The Synthesis of New Linear and Angular Systems useful as Rigid Rods and Spacers in the Design of Molecules

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Various substituted norbornenes are subjected to metal-catalysed [2 + 2] cycloadditions to yield activated cyclobutenes which react further with quadricyclane to yield linear binadienes, or with cyclopentadiene to form angular binadienes; these binadienes are rigid alicyclic frameworks available to synthetic chemists for molecular design.

The ability to separate two groups in a known way is fundamental to the evaluation of chromophoric or functional group interaction.[1,2] Early attempts[3] using simple carbon chains were unsuccessful owing to the conformational mobility of the chain and later workers have used the steroid nucleus to effect separation.[4] Zimmerman introduced the concept of organic [*n*]-rods based on bridge-linked bicyclo[2.2.2]octanes to achieve separation, and these offer special advantages in regard to distal variation.[5] However, all these systems are only suitable if conformational mobility of the interacting groups is not critical.[5] Fusion to alicyclic systems has been used to separate groups in a rigidly aligned fashion in order to avoid conformational problems.[6] Intramolecular interactions can be evaluated using various molecular frameworks for group separation but only with some caution. The cautionary note follows from the experimental work of Paddon-Row and coworkers,[7] in which they amply demonstrated the long-range effects of through-bond interactions which occur in certain alicyclic systems.

We have developed a new group of compounds which we believe will offer considerable versatility as molecular frameworks for separating and evaluating the relationships between substituents. These molecules, termed binanes for nomenclature reasons,† are comprised of a rigid framework of fused cyclobutane and norbornane moieties, and are readily prepared by simple cycloaddition reactions. Both rods and spacer molecules are available (see Figure 1) and these allow considerable versatility in the separation of the end-groups A and

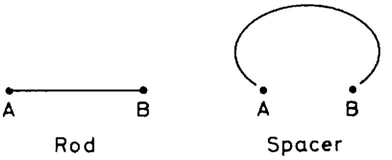

Figure 1. A schematic representation of the types of binanes.

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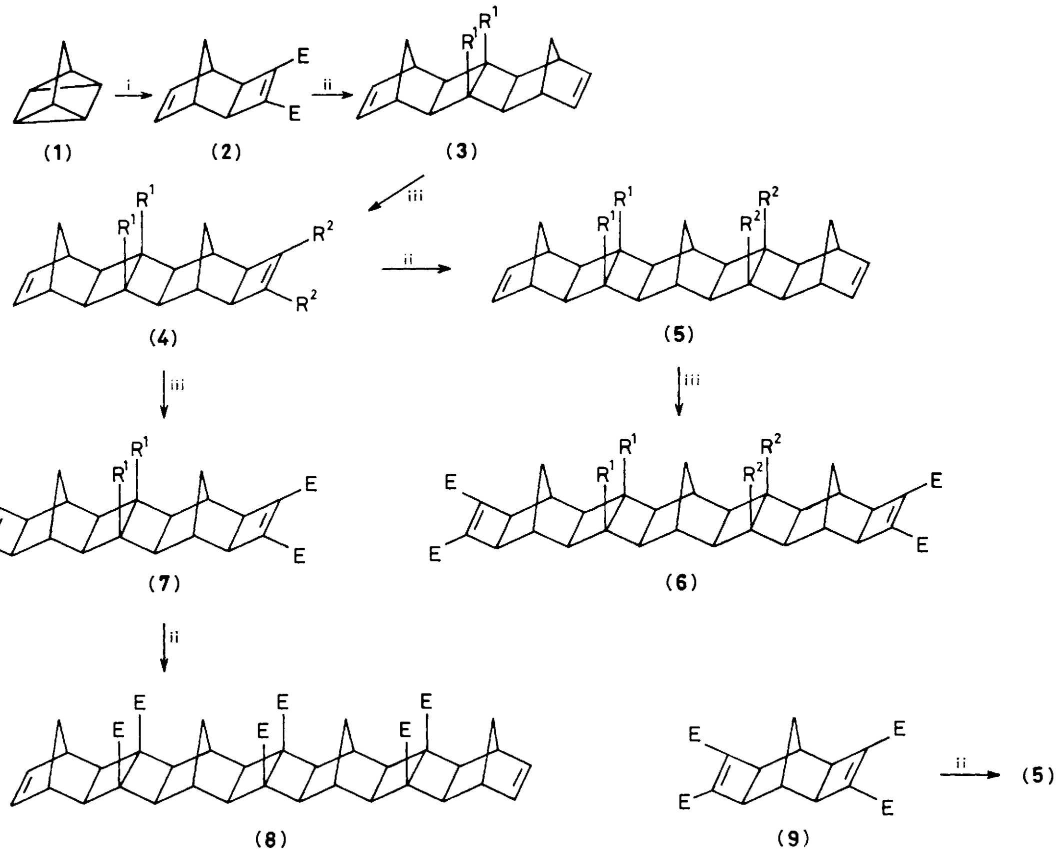
† A simple nomenclature system has been developed to name the binanes which depends on the assignment of a binary number to each system based on the size of the bridging group: methylene (1) or direct linkage (0). This nomenclature has been used in the computer generation of structures from the binary number of the ring system alone, and as well as being exact and brief, it can also be usefully applied by practicing chemists (ref. 8).



