

## A NEW ROUTE TO LINEARLY FUSED POLYQUINANES

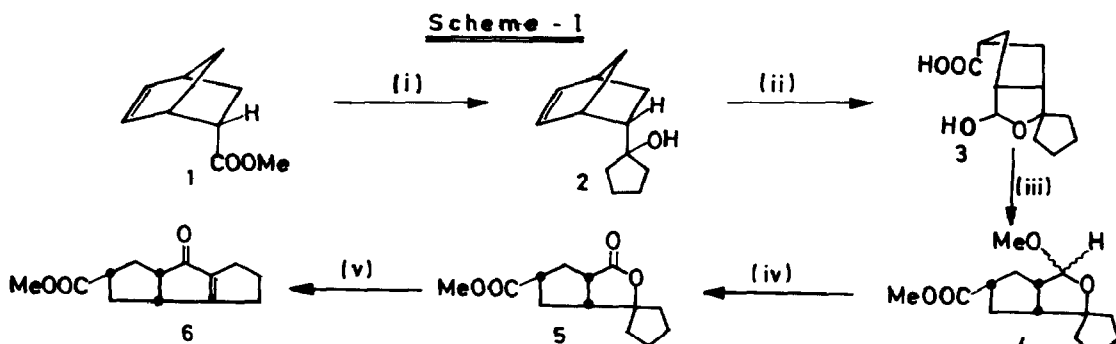
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**Abstract :** Syntheses of the triquinane [6] and the C<sub>17</sub>-pentaquinane [12] are reported starting from bicyclo-[2.2.1]-heptane derivatives utilizing di-Grignard species as key reagents.

Fused cyclopentanes form the basic carbon skeleton in many natural products and also in such synthetic challenges as peristylane and dodecahedrane<sup>1</sup>. Interest in the synthesis of such molecules has led to the development of new routes for the synthesis of a range of polyquinanes. The present communication describes a simple route for polyquinanes utilizing the reaction of the Grignard reagent from 1,4-dibromobutane with esters and lactones which is known to occur by the addition of two nucleophilic centres of the dimagnesium compound on carbonyl<sup>2</sup>. Although, one can find a few reports on reactions involving di-Grignard reagents, their synthetic utility has hardly been explored<sup>3</sup>. As part of our current studies in utilizing these reagents for the syntheses of polyquinane natural products, we have worked out a general methodology for the syntheses of linearly fused polyquinanes. Appropriate bicyclo-[2.2.1]-heptane derivatives were used as the carbonyl precursors so as to fix the stereochemistry at the cyclopentane ring junctions.

The starting material [1] was prepared by the Diels-Alder reaction between cyclopentadiene and methyl acrylate. It has been reported that the desired endo adduct [1] can be obtained by the BF<sub>3</sub> etherate catalysed Diels-Alder reaction<sup>4</sup>. The reaction in our hands gave only meager yields of the desired isomer along with a lot of the dimer and the polymer of the diene. However when the Diels-Alder reaction was carried out with zinc bromide as the catalyst, 96-97% endo selectivity was obtained at 0°C and the dimerisation and polymerisation were totally absent. The generality of this observation in the Diels-Alder reactions of cyclopentadiene is under further investigation. The endo Diels-Alder adduct [1], on reaction with 1,4-di(bromomagnesium)butane at 0°C in THF followed by stirring at room temperature for 6 hours, after work-up, afforded alcohol [2] in 80% yield.

$\text{KMnO}_4$  oxidation of [2] under phase-transfer conditions, interestingly gave the lactol-carboxylic acid [3] instead of the expected lactone-carboxylic acid<sup>5</sup>. This intermediate [3] on refluxing with  $\text{CH}_3\text{OH}/\text{H}^+$  gave the ester-ketal [4] which was further oxidised to the spiro lactone [5] with Jones reagent. Compound [5] was smoothly converted to the triquinane [6] on treatment with 40 equivalents of 5%  $\text{CH}_3\text{SO}_3\text{H}/\text{P}_2\text{O}_5$  mixture<sup>6</sup>. Further elaboration of this methodology towards the syntheses of specific natural products by simple synthetic manipulations on properly substituted lactones of the kind [5] is in progress (Scheme I).



