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Homoladderanes: A Chevron-shaped Motif for Molecular Design

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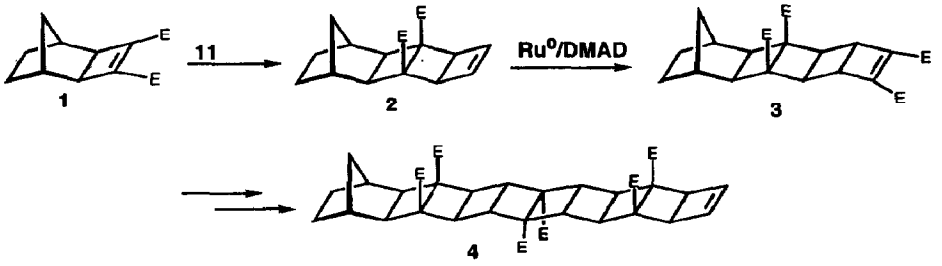
Summary: Serial application of Ruthenium-catalysed [2π+2π] cycloaddition of DMAD followed by cyclobutadiene [4π+2π] cycloaddition is used to construct ladderanes incorporating a central norbornane. The resultant homoladderanes are chevron shaped spacer-units in which the apical angle can be varied by modification of the central methylene bridge of the norbornane unit. Synthesis of 11-oxa and 11-keto tetracyclo[4.4.1.$0^{2,5}$.$0^{7,6}$] undeca-3,8-dien-3,4,8,9-tetraesters is reported as prototype central units for homoladderane construction.

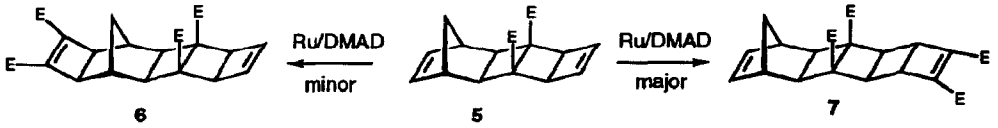
The [n]ladderanes, when *exo*-fused, produce rod-like rigid structures useful as spacer units and as motifs in molecular design. Such systems complement the curved structures already available through binanes and polynorbornanes.[1] In this communication we report on the synthesis of centrosymmetric homoladderanes where the central pair of cyclobutane rings of the [n]ladderane is replaced by a norbornane unit. Such homoladderanes are chevron-shaped with the methylene bridge of the norbornane unit being positioned at the apex. This provides a new building motif for the molecular architect where the apical angle can be varied by modification of the norbornane methylene bridge.

Homoladderanes having a terminal norbornane unit have been prepared *via* the cyclooligomerisation of cyclobutadiene diester (**9**) onto norbornadiene,[2] while other simple homoladderanes of this type are available *via* the photocycloaddition of norbornene onto substituted benzenes.[3] These techniques provide access to bent homoladderanes but are unsuitable for the preparation of chevron-shaped centrosymmetric homoladderanes of the type described herein.

Very recently we reported[1] a tandem cycloaddition approach to [n]ladderanes with the extended, all-*exo* configuration which proceeds in a stepwise manner thereby allowing specific targetting of individual ladderanes, eg **3** and **4**. We now discuss application of this method to the synthesis of centrosymmetric homoladderanes.

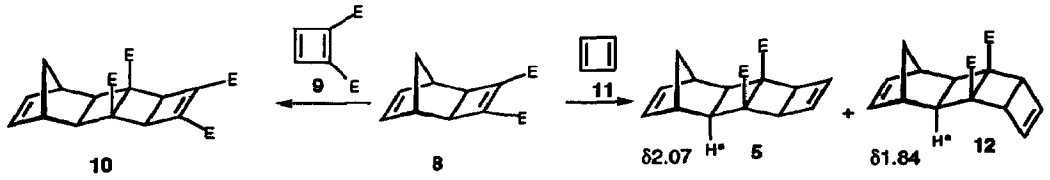


Scheme 1



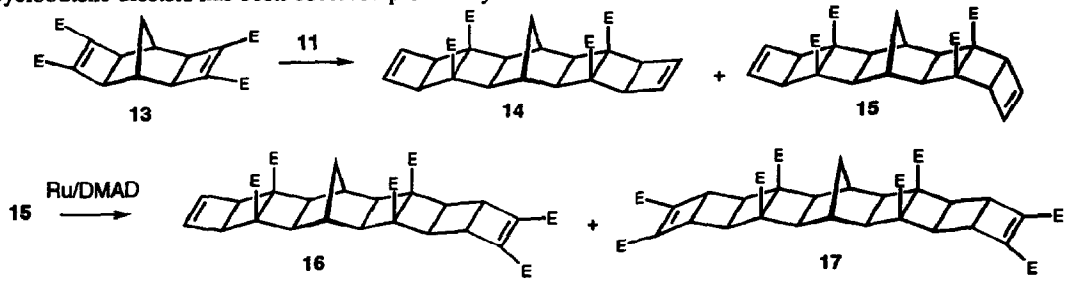
Scheme 2

A key feature of our extension reaction is the *exo*-specific $RuH_2CO(PAr_3)_3$-catalysed[4] coupling of dimethyl acetylene dicarboxylate (DMAD) onto a cyclobutene π-bond. While this cycloaddition is well-documented to occur onto norbornene-π-bonds,[5] it has only recently been found to occur onto cyclobutenyl π-systems.[6] Reaction of polycyclic bisolefin (**5**) with Ru°/DMAD showed that each π-centre was reactive, with cycloaddition at the more-strained cyclobutene (to produce **7**) being favoured 3:1 over formation of the norbornene adduct **6**.[7]



