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LETTERS

Molecular topology : The synthesis of a new class of rigid arc-shaped spacer molecules based on *syn*-facially fused norbornanes and 7-heteronorbornanes in which heterobridges are used to govern backbone curvature

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Abstract: Norbornadienes and 7-heteronorbornadienes are reacted with 7-oxa (or carba or aza) norbornene-fused cyclobutene epoxides (or aziridines) to produce hetero-bridged polynorbornane cycloadducts containing *syn*-facially arranged N,O (or C,N or C,O) bridges. New dual cyclobutene epoxides and dual cyclobutene aziridines are used to prepare multi-fused norbornanes having curved topology in which the heteroatoms modify the curvature in a predictable way C>N>O; AM1 modelling of representative [9]polynorbornanes is presented.

The development of methods for the synthesis of molecules with specific 3D geometry continues to be an important challenge for the molecular architect, eg in cases where host, guest shape is a dominant factor in controlling lock and key selectivity.[1] In this context, it seemed to us that curved components should be considered as one of the fundamental building units, in this case as a subunit of a circle along with the more recognised rods, angles and cavity systems derived from squares and triangles (Figure 1a).

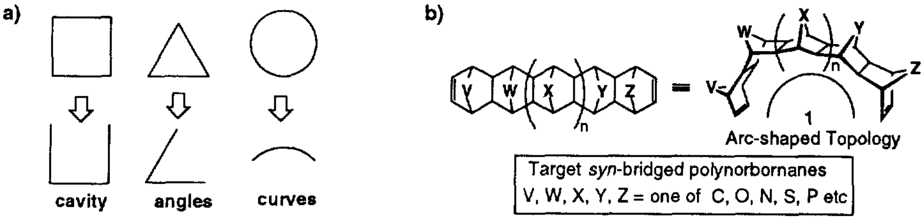

Figure 1

In our earlier work on the production of topologic variants of the polynorbornanes, we showed that linear rods could be produced by linking adjacent norbornane subunits via a σ-bond at the methylene bridges,[2] ie, we could take the curve *out of* the polynorbornane frame. In seeking curved spacers, we appreciated that *syn*-facially fused polynorbornanes were suitable, however, polynorbornanes comprised entirely of norbornane units are extremely rare and difficult to prepare.[3] Accordingly, we turned our attention to molecules based on *syn*-facially fused polynorbornane frameworks incorporating 7-heterobridged norbornanes **1** (Figure 1b). While these were also rare at the commencement of our work,[4] we can now report that they can be synthesised

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using stereoselective coupling methodology recently developed in our laboratories.[9,10] We were encouraged to develop the synthetic chemistry described herein following molecular modelling results (*vide infra,* Figure 2) which indicated that the curvature was maintained following introduction of heteroatoms at the 7-position of the norbornane subunits in *syn*-facially fused polynorbornanes. Further, the degree of curvature could be substantially modified by the nature of the heteroatoms, a feature of design significance to the molecular architect. In this letter, we describe new synthetic routes to realize the synthesis of multi-fused *syn*-facial 7-hetero-bridged norbornanes containing combinations of C, N, and O bridges.

Molecular modelling: The molecular modelling studies were conducted at the AM1 level of theory, and the examples illustrated in Figure 2 have combinations of C, N, O bridges in representative [9]polynorbornane systems. This shows that the alicyclic backbones of these 18σ-spacer molecules **2-7** all have arc-shaped topology, and that there is significant variation in the radius of curvature of the different members. An important finding is that replacement of alternate carbon bridges in [n]polynorbornanes **2** by nitrogen bridges, eg **5**, yields a synthetically accessible product **5** which is almost as curved (r=7.0 Å) as the synthetically inaccessible all carbon analogue **2** (r=5.9 Å). Modelling (see Figure 2) shows that the radius of curvature increases (O>N>C) for hetero-bridged systems **2-4** containing all the same bridge type as well as for the mixed hetero-bridged systems **5-7**, thereby offering a way to tune the shape of these spacers.

