Russian Journal of Organic Chemistry, Vol. 40, No. 3, 2004, pp. 434–437. Translated from Zhurnal Organicheskoi Khimii, Vol. 40, No. 3, 2004, pp. 461–464.

Porphyrins and Their Derivatives: XXIII.* Reaction of Formylporphyrins with Weak CH Acids

Yu. V. Ishkov, Z. I. Zhilina, L. P. Bardai, and S. V. Vodzinskii

Odessa National University, ul. Dvoryanskaya 2, Odessa, 65023 Ukraine
e-mail: zhilina@paco.net

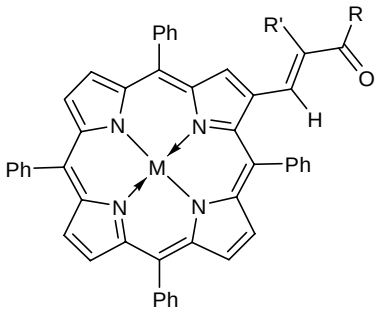
Received April 11, 2003

Abstract—β-Formylporphyrin iminium salts generated *in situ* are more reactive than the initial aldehydes in condensation with ketones having an α-methylene group. A convenient modification of the Claisen–Schimdt reaction has been developed, which makes it possible to involve hydrophobic β-formyltetraphenylporphyrin in the condensation with acetone, 1,4-diacetylbenzene, 2-acetylthiophene, acetylacetone, and acetophenone to obtain β-substituted tetraphenylporphyrins of the general formula PorphCH=CR'COCR.

Quite accessible formylporphyrins are often used as a basic unit for molecular design in the field of porphyrin chemistry; therefore, their chemical transformations are the subject of extensive studies [2–5]. In this connection, very interesting are condensations of formylporphyrins with weak CH acids, e.g., various ketones possessing a methylene group in the α-position. These reactions open wide prospects in purposeful modification of porphyrins.

There are published data on condensations of formylporphyrins only with fairly strong CH acids, specifically with malonic and barbituric acid derivatives and nitroalkanes [6, 7]. It should be noted that such condensations require the presence of strong bases and the use of polar high-boiling solvents, for porphyrins are hydrophobic substances. We have found that condensation of formylporphyrin with various ketones can be effected under mild conditions (boiling chloroform) in the absence of strong bases via intermediate formylporphyrin iminium salts which are generated *in situ*. According to our previous data, β-formylporphyrin iminium salts are formed only in the presence of secondary amines [4]. No condensation occurred when formylporphyrin **Ia** or **Ib** was heated with acetone in boiling chloroform containing piperidine or piperidinium perchlorate. However, addition of a few drops of 70% perchloric acid and piperidine to the reaction mixture promoted formation of an appreciable amount of condensation product **IIa** or **IIb** in several hours. In such a way, we have synthesized a series of previously unknown porphyrin derivatives **IIa**–**VIa** and **IIb**–**VIb**.

Condensations of aldehydes and ketones with strong CH acids (Knoevenagel reaction) are usually catalyzed by amides, amines, and ammonium salts (as a rule, in acid medium). In our case, the catalyst is a secondary ammonium salt in the presence of free amine (alkaline medium). With respect to the initial compounds (aldehydes and ketones) and their transformation products, the reaction can be regarded as a modification of the Claisen–Schmidt (aldol) condensation. Presumably, the reactive species is not a free aldehyde but the corresponding iminium perchlorate; the ease of formation of aldehyde imines is



