

Synthesis of Perhydro-1,2,5,6-tetrazocine and Derivatives

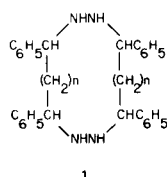
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Synthetic routes to the title compounds were explored. 1,2,5,6-Tetraacetylperhydro-1,2,5,6-tetrazocine (**6**, 36%) was produced from ethylene glycol bis-*p*-toluenesulfonate and the potassium salt of 1,2-bis(*N,N'*-diacetylhydrazino)ethane in refluxing mesitylene. Its acid-catalyzed hydrolysis led to perhydro-1,2,5,6-tetrazocine (**9**), an air-sensitive, crystalline solid, the first reported unsubstituted tetraaza-cyclooctane and the first example of an unsubstituted macrocycle incorporating two or more endocyclic hydrazino groups. 1,2-Bis(hydrazino)ethane (**4**) and diisobutyl oxalate in refluxing dimethylformamide gave 1,4-diamino-2,3-diketopiperazine (**11**) rather than 3,4-diketoperhydro-1,2,5,6-tetrazocine (**12**). The acid-catalyzed reaction of benzil with **4** gave 3,4,7,8-tetraaza-1,2,9,10-tetraphenyl-2,8-decadien-1,10-dione (**20**).

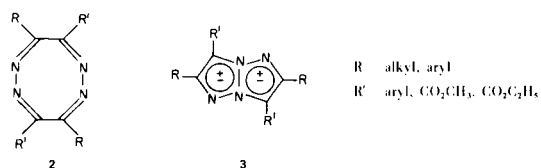
Although numerous macrocyclic polyoxa and polyazacycloalkanes have been described, few macrocycles incorporating two or more endocyclic, unsubstituted hydrazino groups are known (**1**). Cyclic dihydrazines (**1**, $n = 6,8,10$) were synthesized *in situ* by hydrogenation



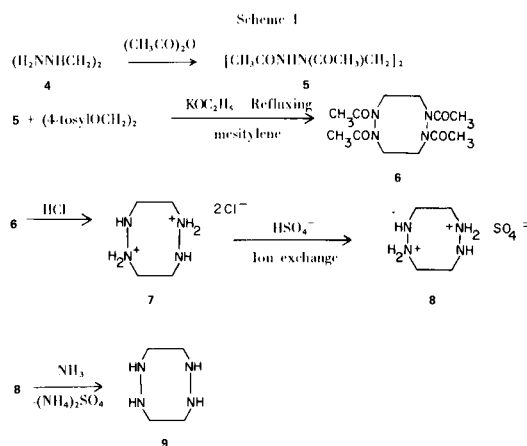
of the parent azines and represent the only known compounds of this type (**2**). However, it was reported that they could not be isolated owing to their facile oxidation to hydrazones (**2**). Substituted macrocyclic poly-1,2-diaza compounds have been described incorporating endocyclic azine, hydrazide, hydrazone, azo and substituted hydrazino groups (**2,3**). Yields are generally low. Most of the synthetic routes leading to these compounds are unsuitable for preparation of unsubstituted macrocycles incorporating endocyclic hydrazino groups. This report describes the first synthesis and isolation of a compound of this type, perhydro-1,2,5,6-tetrazocine.

Two derivatives of 1,2,5,6-tetrazocine have been described previously, perhydrodibenzo[*a,e*]-1,2,5,6-tetrazocine (**3d**) and 1,2,5,6-tetrakis(trifluoromethyl)-3,4,7,8-tetraketoperhydro-1,2,5,6-tetrazocine (**3h**). Two types of tetrazocine derivative have been reported whose structures were later shown to be incorrect. A substance described as 3,7-diketoperhydro-1,2,5,6-tetrazocine (**3d,4**) was shown to be 4-amino-3,5-bis(hydroxymethyl)-*s*-triazole (**5**).

Reported 3,4,7,8-substituted derivatives of 1,2,5,6-tetrazocine (**2**) (**6**) were shown by x-ray crystallography to be substituted 1,4,5,8-tetraazapentalenes (**3**) (**7**). Certain other reported cyclic structures may need to be revised after reinvestigation (**3a,b,d,h,6-9**).