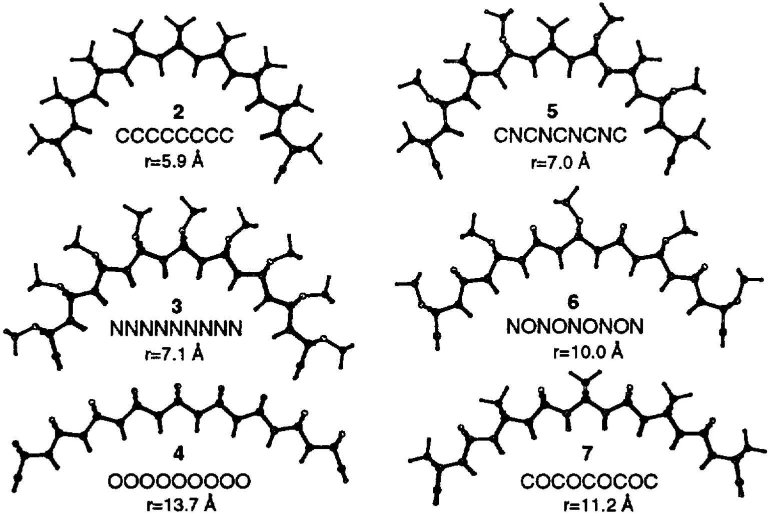
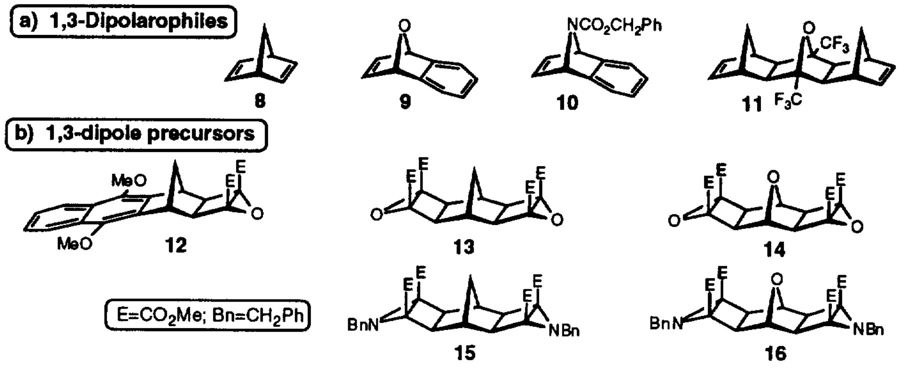


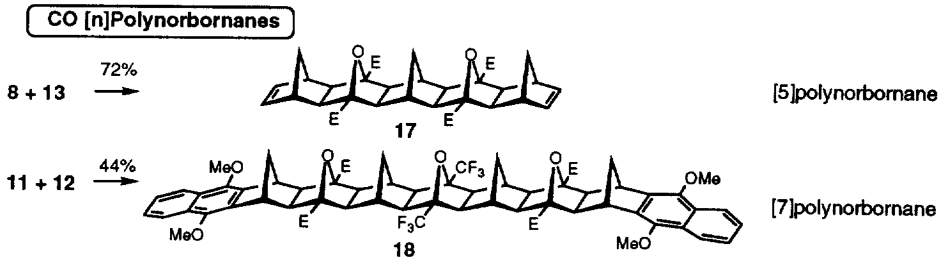
Figure 2. *AM1 optimised structures of representative heterobridged polynorbornanes which illustrate that these systems have an arc-shaped topology. This is reflected in the radius of curvature (r) shown for the H-substituents on the underface of polynorbornanes 2-7, where this radius changes in the order O>N>C.*

Synthesis: Essentially no methods for the preparation of hetero-bridged polynorbornane systems of type **2-6** had been described prior to this work.[4] However, this has now changed owing to our work on the 1,3-dipolar ACE[9] and aza-ACE[10] coupling reactions which has been shown to form 7-oxa(or aza)norbornanes from the reaction of norbornene dipolarophiles with cyclobutene epoxides(or aziridines). In particular, the finding that N,O–bridged polynorbornanes can be produced with complete *syn*-facial stereoselectivity by reaction of oxa-bridged norbornenes with fused cyclobutene epoxides or the reaction of aza-bridged norbornenes with fused aziridinocyclobutanes, offered the breakthrough required for preparation of larger [n]polynorbornanes. These advances have been instrumental in the design of new polynorbornanes related to the CN system **5**, NO system **6** and CO system **7** as well as some other $C_nN_nO_n$ polynorbornanes, and these will be discussed herein. The all-oxygen system **4** and the less developed all-nitrogen system **3** will be presented at a later stage. The dipolarophiles **8-11** (Scheme 1a) used herein are all known compounds, while the 1,3-dipolar precursors **12-16** (Scheme 1b) have been prepared from the related cyclobutene-1,2-diester by epoxidation (^{t}BuO$_2$H, MeLi, -78 °C) or benzyl azide cycloaddition (15 kbar) followed by photochemical ejection of dinitrogen (C_6H_6, 350 nm).



