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Oxidation of Substituted 2-Methylpyrroles With Perhalogenated Metalloporphyrins: A One-pot Synthesis of Dipyrromethanes

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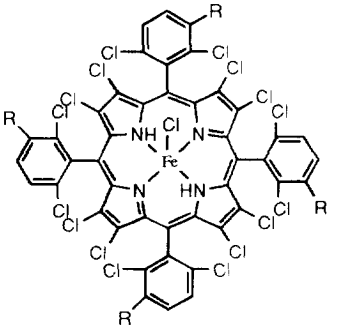
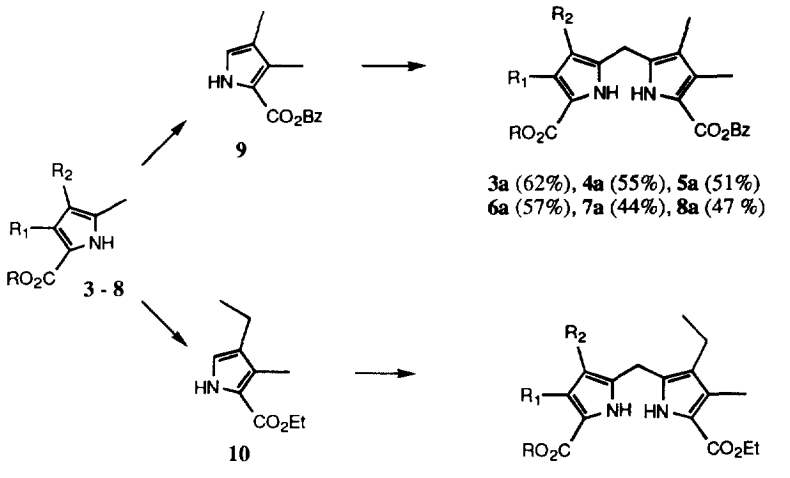
Abstract: A variety of substituted 2-methylpyrroles underwent allylic oxidation with the perchlorinated metalloporphyrin **2** and iodosylbenzene in TFA/CH_2Cl_2 (9:1). Subsequent addition of an α-free pyrrole to the same reaction mixture afforded an efficient one-pot route to dipyrromethanes.

Metalloporphyrins have been used extensively as models for studying cytochrome P-450 monooxygenase activity.[1] Although these catalysts are known to carry out many useful reactions such as alkene epoxidation and hydrocarbon oxidation, their utility in organic synthesis has been limited. Recently we reported that a new type of sulphonated, perchlorinated porphyrin catalyst **1**, can be used to oxidize 2-methyl pyrroles into their corresponding allylic alcohols.[2] In this letter, we report a useful modification to this procedure utilizing the non-sulphonated catalyst **2**, which provides an efficient one-pot preparation of a variety of substituted and functionalized dipyrromethanes.



1, R = SO_3H
2, R = H

More explicitly, when a TFA/CH_2Cl_2 (1:9) solution of the pyrrole **3** was treated with a catalytic amount of the iron III *meso*-tetra(2,6-dichlorophenyl)-β-octachloroporphyrin chloride **2**, followed by 1 equiv of iodosyl benzene (oxygen atom donor), oxidation of the 2-methyl group occurred within 5 min. Then, addition of the α-free pyrrole, 2-benzyloxycarbonyl-3,4-dimethylpyrrole **9**, into the same reaction mixture resulted in *in situ* coupling to provide (after neutralization of the mixture with $NaHCO_3$ and chromatography) the corresponding dipyrromethane **3a** in 62% yield. In a different run, when 3-ethoxycarbonyl-3-ethyl-4-methylpyrrole **10**, was added to the reaction mixture obtained after the initial oxidation, the dipyrromethane **3b** was obtained in 60 % yield. Similarly the dipyrromethanes **4a-8a** and **4b-8b** were prepared from the reaction of the allylic alcohols of the pyrroles **4** - **8** with each of the α-free pyrroles **9** and **10**. Thus, by using the appropriate monopyrrole unit it is possible to synthesize 1,9-dioxycarbonyldipyrromethanes with either symmetric (**8a**, **3b**, **6b**) or asymmetric (**3a-7a**, **4b**, **5b**, **7b**, **8b**) substitution patterns. To the best of our knowledge, this is the first report of a one-pot synthesis of dipyrromethanes starting from the corresponding monopyrrole units. It is important to note that due to its insolubility in most organic solvents, the catalyst **1** is not suitable to be used under these conditions.



3	R=Bz,	R_1=Me, R_2=Et
4	R=Bz,	R_1=Me, R_2=$(CH_2)_2CO_2CH_3$
5	R=Bz,	R_1=Me, R_2=$(CH_2)_7CH_3$
6	R=Et,	R_1=Me, R_2=Et
7	R=Et,	R_1=Et, R_2=Et
8	R=Et,	R_1=Me, R_2=Me

Substituted dipyrromethanes which are functionalized with 1,9-diester groups are precursors in the preparation of the corresponding 1,9-dicyanodipyrromethanes.[3] These dicyano compounds have been successfully employed in the synthesis of porphacyanins, a new class of "expanded" porphyrins[4,5] which have become the focus of much research activity owing to their use in the complexation of large cations,[6] magnetic resonance imaging,[7] and the photodynamic treatment of neoplastic disease.[8] Thus, the methodology described above, which is tolerant to a wide range of substituents, provides access to a large library of symmetrical and unsymmetrical 1,9-diacyldipyrromethanes as key intermediates in the synthesis of porphacyanins and other polypyrrolic macrocyclic systems.

Acknowledgments

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