_{max}$ | $\epsilon\times10^{-3}$ | $\lambda_{max}$ | $\epsilon\times10^{-3}$ | $\lambda_{max}$ | $\epsilon\times10^{-3}$ |
| III | | 266 | 9.80 | | | 274 | 5.28 | | |
| IV | | | | | | 262 | 3.08 | | |
| V | | | | | | 260 | 6.04 | 250–2 | 6.9 |
| VI | | | | | | 256 | 17.10 | | |
| VII | | | | | | | | 246, 282–4 | 12.20, 9.90 |
| VIII (anhyd.) | | | | | | | | 226, 234–6 | 22.10, 22.26 |
| IX | | | | | | | | 250, 270, 326–32 | 12.25, 12.20, 10.80 |
| X | | | | | | | | 242, 280 | 12.30, 7.25 |
| XI | | | | | | | | 252, 272, 330 | 10.60, 11.50, 12.10 |
| XII | | | | | | | | 272, 294–308, 252–6 | 9.80, 5.37, 7.87 |
| XIII | | | | | | | | 226, 252, 270, 304 | 15.50, 17.30, 20.65, 9.58 |
| XV | | | | | | 282–6 | 7.90 | | |
| XVI | | | | | | 266 | 8.31 | | |
| XXI | | 290–2 | 3.74 | 288–90 | 3.50 | 303–06 | 4.85 | | |
| XXII (m.p. 350–4°) | | | | 284–6 | 6.10 | 280 | 4.53 | | |
| XXIII (mp. 292–4°) | | | | 286–92 | 11.20 | 290 | 2.85 | | |
| XXIV | | | | | | | | 260 | 4.33 |

made according to the procedure of Snyder, Handrick, and Brooks.[13] The melting point was 278–280°.

*Anal.* Calcd. for $C_5H_4N_2O_4$: C, 38.40; H, 2.56. Found: C, 38.60; H, 2.86.

*Dimethyl imidazole-4,5-dicarboxylate* (II).[14] This compound was prepared according to procedure *b* of Baxter and Spring.[15] Further purification from hot water gave colorless crystals, melting at 207°.

*Anal.* Calcd. for $C_7H_8N_2O_4$: C, 45.56; H, 4.37. Found: C, 45.76; H, 4.46.

*Imidazole-4,5-dicarboxylic acid bishydrazide* (III). Dimethyl imidazole-4,5-dicarboxylate, II, (14.8 g., 0.08 mole) was dissolved in 250 ml. of methanol on a steam bath. To this solution was added 15 g. (0.468 mole) of hydrazine. After refluxing on the steam bath for 0.5 hr., a white solid was obtained which upon cooling yielded 14.5 g. (99%) of product, m. p. >400°. The crude product was recrystallized from hot water, giving white crystals, m. p. >400°.

*Anal.* Calcd. for $C_5H_8N_6O_2$: C, 32.61; H, 4.65; N, 45.64. Found: C, 32.30; H, 4.31; N, 45.80.

*4,7-Dihydroxyimidazo[4,5-d]pyridazine* (IV). This compound was prepared in a manner similar to that described by Jones[6] method B. A crude yield of 91% was obtained with a melting point greater than 400°. The crude product was purified by dissolving it in 10% sodium hydroxide and precipitating it with glacial acetic acid. The resulting white solid melted above 400°.

*Anal.* Calcd. for $C_5H_4N_4O_2$: C, 39.48; H, 2.56; N, 36.84. Found: C, 39.45; H, 2.99; N, 37.20.

*4,7-Dichloroimidazo[4,5-d]pyridazine* (V). Two grams (0.0133 mole) of dried, finely ground 4,7-dihydroxyimidazo-[4,5-*d*]pyridazine was suspended in 75 ml. of freshly distilled *N,N*-dimethylaniline. To this suspension was added 125 ml. of phosphorus oxychloride and the mixture was refluxed for 2.5 hr. The excess phosphorus oxychloride was distilled off under reduced pressure. The black residue was poured cautiously on ice and the aqueous solution was made basic to litmus with 50% sodium hydroxide and allowed to cool. The *N,N*-dimethylaniline was removed by a siphon. A feathery phosphate salt appeared which was removed by filtration. The aqueous filtrate was then acidified to *p*H 1 with concentrated hydrochloric acid and continuously extracted for 48 hr. with ether, yielding 0.41 g. (17%) of product, m.p. 215–220°. The product was recrystallized twice from absolute ethanol, producing white crystals, m.p. 240.5–241.5°.