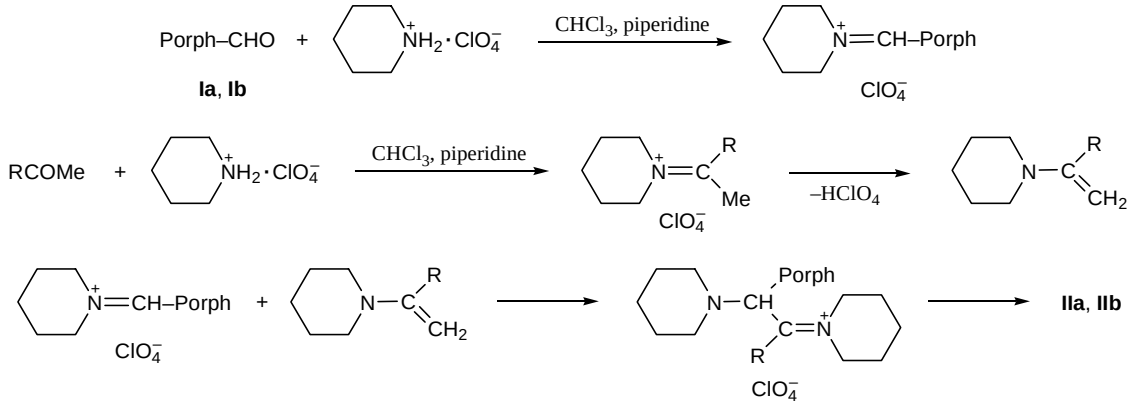
II–VI

IIa, R' = H, R = CH_3, M = 2H; **IIb**, R' = H, R = CH_3, M = Cu; **IIIa**, R' = H, R = *p*-$CH_3COC_6H_4$, M = 2H; **IIIb**, R' = H, R = *p*-$CH_3COC_6H_4$, M = Cu; **IVa**, R' = H, R = α-thienyl, M = 2H; **IVb**, R' = H, R = α-thienyl, M = Cu; **Va**, R' = CH_3CO, R = CH_3, M = 2H; **Vb**, R' = CH_3CO, R = CH_3, M = 2H; **VIa**, R' = H, R = Ph, M = 2H; **VIb**, R' = H, R = Ph, M = Cu.

* For communication XXII, see [1].

1070-4280/04/4003-0434 © 2004 MAIK "Nauka/Interperiodica"

Scheme 1.



well known. In the presence of piperidine, ketone iminium salts can be converted into enamine which is also capable of reacting with aldehydes [7]. A plausible reaction mechanism is shown in Scheme 1. The proposed mechanism resembles that reported in [8, 9] for the condensation of enamines with α-halo enamines but is not the same. As a matter of fact, this is an example of the Claisen–Schmidt reaction which occurs under very mild conditions.

It should be emphasized that in all cases formylporphyrin **Ia** reacts at a higher rate than its copper complex **Ib**. The side chain in the product contains a double bond which has *trans* configuration [10]. This assignment is beyond question for compounds **IIa**, **IVa**, and **VIa**: protons at the double bond therein give rise to two doublets in the ^{1}H NMR spectra with a coupling constant of 13–16 Hz, which is typical of *trans* olefins. However, the corresponding protons in compound **IIIa** appear in the spectrum as a singlet. Compound **IIIa** was assigned *trans* configuration on the basis of the following considerations. First, the larger the substituents, the greater the fraction of the *trans* isomer formed as a result of elimination; second, the signal from the *p*-acetylphenyl fragment in the *cis* isomer should be displaced upfield due to interaction with π-electrons of the macroring.

The low yield of products **Va** and **Vb** in the condensation of formylporphyrins with acetylacetone may be interpreted in terms of the known fact [11] that primary and secondary amines are capable of promoting cleavage of double bonds activated by electron-acceptor groups. In other words, a process reverse to the condensation may occur.

