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New Synthetic Routes to Molrac Spacer and Platform Systems which Incorporate the 1,4-Benzoquinone Chromophore

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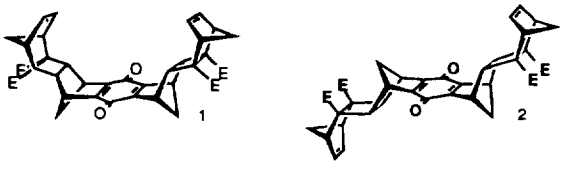
Abstract: Cycloaddition routes are described for the preparation of rigid molrac olefins containing an inbuilt 1,4-benzoquinone chromophore using either a divergent approach as used in the synthesis of platform molrac **1** and its geometrical isomer **2**, or a serial approach used to prepare **20**. A short route to bismethanoanthraquinones **3** and **7** is also reported.

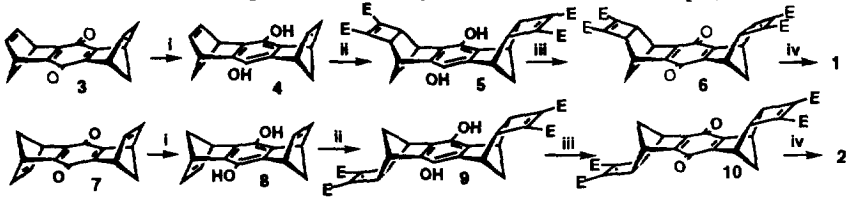
Pioneering work by Paddon-Row and his research group,[1] and subsequently by Zimmt *et al.*[2] have forcefully demonstrated the role of rigid spacer molecules for electron-transfer studies. The limitation of peptide scaffolds in this area has been noted in a recent review, where their lack of conformational rigidity was the major concern.[3] The recent report on the preparation of triad systems incorporating a naphthoquinone within the molecular framework,[1] prompts us to describe our own work in this area. We report herein methodology for preparing molrac olefins with an inbuilt 1,4-benzoquinone. Methods for attachment of bidentate ligands such as dipyridylpyridazine,[4] phenanthroline[5] and 4,5-diazafluorene (see accompanying letter)[6] to molrac olefins are now available,[4-7] so the present compounds should provide access to a new generation of diad and triad systems. Preparation of such compounds and the results of electron-transfer studies using phenanthroline metal complexes as the primary light harvesting centre[5] are under active investigation and results will be reported in due course.



Scheme 1

In selecting platform molecule[8] **1** and its isomeric spacer molecule **2** as initial targets, we found that a common synthetic pathway could be used in their synthesis (Scheme 1). Here, we exploited the fact that literature preparations[9] (and also the new method described in Scheme 5) yield quinone **3** admixed with its *anti*-isomer **7**. Accordingly we take **3** and **7** through the early stages of the synthesis as a mixture and separate at the penultimate quinone stage. The required [2π+2π] cycloaddition of dimethyl acetylene dicarboxylate (DMAD)

to the norbornene π-bond must be conducted at the hydroquinone stage as quinones **3** and **7** are unreactive. Reaction of **4** and **8** (formed from the quinone mixture by reduction with Zn/Cu couple) with DMAD and



i) Zn/Cu, MeOH; ii) DMAD, $RuH_2CO(PPh_3)_3$; iii) Ag_2O; iv) cyclopentadiene in ether

Scheme 2

$RuH_2CO(PPh_3)_3$ as catalyst[10] gave the respective bis-*exo*-cyclobutenes **5**, **9** in 98% yield (lack of vicinal proton coupling to the cyclobutyl methine protons confirms the *exo*-stereochemistry). These were oxidised (Ag_2O) in quantitative yield to the bright yellow-coloured quinones **6**, **10** which were separated by fractional crystallisation (CH_2Cl_2, MeOH): *syn*-isomer **6** (m.p. 260-262 °C) and *anti*-isomer **10** (m.p. 275-277 °C). Reaction of **6** with excess cyclopentadiene (CH_2Cl_2, 6h, RT) occurred site specifically at the cyclobutene π-bonds to form the U-shaped target molecule **1** (m.p. 289-290 °C, 96% yield); similar treatment of **10** gave the quinone rod **2** (m.p. 198-199 °C, 98% yield). The high symmetry of these products is reflected in their simple and almost identical NMR spectra[11] and the exact structure of **2** was established by X-ray analysis (Fig 1).[12]

