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SELECTIVITY IN CYCLOADDITIONS: CRYSTAL AND MOLECULAR STRUCTURE OF (1α,4β,5α)-1,5-DIACETYL-4-HYDROXY-4-METHYLBICYCLO[3.1.0]HEXAN-2-ONE

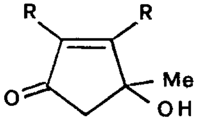
Giorgio Adembri, Donato Donati, Lucia R.Lampariello, Mirella Scotton* and Alessandro Sega

Istituto di Chimica Organica, Piano dei Mantellini, 44 - 53100 Siena (Italy)

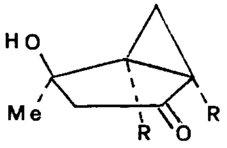
Summary: The stereochemistry of (1α,4β,5α)-1,5-diacetyl-4-hydroxy-4-methylbicyclo[3.1.0]hexan-2-one, the main cycloadduct of 2,3-diacetyl-4-hydroxy-4-methylcyclopent-2-en-1-one and diazomethane, was unambiguously established from a single crystal X-ray analysis.

In the literature there are many studies which deal with regioselectivity of cycloadditions, but very few are devoted to the stereoselectivity of these reactions[1]. Since we are interested in the chemical behaviour of cyclopentenones of type 1[2,3], we decided to study the influence of the chiral centre at 4 position on the stereoselectivity of the cycloadditions.

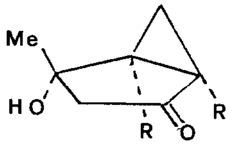
The reaction of the cyclopentenone 1a with diazomethane led to the cycloadducts 2a, 3a and 4a and was largely stereoselective; in the case of the cyclopentenone 1b only one of the possible bicyclo[3.1.0]hexane isomers, 2b, was isolated together with the cyclopenta[b]oxetane 4b and the cyclobutanone 5b. The structures of the cycloadducts obtained were assigned on the basis of spectral data, whereas the stereochemical assignment of 2a, 2b and 3a remained unsolved[4,5].



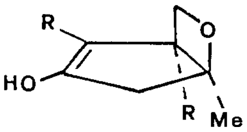
1 a R = Ac
b R = COOEt



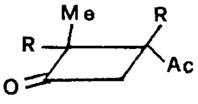
2 a,b



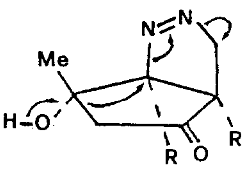
3 a,b



4 a,b



5 b



6 b

Apart from the regioselectivity of the cycloaddition, easily foreseeable on the basis of Frontier Orbitals theory, steric considerations led us to assign the main isomers the structure 2, i.e. with the OH group on the same side of the cyclopropane ring. The stereochemistry of the main isomer obtained from 1a was unambiguously confirmed as 2a from a single crystal X-ray analysis.

Crystal data: $C_{11}H_{14}O_4$, FW = 210.22. Monoclinic, a = 12.999(4), b = 11.728(4), c = 7.414(3) Å, β = 91.89(2)°, V = 1129.66 $Å^3$, D_c = 1.24 g.cm^{-3}, Z = 4, F(000) = 448 (20°C, graphite monochromated Mo-Kα , λ = 0.71069 Å), μ(Mo-Kα) = 0.57 cm^{-1}. Space group $\underline{P}2_1/n$ from systematic absences h0l when $\underline{h}+\underline{l}$ = 2$\underline{n}$+1, 0$\underline{k}$0 when $\underline{k}$ = 2$\underline{n}$+1.

Single crystals of 2a were obtained from ethyl ether/light petroleum (30-50°C). An irregular prism shaped fragment (0.5 x 0.25 x 0.20 mm^3) cut from a larger crystal was mounted on a Philips automated diffractometer. Cell constants were determined by least-squares treatment of angles of 25 reflections. The reflections were collected within $2\vartheta < 50°$ by ω-2ϑ step-scan technique at a scan-speed of 0.05° s^{-1} and a scanwidth of 1.20° in ω . Three standard reflections monitored periodically showed no significant variation. After correction for Lorentz and polarization effects, 1741 reflections with $I > 3\sigma(I)$ were considered observed and used in the structure solution and refinement. Absorption corrections were not applied.

