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Photoisomerisation of Bicyclo[4.2.0]octadienes to Tricyclo[4.2.0.0^{2,5}] octenes: Application to the Synthesis of [n]Ladderanes

Ronald N. Warrener*

Centre for Molecular Architecture, University of Central Queensland, Rockhampton, Queensland 4702, Australia
(fax +61 79 309917 ; internet r.warrener@ucq.edu.au)

Ian G. Pitt and Eric E. Nunn

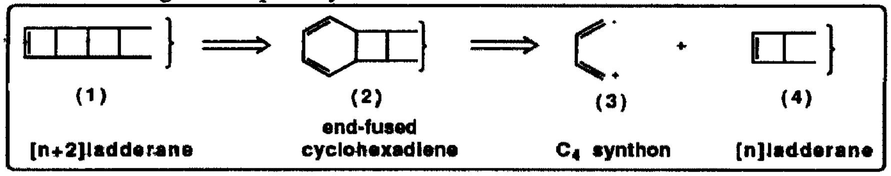
Department of Chemistry, Australian National University, Canberra, 2601, Australia

Colin H.L. Kennard

Small Molecule X-Ray Diffraction Laboratory, University of Queensland, Brisbane, 4067, Australia

Abstract: A new approach for the extension of [n]ladderanes is described which involves formation of an end-fused bicyclo[4.2.0]octadiene and its photoisomerisation to the related tricyclo[4.2.0.0^{2,5}] octene as the ladderane extension step. The protocol is illustrated with the synthesis of [3]ladderane (**9**) from an unsubstituted cyclobutene and nor[5]ladderane (**13**) from an ester activated cyclobutene. The *exo*-stereochemistry of (**13**) is confirmed by reference to intermediate (**23**) for which a single crystal X-Ray structure analysis was obtained.

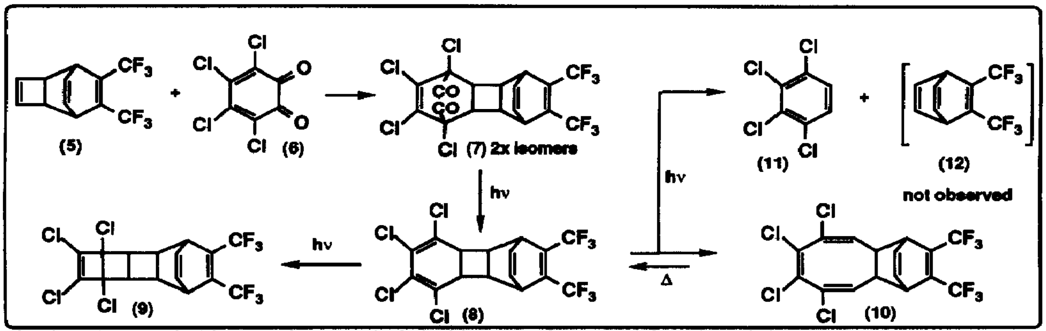
As part of an active program on the synthesis of [n]ladderanes (**4**) as spacer molecules, we have investigated an extension protocol based on the retrosynthetic transform outline in Scheme 1. We were encouraged to pursue this pathway as it was already known that irradiation of several olefinic substrates in aromatic solvents produced [n]ladderanes.[1] Clearly such products can be rationalised by initial formation of a bicyclo[4.2.0]octadiene intermediate of type (**2**) which ring-closes under the photochemical conditions to the [n]ladderane. Accordingly we set out to produce the same bicyclo[4.2.0]octadiene intermediates (**2**) by alternative routes and investigate their photocyclisation.



