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Porphyrins and Their Derivatives: XXV.* Reaction of 2-Formyl-5,10,15,20-tetraphenylporphyrin with Diazomethane

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Abstract—2-Formyl-5,10,15,20-tetraphenylporphyrin and its copper and zinc complexes react with diazomethane in a mixture chloroform–alcohol providing the corresponding 2-acetyl- and 2-acetonyl derivatives. In a pure chloroform main product of diazomethane reaction with 2-formyl-5,10,15,20-tetraphenylporphyrin is 2-acetyl-5,10,15,20-tetraphenylcyclopropa[*b*]chlorin.

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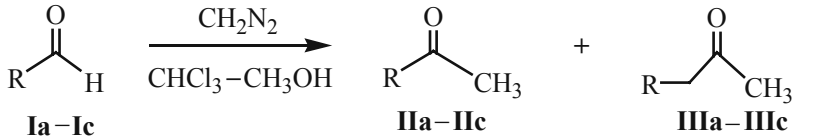
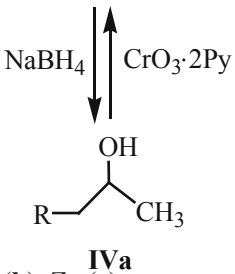
Reactions of ketones and aldehydes with diazomethane are extensively used in the organic synthesis [2]. The main products of diazomethane reaction with aldehydes are methyl ketones, but depending on the structure of substrate, of the solvent and reaction conditions homologous ketones or epoxides might form [3].

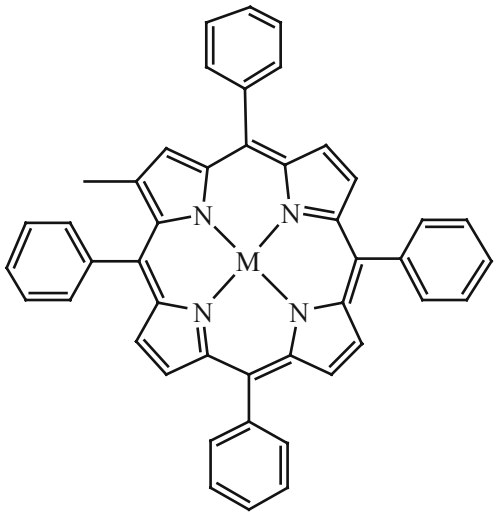
We investigated the reaction of 2-formyl-5,10,15,20-tetraphenylporphyrin (**Ia**) and its copper **Ib** and zinc **Ic** complexes with diazomethane. The target of this study was the preparation of still unknown 2-acetyl-5,10,15,20-tetraphenylporphyrin (**IIa**) that could serve as initial compound for the synthesis of complex porphyrin structures [4]. Reactions with diazomethane of various functional porphyrin derivatives, in particular naturally occurring, were considered in several publications [5], but only a single one treated the reaction with formyl-



Ia–Ic **IIa–IIc** **IIIa–IIIc**



IVa

R = 

, M = 2H (**a**), Cu (**b**), Zn (**c**).

* For communication XXIV, see [1].

porphyrins. Dimethyl ether of diformyldeuteroporphyrin (**IX**) treated with diazomethane gave a complex mixture of compounds: ketones, epoxides, and other unidentified substances [5].

