DIBENZO[f,j]-5.12-DIHYDRODIPYRAZOLO[4,5-c : 5'.4'-m]-[1.2.5.8,9.12]HEXAAZATETRADECYNE – THE FIRST REPRESENTATIVE OF A NEW MACROHETEROCYCLIC SYSTEM

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The first representative of a 14-membered macroheterocyclic system – dibenzodipyrazolo-5,12-dihydro[1,2,5,8,9,12]hexaazatetradecyne – was obtained by template cyclization of 5,5'-dichloro-3,3'-dimethyl-1,1'-diphenyl-4,4'-azopyrazole with 2,2'-diaminoazobenzene in aprotic solvents in the presence of nickel(II) acetate and potassium carbonate.

The synthesis of azaheterocycles containing a 14-membered ring with a high degree of conjugation is attracting the interest of researchers; 1,8-dihydro[1,4,8,11]tetraazatetradecyne [1-3] and 1,8- and 2.9-dihydro-[1,2,4,5,8,9,11,12]octaazatetradecyne [4,5] derivatives are known, but less study has been devoted to 2,9- and 5,12-dihydro[1,2,5,8,9,12]hexaazatetradecyne derivatives [6, 7]. In order to synthesize the dihydro[1,2,5,8,9,12]hexaazatetradecyne system we used template cyclization of 5,5'-dichloro-3,3'-dimethyl-1,1'-diphenyl-4,4'-azopyrazole (I) with 2,2'-diaminoazobenzene (II) in the presence of nickel(II) acetate and potassium carbonate.

A hydrazone structure [8] was assigned to the intermediate for the synthesis of I, obtained by coupling of diazotized 4-aminoantipyrine with 5-methyl-2-phenyl-3H-pyrazole-3-one. The IR spectral data confirm this and indicate the presence of two C=O groups: $\nu_{C=O}$ 1678 cm^{-1} with integral intensity $A_{C=O}$ $7.1 \cdot 10^4$ liter·mole^{-1}·cm^{-2}; IR spectrum of 5-methyl-2-phenyl-3H-pyrazole-3-one: $\nu_{C=O}$ 1714 cm^{-1} with $A_{C=O}$ $3.8 \cdot 10^4$ liter·mole^{-1}·cm^{-2}. A small amount of a bisazo compound – 5-[[2-[(2-aminophenyl)azo]phenyl]amino]-4-[(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)azo]-3-methyl-1-phenylpyrazolato](2-)nickel (IV) – is formed along with macrocyclic[9,20-dihydro-3,6-dimethyl-1,8-diphenyldibenzo[f,j]dipyrazolo[4,5-c:-5'.4'-ml]-1,2,5,8,9,12]hexaazacyclotetradecynato(2-)-N^4,N^9,N^{14},N^{20}]nickel (III) in the reaction in dimethylformamide (DMF) and hexamethylphosphoric triamide (HMP). An increase in the temperature leads to a decrease in the yield of III and to the formation of resinous side products. A decrease in the amount of potassium carbonate causes a decrease in the yield of III. Cyclization to III occurs when IV is refluxed in DMF in the presence of K_2CO_3. Macrocyclic products are not detected when the reaction is carried out without nickel acetate.

Macrocyclic chelate III is characterized by high stability and does not liberate a nickel ion on treatment with concentrated acids; IV is demetallized in mineral acids and forms bisazocompound V.

The molecular ion peaks in the mass spectra correspond to the proposed structures of III-V. The IR spectrum of derivative III does not contain characteristic bands in the region of stretching vibrations of NH bonds, the IR spectrum of azo compound IV has the band of an NH bond at 3330 cm^{-1}, and the spectrum of product V contains a band of an NH bond at 3320 cm^{-1} and bands of an NH_2 group (ν_{sym} 3400 and ν_{as} 3490 cm^{-1}). Bands at 690 and 757 cm^{-1} corresponding to the ν_4 and ν_{11} vibrations of a monosubstituted benzene ring (C_6H_5-N) and at 737 and 757 cm^{-1} (ν_{11} vibrations of o-disubstituted benzene rings) are observed in the region of out-of-plane deformation vibrations in the case of V.

