2-(1-Benzyl-2-benzimidazolylamino)-3-chloro-1,4-naphthoquinone (IXb). This compound was obtained in 40% yield as violet prisms with mp 174-175° (from o-xylene). IR spectrum: 1670 and 1660 cm^{-1} (CO). Found: C 69.7; H 3.7; Cl 8.6; N 11.6%. $C_{24}H_{16}ClN_3O_2$. Calculated: C 69.7; H 3.9; Cl 8.6; N 11.6%.

2-(4-Phenyl-2-thiazolylamino)-3-chloro-1,4-naphtoquinone (XI). This compound was obtained in 36% yield as violet prisms with mp 217-218° (from o-xylene). Found: C 62.2; H 3.4; Cl 9.5; N 7.8; S 8.5%. $C_{19}H_{11}ClN_2O_2S$. Calculated: C 62.2; H 3.0; Cl 9.7; N 7.6; S 8.7%.

5-Ethylbenzimidazo[1,2-a]naphtho[2,3-d]imidazole-7,12-dione (X) Hydrochloride. A solution of 1.3 g (3.7 mmole) of IXa in 10 ml of glacial acetic acid was refluxed for 4 h, after which it was cooled, and the resulting precipitate was removed by filtration and washed with ether to give 0.7 g (77%) of X. IR spectrum: 1660 and 1643 cm^{-1} (CO). Found: C 64.8; H 4.4; Cl 10.2%. $C_{19}H_{13}N_3O_2 \cdot HCl$. Calculated: C 64.8; H 4.0; Cl 10.0%.

Di(2-benzothiazolyl) Disulfide. A 3.34-g (20 mmole) sample of 2-mercaptobenzothiazole was added to a hot solution of 2.14 g (10 mmole) of I in 40 ml of alcohol and 40 ml of dioxane, and the mixture was refluxed for 1 h. The initially dark-red solution became lighter, and colorless needles precipitated. The solution was cooled, and the precipitate was removed by filtration to give 1.5 g of a product with mp 182-184° (from dioxane containing alcohol). The product was insoluble in alkalis but soluble in dilute sulfuric acid. The IR spectrum did not contain the absorption bands of functional groups. The melting point was in agreement with the literature value [4], and the results of elementary analysis were in agreement with the values calculated for di(2-benzothiazolyl) disulfide. Found: C 51.0; H 2.6; N 8.7%. $C_{14}H_8N_2S_4$. Calculated: C 50.6; H 2.4; N 8.4%.

LITERATURE CITED

1. I. I. Popov, Yu. G. Bogachev, P. V. Tkachenko, A. M. Simonov, and B. A. Tertov, Khim. Geterotsikl. Soedin., No. 4, 521 (1976).
2. W. L. Mosby and R. I. Boyle. J. Org. Chem., 24, 374 (1959).
3. Heilbron's Dictionary of Organic Compounds [Russian translation]. Vol. 1, Inostr. Lit., Moscow (1949). p. 480.
4. P. Jakobson, Ber., 21, 2626 (1888).

SYNTHESIS AND PROPERTIES OF CYANOPYRROLES

V. P. Zhestkov, A. F. Mironov, and R. P. Evstigneeva

UDC 547.743.4'746.07

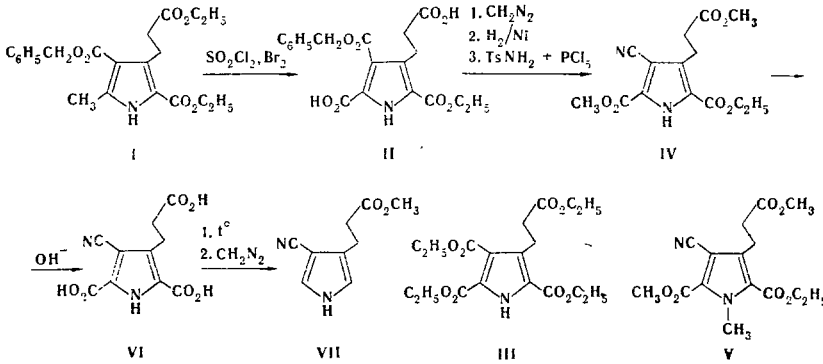
A number of cyanopyrroles were synthesized. The nitrile group was created by treatment of pyrrolecarboxylic acids with p-toluenesulfonamide and phosphorus pentachloride. It was found that the pyrrole ring is rapidly N-methylated in the presence of diazomethane when it contains three electron-acceptor substituents.