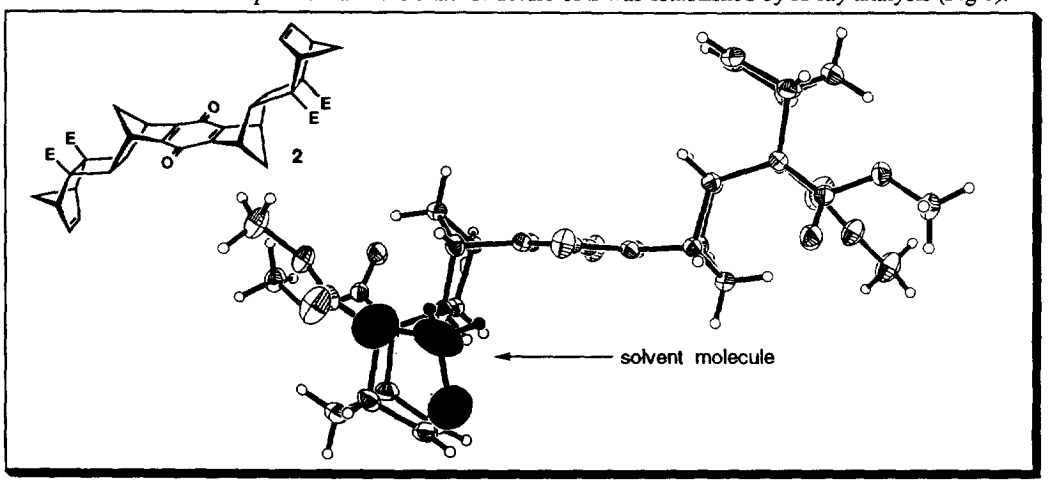
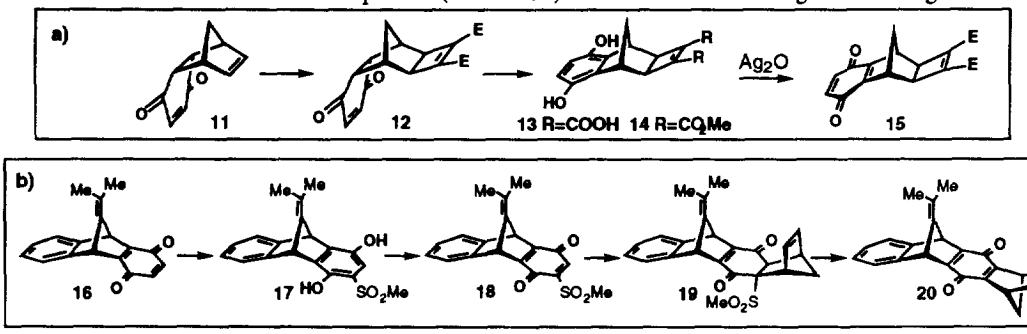


Fig 1. X-Ray structure of **2**.CH_2Cl_2 (Solvent highlighted in black)

