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A General Methodology for the Synthesis of Linearly Fused Polyquinanes

Y.V. Suryanarayana Murthy and C. Narayana Pillai*

Department of Chemistry, Indian Institute of Technology
Madras 600 036, India

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Key words : Polyquinanes; 1,4-dibromomagnesiobutane for spiroannulation; spirolactones to polyquinanes; C-17 pentaquinane; polycyclopentanoids

Abstract : A methodology involving a combination of spiro-annulation by the action of 1,4-dibromomagnesiobutane on succinic acid derivatives followed by cyclization of the spirolactone using P_2O_5-CH_3SO_3H reagent has been developed for the synthesis of polyquinanes. By using bicyclo[2.2.1] heptane carboxylic acids as the precursors for the spirolactones, a triquinane **[8]** and a pentaquinane, **[19]**, have been synthesized.

Polyquinanes comprise a class of fused ring compounds containing only cyclopentane rings. Various members of this family have been the targets of synthetic attempts in the recent past and many original methods for the construction of single or polycyclic five membered rings have been developed[1-3]. However, many of these approaches have been target oriented and lack generality. Thus there is a need for the development of more general and versatile methods to gain access to a range of polyquinanes. Hence studies were initiated in this direction. The objective of the current investigations has been to devise a convenient and stereocontrolled general route to a range of linearly fused polyquinane systems by using bridged bicycles as synthons and by employing di(halomagnesio)alkanes ("di-Griganards") as key reagents[4]. This strategy is based on the fact that the reaction of di(bromomagnesio)alkanes with the carbonyl of carboxylic acid derivatives occurs by the addition of the two nucleophilic centres of the reagent on the same carbonyl[5,6]. This can be made use of in the construction of one of the cyclopentane rings. The basic norbornane skeleton is another important source for one more cyclopentane ring whose formation involves the oxidative cleavage of the carbocycle. The stereochemical rigidity and the structural flexibility of these bicyclo[2.2.1]heptane systems were exploited during the present transformations in realising the targets.

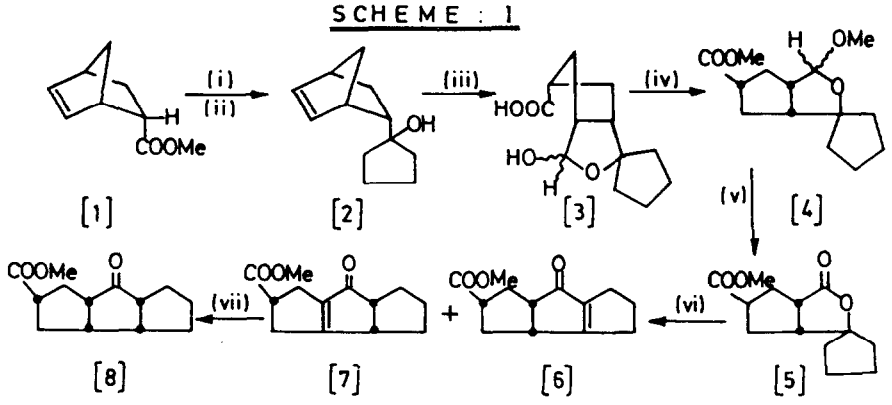
Among all the polyquinanes, the C_{11}-triquinanes have received relatively greater attention due to the fact that these constitute the basic carbon skeleton in many naturally occuring sesquiterpenoids and also because of their potentiality in functioning as the basic building block for dodecahedrane and its precursors. A simple and efficient synthetic methodology was developed starting from the endo Diels-Alder adduct [1] of cyclopentadiene and methyl acrylate. It was reported in our earlier

communication that about 96% endo selectivity can be obtained by employing $ZnBr_2$, a much milder Lewis acid when compared to BF_3-etherate as catalyst[4]. In subsequent studies absolute endo selectivity was achieved for this reaction by employing the combination of Ce-Y zeolite + anhydrous $ZnBr_2$ as the catalyst[7].

The ester [1] in anhydrous THF was added at 0°C under nitrogen atmosphere to one equivalent of the freshly prepared 1,4-di(bromomagnesio)butane from the reaction of magnesium with 1,3-dibromobutane in the same solvent. Hydrolysis with saturated aqueous ammonium chloride furnished the olefinic alcohol [2] in 80% yield as a liquid. The next step is the oxidative cleavage of the double bond of the bicyclo[2.2.1]heptane skeleton. The most versatile reagent that can be employed for this purpose is $KMnO_4$[8]. Phase transfer catalysis has been used to advantage in the permanganate oxidations of alcohols. The advantages are in terms of high yields and selectivity[9,10]. In the present case the PTC employed was tetrabutylammonium bromide. The oxidation was carried out in CH_2Cl_2 in the presence of TBAB with aqueous $KMnO_4$ solution at 0°C. In this reaction one of the carbon atoms has been oxidized to the carboxylic acid whereas the other to aldehyde which formed the five membered hemiacetal without further oxidation. In the ^1H NMR spectrum the characteristic hemiacetal proton adjacent to an oxygen and a hydroxyl appeared as a doublet at δ 5.5. Thus the crucial intramolecular cyclization to five-membered hemiacetal [3] was achieved. At this stage, the crude compound [3] was dissolved in dry methanol and was refluxed in the presence of a few drops of conc.H_2SO_4. This resulted in the formation of the ester ketal [4] as a liquid in 83% yield. In the ^1H NMR, the ketal proton appeared as a broad singlet at δ 4.7, slightly up field when compared to the hemiacetal proton of the compound [3] as expected. Also, the two observed singlets at δ 3.3 and δ 3.6 due to the ketal and ester methyl groups are in accordance with the structure. Oxidation of the above ester ketal [4] at 0°C with Jones reagent for 30 minutes furnished the spirolactone [5] in 92% yield[11]. The disappearance of the signals due to ketal proton and methyl group in ^1H NMR spectrum established the oxidation. The spirolactone [5] can be seen as an immediate precursor for the triquinane system [6] with the required number of carbon atoms, and one can expect [5] to undergo cyclization to [6] in the presence of strong acids[12-14]. Stirring of the compound [5] in a solution of 5% by weight of P_2O_5 in excess (40 moles per mole of the lactone) methanesulfonic acid furnished a liquid product[15]. The TLC and HPLC analysis of the product showed it to be a mixture of two compounds. The premature work up of the reaction showed the presence of only the major component [6] and the formation of the minor product [7] was observed after prolonged reaction times. The spectral characterization of the products suggested the minor component to be an isomer of the major triquinane derivative [6], one possibility being the double bond positional isomer [7] and the other the C_5-epimer. The two compounds were separated over a column of silica gel by very