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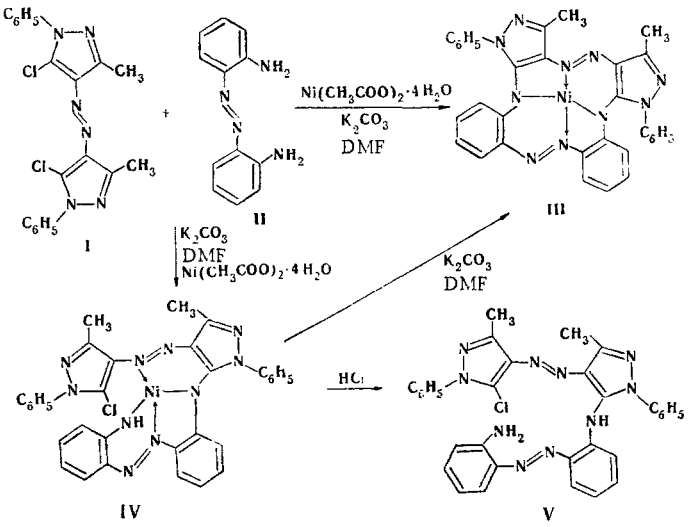

Of the two methyl signals in the PMR spectrum of V, the weak-field signal coincides with the CH_3 singlet of azo compound I and is evidently related to the CH_3 group of the extreme pyrazole ring, whereas the signal at 2.30 ppm can be assigned to the CH_3 group of the middle pyrazole ring. Only one CH_3 signal is observed in the spectrum of product IV because of the random magnetic equivalence of both CH_3 groups. The position of the CH_3 signal in the spectrum of III coincides with the position of the signal of the CH_3 group of the middle pyrazole ring in derivative V. With the exception of the weak-field shift of 0.5 ppm of the signal of one of the protons in the ortho position relative to the azo group in the benzene rings on passing from V to IV, the signals of the CH_3 groups and of the aromatic protons do not experience significant shifts during cyclization and complexing.

EXPERIMENTAL

The electronic spectra of 10^{-4}-10^{-5} M heptane solutions were recorded with an MPS-50L spectrophotometer. The IR spectra of CCl_4 (> 3000 cm^{-1}) and CS_2 (< 2000 cm^{-1}) were recorded with a UR-20 spectrometer; the spectrum of VI was obtained from a $CHCl_3$ solution. The molecular masses were determined with an MS-702 mass spectrometer at an ionizing voltage of 70 eV; the vaporization temperatures of the samples were 160° (III and IV) and 140° (V), and the spectrometer had a source with direct introduction of the sample into the ionization region. The percentage of nickel in chelates III and IV was determined by an x-ray fluorescence method with an RK-5975 quantometer with nickel(III) oxide as the standard. The PMR spectra were recorded with a Varian XL-100-12 spectrometer at 30° with tetramethylsilane as the internal standard.

3-Methyl-1-phenyl-1H-pyrazole-4,5-dione 4-(1,2-Dihydro-1,5-dimethyl-2-phenyl-3H-pyrazol-3-on-4-ylhydrazone) (VI). This compound, with mp 204-205° (from ethanol) (mp 200-205° [8]), was obtained in 93% yield by the method in [8].

5,5'-Dichloro-3,3'-dimethyl-1,1'-diphenyl-4,4'-azopyrazole (I). Triethylamine (10 ml) was added dropwise at room temperature to a mixture of 19.45 g (0.05 mole) of VI and 70 ml of phosphorus oxychloride, after which the mixture was refluxed at 110-115° for 6 h. It was then cooled, and the resulting precipitate was removed by filtration and washed with three 50-ml portions of cold acetone to give 11 g of I. Approximately 50 ml of $POCl_3$ was removed from the mother liquor by vacuum distillation, and the residue was poured over 100 g of ice. The aqueous mixture was cooled and neutralized to pH 7 with 2 M NaOH and filtered, and the solid material was washed with 50 ml of acetone and dried to give another 2 g of I. Recrystallization from glacial acetic acid gave 9.3 g (45%) of I with mp 227-228° (mp 226° [9]). PMR spectrum in CCl_4: 7.33-7.69 (10H) and 2.52 (6H, s).

2,2'-Diaminoazobenzene (II). This compound was obtained by the method in [7, 10]. PMR spectrum in CCl_4: 6.53-7.61 (8H) and 5.43 (NH_2, broad s).

[9,20-Dihydro-3,6-dimethyl-1,8-diphenylbenzo[f,j]dipyrazolo[4,5-c:-5',4'-m][1,2,5,8,9,12]hexaazacyclotetradecyanato(2-)-N^4,N^9,N^{14},N^{20}]nickel (III). A mixture of 2.12 g (0.01 mole) of II, 4.11 g (0.01 mole) of I, 2.48 g (0.01 mole) of nickel(II) acetate tetrahydrate, 5.52 g (0.04 mole) of K_2CO_3 and 70 ml of DMF was refluxed for 7 h. The course of the reaction was monitored by thin-layer chromatography (TLC) on Silufol UV-254 with elution by chloroform. At the end of the reaction, the mixture was cooled and filtered, and the solid