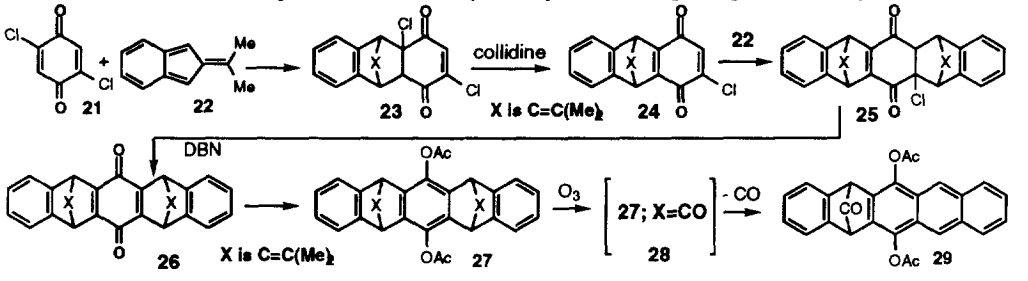
In developing methods for serially extending the molrac superstructure, we have been able to employ a fused cyclohexenedione as a latent quinone as illustrated in the preparation of terminal quinone **15** (Scheme 3a). Catalysed-addition of DMAD (70 °C, 3 days) onto enedione **11** occurs at the norbornene π-bond to provide the cycloadduct **12** in 87% yield, m.p. 123-5 °C. Acid-catalysed enolisation of **12** to the hydroquinone(dil HCl, HOAc, heat) is accompanied by hydrolysis of the ester substituents, thereby yielding diacid **13** (m.p. >300 °C) which can be re-esterified (MeOH, H_2SO_4) to the quinol diester **14** (91%, m.p. 233-235 °C)[11] without affecting the hydroquinone. Conversion to the related quinone **15** (m.p. 164-165 °C) is achieved in quantitative yield by oxidation with Ag_2O.

The next synthetic requirement was to develop a method to build site-specifically onto the external π-bond of the quinone, a known problem with quinones of this type.[13] Our approach is illustrated by conversion of substrate **16** to molrac quinone (Scheme 3b) and involves introducing an activating substituent



Scheme 3

onto the quinone to direct site selectivity. Introduction of a sulfonyl group was achieved by addition of methanesulfinate to molrac quinone **16** thereby yielding hydroquinone **17** (85%, m.p. 193-194 °C) which was oxidised (DDQ) to sulfonylquinone **18** (bright red, moisture sensitive, 95%). Reaction of cyclopentadiene with **18** occurs at the terminal π-bond to form an adduct **19** (37%; non-optimised), which can be returned to the quinone oxidation level by DBN elimination of the sulfonyl group. The gross structure of quinone **20** is supported by ^{1}H NMR but the stereochemistry is tentative, support resting on the fact that the methyl substituents are essentially equivalent in the ^{1}H NMR of precursor adduct **21**; positioning of the sulfonyl group on the *exo*-face of **19** would emphasise the lack of symmetry and cause splitting of the methyl substituents.

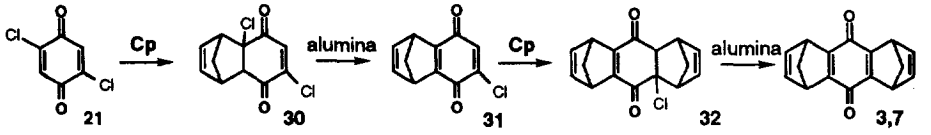


Scheme 4

This cycloaddition, elimination strategy was used (Scheme 4) to prepare initially the orange-coloured chloroquinone **24** (87%, m.p. 199-200 °C) from 8,8-dimethylisobenzofulvene **22**[14] and 2,5-dichloro-1,4-benzoquinone **21** *via* adducts **23** (stereoisomeric mixture treated directly with collidine). Similar addition of isobenzofulvene **22** to **24** provided the *syn*- and *anti*-adducts **25** (97%, m.p. 274-276 °C); dehydrochlorination occurs almost instantaneously with DBN to yield the orange-coloured *syn*- and *anti*-methanobridged quinones **26** (96%, m.p. >340 °C). The duality of proton resonances in the ^{1}H NMR of **25** and **26** confirm that they are mixtures. Reductive acetylation (Zn, Ac_2O) of **26** (83%, m.p. 280 °C), followed by ozonolysis yields the anthracene molrac monoketone **29** (27%, m.p. *ca* 170 °C decomp., ir CO 1790 cm^{-1}) following spontaneous loss of CO from **28** on workup. This procedure provides a new route to end-functionalise molracs containing a latent anthraquinone component.

