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Tetraphenylporphyrinylmethyltriphenylphosphonium Salts: an Improved Synthetic Protocol

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Triphenyl[(5,10,15,20-tetraphenylporphyrin-2-yl)methyl]phosphonium chloride, bromide, and trifluoroacetate were obtained by reacting 2-hydroxymethyl-5,10,15,20-tetraphenylporphyrin with, respectively, hydrogen chloride and triphenylphosphine, triphenylphosphonium hydrobromide, or a mixture of triphenylphosphine, trifluoroacetic acid and trifluoroacetic anhydride. All the salts afforded high yields in a model Wittig reaction with terephthalic aldehyde.

Keywords: Porphyrin, phosphonium salt, chloride, bromide, trifluoroacetate, alkene, Wittig reaction.

Улучшенный метод синтеза тетрафенилпорфиринилметилфосфониевых солей

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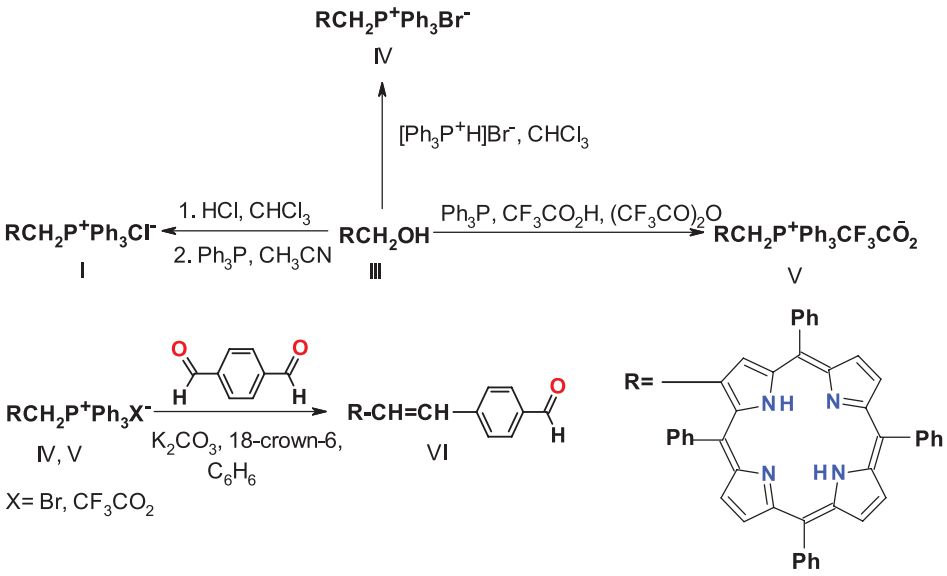
Хлорид, бромид и трифторацетат трифенил[(5,10,15,20-тетрафенилпорфирин-2-ил)метил]фосфония были получены, исходя из 2-гидроксиметил-5,10,15,20-тетрафенилпорфирина. Все эти соли дали высокие выходы целевого продукта в модельной реакции Виттига с терефталевым альдегидом.

Ключевые слова: Порфирин, соль фосфония, хлорид, бромид, трифторацетат, алкен, реакция Виттига.

The Wittig olefin synthesis has found broad application in the chemistry of porphyrins. Since 1988, phosphonium ylides prepared from porphyrinylmethylphosphonium salts are used to create exocyclic double bonds in porphyrins.[1] In order to extend our research in the field of vinylporphyrinic monomers,[2,3] a convenient and scalable synthetic procedure for phosphonium salts, containing triphenyl[(5,10,15,20-tetraphenylporphyrin-2-yl)methyl]phosphonium cation, was required.

Earlier we have demonstrated,[3] that Officer's procedure,[4,6] for the synthesis of triphenyl[(5,10,15,20-tetraphenylporphyrin-2-yl)methyl]phosphonium chloride (**I**), cannot be reproduced even for the step of synthesis of its precursor – 2-chloromethyl-5,10,15,20-tetraphenylporphyrin (**II**). We decided to test the "one-pot" approach to obtain (**I**) – 2-hydroxymethyl-5,10,15,20-tetraphenylporphyrin was converted to the corresponding chloromethylporphyrin (**II**) by a mixture of triphenylphosphine and carbon tetrachloride (Appel reaction), the volatile components were distilled off and the reaction mixture containing porphyrin (**II**) was treated with a fresh triphenylphosphine solution, affording salt (**I**). The best results were achieved when acetonitrile was used as the solvent, however the isolation of product (**I**) was quite tedious as large excesses of the reactants were required, resulting in the formation of side products in significant amounts. The synthesis was also time-consuming and hard to scale-up.

