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PHOTOINDUCED CYCLIZATION OF 3β-ACETOXY-$C_{(14a)}$-HOMO-B-NORLANOSTA-8(14a),9(11)-DIENE AS A ROUTE TOWARDS $B_{(9a)}$-HOMO-C-NORLANOSTANE DERIVATIVES

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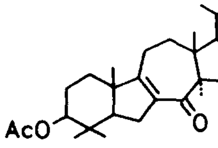
Summary: The synthesis of diketones 6, 7 and 8 starting from diene 3 by photochemical cyclization followed by RuO_4 oxidation is described and stereochemistry of products is proposed.

Recently we have studied [1] chemistry of lanostanes with modified carbon skeleton, namely, $C_{(14a)}$-homo-B-nor derivatives 1 [R= $-CH_2CH(CH_3)_2$; $-COOCH_3$; $-CH=C(CH_3)_2$; $-CH_2C(CH_3)_2OH$]. Such compounds have been synthesized by intramolecular cyclization of the respective 8,9-seco-8,9-diones derived from lanost-8-enes. In spite of theoretical possibility of ketones 2 formation during this type of cyclization, such compounds have never been isolated. The unfavourable formation of $B_{(9a)}$-homo-C-norlanostanes was attributed [2] to the presence of strained trans-condensed bicyclo[3,3,0]octane moiety. This conclusion was additionally supported by synthesis of $B_{(9a)}$-homo-C-norcholane [3] with inverted configuration at C-14 (C/D-cis junction).

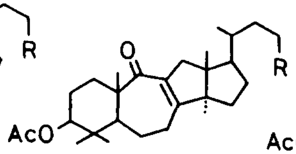
In search for a suitable method of synthesis of C-norlanostanes we have paid our attention to the photochemical cyclization of homoannular dienes. It is known, that excited molecules behave completely differently from those in the ground state providing products which are accessible only with a great difficulty via ground state reactions [4]. Ultraviolet light-induced reactions of 1,3-cycloalkadienes [5] have been extensively studied during the past decades. It has been noticed that 1,3-cycloheptadiene derivatives are very consistent in their photochemical behaviour [6], since valence bond isomerization to bicyclo[3,2,0]heptenes has been observed in almost all instances.

Diene 3, simply prepared [1] by diborane reduction of ketone 1 [R= $-CH_2CH(CH_3)_2$], seemed to be a convenient source of lanostane derivatives with strained trans-bicyclo[3,3,0]octane moiety.

Irradiation of diene 3 (ether, 5°C, 2 hrs, Hanau S 81 quartz lamp) furnished two oily products (4 and 5; 2:1 ratio) in addition to unreacted



1



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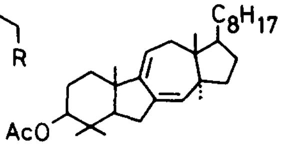

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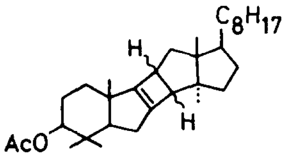
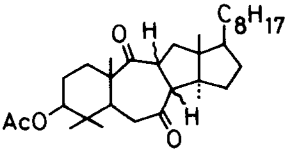