Perhydro-1,2,5,6-tetrazocine (**9**) has been prepared in the present study from 1,2-bis(hydrazino)ethane (**4**) (**10**) (Scheme 1). Acetylation of bishydrazine **4** with excess acetic anhydride at 2-5° leads nearly quantitatively to the tetraacetyl derivative **5**. Reaction of **5** with ethylene

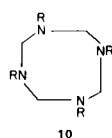


glycol bis-*p*-toluenesulfonate in refluxing mesitylene gave 1,2,5,6-tetraacetylperhydro-1,2,5,6-tetrazocine (**6**) in 36% yield. Substitution of other solvents for mesitylene, or employing no solvent, gave lower yields of **6**, as did use of 1,2-dibromoethane as the alkylating agent.

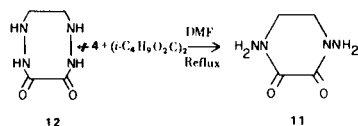
Hydrolysis of the tetraacetyl derivative **6** in concentrated hydrochloric acid led quantitatively to the bis-hydrochloride salt **7**. Conventional methods of isolating the pure, salt-free base **9** from its salts were ineffective owing to the very high solubility of **9** in aqueous solutions of high ionic strength. The sulfate salt **8** was prepared from **7** by ion exchange and the free base **9** liberated in liquid ammonia. The separation of pure **9** from ammonium sulfate was easily effected in absolute ethanol. A stable bis-picrate of **9** forms readily. All operations involving solutions of **9** require rigorous exclusion of oxygen from the solvents owing to the ease of oxidation of the hydrazino groups. Reactions of **9** will be described in forthcoming publications.

Perhydro-1,2,5,6-tetrazocine (**9**) is a crystalline solid whose melting point depends on the rate of heating. It slowly reacts with oxygen of the air at ambient temperature, but may be stored in a well-sealed container at -15° . Its structure is supported by its molecular formula and simple nmr spectrum (two singlets corresponding to ethylene and exchanged NH protons in deuterium oxide solvent).

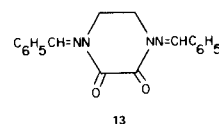
Perhydro-1,2,5,6-tetrazocine (**9**) represents the first unsubstituted tetraazacyclooctane to be isolated. Many *N*-substituted derivatives of isomeric perhydro-1,3,5,7-tetrazocine are known (**10**, R = NO₂, NO, COCH₃, ArSO₂, etc.), but the unsubstituted parent compound (R = H) has not been prepared (11).



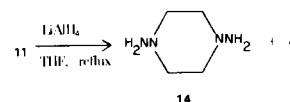
Other synthetic routes to 1,2,5,6-tetrazocine derivatives were investigated. Various amines were heated with diisobutyl oxalate in refluxing dimethylformamide. 1,2-Bis(hydrazino)ethane (**4**) gave 1,4-diamino-2,3-diketopiperazine (**11**, 59%) rather than 3,4-diketoperhydro-1,2,5,6-tetrazocine (**12**) as the only isolated crystalline product (5). The piperazine structure was supported by



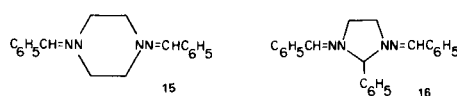
spectral data and formation of a dibenzal derivative (**13**) by reaction of **11** with benzaldehyde (acetic acid catalyst).



Additional support for structure **11** was obtained by reduction with lithium aluminum hydride in refluxing tetrahydrofuran solvent to yield an approximately 1:1 mixture of 1,4-diaminopiperazine (**14**) and 1,2-dihydrazinoethane (**4**). The products (**14**, **4**) were ultimately isolated as their known dibenzal and tribenzal derivatives

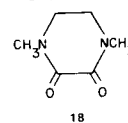


(**15** and **16**, respectively) after reaction of the product mixture of isolated crystalline hydrochloride salts with

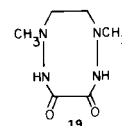


benzaldehyde (10,12). 2,3-Piperazinedione itself was found to be reduced quantitatively to 1,2-diaminoethane with lithium aluminum hydride in refluxing tetrahydrofuran.

