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Synthesis and reactions of dipyrromethane-2,10-dicarboxylates

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Abstract—Dipyrromethane-2,10-dicarboxylates have been prepared. While oxidation and subsequent reaction of **5b** with $BF_3{\cdot}OEt_2$ yields the corresponding complex **10**, ring-closing metathesis of **5d** using $(NHC)(PCy_3)(Cl)_2Ru{=}CHPh$ **7** results in the novel hybrid macrocycle **8**. The structure of **10** has been unequivocally established by an X-ray crystallographic study.

Dipyrromethanes, important precursors to porphyrins,[1] related polypyrrolic macrocycles[2] and pigments,[3] can be oxidatively converted into dipyrromethenes. The latter are fully conjugated flat bipyrrolic moieties and as such are useful ligands for chelation to transition metals.[4] As a result, appropriately 2,10-disubstituted analogs may serve as versatile building blocks for the construction of novel hybrid macrocycles and complexes derived therefrom. However, to the best of our knowledge, such studies have not so far been carried out. Herein, we report our initial investigations towards the elaboration of new macrocyclic structures and coordination compounds derived from dipyrromethane-2,10-dicarboxylates.

We decided to begin our studies with *meso*-aryldipyrromethanes since they can be readily prepared through the acid catalysed condensation of arylaldehydes and pyrroles.[5] A series of 5-unsubstituted pyrrole-2-carboxylates were therefore synthesised. While compounds **4a**–**c** were obtained according to published procedures,[6] the synthesis of the two new pyrrole derivatives **4d**,**e** was accomplished through a similar adaptation of the Barton–Zard protocol.[7] Thus, esterification of glycine with 2 equiv. of each of the alcohols **1d**,**e** and *p*-toluenesulfonic acid (PTSA) gave the corresponding esters **2d**,**e** as the *p*-toluenesulfonate salts in 84 and 95% yield, respectively. *N*-Formylglycinate formation using methyl formate and triethylamine and dehydration with phosphoryl chloride–triethylamine proceeded smoothly to give isocyanates **3d**,**e** in 57 and 63% overall yields (Scheme 1). Subsequent treatment of **3d**,**e** with 3-acetoxy-4-nitrohexane[6a] in the presence of 2 equiv. of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in tetrahydrofuran/isopropanol (1.6:1) gave pyrroles **4d**,**e** in 68 and 95% yield, respectively. Alternatively, transesterification of **4b** with 2 equiv. of the sodium alkoxide derived from **1e** in refluxing tetrahydrofuran gave pyrrole ester **4e** in an unoptimised 60% yield. This latter procedure could prove useful for the synthesis of otherwise inaccessible pyrrole-2-carboxylates (Scheme 1).

With the requisite 5-unsubstituted pyrrole-2-carboxylates in hand, the synthesis of the novel dipyrromethane derivatives **5a**–**d** was undertaken. Compounds **5a**,**b** were best obtained via treatment of **4a**,**b** with *p*-nitrobenzaldehyde (2:1 molar ratio) in dichloromethane in the presence of boron trifluoride diethyl etherate ($BF_3{\cdot}OEt_2$, 0.5 equiv.) (Scheme 1). On the other hand, the more acid sensitive precursor **4c** decomposed upon exposure to $BF_3{\cdot}OEt_2$. However, clean conversion to the desired dipyrromethane **5c** was achieved with catalytic amounts of PTSA (0.1 equiv.). Similarly, *p*-toluenesulfonic acid catalysed condensation of pyrrole ester **4d** and *p*-nitrobenzaldehyde (2:1 molar ratio) in dichloromethane gave the requisite dipyrromethane **5d** in high yield (94%). Interestingly, the same transesterification conditions as before (vide supra) resulted mainly in decomposition of **5b** with only small quantities of the expected dipyrromethane **5e** being formed. A similar result was obtained when bipyrrole **5c** and alcohol **1e** were subjected to acidic conditions. However, reaction of bipyrrole **5b** with a stoichiometric amount of alcohol **1e** in the presence of diphenylammonium triflate[8]

Keywords: dipyrromethanes; dipyrromethenes; ring-closing metathesis; macrocycles; complexes.