A parallel cycloaddition, elimination approach provides a short synthesis of quinones **3**, **7**. Reaction of **21** with cyclopentadiene proceeds readily at RT to form a mixture of adducts **30** (not isolated) which undergo

dehydrochlorination upon chromatography on alumina; repeated Cp addition, alumina dehydrochlorination produces quinones **3** and **7** in around 70% yield; this mixture(1.5:1) is suitable for use as above (Scheme 2).



Scheme 5

Acknowledgements
RNW thanks the Australian Research Council for the award of a Senior Research Fellowship (1992-1996); DNB acknowledges with gratitude the inaugural award of a CMA Senior Visiting Fellowship at CQU (1995).

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8. We have coined the term 'platform' to describe those U-shaped molracs where direct line of sight is available at the termini, *ie* the functionality is attached to a molrac platform (as described by Butler, D. N.; Tepperman, P. M.; Gau, R. A.; Warrener, R. N.; Watson, W. H.; Kashyap, R. P. *Tetrahedron Lett.* **1995**, *36*, 6145-6148).

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11. All new compounds were fully characterised by spectroscopic techniques and their molecular formula established by microanalysis or high resolution mass spectrometry. Representative data follows: **1** ^{13}C NMR δ 42.59, 44.23, 45.53, 51.78, 52.80, 52.86, 58.87, 137.85, 152.88, 172.46. **2**; ^{13}C NMR δ 42.81, 44.09, 45.11, 51.75, 58.74, 58.86, 58.75, 137.84, 152.32, 172.44, 181.00. **15**: ^{1}H NMR δ 1.70, d, 1H; 1.77, d, 1H; 2.81, s, 2H; 3.46, s, 2H; 3.87, s, 6H; 6.65, s, 2H. **18**: ^{1}H NMR δ 1.59, s, 6H; 3.22, s, 3H; 4.94, s, 2H; 7.00-7.17, m, 2H; 7.33, s, 3H; 7.36-7.50, m, 2H. **19**: ^{1}H NMR δ 1.38, bd, 1H; 1.59, s, 6H; 2.14, b rd, 1H; 3.22, s, 3H; 3.3-3.7, m, 2H, 3.93, d, 1H, 4.88, s, 1H; 4.90, s, 1H; 5.42, dd *J* 6.0, 3.0 Hz, 1H; 5.56, dd *J* 6.0, 3.0 Hz, 1H; 6.96-7.16, m, 2H; 7.48-7.30, m, 2H. **20**: ^{1}H NMR δ 1.59, s, 6H; 2.00-2.30, m, 2H; 4.06, m, 2H; 4.94, s, 2H; 6.79, m, 2H; 6.9-7.2, m, 2H; 7.24-7.32, m, 2H. **24**: ^{1}H NMR 1.60, s, 6H; 4.96-4.99, m, 2H; 6.80, s, 1H; 7.04, m, 2H; 7.41, m, 2H. **26**: ^{1}H NMR δ 1.52, 1.56, s, s, 12H, 4.86, s, 4H, 6.90-7.14, m, 4H; 7.26-7.42, m, 4H. m/e 416 (100%), Found: M+ 416.1778, requires $C_{30}H_{24}O_2$ 416.1716. **29**: ^{1}H NMR δ 2.63, s, 6H; 4.80, s, 2H; 7.17-7.28, 2H; 7.41-7.56, m, 4H; 7.92-8.02, m, 2H; 8.39, bs, 2H.

12. Compound **2** crystallised as a monosolvate from CH_2Cl_2 trapped between the two molecules of the unit cell. Submitted to the Cambridge Crystallographic Data Center, 12 Union Rd., Cambridge, CB21E2.

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