4 11β,14aβ

5 11α,14aα



6 8β,9β

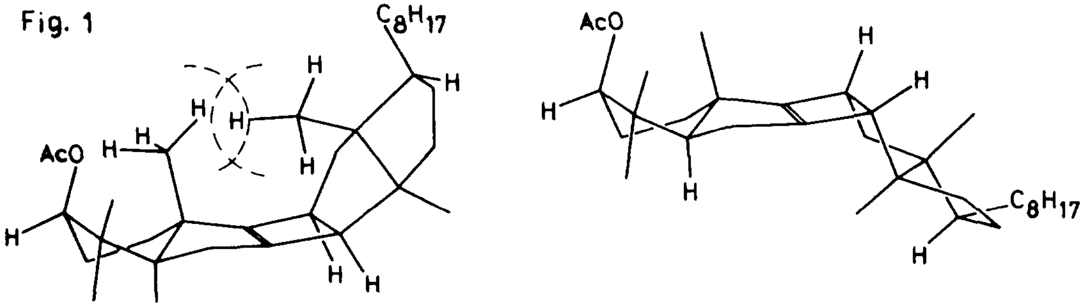
7 8α,9α

8 8β,9α

diene 3 (ca. 20%). Further irradiation (up to 5 hrs) of this mixture did not lead to any change in its composition. Irradiation of isolated [7] cyclolanostene 4 or 5 for 2 hrs resulted in formation of the same mixture of 3, 4 and 5 thus verifying the apparent photoequilibrium $4 \rightleftharpoons 3 \rightleftharpoons 5$ under the reaction conditions. In ^{1}H-NMR spectra of 4 ($[\alpha]_D^{24}$ +3.1°, $CHCl_3$) and 5 ($[\alpha]_D^{24}$ +32.1°, $CHCl_3$) signals of C-11 and C-14a methine protons appeared (4: δ3.78, m, 11β-H, and 3.06, d, J=3.8 Hz, 14aβ-H; 5: δ3.82, m, 11α-H and 2.91, d, J=3.0 Hz, 14aα-H). The presence of the double bond was confirmed by ^{13}C-NMR spectra in which resonances of olefinic carbons C-8 and C-9 were found (4: δ149.4 and 161.7 ppm; 5: δ151.9 and 159.8 ppm). An additional proof of the isomeric nature of photoproducts 4 and 5 was achieved by their thermal reconversion into diene 3 in refluxing n-heptane. Cyclolanostene 5 shows quantitative reaction in 3 hrs, whereas 4 needs 4 hrs for completion. Relatively mild [8] conditions of the thermal opening of cyclobutene ring in 4 and 5 stood in some contrast to the drastic conditions required for an analogical reaction of bicyclo[3,2,0]hept-6-ene (gas phase, 400-500°C)[9]. It is likely that such behaviour of 4 and 5 could be connected with their extremely strained pentacyclic structure.

The configuration at C-11 and C-14a was assigned on the basis of following argumentation. According to Woodward-Hoffman rules [10] photochemical cyclization of butadiene derivatives proceeds in a cleanly disrotatory mode and the obtained products should have, therefore, the cisoidal configuration at C-11 and C-14a. On the other hand examination of Dreiding models reveals that 11α,14aα-isomer should be much more hindered than 11β,14aβ-isomer (cf. projections of models represented in Fig. 1). The observed preference

Fig. 1



5 4

of formation of cyclolanostene 4 and its relatively higher thermal stability enables us to assign to this compound sterically favored 11β,14aβ structure.

Cyclolanostenes 4 and 5 were, in turn, oxidized with RuO_4 (water-acetone, room temp., 5 min) yielding quantitatively diketones 6 (m.p. 210-212^{o}C, $[\alpha]_D^{24}$ +45.3^o, $CHCl_3$) and 7 (amorphous solid, $[\alpha]_D^{24}$ +38.6^o, $CHCl_3$), respectively. It might be expected that epimerization at C-11 and C-14a would not occur during RuO_4 oxidation and thus configuration of B/C ring junction of diketones 6 and 7 have been assigned β-cis and α-cis, respectively. The coupling patterns of methine protons adjacent to the carbonyl groups observed in ^{1}H-NMR spectra of 6 (δ3.02, d, J=11.6 Hz, 8β-H and 4.30, dt, J_1=11.6 Hz, J_2=7.6 Hz, 9β-H) and 7 (δ3.04, d, J=13.0 Hz, 8α-H and 4.29, ddd, J_1=13.0 Hz, J_2=8.7 Hz, J_3=1.4 Hz, 9α-H) were in agreement with those predicted according to Karplus relation [11].

Since 8α,9α-isomer 7 is much more hindered than 8β,9β-isomer 6, as it was evident from models, compounds 6 and 7 were submitted to equilibration (methanolic KOH, reflux, 2 hrs) in order to determine their relative thermodynamical stability. In both cases the same mixture of two products was obtained and after reacetylation and subsequent column chromatography on silica diketone 6 (ca. 15%) and new diketone 8 (ca. 85%; m.p. 168-172^{o}C, $[\alpha]_D^{24}$ +55.2^o, $CHCl_3$) were isolated. Identical mixture was obtained when pure 8 was equilibrated.

The stereochemistry of B/C ring junction of diketone 8, hitherto the only point of ambiguity in the structure has been proposed as 8β,9α from the following arguments. Among the four possible configurations for B/C ring junction two of them, β-cis and α-cis, have to be excluded, as such stereochemistry was already assigned to compounds 6 and 7. Of the remaining two possibilities, 8α,9β and 8β,9α, inspection of ^{1}H-NMR spectrum (δ4.17, dt, J_1=3.2 Hz, J_2=10.6 Hz, 9α-H) as well as examination of the respective models favors the latter form.

The presented results show that previously inknown system of $B_{(9a)}$-homo-C-norlanostane is now possible to be constructed by simple two-step transformation of $C_{(14a)}$-homo-B-norlanostane derivatives.

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References and Notes

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7. All new compounds described here had the appropriate spectral properties and the required composition by elemental analyses. Numbering of the carbon skeleton according to the "IUPAC-IUB 1971 Definitive Rules for Steroid Nomenclature" was used - Pure Appl. Chem., 31, 285 (1971).
8. If thermal isomerization process occured in a conrotatory mode, as predicted by Woodward-Hoffman rules 10), it would result in formation of cis-trans-cycloheptadiene product. Such course of the reaction seems to be extremely energetically unfavoured. Therefore in this case the ring opening should proceed in a forbidden disrotatory mode, slowly and with a great difficulty.
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