We succeeded in obtaining satisfactory electron impact mass spectra only for compounds **IIa**, **IIb**, **VIa**, and **VIb**. In the mass spectra of the other compounds, no molecular ion peak was present, and we observed profound fragmentation of the initial molecules. Informative mass spectra of compounds **IIIa** and **IIIb** were recorded using the MALDI technique. The yields, R_f values, elemental analyses, and electron absorption spectra of compounds **II**–**VI** are given in table.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker DPX-300 spectrometer at 250.15 and 300.13 MHz using $CDCl_3$ as solvent and TMS as internal reference. The electron impact mass spectra (70 eV) were obtained on an MKh-1321 instrument with direct sample admission into the ion source (ion source temperature 220°C). The electron absorption spectra were measured on a Specord M-40 spectrophotometer in $CHCl_3$ ($c = 10^{-5}$ M). Silufol UV-254 plates were used for thin-layer chromatography; elution with benzene or benzene–hexane, 3:1. Column chromatography was performed on silica gel L 40/100 μm. (2-Formyl-5,10,15,20-tetraphenylporphyrinato)copper(II) (**Ib**) and free ligand **Ia** were synthesized by the procedure described in [3].

(*E*)-4-(5,10,15,20-Tetraphenylporphyrin-2-yl)-3-buten-2-one (IIa). A solution of 0.1 g (1.56×10^{-4} mol) of aldehyde **Ia**, 0.058 g (3.12×10^{-4} mol) of piperidinium perchlorate, 0.03 ml (3.0×10^{-4} mol) of piperidine, and 0.2 ml (2.7×10^{-3} mol) of acetone in 6 ml of chloroform was heated under reflux, the progress of the reaction being monitored by TLC using toluene as eluent. When the initial aldehyde disappeared completely (~5 h), 0.2 g of sodium acetate trihydrate was added, and the mixture was heated under reflux for an additional 10 min. The organic phase was separated and evaporated to dryness, the

Yields, R_f values, elemental analyses, and electron absorption spectra of compounds **II**–**VI**

Comp. no.	Yield, %	R_f [a]	Found, %			Formula	Calculated, %			Electron spectrum ($CHCl_3$), λ_{max} (log ε)				
			C	H	N		C	H	N	*I*	*II*	*III*	*IV*	Soret
IIa	77.0	0.42	81.4	5.4	8.9	$C_{48}H_{34}N_4O$	84.4	5.0	8.2	661 (3.49)	603 (3.78)	565.3 (3.89)	523.8 (4.28)	433.8 (5.45)
IIb	74.0	0.58	77.2	4.6	7.2	$C_{48}H_{32}CuN_4O$	77.5	4.3	7.5		589.2 (4.19)	550.3 (4.42)		430.8 (5.57)
IIIa	70.5	0.36	83.9	5.0	7.0	$C_{55}H_{38}N_4O_2$	84.0	4.8	7.1	663 (3.46)	603 (3.52)	571 (3.59)	526 (3.91)	441 (5.31)
IIIb	61.5	0.48	77.5	4.4	6.4	$C_{55}H_{36}CuN_4O_2$	77.8	4.2	6.6		596 (3.89)	553 (3.97)		439 (5.25)
IVa	34.3	0.72	81.3	4.8	7.2	$C_{51}H_{34}N_4OS$	81.6	4.5	7.5	662 (3.78)	603 (4.01)	570 (4.08)	527 (4.51)	437 (5.40)
IVb	26.5	0.82	81.0	4.4	6.5	$C_{51}H_{32}CuN_4OS$	81.3	3.9	6.9		593 (3.85)	550 (4.01)		434 (5.03)
Va	28.5	0.32	82.4	5.4	7.5	$C_{50}H_{36}N_4O_2$	82.6	5.2	7.7	665 (3.96)	605 (4.02)	573 (4.03)	527 (4.44)	440 (5.30)
Vb	21.3	0.42	76.0	5.0	7.0	$C_{50}H_{34}CuN_4O_2$	76.1	4.6	7.1		590 (4.36)	548 (4.10)		429 (5.39)
VIa	76.0	0.56	85.3	5.0	7.2	$C_{53}H_{36}N_4O$	85.5	4.8	7.5	660 (3.61)	603 (3.86)	568 (3.95)	526 (4.31)	437 (5.47)
VIb	42.8	0.74	78.7	4.5	6.7	$C_{53}H_{34}CuN_4O$	78.9	4.2	6.9		593 (4.11)	551 (4.36)		434 (5.42)

