CHAPTER - I

GENERAL INTRODUCTION

Introduction :

The molecules whose structural features such as bond lengths, bond angles, torsion angles etc, significantly differ from their ideal values are said to be strained. Some examples of such strained molecules are depicted in undergraduate organic chemistry text book.[1]

Although strained molecules have been known for about a century, for example the spiropentane was first correctly reported in the 1890's. However, the interest in the chemistry of strained carbocyclics has accelerated greatly during the past three decades and still sustained. This is clearly revealed by the publication of a recent issue of "Chemical Reviews " which is entirely devoted to the chemistry of strained organic molecules.[2]

Apart from the aesthetic nature of strained carbocyclics, the quest to understand physical organic concepts such as strain, strain-energy relationship, the stability and reactivity and the synthetic challenge have been the major reasons for the interest and intense activity in this area of organic chemistry. Indeed, a remarkably large number of strained ring systems have been synthesized and their reactions were studied. The enormous growth in the chemistry of strained ring systems has been probably due to the development of new synthetic methods together with advances in instrumental techniques which allowed experimental access to these species.

Of a vast majority of strained ring systems the molecules such as tetrahedrane (1) Cubane (2) and its homo-logues (3-6), prismanes (7-9) and dodecahedrane (10) (Fig. I.1)
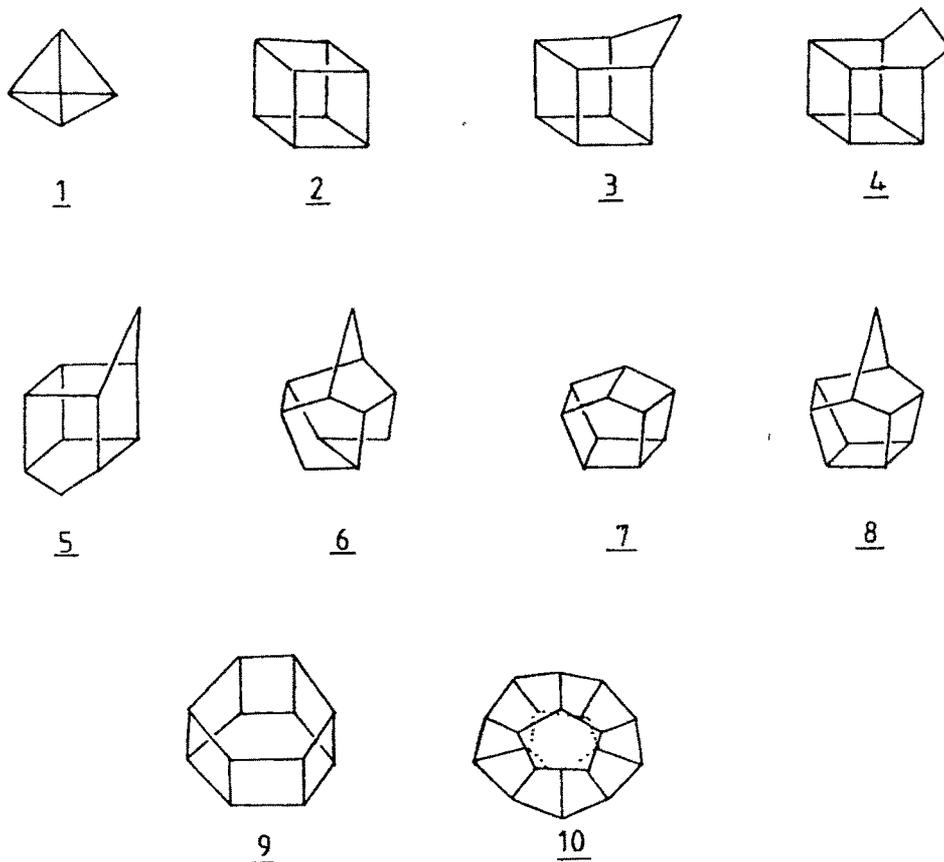

Fig. I.1

have held special fascination among synthetic organic chemists. The synthetic studies on these carbocyclics is presented in the following sections in order to have an overview of this subject.

TETRAHEDRANE[*]

Tetrahedrane (1a) is the carbocyclic analogue $(-CH)_4$ of one of the platonic solids.[3] The parent hydrocarbon and its derivatives have been enticing synthetic target for organic chemists. Although this hydrocarbon has defined its synthesis, its tetralithio derivative (1b) and tetra-tert-butyl analogue (1c) were reported by Schleyer[4] and Maier[5] respectively, despite of the many set backs[6] and discouraging theoretical predictions.[7] The strain energy of tetrahedrane was calculated to be 129-137 Kcal/mol.[7a,8]

The tetralithio derivative 1b was obtained by irradiating a solution of dilithioacetylene (11) in liquid ammonia at -45° with a high pressure Hg lamp (Scheme-I.1). The formation of
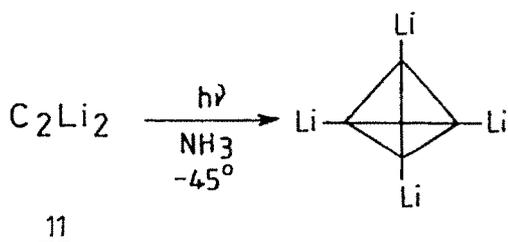

SCHEME - I.1

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* IUPAC name : Tricyclo $(1.1.0.0^{2,4})$ butane

C_4Li_4 was inferred from the disappearance of the signal at δ 75.0 (corresponding to C_2Li_2) and appearance of a singlet at δ 57.2 in ^{13}CNMR. This position of the signal was found to be consistent with expected sp-hybridization of a tetrahedrane carbon.[9]

The tetra-tert-butyltetrahedrane (1c) was synthesized by irradiation of tetra-tert-butyl cyclopentadiendone (12) in a regiosolve matrix at liquid N_2 temperature for about 77 h. The desired tetrahedrane was isolated by column chromatography of the reaction mixture on silicagel at -5° colourless crystals which are stable to air. (Scheme-I.2).

SCHEME - I.2
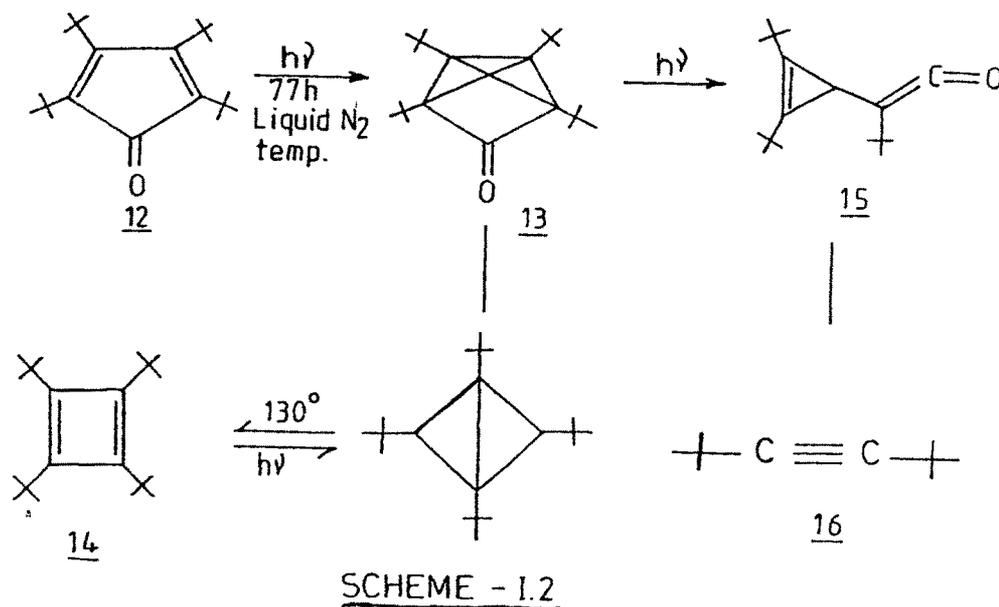
The other products of photolysis were ketone derivative (15) and di-tert-butyl acetylene. The tetrahedrane (14) underwent thermal isomerisation to tetra-tert-butyl cyclobutadiene. It is quite remarkable to note that tri-tert-butyl derivative of cyclopentadienone did not give corresponding tetrahedrane upon irradiation.[10]

Cubane* (Tetraprismane)

The aesthetic appeal and the considerable strain in this molecule is due to bond deformation, in putting eight formally sp^3 hybridized carbon atoms at the vertices of the cube, had posed a major synthetic challenge in the past.[1]

Eaton and Cole[11] reported first synthesis of this strained molecule (strain energy 166 Kcal/mol[12], 14 Kcal/mol per carbon-carbon bond.[13]) Despite the high degree of strain, this molecule was found to be extraordinarily stable, surviving essentially unchanged up to ca 200°.[12b] Eaton and Cole started with cyclo-pentenone (17) and converted it to bromocyclopentadienone (18) which dimerized to 19. The photochemical closure of 19 methanolic HCl furnished the dibromobishomocubanone 20, which after Favorskii type ring contraction gave the cubane dicarboxylic acid 21. The dicarboxylic acid 21 was trans-

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* Pentacyclo $(4.2.0.0^{2,5}0^{3,8}0^{4,7})$ octane

formed into Cubane 2 after its conversion to dibromide

(22) followed by reduction. (Scheme-I.3).

SCHEME -I.3

It is important to note the use of methanolic HCl as a solvent in the intramolecular π^{2s} : π^{2s} cycloaddition of 19. Thus, the species that undergoes photocycloaddition in this reaction to afford 20 is most likely the bis (hemi-ketal) of 19 rather than 19 itself.

Alternatively the required photocyclization can be accomplished by irradiation of that monomethylene ketal of 19 in which only the C-10 carbonyl has been protected.[11] More recent studies by Fuchs and co-workers indicate that photochemical behaviour of halogenated endo cyclopentadienone dimers is complex and, accordingly, that irradiation of these diketones is not a suitable method for the synthesis of halogenated 1,3-bishomocubanediones.[14]

In another approach Eaton et al have synthesised cubane precursors by photochemical 1,3-sigmatropic shift of substituted cis : anti:cis-tricyclo (5.3.0.0^{2,6}) deca-4,9-diene-3,8-diones.[15] Thus irradiation of 23 gave a compound 24, a positional isomer of the dibromo compound 19 which was converted to dimethyl cubane-1,3-dicarboxylate (Scheme-I.4).
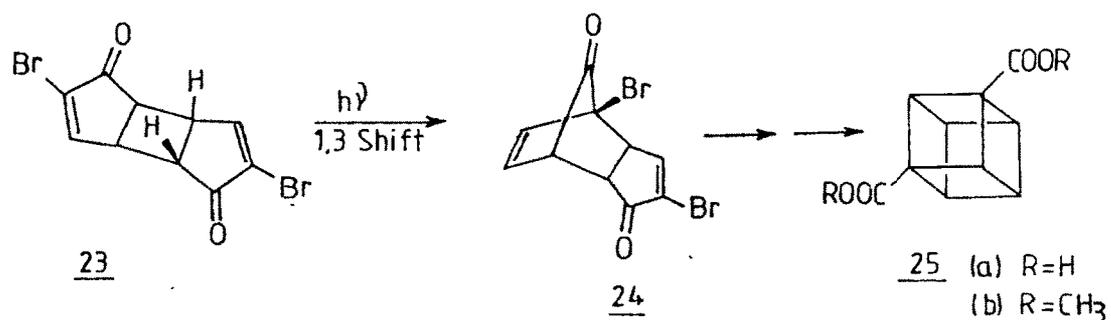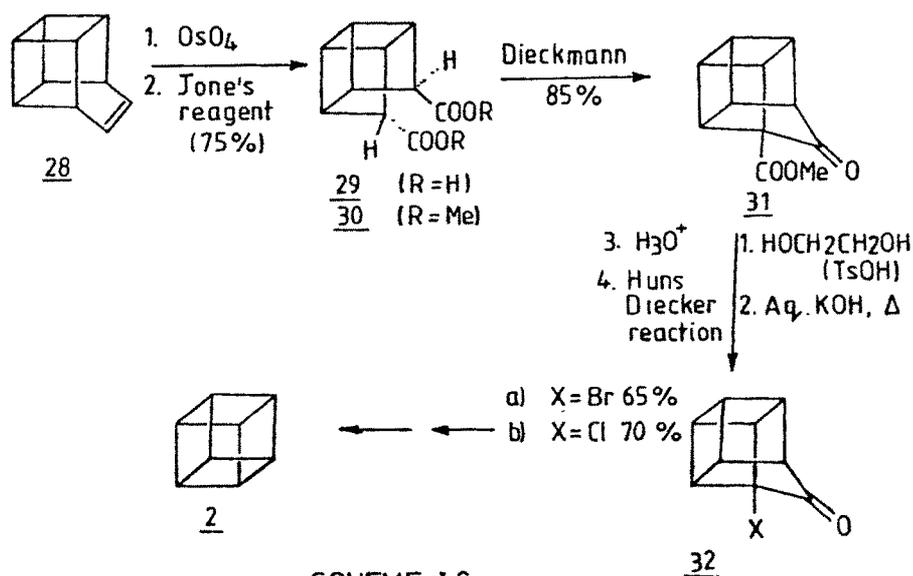
SCHEME -I.4

Pettit and co-workers[16] have synthesized cubane-1,3-dicarboxylic acid in most elegant fashion, via cyclobutadiene-2,5-dibromobenzoquinone adduct (26) which inturn was prepared by oxidative decomposition of (cyclobutadiene) iron tricarbonyl in the presence of 2,5-dibromo benzoquinone. The photocyclization of the endo adduct 26 in benzene furnished the corresponding dibromo-1,2-bishomocubane 27 in 80% yield. Finally the treatment of 27 with aqueous KOH solution at 100° followed

by acidification afforded the cubane 1,3-dicarboxylic acid
25(a) in 80% yield (Scheme-I.5).

SCHEME - I.5
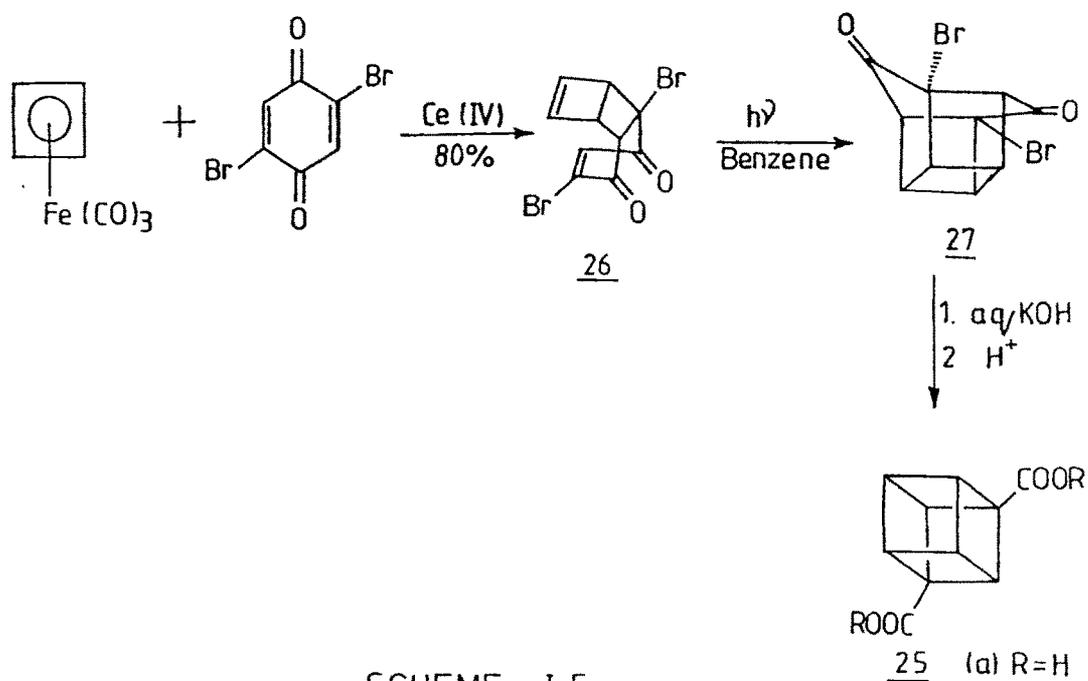
A formal synthesis of cubane from basketene (28) has been
reported by Masamune and his associates.[17] The basketene
(28) was converted into secocubane dicarboxylic acid (29)
by oxidative cleavage of the double bond with OsO_4, followed
by oxidation with Jones reagent.

Esterification of <u>29</u> followed by base promoted Dieckmann condensation of the resulting diester <u>30</u> led to the formation of the substituted homocubanone <u>31</u>. The ketoester <u>31</u> was converted into α-haloketones (<u>32</u>) employing a standard synthetic sequence (<u>Scheme-I.6</u>) which was already been taken to cubane by Eaton et al.[11]
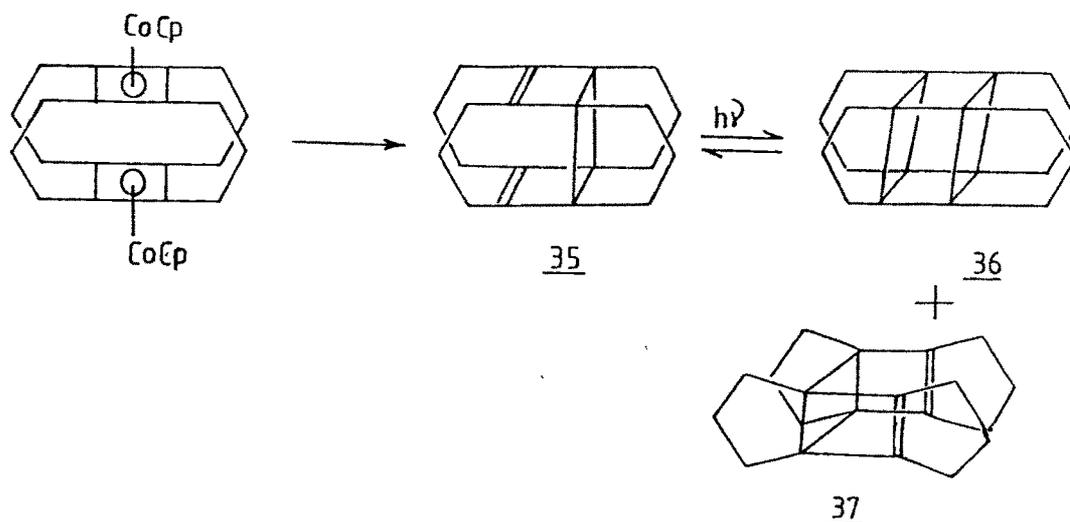

SCHEME-I.6

Among other approaches the intramolecular photochemical $\pi^{2s} + \pi^{2s}$ cycloaddition of appropriately constructed diene or polyene such as 33 (a,b,c) and 34 have been investigated towards synthesis of cubane and its derivatives. However, the photolysis of 33a[18,19] 33b[19,20] or 34[21] have failed to give cubane (Scheme-I.7).