We found that the reaction of 2-formyl-5,10,15,20-tetraphenylporphyrina (**Ia**) with 7-fold molar excess of diazomethane in a mixed solvent chloroform–methanol at room temperature within 18 min resulted in complete disappearance of the initial porphyrin and in the formation of a more polar compound that by mass spectrometry and ^{1}H NMR spectroscopy was identified as a mixture of approximately equal amounts of chromatographically inseparable 2-acetyl-5,10,15,20-tetraphenylporphyrin (**IIa**) and 2-acetonyl-5,10,15,20-tetraphenylporphyrin (**IIIa**) [6]. To separate this mixture we applied the well known difference in the reactivity of aliphatic and aromatic ketones with respect to reduction into alcohols. The treatment of the mixture of porphyrins **IIa** and **IIIa** with sodium borohydride in a mixed solvent chloroform–methanol at room temperature resulted in the quantitative reduction of 2-acetonylporphyrin **IIIa** into corresponding alcohol **IVa** whereas 2-acetylporphyrin **IIa** remained intact. No difficulties were met in the separation of compounds **IIa** and **IVa** by column chromatography on silica gel. Alcohol **IVa** was oxidized with excess Sarett complex in dichloromethane to obtain 2-acetonylporphyrin **IIIa** in 79% yield. Thus the yield of 2-acetonylporphyrin **IIIa** in the reaction of formylporphyrin **Ia** with diazomethane can be estimated at 30%.

Copper complex of aldehyde **Ib** reacted with diazomethane slower; at 7-fold molar excess of diazomethane in a mixed solvent chloroform–methanol within 26 min formed 25% of acetylporphyrin copper complex **IIb** and 46% of acetonylporphyrin copper complex **IIIb**. Unlike free bases **IIa** and **IIIa** copper complexes **IIb** and **IIIb** were easily separated by chromatography.

Under similar conditions zinc complex of aldehyde **Ic** reacted with diazomethane even slower than copper complex **Ib**, and the overall yield of acetylporphyrin **IIc** (41%) and acetonylporphyrin **IIIc** (44%) was higher, and the amount of side reaction products notably less. The separation of zinc complexes **IIc** and **IIIc** by column chromatography was somewhat less easy than that of copper complexes **IIb** and **IIIb**.

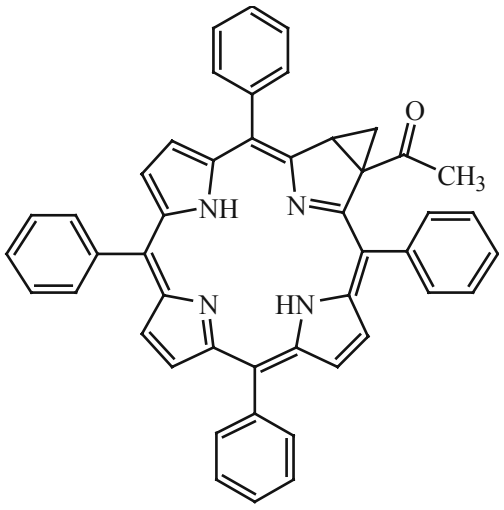
Thus in the mixed solvent $CHCl_3$–CH_3OH the reaction of aldehyde **Ia** and its complexes **Ib** and **Ic** with diazomethane proceeded relatively quickly but acetylporphyrins **IIa–IIc** formed always in somewhat lesser amounts than acetonylporphyrins **IIIa–IIIc**. At replacement of methanol by 2-propanol the reaction time grew to several hours, therefore we increased the amount of the diazomethane to 10 mol per 1 mol of porphyrin. In this case the yields of the main reaction products were moderate, and the yields of acetylporphyrins **IIa–IIc** were always a little greater than that of acetonylporphyrins **IIIa–IIIc** (see the table).

In chloroform without alcohol aldehyde **Ia** reacted with diazomethane faster than in the mixture of chloroform with 2-propanol. The main reaction product was 2-acetylcyclopropa[*b*]chlorin (**Va**), and 2-acetylporphyrin **IIa** and 2-acetonylporphyrin **IIIa** were minor reaction products. In the same conditions copper complex **Ib** was not involved into the reaction, and zinc complex **Ic** yielded considerably less acetylporphyrin **IIc** than acetonylporphyrin **IIIc**.

