NEW ISOINDOLOGENS IN THE SYNTHESIS OF TETRABENZOPORPHINS

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Isoindoline hydrochloride reacts with paraformaldehyde, mesoxalic acid hydrate, N-methylformanilide, diphenylformamide, and methylene iodide in the presence of zinc acetate to give zinc tetrabenzoporphin and with sodium phenylacetate or tribenzylamine to give zinc meso-tetraphenyltetrabenzoporphin. These products are formed, respectively, from o-formylbenzoic acid and ammonium salts of malonic and phenylacetic acids. 1-Imino derivatives of isoindoline react with malonic acid to give mixtures that contain the corresponding tetrabenzoporphins, their mono- and triaza derivatives, and phthalocyanines.

A great deal of attention has recently been directed to the development of convenient methods for the synthesis of tetrabenzoporphins (TBP); this is associated with their ever increasing extensive application in various fields of science and technology. o-Cyanoacetophenone [1], phthalimidine, 3-methylphthalimidine [1] and its N-acyl and N-nitroso derivatives [2], 1-imino-3-carboxymethylene- [3], 3-hydroxy-3-methyl- [4], and 3,3-dimethylphthalimidines [3], 3-R-methylenephthalimidines (R=H, COOH) [5], 3-carboxymethylphthalimidine [3, 6], isoindole [7] and its 1,3,4,7-tetramethyl-substituted derivative [8-10] have been previously used as isoindologens. o-Acetylbenzoic acid [11], which gives Zn-TBP (Ia) in the presence of ammoniated zinc and molecular sieves (Merck, 4 Å) at 400°C, probably through a step involving the intermediately formed 3-methylenephthalimidine, has also been used as the starting compound.

We have previously proposed a one-step method for the synthesis of TBP (up to 26%) based on the condensation of phthalimide with malonic acid or sodium acetate in the presence of zinc acetate in a stream of nitrogen at 340-360°C [12]. This method was also used to obtain meso-tetraaryltetrabenzoporphins [13] for the first time by condensation of phthalimide with arylacetic acids.

Upon examination of the above-indicated isoindologens in the synthesis of TBP it may be concluded that most of the methods are based on their intermolecular cyclic tetramerization around a metal atom (primarily zinc). An isoindole fragment and a donor of a methylidyne group are simultaneously present in a number of isoindologens, whereas in the case of phthalimide and isoindole the introduction of a source of methylidyne groups into the reaction mixture is also required. For phthalimide this source is malonic acid or an alkali metal (lithium, sodium, or potassium) acetate [12], whereas paraformaldehyde is the source for isoindole [7]. The second example is directly analogous to the Rothemund reaction [14]. Most of these methods are not of practical interest. Without examining them in detail, let us note only that the currently most convenient methods for the synthesis of TBP are based on the utilization of 3-carboxymethylphthalimidine and primarily phthalimide.

In order to further develop convenient methods for the synthesis of TBP we continued our synthetic investigations in this direction [15].

In the present communication, as the starting compounds for the synthesis of TBP we used various isoindologens, viz., isoindoline (II) hydrochloride and some of its derivatives such as 3-oxo-1-iminoisoindoline (III), 5(6)-tert-butyl-1-imino-3,3-dimethoxyisoindoline (IV), 1,3-diiminoisoindoline (V), and 1,3-dibenzyliminoisoindoline (VI), as well as o-formylbenzoic acid (VII).

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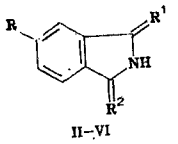
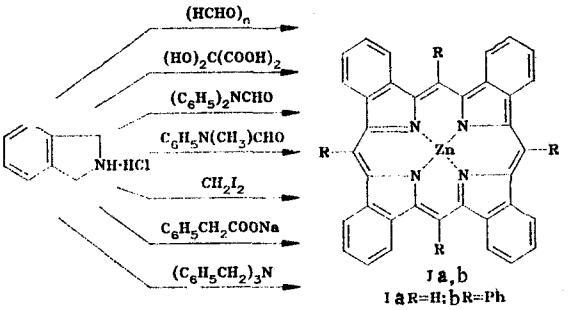