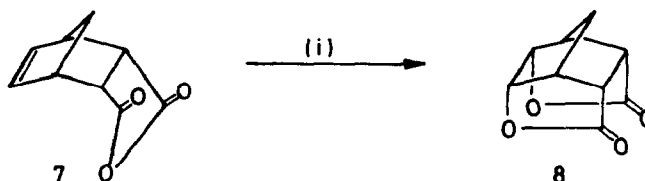
Reagents: (i)  $\text{BrMg}(\text{CH}_2)_2, \text{MgBr}, \text{THF}, 6\text{h}$ . (ii)  $\text{KMnO}_4/\text{TBAB}, \text{CH}_2\text{Cl}_2, 0^\circ\text{C}, 2\text{h}$ .

(iii)  $\text{CH}_3\text{OH}/\text{H}^+, \text{Reflux}, 4\text{h}$ . (iv) Jones Reagent,  $0^\circ\text{C}, 30\text{min}$ .

(v) 5%  $\text{CH}_3\text{SO}_3\text{H}/\text{P}_2\text{O}_5, \text{RT}, 24\text{h}$ .

Although there are well established synthetic routes for tetra and hexaquinanes<sup>7</sup>, much less is known about pentaquinanes<sup>7</sup>. There are no reports available for the synthesis of  $\text{C}_{17}$ -pentaquinanes of the type [12]. Scheme-III provides a simple four step synthesis for the  $\text{C}_{17}$ -pentaquinane derivative [12] starting from the bis-lactone [8], which was prepared in one step in improved yield by a simple modification of the reported procedure<sup>8</sup>. By dissolving freshly prepared [7] in 3 equivalents of aq.  $\text{KOH}$  and subsequent treatment with bromine and heating at  $120^\circ\text{C}$  for 3 hours, [8] was obtained in 70% yield (scheme II).

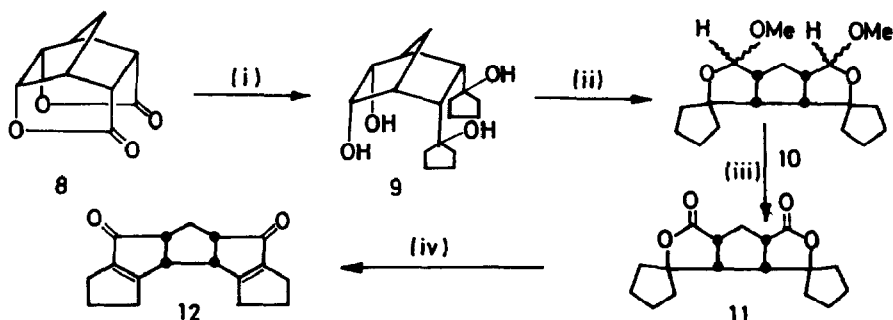
**Scheme : II**



Reagents : Aq  $\text{KOH}, \text{Br}_2, 120^\circ\text{C}, 2\text{h}$ .

Reaction of [8] with two equivalents of 1,4-di(bromomagnesio)butane in dry THF at 0°C followed by stirring the mixture at room temperature for 6 hours followed by work up with ammonium chloride afforded the tetrol [9] in 75-80% yield. Interestingly the reaction is free from complications associated with transannular cyclizations which were however observed in the reactions of [8] with lithium aluminium hydride and methylmagnesium iodide as a result of the spacial proximity of the two lactone carbonyls<sup>9</sup>. Periodic acid oxidation of [9] in aq. methanol then gave the spiro-diketal [10] which on further oxidation with Jones reagent afforded the spiro-dilactone [11]. Compound [11] was finally converted to the target pentaquinane [12] on treatment with  $\text{CH}_3\text{SO}_3\text{H}/\text{P}_2\text{O}_5$  (Scheme III).