Scheme 3

The reaction of cyclobutadiene 1,2-diester (**9**) with Smith's diester (**8**) is most inefficient and produces the 1:1-adduct (**10**) in poor yield (21%) together with the known oligomers of **9**.[8] In contrast, cyclobutadiene cycloaddition to **8** proceeds in good yield to produce a 3:1-mixture of the extended isomer (**5**) and the bent isomer (**12**). Stereochemical assignments follow from the shielding offered protons Ha (see structures **5** and **12**) by the cyclobutene π-bond in the bent isomer (**12**) (δ 1.84) relative to those in the extended stereoisomer (**5**) (δ 2.07). The preference for Alder-addition stereochemistry to occur in cyclobutadiene cycloaddition onto cyclobutene diesters has been observed previously.[9]

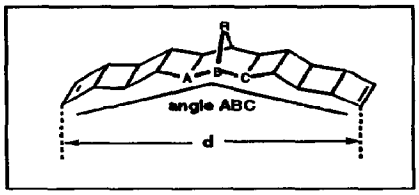


Scheme 4

Indeed, cyclobutadiene cycloaddition onto the biscyclobutene diester (**13**) yields predominantly the dual extended cycloadduct (**14**) (55%) together with some of the bent isomer (**15**) (5%) and a trace of the doubly bent isomer. Application of the Ru/DMAD cycloaddition to biscyclobutene (**15**) yields a mixture of the mono[2π+2π] product (**16**) and the centrosymmetric homo[10]ladderane (**17**) where dual addition has occurred; exclusive *exo*-cycloaddition occurs onto each of the cyclobutene π-bonds.

The homoladderanes differ in geometry from their ladderane counterparts owing to the presence of the norbornane component. This means that the otherwise rod-like spacer unit forms a chevron motif with the norbornane controlling the apical angle. Molecular modelling (MM2) indicates that a series of chevrons are

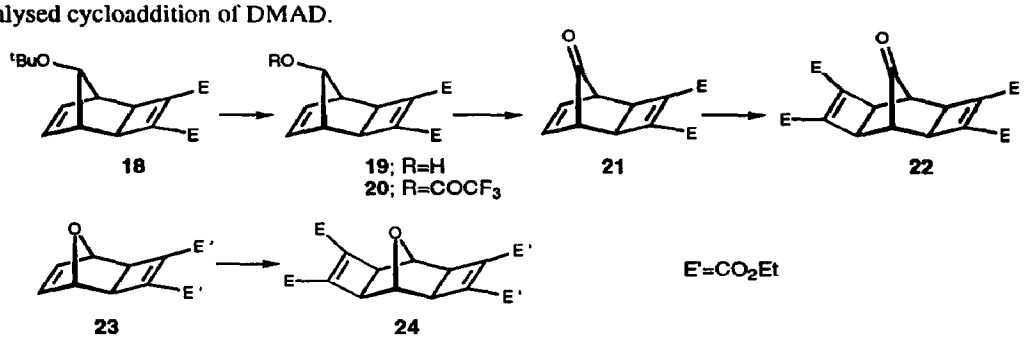
available in which the apical angle can be varied by modifying the norbornane methylene bridge. This affects the distance between the terminii as well as the apical angle and representative data are presented in the table for various homo[10]ladderanes.



	angle ABC[a]	d		angle ABC	d
	110.6	12.94		106.8	12.94
	107.8	12.97		106.1	12.88
	107.9	12.97		104.7	12.88
	108.7* 108.3¶ * planar ¶ pyramidal	12.94* 12.92¶		99.9	12.49

[a]values from biosym, discover (values from MM2).

With this in mind, we report entry to the prototype ring-systems where the methylene bridge in the homo[4]ladderane has been replaced with a carbonyl bridge to produce ketone (**22**) and with an oxygen atom to produce the oxa-tetracycle (**24**). The synthesis of the ketone (**22**) commences from the *tert*-butoxy compound (**18**)[10] which, upon treatment with TFA at RT for 10 min.[12, 13] yielded the alcohol (**19**). Swern oxidation of (**19**) provided the bridge-ketone (**21**),(i.r.CO 1782 cm^{-1}), which yielded the homo[4]ladderane (**22**) on Ru-catalysed cycloaddition of DMAD.



Scheme 5

Similar catalysed addition of DMAD onto tricyclic ester (**23**)[4] yielded the oxabridged homo[4]ladderane (**24**). In this case the ethyl ester (**23**) was used to demonstrate the ability of the method to produce mixed ester products.

Acknowledgements

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6. Indeed our own experience shows that many $RuH_2CO(PAr_3)_3$, [Ar = Ph- or p-FPh-]- catalysed additions of DMAD to strained π-systems are unsucessful. A more versatile catalyst for [2π+2π] cycloaddition of acetylenes onto norbornadienes has recently been reported[7] which should open the way to a larger variety of substituents becoming available on the homoladderane.
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10. Prepared from the thermal cycloaddition of DMAD onto 7-(*tert*-butoxy)quadricyclane according to the method of Smith.[11]
11. Smith, C. D. *J. Am. Chem. Soc.*, **1966**, *88*, 4273-4274.
12. Prolonged treatment of the ether (**18**) with TFA, yields after 24 hrs the trifluoroacetate (**20**) in 54% yield.
13. All new compounds gave satisfactory elemental analysis and spectroscopic data. Compound (m.p. °C): **5** (85-86.5); **6** (146-147); **7** (136-136.5); **10** (191.5-192.5); **14** (187-188); **15** (152-153); **16** (161-162); **17** (163-166); **21** (77-79); **22** (163-165); **24** (118-120).
14. Prepared by transesterification of the corresponding dimethyl ester.[9]

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