The amount of side products was reduced by performing the reaction of hydroxymethylporphyrin (**III**) with gaseous HCl in refluxing chloroform or methylene chloride followed by distillation of the solvent in a stream of HCl. In order to complete the reaction, the procedure had to be repeated twice. The reaction rate in chloroform was significantly higher than in methylene chloride. The formed chloromethylporphyrin (**II**) was not isolated in a pure form and was treated with triphenylphosphine in refluxing



chloroform or acetonitrile. As described in,[3] the formation of phosphonium salt (**I**) was very slow in chloroform, while using acetonitrile allowed to complete the reaction in 30 h with a 76 % overall yield. In comparison to work[3] the isolation and purification work-up for phosphonium salt (**I**) was simplified considerably. Furthermore, the spent quantity of triphenylphosphine was reduced twice. However, some issues may be caused by the use of gaseous HCl and the reaction time increased by 6–7 h.

Literature analysis reveals many procedures for direct transformation of hydroxymethyl derivatives into triphenylmethylphosphonium salts, which are performed without the isolation of the intermediate methyl halide. However, none of these procedures was used for the synthesis of porphyrinylmethyltriphenylphosphonium salts. Among the mentioned procedures is the reaction of primary alcohols with triphenylphosphonium hydrobromide[7] or a mixture of triphenylphosphine and trifluoroacetic acid.[8]

As the reaction of hydroxymethylporphyrin (**III**) with 1.1–2.0 eq. of both reactants proceeded very slowly, we used them in 10-fold excess, which allowed to reduce the time required to obtain triphenyl[(5,10,15,20-tetraphenylporphyrin-2-yl)methyl]phosphonium bromide (**IV**) and triphenyl-[(5,10,15,20-tetraphenylporphyrin-2-yl)methyl]phosphonium trifluoroacetate (**V**).

Acetonitrile, dichloromethane and chloroform were used as solvents for the reaction of hydroxymethylporphyrin (**III**) with triphenylphosphonium bromide. The best results were achieved in chloroform – 87 % yield of salt (**IV**) after a 21 h reaction time. However, we consider the optimal procedure for the synthesis of porphyrinylmethylphosphonium building block to be the one for trifluoroacetate (**V**). The yield was 87 % after an 18 h reaction time. The addition of 2 eq. of trifluoroacetic anhydride to the reaction mixture followed by 1 h stirring at ambient temperature and 17 h refluxing resulted in an improved yield (92 %).

As expected, using triphenylporphyrinylmethylphosphonium bromide (**IV**) or trifluoroacetate (**V**) instead of the corresponding chloride (**I**) in a model Wittig reaction with terephthalic aldehyde under conditions similar to[3] did not have a considerable effect on the reaction time and yield of 2-[2-(4-formylphenyl)ethene-1-yl]-5,10,15,20-tetraphenylporphyrin (**VI**).

In conclusion, a convenient, reproducible, and easily scalable procedures for the synthesis of valuable porphyrin-containing Wittig reagents were proposed. This allows for extended diversity of synthetic porphyrins.

Experimental

The ^{1}H NMR spectra were recorded in $CDCl_3$ on a Brucker DPX-300 spectrometer operating at 300.13 MHz, using TMS as the internal standard. The FAB mass spectra were recorded on a VC 7070 EQ instrument. Ion desorption was performed by a 8 keV xenon particle beam from a 3-nitrobenzyl alcohol matrix. The exact molecular ion masses were determined at the instrument resolution of 10000. The electronic absorption spectra were recorded on a Specord M-40 spectrophotometer in $CHCl_3$ (C=10^{-5} mol·L^{-1}). Thin layer chromatography was performed on Silufol plates. Column chromatography was conducted on silica gel 60 type 9385 (40-63 μm) from Merck. 2-Hydroxymethyl-5,10,15,20-tetraphenylporphyrin was synthesized according to the literature.[4]