33 a) R = H
33 b) R = CH₃
33 c) R = CF₃

2 c (R = CF₃)

34   2
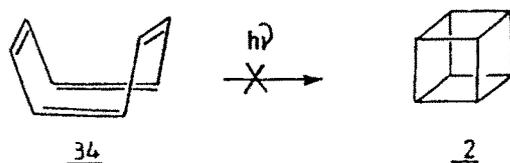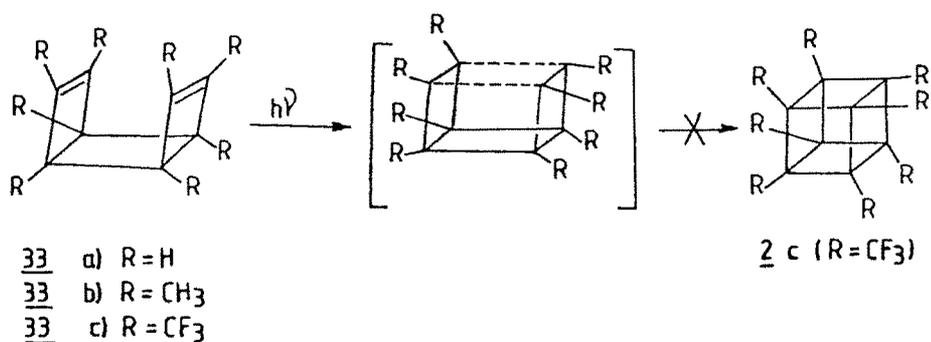
SCHEME - I.7

The reason for failure of eg, <u>33a</u> towards π^{2s}+ π^{2s} cyclo-addition is believed to be due to dominant through bond (rather than through space) interaction between C=C centres of <u>33a</u> which reverse the relative energies of the in-phase and out-phase π combinations. This reversal in energy levels renders the suprafacial (2+2) photocyclization symmetry forbidden.[18,22-25] In contrast to this observation, the tricyclo (4.2.0.0[2,5]) octa-3,7-diene <u>33c</u> has been photocyclized to give corresponding cubane.[26]

More recently Gleiter and Karchav have reported a striking example of photocycloaddition of <u>35</u> to corresponding cubane <u>36</u> (Scheme-I.8).

SCHEME - I.8

Synthetic routes which relied on thermal and/or photoche-
mical extrusion of (a neutral molecule such as) N_2 from diazo-
basketene (38) have also failed[27,28] to give cubane. Similarly
thermal decomposition of 42 was also unsuccessful[29] towards
synthesis of cubane (Scheme-I.9).
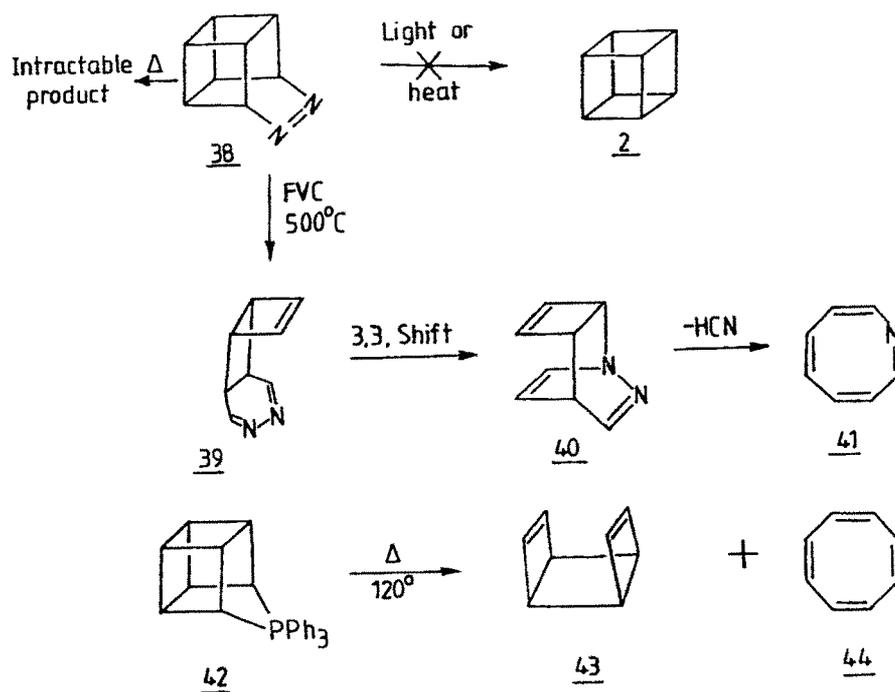
SCHEME - I.9

A detailed review on synthesis and reactions of cubane is presented in the recent article.[30]
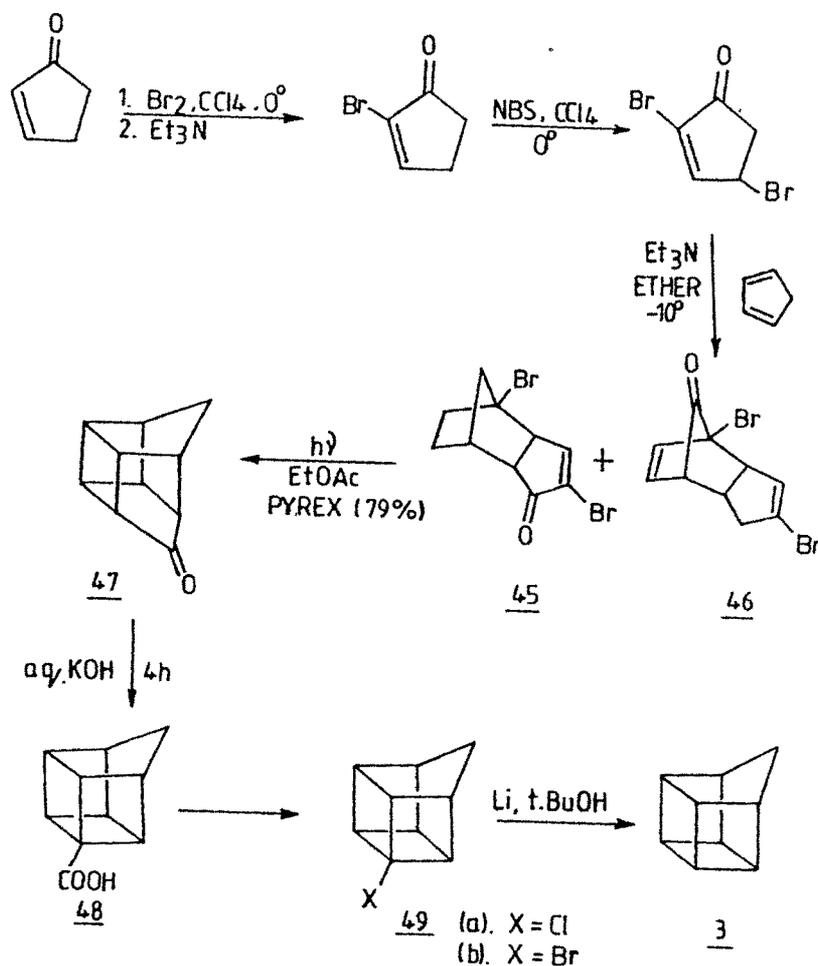
Homocubanes[*]

Although less strained than cubane (1), the homocubanes have equally fascinated the organic chemist for a long time. Homocubane contains long carbon-carbon sigma bond, unusual -C-C-C- bond angles that deviate from 109.5°. They also possess negative heats of combustion and positive heats of formation when compared to non strained systems. These characteristics of (Caged molecules) homocubanes often reflected through their unusual chemical reactivity patterns. The interest in this area has culminated into synthesis of a large number of homocubanes and studies on their chemical reactions. These developments have been reviewed in an excellent article by Marchand.[31] In the following sections we shall briefly outline the general methods for the synthesis of various homocubanes and their derivatives.

The success of base promoted ring contraction of α - halo ketones during synthesis of cubane[11] stimulated other workers to employ and extend this method for the synthesis of other homologues of Cubane.

Pentacyclo $(4.3.0.0^{2,5}, 0^{3,8}, 0^{4,7})$ nonanes

15

Dunn and coworkers synthesized[32] homocubane (3) through
ring contraction of 1,3-bishomocubanone derivative (47) which
gave homocubane-4-carboxylic acid (48). Halodecarboxylation
of 48 followed by reduction of halohomocubane (49) with Lithium-
t-butanol gave the homocubane (3) (Scheme-I.10).

SCHEME - I.10

The desired cage precursor in this approach was synthesized by irradiation of the adduct 45, obtained by trapping bromocyclopentadienone with cyclopentadiene.

Chlorinated homocubane derivatives were synthesized by Scherer and coworkers[33] starting from bisethylene ketal of cyclopentadienone dimer (50) as shown in Scheme-I.11.
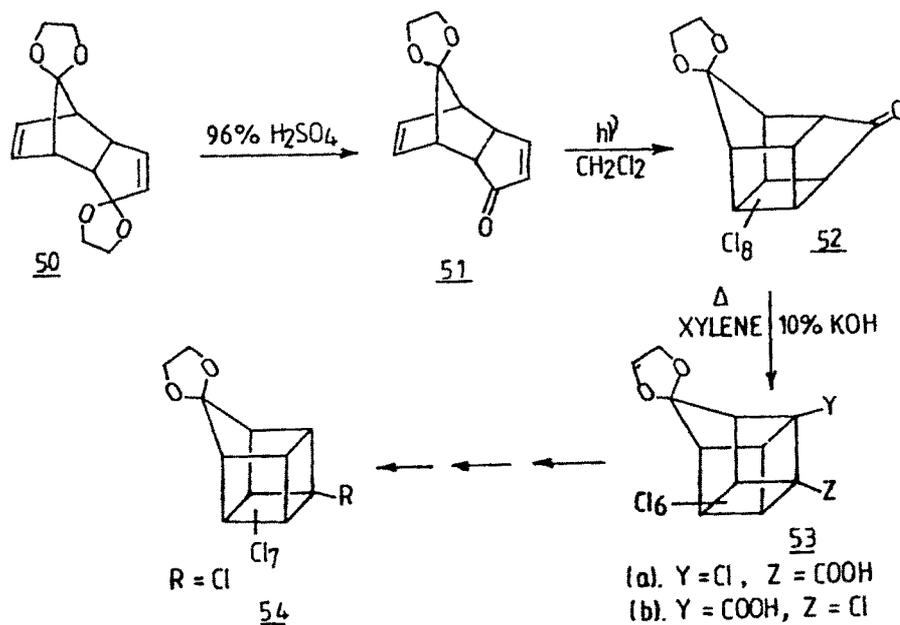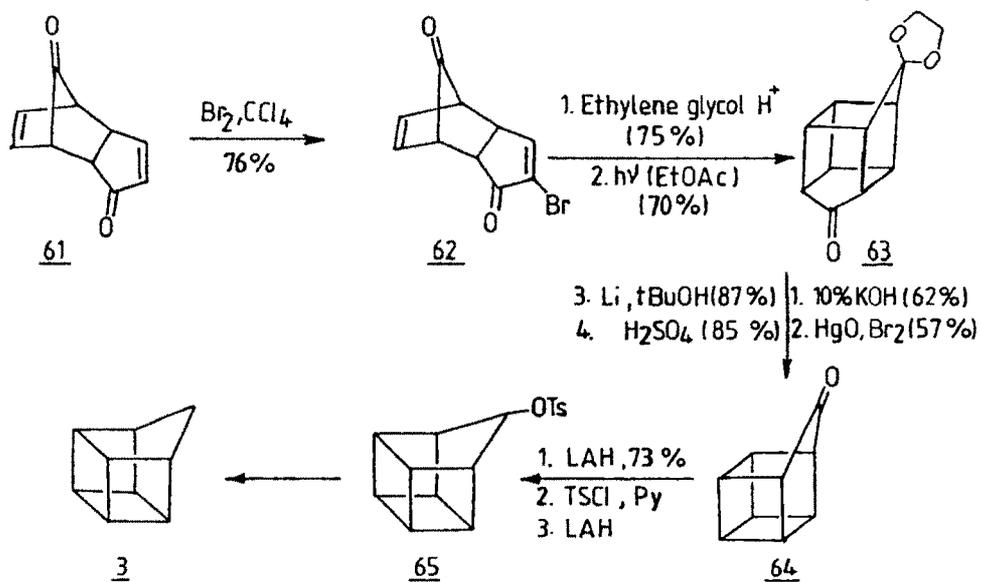

SCHEME - I.11

Similar approach by Chapman[34] employing bis ethyleneketal of dibromocyclopentadienone dimer (55) is outlined in the following Scheme-I.12.·
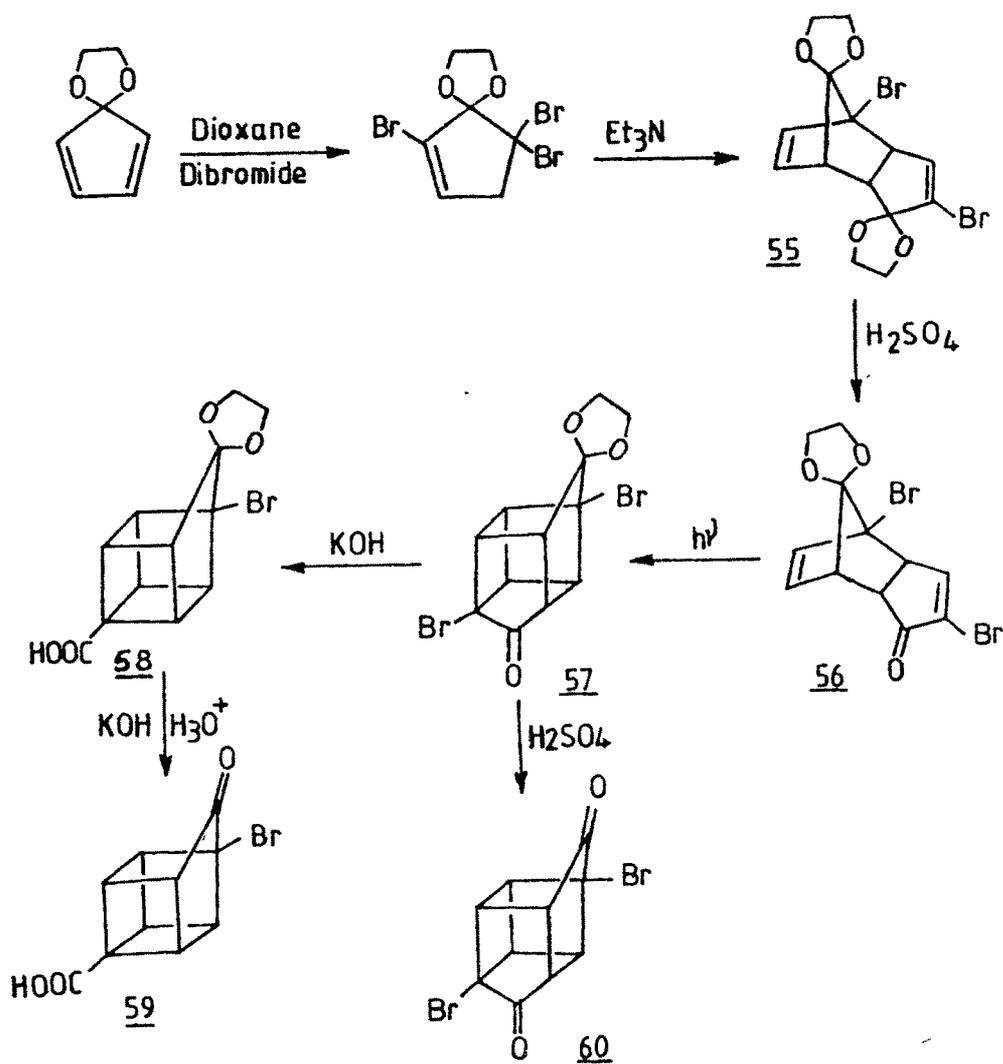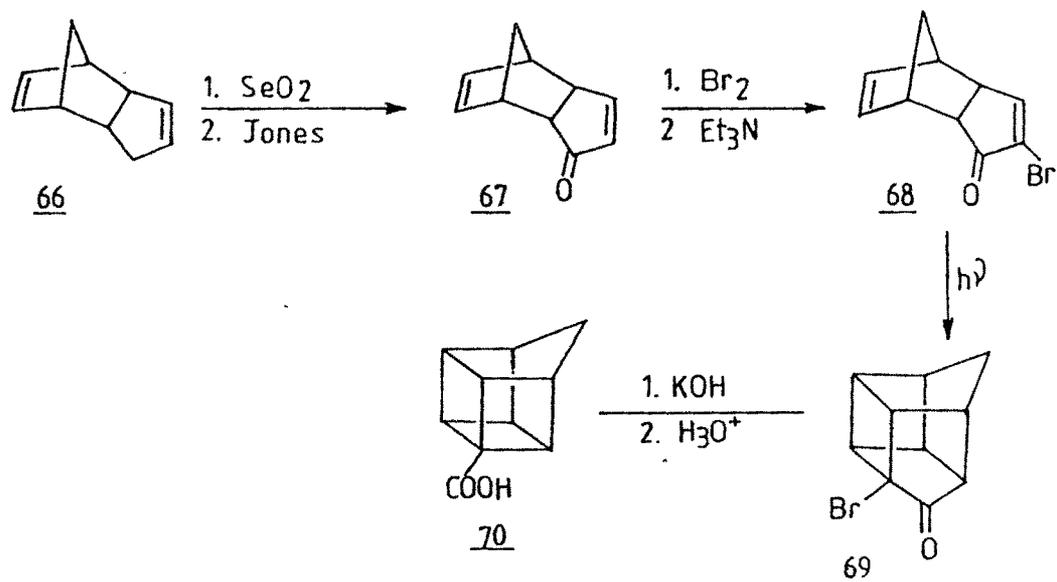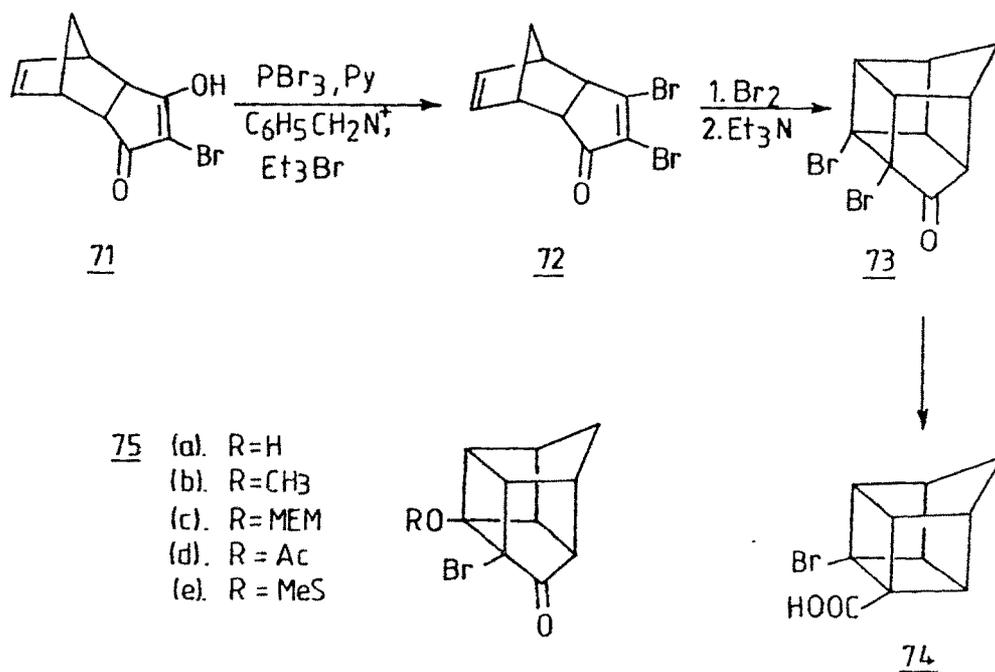

SCHEME - I.12

Other routes based on the ring contraction of α-halo ketones[35,36,37] are shown in the following Schemes-I.13, 14 and 15.