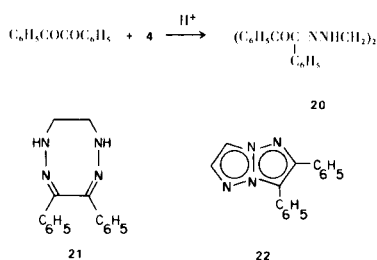
Reaction of 1,2-bis(methylamino)ethane (**17**) with diisobutyl oxalate in refluxing dimethylformamide led to 1,4-dimethyl-2,3-diketopiperazine (**18**, 41%). 1,2-Bis(1-



methylhydrazino)ethane in a parallel experiment gave a low yield of crystalline material (the nmr spectrum revealed isobutyryl groups and the infrared spectrum showed ester and amide carbonyl bands). The unidentified material is believed to contain unknown proportions of acyclic 1:1 and 2:1 ester:amine condensation products and possibly a very low yield of the tetrazocine derivative **19**.

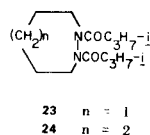


The acid-catalyzed reaction of benzil with 1,2-bis(hydrazino)ethane (**4**) in ethanol gave 3,4,7,8-tetraaza-1,2,9,10-tetraphenyl-2,8-decadien-1,10-dione (**20**, 8%) as the only crystalline product. None of the tetrazocine derivative (**21**) or the derived tetraazapentalene (**22**) could be isolated. As noted above, benzil reacts with hydrazine to provide low yields of substituted tetraazapentalenes



(3) rather than tetrazocines (2) (R, R' = aryl) (5,6,7). The parent, unsubstituted 3 (R, R' = H) has not been prepared (6d,7).

1,2-Diazacyclooctane had not been synthesized at the time this work was initiated. Its preparation (13,14) and that of 1,2-diazacycloheptane (15) have now been described. Procedures for preparation of new precursors of these 1,2-diazacycloalkanes by a modified Stetter procedure are described in the experimental section (16). Reaction of 1,5-dibromopentane or 1,6-dibromohexane with the potassium salt of *N,N'*-diisobutyrylhydrazine in refluxing dimethylformamide led to 1,2-diisobutyryl-1,2-diazacycloheptane (23) or 1,2-diisobutyryl-1,2-diazacyclooctane (24), respectively.



EXPERIMENTAL

Infrared spectra were determined on a Perkin Elmer Model 137, 1H nmr spectra on a Varian A-60 or XL-100, and ^{13}C nmr spectra on a Varian XL-100 spectrometer with Transform Technology TT-100 phased Fourier transform system; 1H and ^{13}C chemical shift measurements were determined at ca. 30° and are referenced to tetramethylsilane internal standard (sodium 3-(trimethylsilyl)-1-propanesulfonate in deuterium oxide). Melting points were determined on a Kofler hot stage, unless otherwise stated, and are corrected. Elemental analyses and molecular weights were determined by Galbraith Laboratories, Knoxville, Tennessee. Atmospheric pressures of 700-710 mm apply for all temperatures recorded when pressures are not stated.

1,2-Bis(*N,N'*-diacetylhydrazino)ethane (5).

To 1,2-bis(hydrazino)ethane (46.0 g., 0.50 mole, 98% assay, Dow Chemical Co.) in 100 ml. of water was added acetic anhydride (256 g., 2.5 moles) dropwise with stirring during 4.5 hours keeping the temperature of the reaction mixture at 5°. Stirring was continued for an additional 17.5 hours at 2-5° (nitrogen atmosphere maintained). The mixture was concentrated to dryness and the solid residue treated with ethanol (100 ml.) and heated on the steam bath to obtain a solution. Dilution of the the solution with ether (100 ml.) gave 123.6 g. (95.6%) of 5, m.p. 162-163°; recrystallization from acetone gave prisms, m.p. 163-165°; ir (potassium bromide): 3200 cm^{-1} (NH), 1660 (C=O); nmr (deuteriochloroform, -30°): δ 8.85 (s, 2, NH), 4.57,

3.02 (AB, J = 10.5 Hz, 4, CH₂CH₂, coalesces to a very broad singlet at 25°), 2.15 (s, 6, CH₃), 2.07 (s, 6, CH₃).