*Triphenyl[(5,10,15,20-tetraphenylporphyrin-2-yl)methyl] phosphonium chloride (**I**).* A stream of dry HCl was passed for 5 h through a refluxing solution of 0.562 g (8.72·10^{-4} mol) of hydroxymethylporphyrin (**III**) in 125 mL of chloroform. The solvent was then distilled off while the stream of HCl still on. The procedure was repeated twice using 100 and 75 mL of chloroform. Then 2.287 g (8.72·10^{-3} mol) of triphenylphosphine in 100 mL of acetonitrile was added to the dry residue and the mixture was refluxed for 30 h. The solvent was evaporated, the residue was dissolved in 270 mL of chloroform, washed with water, cold 0.5 % sodium hydrocarbonate solution, again water, the organic layer was collected, the solvent was evaporated. The residue was dissolved in chloroform (100 mL) and applied onto column with silica (2.5×10 cm). The column was eluted with chloroform followed by a chloroform-methanol mixture (10:1). The major band containing the phosphonium salt (**I**) was collected, the eluent was evaporated and the residue was crystallized from a mixture of chloroform-ethyl acetate (1:3). Yield 0.613 g (76 %). *m/z* (%) 889 [M–Cl]$^+$ (100), 890 (45), 891 (18), 627 [M–CPh_3Cl]$^+$ (72). UV-Vis λ_{max} (lgε) nm:

425 (5.14), 522 (4.12), 551 (3.96), 598 (3.86), 655 (3.54). ^{1}H NMR δ_H ppm: 8.85 d, 8.78 m, 8.45 d, 8.28 d (7H, β-pyrrole), 8.16 d (4H, *o*-phenyl), 7.50–7.85 m (17H, *m*-, *p*-, *o*-phenyl, *p*-phenyl.phosph.), 7.40 d (2H, *o*-phenyl), 7.27 m (6H, *m*-phenyl.phosph.), 7.10 d (6H, *o*-phenyl.phosph.), 5.13 d (2H, -CH_2-), -2.75 wid. s. (2H, NH).

*Triphenyl[(5,10,15,20-tetraphenylporphyrin-2-yl)methyl]phosphonium bromide (**IV**).* A mixture of 0.412 g ($6.39\cdot10^{-4}$ mol) of hydroxymethylporphyrin (**III**), 2.193 g ($6.39\cdot10^{-3}$ mol) triphenylphosphine hydrobromide[5] and 120 mL of chloroform was refluxed for 20 h, then the solvent was slowly distilled off during 1 h. The residue was dissolved in 200 mL of chloroform, washed with water, cold 1 % sodium hydrocarbonate solution, again water, the organic layer was collected, the solvent was evaporated. The crude product was dissolved in 75 mL of chloroform and applied onto a silica column (2.5×8 cm). The major porphyrinic band was collected, the eluent was evaporated and the residue was crystallized from a mixture of chloroform-ethyl acetate (1:3). Yield 0.533 g (86 %). *m/z* (%) 889 $[M–Br]^+$ (100), 890 (40), 891 (22), 627 $[M–CPh_3Br]^+$ (69). UV-Vis λ_{max} (lgε) nm: 424 (5.07), 521 (4.06), 552 (3.88), 596 (3.80), 653 (3.49).

*Triphenyl[(5,10,15,20-tetraphenylporphyrin-2-yl)methyl] phosphonium trifluoroacetate (**V**).* 0.3 mL ($2.1\cdot10^{-3}$ mol) of trifluoroacetic anhydride was added to a mixture of 0.664 g ($1.03\cdot10^{-3}$ mol) hydroxymethylporphyrin (**III**), 2.702 g ($1.03\cdot10^{-2}$ mol) of triphenylphosphine, 25 mL of trifluoroacetic acid. The mixture was stirred at ambient temperature for 1 h, then it was refluxed for 17 h, the solvent was evaporated, the residue was dissolved in 320 mL of chloroform, washed with water, cold 0.5 % sodium hydrocarbonate solution, again with water, then organic layer was collected, the solvent was evaporated. The residue was dissolved in 120 mL of chloroform and applied onto silica column (2.5×9 cm). The column was eluted with chloroform followed by a chloroform-methanol 10:1 mixture. The major porphyrinic band was collected, the solvent was evaporated and the residue was crystallized from a chloroform-ethyl acetate mixture (1:3). Yield 0.950 g (92 %). *m/z* 889 $[M–CF_3CO_2]^+$ (100), 890 (46), 891 (25), 627 $[M–CPh_3CF_3CO_2]^+$, (75). UV-Vis λ_{max} (lgε) nm: 424 (5.16), 522 (4.16), 550 (4.01), 598 (3.88), 654 (3.58).