SCHEME-I.13

19

SCHEME -I.14

75 (a). R=H
    (b). R=CH3
   (c). R=MEM
    (d). R = Ac
    (e). R = MeS

SCHEME -I.15

Although the base promoted ring contraction of ⍺-halo ketones appears to be a general pathway for synthesizing homocubanes and other cage compounds,[38] the cage ketones bearing oxysubstituent ⍺ to a halogen such as 75 failed to undergo such a ring contraction upon treatment with base.[37]

Most of the approaches described above, employed ⍺-haloketones for ring contraction, Dauben[39] synthesized homocubanes through ring contraction of ⍺-diazoketone as shown in Scheme-I.16.

SCHEME - I.16

3
a. R = COOH
b. R = Br
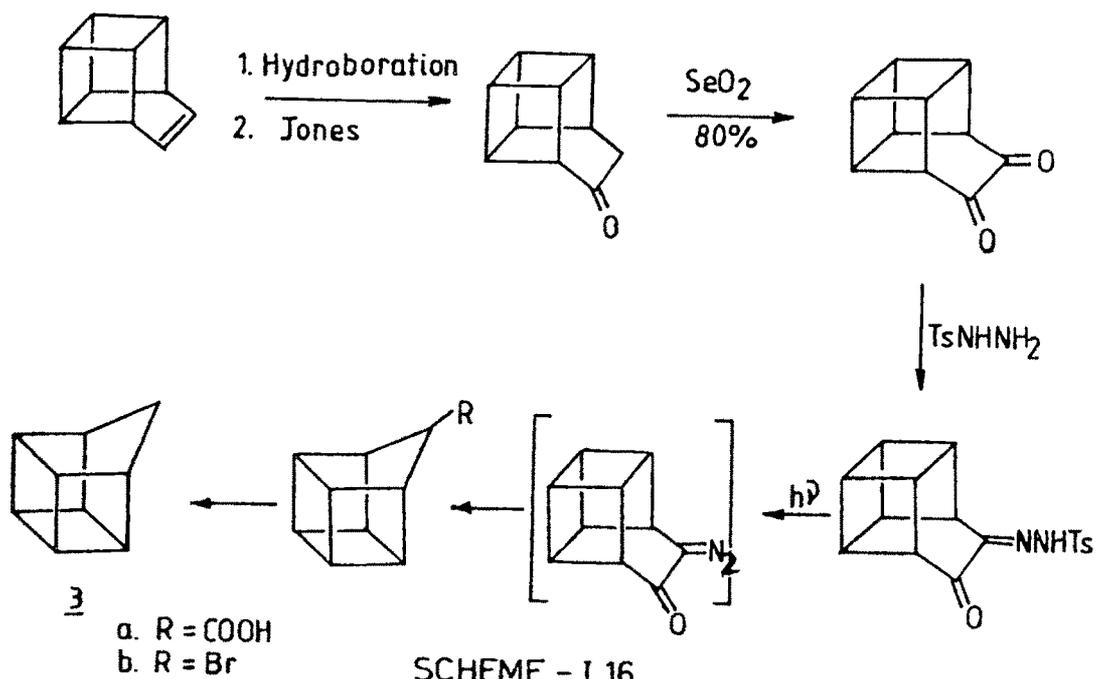
Other approach which proved successful towards synthesis of homocubanes involves $\pi^{2s} + \pi^{2s}$ cycloaddition of appropriately substituted to bicyclic diene ring systems. Thus Pettit and Barborak[40] prepared 76 by cycloaddition of cyclobutadiene and cyclopentadiene ketal and photolyzed to give homocubanone (64) which was converted into homocubyl alcohol (78). Alternatively the tricyclic system 76 was reduced to the alcohol (77) and irradiated to give 78. (Scheme-I.17)
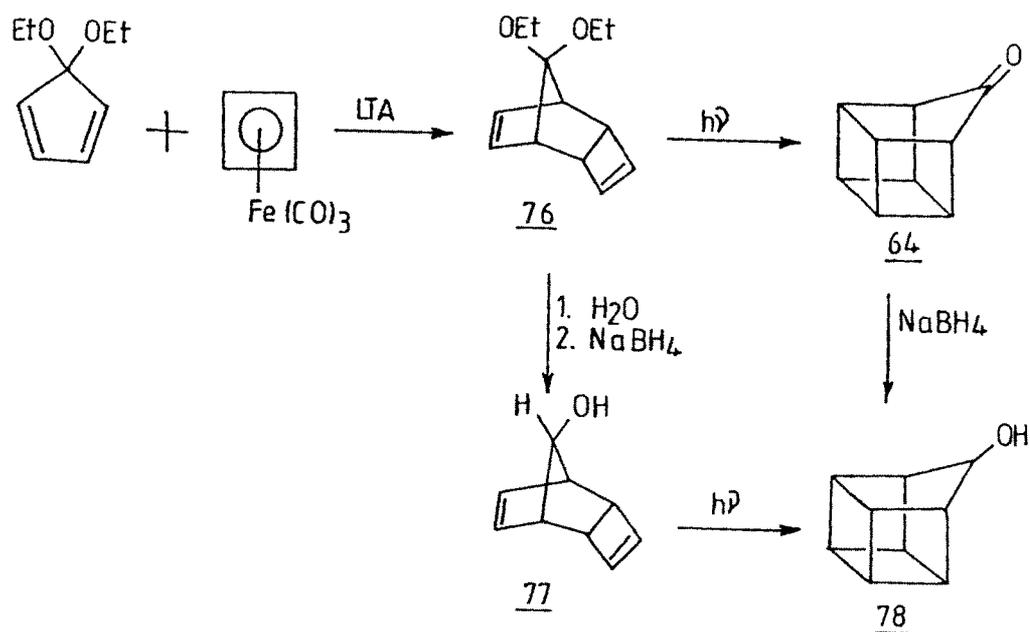
SCHEME-I.17

Paquette and Stowell have also employed cyclobutadiene
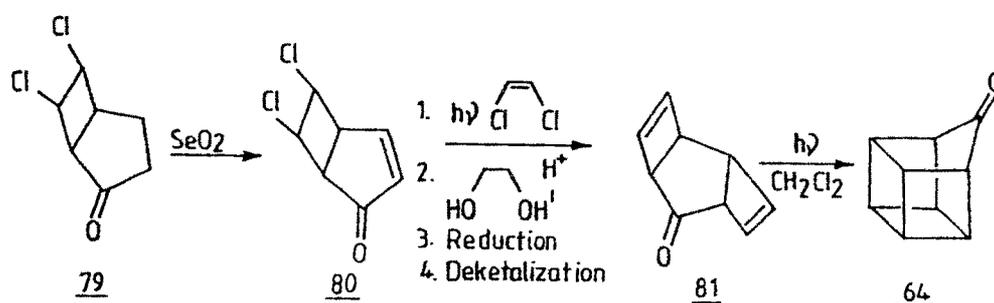in their synthesis of homocubane.[41] (Scheme-I.18)
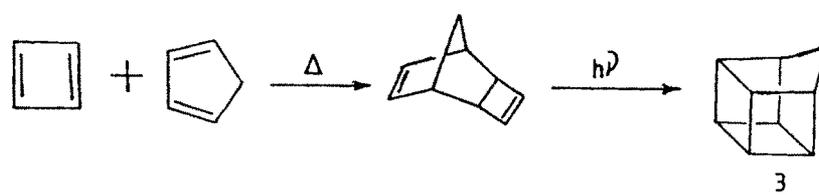
SCHEME I.18

Gargil and his co-workers have reported synthesis of
homocubanones in most interesting way employing photoaddition
of cis:anti:cis tricyclic dieneone (81) (Scheme-I.19). The
photolysis of 81 proceeds via Buchi rearrangement.[42]

SCHEME-I.19

Dauben and Warrener[43] used the adduct 82 obtained from cyclooctatetraene (44) and DMAD (Dimethyl Acetylenedicarboxylate) as source of cyclobutadiene for the preparation of chlorinated tricyclic diene (84) which was converted to homocubane employing standard synthetic sequences (Scheme-I.20).
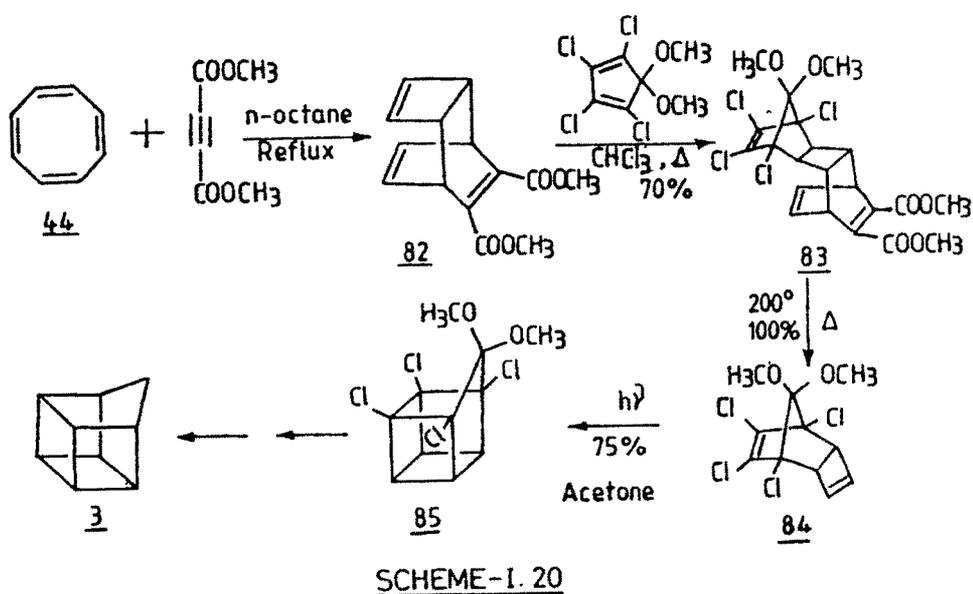
SCHEME-I.20

Homocubane (64) has also been prepared by reaction of transition metal complexes with cubane. Thus the reaction

of Cubane (2) with Rh(CO)$_2$Cl$_2$ affords homocubanone (64) (Scheme-I.21).[44]
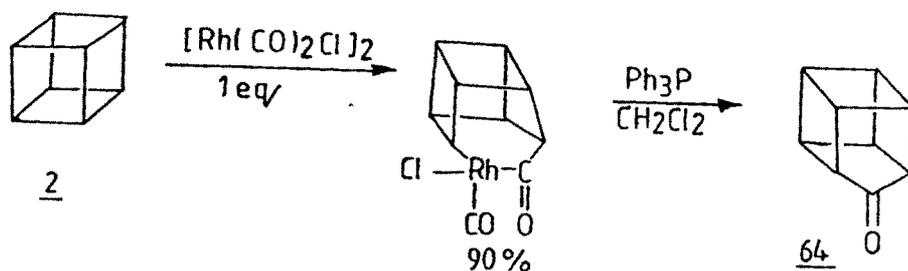
SCHEME - I. 21

Substituted homocubanes have been synthesised via carbene mediated ring expansion of cubanes. For example, thermolysis[45] of diazoalkane (86) in ethanolic sodium ethoxide gave a 3:2 mixture of isomeric ethers (89 and 90 respectively), via intermediacy of 87 and 88. (Scheme-I.22).
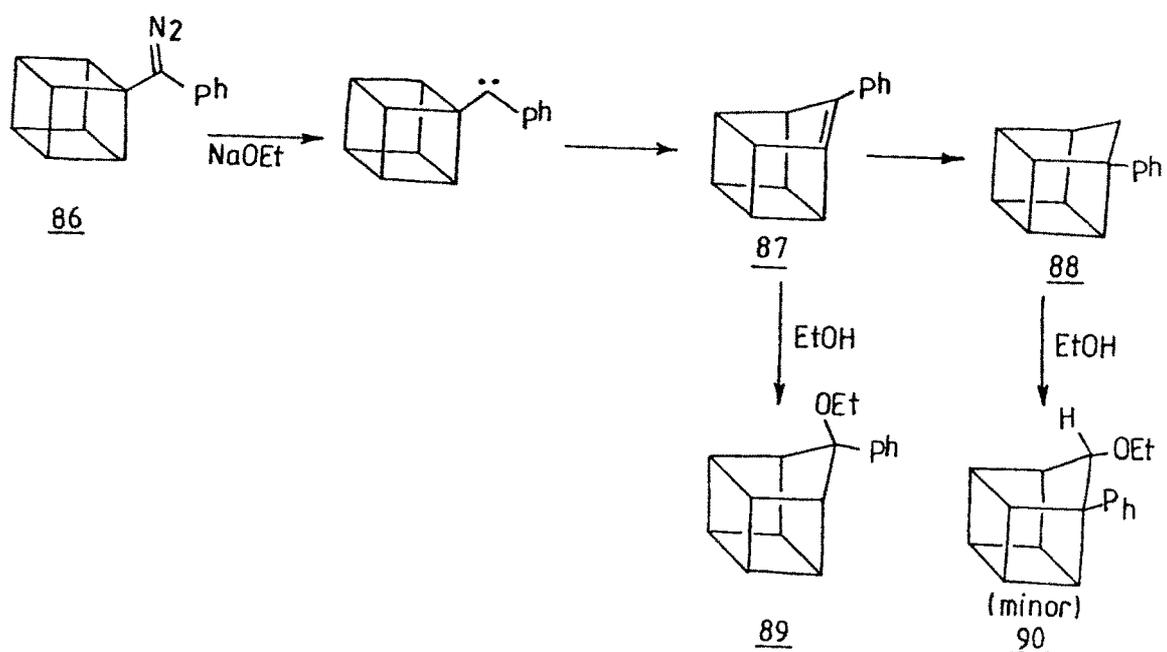
SCHEME – I.22

Bishomocubanes :

1,8 (or 1,1') Bishomocubane (Basketene) : Basketene (4)
was first reported in 1966 by Masamune and his associates[46]
and Dauben and Whalen[39] independently (Scheme-I.23).
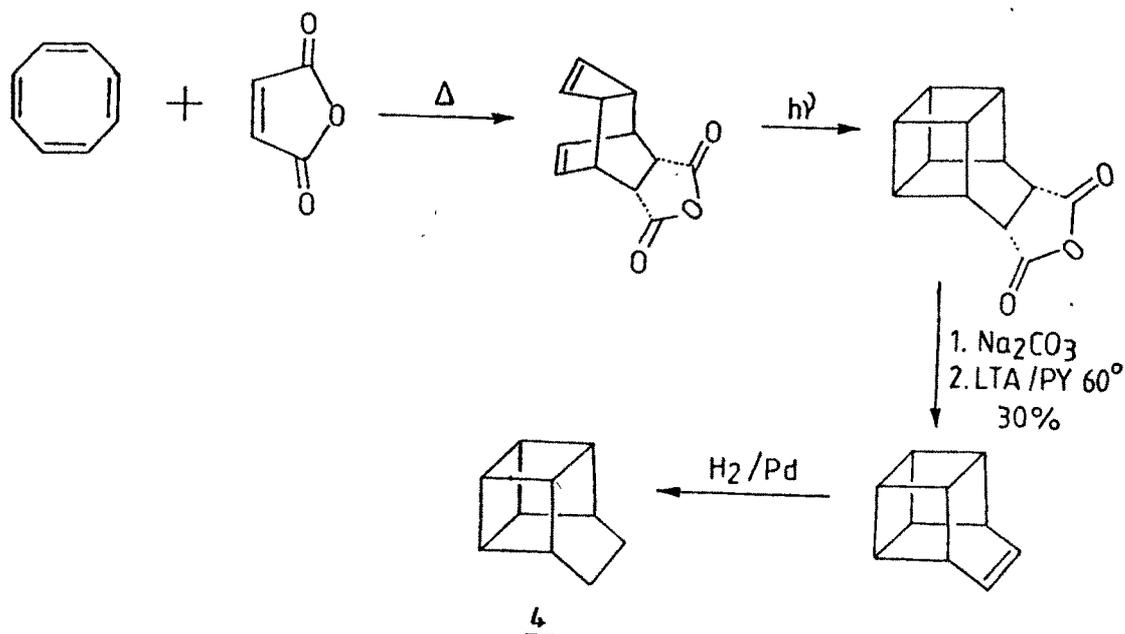
SCHEME - I.23