Scheme 1. *Retrosynthetic transform for the photoisomerisation route to [n]ladderanes*

The synthesis of small [n]ladderanes is well documented but essentially no method is available for producing members where n is greater than four in which the all-*exo* configuration obtains.[2] The pterodactyladiene ring system, a [4]ladderane, was described by Pettit[2] and by Martin[3] and represents the best characterised of the smaller ladderanes having the extended all *exo*-configuration. Larger [n]ladderanes have been reported but they are either bent[4] or of uncharacterised geometry.[6,7]

This communication describes assessment of a route for extending the length of [n]ladderanes based on the production of an end-fused cyclohexadiene (**2**) and its photoconversion to a bicyclo[2.2.0]hexene



Scheme 2. *Synthesis of chloro-substituted [3]ladderanes from end-fused cyclobutenes*

valence-isomer as the [n]ladderane-extension step as outlined in the retrosynthetic transform shown in *Scheme 1.* o-Chloranil (**6**) is used in a transfer technology role[8] to supply the C_4 synthon (**3**) when unsubstituted cyclobutene compounds (**4**) are involved, while cyclopentadienones (**19**) are assigned this role when the cyclobutene π-bond has electron-withdrawing ester substituents as in (**18**).

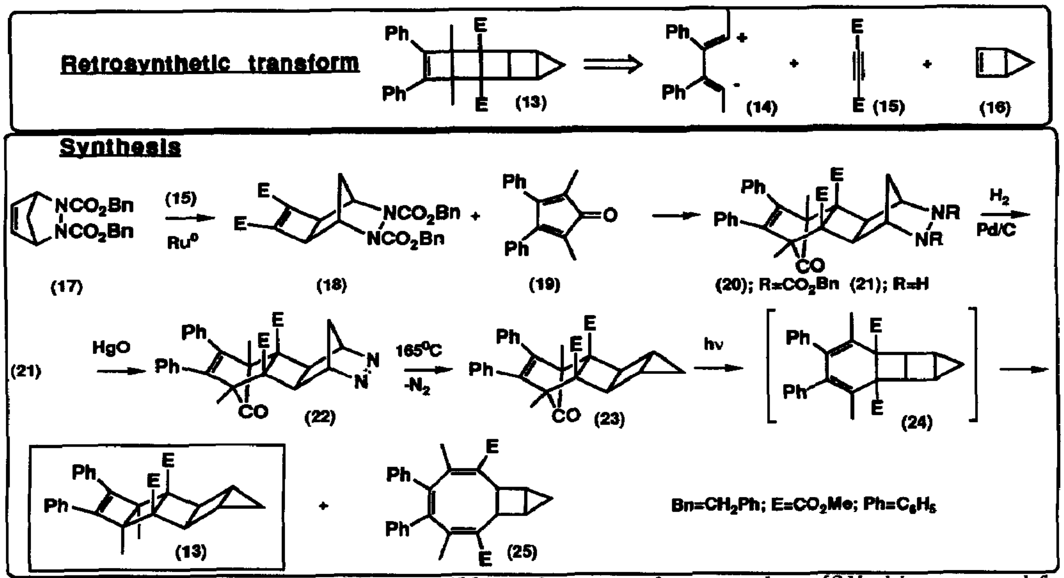
Reaction of o-chloranil (**6**) with the Nenitzescu hydrocarbon derivative (**5**) produces a mixture of 1:1-adducts (**7**) as described elsewhere.[9] They do not require separation as photoinduced loss of the α-dicarbonyl bridge yields a common cyclohexadiene product (**8**), accompanied in this case with secondary photoproducts, valence-isomers (**9**) and (**10**)[10] (Scheme 2). Changes in solvent and substrate concentration can be used to vary the proportion of isomers in the mixture and conditions can be found which provide enriched samples of each product (see Table). In particular, irradiation of α-diones (**7**) in benzene solution provides, in 71% yield, a 7:2 mixture of the fused [3]ladderane (**9**) and the cyclooctatriene valence-isomer (**10**) which can be separated by chromatography. The cyclooctatriene (**10**) is converted quantitatively to the bicyclo [4.2.0] octatriene (**8**) at its melting point or by heating in chloroform solution ($t_{0.5}$ 80° = 27 minutes), so further irradiation of (**8**) can be used to boost the overall yield of fused [3]ladderane (**9**).