Anal. Calcd. for C₁₂H₂₂N₄: C, 46.50; H, 7.02; N, 21.69; mol. wt. 258.3. Found: C, 46.49; H, 7.07; N, 21.53; mol. wt. 261 (dimethylformamide).

1,2,5,6-Tetraacetylperhydro-1,2,5,6-tetrazocine (6).

1,2-Bis(*N,N'*-diacetylhydrazino)ethane (38.5 g., 0.149 mole) was added to a solution of ethanolic potassium ethoxide [prepared by cautious, slow addition of potassium (11.7 g., 0.298 mole) to absolute ethanol (150 ml.)]. Warming slightly gave a solution which was concentrated to dryness under reduced pressure and treated with dry mesitylene (1600 ml.) and ethylene glycol bis-*p*-toluenesulfonate (55.4 g., 0.149 mole of recrystallized material, m.p. 127-128°, prepared by the procedure of Sakellarios (17)). The mixture was distilled with stirring (nitrogen atmosphere) and 125 ml. of distillate removed and discarded; the temperature within the reaction flask reached 162° when distillation was stopped. The mixture was heated under reflux with stirring for 20 hours (Dean-Stark tube attached). The reaction mixture was cooled to 120° with continued stirring and then filtered hot through a sintered glass Buchner funnel leaving insoluble material adhering to the reaction flask. Chilling of the filtrate gave 17.7 g. of crude product, m.p. 155-175°. The filtrate was added to the reaction flask containing solid (principally potassium tosylate) and heated under reflux with stirring for 2 hours. After filtering hot and chilling the filtrate a second crop of material was obtained, 9.0 g., m.p. 160-180°. Concentration of the filtrate to dryness gave 7.0 g. of additional product. The combined crude product (33.7 g.) was crystallized from 2-propanol (*Darco* charcoal treatment) to yield by fractional crystallization 6, 12.26 g., m.p. 183-191°, and 3.10 g. m.p. 173-183°; total yield of crystalline 6, 15.36 g. (36.4%); recrystallization from acetone gave small prisms, m.p. 192-193°; ir (potassium bromide): 1675 cm^{-1} (C=O); nmr (deuteriochloroform): δ 4.73, 3.05 (AB, J = 13.5 Hz, 8, CH₂CH₂), 2.02 (s, 12, CH₃).

Anal. Calcd. for C₁₂H₂₀N₄O₄: C, 50.69; H, 7.09, N, 19.71, mol. wt. 284.3. Found: C, 50.54; H, 7.14; N, 19.50; mol. wt. 281 (chloroform).

The above procedure was repeated substituting dimethylformamide solvent for mesitylene to provide a 28% yield of 6. Conducting the reaction with tetralin solvent or no solvent gave 15-20% yields of 6. Substitution of 1,2-dibromoethane for ethylene glycol bis-*p*-toluenesulfonate reactant (cyclohexane solvent or no solvent) gave 4-5% yields of 6.

Perhydro-1,2,5,6-tetrazocine Bishydrochloride (7).

A mixture of 1,2,5,6-tetraacetylperhydro-1,2,5,6-tetrazocine (6, 11.37 g., 0.040 mole), concentrated hydrochloric acid (100 ml.) and water (100 ml.) was heated on the steam bath for 24 hours. Concentration to dryness followed by crystallization of the residue from concentrated hydrochloric acid gave, in successive crops, 7.48 g. (99%) of crystalline bishydrochloride 7, m.p. 208-210° dec.; ir (potassium bromide): 1580 cm^{-1} (NH), carbonyl bands absent; nmr (deuterium oxide): δ 5.07 (s, 6, NH), 3.78 (s, 8, CH₂); an analytical sample was dried at 100° for 3 hours.

