New easy access to cyclopentanoid structures

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<u>Abstract</u>: We describe new easy synthesis of functionalized di and tricyclic cyclopentane containing derivatives. The stereochemistries of the ring junction are well defined. The starting material tricyclic methylene cyclobutanols are easily obtained on large scale from inexpensive substrates.

A carbocyclic five-membered ring is the basic structure of a large number of interesting natural as well as synthetic products endowed with biological or therapeutic activity.¹ It is thus not surprising that the synthesis of cyclopentane derivatives is always under very active investigation.² As part of our program aiming at the design of new biomolecules³ we needed an easy and inexpensive access to polycyclic cyclopentanes. In the present communication we wish to report the first very encouraging results obtained in this way.

A first family of cyclopentane derivatives was synthesized according to Scheme I.



1 was easily prepared on a large scale⁴ by condensation of the nucleophilic Complex Bases⁵ NaNH₂ketone enolate on 1-chlorocyclohexene. Yields of 3 and 4 were calculated from 1. 2 $(n=1, R=Me)^6$ reacted with mesyl chloride and pyridine⁷ to give 3 $(n=1)^8$ accompanied by a small amount of 4 (n=1).⁹ Curiously 4 $(n=2)^9$ was the only product formed from 2 (n=2, R=Me) and TsCl must be used instead of MsCl in order to obtain acceptable yields. Interestingly, during this reaction performed on 2 (n=1, R=Me), we were able to isolate a small amount of the mesylate 5. Its structure, established by X-ray diffraction data, shows that rearrangement of 2 seems to be due to the migration of antiperiplanar four membered ring bonds relative to the broken C-O bond. A second kind of cyclopentane derivatives has been obtained according to Scheme II.¹⁰

Scheme II



The formation of 7 results from an obvious rearrangement and may be used as starting material for further syntheses. For example, a functional group may be incorporated into the five-membered ring as exemplified in Scheme III where the procedure of Bakuzis and Bakuzis¹² was used.





The configuration of 8 was deduced from its 1 H NMR spectra, the coupling constant of the protons indicated being 11 Hz. Extension of the first results and their application to the synthesis of biomolecules is actively being pursued.

References and notes

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 The structure of 3 (n=1) was deduced from X-ray diffraction data performed on one of the two isomers obtained by reduction of 3 (n=1) with LiAlH4.

9) The configuration of 4 (n=1, 2) was assigned after comparison of their ¹H and ^{13}C NMR spectra with those of 3. Furthermore, the coupling constant of the two hydrogens of the cycle junction is J=10 Hz which is correct for a cis junction, a trans junction would give a greater value (J=18 Hz). R.L. Funk, G.L. Bolton, Y.U. Daggett, M.M. Hansen, L.H. Morcuer, Tetrahedron, 1985, <u>41</u>,, 3479.

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