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A SIMPLE APPROACH TO THE CONSTRUCTION OF BICYCLO[5.2.1] AND [5.3.1] RING SYSTEMS FROM BICYCLO[2.2.1]HEPTANE PRECURSORS

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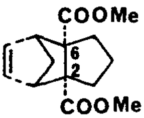
Abstract: A simple two step sequence for the construction of highly functionalised bicyclo[5.2.1]decane and its transformation to bicyclo[5.3.1]-undecane is described for entry into bridged ring terpenoids.

Development of an efficient strategy for the construction of bicyclo[5.n.1] ring systems (n=2,3) is of great importance because of their presence in large number of terpenoids. Conceptually,[1] a bicyclo[2.2.1]heptane derivative e.g. **1**, easily accessible through cycloaddition between cyclopentadiene and an appropriate dienophile, may lead to bridged rings of higher member through cleavage of the ring fusion bond (C_2-C_6 in **1**). Herein, we report the realisation of this concept leading to a new strategy for an easy access to otherwise difficultly accessible bicyclo[5.n.1]ring systems for entry into the sesquiterpene **2**[2] and the diterpenes of the taxane family.[3]

The diester **1** was prepared[4] in near quantitative yield by (4+2) cycloaddition between cyclopentadiene and cyclopentene-1,2-dicarboxylic anhydride followed by hydrolysis and esterification. Treatment of **1** with sodium (10-12 equiv) in liquid ammonia[5] at -55°C effected the fragmentation leading to **3**, m.p. 76°C in 70% yield. The diagnostic information that 2,6-bond breaking in **1** has really been taken place follows from the appearance of a two proton doublet of doublet at δ 3.34 (J = 10.4 and 4.4 Hz) in ^{1}H NMR[6] of **3** assigned to C_2, C_6-H's. This assignment was further corroborated by ^{13}C NMR (DEPT) data showing the presence of additional methine units (C_2, C_6) at δ 46.7. The <u>exo</u>-assignment of the carbomethoxyl groups in **3** follows from an upfield shift of the olefinic protons as a singlet by 0.3 ppm over the epimer **4** (obtained by epimerisation of **3** as a 1:1 mixture of **3** and **4**). The bicyclo[5.2.1]decanes thus generated are sufficiently functionalised for further elaboration to either the sesquiterpene **2** or the bicyclo[5.3.1]undecane system.

The wide applicability of this two-step sequence is demonstrated by a convergent synthesis of the tricyclic diester **9** bearing close structural relationship with the taxane nucleus. The reaction of the anhydride **5**[7] with cyclopentadiene in refluxing toluene followed by hydrolysis afforded the dicarboxylic acid **6**, m.p. 188°C (dec) in 88% yield. Exposure of **6** to diazomethane gave quantitatively the diester **7**, m.p. 59°C. The structure and <u>endo</u> stereochemistry of **6** was unequivocally established by its facile lactonisation (I_2, $NaHCO_3$) to the dilactone **8** (76%), m.p. 218°C. Treatment of **7** with $Na\text{-}NH_3(l)$ at -55°C afforded the diester **9** in 34% yield as a 1:1 diastereoisomeric mixture. The structure **9** follows from ^{1}H NMR [δ 3.34-3.6 (H), 3.7, 3.72, 3.74, 3.76, (4s, 6H), 3.95 (m, H), 5.32-6.34 (2H) and 7.04-7.48 (4H)] and mass spectral (M^+ 300) data as well as its mode of formation.

The synthetic potential of this two step sequence was further increased by a facile transformation of bicyclo[5.2.1]decane to bicyclo[5.3.1]undecane. The diester **3** on hydroboration (BH_3-THF-NaOH-H_2O_2) followed by Jones oxidation afforded the keto-diester **10** (85%). Treatment of **10** with ethyl diazoacetate under $Et_3O^+BF_4^-$ catalysis[8] afforded the bicyclo[5.3.1]undecane **11** (51%). Utilising the above concept, a synthetic approach to the sesquiterpene **2** and a few taxane diterpenes starting with an appropriately functionalised cyclopentadiene derivative is under active investigation and will be reported in due course.



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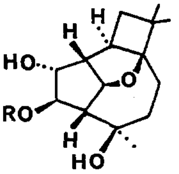

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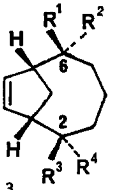
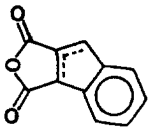
R=$HO_2C(CH_2)_2CO$



3, $R^1=R^3=COOMe$; $R^2=R^4=H$
4, $R^1=R^3=H$; $R^2=R^4=COOMe$



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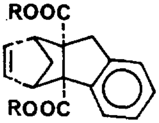
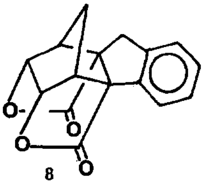


6, R = H
7, R = Me



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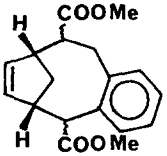

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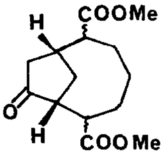

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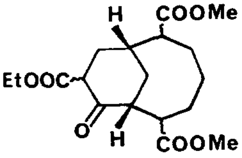

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References and Notes

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