One of the most complex problems that arise in the synthesis of heme *a* – the prosthetic group of cytochromoxidase – is the introduction of a formyl group in the 8 position of the macrocycle. The preparation of porphyrins with a nitrile group and their subsequent reduction to formylporphyrins may serve as a possible approach to the solution of this problem. A recently proposed method [1] makes it possible to selectively reduce the nitrile group in the presence of vinyl and keto groups, and this is particularly valuable in the synthesis of compounds similar to heme *a*.

M. V. Lomonosov Moscow Institute of Fine Chemical Technology. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 786-789, June, 1976. Original article submitted August 18, 1975; revision submitted October 23, 1975.

In the present research we accomplished the synthesis of a number of cyanopyrroles that are intermediates in the preparation of porphyrins.

The starting 2-methyl-3-carbobenzoxy-4-(β-carbethoxyethyl)-5-carbethoxypyrrole (I) was oxidized to a pyrrolecarboxylic acid (II) by treatment with sulfuryl chloride and bromine.



Acid II was esterified in alcohol in the presence of acid catalysts (HCl, TsOH, and H_2SO_4), during which it was observed that the benzyl ester undergoes partial transesterification. The benzyl residue is replaced completely when acid II is refluxed in ethanol containing HCl for 3 h. The structure of tetraethyl ester III was confirmed by mass spectrometric data and also by the PMR spectrum, in which four triplets with intensities of three proton units each are present at 1.17-1.31 ppm, and four quartets with intensities of two proton units each are present at 4.06-4.31 ppm (this is in agreement with four carbethoxy groups).

In this connection, the subsequent esterification of acid II was carried out by means of diazomethane. The reaction mixture was vacuum distilled and subjected to hydrogenolysis over Raney nickel. The product was treated with p-toluenesulfonamide (tosyl amide) and phosphorus pentachloride and chromatographed with a column filled with silica gel. The yield of 3-cyano-4-(β-carbomethoxyethyl)-2-carbomethoxy-5-carbethoxypyrrole (IV) was 40% based on carboxylic acid II.

In addition to the NH absorption bands at 3260 cm^{-1} and the absorption bands of ester groups at ~1740 and 1710 cm^{-1}. the IR spectrum of pyrrole IV contains the characteristic frequency of the nitrile group at 2250 cm^{-1}. Signals at 2.60 and 3.16 ppm. which correspond to the propionic acid residue, and two singlets at 3.61 and 3.92 ppm of two carbomethoxy groups are present in the PMR spectrum; the triplet at 1.33 ppm and the quartet at 4.35 ppm with an overall intensity of five protons units are affiliated with a carbethoxy group. The mass spectrum of pyrrole IV contains a molecular ion peak at m/e 308.

Chromatography of the reaction mixture gave, in addition to the chief product IV, a small amount of an N-methyl-substituted pyrrole (V). In contrast to major product IV, the IR spectrum of V does not contain an NH absorption band at ~3300 cm^{-1}. In addition to the signals that are present in the PMR spectrum of pyrrole IV, the PMR spectrum of V contains a singlet at 4.17 ppm corresponding to a methyl group attached to the nitrogen atom. The mass spectrum contains a molecular ion peak with m/e 322.

The nitrogen atom is evidently alkylated in the esterification of acid II with gaseous diazomethane, as a result of which a small amount of the N-methyl derivative, which gives N-methylpyrrole V after hydrogenation and treatment with tosyl amide and phosphorus pentachloride, is formed along with the required methyl ester. In contrast to the available data [2], N-methylation occurs even on brief treatment of pyrrolecarboxylic acid II with diazomethane.

It should be noted that the method that we used to introduce a nitrile group into the pyrrole ring by treatment of the β-carboxy group with p-toluenesulfonamide and phosphorus pentachloride differs favorably from the known syntheses [3] with respect to the smaller number of steps and the higher yields.