Anal. Calcd. for C₄H₁₄Cl₂N₄: C, 25.41; H, 7.46; Cl, 37.50; N, 29.63. Found: C, 25.15; H, 7.20; Cl, 37.36; N, 29.46.

Perhydro-1,2,5,6-tetrazocine (9).

Ion exchange resin, polystyrene quaternary ammonium chloride type (Biorad AG1X-10, 200-400 mesh, 150 g.), was thoroughly

exchanged with aqueous saturated potassium bisulfate solution until tests for chloride ion were negative. To this bisulfate resin in a column was introduced a solution of perhydro-1,2,5,6-tetra-zocine bishydrochloride (**7**, 5.76 g., 30.4 mmoles) in 40 ml. of water. The eluate gave a negative test for chloride ion. The column was rinsed with water and the combined solutions concentrated to dryness (100°, 0.1 mm) to yield 6.1 g. (94%) of perhydro-1,2,5,6-tetrazocine sulfate (**8**) as an amorphous solid, m.p. 205-210° dec.; attempts to crystallize the sulfate salt were unsuccessful.

The sulfate salt **8** (6.1 g.) was placed in a 3-necked flask flushed with oxygen-free dry nitrogen and equipped with a dry-ice-acetone condenser, *ascarite* tube and magnetic stirrer and surrounded by a dry-ice acetone cold bath. Ammonia (100 ml.) was condensed into the apparatus during 3 hours with stirring. The ammonia inlet was replaced by oxygen-free dry nitrogen and the cold bath was removed. The ammonia was allowed to evaporate completely at ambient temperature with stirring. To the residue was added 50 ml. of oxygen-free absolute ethanol (degassed by passing through oxygen-free nitrogen) and the mixture stirred at ambient temperature for 4 hours. The mixture was filtered (to remove ammonium sulfate) into a distilling flask equipped with an oxygen-free nitrogen capillary inlet. Solvents were removed at 30 mm pressure keeping the bath temperature below 50°. A white solid precipitates from the ethanol solution as the distillation proceeds; after all solvents are removed there remains 2.75 g. (83%) of the amine **8**, capillary m.p. 145-155° (dec. with gas evolution and sublimation from 110°; recrystallization from oxygen-free 95% ethanol gave chunky crystals (50% recovery); m.p. in sealed capillary 149-165° dec.; d_4^{25} 1.21 (compression @ 40,000 psi); in air at 25° a sample turns dark brown and becomes oily after a few hours; ir (potassium bromide): 3120 cm^{-1} (sharp, NH, carbonyl bands absent); nmr (deuterium oxide): δ 4.63 (s, 4, NH), 2.93 (s, 8, CH_2).

Anal. Calcd. for $\text{C}_4\text{H}_{12}\text{N}_4$: C, 41.35; H, 10.41; N, 48.23; mol. wt. 116.2. Found: C, 41.09; H, 10.64; N, 48.35; mol. wt. 116 (mass spectrum).

Amine **9** (0.116 g., 1.0 mmole) and picric acid (0.458 g., 2 mmoles), each dissolved in 5 ml. of oxygen-free ethanol, were mixed at 25°. After 3 hours water was added (ca. 10 ml.) and the mixture heated on the steam bath to obtain a clear solution. Chilling at 0° gave 0.40 g. (70%) of the amine **9** bispicrate derivative, m.p. 173-175°; recrystallization from 50% aqueous ethanol gave flat yellow prisms, m.p. 177-180°, with decomposition and gas evolution to form some small prisms, m.p. 235-240°.

Anal. Calcd. for $\text{C}_{16}\text{H}_{18}\text{N}_{10}\text{O}_{14}$: C, 33.46; H, 3.16; N, 24.39. Found: C, 33.64; H, 3.21; N, 25.54.

1,4-Diamino-2,3-diketopiperazine (**11**).