careful elution with a 1:1 mixture of benzene-hexane. As the 10% Pd/C-H_2 reduction of the mixture [6+7] furnished a single product, the isomer formation was assumed to be due to the double bond shift and the structure [7] was assigned. The ir spectrum of the reduced compound [8] showed a strong absorption of 1734 cm^{-1} indicating the carbonyl group. The absorptions at 1680 cm^{-1} and 1620 cm^{-1} of the enone moiety were absent thereby establishing the hydrogenation of the double bond. The 13 line ^{13}C NMR spectrum of the compound [8] was totally in support of the formation of only one product during the hydrogenation. The complete disappearance of the olefinic carbons of the enone firmly established the reduction (Scheme I).

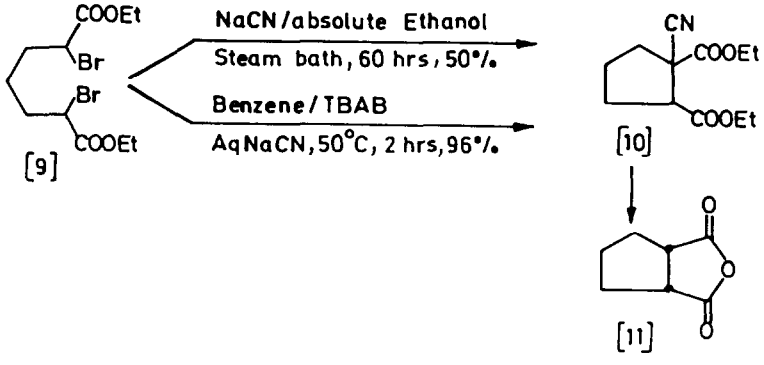
SCHEME : I



(i) $BrMg(CH_2)_4MgBr$, RT, 12 hrs (ii) Aq NH_4Cl (iii) Aq $KMnO_4$/TBAB, CH_2Cl_2, 0°C, 3 hrs. (iv) CH_3OH/H^+, Reflux (v) Jones reagent, 0°C, 30 min (vi) CH_3SO_3H/P_2O_5, 24 hrs, RT (vii) Pd-C/H_2, Ethyl acetate.

When the transformation of [5] to [6] was tried with polyphosphoric acid, even after several hours of heating, it was found that the reaction was incomplete and much of the unreacted lactone was left behind.

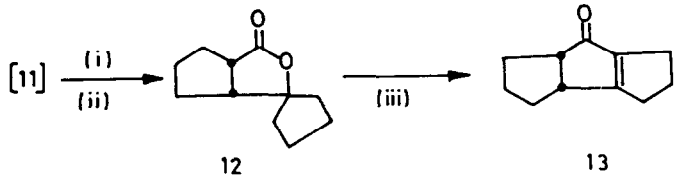
SCHEME : II



As the spirolactone [5] was found to be an effective precursor for the triquinane [6] it was expected that the corresponding unsubstituted spirolactone [12] could be obtained directly from cis-1, 2-cyclopentanedicarboxylic anhydride [11] by utilizing Canonne's procedure and then taken over to [13][6,16]. With this reasoning in mind, the synthesis of anhydride [11] was carried out starting from pimelic acid. The procedure reported by Fuson et al. was followed after effecting a few modifications to improve the yield[17] (Scheme II).

Fuson has effected the crucial ring closure of the α,α'-dibromopimelate [9] to the cyanocyclopentane derivative by refluxing [10] with powdered NaCN in absolute ethanol over a steam bath for 60 hours. Problems were faced with yields and the work-up of the reaction. Due to the low solubility of the NaCN in ethanol, distillation of the product was found difficult. Ring closure was tried under phase transfer catalysis conditions. The reaction was carried out in benzene in the presence of tetrabutylammonium bromide with aqueous NaCN at 50°C with vigorous stirring to furnish the ethyl 1-cyano-1,2-cyclopentanedicarboxylate [10]. In this modified PTC procedure, the reaction time was reduced substantially from 60 h to 2 h and 95% yield was obtained. Just by separating out the benzene layer the product could be obtained, the excess NaCN remaining in the aqueous layer. Compound [10] was transformed to the cis-1,2-cyclopentanedicarboxylic anhydride [11] as reported earlier[17]. Compound [11] on reaction with one equivalent of 1,4-di(bromagnesio)butane followed by work up with dil. HCl furnished the spirolactone [12] in 80% yield as a liquid. The spirolactone [12] was then on treatment with 5% (w/w) solution of P_2O_5 in 40-fold molar excess of CH_3SO_3H smoothly converted to triquinane [13] in 90% yield. Strong absorptions at 1686 cm^{-1} and 1628 cm^{-1} due to α,ß-unsaturated carbonyl moiety confirmed the transformation. The 11 line ^{13}C NMR spectrum contained a singlet at 206.66 due to the carbonyl carbon and two more singlets at 188.99 and 149.31 due to the two characteristic olefinic carbons of enone further established the formation of [13] (Scheme III).