II–VI

II, III, V, VI R=H; IV R=*t*-Bu; II $R^1=R^2=H_2$; III $R^1=O$, $R^2=NH$; IV $R^1=(OMe)_2$, $R^2=NH$; V $R^1=R^2=NH$; VI $R^1=R^2=NCH_2C_6H_5$

The reaction of II with various carbonyl components, viz., paraformaldehyde, mesoxalic acid hydrate, diphenylformamide, and N-methylformanilide, in the presence of zinc acetate and alkali at 300-360°C for 6 min to 1 h in a stream of an inert gas (nitrogen, helium) gives Ia in up to 20-25% yields, which are comparable to the yields of meso-tetraarylporphyrins in the reaction of pyrrole with aromatic aldehydes in organic acids [14].

Methylene iodide can also be used in the reaction that we proposed; however, the yields of Ia do not exceed 2%.



When paraformaldehyde and N-methylformanilide are used in this reaction, the initial product is probably the 1-formyl derivative of II, four molecules of which are coordinate around the zinc cation with the simultaneous splitting out of water and the formation of Ia. However, in the case of mesoxalic acid hydrate and methylene iodide, the formation of Ia occurs as a result of their intermolecular cyclic condensation directly with isoindologen II. Attempts to use benzaldehyde in this reaction were unsuccessful, i.e., the hypothetical meso-tetraphenyltetrabenzoporphin Ib was not obtained. It is interesting that the latter is formed in up to 10% yield with sodium phenylacetate or tribenzylamine. The stable benzyl radical, which is generated under the conditions of the thermal reaction and then attacks the α-carbon atom of isoindoline, probably acts as the active component. We link the insufficiently high yields of the final product to further transformations of the benzyl radical, viz., disproportionation, etc.

On the basis of the data set forth above it may be concluded that our method for the synthesis of TBP from the extremely accessible II [16] by the reaction with several carbonyl components such as diphenylformamide and N-methylformanilide can compete successfully with other methods [3, 7].

The possibility of the formation of phthalocyanine (Pc) and other aza analogs of TBP was not excluded when the more reactive (as compared with phthalimide) imino derivatives III-VI were used in the synthesis of Ia. The reaction of III with potassium malonate or sodium acetate in the presence of zinc acetate at 330-360°C for 1-2 h leads only to zinc complex Ia in 12% and 8% yields, respectively. However, the condensation of IV-VI with malonic acid in the presence of zinc acetate under the same conditions gives mixtures of reaction products, in the electronic absorption spectra of which maxima at 674, 646, 628, and 426 nm with slight differences in their intensity ratios are observed. We were unable to separate these mixtures in the case of V and VI. The presence of a tert-butyl group in isoindologen IV led to a substantial increase in the solubility of the resulting mixture of reaction products in low-polarity organic solvents. This made it possible to separate the mixture chromatographically on aluminum oxide into two fractions, the first of which contained tetra-4-tert-butyl-Pc (VIII) [17], and the second of which consisted of a mixture of zinc complexes of tetra-4-tert-butyl-TBP (IX) [18], tetra-4-tert-butyltetrabenzomonoazaporphin (X), tetra-4-tert-butyltetrabenzotriazaporphin (XI), and tetra-4-tert-butyl-Pc (XII) [17].

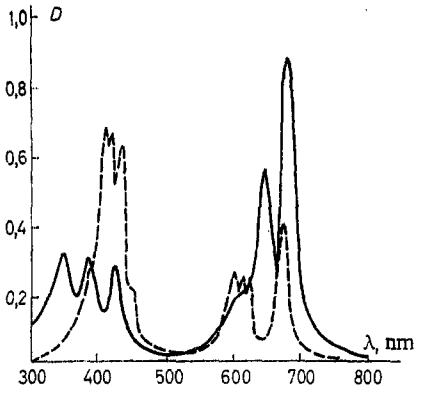
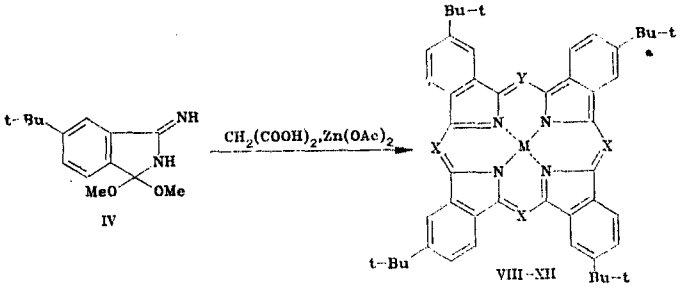


Fig. 1. Electronic absorption spectra of mixtures of XI and XII (———) and XIII and XIV (– – – – –) in chloroform.