To 1,2-bis(hydrazino)ethane (1.1 g. of 98% assay, 0.10 mole) in refluxing dimethylformamide (500 ml.) was added diisobutyl oxalate (20.2 g., 0.10 mole) during 1.5 hours with stirring. After heating under reflux for an additional 4 hours the yellow solution was allowed to cool to room temperature overnight to deposit 6.01 g. of crystals, m.p. 281-221°. Concentration of the filtrate to dryness, followed by trituration of the residue with methanol (25 ml.) gave 2.42 g. of additional product, m.p. 210-220°; total yield of crystalline **11**, 8.43 g. (59%). The remaining reaction product was an orange oil (9.2 g.) from which no crystalline product could be isolated; spectra: ir (potassium bromide): 3320 cm^{-1} (sharp, NH), 1680, 1660 (C=O); nmr (dimethyl sulfoxide- d_6): δ 3.58 (s, 4, NH), 3.0-3.8 (m, 4, CH_2CH_2).

Anal. Calcd. for $\text{C}_4\text{H}_8\text{N}_4\text{O}_2$: C, 33.33; H, 5.59; N, 38.87; mol. wt. 144.14. Found: C, 33.36; H, 5.75; N, 38.84; mol. wt. 143 (osmometry, dimethylformamide).

Heating a premixed solution of 1,2-bis(hydrazino)ethane (0.90 g.) and diisobutyl oxalate (2.02 g.) under reflux in dimethylformamide (100 ml.) for 5 hours gave a 35% yield of **11**, m.p. 206-216°. Heating 1,2-bis(hydrazino)ethane (0.90 g.) and diethyl oxalate in dioxane (100 ml.) on the steam bath for 15 hours gave a 21% yield of **11**.

1,4-Bis(benzalamino)-2,3-diketopiperazine (**13**).

A solution of 1,4-diamino-2,3-diketopiperazine (**11**, 0.15 g., 1.1 mmoles), benzaldehyde (0.24 g., 2.3 mmoles) and a few drops of acetic acid in 15 ml. of ethanol and 5 ml. of dioxane was heated on the steam bath for 2 hours. Cooling gave 0.23 g. (70%) of the dibenzal derivative **13** as pale yellow prisms, m.p. 298-300°; recrystallization from dimethylformamide gave flat prisms, m.p. 301-302°; ir (potassium bromide): 1570 (C=O); NH absent.

Anal. Calcd. for $\text{C}_{18}\text{H}_{16}\text{N}_4\text{O}_2$: C, 67.48; H, 5.03; N, 17.49. Found: C, 67.40; H, 5.19; N, 17.45.

Lithium Aluminum Hydride Reduction of 1,4-Diamino-2,3-diketopiperazine (**11**).

To 1,4-diamino-2,3-diketopiperazine (**11**, 1.44 g., 1.0 mmole) in tetrahydrofuran (25 ml.) was added lithium aluminum hydride (0.76 g., 2.0 mmoles) and the mixture heated under reflux with stirring for 100 hours. The cooled mixture was treated with 30 ml. of 5% sodium hydroxide solution and stirred for 6 hours. After filtering and washing the solid with water, the filtrate was treated with potassium carbonate (ca. 20 g.) and distilled, water in the flask being replaced continuously, until 700 ml. of distillate was collected. Neutralization of the distillate with 1 *N* hydrochloric acid followed by concentration to dryness gave 0.96 g. of crystalline hydrochloride salts. Treatment of the salts in 30 ml. of ethanol-water (2:1) with benzaldehyde (2.0 g.), followed by warming on the steam bath for 5 minutes and dilution of the mixture with water gave 0.90 g. of prisms, m.p. 100-180°, fractional crystallization of which gave 0.18 g. of long, flat prisms, m.p. 214-216°, and 0.20 g. of chunky prisms, m.p. 132-135°. The higher melting derivative when mixed with authentic 1,4-bis(benzalamino)piperazine, m.p. 213-214°, melted at 214-215° (lit m.p. 212-213.5° (12)). The lower-melting derivative was recrystallized from ethanol to yield 0.14 g. of 1,3-bis(benzalamino)-2-phenylimidazolidine, m.p. 134-136°; when mixed with an authentic sample, m.p. 135-136°, the melting point was 133-135° (lit m.p. 139.5-140° (10)).

Lithium Aluminum Hydride Reduction of 2,3-Piperazinedione.