*2-[2-(4-Formylphenyl)ethene-1-yl]-5,10,15,20-tetraphenylporphyrin (**VI**).* A mixture of 0.151 g (0.163 mmol) of porphyrinylmethylphosphonium chloride (**I**) [or 0.158 g (0.163 mmol) of porphyrinylmethylphosphonium bromide (**IV**), or 0.164 g (0.163 mmol) of porphyrinylmethylphosphonium trifluoroacetate (**V**)], 0.066 g (0.489 mmol) of terephthalic aldehyde, 0.225 g (1.63 mmol) of potassium carbonate, 0.008 g (0.03 mmol) of 18-crown-6 in 30 mL of benzene was refluxed for 11 h. The mixture was then cooled, filtered through a plug of alumina (3×5 cm), evaporated to a volume of 7 mL and diluted with 14 mL of methanol. The obtained suspension was warmed to 50 °C, then a solution of 0.05 g ammonium chloride in 9 mL of water with a temperature of 50 °C was introduced. The mixture was stirred, maintaining the temperature, for 30 min, then cooled and the precipitate was filtered. The precipitate was then washed with 10 mL of 50 % aqueous ethanol, 30 mL of water at 50 °C and dried for 5 h at 110 °C, redissolved in a minimum of a benzene-carbon tetrachloride mixture and subjected to chromatography on silica (2.5×30 cm). The eluent was a 1:1 mixture of benzene-carbon tetrachloride. The product was crystallized from a chloroform-methanol mixture (1:2). Yield 0.104 g (86 %), [0.103 g (85 %) from bromide (**IV**), 0.104 g (86 %) from trifluoroacetate (**V**)], R_f 0.27 (benzene). *m/z* (%) 744 $[M]^+$ (100). UV-Vis λ_{max} (lgε) nm: 428 (5.35), 525 (4.24), 565 (4.05), 601 (3.85), 657 (3.62). ^{1}H NMR δ_H ppm: 10.02 s (1H, CHO), 9.04 s (1H, β-pyrrole), 8.85–8.71 m (6H, β-pyrrole), 8.28–8.17 m (6H, *o*-phenyl), 7.85–7.70 m (14H, *m*-, *p*-phenyl, *o*-, *m*-phenylene), 7.39 d (2H, *o*-, *m*-phenylene), 7.33 d (1H, *J*=16.1 Hz, ethylene), 7.15 d (1H, *J*=16.1 Hz, ethylene), -2.59 wid. s. (2H, NH).

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References

1. Burrell A.K., Officer D.L. *Synlett* **1998**, *12*, 1297–1307.
2. Berezovskii V.V., Ishkov Yu.V., Mazepa A.V. *Russ. J. Org. Chem.* **2010**, *46*, 1409–1413.
3. Berezovskii V.V., Ishkov Yu.V., Mazepa A.V. *Macroheterocycles* **2013**, *6*, 251–256.
4. Bonfantini E.E., Burrell A.K., Campbell W.M., Crossley M.J., Gosper J.J., Harding M.M., Officer D.L., Reid D.C.W. *J. Porphyrins Phthalocyanines* **2002**, *6*, 708–719.
5. Hercouet A., Le Corre M. *Synthesis* **1988**, 157–158.
6. Bonfantini E.E., Officer D.L. *Tetrahedron Lett.* **1993**, *34*, 8531–8534.
7. Zang J-X., Dubois Ph., Jerome R. *Synth. Commun.* **1996**, *26*, 3091–3095.
8. Lee K.Y., Kim J.N. *Bull. Korean. Chem. Soc.* **2000**, *21*(8), 763–764.

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