VII M=HH, X=Y=N; IX—XII M=Zn; IX X=Y=CH; X X=CH; Y=N; XI X=N, Y=CH; XII X=Y=N

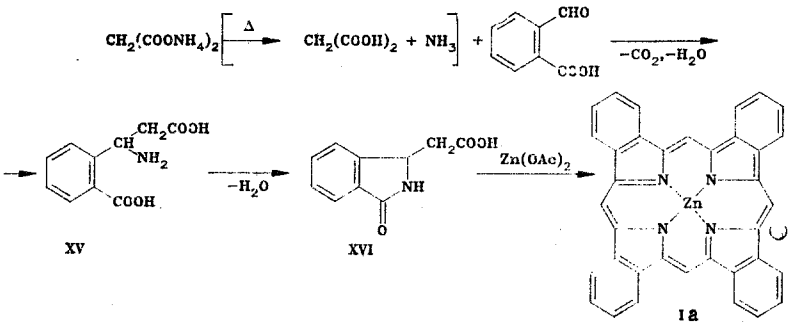
For the separation and identification of zinc complexes IX-XII we used their different capacities for demetallation in acidic media, which decrease on passing from IX to XII [3]. Thus reaction products, which were subsequently separated into two fractions by chromatography, were obtained after passing a stream of hydrogen chloride into a sulfuric acid solution of this mixture. An analysis of the electronic absorption spectra and the results of elementary analysis made it possible to establish a mixture of H_2TBP (XIII) and tetrabenzomonoazaporphin (XIV) in a ratio of 4:1 in the first fraction. Bands at 666, 616, 608, 600, 446, 430, 416, and 412 nm are observed in the electronic absorption spectrum of this fraction in chloroform (Fig. 1). It was noted that in the triplet at 616, 608, and 600 nm the first band is located in the longer-wave region than in the case of XIII [18], whereas the second and third bands are located in a shorter-wave region than in the case of XIV [3].* The intensity of the band at 666 nm is markedly increased as compared with the triplet. Bands related to XIII (412 nm) and XIV (416 nm) are also observed in the short-wave region, and the broad band at 430 nm is related to both products. Thus the electronic spectrum of the first fraction is the result of superimposition of the spectra of XIII and XIV.

The second fraction is a mixture of complexes XI and XII in a ratio of 4:1. Bands at 674, 648, 600 (sh), 422, 380, and 344 nm are observed in the electronic absorption spectrum of this mixture in chloroform (Fig. 1). The bands at 674 and 648 nm can be assigned to both compounds; however, their intensity ratio is different in the spectra of the individual compounds. Thus in the spectrum of XII [17] the first band is considerably more intense than the second, whereas the intensities are commensurable in the spectrum of XI [3]. The bands at

*It is known that the presence of tert-butyl groups in porphin-like compounds has virtually no effect on the positions of the absorption bands in their electronic spectra [17-19] as compared with the unsubstituted compounds, and data from the electronic spectra for unsubstituted monoaza- and triaza-TBP were therefore used in the analysis of the mixtures.

422 and 380 nm in the short-wave region of the spectrum belong to XI, and the band at 344 nm belongs to XII.

The reaction of o-formylbenzoic acid (VII) — the product of the oxidation of naphthalene with an alkaline solution of potassium permanganate [20] — with diammonium malonate or ammonium phenylacetate in the presence of zinc acetate for 0.5-1 h gives Ia and Ib in 12% and 10% yields, respectively. The reaction probably proceeds through a step involving the intermediate formation of 3-carboxymethylphthalimidine (XVI) in analogy with the known reaction of VII with malonic acid in the presence of ammonia [20].



The malonic acid and ammonia formed in the thermal decomposition of diammonium malonate condense at the formyl group of VII to give amino acid XV. The latter gives off a molecule of water and undergoes cyclization to XVI. The condensation of o-formylbenzoic acid with ammonium phenylacetate also proceeds via a similar scheme.