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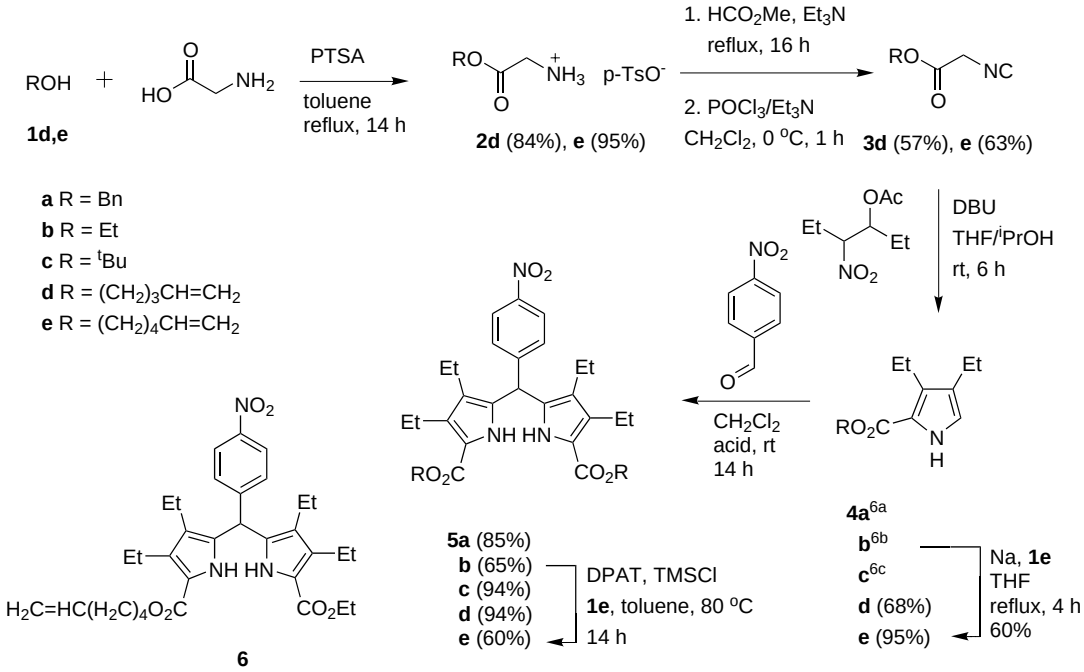
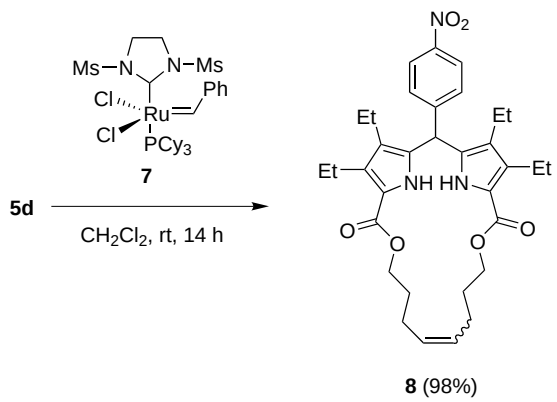


Scheme 1.

(DPAT, 10 mol%) and chlorotrimethylsilane (TMSCl, 10 mol%) in toluene gave the desired product **5e** (60%) along with the mixed diester **6**.

As the next step, the ring-closing metathesis of bisalkene **5d** was examined. Thus, a solution (0.01 M) of **5d** in dichloromethane was treated with 5 mol% of $(NHC)(PCy_3)(Cl)_2Ru{=}CHPh$ **7**[9] (Scheme 2). After fourteen hours at ambient temperature the formation of a new less polar material could be detected along with what was initially believed to be the starting material. However, no change in composition occurred upon the addition of a further 5 mol% of Grubb's catalyst **7**. Fortuitously, proton and carbon NMR analysis of the product revealed it to consist only of a *cis*/*trans*-mixture of the desired macrocycle **8**.[10] In addition, high-resolution mass ion measurement and all other spectroscopic data were consistent with the proposed structures.



Scheme 2.

In parallel, oxidation of **5a**,**b** to their corresponding dipyrromethene derivatives **9a**,**b** occurred readily with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in dichloromethane (Scheme 3). Subsequent treatment of **9b** with an excess of $BF_3{\cdot}OEt_2$ in toluene in the presence of triethylamine at ambient temperature gave the corresponding boron complex **10** in high yield (95%). The solid state structure of **10** is illustrated in Fig. 1.[11] The two pyrrole rings and their linking carbon atom are co-planar to within 0.09 Å, the boron atom lying 0.18 Å out of this plane. Thus, the central C_3N_2B ring has a slightly folded conformation, there being a ca. 8° fold about the N···N vector (the C_3N_2 portion being planar to within 0.008 Å), and this results in a pseudo axial/equatorial disposition of the two fluorine substituents. The *para*-nitrophenyl unit is oriented orthogonally (88°) to the plane of the central six-membered heterocyclic ring.