The reaction of diazomethane with aldehydes is known to proceed through an intermediately formed

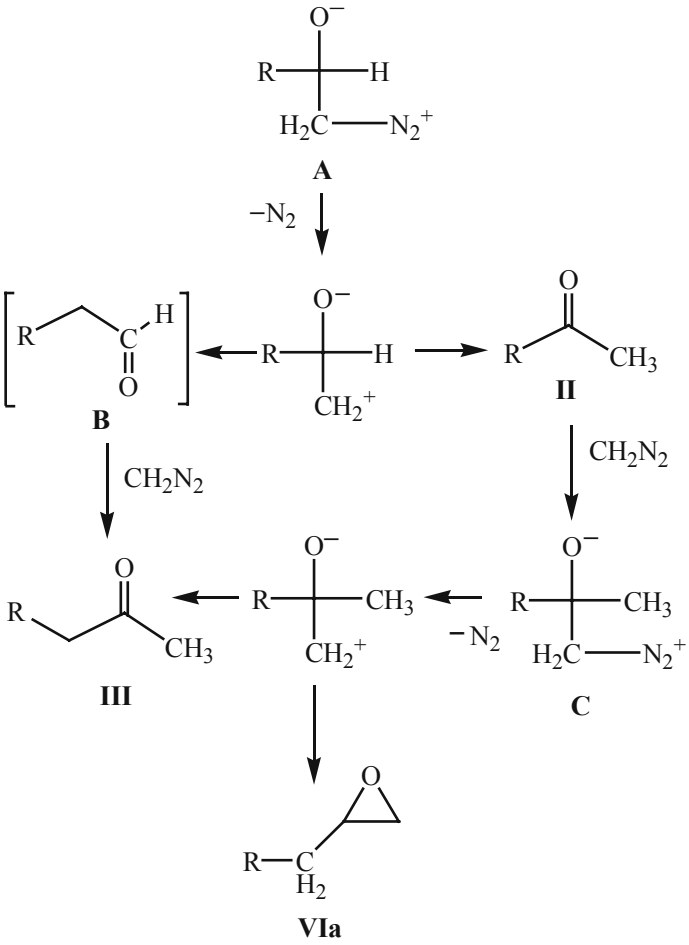
Yields of products of reaction between aldehydes **Ia–Ic** and diazomethane in various solvents at 20°C.

Compound no.	$CHCl_3$–CH_3OH, 3:1		$CHCl_3$–*i*-PrOH, 3:1		$CHCl_3$	
	Reaction time, min	Yield, %	Reaction time, h	Yield, %	Reaction time, h	Yield, %
IIa	18	28	25	26	2.5	7
IIIa		30		19		17
Va		0		0		33
IIb	26	25	25	25	2	0
IIIb		46		20		0
IIc	35	41	20	29	11	16
IIIc		44		23		36



Va

betaine **A** that is capable to suffer rearrangements [3]. In our case the migration of a hydrogen atom resulted in the formation of acetylporphyrin **II**, and the migration of the porphyrin macrocycle via intermediate formation of aldehyde **B** (which could not be isolated since it immediately reacted with diazomethane) led to 2-acetonylporphyrin **III**.



The formation of comparable quantities of porphyrins **II** and **III** shows that the migration both of hydrogen and macrocycle in betaine **A** occurred with comparable rates. A sufficiently high yield of 2-acetonylporphyrins **III** might originate from the reaction of diazomethane with 2-acetylporphyrins **II** via betaine **C**. However individual 2-acetylporphyrins **IIa–IIc** did not react with diazomethane at room temperature both in chloroform and the mixture chloroform–2-propanol. In the mixture chloroform–methanol, 3:1, diazomethane was involved into the reaction with metal complexes of 2-acetylporphyrins **IIb** and **IIc**, but the process was so slow that it could not significantly affect the yield and the ratio of porphyrins **IIb, IIc** and **IIIb, IIIc**. Considerably stronger reacted with diazomethane the free base 2-acetylporphyrin **IIa** forming within 2 h at room temperature 52% of 2-acetonylporphyrin **IIIa** and 39% of porphyrin-epoxide **VIa**. In this event both compounds obtained **IIIa** and **VIa** were products of migration of the macrocycle in betaine **C**.