EXPERIMENTAL

The electronic absorption spectra of solutions of the compounds in chloroform were obtained with a Hitachi-356 spectrophotometer.

Zinc Tetrabenzoporphin (Ia). A) A mixture of 0.155 g (1 mmole) of isoindoline (II) hydrochloride [16], 0.219 g (1 mmole) of zinc acetate dihydrate, 0.07 g of paraformaldehyde, and 0.056 g (1 mmole) of potassium hydroxide was heated in a stream of helium at 350°C for 1 h, after which it was cooled to room temperature and washed with 25 ml of hot water and 25 ml of 80% ethanol. The precipitate was dried at 60-80°C and 0.01 mm (mercury column) and dissolved in 10 ml of pyridine. The solution was transferred to a chromatographic column (4 by 25 cm) packed with Brockmann activity II aluminum oxide and eluted with pyridine—ether (1:4) to give 30 mg of a crude product, which, according to data from the electronic absorption spectra, contained 20 mg (13%) of spectrally pure Ia. Here and subsequently, to determine the yield of the pure substance we used the intensity of the long-wave band at 632 nm with log ε 5.18 [6].

B) A 7-mg sample of a crude product containing 5 mg (3.6%) of Ia was obtained as in method A from 0.155 g (1 mmole) of II•HCl, 0.219 g (1 mmole) of zinc acetate dihydrate, 0.22 g (1.6 mmole) of mesoxalic acid hydrate, and 0.22 g (4 mmole) of potassium hydroxide.

C) A mixture of 0.155 g (1 mmole) of II•HCl, 0.219 g (1 mmole) of zinc acetate dihydrate, and 0.25 g (1.3 mmole) of diphenylformamide was heated in a stream of nitrogen at 300°C for 1 h. Workup of the reaction mixture by method A gave 25 mg of a crude product containing 18 mg (12%) of Ia. In a similar method at 330-340°C the yield of the desired product increased to 16%.

D) A mixture of 0.155 g (1 mmole) of II•HCl, 0.135 g (1 mmole) of N-methylformanilide, and 0.183 g (1 mmole) of zinc acetate dihydrate was heated at 350-360°C for 1 h, after which it was cooled, triturated, and washed successively with 50 ml of water, 50 ml of dilute hydrochloric acid (1:1), 50 ml of 5% sodium hydroxide, and 25 ml of aqueous ethanol (1:1). The residue was dried at 60-80°C and 0.01 mm (mercury column) and dissolved in 10 ml of pyridine. The solution was chromatographed with a column (4 by 30 cm) packed with Brockmann activity II aluminum oxide in a pyridine—ether system (1:1). The solvent was removed by distillation, and the residue was dissolved in 7 ml of pyridine. The solution was chromatographed with a column (4 by 35 cm) packed with aluminum oxide by elution with pyridine—ether (1:1) to give 29-36 mg (20-25%) of Ia.

E) An 11-mg (2%) sample of Ia was obtained by method A from 0.155 g (1 mmole) of II•HCl, 0.268 g (1 mmole) of methylene iodide, and 0.183 g (1 mmole) of zinc acetate dihydrate.

F) A mixture of 0.5 g (3.4 mmole) of 3-oxo-1-iminoisoindoline (III) [21], 0.56 g (2.6 mmole) of zinc acetate dihydrate, and 4.59 g (55.5 mmole) of sodium acetate was heated in a stream of helium for 2 h at 330°C, after which it was cooled to room temperature and worked up as in method A to give 60 mg of a product containing 40 mg (8%) of Ia.

G) A mixture of 0.5 g (3.4 mmole) of III, 0.56 g (2.6 mmole) of zinc acetate dihydrate, and 0.74 g (4.1 mmole) of potassium malonate was heated in a stream of helium for 1 h at 360°C, after which it was worked up as in method A to give 85 mg of a product containing 60 mg (12%) of Ia.

H) A mixture of 0.15 g (1 mmole) of o-formylbenzoic acid (VII) [20], 0.165 g (0.8 mmole) of zinc acetate dihydrate, and 0.28 g (2 mmole) of diammonium malonate was heated in a stream of helium at 360°C for 1 h, after which it was cooled to room temperature and worked up via method D to give 17 mg (12%) of Ia.