Scheme 1

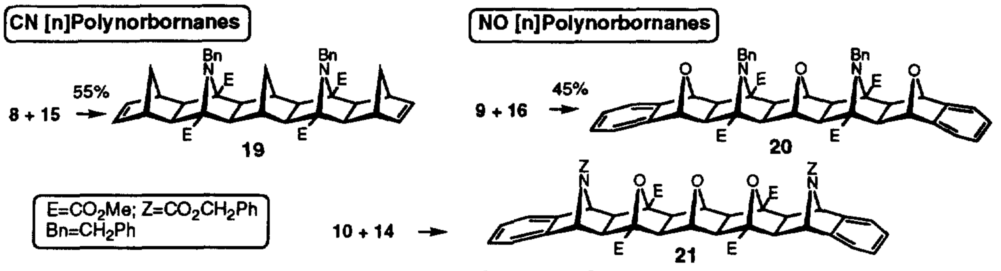
For the preparation of CO [n]polynorbornanes of type **7**, the ACE method was used to introduce one or more of the 7-oxanorbornane units in the course of construction, and the high stereoselectivity of the coupling with norbornenes provided the desired *syn*-alignment of the norbornene bridge-components. Accordingly, CO[5]polynorbornane **17** was produced exclusively by heating *bis*-epoxide **13**[9] with excess norbornadiene **8** (140 °C, sealed tube, THF or DCM).[11] In this case, both 7-oxanorbornane subunits were formed in the linking procedure. An alternative dual coupling combination, this time using excess epoxide **12**[9] with *bis*-alkene **11** yielded CO[7]polynorbornane **18**. Production of **18** could be achieved either thermally (140 °C, 2 h) or photochemically (350 nm, acetone). A feature of the production of **18** is the ability to attach effector groups to the curved frame: indeed crown ether functionality has been attached to CO[5], CO[7], and CO[9] polynorbornanes to form bis-crown systems.[12]



Scheme 2

Aza-ACE coupling of *bis*-aziridine **15** with norbornadiene **8** (benzene at reflux) produced the CN[5]polynorbornane **19** and serves as the protoype reaction to access systems containing juxtaposed C,N bridges related to system **5**.

The construction of ON [n]polynorbornanes can be illustrated by the aza-ACE reaction of 7-oxabenzonorbornadiene **9** with *bis*-aziridine **16** to form the ON[5[polynorbornane **20** (Scheme 3). While the inverted NO [n]polynorbornane still remains to be achieved, we have demonstrated that ACE chemistry for this goal by establishing the stereoselectivity for the reaction of *N*-Z-7-azabenzonorbornadiene **10** with *bis*-epoxide **14** which forms the [5]polynorbornane **21**.



Scheme 3

Conclusion: We have presented convenient and versatile methodology to construct hetero-bridged polynorbornanes of type **3-7** thereby setting them aside from the longer all-carbon series **2** which remain synthetically inaccessible. This range of curved spacer systems opens the way for their use in developing new molecular architecture based on classical arc-shaped components.

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References

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10. Aza-ACE coupling: Butler, D. N.; Malpass, J. R.; Margetic, D.; Russell, R. A.; Sun, G.; Warrener, R. N. *Synlett*, **1998**, 588-589.
11. All compounds were characterised by NMR and mass spectral analysis,: mp °C:
14, 314 dec; **15**, 86-88; **16**, 116-119; **17**, >300; **18**, 289-291; **19**, 233-235; **20**, 285-287; **21**, 248-251.
Selected ^{1}H NMR δ (300 MHz, $CDCl_3$), **13** 1.94, s, 2H; 2.27, s, 4H; 3.29, s, 2H; 3.83, s, 6H. **14** 2.60, s, 4H; 3.83, s, 12H; 5.68, s, 2H. **15** 1.90, s, 2H; 2.15, s, 4H; 3.30, s, 2H; 3.72, s, 12H; 3.99, s, 4H, 7.22-7.44, m, 10H. **16** 2.46, s, 4H; 3.74, s, 12H; 4.02, s, 4H; 5.78, s 2H; 7.31, m, 10H. **17** 0.99, d *J*=8.7 Hz, 2H; 1.93, s, 2H; 1.95, s, 4H; 2.03, s, 12H; 2.32, d *J*=8.7 Hz, 2H; 2.62, s, 4H; 3.83, s, 12H; 6.11s, 4H. **18** 1.39, d *J*=9.0 Hz, 2H; 1.61, m, 2H; 1.77, s, 4H; 1.86, s, 4H; 2.07, d, *J*=11 Hz, 2H; 2.30, s, 4H; 2.41, s, 4H, 2.70, d, *J*=9.0 Hz, 2H; 3.59, s, 4H, 3.96, s, 24H, 7.44-7.46, m, 4H,; 8.05-8.06, m, 4H. **19** 0.70, d *J*=8.1 Hz, 2H; 1.80, s, 2H; 1.83, s, 4H; 1.91, s, 4H; 2.18, s, 2H; 2.55, d *J*=8.1 Hz, 2H; 2.56, s, 4H; 3.79, s, 12H; 4.15, s, 4H; 6.07, s, 4H; 7.14-7-42, m, 10H; **20** 2.00, s, 4H; 2.09, s, 4H; 3.68, s, 12H; 4.08, br s, 4H; 4.55, s, 2H; 5.29, s, 4H; 7.11-7.30, m, 14H; 7.70, d *J*=7.3Hz, 4H.
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