

Article

Polyquadranoïd Frameworks: Design and Chemistry of [n]-Ladderanes

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Received: June 28, 1996

Tendo por base a oligomerização de um ciclobutadieno, concebeu-se uma rota de uma só etapa para a obtenção de [n]laderanos. Neste contexto, o 1,2-*bis*-carbometoxiciclobutadieno **9c** foi identificado com um monômero adequado, a partir da avaliação das interações HOMO-LUMO no nível AM-1 no ciclobutadieno e em alguns de seus derivados substituídos. De fato, 1,2-*bis*-carboximetoxiciclobutadieno, desconectado de seu complexo de ferrottricarbonila **13**, sofreu a oligomerização prevista para dar [3]-**14**, [5]-**15**, [7]-**16**, [9]-**17**, [11]-**18** e [13]-laderano **19** com rendimento de 60%. Estereoestruturas para **14-19** foram deduzidas com base em análise incisiva de dados de NMR de alto campo (1 e 2D). Este trabalho se constitui na primeira caracterização de inéditos arranjos moleculares de dimensão nanométrica que contêm até 13 anéis de ciclobutano linearmente fundidos. Alguns resultados preliminares sobre a química desses laderanos também são discutidos. Nossa estratégia de oligomerização abre novas oportunidades para se obter acesso a muitas estruturas inéditas.

A one-step approach to [n]-ladderanes, based on the oligomerization of a cyclobutadiene, has been conceived. In this context, 1,2-*bis*-carbomethoxycyclobutadiene **9c** was identified as a suitable monomer on the basis of evaluation of HOMO-LUMO interactions at the AM-1 level in cyclobutadiene and some of its substituted derivatives. Indeed, 1,2-*bis*-carbomethoxycyclobutadiene, disengaged from its iron tricarbonyl complex **13**, underwent the predicted oligomerization to furnish [3]-**14**, [5]-**15**, [7]-**16**, [9]-**17**, [11]-**18** and [13]-ladderane **19** in ~60% yield. Stereostructures of **14-19** have been deduced on the basis of incisive analysis of high-field NMR (1 and 2D) data. The present study constitutes the first characterization of the novel molecular arrays of nanometric dimension and containing as many as 13-linearly-fused cyclobutane rings. Some preliminary results on the chemistry of these ladderanes are also discussed. Our oligomerization strategy opens new avenues for gaining access to many novel frameworks.

Keywords: [n]-ladderanes, 1,2-*bis*-carbomethoxycyclobutadiene, oligomerization, [n]-prismanes

Introduction

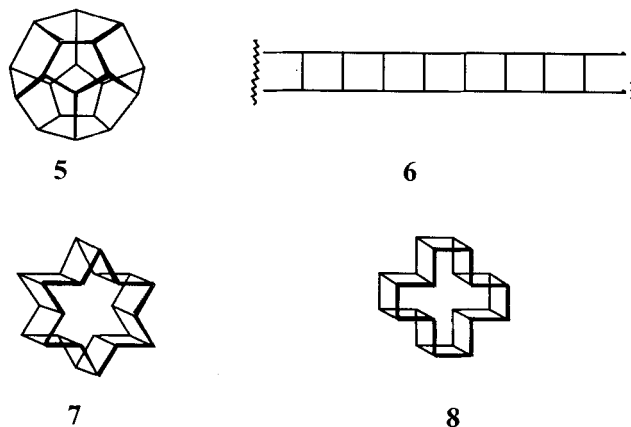
Construction of linearly-fused molecular arrays, composed of cyclic rings of varying size, shape and of nanometric length, has attracted a great deal of attention from organic chemists as the resulting molecular entities are expected to exhibit interesting physico-chemical characteristics and may find utility in areas ranging from supramolecular chemistry to microelectronics. Recent reports of synthesis of molecular 'rods' **1**¹, 'wires' **2**² and 'belts' **3**³ are examples of creation of nanometric level architecture employing six-membered rings. These efforts, to a large

extent, have been successful through the imaginative use of both the inter- and intramolecular versions of the Diels-Alder reaction for the rapid construction of six-membered rings. The assembly of large arrays made-up of fused five-membered rings (polyquinanes) *e.g.*, **4**⁴, has proved to be a more challenging task and met with only limited success, notwithstanding the spectacular attainment of the 'supercyclopentanoïd' dodecahedrane **5**⁵. By comparison, the polycarbocyclic frameworks composed exclusively of four-membered rings *e.g.*, **6**, has received even lesser attention and only a few, scattered examples of multi-fused cyclobutanoids (polyquadranoïds) are documented in the