A mixture of 2,3-piperazinedione (6.7 g., 0.05 mole (18)) and lithium aluminum hydride (2.85 g., 0.075 mole) in tetrahydrofuran (100 ml.) was heated under reflux with stirring for 41 hours. Aqueous sodium hydroxide solution (20 ml. of 10%) was carefully added, followed by 150 ml. of water and the mixture distilled, water in the flask being replaced continuously until 700 ml. of distillate was collected. Neutralization of the filtrate with 1 *N* hydrochloric acid (100 ml., 0.10 mole), followed by concentration to dryness gave 6.8 g. (100%) of white, crystalline ethylenediamine dihydrochloride; an aliquot sample was treated with 10% aqueous sodium hydroxide solution and benzoyl chloride to yield, quantitatively, 1,2-dibenzoyl-1,2-diaminoethane as needles, m.p. 249-250° (lit m.p. 250° (19)); 1,4-dibenzoylpiperazine, m.p. 191° (20) 192° (21).

1,4-Dimethyl-2,3-diketopiperazine (**18**).

To a solution of 1,2-bis(methylamino)ethane (1.76 g., 2.0 mmoles) in dry dimethylformamide (200 ml.) heated under reflux was added diisobutyl oxalate (4.04 g., 2.0 mmoles) dropwise with stirring during 3 hours; refluxing was continued for 15 hours. The solution was concentrated to dryness and the residue triturated with ether to yield 1.73 g. of slightly oily crystals, m.p. 150-170°; crystallization from 2-propanol gave 1.16 g. (41%) of flat prisms, m.p. 172-176°; recrystallization from 2-propanol gave 0.82 g., m.p. 176-177°; ir (potassium bromide): 1680 cm^{-1} (C=O), NH bands absent; nmr (deuteriochloroform): δ 3.64 (s, 4, CH_2), 3.07 (s, 6, CH_3).

Anal. Calcd. for $\text{C}_6\text{H}_{10}\text{N}_2\text{O}_2$: C, 50.69; H, 7.09; N, 19.71; mol. wt. 142.16. Found: C, 50.81; H, 7.09; N, 19.51; mol. wt. 150 (osmometry, chloroform).

The above procedure was tried with 1,2-bis(1-methylhydrazino)ethane. A solution of 1,2-bis(1-methylhydrazino)ethane, b.p. 76-78° (3.5 mm) (22) 1.18 g., 1.0 mmole and diisobutyl oxalate (2.02 g., 1.0 mmole) in dry dimethylformamide (100 ml.) was heated under reflux for 15 hours (nitrogen atmosphere). The pale yellow solution was concentrated to dryness and the residue (1.6 g. of oil) triturated with ether (25 ml.) to yield 0.46 g. of yellow crystals, m.p. 185-215°; fractional crystallization from ethanol and 2-propanol gave 0.08 g., m.p. 216-231°; ir (potassium bromide): 3160 cm^{-1} (NH), 1730, 1670, 1650 (C=O); nmr (pyridine- d_5): δ 5.00 (s, NH), 4.32 (d, $J = 7$ Hz, CH_2O), 3.2-3.5 (m, CH_2N), 2.7-3.1 (m, CH_2N), 2.91 (s, CH_3N), 2.67 (s, CH_3N), 1.9-2.3 (m, CH), 0.98 [d, $J = 7$ Hz, (CH_3) $_2$ CH]; based on peak intensities the sample is a mixture (see discussion). The reaction was repeated with reaction times of 7 and 48 hours to give a similar product in lower yield.

3,4,7,8-Tetraaza-1,2,9,10-tetraphenyl-2,8-decadiene-1,10-dione (20).