The formation of chlorin **Va** may originate from the primary attack of diazomethane on the most electron-deficient β-pyrrole position in the macrocycle contiguous to the formyl group followed by cyclization and the attack of the second diazomethane molecule just on the carbonyl carbon atom. A similar formation of cyclopropachlorin was observed at the addition of diazomethane to the β-pyrrole position of porphyrin containing 4 electron-acceptor pentafluorophenyl *meso*-substituents [7].

EXPERIMENTAL

^{1}H NMR spectra were registered on a spectrometer Bruker DPX-300 at operating frequency 300.13 MHz, internal reference TMS, solvent $CDCl_3$. Mass spectra FAB were recorded on a VC 7070 EQ instrument. Desorption of ions was performed by a xenon atoms beam of 8 keV from a matrix consisting of the solution of compound under study in 3-nitrobenzyl alcohol. The precise mass of molecular ions was measured at the mass spectrometer resolution 10000. Electron absorption spectra were measured on a spectrophotometer Specord M-40 in benzene (c 10^{-6}–10^{-4} mol l^{-1}). TCX was performed on Silufol UV-254 plates, column chromatography was carried out on silica gel L 40/100, eluent toluene. The diazomethane solution in ether was obtained by procedure [8], concentration 0.38 mol l^{-1}, reactions

of carbonyl compounds with diazomethane were carried out at 20°C. 2-Formyl-5,10,15,20-tetraphenylporphyrin (**Ia**) was prepared by procedure [9].

Reaction of aldehydes Ia–Ic with diazomethane in a mixture chloroform–methanol, 3:1. To a solution of 0.104 g (1.48×10^{-4} mol) of 2-formyl-5,10,15,20-tetraphenylporphyrin zinc complex (**Ic**) in a mixture of 30 ml of chloroform and 10 ml of methanol was added 2.74 ml (1.04×10^{-3} mol) of diazomethane ether solution (*c* 0.38 mol l^{-1}), and the reaction mixture was stirred for 35 min. Then 0.2 ml of acetic acid was added, the solvent was distilled off to dryness at a reduced pressure, the residue was dissolved in toluene and subjected to chromatography on a column (30 × 1 cm) packed with silica gel.

1-(5,10,15,20-Tetraphenylporphinatozinc-2-yl)-propan-2-one (IIIc). The first zone was collected, evaporated to dryness, and the residue was crystallized from a mixture chloroform–hexane, 1:3. Yield 0.048 g R_f 0.14. Electronic spectrum, λ_{max} (log ε): 425 (5.12), 552 (4.12). Mass spectrum: *m/z* 732.188 $[M]^+$.

1-(5,10,15,20-Tetraphenylporphinatozinc-2-yl)-ethanone (IIc) was eluted from the column after compound **IIIc**. The solvent was evaporated to dryness, and the residue was crystallized from a mixture chloroform–hexane, 1:3. Yield 0.044 g, R_f 0.11. Electronic spectrum, λ_{max} (log ε): 427 (5.55), 554 (4.25), 595 (3.72). Mass spectrum: *m/z* 718.172 $[M]^+$.

Reaction of aldehydes Ia–Ic with diazomethane in a mixture chloroform–2-propanol, 3:1. To a solution of 0.202 g (2.68×10^{-4} mol) of 2-formyl-5,10,15,20-tetraphenylporphinatocopper (**Ib**) in a mixture of 60 ml of chloroform and 20 ml of 2-propanol was added at stirring 7.63 ml (2.90×10^{-3} mol) of diazomethane ether solution (*c* 0.38 mol l^{-1}). On completion of the reaction 0.4 ml of acetic acid was added, the stirring was continued for 2 min more, the solvent was evaporated to dryness at a reduced pressure, the residue was dissolved in toluene and subjected to chromatography on a column (30×2 cm) packed with silica gel.

