

CIRCULAR DICHROISM OF SOME CYCLOPROPANE RING CONTAINING 1,3-CYCLO-5,10-SECO-STEROIDAL KETONES¹

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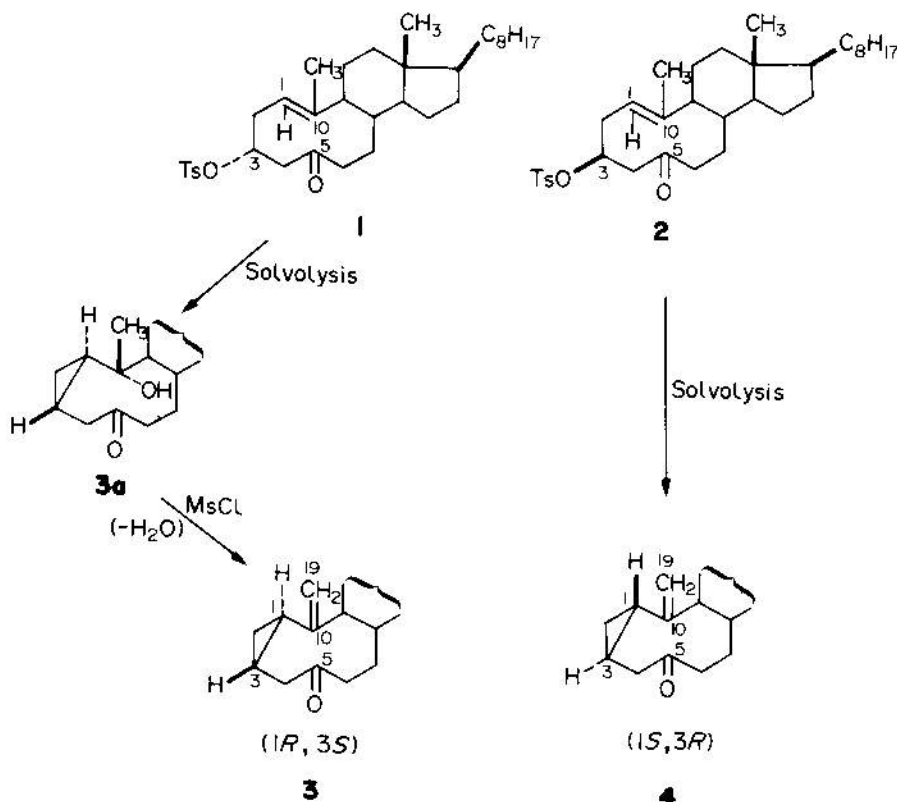
Abstract—Circular dichroism of the rearranged keto steroids **3** and **4**, containing a condensed three and nine-membered ring system, shows that the conformation of the nine-membered ring is the same in solution as in the crystal; reduction of the keto group does not change this situation. CD also indicates that epimerization at C(5) in the pair **7/8** and the pair **11/12** leaves the cyclononanone ring conformation unchanged.

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‡The primarily formed product from the 3α -tosylate **1** being, actually, the 10-methyl-10-hydroxy-1,3-cyclo derivative **3a**, which can readily be dehydrated (by means of mesyl chloride) to the corresponding olefinic compound **3**.³

As previously reported,^{2,3} solvolysis of the epimeric (*E*)- 3α - and (*E*)- 3β -tosyloxy-5,10-seco-cholest-1(10)-en-5-ones **1** and **2** in buffered acetone-water (90:10 v/v) solution at reflux proceeds with homoallylic π -bond participation and internal C(1)-C(3) bond formation, affording (among other products) the diastereomeric 1,3-cyclo-5,10-seco-steroidal 5-ketones **3** (upon dehydration)[§] and **4** (direct product), respectively (Scheme 1), which both contain a bicyclo[7.1.0]-decane system instead of the two 6-membered rings A and B.



Scheme 1.

Since, owing to the conformational mobility of the 9-membered ring, configurational assignments at C(1) and C(3) by the usual physical methods (CD, ^1H - and ^{13}C -NMR spectra) proved to be impossible, the *trans* 1*R*,3*S*-configuration of the cyclopropane derivative 3 (obtained from the 3 α -tosylate 1) and the *trans* 1*S*,3*R*-configuration of the diastereomeric ketone 4 (produced from the 3 β -tosylate 2) were established by X-ray analysis.⁴ It was also shown that the solid-state conformation of the 9-membered ring in compound 3 closely approximates to a twist-chair-chair (C_2) form,⁵ with the two-fold axis of symmetry passing through C(8) and the mid-point of the C(3)-C(4) bond (3-A, Scheme 2), while the corresponding 9-membered ring in the cyclopropane derivative 4 is best considered as a distorted chair-boat (C_s) form,⁵ in which a mirror plane of symmetry passes through C(9) and the mid-point of the C(4)-C(5) bond (4-B, Scheme 2).