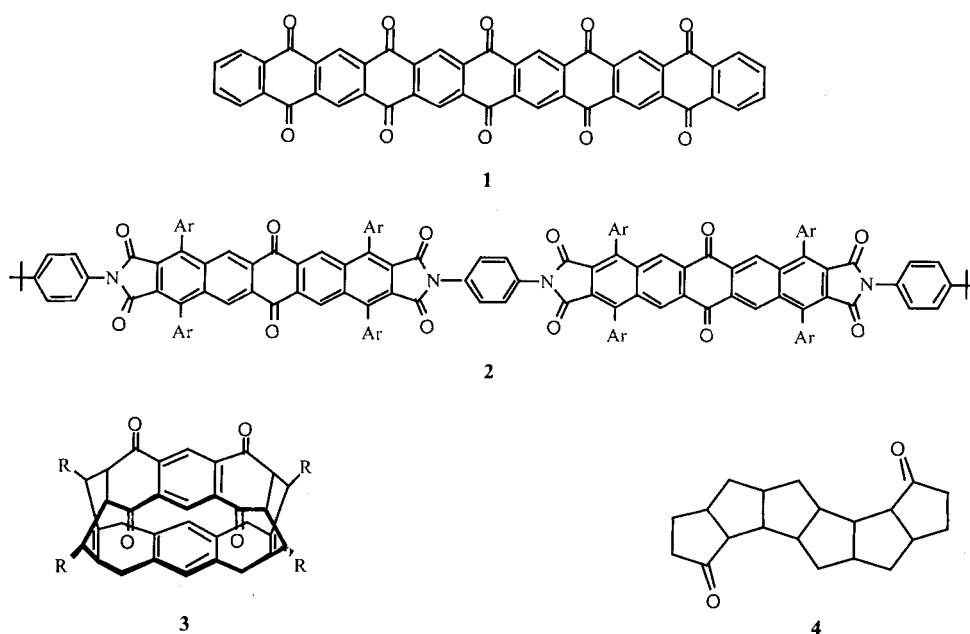
literature⁶⁻⁸. Herein, we describe the synthesis, characterization and selected reactions of a range of polyquadranoid systems.

The name [n]-ladderanes is bestowed on novel molecular arrays constituted entirely of linearly concatenated cyclobutane rings *e.g.*, **6**. Thus, cyclobutane, bicyclo[2.2.0]hexane and tricyclo[4.2.0.0^{2,5}]octane are [1]-, [2]- and [3]-ladderanes, respectively. [n]-Ladderanes, besides their beautiful architecture, can exist in several interesting stereochemical patterns *e.g.*, all *exo*- or zig-zag and hold promise as excellent, rigid, modular spacers for electron and energy transfer⁹. Indeed, [2]-ladderanes have been used as spacers, but higher ladderanes, due to lack of ready access, have not been exploited so far. Doubly end-functionalized [n]-ladderanes with *cis,syn,cis*-stereochemistry can, through an intramolecular [2+2]-photocycloaddition, furnish the corresponding [n]-prismanes, an exotic class of C_nH_n hydrocarbons. In particular, [n]-ladderanes of appropriate stereochemical pattern with $n \geq 11$ have been considered as precursors of higher prismanes *e.g.*, israelane **7** and helvetane **8**¹⁰. Higher ladderanes, on exposure to heat and light, are also expected to undergo novel cascade reorganizations in view of the inherent strain present in them. Despite such promise, a major impediment in the exploitation of the potentially rich chemistry of ladderanes has been their inaccessibility. Prior to our present effort, it had not been possible to assemble a linear array of more than four cyclobutane rings and only a handful of [4]-ladderanes were known⁶⁻⁸.

While considering various strategies for the efficient construction of array **6**, we recognized that just as squares serve as versatile building blocks for shapes in art and architecture, an appropriately substituted cyclobutadiene is



an effective molecular module for the rapid assembly of linearly-fused and doubly end-functionalized polyquadranoid frameworks. Thus, controlled oligomerization of cyclobutadiene should constitute a short and practical way of accessing a diverse range of ladderanes. However, a literature search revealed that cyclobutadiene and its derivatives are known to dimerize only to *cis,syn,cis*- and/or *cis,anti,cis*-tricyclo[4.2.0.0^{2,5}]octanes depending on the nature of the substitution. Thus, we posed the question "why the oligomerization of cyclobutadiene does not proceed beyond the dimer stage?" and sought the answer through the examination of the frontier orbitals involved in the oligomerization process through molecular orbital calculations at the AM1 level, Scheme 1.¹¹ The HOMO-LUMO gap of 8.46 eV for the dimerization of parent cyclobutadiene **9a** to **10a** is within the normal range of observed [4+2]-cycloadditions but the HOMO-LUMO or LUMO-HOMO gap for further addition of **9a** to the dimer **10a** and trimer **11a**, are significantly larger ~9.65-9.70 eV