a; $R^1 = CO_2Me$, $R^2 = CO_2Me$
b; $R^1 = CH_2OH$, $R^2 = CH_2OH$
c; $R^1 = CH_2OSO_2Me$, $R^2 = CH_2OSO_2Me$
d; $R^1 = Me$, $R^2 = Me$
e; $R^1 = Me$, $R^2 = CO_2Me$

$E = CO_2Me$

Scheme 1. Linear binanes. i, Heat, DMAD; ii, heat, (**1**); iii, $RuH_2CO(PPh_3)_3$, DMAD.

Table 1

Coreagent	Product(s)	Yield (%)	M.p./ °C
[a] (**2**)	(**3a**)	67	181
(**4a**)	(**5a**)	64	259—261
(**9**)	(**5a**)	48	259—261
(**7a**)	(**8a**)	44	>350
(**4e**)	(**5e**)	48	—
[b] (**2**)	(**10**)	72	65—67
(**9**)	(**11**)	91	210—212
[c] (**3a**)	(**4a**)	28	165—167
	(**7a**)	40	217—218
(**5a**)	(**6a**)	71	>350
(**3e**)	(**4e**)	56	103—104
	(**7e**)	34	246—247

[a] Quadricyclane cycloadditions: sealed tube, 180 °C, 15 h. [b] Cyclopentadiene cycloadditions: 56 °C, $CHCl_3$, 48 h. [c] Ruthenium catalysed DMAD cycloaddition: $RuH_2CO(PPh_3)_3$, C_6H_6, 80 °C, 24 h.

B and in their angular interrelationship, while maintaining A and B conformationally locked onto the rigid binary framework.

These binanes owe their existence largely to the ability of quadricyclane (**1**) to undergo the bishomo Diels–Alder reaction,[9] in this case with activated cyclobutenes. This specific variant, unknown prior to this study, has been exploited in combination with the metal-catalysed [2 + 2] cycloaddition of dimethyl acetylenedicarboxylate (DMAD) to norbornenes.[10] This provides a sequential series of reactions, shown in Scheme 1, which yield linear binane rods of varying distal separation. The stereospecificity of each reaction ensures the *exo*-fusion of the cyclobutene ring to the norbornane moiety and the production of the rigid binane. In this way we have prepared the representative binanes (**3a**), (**5a**),‡ and (**8a**) in which the terminal norbornene π-bond is separated by 6, 10, or 14 σ-bonds, respectively, starting from the appropriate cyclobutene (see Scheme 1 and Table 1). The binane (**5a**) can also be formed directly from (**9**)§ on heating with a large excess of quadricyclane. These reactions clearly illustrate that extension can be carried out bimodally with molecules containing two activated