*Anal.* Calcd. for $C_5H_2N_4Cl_2$: C, 31.77; H, 1.07; N, 29.64. Found: C, 31.74; H, 1.24; N, 29.48.

A side product Va was obtained in very small yield which was only slightly soluble in absolute ethanol and proved to be 4(7)-chloro-7(4)-hydroxyimidazo[4,5-*d*]pyridazine, Va, which decomposed 358–360° in a sealed tube under nitrogen.

*Anal.* Calcd. for $C_5H_3N_4ClO$: C, 35.50; H, 1.80. Found: C, 36.00; H, 1.98.

*4,7-Dimercaptoimidazo[4,5-d]pyridiazine* (VI). 4,7-Dihydroxyimidazo[4,5-*d*]pyridazine, IV, (10.0 g., 0.0656 mole) was mixed with 1000 ml. of freshly dried pyridine. To this suspension was added 90 g. of phosphorus pentasulfide and refluxed for 10 hr. The pyridine was removed under reduced pressure. To the residue was added slowly in a hood, 2 l. of crushed ice with continuous shaking. The mixture was then heated on a steam bath for 8 hr. The solution was filtered while hot. To the cooled filtrate was added concentrated hydrochloric acid until a tan precipitate was formed, yield 9.62 g. (79%) of product m.p. 307–311°. The crude product was further purified by dissolving it in 10% sodium hydroxide and precipitating with glacial acetic acid, m.p. 309–311.°

*Anal.* Calcd. for $C_5H_4N_4S_2$: C, 32.60; H, 2.19; N, 30.41. Found: C, 32.70; H, 2.32; N, 30.35.

*4,7-Bismethylmercaptoimidazo[4,5-d]pyridazine* (VII). 4,7-Dimercaptoimidazo[4,5-*d*] pyridazine, VI, (10.0 g., 0.0544 mole) was dissolved in 100 ml. of 1.25*N* potassium hydroxide solution. To this solution was added 24.9 g. (0.175 mole) of methyl iodide and it was refluxed on a steam bath for 1 hr. Upon filtration 8.38 g. (73%) of the product, m.p. 195–200° was obtained. The crude product was recrystallized from absolute ethanol, yielding a white solid, m.p. 243–245°.

*Anal.* Calcd. for $C_7H_8N_4S_2$: C, 39.60; H, 3.79; N, 26.39. Found: C, 39.87; H, 3.63; N, 26.96.

*4,7-Diaminoimidazo[4,5-d]pyridazine* (VIII). 4,7-Bismethylmercaptoimidazo[4,5-*d*]pyridazine, VII, (2.15 g., 0.01 mole) was placed in a 500 ml. stainless steel bomb with 250 ml. of a saturated solution of ammonia in absolute ethanol. The ammoniacal ethanolic solution contained approximately 18 g. of ammonia. The bomb was heated at

(13) H. R. Snyder, R. G. Handrick, and L. A. Brooks, *Org. Syntheses*, **Coll. Vol. III,** 471 (1955).

(14) This compound was later supplied through the courtesy of Dr. Howard W. Bond, National Cancer Institute, Bethesda 14, Md.

(15) R. A. Baxter and F. S. Spring, *J. Chem. Soc.*, 232 (1945).

195–205° for 26 hr. The solution was removed from the bomb, heated on a steam bath and filtered while hot. The filtered solution was evaporated on a steam bath to dryness. The reaction yielded 0.75 g. (44%) of product, m.p. 265–270°. On a Kofler micro hot stage, water was given off at approximately 200°. The crude product was recrystallized twice from ethanol, m.p. 314–316°. This proved to be the hydrate.

*Anal.* Calcd. for $C_5H_8N_6O$: C, 35.71; H, 4.80. Found: C, 36.35; H, 4.93.

Upon recrystallization of the crude product from absolute ethanol the anhydrous compound, in the form of white crystals, was obtained, m.p. 340–342°.

*Anal.* Calcd. for $C_5H_6N_6$: N, 55.98. Found: N, 55.82.

*4(7)-Methylmercapto-7(4)-mercaptoimidazo[4,5-d]pyridazine* (IX). 4,7-Dimercaptoimidazo[4,5-*d*]pyridazine, VI, (3 g., 0.0163 mole) was dissolved in 36 ml. of *N* potassium hydroxide. To this solution was added 2.4 g. (0.0169 mole) of methyl iodide and the solution was shaken until the methyl iodide layer disappeared. To the cooled solution glacial acetic acid was added until a precipitate appeared. The crude yield was 2.15 g. (67%), m.p. 300–308°. The crude product was recrystallized from absolute ethanol giving a light brown solid, m.p. 331–333°.