SCHEME : III

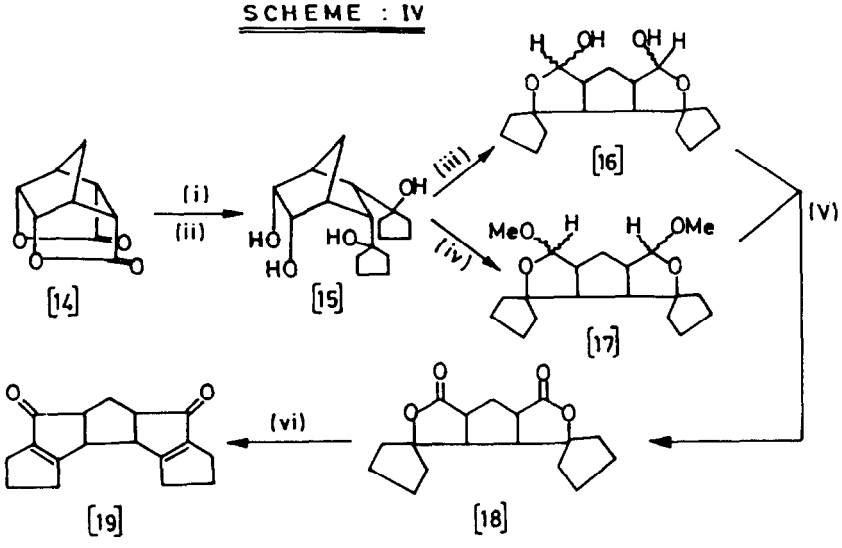


(i) $BrMg(CH_2)_4MgBr$, THF, 10 hrs. (ii) Dil. Hcl (iii) P_2O_5/CH_3SO_3H, 24 hrs., RT

The chemistry of the higher polyquinanes has developed particularly rapidly in the last two decades[1-3]. The more complex members of this class are those which are endowed with all cis-stereochemistry. Attempts to synthesize the $C_{20}H_{20}$ dodecahdrane, have resulted in a variety of

newer ways of assembling mutually cis-fused cyclopentane rings, resulting in the synthesis of useful intermediates such as the C_{10}-triaquinacene, C_{15}-peristylane[21], the C_{16}-hexaquinane[22], C_{17}-heptaquinane[23] and C_{20}-hexaquinane[24]. Of all the polyquinanes, relatively less is known about pentaquinanes. The only report that is available is of Eaton who has synthesised the C_{14}-pentaquinane system en route to peristylane[21]. With this background, one of the C_{17}-pentaquinane systems **[19]**, which is hitherto unknown was chosen as the target molecule for further establishing the generality of the methodology developed in the present study. A simple four step synthesis of the C_{17}-pentaquinane derivative **[19]** starting from the dilactone **[14]** was developed. The complete transformations effected during the synthesis are shown in Scheme IV.

SCHEME : IV



(i) $BrMg(CH_2)_4MgBr$, THF, TR, 6h. (ii) Aq. NH_4Cl.

(iii) H_5IO_6/CH_2Cl_2, RT, 6h. (iv) H_5IO_6/MeOH, RT, 6h.

(v) Jones reagent, 0°C, 30 min.

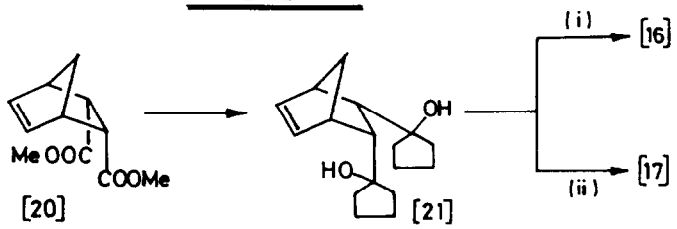
(vi) 5% P_2O_5/CH_3SO_3H, RT, 24 h.

Surprisingly, very little chemistry of the dilactone [14] has been reported although it was first synthesized almost 50 years ago. The crux of the present synthetic scheme in utilizing this dilactone [14] as the precursor is to open up both the lactone rings by reacting with the di-Grignard reagent to

get the expected tetrol [15]. One immediate problem that crops up is the reactivity of the lactone rings towards normal ring opening reactions. It was understood from the earlier studies in this laboratory that one of the lactone rings is totally inert towards usual nucleophiles[25]. The second serious problem is the likelihood of interference by transannular cyclizations which is the case when the dilactone [14] was reacted with normal Grignard reagents[26]. With all these apprehensions in mind the reaction of the compound [14] with di(bromomagnesio)butane was carried out. However, no complications due to transannular cyclizations were observed and the tetrol [15] was obtained as the sole product in 80% yield. The 9 line ^{13}C NMR spectrum of the compound was indicative of the symmetry of the structure. The four methylene carbons and the tertiary carbon of the cyclopentane ring adjacent to hydroxyl were observed as four triplets and a singlet at δ 42.8, 42.7, 25.9, 24.2 and 82.2 respectively. The magnetic nonequivalence of the methylenes suggests that the rotation around the single bond connecting the cyclopentane ring to the bicyclic system is restricted. The C_2, C_3 vicinal hydroxyl groups now provide the site for the cleavage of the parent bicyclo[2.2.1]heptane system. Periodic acid was preferred over sodium metaperiodate for the oxidation as it can easily go into organic solvent[27]. When the oxidation was carried out in CH_2Cl_2, it afforded the dispirohemiacetal [16] in 90% yield as a thick viscous mass. The characteristic hemiacetal protons were observed as a clear doublet at δ 5.2. However, when the oxidative cleavage was carried out in methanol, it furnished the corresponding methyl ketal[17] in 83% yield as a thick liquid. In ^1H NMR the ketal methyl protons were observed as a broad singlet at δ 4.6 and methoxy protons appeared as a singlet at δ 3.2. Hence, the crucial dispiroannulation was successfully achieved during this oxidation in a single step via the carbon-carbon bond cleavage followed by intramolecular hemiacetal ring formation. Both the crude spirohemiacetal [16] and the dispiroketal [17] without further purification, on oxidation with Jones reagent at 0°C afforded the dispirodilactone [18] as a white solid in 86% yield. Oxidation of the dispiroketal [17] to the dispirodilactone [18] took place probably through the hemiacetal intermediate[11]. The 9 line ^{13}C NMR spectrum was in accordance with the symmetric structure, the spiro carbons adjacent to the oxygen appearing as a singlet at 94.4. In the next step, compound [18] was converted to the all-cis pentaquinane by the treatment with P_2O_5/CH_3SO_3H. After the purification over silica gel by eluting with 1:1 benzene-hexane mixture, [19] was obtained as a viscous liquid in 40% yield. The ir spectrum of the compound [19] showed characteristic absorptions at 1680 cm^{-1} and 1620 cm^{-1} corresponding to α,β-unsaturated carbonyl moiety. The UV in methanol had a maximum at 249 nm and a shoulder at 300 nm. This was in accordance with the presence of the tetrasubstituted cyclopentenone moiety. The 9 line ^{13}C NMR spectrum was indicative of the symmetric nature of the molecule. The ketone carbons were observed as a singlet at 204.13. The characteristic enone methine carbons were observed as two doublets at 183.48 and 149.22.