A mixture of 1,2-bis(hydrazino)ethane (1.80 g., 0.02 mole), benzil (4.20 g., 0.02 mole), 2 drops of concentrated hydrochloric acid and 100 ml. of ethanol was heated on the steam bath for 10 minutes to produce a clear yellow solution. After standing at 25° for 3 days the solution was concentrated to dryness under reduced pressure on the steam bath to yield a dark oil (4.7 g.). Extraction of the residue with several portions of boiling heptane, followed by slow evaporation of the extracts produced 0.39 g. (8%) of 20, m.p. 126-150°; recrystallization from benzene-heptane gave 0.25 g. of square, flat prisms, m.p. 65-70° (solvate), with resolidification to rectangular prisms, m.p. 145-150°; on cooling, the melt resolidifies, m.p. 147-150°; an analytical sample was dried at 100° (0.1 mm) for one hour, m.p. 149-150°; ir (potassium bromide): 3280 cm^{-1} (NH); 1625 (C=N); nmr (deuteriochloroform): δ 7.0-7.9 (m, 10, C_6H_5), 6.3-6.5 (m, 2, NH; disappears on addition of deuterium oxide), 3.35-3.6 (m, 4, CH_2CH_2 ; changes to sharp singlet on addition of deuterium oxide).

Anal. Calcd. for $\text{C}_{30}\text{H}_{26}\text{N}_4\text{O}_2$: C, 75.93; H, 5.52; N, 11.81; mol. wt. 474.5. Found: C, 75.67; H, 5.58; N, 11.67; mol. wt. 485 (chloroform).

1,2-Diisobutyl-1,2-diazacycloheptane (23).

To *N,N'*-diisobutylhydrazine (68.9 g., 0.40 mole (16)) in absolute ethanol (200 ml.) was added during 15 minutes a solution of ethanolic potassium ethoxide (0.40 mole prepared from 16.0 g. of potassium and 200 ml. of absolute ethanol) with vigorous stirring. After stirring for 1 hour the resulting solution was concentrated to dryness under reduced pressure (steam bath). Anhydrous dimethylformamide (500 ml.) was added to the residue and the mixture heated under reflux, with stirring, until a clear solution is obtained (ca. 30 minutes). 1,5-Dibromopentane (46.0

g., 0.20 mole) was added dropwise with stirring during 17 hours to the refluxing solution; refluxing was continued for an additional 3 hours. The cooled solution (0°) was filtered and the collected solid washed with dimethylformamide. The filtrate was concentrated under reduced pressure, the residue filtered and the solid washed with dimethylformamide to yield 14.7 g. of diisobutylhydrazine, m.p. 245-247°; a second crop was obtained by concentration of the filtrate, 9.1 g., m.p. 240-243°. The filtrate was distilled to yield 24.3 g. of oily solid, b.p. 90-160°, principally b.p. 124° (0.6 mm), after a small forerun and 18.8 g. of residue (bath temperature 210°); redistillation of the principal fraction gave 16.7 g. (35%) of 23, b.p. 120-124° (0.5 minutes), flat prisms, m.p. 45-53°; ir (*Nujol*): 1680 cm^{-1} (C=O); NH band absent.

Anal. Calcd. for $\text{C}_{13}\text{H}_{24}\text{N}_2\text{O}_2$: C, 64.96; H, 10.07; N, 11.66; mol. wt. 240.34. Found: C, 64.77; H, 10.08; N, 11.59; mol. wt. 241 (dimethylformamide).

1,2-Diisobutyl-1,2-diazacyclooctane (24).

The procedure above employed for preparation of 1,2-diisobutyl-1,2-diazacycloheptane was used (34.44 g., 0.20 mole of *N,N'*-diisobutylhydrazine and 24.4 g., 0.10 mole, of 1,6-dibromohexane) to yield 7.62 g. (30%) of 24, b.p. 124-128° (0.1 mm), m.p. 61-64°; ir (neat, supercooled) 1680 cm^{-1} (C=O); nmr (deuteriochloroform): δ 2.9-4.7 (m, 4, CH_2N), 2.3-3.0 (m, 2, CH), 1.6 [broad s, 8, (CH_2) $_4$ CH $_2$ N], 1.0-1.3 (doublets, 12, CH_3).

Anal. Calcd. for $\text{C}_{14}\text{H}_{26}\text{N}_2\text{O}_2$: C, 66.10; H, 10.30; N, 11.01; mol. wt. 254.36. Found: C, 66.21; H, 10.34; N, 11.22; mol. wt. 253 (dimethylformamide).

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