*Anal.* Calcd. for $C_6H_6N_4S_2$: C, 36.34; H, 3.05; N, 28.26. Found: C, 36.49; H, 3.60; N, 28.47.

*4-Methylmercaptoimidazo[4,5-d]pyridazine* (X). 4(7)-Methylmercapto-7(4)-mercaptoimidazo[4,5-*d*]pyridazine, IX, (2.5 g., 0.0126 mole) was added to 150 ml. of absolute ethanol. To this mixture was added approximately 3 g. of Raney nickel and the mixture was refluxed for 5.5 hr. The Raney nickel was removed through the use of a Büchner funnel and washed rapidly with 500 ml. of hot ethanol. Upon evaporation of the ethanol 0.86 g. (41%) of crude product was obtained. The crude product was recrystallized twice from absolute ethanol, consisting of a light tan solid, m.p. 230–232°.

*Anal.* Calcd. for $C_6H_6N_4S$: C, 43.36; H, 3.63; N, 33.70. Found: C, 43.22; H, 3.72; N, 33.71.

*4(7)-Ethylmercapto-7(4)-mercaptoimidazo[4,5-d]pyridazine* (XI). 4,7-Dimercaptoimidazo[4,5-*d*]pyridazine, VI, (4.3 g., 0.0234 mole) was dissolved in 30 ml. of *N* potassium hydroxide. To this solution was added 4.38 g. (0.028 mole) of ethyl iodide. The same procedure was followed as in the preparation of compound IX. The yield was 2.6 g. (53%), m.p. 269–274°. The crude product which upon recrystallization from absolute ethanol gave a light tan solid which melted at 279–282°.

*Anal.* Calcd. for $C_7H_8N_4S_2$: C, 39.66; H, 3.80; N, 26.39. Found: C, 40.29; H, 4.32; N, 26.47.

*4,7-Bisethylmercapto-1-ethylimidazo[4,5-d]pyridazine hydrogen iodide* (XII). 4,7-Dimercaptoimidazo[4,5-d]pyridazine, VI, (9 g., 0.049 mole) was dissolved in 75 ml. of 0.85 *N* potassium hydroxide (0.0637 mole). To this solution was added 21.2 g. (0.149 mole) of ethyl iodide and it was refluxed on a steam bath for 4.5 hr. The solid was filtered, resulting in 8.1 g. (42%) of product, m.p. 245–248°. The crude product was recrystallized twice from absolute ethanol, m.p. 256–259°. The light tan crystals gave a positive ionic halogen test.

*Anal.* Calcd. for $C_{11}H_{17}N_4S_2I$: C, 33.34; H, 4.32; N, 14.14. Found: C, 33.86; H, 4.41; N, 13.90.

*4,7-Bisethylmercapto-1-ethylimidazo[4,5-d]pyridazine* (XIII). A portion of the 4,7-bisethylmercapto-1-ethylimidazo[4,5-*d*]pyridazine hydrogen iodide, XII, was dissolved in water. To this solution was added, dropwise, 10% sodium hydroxide until a white precipitate appeared. Upon filtration and drying, the solid melted at 121–123°. After recrystallization from absolute ethanol and sublimation at 100° (0.15 mm.) it melted at 122–124°.

*Anal.* Calcd. for $C_{11}H_{16}N_4S_2$: C, 49.22; H, 6.01; N, 20.88. Found: C, 49.01; H, 6.01; N, 21.15.

*4,5-Dimethylimidazole* (XIV). Dimethyl imidazole-4,5-dicarboxylate, II, (3 g., 0.0163 mole) was placed in a Soxhlet thimble. Lithium aluminum hydride (11.4 g.) was dissolved in approximately 250 ml. of diglyme (diethylene glycol dimethyl ether). The lithium aluminum hydride slurry was refluxed in a Soxhlet extractor with the ester for 96 hr. Wet ether was added to destroy the excess lithium aluminum hydride. The ethereal solution was extracted with two 300-ml. portions of water. On standing an inorganic solid formed in the aqueous solution which was removed. The aqueous solution was then extracted with ether in a liquid-liquid extractor for one week. The ethereal solution was dried and the ether evaporated to yield 0.45 g. (29%) of a brown residue, m.p. 95–112°. The crude product was sublimed twice at room temperature and 0.5 mm. Hg to give white needles, m.p. 118.5–119.5°. This has been previously reported.[16]

*Anal.* Calcd. for $C_5H_8N_2$: C, 62.47; H, 8.39; N, 29.15. Found: C, 62.00; H, 8.29; N, 29.60.