The structure was solved by using phasing program of MULTAN 80[6] and the E map showed all non-hydrogen atoms. The refinement was pursued using SHELX-76 program system[7]. Two cycles of full matrix least-squares refinement with isotropic temperature factors reduced the R value to 0.18. Subsequently, two full matrix least-squares cycles with anisotropic temperature factors converged at R = 0.095. All the hydrogen atoms were located in the difference Fourier maps and all the hydrogen atoms, but those of the acetyl groups, were isotropically refined. The hydrogen atoms of the acetyl groups were kept fixed in the final two cycles of least-squares owing to some higher than 0.5 correlation matrix elements. The final disagreement indexes obtained were R = 0.045 and R_w = 0.050. The weighting scheme used was $w = [\sigma^2(F_o)]^{-1}$ where $\sigma(F_o)$ is the individual estimated standard deviation for each reflection from diffractometer counting statistics.

A complete list of the refined coordinates, the observed and calculated structure factors, and a table of angles and bond distances have been deposited in the Cambridge Crystallographic Data Centre (C.C.D.C.).

The ORTEP plot[8], shown in Fig.1, clearly demonstrates the configuration of ($1\alpha,4\beta,5\alpha$)-1,5-diacetyl-4-hydroxy-4-methylbicyclo[3.1.0]hexan-2-one, 2a. The bicyclo[3.1.0]hexane system shows a boat-like conformation. The C(1), C(2), C(4) and C(5) atoms are coplanar and the angles between this plane and C(2)-C(3)-C(4) and C(1)-C(5)-C(6) planes are 29.06° and 70.06° respectively (Fig.2). These data agree with those reported in the literature for bicyclo[3.1.0]hexane[9-13] and bicyclo[3.1.0]hexan-3-one[14] systems. We found only one paper[15] which reported the crystal

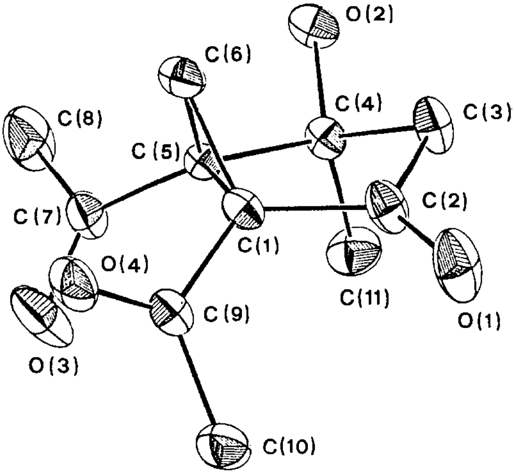


Fig.1 - ORTEP drawing of 2a and atom labelling system used in the crystallographic analysis.

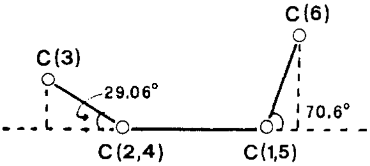


Fig.2 - Displacements of C(3) and C(6) from the plane of C(1),C(2),C(4),C(5).

structure of a bicyclo[3.1.0]hexan-2-one (crispatone): in this case the five-membered ring was nearly planar.

Packing of 2a shows an intermolecular H-bond between the OH group and the acetyl group of the molecules related by 0.5-x, 0.5+y and 1.5-z symmetry operation.

On the basis of the concordance between the predicted course of the reaction and the data of X-ray analysis it seems reasonable to suppose that the bicyclo[3.1.0]hexane adduct obtained from 1b has the stereochemistry shown in 2b.

It is noteworthy that also the nature of the substituents at 2 and 3 positions must have a certain influence on the stereochemistry of the cycloadducts: in fact examination by ^{1}H-nmr spectroscopy of all the different fractions of the reaction mixture separated by column chromatography showed no traces of the stereoisomer 3b. The yield of the isolated 2a, 3a and 4a was 43.5%, 3.1% and 24.6% respectively and that of compounds 2b, 4b and 5b was 70%, 16% and 2% respectively.

In the case of the cyclopentenone 1b we must suppose that the regioselectivity was not complete in so much as we isolated a small quantity (2%) of 1-acetyl-2-methyl-3-oxocyclobutane-1,2-dicarboxylate, 5b, which can arise by a contraction of the isomeric pyrazoline intermediate 6b.

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