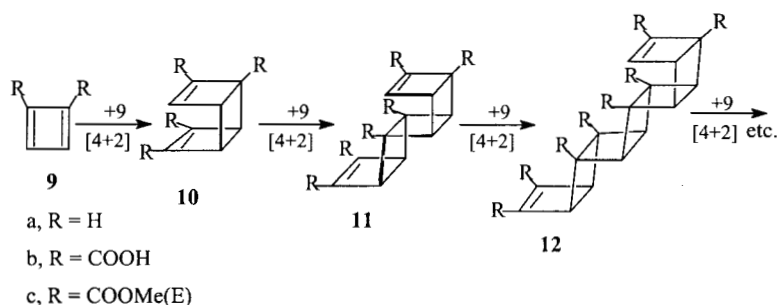


and fall in the category of disfavoured reactions¹². Electron withdrawing substituents in the 1,2-position, as in **9b**, are known to reduce the HOMO and LUMO of the system, and with this aim in mind, the **9b** → **12b** cycloaddition cascade was optimized. While considerable lowering in the HOMO-LUMO gap (8.12 eV) for **9b** → **10b** dimerization was noticed as expected, what was most gratifying was the sharp reduction (~1 eV) in the HOMO-LUMO gap (~8.3 eV) for the **10b** → **11b** → **12b** cycloadditions, which now came within the range of normal [4+2]-cycloadditions. These observations offered some rationale for the non-observation of oligomerization in parent cyclobutadiene and propelled 1,2-dicarbomethoxycyclobutadiene **9c** as the lead candidate for exploring the proposed oligomerization process.

Results and Discussion

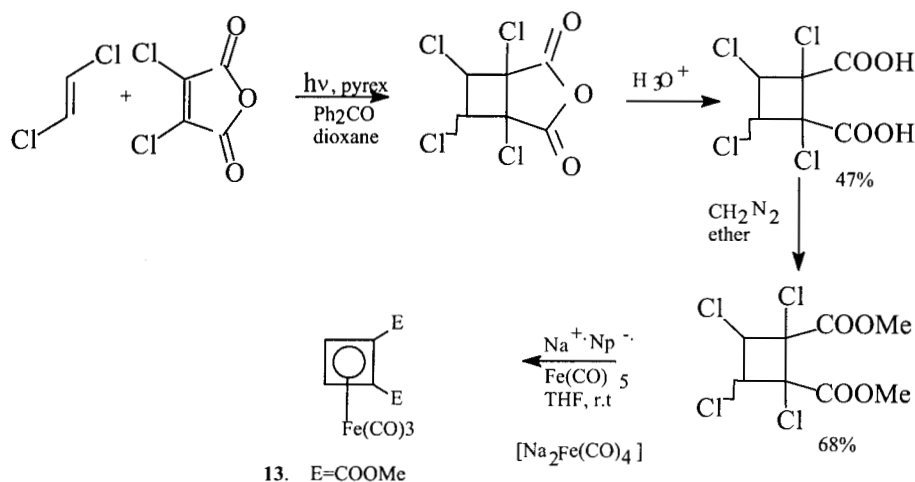
The starting 1,2-dicarbomethoxycyclobutadiene **9c** precursor **13** was readily synthesized from the commer-

cially available starting materials as shown in Scheme 2, following a marginally modified literature procedure¹³. A slurry of tricarbonyl iron complex **13** (0.8 mmol) and ceric (IV) ammonium nitrate in minimal amount of dry acetone (1-2 mL) was stirred (3-4h) at -20 °C and the resulting product mixture was column chromatographed on silica gel. To our delight, we observed that the contemplated oligomerization had unfolded and as many as six odd-membered ladderanes **14-19** could be isolated in ~60% yield, Scheme 3. Structures to [3]-**14**, [5]-**15**, [7]-**16**, [9]-**17**, [11]-**18** and [13]-ladderane **19** were assigned on the basis of FAB-MS and incisive analyses of high field (400 MHz) ¹H- and ¹³C-NMR data. In particular, extensive use of n.O.e. and NOESY proved to be decisive in arriving at the regio- and stereochemistry of these ladderanes. Several features associated with the stereostructure as well as formation of **14-19** deserve to be highlighted.