[a] Eluent benzene.

residue was dissolved in a minimal amount of benzene, and the solution was applied to a column (1.5×15 cm) charged with silica gel. The column was eluted first with benzene and then with benzene–acetone (100:1) to wash off the red zone (product **IIa**). The eluate was evaporated, and the residue was recrystallized from methanol–chloroform (5:1). Yield 0.082 g. ^{1}H NMR spectrum, δ, ppm: –2.595 s (2H, NH), 2.07 s (3H, CH_3), 7.34 d and 6.77 d (2H, CH=CH, J = 16.2 Hz), 7.76 m (12H, *m*-H, *p*-H), 8.202 m (8H, *o*-H), 8.998 s and 8.8 m (7H, β-H). Mass spectrum: m/z 683 $[M]^+$; calculated: M 682.

[2-[(*E*)-3-Oxo-1-butenyl]-5,10,15,20-tetraphenylporphyrinato]copper(II) (IIb) was synthesized in a similar way from 0.110 g (1.56×10^{-4} mol) of complex **Ib**. Reaction time 7 h. Yield 0.086 g.

(*E*)-1-(4-Acetylphenyl)-3-(5,10,15,20-tetraphenylporphyrin-2-yl)propenone (IIIa) was synthesized in a similar way from 0.100 g (1.56×10^{-4} mol) of aldehyde **Ia** and 0.123 g (7.8×10^{-4} mol) of 1,4-diacetylbenzene. Yield 0.087 g. ^{1}H NMR spectrum, δ, ppm: –2.57 s (2H, NH), 2.697 c (3H, CH_3), 7.47 s (2H, CH=CH), 7.57 m and 7.75 m (12H, *m*-H, *p*-H), 7.936 d and 8.067 d (4H, 4-$CH_3COC_6\mathbf{H}_4$), 8.067 d and 8.2 m, (8H, *o*-H), 8.802 m and 9.086 s (7H, β-H). Mass spectrum: m/z 787.7 $[M]^+$; calculated: M 786.

[2-[(*E*)-3-(4-Acetylphenyl)-3-oxo-1-propenyl]-5,10,15,20-tetraphenylporphyrinato]copper(II) (IIIb) was synthesized as described above for compound **IIb** from 0.100 g (1.56×10^{-4} mol) of complex **Ib** and 0.126 g (7.8×10^{-4} mol) of 1,4-diacetylbenzene. Yield 0.082 g.

(*E*)-3-(5,10,15,20-Tetraphenylporphyrin-2-yl)-1-(2-thienyl)-2-propenone (IVa) was synthesized as described above for compound **IIa** from 0.100 g (1.56×10^{-4} mol) of aldehyde **Ia** and 0.084 g (7.8×10^{-4} mol) of 2-acetylthiophene. Yield 0.040 g. ^{1}H NMR spectrum, δ, ppm: –2.57 s (2H, NH); 7.18 d, 7.73 d, and 7.74 d (3H, thienyl); 7.46 d and 7.59 d (2H, CH=CH, J = 15.3 Hz); 7.76 m (12H, *m*-H, *p*-H); 8.115 d (J = 7.8 Hz) and 8.2 m (8H, *o*-H); 8.802 m and 9.061 s (7H, β-H).

[2-[(*E*)-3-Oxo-3-(2-thienyl)-1-propenyl]-5,10,15,-20-tetraphenylporphyrinato]copper(II) (IVb) was synthesized as described above for compound **IIb** from 0.110 g (1.56×10^{-4} mol) of complex **Ib** and 0.084 g (7.8×10^{-4} mol) of 2-acetylthiophene. Yield 0.034 g.