The spirodilactone [18] was also synthesized by an alternate route, starting from bicyclo [2.2.1] hept-5-en-2, 3-dicarboxylate [20] (Scheme V).

SCHEME : V



(i) Aq $KMnO_4/CH_2Cl_2$, TBAB, 0°C, 2 hrs.

(ii) Aq $KMnO_4$, 0°C, 3 hrs.

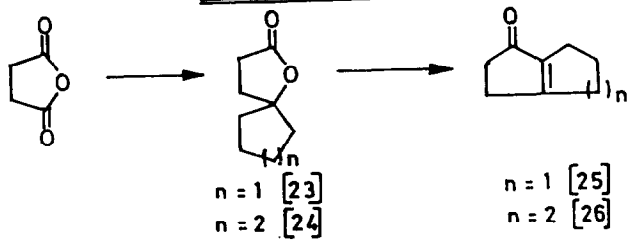
The diester [20] in dry THF was reacted with two moles of the freshly prepared 1,4-di(bromagnesio)butane to obtain the ene diol[21] as the sole product. Here again no transannular cyclization products were isolated. The 9 line ^{13}C NMR spectrum was in accordance with the structure of the compound. The olefinic carbons were observed as a doublet as 135.00 and the quaternary carbons adjacent to hydroxyls appeared as singlet at 83.17. In the compound [21], the norbornene skeletal double bond is the site for oxidative cleavage. The reagent used here was $KMnO_4$ as in the case of the compound [2]. The oxidative cleavage was effected under phase transfer conditions. To the dichloromethane solution of the diol[21], containing tetrabutylammonium bromide, a freshly prepared aqueous solution of $KMnO_4$ was added slowly. After the usual work up compound [16] was obtained in 70% yield. Interestingly, under PTC conditions the oxidation of both the carbons stopped at the aldehyde stage. When the oxidation was carried out in the absence of PTC, the oxidation was complete and the compound [18] was obtained directly in 35% yield [28]. It can be noticed that in the absence of PTC both the carbon atoms were oxidized to carboxylic acids. It was found that the yield of the dispirodilactone [18] was very poor and the reaction was not clean as several side products were observed.

By using the present procedure various synthetically useful bicyclic and tricyclic enones were synthesized. There are several reported syntheses of natural products which utilize diquinanes as building blocks. For example starting from the enone [25], racmodhephene a sesquiterpene with a propellane C skeleton and its epimer have been synthesized[29]. Realizing the importance of this molecule in synthesis, the present procedure was applied to the preparation of [25] (Scheme VI).

The spirolactone [23] was prepared according to Canonne's procedure[6,16]. The spirolactone [23] was then dissolved in exess of freshly prepared 5% P_2O_5/CH_3SO_3H and stirred for 12 hours. Usual work up afforded the target enone [25] in excellent yield (95%). The corresponding

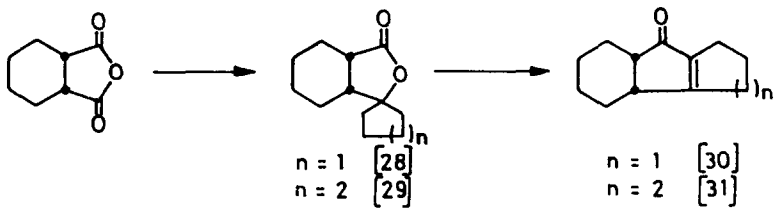
tetrahydroindenone [26] is also a potential starting material for natural product synthesis. The present annulation method was used for the preparation of the bicyclic enone [26]. The spirolactone [24] was prepared according to Cannone's procedure from succinic anhydride and 1,5-di(bromomagnesio)pentane[6,16]. This on treatment with P_2O_5/CH_3SO_3H furnished the enone in 90 - 95% yield.

SCHEME : VI



Spirolactones prepared from cis-1,2-cyclohexanedicarboxylic anhydride were also smoothly converted to the tricyclic enones, which were required for another synthetic project, thereby establishing easy access to these enones. Spirolactones [28 and 29] were prepared according to Canonne's procedure[6,16] and were treated with excess of 5% P_2O_5/CH_3SO_3H mixture. The tricyclic enones [30 and 31] were obtained in over 90% yield after the usual work-up (Scheme VII).

SCHEME : VII



Thus the present studies constitute a short, stereocontrolled and general methodology for the construction of the linearly fused polyquinanes and offer a lot of scope for exploitations in natural product chemistry.

EXPERIMENTAL

General procedure for the preparation of di(bromomagnesio)alkanes

In a typical experiment, into a three-necked 250 ml flask provided with mechanical stirrer, 728 mg (20 mmols) of magnesium and 20 ml of dry THF were introduced in an atmosphere of dry nitrogen. Then a solution of 10 mmoles of dibromide in 60 ml of dry THF was added dropwise at a rate just

sufficient to keep the reaction mixture boiling. The contents of the flask were further refluxed for an hour till all the magnesium reacted. After cooling the reaction flask to 0°C, the organodimagnesium reagent was ready for use.

Endo-2-(1-hydroxycyclopentyl)bicyclo[2.2.1]hept-5-ene[2]

1,4-Di(bromomagnesio)butane was prepared according to the above standard procedure from 728 mg of magnesium and 2.4 g of 1,4-dibromobutane in dry THF under nitrogen atmosphere. The reagent was then cooled to 0°C and a solution of endo-ester **[1]** (1.52) in 20 ml of dry THF was allowed to flow in dropwise with stirring. The stirring was continued for 6 hours at room temperature and the reaction mixture was treated with a saturated aqueous solution of NH_4Cl at 0°C. The resulting mixture was extracted with ether (3 x 50 ml) and the extracts were dried over anhydrous sodium sulphate. Evaporation of the solvent and distillation of the resultant liquid under reduced pressure in a bulb to bulb distillation apparatus furnished the alcohol **[2]** as a colourless liquid. Yield : 80%. i.r (CCl_4):3550-3500 and 2950 cm^{-1}: 1_H NMR (200 MHz, $CDCl_3$/TMS): δ 6.2 (m, 1H), 6.0(m,1H), 2.9 (bs, 1H), 2.8 (bs,1H), 2.3(m,1H), 3.5(broad hump, exchanges with D_2O, 1H) and 1.2-2.0 (series of multiples, 12H); ^{13}C NMR (400 MHz, $CDCl_3$/TMS): 138.14(d), 132.39(d), 83.39(s), 51.13(d), 48.16(d), 45.05(d), 42.64(t), 40.36(t), 39.98(t), 27.95(t), 23.82(t) and 23.56(t); Mass spectrum (m/z); $M^{+\cdot}$ 178(8), 160(40), 111(20), 95(45), 83(30) and 66(100); High resolution mass: Calculated for $C_{12}H_{18}0$: 178.13577, Observed: 178.13392.