Saponification of pyrrole IV with 2 N alkali gives a tricaboxylic acid (VI), which, as one should have expected. is an extremely stable compound and does not undergo decarboxylation even when it is heated to 260°. Iodination of VI also does not lead to removal of the carboxyl group. An α,α'-unsubstituted pyrrole, which was esterified with diazomethane to 3-cyano-4-(β-carbomethoxyethyl)pyrrole (VII), was obtained only when sodium and potassium acetates were used.

The absence of substituents in the 2 and 5 positions of the pyrrole ring follows from the PMR spectrum, which contains signals at 6.57 and 7.20 ppm, each with an intensity of one proton unit. The structure of pyrrole VII was also confirmed by mass spectrometric data.

3-Cyano-4-(β-carbomethoxyethyl)pyrrole VII can be used in the synthesis of porphyrins containing a nitrile group in the 8 position.

EXPERIMENTAL

The IT spectra of KBr pellets (for crystalline substances) and films (for the liquid compounds) were recorded with a Perkin–Elmer 257 spectrometer. The PMR spectra of deuterochloroform solutions of the compounds were recorded with a Tesla BS-487C spectrometer: the chemical shifts (δ in parts per million) are presented with respect to hexamethyldisiloxane. The mass spectra were measured with an MKh-1309 spectrometer.* Chromatography was carried out with L40/100 μm silica gel (Czechoslovakian SSR).

2-Carbethoxy-3-(β-carboxyethyl)-4-carbobenzoxy-5-carboxypyrrole (II). A solution of 9.6 ml (0.12 mole) of sulfuryl chloride and 1.45 ml (0.029 mole) of bromine in 15 ml of glacial acetic acid was added with stirring and ice cooling in the course of 30 min to a suspension of 10 g (0.026 mole) of 2-methyl-3-carbobenzoxy-4-(β-carbethoxyethyl)-5-carbethoxypyrrole (I) [4] in 60 ml of glacial acetic acid and 2 ml of acetic anhydride, after which the mixture was stirred at room temperature for 0.5 h and allowed to stand at 5° for 16 h. It was then heated to 70°, and water was added cautiously at this temperature in the course of 40 min up to a volume of 400 ml. The mixture was then cooled, and dicarboxylic acid II was removed by filtration, washed with 20 ml of 50% acetic acid, and vacuum dried to give 7.3 g (73%) of a product with mp 206-207° (from aqueous acetic acid). IR spectrum: 3270 (NH), 2620, 1720, and 1625 (COOH) cm^{-1}. Found: C 58.3; H 4.8; N 3.7%. $C_{19}H_{19}NO_8$. Calculated: C 58.6; H 4.9; N 3.6%.

3-(β-Carbethoxyethyl)-2,4,5-tricarbethoxypyrrole (III). A solution of 5.5 g (0.014 mole) of pyrrole II in 80 ml of absolute ethanol saturated with dry hydrogen chloride was refluxed for 3 h, after which the solvent was vacuum evaporated, and the residue was distilled to give 4.8 g (89%) of pyrrole III was a colorless viscous oil with bp 194-196° (0.06 mm). IR spectrum: 3280 (NH) and 1730 (CO_2Et) cm^{-1}. PMR spectrum, δ, ppm: 1.17 (3H, t, $CH_2CH_2CO_2CH_2\mathbf{CH_3}$), 1.28, 1.30, 1.31 (9H, 3t, **2,4,5-$CO_2CH_2CH_3$**), 2.50 (2H, t, $CH_2CH_2CO_2C_2H_5$), 3.13 (2H, t, $CH_2\mathbf{CH_2}CO_2C_2H_5$), 4.06 (2H, q, $CO_2\mathbf{CH_2}CH_3$), 4.29, 4.31 (6H, 2q, 2,4,5-$CO_2CH_2CH_3$), 9.86 (1H, s, NH). Mass spectrum, m/e (%): 383 (M^+, 9.2), 338 (35), 337 (30), 310 (15), 309 (100), 292 (6), 265 (7), 264 (12), 263 (10): m*: 284.3 (338→310), 227.3 (309→265).