3-(5,10,15,20-Tetraphenylporphyrin-2-ylmethylene)pentane-2,4-dione (Va) was synthesized as described above for compound **IIa** from 0.100 g (1.56×10^{-4} mol) of aldehyde **Ia** and 0.08 ml (7.8×10^{-4} mol) of acetylacetone. Yield 0.032 g. ^{1}H NMR spectrum, δ, ppm: –2.68 s (2H, NH), 2.09 s and 2.27 s (6H, CH_3), 7.51 s (2H, CH=CH), 7.77 m (12H, *m*-H, *p*-H), 8.195 d (8H, *o*-H), 8.78 m and 8.89 s (7H, β-H).

[2-(2-Acetyl-3-oxo-1-butenyl)-5,10,15,20-tetraphenylporphyrinato]copper(II) (Vb) was synthesized as described above for compound **IIb** from 0.110 g (1.56×10^{-4} mol) of complex **Ib** and 0.08 ml (7.8×10^{-4} mol) of acetylacetone. Yield 0.026 g.

(*E*)-1-Phenyl-3-(5,10,15,20-tetraphenylporphyrin-2-yl)propenone (VIa) was synthesized as described above for compound **IIa** from 0.100 g (1.56×10^{-4} mol) of aldehyde (**Ia**) and 0.09 ml (7.8×10^{-4} mol) of acetophenone. Yield 0.089 g. ^{1}H NMR spectrum, δ, ppm: –2.57 s (2H, NH), 7.48 m and 7.89 d (5H, 1-Ph), 7.465 d and 7.52 d (2H, CH=CH, J = 13 Hz), 7.57 m and 7.74 m (12H, *m*-H, *p*-H), 8.04 m and 8.2 m (8H, *o*-H), 8.77 m and 9.086 s (7H, β-H). Mass spectrum: m/z 744 $[M]^+$; calculated: M 744.

[2-[(*E*)-3-Oxo-3-phenyl-1-propenyl]-5,10,15,20-tetraphenylporphyrinato]copper(II) (VIb) was synthesized as described above for compound **IIb** from 0.110 g (1.56×10^{-4} mol) of complex **Ib** and 0.09 ml (7.8×10^{-4} mol) of acetophenone. Yield 0.054 g.

REFERENCES

1. Ishkov, Yu.V., *Russ. J. Org. Chem*., 2001, vol. 37, p. 288.
2. Arnold, D.P., Gaete-Holmes, R., Johnson, A.W., Smith, A.R.P., and Williams, G.A., *J. Chem. Soc., Perkin Trans. 1*, 1978, p. 1660.
3. Ponomarev, G.V. and Maravin, G.B., *Khim. Geterotsikl. Soedin*., 1982, p. 59.
4. Ishkov, Yu.V., Zhilina, Z.I. Grushevaya, Zh.V., and Shul'ga, A.M., *Zh. Org. Khim*., 1993, vol. 29, p. 2270.
5. Ishkov, Yu.V. and Zhilina, Z.I., *Russ. J. Org. Chem*., 1995, vol. 31, p. 123.
6. Rish I.G., Pshezhetskii, V.S., Askarov, K.A., and Ponomarev, G.V., *Khim. Geterotsikl. Soedin*., 1985, p. 936.
7. Chen, Ch.-T., Yeh, H.-Ch., Zhang, X., and Yu, J., *Organic Lett*., 1999, vol. 1, p. 1767.
8. Birkofer, L., Kim, S.M.., and Engels, H.D., *Chem. Ber*., 1962, vol. 95, p. 1495.
9. Böhme, H., Osmers, K., and Wagner, P., *Tetrahedron Lett*., 1972, p. 2785.
10. March, J., *Advanced Organic Chemistry. Reactions, Mechanisms, and Structure*, New York: Wiley, 1985.
11. Layer, R.W., *Chem. Rev*., 1963, vol. 63, p. 489.