*Imidazole-4,5-dicarboxylic acid bismethylhydrazide* (XV). To a solution of dimethyl imidazole-4,5-dicarboxylate, II, (14.8 g., 0.08 mole) in 250 ml. of methanol was added 20.7 g. (0.468 mole) of methylhydrazine and the solution refluxed on a steam bath for 3 hr. The reaction mixture was allowed to stand in an ice box for three days. A white granular precipitate was removed, amounting to 8.25 g. (48%), m.p. 187–192°. White needles were obtained upon recrystallization from water, m.p. 210–212°.

*Anal.* Calcd. for $C_7H_{12}N_6O_2$: C, 39.60; H, 5.60; N, 39.61. Found: C, 39.54; H, 5.68; N, 39.54.

Compound XV (7 g., 0.033 mole) was refluxed with 100 ml. of 10% hydrochloric acid for 3.5 hr. This product proved to be imidazole-4,5-dicarboxylic acid by analysis and mixed melting point.

*Methyl 4(5)-imidazolecarboxylate-5(4)-phenylhydrazide* (XVI). Dimethyl imidazole-4,5-dicarboxylate, II, (3.68 g., 0.02 mole) was dissolved in 90 ml. of methanol and to this solution was added 12 g. (0.112 mole) of phenylhydrazine. The solution was refluxed on a steam bath for 0.5 hr., and a tan solid was removed, yield 1.95 g. (37%), m.p. 244–246°. The crude product gave white crystals after recrystallization three times from large amounts of methanol, m.p. 254–255°.

*Anal.* Calcd. for $C_{12}H_{12}N_4O_3$: C, 54.90; H, 4.57; N, 21.53. Found: C, 54.50; H, 4.76; N, 21.74.

Compound XVI (1.0 g., 0.0038 mole) was refluxed with 15 ml. of 10% hydrochloric acid for 2 hr. This product proved to be imidazole-4,5-dicarboxylic acid by analysis and mixed melting point.

*4,5-Dichloro-3-pyridazone* (XXI). This product was prepared by the method of Mowry,[16] giving a melting point range of 202–203°.

*4 or 5-Amino-5 or 4-chloro-3-pyridazone* (XXII). 4,5-Dichloro-3-pyridazone, XXI (30 g., 0.183 mole), was placed in a large stainless steel bomb. To this was added 400 ml. of liquid ammonia and 1200 ml. of absolute ethanol. The bomb was rocked and heated to 185° for 60 hr. The residue was removed and the solution was evaporated to dryness. The yield was 15.7 g. which contained a large portion of ammonium chloride. The crude product gave white crystals after recrystallization three times from absolute ethanol, m.p. 350–354°.

*Anal.* Calcd. for $C_4H_4N_3OCl$: C, 33.00; H, 2.77; N, 28.87; Cl, 24.36. Found: C, 33.38; H, 3.06; N, 29.00; Cl, 24.53.

*4 or 5-Amino-5 or 4-chloro-3-pyridazone* (XXIII). 4,5-Dichloro-3-pyridazone, XXI (49 g., 0.29 mole), was placed in a large stainless steel bomb. To this was added 400 ml. of liquid ammonia and 1200 ml. of absolute ethanol. The bomb was rocked for 84 hr. at 260°. The residue was removed and the solution was evaporated to dryness. The yield was 18.8 g. which contained a large portion of ammonium chloride. The solid was extracted in a Soxhlet extractor with dry chloroform for three weeks. Upon evaporation of the chloro-

(16) R. G. Fargher and F. L. Pyman, *J. Chem. Soc.*, **115**, 232 (1919).

form 1.8 g. of solid was obtained, m.p. 260–265°. White crystals were obtained upon recrystallization from absolute ethanol, m.p. 292–294°.

*Anal.* Calcd. for $C_4H_4N_3OCl$: C, 33.00; H, 2.77; N, 28.87. Found: C, 33.55; H, 3.21; N, 28.25.