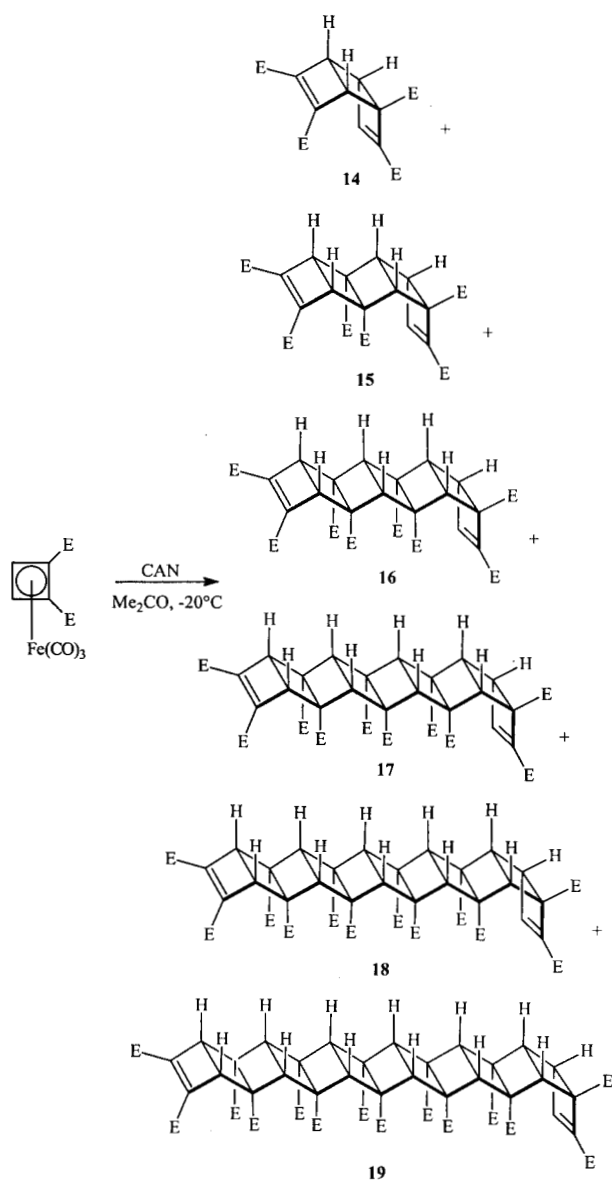


Reaction	HOMO-LUMO (LUMO-HOMO) [eV]	
	R = H	R = COOH
9 + 9 → 10	8.46	8.12
9 + 10 → 11	9.64 (9.70)	8.37 (9.29)
9 + 11 → 12	9.68 (9.64)	8.35 (9.29)

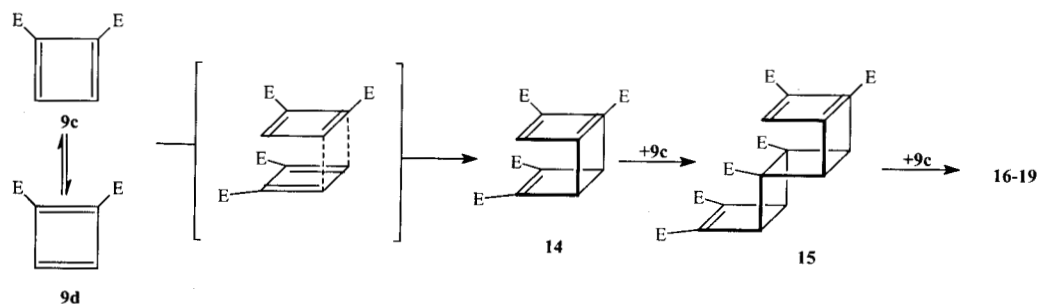
Scheme 1.



Scheme 2.



Scheme 3.

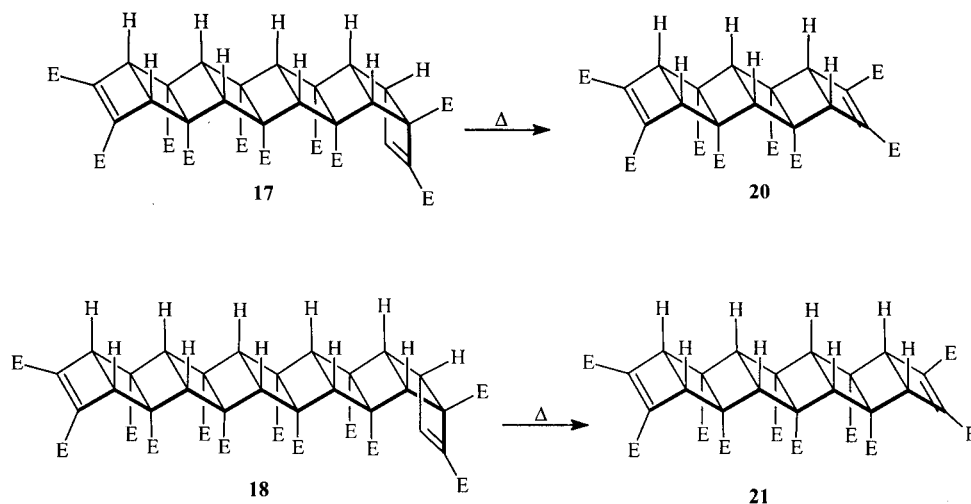


Scheme 4.