3-Oxa-4,4-tetramethylene-7-carboxybicyclo[3.3.0]octan-2-ol [3]

To a stirred solution of the endo alcohol **[2]** (1.69 g, 9 mmols) and tetrabutylammonium bromide (2.5g) in dichloromethane (60 ml), was added dropwise the oxidant solution freshly prepared with $KMnO_4$ (2.144 g, 13 mmols) in water at such a rate that the temperature was maintained at 0-30°C under cooling in an ice bath. After the addition was complete, stirring was continued for an additional 2 hours. The heterogeneous dark brown mixture was then treated with solid sodium metabisulphite till the reaction mixture became colourless. Later the contents were acidified with dil. HCl. The reaction mixture was then diluted with 50 ml of CH_2Cl_2 and the organic layer was separated, washed with brine solution (2 x 20 ml) and finally dried over sodium sulphate. Evaporation of the solvent furnished the lactolcarboxylic acid **[3]** as a thick mass. Yield: 72%; i.r. ($CHCl_3$): 3600 - 3200, 2900, 1725 and 1450 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$/TMS); δ 5.5 (d,1H) and 1.03-3.5 (series of multiplets, 17H); Mass spectrum (m/z): $M^{+\cdot}$ 226 (7), 208 (20), 135(50), 91(40) and 55(100).

2-Methoxy-3-oxa-4,4-tetramethylene-7-carbomethoxybicyclo [3.3.0] octane [4]

Crude compound **[3]** was dissolved in 40 ml of dry methanol and the solution was cooled to 0°C. Then a few drops of conc. H_2So_4 were added and the mixture was refluxed over a steam-bath for 4 hours. The excess methanol was distilled off and the contents were diluted with 150 ml of cold

water. Then the mixture was extracted with ether (3 x 40 ml). The ether layer was washed with saturated $NaHCO_3$ solution (2 x 20 ml), saturated brine solution (2 x 20 ml) and dried over anhydrous sodium sulphate. The solvent ether was removed in a rotary evaporator and the resultant liquid was purified by eluting through a silica gel column with 3:1 benzene-hexane mixture to furnish the esterketal [4]. yield: 83%; i.r. (CCL_4): 2900, 1715, 1450, 1150 and 1100 cm^{-1}; ^1H NMR(60 MHz, CCl_4/TMS): δ 4.7(s,1H), 3.6(s,3H), 3.3(s,3H), 1.0 - 3.0(series of multiplets, 15H); Mass spectrum (m/z): $M^{+\cdot}$ 254(6), 225(40), 212(30), 194(30), 169(40), 149(40), 135(80), 91(60) and 67(100).

3-Oxa-4,4-tetramethylene-7-carbomethoxybicyclo[3.3.0]octen-2-one [5]

The esterketal [4] (2.5 g) was dissolved in 35 ml of acetone and the oxidation with Jones reagent was carried out. Purification of the product by passing through a short column of silica gel and elution with 1:1 benzene-hexane mixture furnished a white solid which was later recrystallized in ether-CH_2Cl_2 mixture to get the spirolactone [5]. Yield:78%; m.p.56 °C.i.r. (KBr):3000, 1760 and 1720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$/TMS): δ 3.8(s, 3H), 3.1(m, 1H), 2.7(m,1H),2.8(m.1H) and 1.4-2.4(series of m, 12H); ^{13}C NMR (400 MHz, $CDCl_3$/TMS): 179.27(s), 174.13(s), 94.75(s), 51.94(q), 49.56(d), 45.79(d), 44.94(d), 40.16(t), 34.19(t), 32.62(t), 31.41(t), 23.67(t) and 23.42(t); Mass spectrum (m/z): $M^{+\cdot}$238(15), 209(80), 196(50), 181(25), 135(50) and 67(100); High resolution mass: Calculated for $C_{13}H_{18}O_4$: 238.12051, Observed : 238.12590; Microanalytical data: calculated for $C_{13}H_{18}O_4$: C, 65.51; H, 7.61, Observed: C, 65.69: H,7.78.

10-Carbomethoxytricyclo[6.3.0.0^{3,7}]undec-$\Delta^{3,7}$-en-2-one[6]

Phosphorus pentoxide (2.5 g) was suspended in 48 g of methanesulfonic acid (freshly distilled) and the mixture was stirred at 50 °C under nitrogen until homogeneous (40 min. - 1 h). Compound [5] (1.20 g) was added and it got dissolved in about 40 minutes. The reaction mixture gradually became reddish brown and it was stirred for 24 h ours at room temperature. Then the contents were cooled to 5 °C and was added to 100 ml of ice water. The aqueous mixture was extracted with ether (3 x 60 ml) and the organic layer was washed with dil. $NaHCO_3$ solution, brine solution (2 x 25 ml) and dried over anhydrous sodium sulphate. Ether was evaporated by using a rotary evaporator and the resultant liquid was eluted over a small silica gel column with 1:1 benzene-hexane mixture to furnish the triquinane [6] as a colourless liquid. Yield. 88% i.r. (CCl_4): 2960, 1720, 1680, 1620, 1200 and 1150 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$/TMS): δ 3.7(s, 3H), 3.2(m, 2H), 2.9(m, 1H), 2.6(m,1H), 2.4(m,1H), 2.2(m,4H) and 1.9-2.1(series of multiplets, 4H); ^{13}C NMR (400 MHz, $CDCl_3$/TMS): 204.38(s), 188.41(s), 174.58(s), 148.00(s), 56.81(d), 51.76(q), 45.42(d), 42.92(d), 31.90(t), 30.99(t), 30.28(t), 27.61(t) and 24.51(t); High resolution mass: Calculated for $C_{13}H_{16}O_3$: 220.04918;Observed:220.04618.