Mehta and coworkers[47] have reported an efficient synthesis of basketene from cycloocta-tetraene-acrylonitrile adduct (Scheme-I.24).
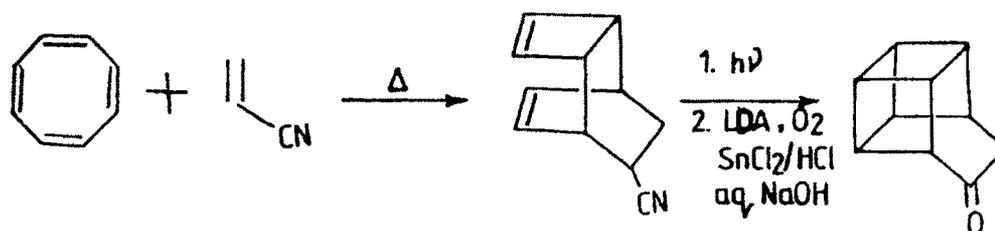
SCHEME - I. 24

Since cyclooctatetraene is an expensive starting material none of the aforementioned routes are suitable for large scale preparation of basketene and its derivatives. Gassman and Yamaguchi reported[48] an improved synthesis of 4 starting from rather easily available starting materials, cyclohexa-1,3 diene and 2,5-dibromobenzoquinone as outlined in Scheme-I.25.
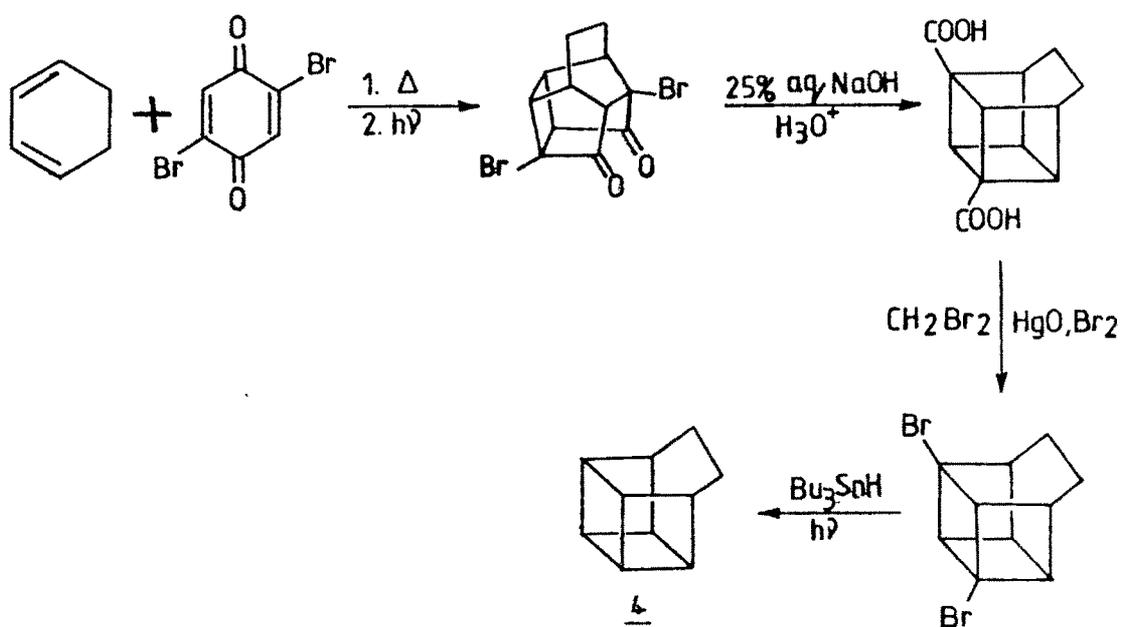
SCHEME - I.25

Some substituted basketenes have been synthesized by regiospecific one carbon homologation of 4-substituted homocubanes[49] (Scheme-I.26). The regiospecificity of such homologation is probably controlled by bromine substituent at C-1.
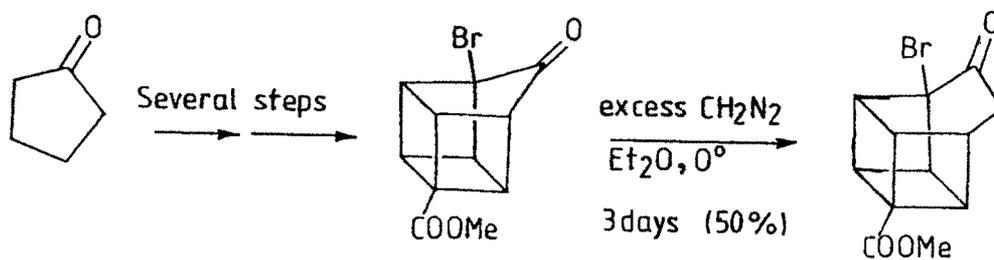
SCHEME - I.26

1,3-Bis homocubanes:

Intramolecular $\pi^{2s} + \pi^{2s}$ photocycloaddition of substituted endo tricyclo $(5.2.1.0^{2,6})$ deca-4,8-dienes of type 91 has proved to be a general route towards synthesis of a variety of 1,3-bishomocubanes (92) and a number of examples have been reported.[50] The parent hydrocarbon endo dicyclopentadiene (93), was converted to 1,3-bishomocubane (5) by acetone sensitized irradiation.[51] Similarly endo dicyclopentadienone (94) and its chlorinated derivative (95) were smoothly converted

to $\underline{64}^{52}$ and $\underline{96}^{53}$. Interestingly intramolecular photocycliza-
tion has been utilized to establish, unequivocally,[54] the
structure of thiels ester[55] (97). (Scheme-I.27)
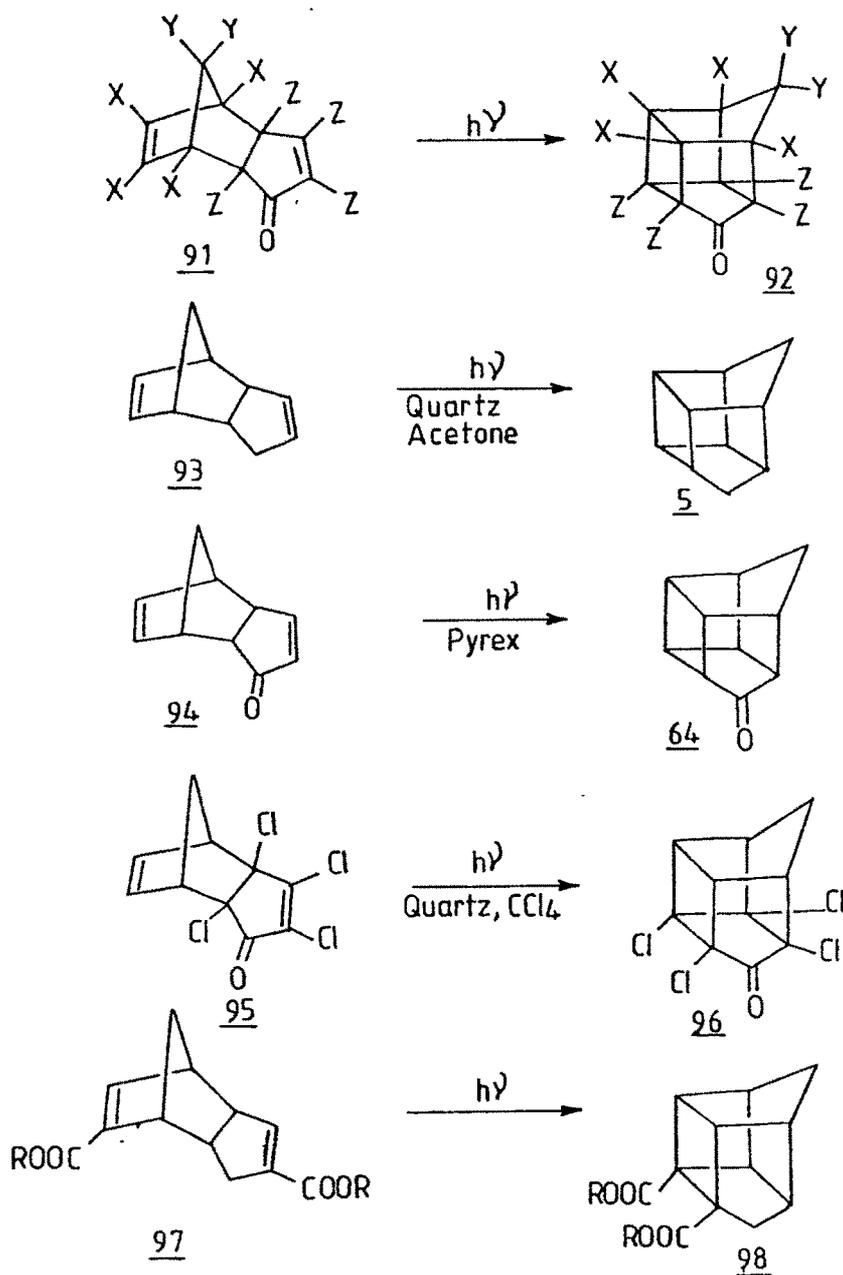
SCHEME -I.27

Although <u>endo</u> tricyclo $(5.2.1.0^{2,6}$) deca-4,8-dienes

(<u>endo</u>-cyclopentadiene dimers) such as those described above

undergo smooth photocycloaddition to corresponding cage isomers,

the behaviour of substituted <u>endo</u> cyclopentadienone dimers

has been found to be more complicated.[56-63]

Thus irradiation of <u>endo</u> dicyclopentadienone dimer (<u>99</u>)

affords products corresponding to various possible modes

of molecular interconversion (Scheme-I.28).[59] All the intercon-

versions depicted in Scheme-I.28 with the exception of the

Cope rearrangement are photochemically allowed processes.[64]
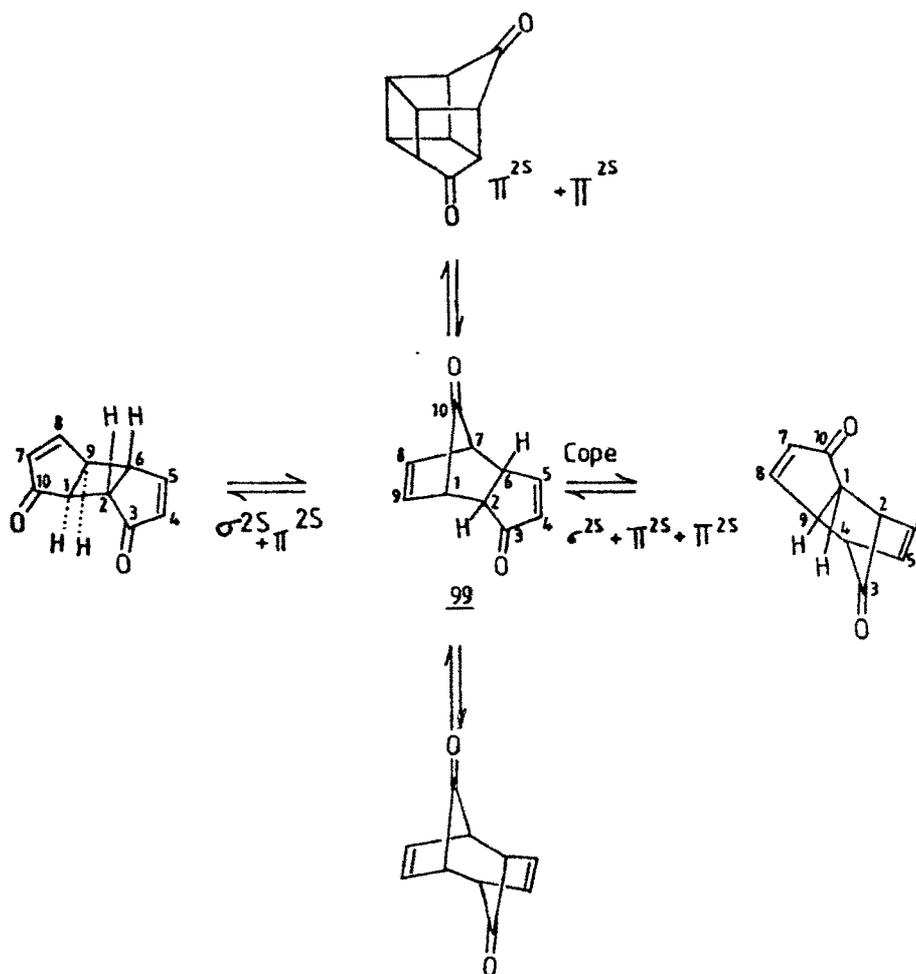
SCHEME - I.28

Therefore, substituted <u>endo</u> cyclopentadienone dimers can be used as precursors for 1,3-bishomocubanes provided that the hybridization of C(10) in the substrate is sp^3. This can be accomplished in any of the many ways e.g. (i) by selective reduction of nonconjugated (C-10) carbonyl group with NaBH$_4$[60,65] (ii) by selective hemiketal formation at C(10)[11] or (iii) by selective hydrolysis of ethylene ketal functionality at C(3) in a substituted <u>endo</u> tricyclo (5.2.1.0^{2,6}) deca-4,8-diene-3,10-dione bis(ethylene ketal).[66-68] Examples of each these reactions to the synthesis of 1,3-bis homocubanes are shown in Scheme-I.29.
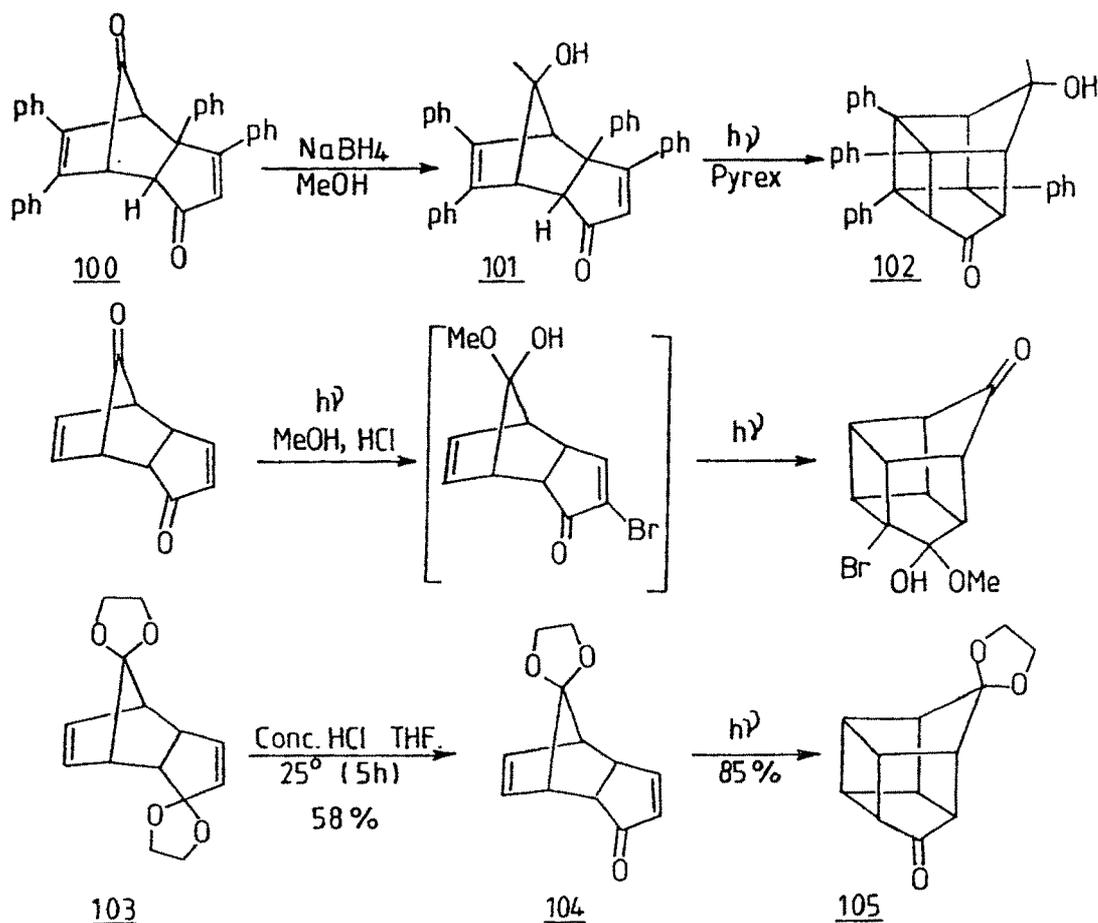
SCHEME-I.29

Since 1,3-bishomocubane possessing C_2-symmetry is chiral,
Nakazaki and coworkers[70] have reported synthesis of optically
active 1,3-bishomocubanes and studied their chiroptical proper-
ties.[70,71](Scheme-I.30).
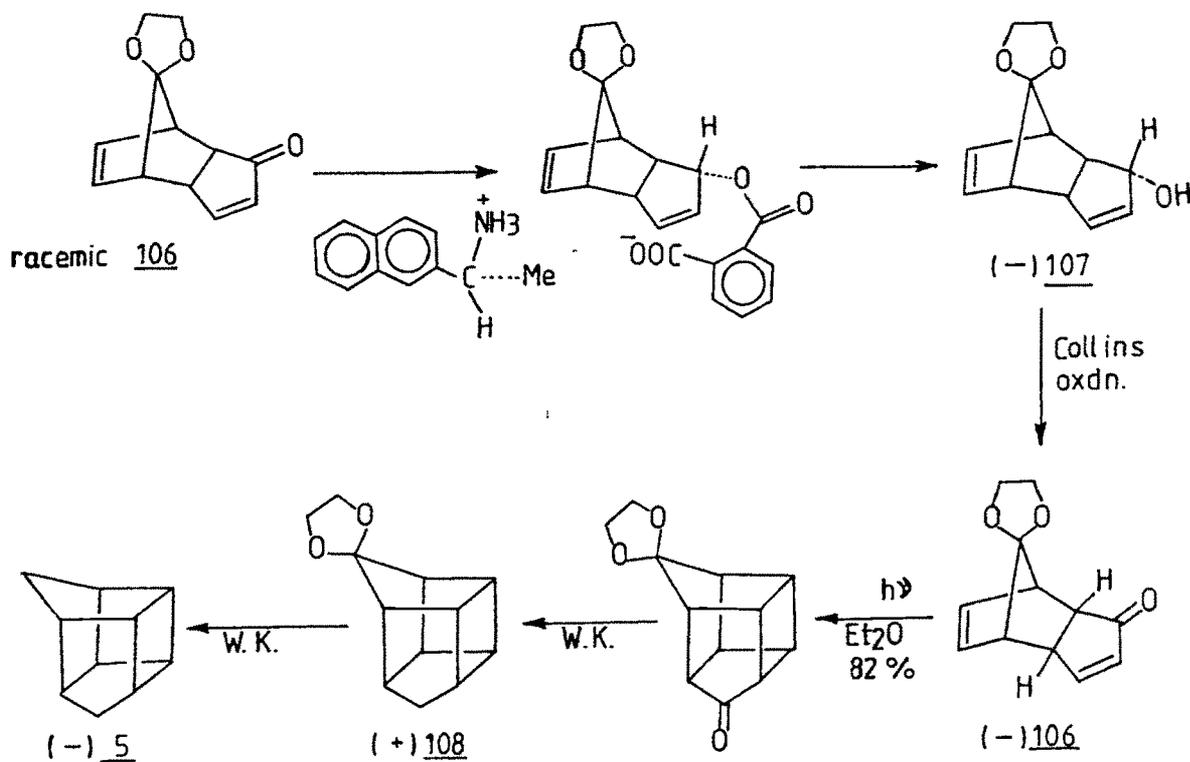
SCHEME-I.30