Zinc meso-Tetraphenyltetrabenzoporphin (Ib). A) A mixture of 0.78 g (0.5 mmole) of II•HCl, 0.144 g (0.5 mmole) of tribenzylamine, and 0.09 g (0.4 mmole) of zinc acetate dihydrate was heated in a stream of helium at 360°C for 5 min, after which it was cooled to room temperature and dissolved in 5 ml of chloroform. The solution was transferred to a column (1.5 by 2.5 cm) packed with Brockman activity II aluminum oxide and eluted with chloroform. The eluate was evaporated to dryness, and the residue was dissolved in 3 ml of chloroform. The solution was transferred to a similar chromatographic column packed with aluminum oxide and eluted with chloroform–hexane (1:1) to give 1 mg (10%) of the zinc complex (Ib) of meso-tetraphenyltetrabenzoporphin, which was spectrally identical to a sample obtained by the method in [13].

B) A mixture of 0.156 g (1 mmole) of II•HCl, 0.158 g (1 mmole) of sodium phenylacetate monohydrate, and 0.154 g (0.7 mmole) of zinc acetate dihydrate was heated for 10 min at 360°C in a stream of helium, after which it was cooled and purified by method A to give 12 mg (5%) of Ib.

C) A mixture of 0.15 g (1 mmole) of VII, 0.306 g (2 mmole) of ammonium phenylacetate, and 0.165 g (0.75 mmole) of zinc acetate dihydrate was heated in a stream of helium at 360°C for 30 min. Chromatographic purification as in method A gave 21 mg (10%) of Ib.

5(6)-tert-Butyl-1-imino-3,3-dimethoxyisoindoline (IV). A 5-g (20 mmole) sample of 4-tert-butylphthalonitrile [17] was added at no higher than 25°C to a solution of sodium methoxide (obtained from 0.34 g of sodium and 30 ml of methanol), and the mixture was stirred for 1.5 h. It was then evaporated to 10 ml, and the concentrate was cooled to 0°C. The resulting precipitate was removed by filtration, washed on the filter with 50 ml of ice water, and dried at 20-25°C and 0.01 mm to give 4.7 g (70%) of IV with mp 135°C (dec.). Found: N 11.1%. $C_{14}H_{20}N_2O_2$. Calculated: N 11.3%.

Reaction of Isoindologens IV-VI with Malonic Acid and Zinc Acetate. A) A mixture of 0.9 g (3.6 mmole) of IV, 0.63 g (3.6 mmole) of zinc acetate dihydrate, and 1.5 g (13.4 mmole) of malonic acid was heated for 1 h at 360°C in a stream of helium, after which it was cooled to room temperature and washed with 100 ml of hot water and 100 ml of 60% ethanol. The residue was dissolved in 25 ml of chloroform, and the solution was chromatographed with a column (5 by 50 cm) packed with Brockmann activity II aluminum oxide with collection of the fraction with R_f 0.83 (Al_2O_3, chloroform). Removal of the solvent gave 25 mg (3.7%) of tetra(4-butyl)phthalocyanine (VIII). The next fraction (0.25 g), with R_f 0.22 (Al_2O_3, chloroform), was dissolved in 20 ml of concentrated H_2SO_4, and a stream of HCl was passed into the solution at 0°C. The mixture was then poured over ice, the aqueous mixture was neutralized to pH 7 with ammonium hydroxide, and the resulting precipitate was removed by filtration and dissolved in 15 ml of chloroform. The solution was chromatographed with a column (3 by 50 cm) packed with Brockmann activity II aluminum oxide to give two fractions: one fraction contained 80 mg (12%) of a product with R_f 0.7 (Al_2O_3, chloroform), and the other fraction contained 50 mg (6.7%) of a product with R_f 0.22 (Al_2O_3, chloroform). According to the results of elementary analysis, the first fraction contained ~80% tetra(4-tert-butylbenzo)porphin ($C_{54}H_{54}N_5$) (XIII) and 20% tetra(4-tert-butyl)tetrabenzomonoazaporphin ($C_{51}H_{53}N_5$) (XIV). Found: N 8.1%. Calculated: N 7.6% (for $C_{52}H_{54}N_5$) and 9.5% (for $C_{51}H_{53}N_5$). According to the results of elementary analysis, the second fraction contained 80% zinc tetra(4-tert-butyl)tetrabenzotriazaporphin (XI) and 20% zinc tetra(4-tert-butyl)phthalocyanine (XII). Found: N 12.5%. Calculated: N 12.2% (for $C_{49}H_{49}N_7Zn$) and 14.0% (for $C_{48}H_{48}N_8Zn$).