Further elution of the column afforded the triquinane[7] as a colourless liquid.

5-Carboxytricyclo[6.3.0,$0^{3,7}$]undec- $\Delta^{3,7}$-en-2-one [7]

i.r.(CCl_4): 2970, 1730, 1668 and 1620 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$/TMS) 3.7(s, 3H), 3.3(m,1H), 3.2 (m, 1H) 2.9(m, 1H), 2.3- 2.6(series of m, 4H) and 1.8-2.1(series of m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$/TMS):200.33(s), 173.14(s), 167.33(s), 137.59(s), 51.68(q), 49.86(d), 47.56(d), 42.36(t), 42.14(t), 36.88(t), 28.36(t), 28.23(t) and 22.26(t): High resolution mass : Calculated: 220.04918; Observed. 220.04818.

Reduction of the mixture [6] and [7]

A solution of **[6]** and **[7]** (200 mg) in 20 ml of dry ethyl acetate was hydrogenated (40 psi H_2 pressure) over 10% Pd/C (10 mg) for a period of 4 hours. Pd/C was filtered off and the solvent removed to furnish **[8]** as a colourless liquid. Yield: 92%.i.r: 2995 and 1734 cm^{-1}; ^1H NMR (60 MHz, CCl_4/TMS): δ 3.62(s, 3H) and 1.63-3.15 (series of multiplets, 15H); ^{13}C NMR (400 MHz, $CDCl_3$/TMS); 221.22(s), 179.93(s), 54.34 (q), 45.56(d), 45.36(d), 42.88(d), 42.76(d), 40.18(d), 32.42(t), 29.93(t), 29.77(t), 27.88(t) and 27.55(t); Mass spectrum (m/z): $M^{+\cdot}$ 222(62), 191(30), 190(35), 162(100), 163(30), 119(70) and 67(40).

Ethyl 1-cyanocyclopentane-1, 2-dicarboxylate [10]

To the solution of the dibromoester **[9]** (15 g) in 120 ml of distilled benzene, 3 g of tetrabutylammonium bromide was added. To this vigorously stirring reaction mixture, an aqueous solution of sodium cyanide (8 g in 25 cc. of water) was added drop by drop while maintaining the emperature at 50°C. After the addition was over the stirring was continued vigorously for an additional 2 hours. Later the reaction mixture was diluted with 100 cc. of water and the organic layer was separated. Removal of the solvent benzene by rotary evaporator followed by distillation of the resultant liquid under reduced pressure furnished the cyanodiester **[10]** as a colourless liquid. Yield: 92%. i.r. (CCl_4): 2985, 2220 and 1380 cm^{-1}; ^1H NMR (60 MHz, CCl_4/TMS): δ4.01-4.5(m,4H), 3.28-3.39(m,1H), 2.05-2.35(m,6H) and 1.17-1.52(m, 6H).

3-Oxa-4,4-tetramethylenebicyclo[3.3.0]octan-2-one[12]:

1,4-Di(bromomagnesio)butane was prepared from 728 mg of magnesium and 2.4 g of 1,4-dibromobutane. Then 1.40 g of the cis-anhydride **[11]** was added dropwise to the reagent as a solution in dry THF. After stirring the reaction mixture for 10 hours, 10% dil. HCl was added and further stirred for an additional hour. Then the resulting mixture was extracted with ether (3x40 ml) and dried over anhydrous sodium sulphate. Solvent ether was evaporated and the resultant liquid was purified by passing through a small silica gel column with 1:1 benzene-hexane mixture to furnish the spirolactone **[12]** as a colourless liquid. Yield : 76%. i.r. (CCl_4) : 2970, 1760 and 1150 cm^{-1}; ^1H NMR (60 MHz, CCl_4/TMS) : 3.03(m,1H),2.5(m,1H) and 1.0-2.05(m,14H); ^{13}C NMR(400 MHz, $CDCl_3$/TMS) : 180.48(s), 95.78(s), 48.82(d), 46.89(d), 40.67(t), 34.32(t), 29.40(t), 29.30(t), 26.17(t), 23.50(t) and

23.33(t); Mass spectrum (m/z) : $M^{+\cdot}$ 180(60), 132(100) and 131(40); High resolution mass : Calculated for $C_{11}H_{16}O_2$: 180.11503, Observed : 180.11544.

Tricyclo[6.3.0^{3,7}]undec-$\Delta^{3,7}$-en-2-one [13]

The procedure described for compound **[6]** was adopted. Compound **[12]** (1.25 g) was treated with the P_2O_5/CH_3SO_3H mixture (2.5 g of P_2O_5 and 48 g of CH_3SO_3H) for 24 hours. Compound **[13]** was obtained as a colourless liquid after purification over a small silica gel column with 1:1 benzene-hexane mixture. Yield: 90%. i.r. (CCl_4) : 2900, 1686 and 1628 cm^{-1}; UV : λ_{max}^{EtOH} 244 nm (ϵ 7,600) in methanol; ^{1}H NMR (400 MHz, $CDCl_3$/TMS) : δ 3.1 - 3.2 (m,2H), 2.3(m,1H), 2.5(m,3H), 1.9(m,1H), 1.6(m,5H) and 1.3(m,2H); ^{13}C NMR (400 MHz, $CDCl_3$/TMS) : 206.66(s), 188.99(s), 149.31(s), 57.49(d), 42.91(d), 30.34(t), 29.31(t), 27.82(t), 27.61(t), 24.56(t) and 24.27(t); Mass spectrum (m/z) : $M^{+\cdot}$ 162(70) and 134(100).

endo,endo-5,6-Bis(1-hydroxycyclopentyl)bicyclo[2,2,1]heptane-endo, endo-2,3-diol [15]