(D$_3$)-Trishomocubanes:

(D$_3$)-Trishomocubane and its derivatives have been the
subject of numerous studies. The rigid carbocyclic network
of (5) belonging to the chiral symmetry group D$_3$, represents
a unique assembly of six identical twist cyclopentane rings

and is a tricycloundecane $\underline{\text{stabilomer}}$.[73] Majority of the synthetic routes to D_3-Trishomocubane have employed Cookson's[74] cage dione ($\underline{109}$) as the starting material. Underwood and Ramamoorthy[75] reported its first synthesis in 1970, starting from pentacyclic dione ($\underline{109}$) as shown in Scheme-I.31.
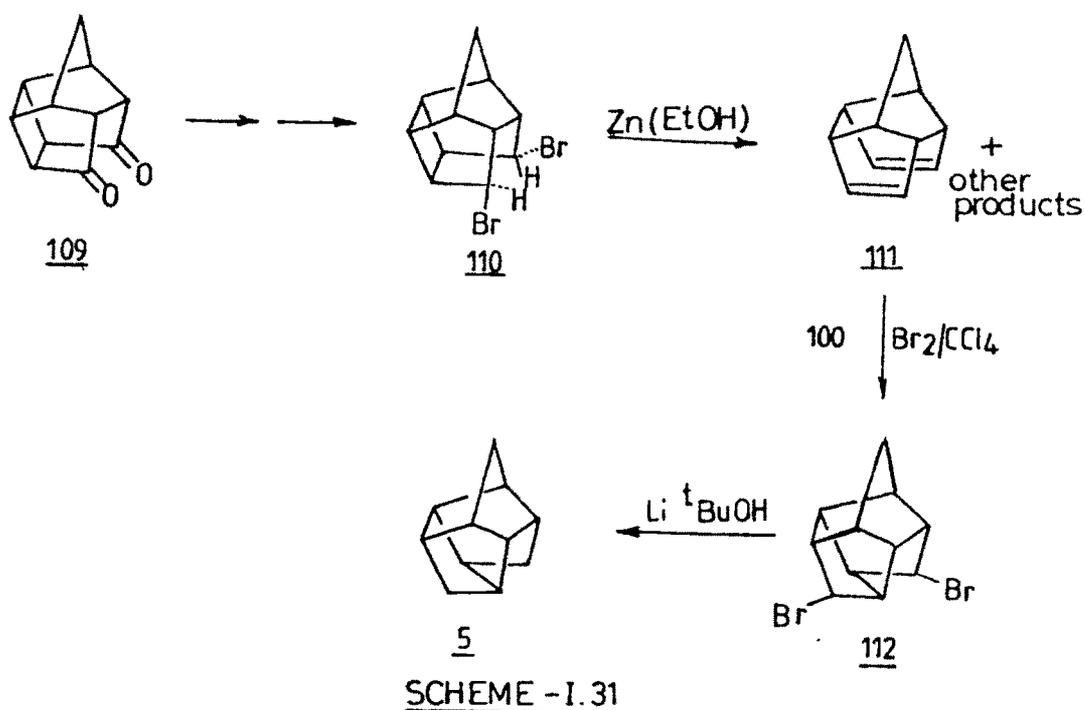
SCHEME -I.31

Subsequently, Schleyer and coworkers[73,76] synthesized ($\underline{5}$) 93% yield via $AlBr_3$ - catalyzed isomerization of pentacyclo ($5.4.0.0^{2,6}0^{3,10}0^{5,9}$) undecane ($\underline{113}$) (Scheme-I.32).

SCHEME - I.32

Eaton[77] and his associates synthesized the D_3-trisho-mocubane from cyclopentadiene-p-benzoquinone adduct.[74] (Scheme-I.33).
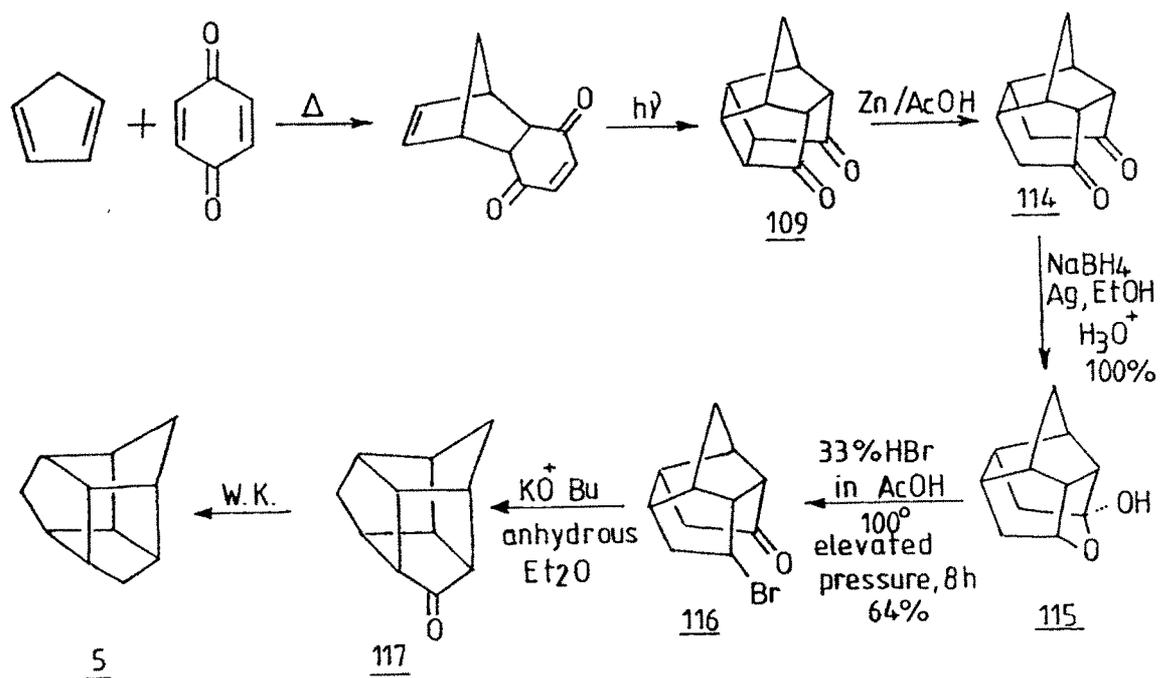
SCHEME - I.33

Starting from the same pentacyclic dione (109) two methods for synthesis of (5) were reported[78,79] via reduction of iodinated pentacyclo $(6.3.0^{2,6}0^{3,10}.0^{5,9})$ undecanes 118a and 118b (Scheme-I.34).
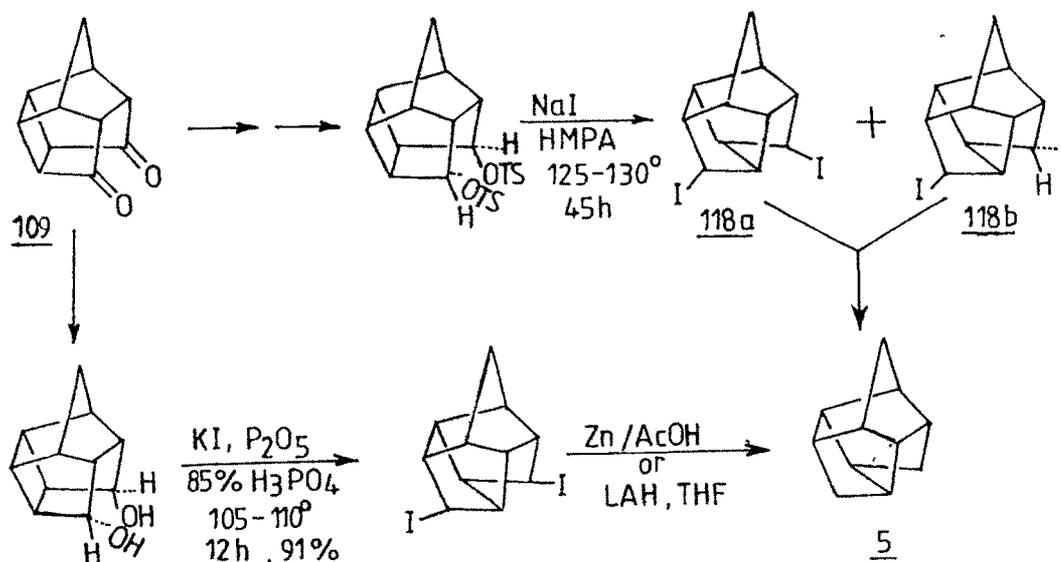
SCHEME - I. 34

Subsequently Mehta and Chaudhuri[80] also reported a synthesis of D_3-trishomocubane (Scheme-I.35).
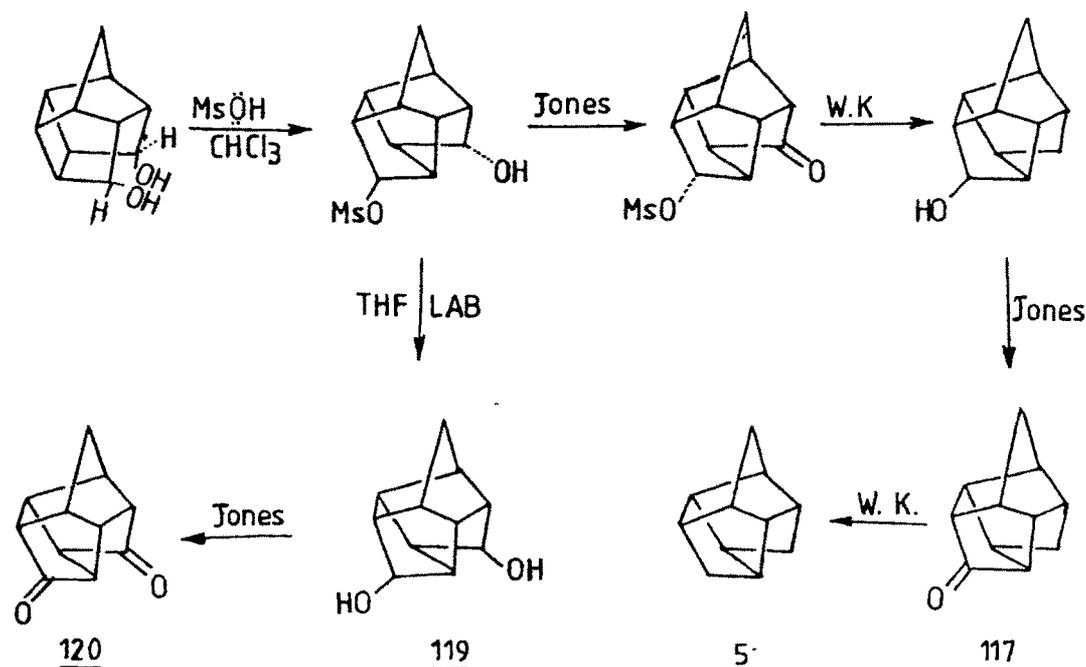
SCHEME - I.35

Soon after racemic trishomocubane (5) had been synthesized. Three research groups independently developed routes for preparation of the enantiomers of 5 in optically pure form and absolute configuration of each enantiomer was then determined.[81-84] Helmchen and Staiger[81] separated the diastereomeric esters obtained from the reaction of iodoalcohol 121 with (-) Camphanic acid converted it to enantiomerically pure (-) (5) as shown in the Scheme-I.36.
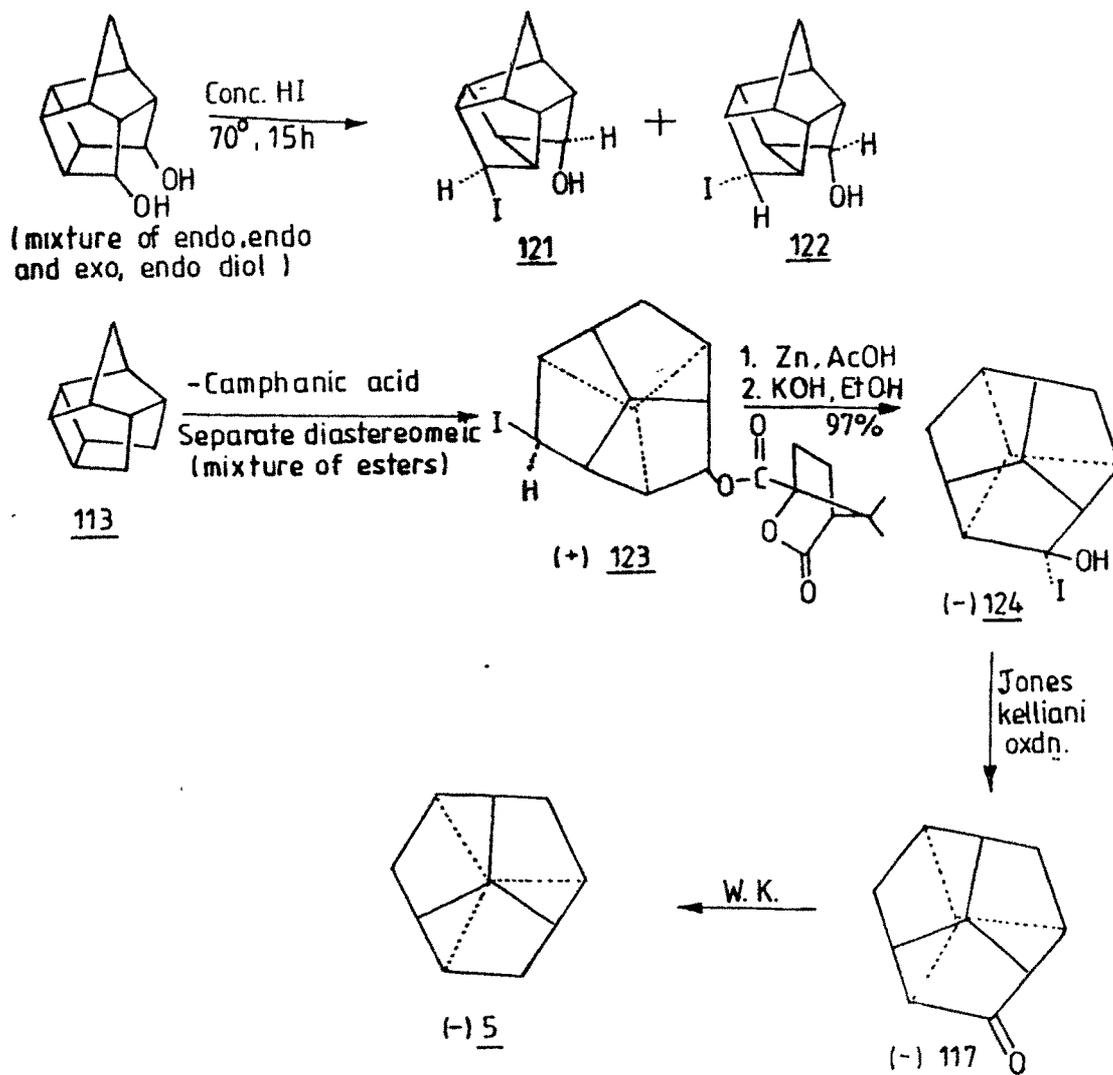
SCHEME -I.36

Nakazaki and coworkers[82] attempt to resolve the diol

125 failed, accordingly they converted it to trishomocubanol

(124) and then resolved it via the hydrogen phthalate using

(+)-2-(1-amino ethyl) napthalene as resolving agent, and

obtained optically pure (+)-124. Oxidation of (+)-124 followed by Wolf-Kishner gave the (+)-5 (Scheme-I.37).