3-Cyano-4-(β-carbomethoxyethyl)-2-carbomethoxy-5-carbethoxypyrrole (IV). A suspension of 0.86 g (2.2 mmole) of pyrrole II in 10 ml of methanol was saturated with gaseous diazomethane [5], after which it was vacuum evaporated, and the residue was distilled and hydrogenated over Raney nickel in 15 ml of methanol until hydrogen absorption ceased. The solution was poured into 100 ml of 5% sodium carbonate solution, and the catalyst was removed by filtration. The filtrate was acidified to pH 2 with dilute hydrochloric acid solution and extracted with four 10-ml portions of chloroform. The combined extracts were vacuum evaporated, the oily residue was triturated in 4 ml of petroleum ether–ether (1 : 1), and the solid material was removed by filtration.

The product was mixed with 0.32 g (1.87 mmole) of p-toluenesulfonamide and 0.8 g (3.84 mmole) of phosphorus pentachloride, and the mixture was then heated at 120° until gas evolution ceased. The phosphorus oxychloride was removed by vacuum distillation, and the hot residue was cooled, treated with 10 ml of ether and 2 ml of pyridine, and diluted to three times its original volume with water. The aqueous mixture was extracted with four 20-ml portions of chloroform, and the extracts were dried and vacuum evaporated. The residue was chromatographed with a column (1.5 × 20 cm) filled with silica gel with elution by chloroform to give 0.27 g (40% based on acid II) of IV with mp 139-140° (from chloroform containing hexane). IR spectrum: 3260 (NH). 2250 (CN), 1740, 1710 (COOR) cm^{-1}. Mass spectrum, m/e (%): 308 (M^+, 29), 278 (25), 250 (40), 249 (83), 235 (15), 222 (14), 208 (26), 202 (20), 192 (15), 176 (42), 172 (100). PMR spectrum, δ, ppm: 1.33 (3H, t, $CO_2CH_2\mathbf{CH_3}$), 2.60 (2H, t, $\mathbf{CH_2}CH_2CO_2CH_3$), 3.16 (2H, t, $CH_2\mathbf{CH_2}CO_2CH_3$), 3.61 (3H, s, $CH_2CH_2CO_2\mathbf{CH_3}$), 3.92 (3H, s, $CO_2\mathbf{CH_3}$), 4.35 (2H, q, $CO_2\mathbf{CH_2}CH_3$). Found: C 54.2; H 5.1; N 8.8%. $C_{11}H_{16}N_2O_6$. Calculated: C 54.5; H 5.2; N 9.1%.

In addition to the required pyrrole IV, a fast-moving fraction was also eluted from the column. Evaporation of this fraction gave 0.09 g (13% based on acid II) of a viscous oil, which was identified as 1-methyl-2-carbomethoxy-3-cyano-4-(β-carbomethoxyethyl)-5-carbethoxypyrrole (V). IR spectrum: 2245 (CN), 1740, 1700 (COOR) cm^{-1}. Mass spectrum, m/e (%): 322, (M^+, 46). PMR spectrum, δ, ppm: 1.37 (3H, t, $CO_2-CH_2-\mathbf{CH_3}$), 2.46 (2H, t, $\mathbf{C}H_2CH_2CO_2CH_3$), 3.07 (2H, t, $CH_2\mathbf{CH_2}CO_2CH_3$), 3.61 (3H, s, $CH_2CH_2CO_2\mathbf{CH_3}$), 3.93 (3H, s, $CO_2\mathbf{CH_3}$), 4.17, (3H, s, $N-\mathbf{CH_3}$), 4.34 (2H, δ, $CO_2\mathbf{CH_2}CH_3$).

* The authors thank B. V. Rozynov (Institute of Biochemistry Academy of Sciences of the USSR) for recording the mass spectra.