material was washed with water until the wash waters gave a negative reaction for carbonate and chloride ions. It was then dried and crystallized twice from benzene–methanol (1 : 3) to give 1.4 g (23%) of greenish finely crystalline II with mp 285-290° (dec.). The solubility of the product in $CHCl_3$ was $\sim 10^{-1}$ M, as compared with $\sim 5 \cdot 10^{-2}$ M in benzene and carbon tetrachloride; it was less soluble in DMF, acetone, methanol, hexane, cyclohexane, and ether. It was soluble in concentrated H_2SO_4 (II was obtained when this solution was diluted and neutralized) but insoluble in other mineral acids and water. Found: C 62.6; H 3.8; N 23.1; Ni 9.1%. Mass spectrum: 605, 606, 607, 608, 609. $C_{32}H_{24}N_{10}Ni$. Calculated: C 63.0; H 4.0; N 23.3; Ni 9.8%, M 607.32. R_f 0.82 [benzene–chloroform (1 : 1)]. PMR spectrum (in $CDCl_3$): 6.10-7.40 (18H, complex m) and 2.30 (6H. s). Electronic spectrum (n-heptane): λ_{max}, nm (log ε): 238 (inflec.) (5.12), 242 (5.13), 248 (5.13), 257 (inflec.) (5.03); 268 (inflec.) (4.76), 272 (inflec.) (4.70), 280 (sh.) (4.57), 291 (4.63), 300 (inflec.) (4.58), 319 (inflec.) (4.49), 362 (sh.) (4.19), 386 (sh.) (4.17), 468 (4.53), 670 (sh.) (3.42), 722 (3.66).

The solution in DMF after separation of II was diluted with a fivefold volume of water, and the resulting black precipitate was removed by filtration, dried, and dissolved in 50 ml of $CHCl_3$. The $CHCl_3$ solution was chromatographed with a column filled with Chemapol L100/160 μ silica gel with elution by $CHCl_3$ to give III and IV. Compound III was recrystallized from benzene–methanol (1 : 5) to give 0.35 g of III. The overall yield of III was 1.74 g (29%). Two recrystallization from benzene–hexane (1 : 6) gave 0.2 g of IV.

5-[[2-[(2-Aminophenyl)azo]phenyl]amino]-4-[(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)azo]-3-methyl-1-phenylpyrazolato](2-)nickel (IV). The synthetic conditions were similar to those in the preparation of III, but 1.38 g (0.01 mole) of K_2CO_3 was used. At the end of the reaction, the mixture was cooled, and the resulting precipitate was removed by filtration, dried, and refluxed in benzene–methanol (1 : 5). The hot mixture was filtered to remove 0.35 g of III, and the solvent was removed from the filtrate by distillation. The residue was crystallized twice from benzene–hexane (1 : 4) to give 1.06 g (16%) of brown-greenish fine crystals of IV with mp 250° (dec.). The solubility of the product in $CHCl_3$ was $\sim 5 \cdot 10^{-1}$ M, as compared with $\sim 10^{-1}$ M in benzene and CCl_4 and $5 \cdot 10^{-2}$–10^{-2} M in acetone, cyclohexane, and toluene. It was less soluble in ethanol, methanol, and hexane, insoluble in water, and soluble, with decomposition, in mineral acids. Found: C 59.1; H 3.9; N 21.5; Cl 5.6; Ni 9.6%. Mass spectrum: 642, 643, 644, 645, 646. $C_{32}H_{25}N_{10}ClNi$. Calculated: C 59.5; H 4.0; N 21.8; Cl 5.6; Ni 9.1%. M 643.78. R_f 0.69 [benzene–chloroform (1 : 1)]. PMR spectrum in CCl_4: 8.31 (1H, d, J = 8 Hz). 6.14-7.78 (17H, m), 5.46 (H, broad s), and 2.47 (6H, s). Electronic spectrum (n-heptane): λ_{max}, nm (log ε): 239 (inflec.) (4.60), 253 (4.65), 281 (sh.) (4.54), 311 (inflec.) (4.39), 375 (4.23), 443 (4.27), 550 (inflec.) (3.70), 630 (sh.) (3.53), 676 (3.66).

Preparation of III by Cyclization of IV. A 0.64-g (1 mmole) sample of IV was refluxed in 50 ml of DMF in the presence of 0.28 g (2 mmole) of K_2CO_3 for 3 h (monitoring by TLC with elution by $CHCl_3$), after which it was diluted with 200 ml of water, and the resulting precipitate was removed by filtration, washed with water, and crystallized from benzene–methanol (1 : 3) to give 0.42 g (69%) of III. According to the PMR and IR spectra and the TLC data, the product was identical to the III obtained above.