Table: Photolysis of α-diones (7)

Entry	Solvent	Concentration (g/l)	Time (h)	Product ratio (**8**) :	(**9**) :	(**10**)	Total Yield * (%)
1.	THF	8	1	4	0	1	48
2.	THF	4	0.5	2.5	0.5	1	45
3.	THF	4	1.25	0.2	0.9	1	46
4.	THF	2	0.5	1	0	1	49
5.	THF	2	1	0	1	1	47
6.	C_6H_6	1.5	1	0	3.5	1	71

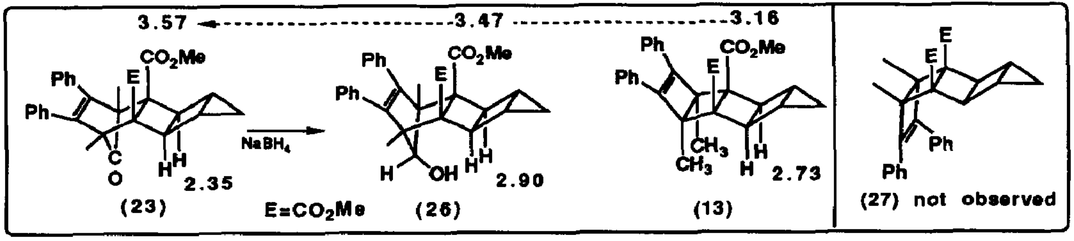
* Yield refers to the sum of (**8**), (**9**) and (**10**). 1,2,3,4-tetrachlorobenzene is also identified in this reaction. It is presumed to arise by 1,2-photoaromatisation of cyclohexadiene (**8**),[7] but the other expected product, barrelene (**12**) is not observed.

The synthesis of nor[5]ladderane (**13**), has already been described without stereochemical support by us earlier.[11] The *exo*-fused cyclobutene (**18**) is reacted with hemicyclone (**19**) rather than o-chloranil[13] to produce the bridged carbonyl adduct (**20**) in 98% yield. Elaboration of the diazanorbornane component in (**20**) to the bicyclo [2.1.0] pentane unit in (**23**) commenced by selective removal of the carbamate benzylic ester groups by hydrogenolysis (H_2, Pd/C) followed by *in situ* oxidation (HgO) of the resultant hydrazo-compound (**21**) to the crystalline diazo-compound (**22**) which on heating (165°) ejected dinitrogen with concomitant inversion,[14] to form the pentacyclic bridged ketone (**23**) in 71% overall yield (3 steps). Loss of carbon monoxide was induced photochemically (acetone-d_6, -35°, 254nm, 90 min) to provide access to a mixture of the cyclooctatriene (**25**)



Scheme 3. *Synthesis of nor[5]ladderane (13) and a general approach to [3]ladderanes end-fused to ring-systems containing cyclobutene-1,2-diesters.*

(55%) and the target nor[5]ladderane (**13**) (16%), presumably by way of cyclohexadiene (**24**).[15] The stereochemistry of nor[5]ladderane (**13**) is confirmed as that shown in the box (Scheme 3) by reference to precursor bridged ketone (**23**) for which a single crystal X-Ray structure analysis (Fig. 1) was obtained.[16] The key to this interrelationship is provided by the relative chemical shift position of the bicyclobutyl protons and the ester methyl resonances in the series of related compounds: ketone (**25**), the derived alcohol (**26**) and the nor[5]ladderane (**13**) (chemical shifts are annotated on the relevant structures in Scheme 4). The ester methyl groups normally resonant at δ 3.70 or thereabout in polyalicyclic compounds: thus the downfield shift in ketone (**25**) (δ 3.57); alcohol (**26**) (δ 3.46); nor[5]ladderane (**13**) (δ 3.18) all indicate significant shielding from the phenyl substituents which increases as they become closer to the ester groups. The relative chemical shifts of the bicyclobutyl protons in this series are also of diagnostic significance. The shift changes reflects the removal of the shielding of the carbonyl group in (**23**) (δ 2.35) upon reduction to alcohol (**26**) (δ 2.90) and a small upfield shift in nor[5]ladderane (**13**) (δ 2.73) relative to (**26**) owing to the shielding from the aligned C8,11 methyl groups.