1,4-Di(bromomagnesio)butane was formed according to the standard procedure from 960 mg of magnesium and 4.23 g of 1,4-dibromobutane in 80 mg of dry THF under nitrogen atmosphere. The reagent was cooled to 0°C and the solid dilactone **[14]** (1.80 g) was added with the help of an elbow flask slowly with vigorous stirring. The reaction was continued for 6 hours at room temperature and then the reaction mixture was treated with staturated NH_4Cl solution. the contents were then extracted with dichloromethane (3x30 ml) and the organic layer was washed with brine (2x20 ml) prior to drying over anhydrous sodium sulphate. After removing the solvent in a rotary evaporator, a sticky solid was obtained. This solid on recrystallization in CH_2Cl_2-ether mixture furnished the tetrol **[15]**. Yield : 75%; m.p. : 172°C. i.r. (KBr) : 3500 - 3200, 2965 and 1450 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$/TMS) : δ6.65 (broad signal, exchanged with D_2O), 3.95(bs,2H), 2.71(bs,2H), 2.35(bs,2H), 1.27-2.11(series of m, 18H); ^{13}C NMR (200 MHz, $CDCl_3$/TMS) : 81.55(s), 69.99(d), 52.91(d), 47.12(d), 42.17(t), 42.12(t), 32.62(t), 25.30(t) and 23.61(t); Mass spectrum (m/z) $M^{+\cdot}$ 296(6), 278(8), 246(55), 181(40), 105(78), 92(100), 77(95) and 65(80) : Microanalytical data : Calculated for $C_{17}H_{28}O_4$: C, 68.87; H, 9.5, Observed : C, 69.08; H, 9.71.

5,10-Dioxa-6,6-tetramethylene-9.9-tetramethylenetricyclo[6.3.0.0^{3,7}]-undecane-4,11-diol [16]

To a solution of tetrol **[15]** (2.96 g) in 40 ml of dichloromethane was added 2.28 g of periodic acid. The reaction mixture was stirred at room temperature for 4 hours and was poured into water. The CH_2Cl_2 layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2x40 ml). Combined organic layers were then washed with saturated brine solution (2x30 ml) prior to drying over anhydrous sodium sulphate. Evaporation of the solvent furnished the dispirohemiacetal **[16]** as a thick mass. Yield : 74% i.r. (neat) : 3500-3200, 2900, 1440 and 1250 cm^{-1}; i.r. ($CHCl_3$) : 3500 - 3200, 2900 and 1710 cm^{-1} (weak absorption); ^{1}H NMR (60 MHz, $CDCl_3$/TMS) : δ5.2(d,2H), 4.0 (broad signal,

exchanged with D_2O), 2.88(m,2H), 2.26(m, 2H) and 1.24-1.78(m,18H); Mass spectrum (m/z) : $M^{+\cdot}$ 294(2), 276(10), 248(25), 219(40), 206(40), 163(25) and 55(100).

4,11-Dimethoxy-5,10-dioxa-6,6-tetramethylene-9,9-tetramethylenetricyclo[6.3.0.$0^{3,7}$] undecane [17]

The oxidation was carried out as in the above case by replacing CH_2Cl_2 with dry methanol. Tetrol **[15]** (2.96 g) was dissolved in 40 ml of methanol and then 2.28 g of periodic acid was added. After the reaction, excess methanol was distilled out by using rotary evaporator under reduced pressure and then the contents were diluted with 50 ml of H_2O. Then the contents were extracted with CH_2Cl_2 and the organic layer was dried over anhydrous Na_2SO_4. Evaporation of the solvent furnished the ketal **[17]** as a viscous liquid. Yield : 72%. i.r.(CCl_4) : 2965, 1550, 1450, 1250, 1110 and 1050 cm^{-1}; ^1H NMR (60 MHz, CCl_4/TMS) : δ4.6(s,2H), 3.2(s,6H) and 1.2-2.8 (series of m,22H); Mass spectrum (m/z) : $M^{+\cdot}$322(10), 307(8), 291(20), 290(30), 262(80), 238(100), 229(60), 174(58), 91(78) and 67(70).

Oxidation of [16] or [17] to 5,10-dioxa-6,6-tetramethylene-9,9-tetra-methylene tricyclo[6.3.0.$0^{3,7}$]undecane-4,11-dione [18]

The procedure described for the compound **[4]** was followed. 1.5 g of the hemiacetal **[16]** or ketal **[17]** was dissolved in 25 ml of acetone. After the oxidation, dichloromethane was used for the extraction of the product. The product was purified by passing through a small column of silica gel with 1:1 benzene-hexane followed by recrystallization in CH_2Cl_2 - ether mixture. Yield : 78% m.p. 156°C; i.r. (KBr) : 2980, 1760, 1200, 1170 and 980 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$/TMS) : δ 3.2(m, 2H), 2.6(m,1H), 2.2(m,1H), and 1.6-2.0(series of m, 18H); ^{13}C NMR (400 MHz, $CDCl_3$/TMS) : 176.26(s), 94.40(s), 52.49(d)), 48.17(d), 41.82(t), 34.88(t), 29.10(t), 24.16(t) and 22.22(t); Mass spectrum (m/z) : $M^{+\cdot}$ 290(70), 272(80), 244(60), 233(55), 178(78), 150(75), 122(95) and 66(100); Microanalytical data : Calculated for $C_{17}H_{22}O_4$: C, 70.30, H, 7.64 Observed : C, 70.12; H, 7.41.