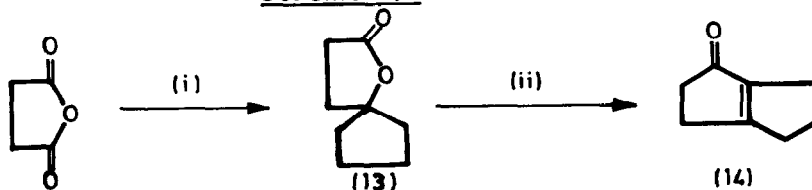
Scheme : III



Reagents : (i)  $\text{BrMg}(\text{CH}_2)_4$ ,  $\text{MgBr}$ , 0°C, THF, 6h. (ii)  $\text{H}_5\text{IO}_6$ , Aq  $\text{CH}_3\text{OH}$ , 4h, RT  
 (iii) Jones Reagent, 0°C, 30min. (iv) 5%  $\text{CH}_3\text{SO}_3\text{H}/\text{P}_2\text{O}_5$

Using our procedure, the spiro-lactone [13] prepared from succinic anhydride<sup>3a</sup> was converted by the action of  $\text{CH}_3\text{SO}_3\text{H}/\text{P}_2\text{O}_5$  to [14] in 90% yield (Scheme IV). The bicyclic enone [14] has been previously prepared via ethynylcyclopentanol in an overall yield of 7%<sup>10</sup>.

Scheme IV



Reagents: (i)  $\text{BrMg}(\text{CH}_2)_4$ ,  $\text{MgBr}$ , THF, 6hr.  
 (ii) 5%  $\text{CH}_3\text{SO}_3\text{H}/\text{P}_2\text{O}_5$ , RT, 24hr.

All the new compounds reported above were fully characterised on the basis of spectral and analytical data<sup>11</sup>.

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### References and Notes

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- Spectral data for selected compounds are given below:

#### Compound 5

i.r.:  $\text{cm}^{-1}$  1760, 1735.  
 $^1\text{H}$ -nmr: 3.8 (s, 3H), 2.8 (m, 1H), 2.7 (m, 1H), 2.4 (m, 1H),  
 2.2 (m, 1H), 2.1 (m, 1H), 2.0 (m, 1H), 1.6-1.9 (m, 9H)  
 $^{13}\text{C}$ -nmr: 179.27(s), 174.13(s), 94.75(s), 51.94(q), 49.5(d), 45.79(d),  
 44.9(d), 40.16(t), 34.19(t), 32.62(t), 31.41(t), 23.67(t),  
 23.42(t).  
 mass: m/z 238.

#### Compound 6

i.r.:  $\text{cm}^{-1}$  1720, 1680, 1620.  
 $^1\text{H}$ -nmr: 3.7 (s, 3H), 3.2 (m, 2H), 2.6 (m, 1H), 2.4 (m, 1H),  
 2.2 (m, 4H), 1.9-2.1 (m, 4H), 2.9 (m, 1H)  
 $^{13}\text{C}$ -nmr: 204.8(s), 188.4(s), 174.5(s), 148.0(s), 56.8(d), 51.7(q)  
 45.4(d), 42.9(d), 31.9(t), 30.9(t), 30.2(t), 27.6(t), 24.5(t)

#### Compound 9

i.r.:  $\text{cm}^{-1}$  3400.  
 $^1\text{H}$ -nmr: 6.65 (broad s, exchanged with  $\text{D}_2\text{O}$ ), 3.95 (s, 2H), 2.71  
 (s, 2H), 2.35(s, 2H), 1.27-2.11 (m, 18H)  
 $^{13}\text{C}$ -nmr: 81.55(s), 69.99(d), 52.91(d), 47.12(d), 42.17(t), 42.12(t),  
 32.62(t), 25.30(t), 23.61(t).  
 mass: m/z 296.

#### Compound 11

i.r.:  $\text{cm}^{-1}$  1775.  
 $^1\text{H}$ -nmr: 3.3(m, 2H), 2.6 (m, 1H), 2.2 (m, 1H), 1.6-2.1 (m, 18H).  
 $^{13}\text{C}$ -nmr: 176.26(s), 94.40(s), 52.49(d), 48.17(d), 41.82(t), 34.88(t),  
 29.10(t), 24.16(t), 22.22(t).  
 mass: m/z 290.

#### Compound 12

i.r.:  $\text{cm}^{-1}$  1680, 1620.  
 $^1\text{H}$ -nmr: 3.0-3.5(series of m, 4H), 2.2-2.6 (series of m, 14H).  
 $^{13}\text{C}$ -nmr: 204.1(s), 183.4(s), 149.2(s), 62.6(d), 45.0(d),  
 32.2(t), 27.6(t), 26.1(t), 24.4(t).  
 mass: m/z 254.