Scheme 4. *Chemical shifts of ketone (23), alcohol (26) and ladderane (13)*

In conclusion it has been established that this technique for the extension of [n]ladderanes is viable, although the yields in the photoisomerisation step need improvement in some cases.

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4. Mehta, G. and his co-workers[5] have reported that a [5]ladderane and a [7]ladderane are formed from the oligomerisation of 1,2-dicarbomethoxy cyclobutadiene, but these higher order ladderanes have bent geometry being derived from the cycloaddition onto the initially formed *syn*-dimer
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10. All compounds gave correct elemental analytical data and exhibited n.m.r. spectral data consistent with their structures. The melting points of new compounds are as follows: (compound number), m.p. in °C: (**8**), 147-8; diene (**8**) formed a single adduct with *N*-phenyltriazoline dione, m.p. 202-3; (**9**), 162-3; (**10**), 145-6; (**13**), 162-3;(**18**), 117-20; (**20**), 183-4; (**22**), 166-8; (**23**), 165-6; compound (**23**) produced a single alcohol (**26**) on treatment with $NaBH_4$, m.p. 213-4; (**25**), 133-5.
11. The original report[12] incorrectly assigned the major photoproduct from irradiation of (**23**) as cyclohexadiene (**24**) rather than cyclooctatriene (**25**).
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15. All three isomers must be in photoequilibrium since continued irradiation produces dimethyl 3,6-dimethyl-4,5-diphenylphthalate, a product of 1,2-photoaromatisation of cyclohexadiene (**24**) as the sole C-methyl containing product. No solvent or concentration study of the photochemistry of (**23**) was conducted.
16. *Empiral formula:* $C_{30}H_{28}O_5$; *Formula weight:* 468.52; *Temperature: 298(2) K; Wavelength:* 0.71073 A; *Crystal system:* Monoclinic; *Space group:* C 2/c; *Unit cell dimensions:* a = 26.237(9) A α= 90 deg., b = 15.216(2) A β = 115.46(2) deg., c = 13.413(3) A γ = 90 deg.; *Volume:* 4835(2) A^3; *Z:* 8; *Density (calculated):* 1.287 Mg/m^3; *Absorption coefficient:* 0.087 mm^{-1}; *F(000):* 1984; *Crystal size:* .50 x .40 x .30 mm; *Theta range for data collection:* 1.59 to 24.97 deg.; *Index ranges:* 0<=h<=31, 0<=k<=18,m -15<1<=14; *Reflections collected:* 4332; *Independent reflections:* 4235 [Rz(int) = 0.0209]; *Absorption correction:* Psi scan; *Refinement method:* Full-matrix least-squares on F^2; *Data / restraints / parameters:* 4235 / 0 / 321; *Goodness-of-fit: on* F^2 1.019; *Final R indices [I>2sigma(I)]:* R1 = 0.0386, wR2 = 0.0992; *R indices (all data):* R1 = 0.0628, wR2 = 0.1153; *Largest diff. peak and hole:* 0.192 and -0.159 $e.A^{-3}$.

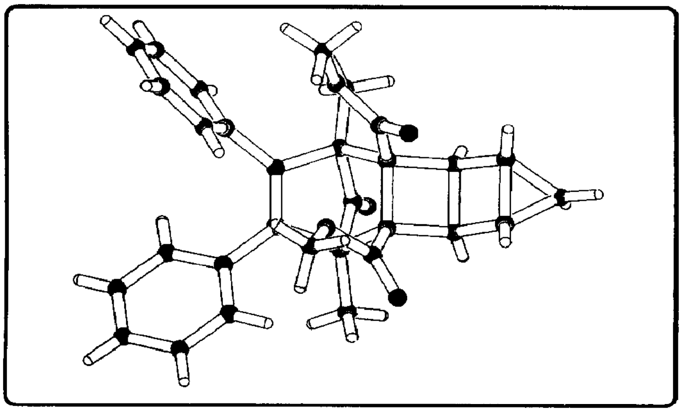

Fig 1 *Pluton diagram of bridged ketone (23) based on the X-ray structure analysis*

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