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On the synthesis of water-soluble Mn(III) 2-*N*-alkylpyridylporphyrins of interest for developing biomimetic catalysts and redox-active therapeutics

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Mn(III) 2-*N*-alkylpyridylporphyrins have been intensively studied as biomimetic catalysts and redox-active therapeutics. This class of compounds provided an entry to homogeneous or heterogenized cytochrome P450 models, potent superoxide dismutase (SOD) mimics, peroxynitrite decomposition catalysis, and HNO/NO traps [1, 2]. Here we report on an alternative synthesis route for a series of Mn(III) 2-*N*-alkylpyridylporphyrins compounds (alkyl = Me, Et, nBu, nHex) via the direct alkylation of a single common intermediate, *meso*-tetrakis(2-pyridyl)porphyrinatomanganese(III) (MnT-2-PyP$^+$). A new, organic-solvent-free method for preparing MnT-2-PyP$^+$ was developed using aqueous inorganic acid conditions. Thus, Mn-metallation of H_2T-2-PyP in aqueous H_2SO_4 to yield MnT-2-PyP$^+$ was optimized via chemometrics using a 3-factor Doehlert experimental design to optimize solvent acidity, Mn/H_2T-2-PyP ratio, and reaction temperature. A chromatography-free purification method using NaCl as precipitating agent produced MnT-2-PyPCl. Overall, the new routes for metallation and alkylation reduced by at least 50% the use of organic solvents and precipitating agents (such as, NH_4PF_6 and organic quaternary ammonium salts) with mild workup requirements, which represented a more affordable procedure of lower environmental impact. The new metallation-followed-by-alkylation route led to Mn(III) porphyrins in yields comparable to the classic alkylation-followed-by-metallation routes [3]. However, whereas the classic procedure was found of universal use among the various Mn(III) porphyrin alkyl-series, the new method was particularly successful for shorter alkyl derivatives (e.g., Me and Et), presenting some limitations with longer alkyl chains tosylates (e.g., nBu and nHex). Finally, we also highlight some useful experimental tips that our groups collected over two decades working on the synthesis of these water-soluble 2-*N*-alkylpyridylporphyrin complexes of interest to the development of experimental therapeutics and biomimetic models.

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References

[1] V. H. A. Pinto *et al.*, Dalton Transactions, **45**, 1030 (2020).
[2] I. Batinic-Haberle *et al.*, Antioxidant & Redox Signalling, **29**, 1691 (2018).
[3] I. Batinic-Haberle *et al.*,Dalton Transactions, **13**, 2689 (2002).