It is quite remarkable that ladderanes of nanometric dimension and having as many as 13-cyclobutane rings (see **19**) are assembled in a single-pot reaction. To our knowledge, no fused carbocyclic array, composed of 13 rings, identical or mixed, is known up-to-date. No less significant is the observation of a highly regio- and stereoselective oligomerization process. Dicarbomethoxycyclobutadiene **9c** seems to be reacting exclusively in the form **9c** with very little contribution from **9d**. The calculated energy difference between **9c** and **9d** is very small. The initial dimerization ([4+2]-cycloaddition) is controlled by secondary orbital interactions, and the unsymmetrical dimer, the [3]-ladderane **14** with folded *cis,syn,cis*-stereochemistry is exclusively formed, Scheme 4. Further cycloaddition of **9c** to **14** to give **15** and higher ladderanes occurs regioselectively at the more substituted olefinic center (larger LUMO coefficient) and now an *all exo,cis,anti,cis*-stereochemistry is generated. Further oligomerization follows this regio- and stereochemical trend. This stereoselective cycloaddition cascade, interestingly places all the ester groups (except in the initial dimerization step) on to the one face of the ladderane and hydrogen atoms on the other, thus imparting a dipolarifacial character to these entities. This characteristic, in particular, augurs well for the further exploitation of these entities as specialty materials.

While the ready formation of [n]-ladderanes **14-19** was a gratifying outcome, we were a bit concerned about the two limiting features of the present oligomerization process that needed to be remedied. Firstly, the intrinsic nature of the cascade cycloaddition route leading to ladderanes provided access to only odd-numbered ladderanes. Thus, the even-numbered ladderanes, by this approach, eluded us. Secondly, the initial secondary orbital dominated cycloaddition leads to the folded *cis,syn,cis*-stereochemistry in the dimer **14** and while the subsequent cycloadditions consistently lead to the all *exo*-stereochemistry, this initial defect persisted all through in all the ladderanes.

To overcome these limitations, we sought a solution in which the wrong, unsymmetrical end of the ladder could be corrected by sacrificing the cyclobutane rings in the fold. This manoeuvre should result in shorter but perfect, even



Scheme 5.

numbered $[n]$ -ladderanes. Heating a benzene solution of [9]-**17** and [11]-ladderanes **18** and chromatography on silica gel led to the isolation of [6]-ladderane **20** and [8]-ladderane **21**, respectively, in reasonable yield, Scheme 5. The structural identity of **20** and **21** and the emergence of symmetry manifested in the simplified ^1H - and ^{13}C -NMR features of these even-numbered ladderanes. The folded, dissected portion of the ladders **17** and **18** showed-up as dimethylphthalate. A remarkable and efficacious aspect of this 'step-down' process is that the cyclobutene ring opening and fragmentation occurs regioselectively at the required 'wrong-end'.

While the higher ladderanes exhibit propensity towards thermally induced self-correction, the lower members i.e., [3]-**14**, [5]-**15** and [7]-ladderanes **16** undergo some interesting, thermally induced, deep-seated reorganizations¹⁴. We have also observed that the 'ladders' can be grown on norbornene and other related olefins to generate systems that should be amiable towards energy and electron transfer¹⁵.

Conclusions

In summary, we have described a simple and practical approach to both even- and odd-numbered $[n]$ -ladderanes (upto $n = 13$) from a readily available substituted cyclobutadiene precursor. These novel molecular arrays are of record length and the higher members are of nanometric dimension. We have studied thermally induced, deep-seated rearrangements of these ladderanes and also explored their utility as spacer groups. Our observations augur well for the application of these novel entities in material science.

Acknowledgments

The authors would like to thank Prof. E.D. Jemmis, Dr. A.C. Kunwar and Dr. D.S.K. Reddy for their collaboration and interest in this project. GM thanks INSA for the award

of S. Ramanujan Research Professorship and MBV thanks CSIR for a Research Fellowship. This research was supported in part by the Jawaharlal Nehru Center for Advanced Scientific Research, Bangalore.

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