Pentacyclo[9.6.0.$0^{3,10}$.$0^{5,9}$,$0^{12,16}$]heptadeca-$\Delta^{5,9}$,$\Delta^{12,16}$-diene-4,17-dione [19]

The procedure was the same as was used for compound **[5]**. The dispirodilactone **[18]** (1.5 g) was dissolved in freshly prepared P_2O_5/CH_3SO_3H (3 g of P_2O_5 and 57 g of CH_3SO_3H) and stirred for 24 hours. After the work-up with water and extraction with CH_2Cl_2, a highly coloured mass was obtained. The brown mass was purified on a column of silica gel. Careful elution with 1:1 benzene-hexane furnished the pentaquinane**[19]** as a colourless viscous liquid. Yield : 35%. i.r. ($CHCl_3$) : 2985, 1680, 1620, 1380 and 1170 cm^{-1}; UV : λ_{max} 249 nm and a shoulder at 300 nm in methanol; ^1H NMR (400 MHz, $CDCl_3$/TMS) : δ3.4(m,2H), 3.1(m, 2H) and 2.2-2.6(series of m, 14H), ^{13}C NMR (400 MHz, $CDCl_3$/TMS) : 204.12(s), 183.48(s), 149.22(s), 62.62(d), 46.06(d), 32.24(t), 27.62(t), 26.18(t) and 24.42(t); Mass spectrum (m/z) : $M^{+\cdot}$ 254(50), 226(40), 225(25), 198(30), 160(35), 149(40), 91(47) and 57(100). High resolution mass : Calculated for $C_{17}H_{18}O_2$: 254.13068, Observed : 254.13047.

endo,endo-5,6-di(1-hydroxycyclopentyl)bicyclo[2.2.1]hept-2-ene [21]

1,4-Di(bromomagnesio)butane was prepared according to the standard procedure from 960 mg of magnesium and 4.32 g of 1,4-dibromobutane. To this reagent, diester **[20]** (2.10 g) was added drop by drop as a solution in anhydrous THF at 0°C and the reaction mixture was stirred for 6 hours. After work-up as in the case of the compound **[15]** **diol [21]** was obtained as a colourless solid which was recrystallied from 1:1 benzene-hexane mixture. Yield : 72% m.p. : 124°C. i.r. (KBr) : 3500-3250 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$/TMS) : δ 6.3(m,2H), 3.1(s,exchanged withD_2O, 2H), 3.0(m,2H), 2.5(m,2H), 1.5-2.1 (series of m, 16H) and 1.3(m,2H); ^{13}C NMR (200 MHz, $CDCl_3$/TMS) : 135.00(d), 83.18(s), 56.18(d), 50.12(t), 48.08(d), 43.85(t), 42.76(t), 25.18(t) and 23.65(t); Mass spectrum (m/z) : $M^{+\cdot}$ 262(10), 244(40), 215(30), 178(40), 160(100), 149(96) and 66(65); Microanalytical data : Calculated for $C_{17}H_{26}O_2$: C, 77.80; H, 9.99, Observed : C, 77.71; H, 9.72.

Oxidative cleavage of endo,endo-5,6-di(1-hydroxycyclopentyl) bicylco[2.2.1]hept-2-ene [21] to [16] under PTC conditions

The procedure followed was similar to that for compound **[2]**. The quantities of the substances used were (i) compound **[2]** (2.358 g) (ii) tetrabutylammonium bromide (2.5 g) (iii) $KMnO_4$ (2.1 g). After the reaction and usual work-up, compound **[16]** was obtained as a thick mass. Yield : 65%.

Oxidative cleavage of endo, endo-5,6-di(1-hydroxycyclopentyl)bicyclo [2.2.1]hept-2-ene [21] to [18] in the presence of PTC

Compound **[21]** (2.358 g) was dissolved in a minimum of acetone (around 6 ml) and cooled in an ice-bath. To the cold solution the freshly prepared oxidant solution (2.144 g) of $KMnO_4$ in 80 ml of H_2O was added dropwise with vigorous stirring. After the addition was complete, the contents were stirred for 3 more hours. Work-up of the reaction by following the procedure similar to that for **[2]** afforded a gummy solid, which on purification by column chromatography furnished the dispirodilactone **[18]**.

Bicyclo[4.3.0]nona-5-en-2-one [26]

The procedure adopted is similar to that for compound **[6]**. The quantities of the substances used were (i) spirolactone **[24]** (1.5 g) (ii) P_2O_5 (3 g) (iii) CH_3SO_3H (57 g). Yield : 94%. i.r. (CCl_4) : 2960, 1677, 1630, 1430 and 1380 cm^{-1}; ^1H NMR (60 MHz, CCl_4/TMS) : δ2.0-2.55(m,6H) and 1.50-1.78(m,6H).

Tricyclo[6.4.0.0^{3,7}]dodec-$\Delta^{3,7}$-en-2-one [30]

The procedure adopted was similar to that for compound **[6]**. The quantities of the substances used were (i) spirolactone **[18]** (1.5 g) (ii) P_2O_5 (3 g) and (iii) CH_3SO_3H (57 g). Product obtained was passed through a small column of silica gel by eluting with 3:2 hexane-benzene mixture to obtain the enone **[30]** as a colourless liquid. Yield : 82%. i.r. (CCl_4) : 2900, 1694 and 1620 cm^{-1}; UV : λ_{max} 241

nm (ϵ 6,800) in methanol; ^{1}H NMR (60 MHz, CCl_4/TMS) : δ 3.19 (m,1H), 2.83(m, 1H), 2.21-2.42(m,4H) and 1.24-1.82(m, 10H); ^{13}C NMR (200 MHz, $CDCl_3$/TMS) : 206.08 (s), 176.21(s), 136.77(s), 45.69(d), 41.60(d), 26.81(t), 26.32(t), 22.68(t), 22.26(t), 22.89(t), 21.02(t) and 19.95(t); Mass spectrum (m/z) : M^+ 176(65), 148(100), 147(40), 91(60) and 65(30); High resolution mass : Calculated for $C_{12}H_{16}O$: 176.1201, Observed : 176.1213.

Tricyclo[7.4.0.0^{3,8}]tridec-$\Delta^{3,8}$-en-2-one [31]

Procedure adopted was similar to that for compound **[6]**. The quantities of the substances used were (i) spirolactone **[29]** (1.5 g) (ii) P_2O_5 (3 g) and (iii) CH_3SO_3H (57 g). The product obtained was passed through a small column of silica gel by eluting with 3:2 hexane-benzene mixture to obtain the enone **[31]** as a colourless liquid. Yield : 80%. i.r. (CCl_4) : 2910, 1691 and 1636 cm^{-1}; UV : λ_{max} 238 nm (ϵ 7,800) in methanol; ^{1}H NMR (60 MHz, CCl_4/TMS] : δ 2.78(m, 1H) and 1.3-2.70(series of m,17H); Mass spectrum (m/z) : M^+ 190(60), 162(100), 161(55), 149(40), 107(30) and 79(80); High resolution mass : Calculated for $C_{13}H_{18}O$: 190.1357, Observed : 190.1348.

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