*4-Aminoimidazo[4,5-d]pyridazine* (XXIV). 4-Methylmercaptoimidazo[4,5-*d*]pyridazine, X (1.3 g., 0.008 mole), was placed in a 500 ml. stainless steel bomb with 150 ml. of ethanol containing approximately 9 g. of ammonia. The same procedure was followed as in the preparation of compound VIII. The yield was 1.0 g. (87%) of crude product. On a Kofler micro hot stage, water was given off at approximately 215°. The crude product was recrystallized twice from ethanol. A tan solid was obtained with a decomposition point of approximately 315°.

*Anal.* Calcd. for $C_5H_7N_3O$: N, 45.73. Found: N, 45.53.

Infrared spectra were determined on the following compounds: V, VI, VII, VIII (anhydrous), IX, X, XI, XII, XIII, XV, XVI, and XXIV.

ALBUQUERQUE, N. M.

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

# Dibenzopentalene[1]

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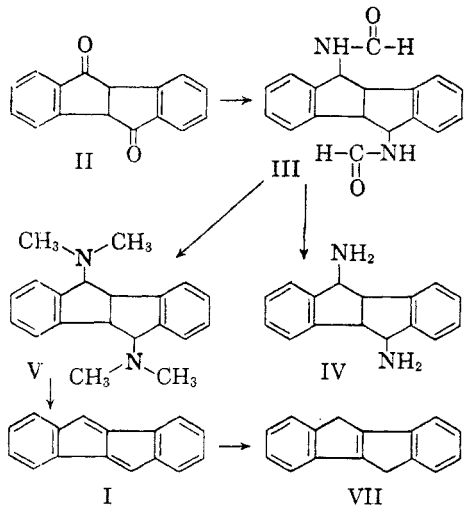
*Received April 7, 1958*

A new synthesis of 1,2:5,6-dibenzopentalene is described.

In 1952 Blood and Linstead[3] described a synthesis of the hydrocarbon 1,2:5,6-dibenzopentalene-(I). This red compound is the simplest relative of pentalene which has been prepared. Bicyclo-[3.3.0]octa-1,4-diene-3,6-dione, which might be considered to be the ketonic form of a pentalenediol, has been prepared[4] but could not be induced to enolize. The present work describes a new synthesis of I and some of its reactions.

The key intermediate in the present sequence was 9,12-diphensuccinadione(II) which was prepared in 50–70% yield by cyclization of *meso*-diphenylsuccinic acid with hot, concentrated sulfuric acid. Treatment of II with formamide and formic acid yielded the bisformyl derivative (III) in 69% yield. Acid hydrolysis of this amide gave the base, 9,12-diaminodiphensuccindane(IV) which was characterized as the dipicrate. This diamine was readily methylated with formic acid and formaldehyde to give the ditertiary amine(V). V was extremely hydroscopic and formed a dipicrate which was obtained as a dihydrate. The water of crystallization was removed by prolonged heating under reduced pressure. The ditertiary amine(V) was also obtained directly from III by treatment with a solution of formic acid in formalin. Treatment of V with methyl iodide yielded the methiodide(VI).




When an aqueous solution of VI was basified at room temperature, two molecular equivalents of trimethylamine were eliminated giving the blood red dibenzopentalene(I) in 30% yield. The usual procedure for the Hofmann elimination reaction involving treatment of the methiodide with silver oxide followed by thermal decomposition of the quaternary hydroxide proved to be rather ineffective in this case as the product tended to coat the insoluble oxide and prevent further reaction.

The identity of I was established by mixture melting point, comparison of infrared and ultraviolet spectra, and comparison of x-ray diffraction patterns of this substance with an authentic sample prepared according to the method of Blood and Linstead.[3] Reduction of I with zinc and acetic acid gave 10-diphensuccindene(VII) in 77% yield. The mixture melting point and infrared spectrum of VII were identical with that of an authentic sample.[5]

Dibenzopentalene polymerized fairly readily. When I was heated at the reflux temperature with glacial acetic acid, an amorphous yellow product was obtained which was insoluble in toluene, benzene, chloroform, ether, or alcohol. A similar prod-

(1) Supported in part by a grant from the Rohm & Haas Co., Philadelphia.

(2) Abstracted from the M.S. Thesis of Miss Chen C. Chuen, University of Minnesota, January 1954.

(3) C. T. Blood and R. P. Linstead, *J. Chem. Soc.*, 2263 (1952).

(4) C. T. Blood and R. P. Linstead, *J. Chem. Soc.*, 2255 (1952).

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