5-[[2-[(2-Aminophenyl)azo]phenyl]amino]-4-[(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)azo]]-3-methyl-1-phenylpyrazole (V). A 1.29-g (2 mmole) sample of IV was dissolved in 80 ml of concentrated HCl, and the solution was poured over 200 g of ice. The aqueous mixture was cooled and neutralized to pH 6-7 with 6 N ammonium hydroxide, and the precipitate was washed with water, dried, and dissolved in 20 ml of $CHCl_3$. The $CHCl_3$ solution was chromatographed with a column filled with silica gel (elution with $CHCl_3$). The solvent was removed from the eluate by distillation, and the residue was crystallized twice from methanol to give 0.24 g (21%) of orange crystals of V with mp 118-119°. The solubility of the product in benzene, toluene, $CHCl_3$, acetone, and ether was $5 \cdot 10^{-1}$–10^{-1} M, as compared with $5 \cdot 10^{-2}$–10^{-2} M in methanol, ethanol, cyclohexane, and CCl_4. It was less soluble in hexane, heptane, and petroleum ether. Found: C 65.3; H 4.4; Cl 5.9; N 23.5%. Mass spectrum: 586, 587, 588, 589. $C_{32}H_{27}N_{10}Cl$. Calculated: C 65.5; H 4.5; Cl 6.1; N 23.9%. M 587.09. R_f 0.63 [benzene–$CHCl_3$ (1 : 1)]. PMR spectrum in CCl_4: 6.55-7.63 (18H, m), 5.50 (NH_2, broad s), 10.06 (NH, s). 2.54 (3H, s), and 2.30 (3H, s). Electronic spectrum (n-heptane), λ_{max}, nm (log ε): 217 (4.50), 252 (inflec.) (4.37), 329 (4.40), 382 (4.34), 405 (inflec.) (4.27), 4.65 (inflec.) (4.01).

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RESEARCH ON BENZIMIDAZOLE DERIVATIVES

XLI.* SYNTHESIS OF 2-METHYLPYRROLO[1,2-a]BENZIMIDAZOLE DERIVATIVES

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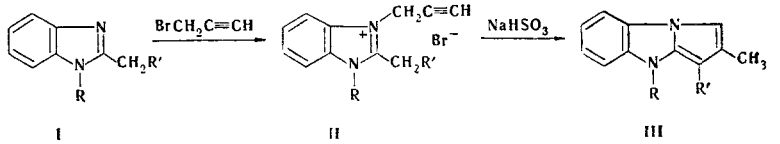
It is shown that 1,2-dialkylbenzimidazoles react with propargyl bromide to give 1,2-dialkyl-3-(2-propynyl)benzimidazolium hydrobromides, the cyclization of which leads to 2-methylpyrrolo[1,2-a]benzimidazole derivatives.

1,2-Dialkylbenzimidazoles (Ia-e) react with propargyl bromide in refluxing ethanol or n-butanol to give 1,2-dialkyl-3-(2-propynyl)benzimidazolium bromides (IIa-e) in good yields. Pyrrolo[1,2-a]benzimidazole derivatives (IIIa-e) are formed in low yields (3-5%) when salts II are refluxed in aqueous sodium carbonate or bicarbonate solutions [2]. The yields of derivatives III can be raised (to 30-40%) by refluxing salts II in an aqueous sodium bicarbonate solution in the presence of sodium hydrosulfite, which prevents oxidation of the intermediately formed methylene bases (see [3]).

The use of a suspension of potassium hydroxide in absolute tetrahydrofuran (THF) at room temperature for the cyclization of salts II led to pyrrolo[1,2-a]benzimidazoles IIId, e in good yields only in the case of IId, e ($R' = C_6H_5$); resinification of the reaction mixture occurs when $R' = H$, CH_3.



I II III

I—III a $R=CH_3$, $R'=H$; b $R=C_2H_5$, $R'=H$; c $R=R'=CH_3$; d $R=CH_3$, $R'=C_6H_5$; e $R=C_2H_5$, $R'=C_6H_5$

Considerable amounts (up to 25%) of 1,2-dialkylbenzimidazoles Ia-e, which are formed as a result of alkaline cleavage of starting quaternary salts II (see [4]), are formed during the cyclization.

The mechanism of the conversion of salts IIa-e to derivatives IIIa-e is evidently analogous to the mechanism of the cyclization of 1-alkyl-2-imino-3-(2-propynyl)benzimidazolines to imidazo[1,2-a]benzimidazole derivatives [5], which includes rearrangement of the propargyl group to an allenic group.

*See [1] for communication XL.

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