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SYNTHESIS OF A TETRACYCLODECENONE WITH TWO ORTHOGONAL π-ELECTRON SYSTEMS VIA A 1,3-THROUGH CAGE ELIMINATION IN A BRIDGEHEAD SUBSTITUTED 1,3-BISHOMOCUBYL ACETATE

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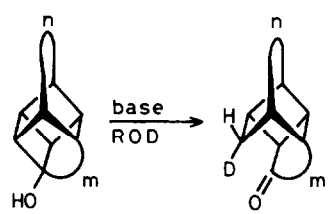
Abstract Stereoselective reduction of 1,3-bishomocubanone acetate 1 followed by mesylation leads to an epimeric mixture of mesylates 3. Base induced homoketonization of the anti-epimer 3b affords tetracyclo[5.3.0.$0^{2,5}$ $0^{4,8}$]decenone 4.

Highly strained bridgehead cage alcohols of the cubane type are reactive substrates which under basic conditions give rise to a regio- and stereospecific cage opening reaction[1] (Scheme 1). The regiochemistry of this homoketonization process is primarily determined by the relative thermodynamic stabilities of the conceivable cage opened products[2].

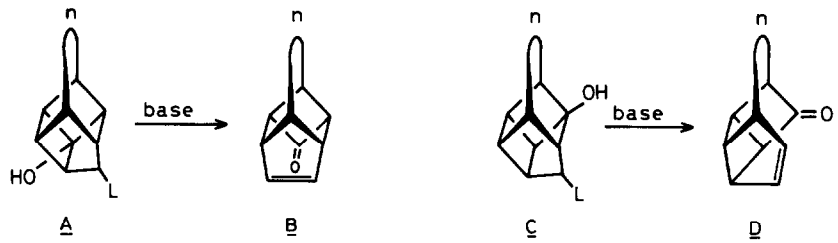
Scheme 1

cubane	n=m=0
homocubane	n=1 m=0
basketane	n=2 m=0
1,3-bishomocubane	n=1 m=1



However, this thermodynamic control may be disturbed if one of the three possible carbon-carbon bond cleavages leads to a carbanionic intermediate which is stabilized by an adjacent carbonyl function[3]. An alternative possibility to enforce the homoketonization to proceed in a 'contra thermodynamic' direction would be a 1,3-through cage elimination reaction in an appropriately β-functionalized bridgehead cage alcohol (or acetate) with the general structures A and C in which L is an efficient leaving group (Scheme 2). Assuming that the eliminative cage opening indeed takes the predicted course then the tetracyclic compounds B and D would arise. These structures are of particular interest as they contain two isolated orthogonal π-electron systems which are in close spatial proximity due to the rigidity of the polycyclic skeleton[5].
This communication deals with the synthesis of a suitable substrate of the type A and its subsequent cage opening.

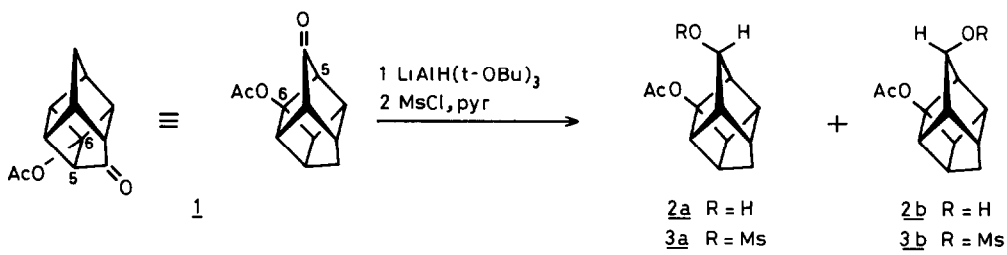
Scheme 2



A B C D

As starting material the 1,3-bishomocubyl acetate 1 was chosen (Scheme 3). This material is readily available from the Diels Alder adduct of cyclopentadiene and cyclopenten-1,3-dione by first acylation to the corresponding enol-acetate and subsequent photocyclization[4].