In the present paper, CD spectra of these 10(19)-unsaturated 1,3-cyclo-5-ketones 3 and 4, as well as of the derived compounds, i.e. the 10(19)-olefinic 5-acetates 9 and 10, and also of the corresponding 1,3-cyclo-10-keto-5-acetates 7, 8, 11 and 12 (Scheme 3), are discussed in order to deduce the conformation(s) of the 9-membered ring in these modified steroid molecules in solution.

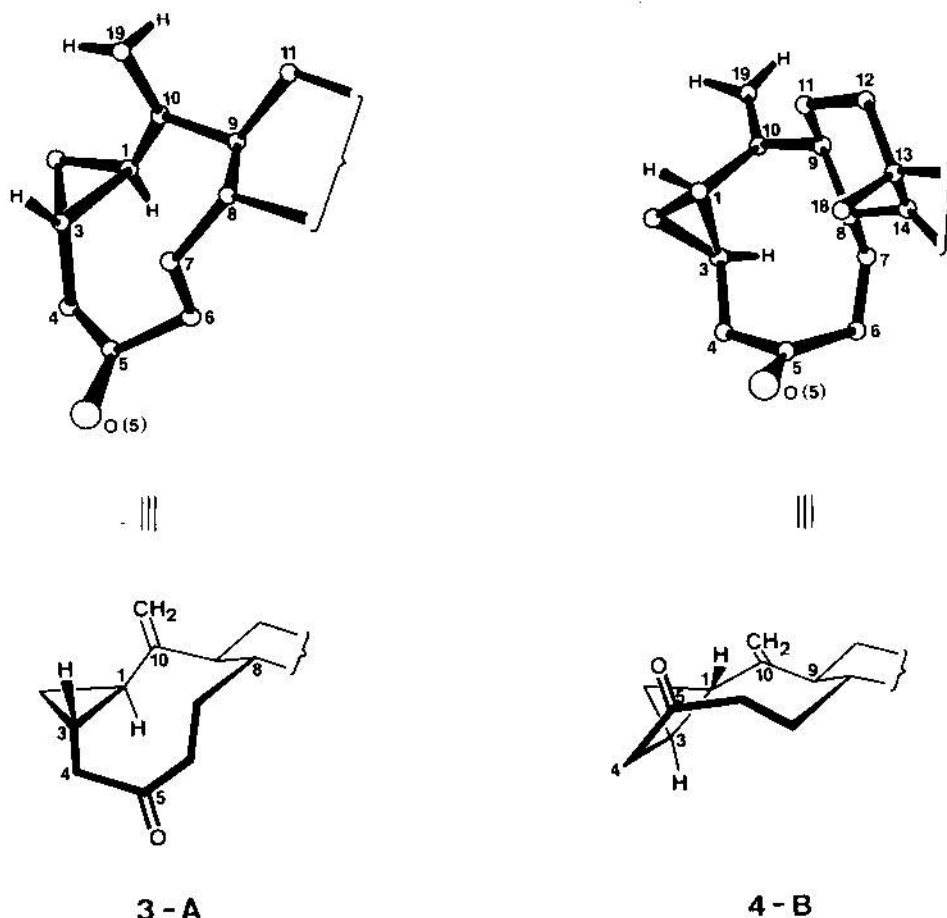
[†]Besides the arguments given there,^{4a} we found, in addition, a pronounced upfield shift (6.6 ppm) for the signal of C(1) of 4 (δ 22.0 ppm) compared to that of 3 (δ 28.6 ppm); this can be assigned to the γ_{gauche} effect of C(11) which only in 4 has the proper geometry.