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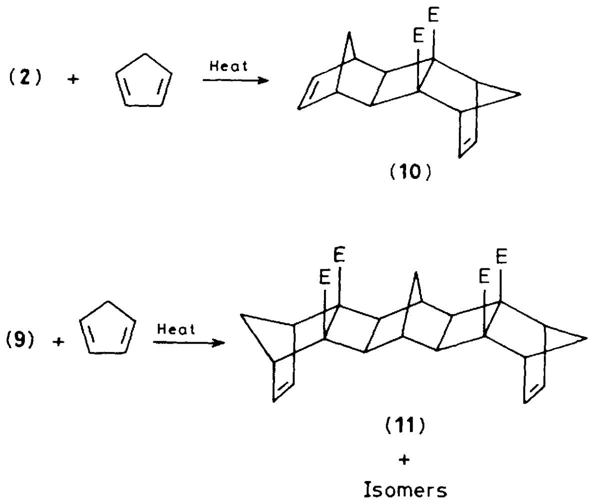
‡ *E.g.* binadiene (**5a**): ^1H n.m.r. ($CDCl_3$) δ 1.06 (d, J 9.8 Hz), 1.78 (d, J 9.8 Hz, 4H, 23-H, 25-H), 2.10 (s, 6H, 2-H, 11-H, 13-H, 22-H, 24-H), 2.17 (s, 2H, 1-H, 12-H), 2.26 (s, 4H, 4-H, 9-H, 15-H, 20-H), 2.80 (br. s, 4H, 5-H, 8-H, 14-H, 19-H), 3.69 (s, 12H, $-CO_2Me$), 6.04 (t, J 1.6 Hz, 4H, 6-H, 7-H, 17-H, 18-H); ^{13}C n.m.r. δ 27.29, 39.76, 40.54, 43.79, 47.17, 49.77, 50.94, 53.67, 136.06, and 170.36 p.p.m.

§ A significant improvement over the yield reported in the literature (ref. 10) can be obtained in the conversion of (**2**) into (**9**) by using $RuH_2CO(PPh_3)_3$ as catalyst (80 °C, 4 days, benzene, m.p. 142—143 °C, 85%).



Scheme 2. Non-linear binanes.

dienophilic centres, *e.g.* (**6**) or (**9**), or unidirectionally with binanes like (**2**) or (**4**).¶

In addition to the linear binane rods, the framework can be bent to provide a range of non-linear binane spacer molecules. This is achieved experimentally by using the cyclobutenes as dienophiles in [4 + 2] cycloaddition reactions with cyclopentadiene, *e.g.* the binane (**10**) from (**2**) and the binane spacer (**11**) from (**9**) (Scheme 2).**

The central ester groups offer an excellent opportunity to modify the physical or chemical characteristics of the binane. For example reduction ($LiAlH_4$) of (**3a**) yields the 1,4-diol (**3b**) (60%; m.p. 188—189 °C) which markedly increases its hydrophilicity, while mesylation of alcohol (**3b**) forms the bismethanesulphonate (**3c**) (99%; m.p. 151 °C) which yields the corresponding methyl-substituted hydrocarbon (**3d**) (85%; m.p. 122—123 °C) on treatment with $LiAlH_4$. In the production of the tetramethyl binane (**5d**) it was found advisable to proceed stepwise *via* (**3d**) rather than directly by reduction of (**5a**).

A study of end group functionalisation is underway in order to exploit the spacer properties of binanes in energy transfer evaluation and drug design.

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¶ The rate of Ru catalysed [2 + 2] cycloaddition of DMAD onto the norbornene moiety of binenes is markedly different. Linear binane formation is strongly favoured, as illustrated by the reaction of (**10**) where the reaction essentially stops under normal conditions after the addition of only one DMAD unit. D. L. Officer, unpublished results.

** The stereospecificity of this reaction can be modified by use of Lewis acid catalysts or by using the related diacids. Details will be provided in the full paper (ref. 8).

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