SCHEME - I.37
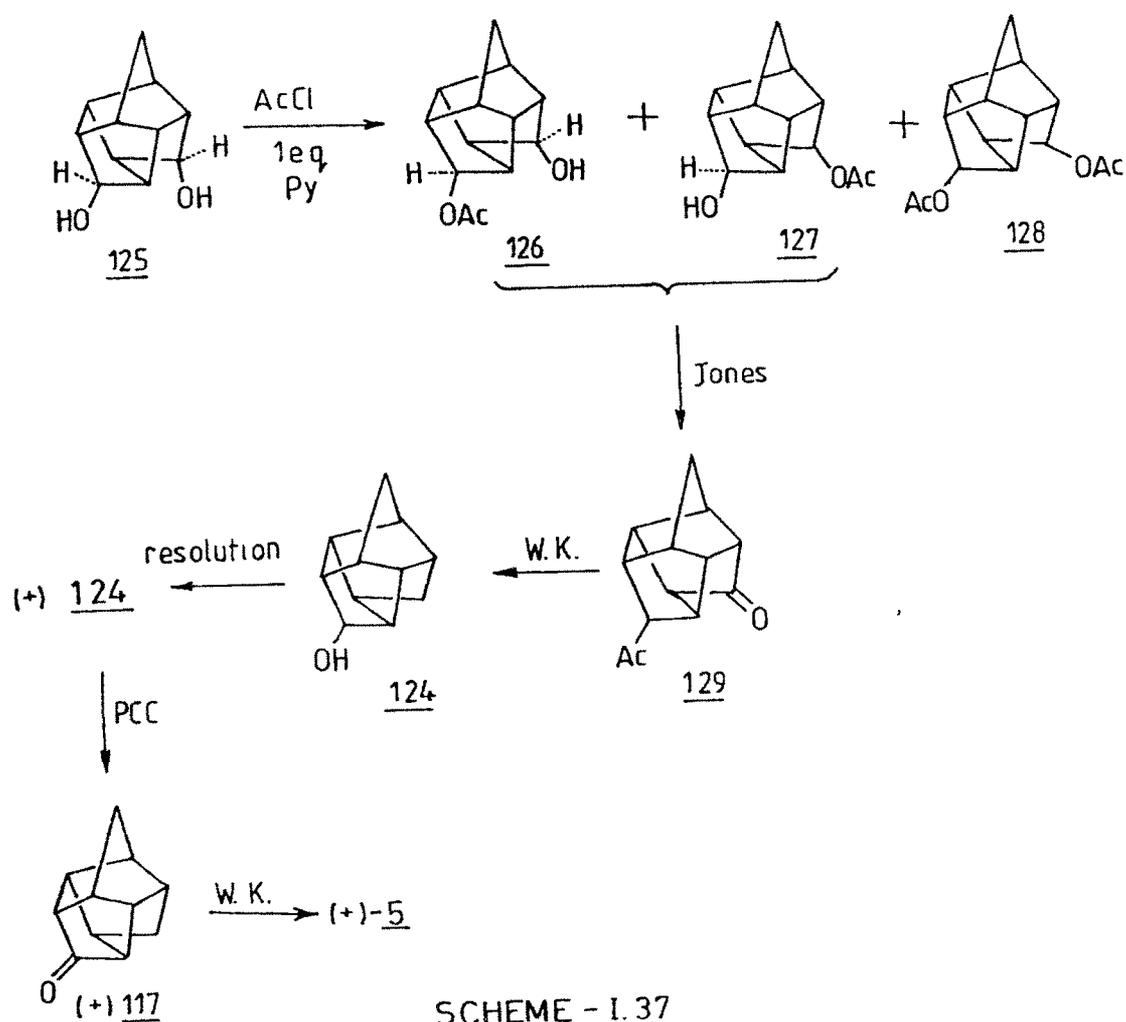
In addition, Naemura et al.[83] have performed an asymmetric reduction of the Cage diketone 109 with horse liver alcohol dehydrogenase (HLADH), the optically active alcohol 130 was transformed into optically active trishomocubanol (+)-124 as shown in Scheme-I.38.
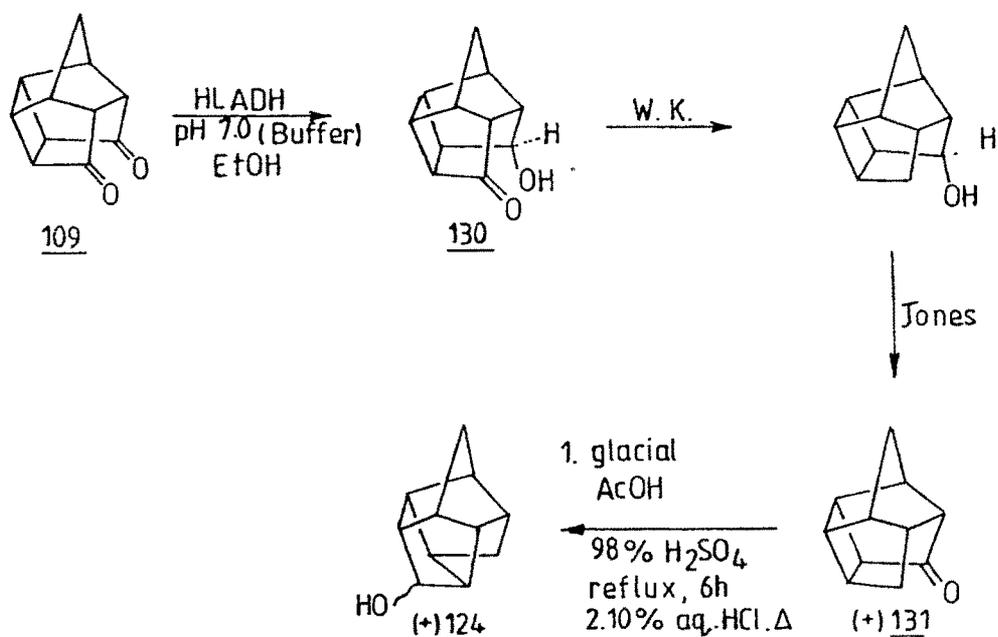
SCHEME I.38

Optically active ketone (+)-131 was subsequently converted into homologated trishomocubane (Scheme-I.39). A similar approach had been reported earlier by Dekker and coworkers[84] for the synthesis of rac.(-)135.
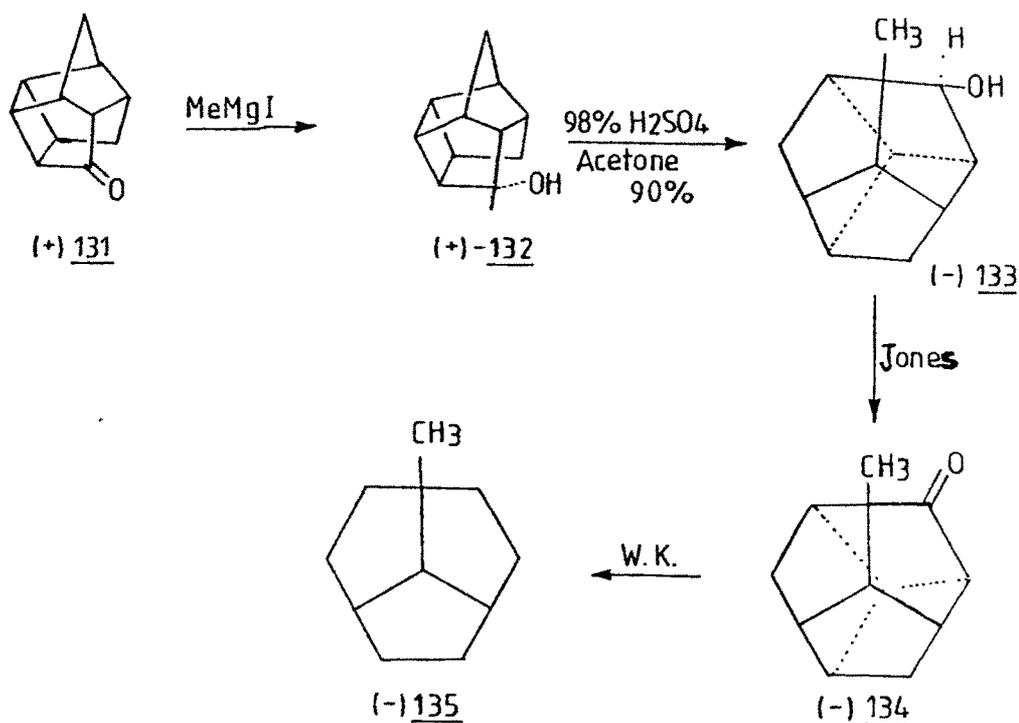
SCHEME - I. 39

Eaton and Leipzig[85] resolved the trishomocubanone (rac.117) by its reaction with L-ephedrine followed by acid hydrolysis of each diastereomer. The absolute configuration of each ketone enantiomer was established by Wolf-Kishner reduction of the corresponding optically active D_3-trishomocubane.

The synthesis of rac-D_3-trishomocubane trione (136) has been reported from two laboratories.[85,86] 4,4-Dimethoxy-pentacyclo (5.4.0.0^{2,6} 0^{3,10} 0^{5,9}) undecane-8,11-diol (137a

or <u>137b</u>) was used as a starting material for both routes. Their key step in each route involved the acid catalyzed Wagner-Meerwein rearrangement from an appropriately substituted pentacyclo $(5.4.0.0^{2,6}.0^{3,10}.0^{5,9})$ undecane to the corresponding substituted undecane system (<u>Scheme-I.40</u>).
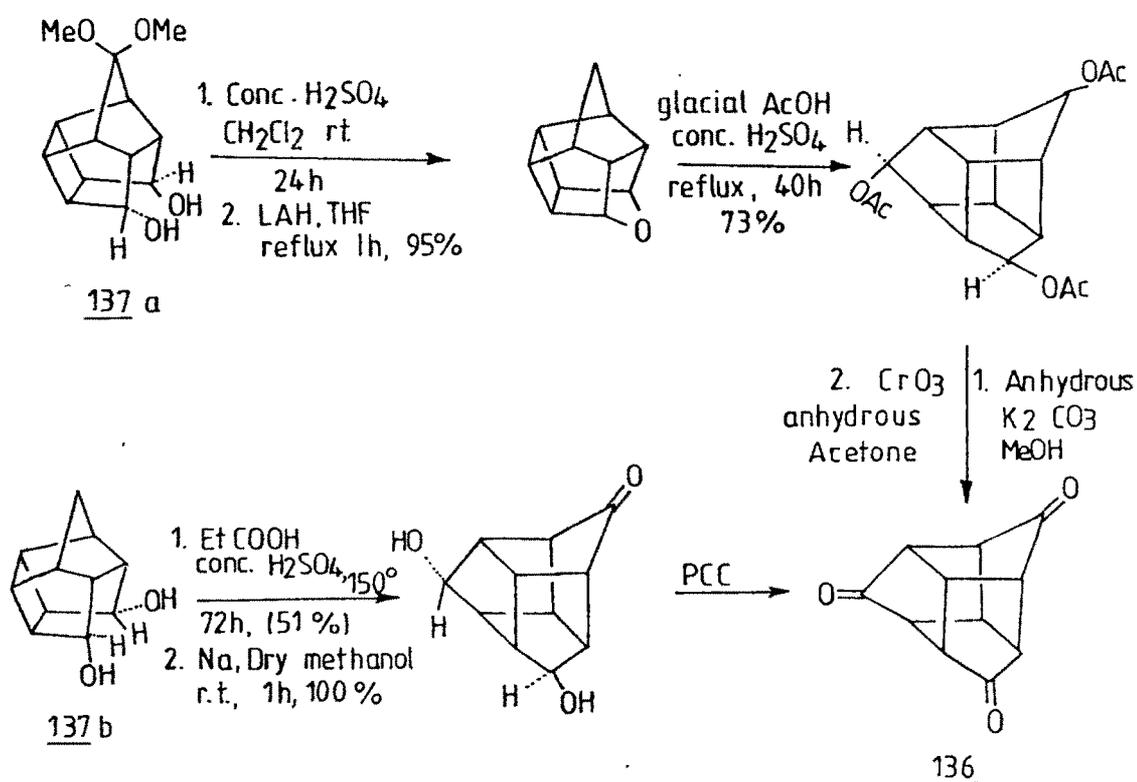
SCHEME - I.40

Optical resolution of rac-<u>136</u> was performed by reaction of this triketone with (R,R)-2,3-butanediol followed by fractional recrystallization of the mixture of diastereomeric trisketals, <u>138</u> thereby obtained from CH_2Cl_2-hexane. Reaction

of pure (-)-138 and (+)-138 with HBr in glacial acetic acid gave optically active (+)-136 and (-)-136 respectively, whose absolute configurations were established through their facile reduction to (-)-5 and (+)-5 respectively (Scheme-I.41).[85]

SCHEME -I.41
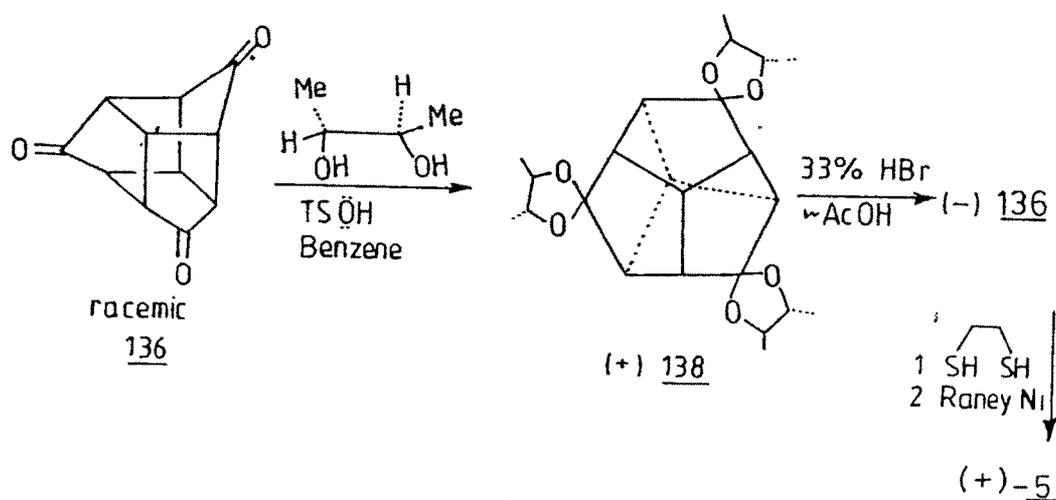
Rac-D_3-trishomocubane dione (120) has been synthesized by oxidation of diol 119 by Mehta and Chaudhuri.[80] Many other interesting facets of chemistry of cubanes and homocubanes such as their reactions and rearrangements have been described in recent articles.[30,31]

Pentaprismane*

The third member of this family[87a] (the first member triprismane (139) has been synthesized[87b]) has long defied its synthesis until recently[88] despite its rather facile appearence as a synthetic target. In addition to its synthetic appeal, the high strain energy, estimated[89] to be 135.7 Kcal/mole^{-1} and its intriguing chemical behaviour have been the reasons for interest in this molecule.

Many indigenious synthetic efforts, most notably the attempted photochemical closure of hypostrophene[90-92] (140) and the thermal extrusion of N_2 either from (141)[93] or from (142)[94] have proved futile. (Scheme-I.42)

139   140   141   142
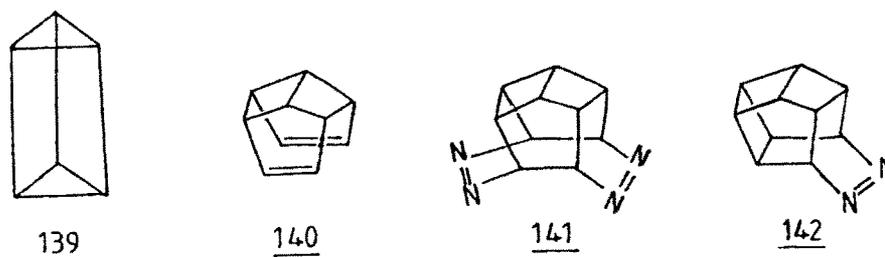
SCHEME-I.42

Eaton and coworkers[88] reported the first successful synthesis of pentaprismane from readily available dimethylketal

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* Hexacyclo [5.3.0.0^{2,6}0^{3,10}.0^{4,9}.0^{5,8}] decane

of tetrachloro pentacycloundecatrione (143)[74,95] employing
ring contraction of α-keto tosylate (150) as a key step (Scheme-
I.43).
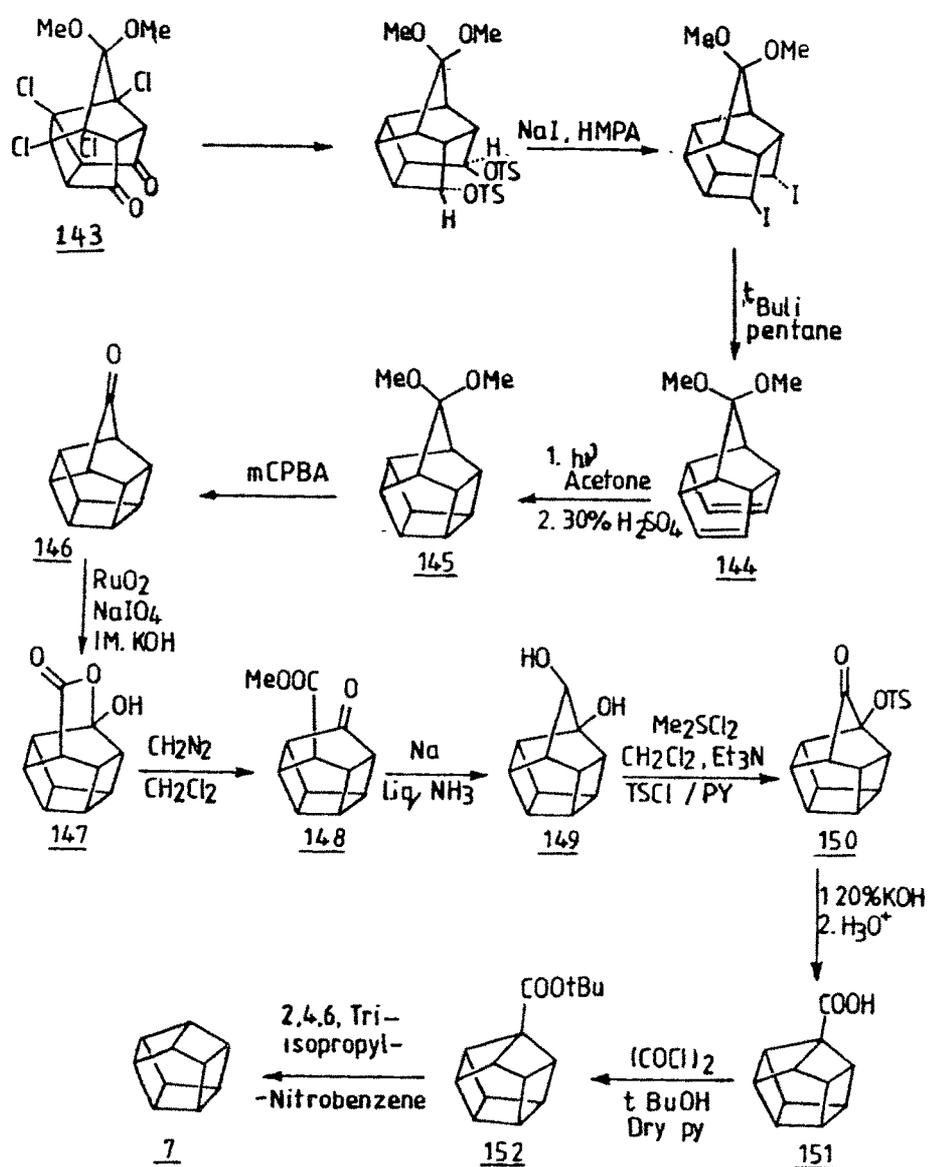
SCHEME -I.43