1-(5,10,15,20-Tetraphenylporphinatocopper-2-yl)-propan-2-one (IIIb). The first zone was collected, evaporated to dryness, and the residue was crystallized from a mixture chloroform–methanol, 1:3. Yield 0.042 g, R_f 0.36. Electronic spectrum, λ_{max} (log ε): 419 (5.71), 541 (4.39). Mass spectrum: *m/z* 731.198 $[M]^+$.

1-(5,10,15,20-Tetraphenylporphinatocopper-2-yl)ethanone (IIb) was eluted from the column after compound **IIIb**. The solvent was evaporated to dryness, and the residue was crystallized from a mixture chloroform–methanol, 1:3. Yield 0.052 g, R_f 0.29. Electronic spectrum, λ_{max} (log ε): 422 (5.44), 546 (4.16), 584 sh (3.53). Mass spectrum: *m/z* 717.183 $[M]^+$.

Reaction of aldehydes Ia and Ic with diazomethane in chloroform. To a solution of 0.164 g (2.56×10^{-4} mol) of 2-formyl-5,10,15,20-tetraphenylporphyrin (**Ia**) in 55 ml of chloroform was added at stirring 6.75 ml (2.56×10^{-3} mol) of diazomethane ether solution (*c* 0.38 mol l^{-1}). On completion of the reaction 0.4 ml of acetic acid was added, the stirring was continued for 2 min more, the solvent was evaporated to dryness at a reduced pressure, the residue was dissolved in toluene and subjected to chromatography on a column (45×2 cm) packed with silica gel. In the first fraction initial aldehyde **Ia** was eluted, then a small portion of unidentified impurities.

1-(5,10,15,20-Tetraphenyl-2,3-dihydrocyclopropa[*b*]porphyrin-2-yl)ethanone (Va). The third fraction eluted from the column with toluene was a dark-violet zone. Toluene was distilled off to dryness, the residue was crystallized from a mixture chloroform–methanol, 1:7. Yield 0.057 g R_f 0.23. Electronic spectrum, λ_{max} (log ε): 421 (5.49), 522 (4.42), 550 (4.35), 602 (4.03), 656 (4.66). ^{1}H NMR spectrum, δ, ppm: 8.647 m, 8.470 m, 8.410 d (6H, β-pyrrole), 8.265 m, 8.147 m, 8.025 m (8H, *o*-phenyl), 7.706 m (12H, *m-, p*-phenyl), 4.028 d.d (1H, cyclopropyl, *J* 8.8, 4.6 Hz), 2.815 d.d (1H, cyclopropyl, *J* 8.8, 4.5 Hz), 1.823 s (3H, CH_3), 1.554 t (1H, β- pyrrole, *J* 4.6 Hz), –1.706 br.s (2H, NH). Mass spectrum: *m/z* 671.275 $[M+1]^+$.

The fourth fraction (mixture of compounds **IIa** and **IIIa**) was collected, toluene was evaporated to obtain 0.043 g of dry residue. The latter was dissolved in 8 ml of chloroform, 4 ml of methanol and 65 mg (1.71×10^{-3} mol) of sodium borohydride was added. The mixture was stirred for 25 min at room temperature, then 40 ml of water was added, chloroform layer was separated, washed with water (3×15 ml), evaporated to dryness, the residue was dissolved in a minimum amount of toluene, and subjected to chromatography on a column (12×1 cm) packed with silica gel.

1-(5,10,15,20-Tetraphenylporphyrin-2-yl)-ethanone (IIa). First fraction. The solvent was evaporated, the residue was crystallized from a mixture chloroform–methanol, 1:7. Yield 0.012 g, R_f 0.17. Electronic spectrum, λ_{max} (log ε): 424 (5.52), 520 (4.22), 556 (3.77), 598 (3.63), 655 (3.64). ^{1}H NMR spectrum,

δ, ppm: 8.985 d, 8.894 m, 8.776 s (7H, β-pyrrole), 8.212 m (8H, *o*-phenyl), 7.753 m (12H, *m-, p*-phenyl), 2.312 s (3H, CH_3), –2.676 br.s (2H, NH). Mass spectrum: *m/z* 657.258 $[M+1]^+$.