Scheme 3



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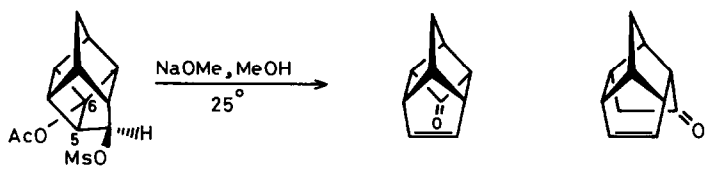
In spite of the sensitive nature of the acetate function in the 1,3-bishomocubanone acetate 1, the bridge ketone function could be selectively reduced by using either $NaBH_4$ in methanol or $LiAlH(t\text{-}OBu)_3$ in diethyl ether. In either case a 5 1 mixture of epimeric alcohols 2 was obtained in yields of 60 and 80%, respectively. Separation of these epimers could not be accomplished. Mesylation in pyridine produced the corresponding mesylates in the aforementioned ratio (yield 80%). Repeated crystallization from methanol afforded the major epimer analytically pure. Its ^1H NMR spectrum did not allow an unequivocal structural assignment. On merely steric grounds the formation of 2a as the predominant product from the reduction of 1 seems plausible. On the other hand, a participation of the acetate function in the complexation of the hydride reducing agent can be envisaged with the consequence of a stereoselective preference for the formation of the anti-isomer 2b[6]. An X-ray analysis of the major mesylate[7] unambiguously showed it to possess the anti-structure 3b thus proving the anchimeric effect of the acetate function on the reduction process In this structure 3b the mesylate group has the proper *trans-anti* parallel orientation with respect to the central C5-C6 bond which is to be cleaved in the through-bond fragmentation reaction[8].

The acetate 3b appeared to be highly reactive towards base. Upon treatment with sodium methoxide in methanol at room temperature an almost instantaneous reaction took place leading to a single

crystalline compound (yield 60%), m.p. 129-130° (sealed tube). On the basis of its spectral properties the tetracyclic structure 4 was assigned (Scheme 4). In contrast, under identical conditions, the *syn*-epimer 3a did not undergo such a facile cage opening reaction, only the corresponding mesylate alcohol was obtained. This means that the through-cage elimination process is subject to stringent stereoelectronic control and proceeds in a concerted manner[8].

Both the ^1H NMR and ^{13}C NMR are particularly decisive in assigning the structure as they show a relatively simple resonance pattern due to the high symmetry of 4. In the ^1H NMR spectrum ($CDCl_3$) both the olefine protons and bridge protons appear as a singlet at δ6.20 and δ1.95 ppm, respectively, while the remaining six cage protons are found as a multiplet between δ2.7 and 3.3 ppm.

Scheme 4



3b 4 5

The ^{13}C NMR spectrum ($CDCl_3$) shows the expected seven carbon signals at δ199.5 (s, C=O), 137.8 (d, olefinic carbons), 65.1 (d), 61.2 (d), 53.5 (d), 43.5 (d), 36.8 (t). The C=O absorption at δ199.5 ppm and the observation of a high C=O absorption (1760 cm^{-1}) in the IR-spectrum proves the presence of a cyclobutanone ring. The UV spectrum of 4 which exhibits a maximum at 204 nm (n-hexane, ε 3200)[9], is of particular interest as it suggests the occurrence of substantial orbital interaction between the two orthogonal π-electron systems. In contrast such an absorption in the low wave length region is absent in the UV spectrum of the closely related but less rigid tetracycloundecenone 5[10].

The alkenone 4 is extremely volatile and reacts readily with moisture from the air to form an insoluble hydrate. Currently, we are studying the chemistry of this particular π-electron system with emphasis on π-participation between the two double bonds.

REFERENCES and NOTES

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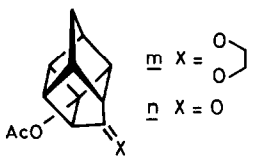
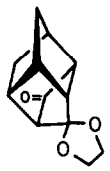
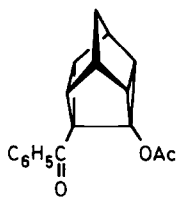
actates m and n. While the ketal acetate m yielded exclusively the thermodynamically controlled homoketonization product o, cage fission of the β-keto-substituted compound n resulted in a rapid and regiospecific formation of p. The stabilizing effect of a β-keto-substituent is



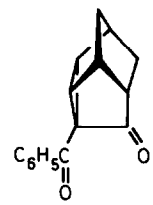


o

p



q



r

not always sufficient to direct the regiochemistry of such a homoketonization reaction in highly strained cage molecules. This is exemplified by the base induced cage opening of 4-acetoxy-5-benzoylhomocuneane q, which leads exclusively to the thermodynamically most stable product r[11].

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