This work clearly illustrates that dipyrromethane-2,10-dicarboxylates are indeed useful molecular platforms for the potential development of novel hybrid macrocycles and complexes derived thereof. Further aspects of the chemistry of such systems will be reported in due course.

Acknowledgements

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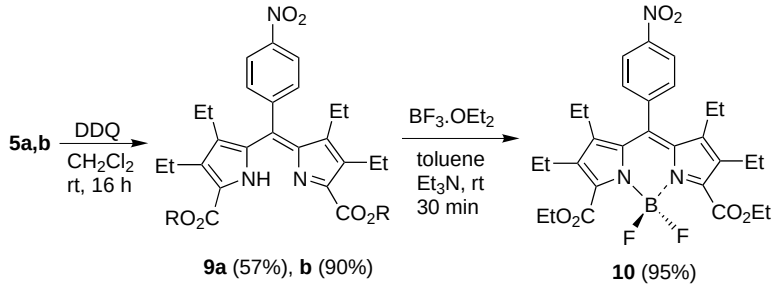

Scheme 3.

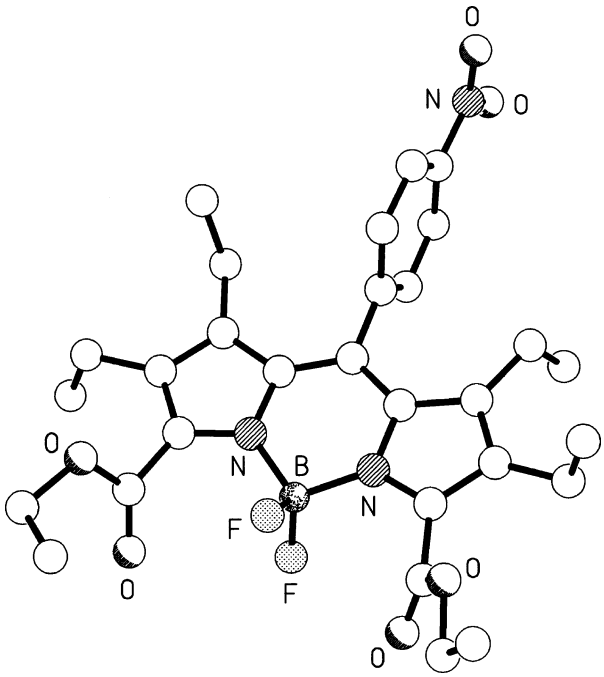

Figure 1. X-Ray crystal structure of **10**.

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10. *Selected data for* ***8***: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.95–1.05 (m, 6H), 1.14–1.25 (m, 6H), 1.64–1.74 (m, 4H), 2.06–2.15 (m, 4H), 2.34–2.44 (m, 4H), 2.75–2.85 (m, 4H), 4.24 (t, $J=5.2$ Hz, 4H, OCH_2), 5.38 (t, $J=4.8$ Hz, 2H, CH=CH), 5.67 and 5.70 (two singlets in the ratio 1:2.3, respectively, 1H, ArCH), 7.25 (d, $J=8.6$ Hz, 2H), 8.17 and 8.18 (two doublets in the ratio 2.3:1, respectively, $J=8.6$ Hz, 2H, Ar), 8.23 (br s, 2H). HRMS (FAB) calcd for $C_{33}H_{41}N_3O_6$: ($M^{+\bullet}$) 575.2995; found: ($M^{+\bullet}$) 575.3020.
11. *Crystal data for* ***10***: $C_{29}H_{34}BF_2N_3O_6$, $M=569.4$, monoclinic, $P2_1/c$ (no. 14), $a=20.478(3)$, $b=17.580(2)$, $c=8.131(3)$ Å, $\beta=100.99(2)°$, $V=2873(1)$ Å^3, $Z=4$, $D_{calcd}=1.316$ g cm^{-3}, μ(Cu Kα)$=8.37$ cm^{-1}, $T=193$ K, orange platy needles; 4238 independent measured reflections, F^2 refinement, $R_1=0.107$, $wR_2=0.267$, 3112 independent observed reflections [$|F_o|>4\sigma(|F_o|)$, $2\theta\leq120°$], 386 parameters. The high final value for R_1 is a consequence of the very poor quality of the crystalline sample which suffered from multiple twinning effects; the constitution and structure of the compound is, however, unambiguous. CCDC 177980.