Dauben and Cunningham[96] have also synthesized the keto-
ester (148) and thereby achieved a formal synthesis of penta-
prismane. They employed cyclobutadiene and monoketal of
benzoquinone[97,98] (153) as starting material, which after
cycloaddition followed by a $\pi^{2s} + \pi^{2s}$ photoclosure furnished
monoketal of cage-dione (155). Wittig olefination of 155
followed by hydroboration gave 157 which was transformed
into ketoester 148 (Scheme-I.44).
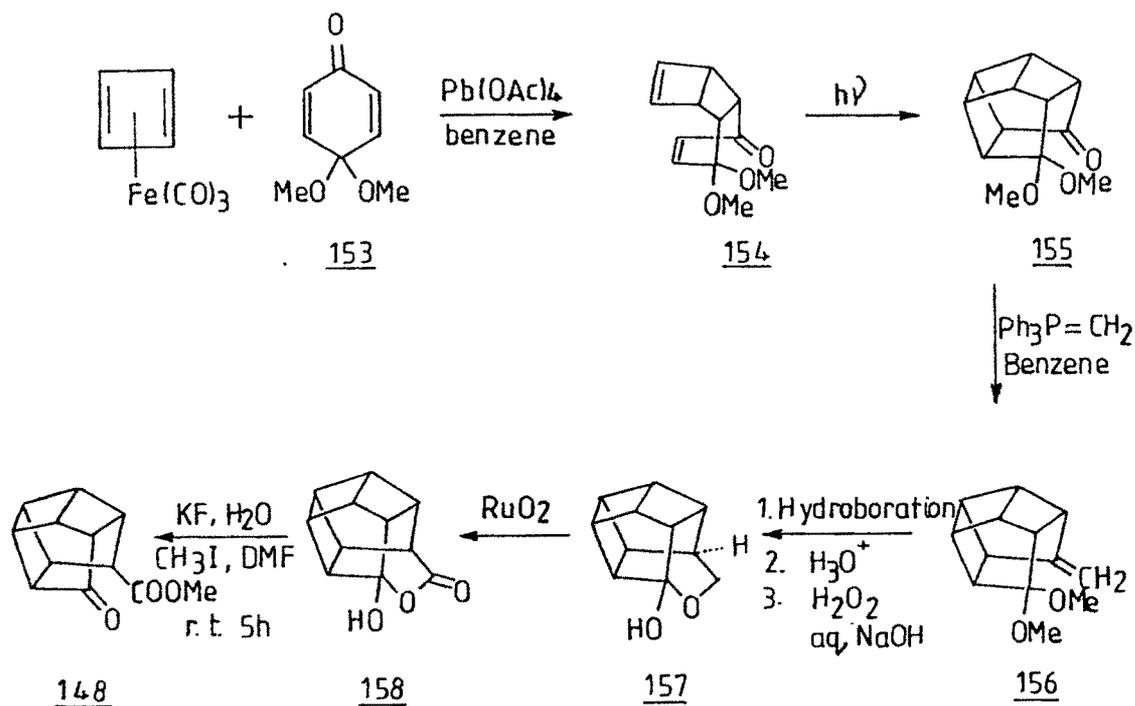
SCHEME - I.44

The reluctance of hypostrophene towards $\pi^{2s} + \pi^{2s}$ photo-cyclization was explained on the basis of more effective through bond interaction between "π" bonds which reverses the normal ordering of inphase and out of phase combinations.[99] This is a result of interaction of highlying orbitals and the π bond. Although hypostrophene (140) did not serve as a source of pentaprismane (7), it generated some chemistry of its own.[100]

Homopentaprismane : (8)

The initial report of its synthesis by Underwood and Ramamoorthy is now known to be incorrect.[101] Eaton and his associates[102] have synthesized this molecule, a homologue of penta-prismane. The key precursor to pentaprismane, homohypostrophene has been synthesized in the laboratories of Barborak[103] and Marchand.[104] All the three routes to homohypostrophene (164) which was subsequently converted to homopentaprismane employ, Cookson's pentacyclic cage dione (109) as starting material which is readily available.

In Eaton's approach the dione (109) was monoketalized and then reduced with sodiumborohydride to give hydroxy ketal (159) which was further transformed into bromo ketone (160). The zinc reduction of 160 furnished the enone (161) which after reduction with LAH followed by its treatment with $POCl_3$-Py gave bromo olefin (163). Elimination of halogen with KotBu

gave the air sensitive homohypostrophene (164) which was irradiated to give homopentaprismane (8) (Scheme-I.45).
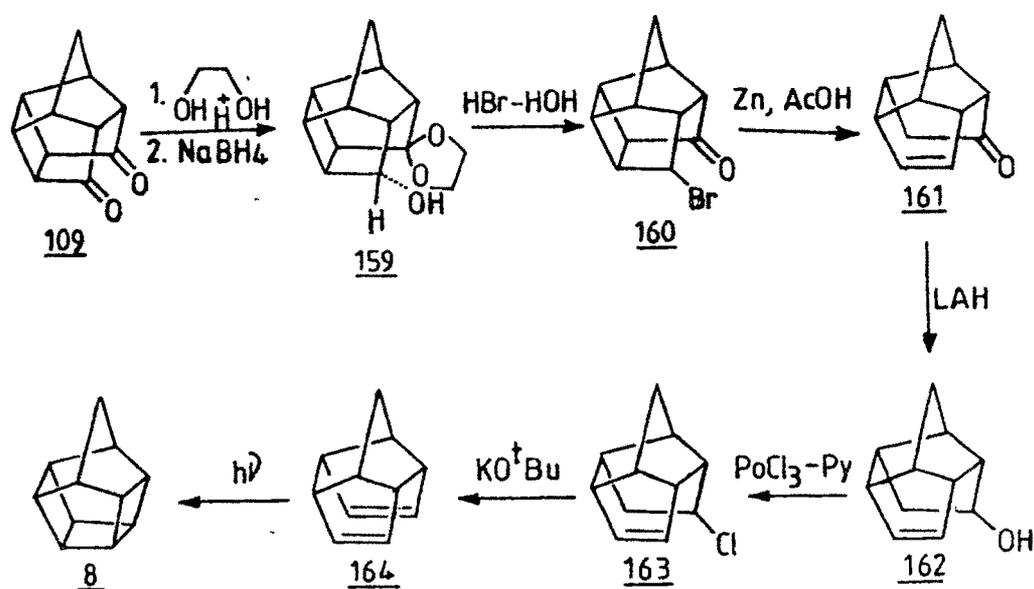
SCHEME - I.45

Barborak and Marchand prepared homohypostrophene starting from the same cage dione (109) as shown in Scheme-I.46 and I.47 respectively.
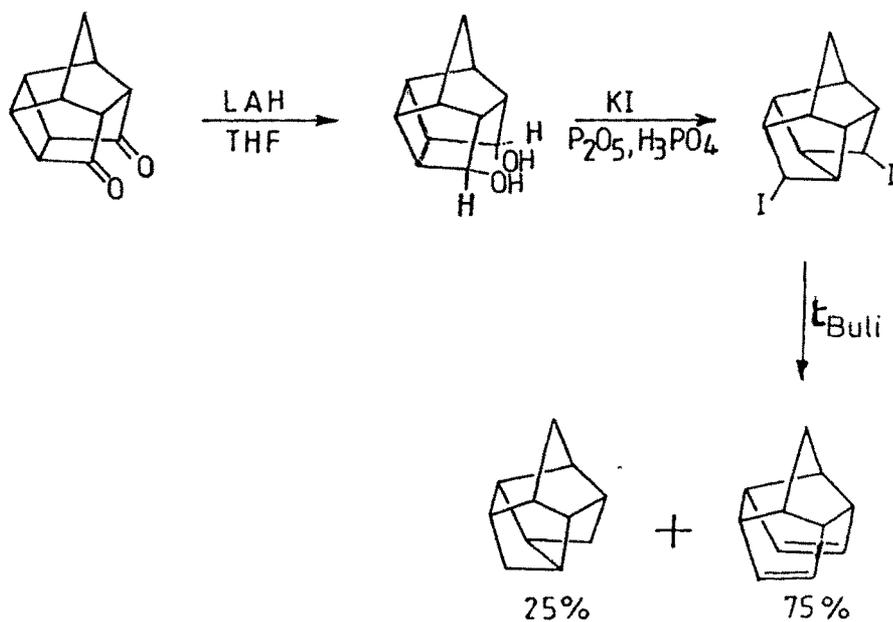
SCHEME – I. 46
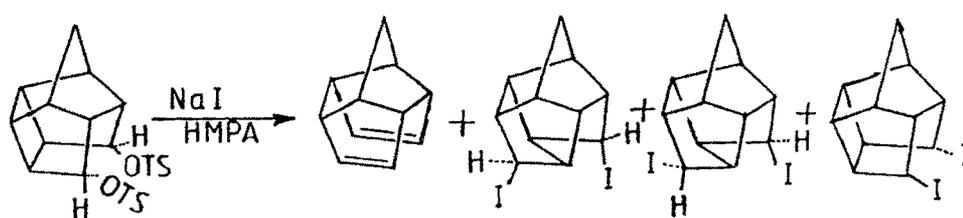
SCHEME – I.47

A $C_{12}H_{12}$ hydrocarbon, a formal face-to-face dimer of benzene having D_{6h} symmetry and high strain energy,[105] 160 Kcal/ mole has now attracted the attention of many research groups[105-109] in this area. However only progress towards it has been forthcoming.

Mehta et al.[110] have recently reported the synthesis of secohexaprismane (175) a one bond away, secologue of (9). The readily available[111] Diels-Alder adduct (165) of 1,5-cyclooctadiene and 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene, was transformed into the symmetrical 1,3-diene (166) via allylic bromination and dehydrobromination. The cycloaddition of $^1O_2$ with diene (166) furnished the peroxide whose LAH reduction and acetylation gave the diacetate (168) which underwent $\pi^{2s} + \pi^{2s}$ cycloaddition on acetophenone sensitized irradiation to furnish the caged pentacyclic endo, endo, diacetate (169). This diacetate (169) was converted into a key diene (172) which on photolysis and ring contraction gave the carboxy derivative (174), followed by three step sequence finally gave the secohexaprismane (175) (Scheme-I.48). It is disappointing to note that the precursors to hexaprismane 176 and 177 did not undergo the desired $\pi^{2s} + \pi^{2s}$ cycloaddition.
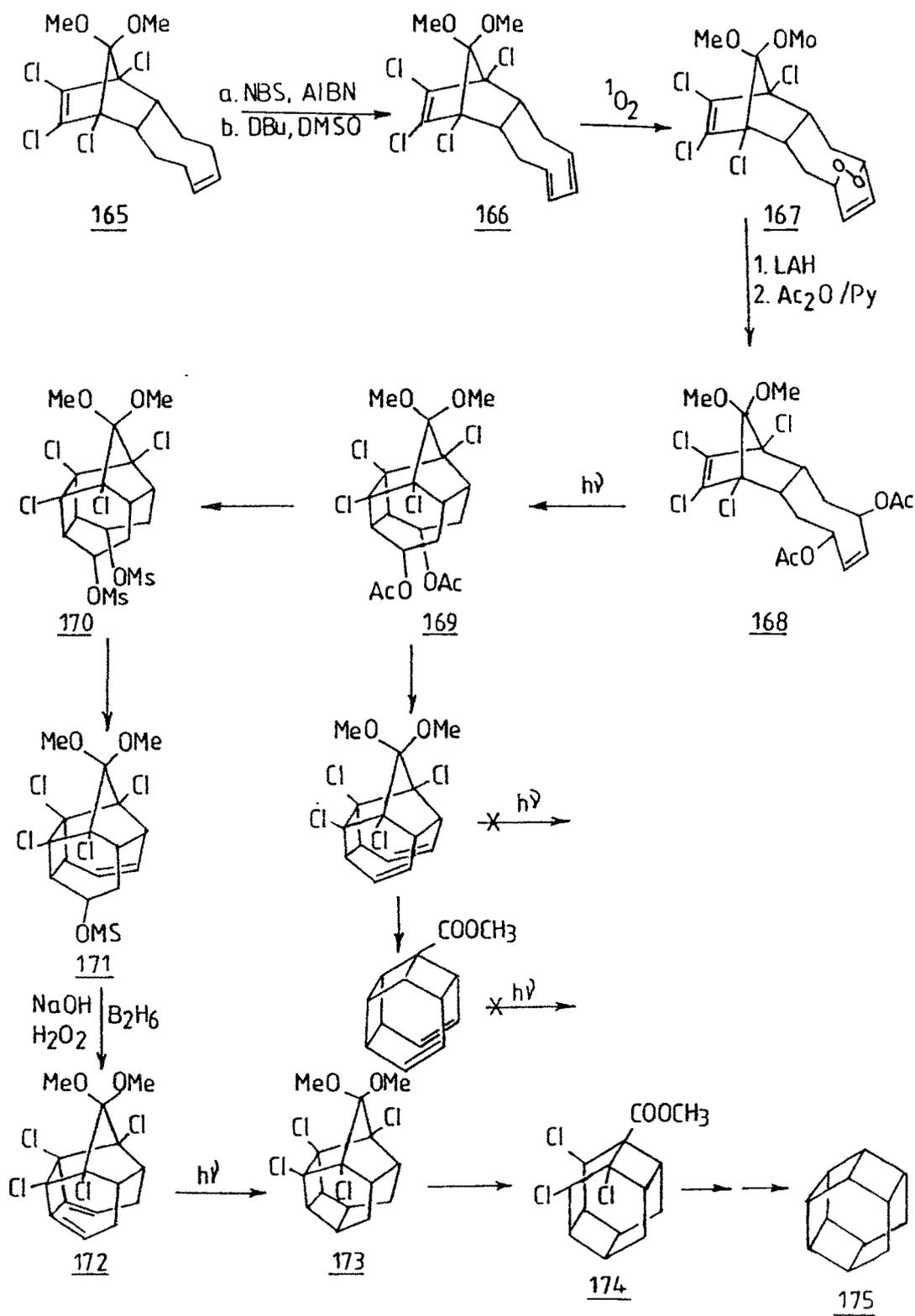
SCHEME - I. 48

Dodecahedrane : (10)

Dodecahedrane, though not really strained in the same way as the earliest member of the (tetrahedrane, cubane) belonging to platonic solids, has been the most fascinating and challenging target for synthesis. There has been a very high level of worldwide interest in this highly symmetric molecule (In symmetry 120 symmetry operations) and many research groups have been engaged in developing synthetic route to dodecahedrane (10).[112] Paquette and his coworkers[113] after a decade intense effort, have realized this goal recently.

Among early approaches to dodecahedrane Woodward[114] and Jacobson[115] almost 25 years ago, independantly contemplated that dimerization of triquinacene (176) would give the dodecahedrane (10). However all the attempts to dimerize triquinacene have proved unsuccessful under a variety of conditions. The overall dimerization process though expected to be exothermic by approximately 97 Kcal/mole is disallowed because of statistical, entropic and steric factors.

Other schemes of dimerization of triquinacene derivatives such as 117[116], 178[117], 179[118] and 180[119] have also been unsuccessful towards the synthesis of dodecahedrane.

176

178

177

179

180
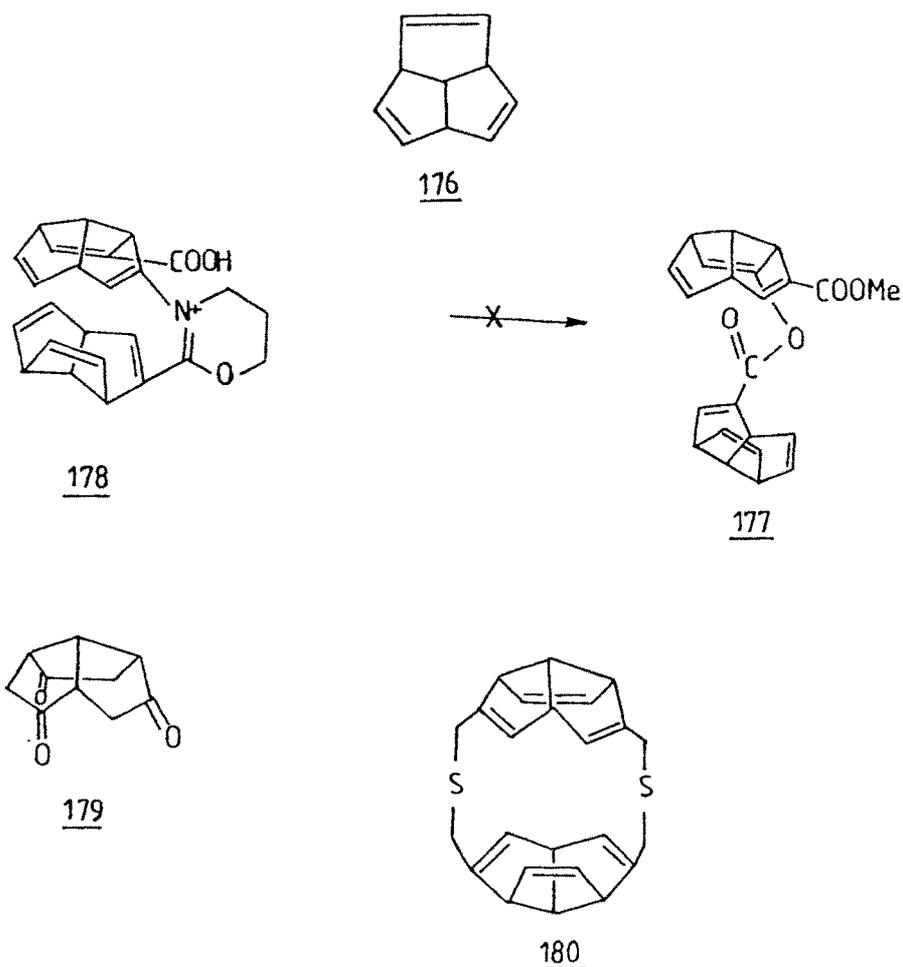
The Eaton's[120] approach to dodecahedrane (10) by capping of a properly functionalized C_{15} -hexaquinane such as (181) have also been unsuccessful towards 10. Exposure of 181 to the base under mild conditions induced elimination of acetate ion leading to very reactive peristylenone 182. Similarly Paquette's attempts to elaborate 183 to dodecahedrane have also met with complications.[121] Many other novel approaches involving the hexaquinanes 184[122], 185[123], 186[124] as potential dodecahedrane precursors have also not been successful.