3-Cyano-4-(β-carboxyethyl)-2,5-dicarboxypyrrole (VI). A mixture of 0.89 g (2.9 mmole) of pyrrole IV and 12 ml of 2 N sodium hydroxide solution was refluxed for 1 h. after which it was cooled and extracted with eight 30-ml portions of ether. The extracts were dried, the solvent was removed by vacuum evaporation, and the residue was recrystallized from acetic acid containing heptane to give 0.61 g (83%) of a product with mp 270° (mp 272-273° [6]). IR spectrum: 3180 (NH), 2630 (COOH), 2245 (CN), 1730, 1680 (COOH) cm^{-1}.

3-Cyano-4-(β-carbomethoxyethyl)pyrrole (VII). A mixture of 100 mg of tricarboxylic acid VI, 2 g of sodium acetate, and 3 g of potassium acetate was heated in a stream of nitrogen at 180-190° for 10 min and at 230° for 2 min. The mixture was then cooled and dissolved in 40 ml of water. The aqueous solution was extracted with four 10-ml portions of ether, and the extracts were dried, concentrated in vacuo to a small volume, and treated with excess diazomethane. The solvent was evaporated, and the residue was chromatographed with a column (1.5 × 15 cm) filled with silica gel with elution by chloroform. The slow-moving fraction, which gave a rose coloration with Ehrlich's reagent on Silufol UV-254, was evaporated and the residue was recrystallized from benzene containing hexane to give 4.5 mg (6.5%) of a product with mp 81-81.5°. IR spectrum: 3340 (NH), 2240 (CN). 1725 CO_2CH_3) cm^{-1}. Mass spectrum, m/e (%): 178 (M^+, 30), 147 (9), 119 (35), 118 (100), 105 (53), 92 (8); m*: 126.4 (178→150), 96.3 (147→119), 71.1 (119→92). PMR spectrum, δ, ppm: 2.63 (2H, t, $CH_2CH_2CO_2CH_3$), 2.90 (2H, t, $CH_2CH_2CO_2CH_3$). 3.61 (3H, s, $CH_2CH_2COOCH_3$), 6.57 (1H, s, 7.20 (1H, s).

LITERATURE CITED

1. J. L. Fry, Chem. Commun., 45 (1974).
2. G. A. Swan and A. Waggott, J. Chem. Soc., C, 285 (1970).
3. H. Fischer and H. Orth. Chemis Des Pyrrols, Johnson Repr. (1969).
4. S. F. McDonald, J. Chem. Soc., 4176 (1952).
5. L. Vanino, Preparative Chemie. Vol. 2, Stuttgart (1923), p. 305.
6. M. Piattelli, Tetrahedron. 8, 266 (1960).

NEW SYNTHESIS OF PYRROLES

I. I. Ibragimov, A. N. Kost.
M. M. Guseinov, R. A. Gadzhily,
S. P. Godzhaev, V. G. Dzhafarov,
R. A. Agaev, and A. K. Murguzov

UDC 547.742.07

The reaction of ammonia or a primary amine with alkyl(cycloaklyl, phenyl)-β,γ-dihalopropyl ketones gives 2-, 2,4-, and 1,2- or 1.2,4-substituted pyrroles in high yields.

We have previously shown that reaction of carboxylic acid chlorides with allyl chloride in the presence of aluminum chloride gives dichloropropyl ketones, which are converted to 2-alkyl- or 2-cycloalkylfurans on vacuum distillation [1].

In the present research we have established that pyrroles are formed in the reaction of the above-indicated dichloro ketones with excess ammonia or a primary amine (in water or in water-ether). Nitrogen-unsubstituted compounds (in the case of the reaction with ammonia) were obtained in 60-70% yields, the yields of 1-phenylpyrroles reached 75%, and pyrroles with an alkyl, allyl, or cycloalkyl group in the 1 position were obtained in yields above 80%. No substantial difficulty was observed in the synthesis of 1,2-dialkylpyrroles even in the case of those with bulky substituents.

For the preparation of 2,4- or 1,2,4-substituted pyrroles we used dichloro ketones formed by reaction of the appropriate acid chloride with methallyl chloride in the presence of aluminum chloride, but we did not

Simgait Branch, Institute of Petrochemical Processes, Academy of Sciences of the Azerbaidzhan SSR. M. V. Lomonosov Moscow State University.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 790-793. June, 1976. Original article submitted July 18, 1975.