B) A mixture of 1 g (6.9 mmole) of 1,3-diiminoisoindoline (V), 0.78 g (3.8 mmole) of malonic acid, and 0.44 g (2 mmole) of zinc acetate dihydrate was heated for 1 h at 360°C, after which it was cooled to room temperature, washed successively with 100 ml of water and 100 ml of 60% ethanol, and dried at 60-80°C and 0.01 mm to give 0.17 g (59%) of a mixture of Pc-H_2, Pc-Zn, TBP-Zn, and monoaza- and triaza-TBP-Zn.

C) A mixture of 0.323 g (1 mmole) of 1,3-dibenzyliminoisoindoline (VI), 0.208 g (2 mmole) of malonic acid, and 0.219 g (1 mmole) of zinc acetate dihydrate was heated in a stream of helium at 360°C for 1 h, after which it was worked up via method B to give 99 mg (66%) of a mixture of complexes similar to those indicated in method B.

LITERATURE CITED

1. J. H. Helberger, A. Rebay, and D. B. Hever, Ann. Chem., 533, 197 (1938).
2. J. H. Helberger and D. B. Hever, Ann. Chem., 536, 173 (1938).
3. P. A. Barrett, R. P. Linstead, and G. A. P. Rundall, J. Chem. Soc., No. 2, 1079 (1940).
4. V. F. Borodkin and Kh. A. Khaidarov, USSR Inventor's Certificate No. 833974; Byull. Izobret., No. 20, 105 (1981).
5. C. E. Dent, J. Chem. Soc., No. 1, 1 (1938).
6. R. P. Linstead and F. T. Weiss, J. Chem. Soc., No. 11, 2975 (1950).
7. D. E. Remy, Tetrahedron Lett., 24, 1451 (1983).
8. R. Bonnett, British Patent No. 1193671; Chem. Abstr., 73, 45553f (1970).
9. C. O. Bender, R. Bonnett, and R. G. Smith, J. Chem. Soc., C, No. 9, 1251 (1970).
10. C. O. Bender, R. Bonnett, and R. G. Smith, J. Chem. Soc., Perkin Trans. 1, No. 6, 771 (1972).
11. A. Vogler and H. Kunkely, Angew. Chem., 90, 808 (1978).
12. V. N. Kopranenkov, E. A. Makarova, and E. A. Luk'yanets, Zh. Obshch. Khim., 51, 2727 (1981).
13. V. N. Kopranenkov, S. N. Dashkevich, and E. A. Luk'yanets, Zh. Obshch. Khim., 51, 2513 (1981).
14. P. Rothemund, J. Am. Chem. Soc., 57, 2010 (1935).
15. V. N. Kopranenkov, E. A. Makarova, S. N. Dashkevich, and E. A. Luk'yanets, Khim. Geterotsikl. Soedin., No. 11, 1563 (1982).
16. M. A. Kolesnikov, N. A. Red'kin, and A. I. Tochilkin, USSR Inventor's Certificate No. 287944; Byull. Izobret., No. 42, 30 (1971).
17. S. A. Mikhalenko, S. V. Barkanova, O. L. Lebedev, and E. A. Luk'yanets, Zh. Obshch. Khim., 41, 2735 (1971).
18. V. N. Kopranenkov, E. A. Tarkhanova, and E. A. Luk'yanets, Zh. Org. Khim., 15, 642 (1979).
19. V. N. Kopranenkov, L. S. Goncharova, and E. A. Luk'yanets, Zh. Obshch. Khim., 47, 2143 (1977).
20. V. M. Rodionov and E. I. Chukhina, Zh. Obshch. Khim., 14, 325 (1944).
21. A. Braun and J. Tcherniac, Chem. Ber., 40, 2709 (1907).
22. P. F. Clark, J. A. Elvidge, and J. H. Golden, J. Chem. Soc., No. 11, 4135 (1956).