181 **182** **183**

184 **185** **186**
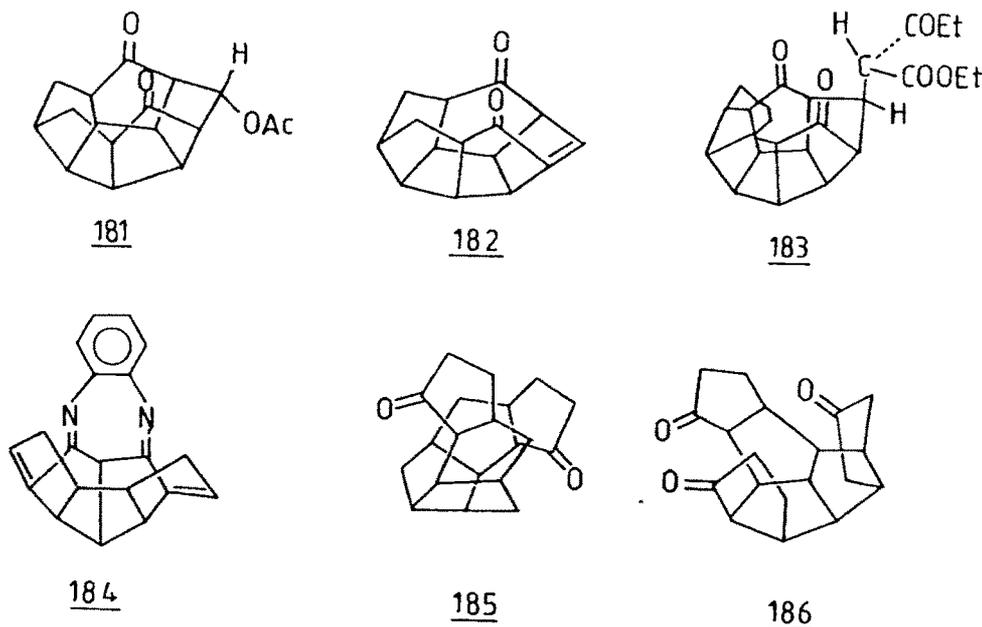
Paquettes successful route to dodecahedrane from dihydrofulvalene and dimethyl acetylene dicarboxylate is as follows. The domino Diels-Alder adduct (**187**)[125,126] was converted into **188b** which after reaction with sulfur ylide (**189**) gave the cyclobutanone (**190**). Baeyer-Villiger oxidation of **190** followed by cyclization with P_2O_5 furnished the bis enone (**192**). Reduction of the bis enone **192** with H_2 on Pd/C furnished the all cis dione diester **193**, since the delivery of hydrogen occured from the less hindered convex face of the bis enone **192**. The reduction of the ketoester **193** with NaCNBH$_4$ gave the dilactone **194**[127] which was converted into chloro ester **195**. The chloroester (**195**) underwent monoalkylation under the influence of Lithium in liquid ammonia to give **196**.[128] Photocyclization of **196** followed by reduction

of the ester group gave the aldehyde (197), which after
sequential photocyclization, Birch reduction, acid hydrolysis
and PCC oxidation furnished the keto aldehyde (198). Irradia-
tion of 198 induced the ring closure and decarbonylation
which gave the seco⊃dodecahedrane (199). The cast bond
was made through dehydrogenation of 199 which finally furnished
the dodecahedrane (10) itself (Scheme-I.49). This methodology
employed above was first developed for the synthesis of
dimethyl dodecahedrane (200) from the dilactone (196).[129]

192 → (Pd-H₂) → **193** → (NaCNBH₄) → **194**

194 → (MeOH HCl) → **195**

195 → (Reductive cleavage of Central bond, ⟨O⟩-OCH2Cl, Li NH₃) → **196**

196 → **197**

197 → **198**

198 → **199** Secododecahedrane

199 → **10** Dodecahedrane

200
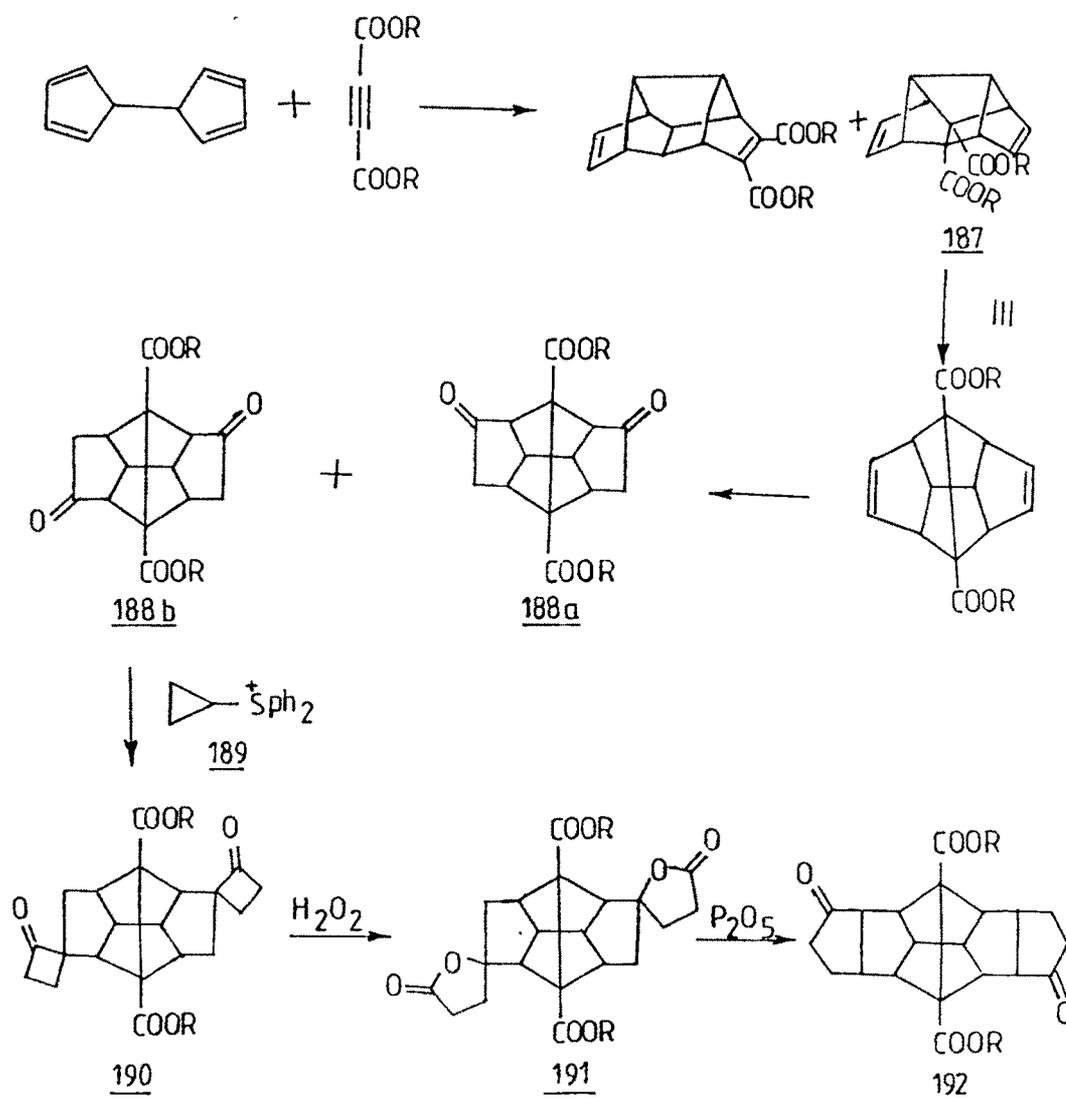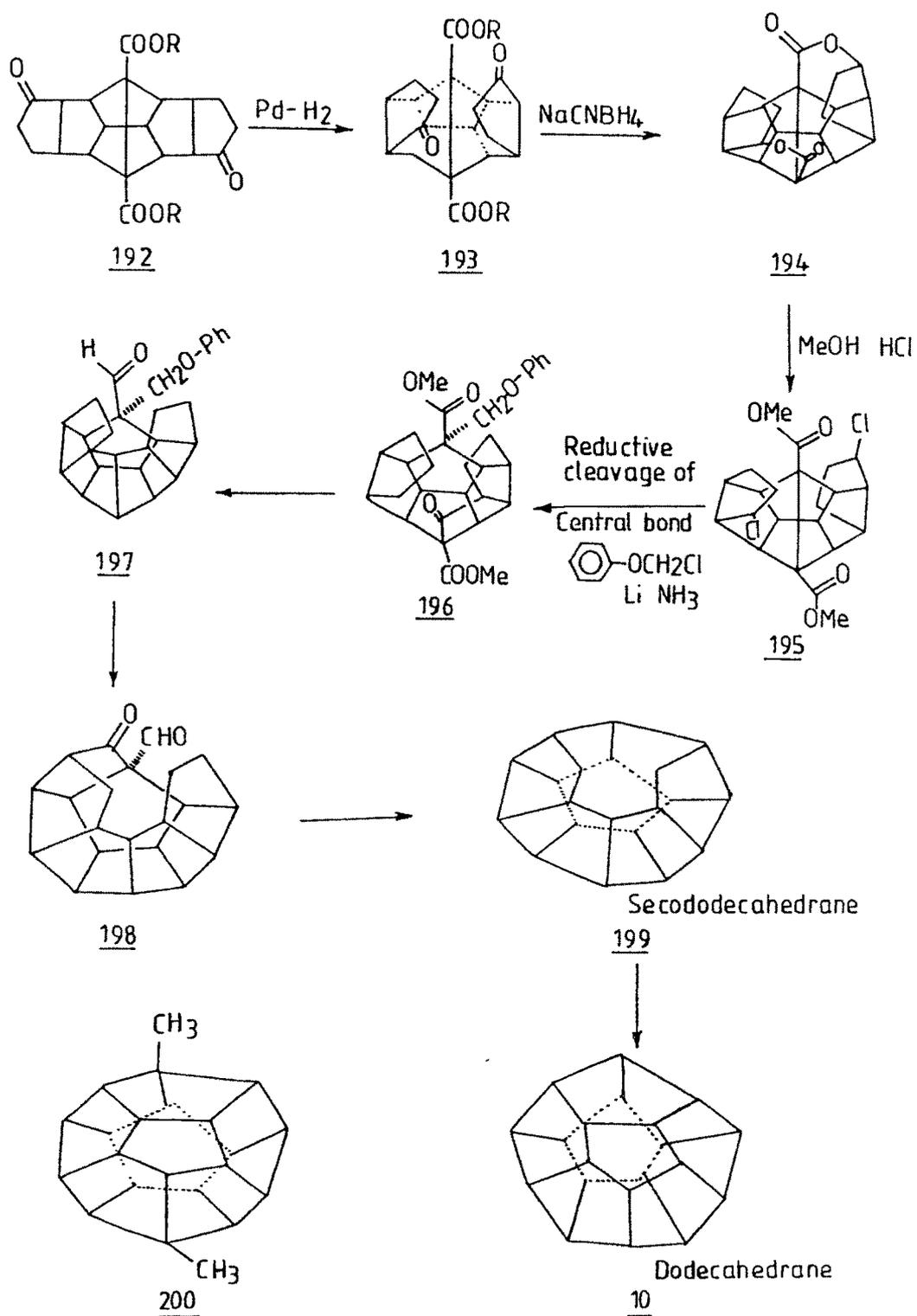
SCHEME - I.49

Based on Schleyer's isomerization route,[130] several attempts have been made to obtain dodecahedrane and its dimethyl analogue. This thrust was supported by molecular mechanics calculations which showed dodecahedrane to be the $C_{20}H_{20}$ stabilomer.[131]

However, it was quite diappointing to note that the isomerisation of 201[132] did not yield any dodecahedrane despite the potential release of 178 Kcal/mole of strain energy. Similarly, attempts to isomerise $C_{22}H_{24}$ hydrocarbon (202-205)[133] have also come to a naught. (Scheme-I.50).
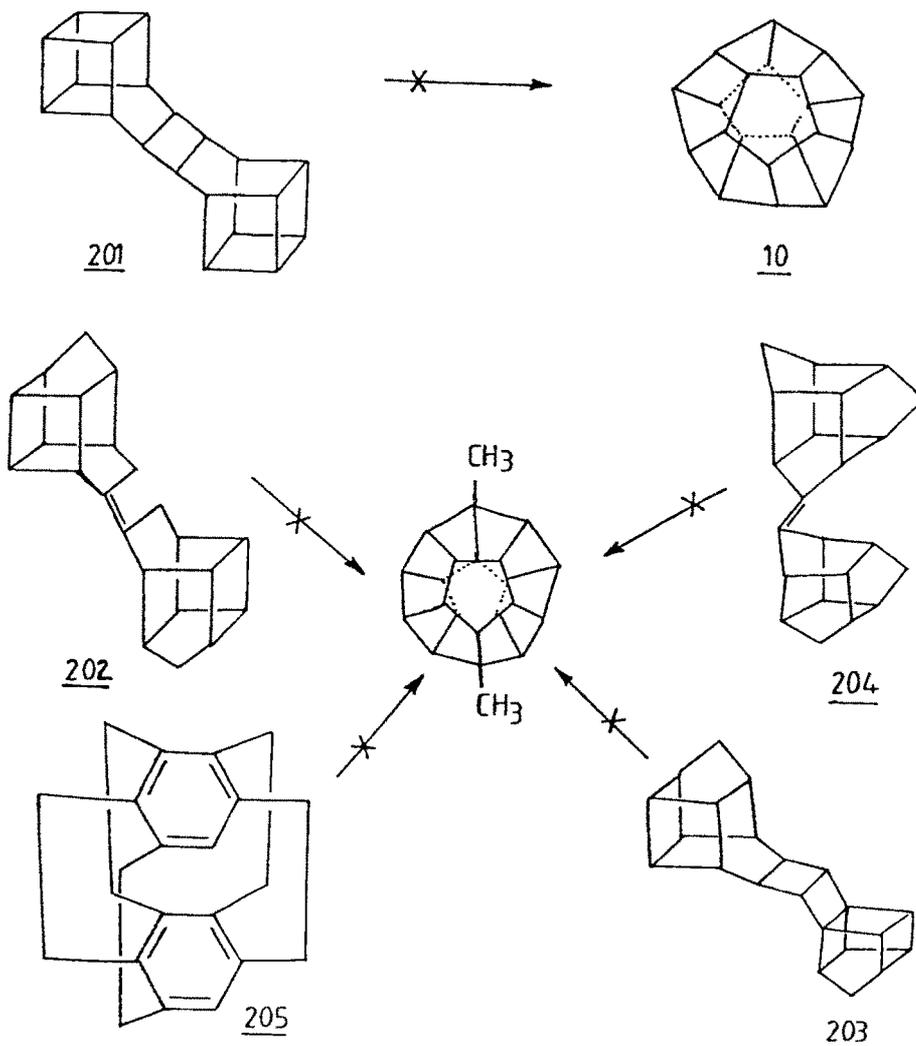
SCHEME - I.50

However, Prinzbach[134] has been successful in isomerising the pagadane (212) in vapour phase in a flow apparatus over various catalysts at 250-450° to a mixture of compounds containing dodecahedrane upto 0.1% which was later optimized to 8%.[135] (Scheme-I.51)

206   207   208

C_6H_6 , Δ

KOH, MeOH
$C u_2 O$,
Quinolene

211   210   209

$h \nu$
THF H_2O

1. LTA , I_2 , CCl_4
2. Na ,K , tBuOH
    THF

212   10

Catalyst
Δ
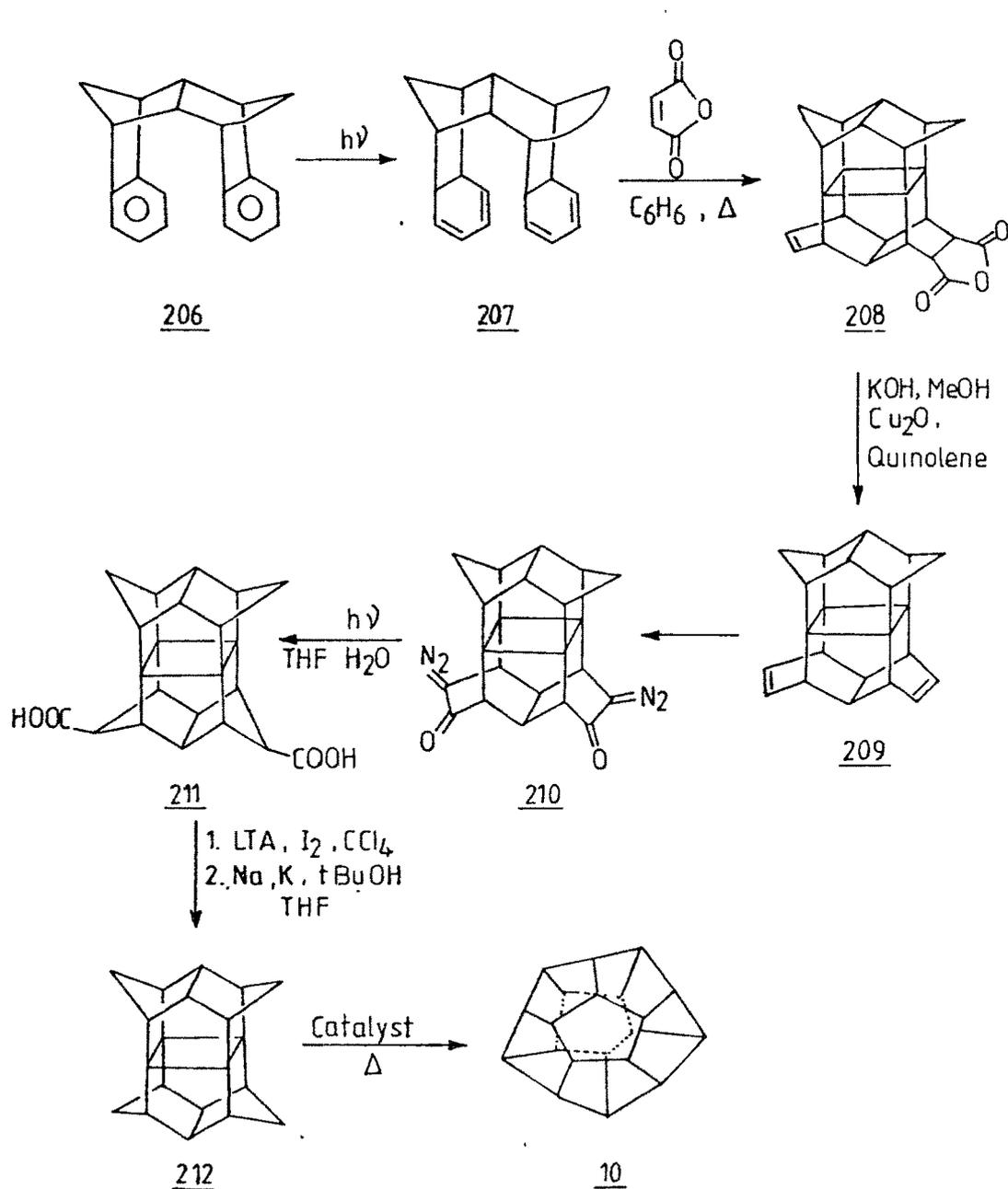
SCHEME - I.51

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