1-(5,10,15,20-Tetraphenylporphyrin-2-yl)propan-2-ol (IVa). Second fraction. The solvent was evaporated, the residue was crystallized from ethanol. Yield 0.029 g, R_f 0.06. Electronic spectrum, λ_{max} (log e): 420 (5.36), 516 (4.03), 550 (3.54), 591 (3.50), 646 (3.28). ^{1}H NMR spectrum, δ, ppm: 8.865 s, 8.770 m, 8.635 d (7H, β-pyrrole), 8.212 m, 8.118 m (8H, *o*-phenyl), 7.765 m (12H, *m-, p*-phenyl), 4.029 br.s (1H, OH), 3.005 s (2H, CH_2), 1.470 m (1H, CH), 1.118 d (3H, CH_3, *J* 3.5 Hz), –2.735 br.s (2H, NH). Mass spectrum: *m/z* 673.291 $[M+1]^+$.

1-(5,10,15,20-Tetraphenylporphyrin-2-yl)-propan-2-one (IIIa). To a solution of 0.042 g (6.24×10^{-5} mol) of alcohol **IVa** in 3 ml of dichloromethane was added 0.108 g (4.2×10^{-4} mol) of Sarett complex ($CrO_3 \cdot 2Py$), and the mixture was stirred for 17 h. The mixture turned bright green and in the course of the reaction the color changed to red-violet. Then the reaction mixture was filtered through alumina, washed with benzene, the solvent was evaporated to dryness at a reduced pressure, the residue was dissolved in toluene and subjected to chromatography on a column (12 × 1 cm) packed with silica gel. Ketone **IIIa** was collected, toluene was distilled off, and the residue was crystallized from methanol. Yield 0.033 g (79%), R_f 0.18. Electronic spectrum, λ_{max} (log ε): 421 (5.53), 516 (4.21), 549 (3.77), 592 (3.66), 647 (3.41) ^{1}H NMR spectrum, δ, ppm: 8.780 m, 8.630 m, 8.570 d (7H, β-pyrrole.), 8.235 m, 8.059 d (8H, *o*-phenyl), 7.759 m (12H, *m-, p*-phenyl). 4.109 s (2H, CH_2), 1.970 s (3H, CH_3), –2.735 br.s (2H, NH). Mass spectrum: *m/z* 671.274 $[M+1]^+$.

Reaction of diazomethane with 2-acetyltetraphenylporphyrin (IIa). To a solution of 0.056 g (8.72×10^{-5} mol) of acetylporphyrin **IIa** in a mixture of 15 ml of chloroform and 5 ml of methanol was added 2.30 ml (8.72×10^{-4} mol) of diazomethane ether solution (*c* 0.38 mol l^{-1}). The mixture was stirred for 2 h, then 0.1 ml of acetic acid was added, the stirring was continued for 2 min more, the solvent was distilled off in a vacuum. The residue was dissolved in toluene and subjected to chromatography on a column (25×1 cm) packed with silica gel.

2-Oxiranylmethyl-5,10,15,20-tetraphenylporphyrin (VIa). First fraction. The solvent was evaporated, the residue was crystallized from methanol. Yield 0.022 g (39%), R_f 0.23. Electronic spectrum, λ_{max} (log ε): 421 (5.55), 516 (4.26), 549 (3.88), 593 (3.72), 654 (3.71). ^{1}H NMR spectrum, δ, ppm: 8.888 s, 8.818 m, 8.647 d (7H, β-pyrrole), 8.224 m, 8.088 m (8H, *o*-phenyl), 7.765 m (12H, *m-, p*-phenyl), 3.367 m (1H, CH-oxirane), 3.084 m (2H, CH_2), 2.778 t, 2.444 q (2H, CH_2-oxirane), –2.765 br.s (2H, NH). Mass spectrum: *m/z* 671.273 $[M+1]^+$.

Second fraction: 2-acetonylporphyrin **IIIa**. Yield 0.030 g (52%).

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