Compounds 7-12 were prepared from the 5-ketones 3 and 4 by the reaction sequences outlined in Scheme 3. The configuration at C(5) in 9 and 10, and also in 11 and 12, follows from the fact that the 5-acetate 9, upon acetolysis, undergoes opening of the 3-membered ring to give the known (*E*)-3 β ,5 α -diacetoxo-5,10-seco-1(10)-cholesten-5-one 13,⁶ while the acetate 10, under similar experimental conditions, produces the epimeric compound (*E*)-3 β ,5 β -diacetoxo-5,10-seco-1(10)-cholesten-5-one 14.⁷ By comparing ^1H -NMR spectral data (Table 1), it was possible to correlate the stereochemistry at C(5) of the 10-keto-5-acetates 7 and 8 (in the 1*R*,3*S*-series) with that of the respective compounds 11 and 12 (in the 1*S*,3*R*-series).

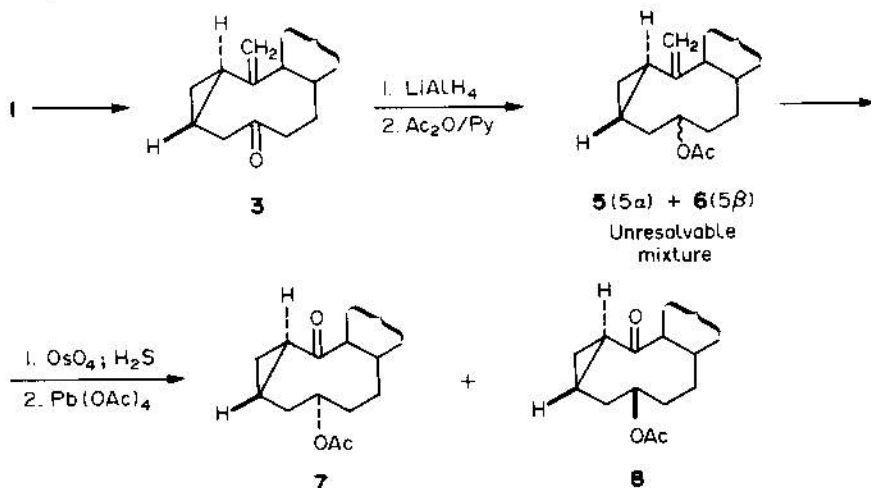
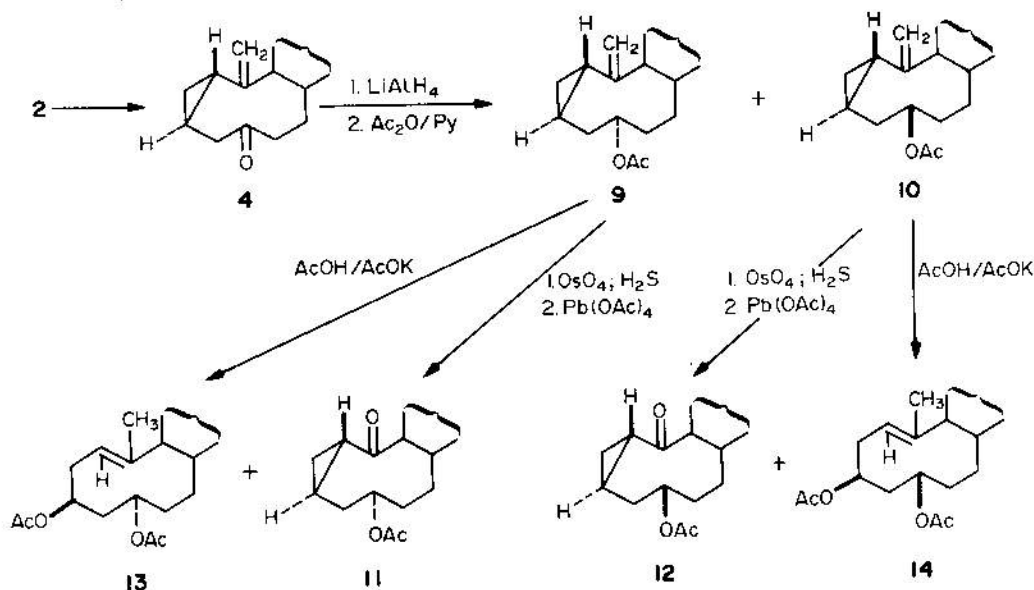
CD Spectra

The CD maxima are summarized in Table 2. Compounds 3 and 4 contain each two chromophores which have well been investigated, *viz.* the saturated carbonyl and the vinyl cyclopropane. There are now many cases known where the preferred conformation in solution is very similar to that in the crystal, and so we shall too assume at first the same for the cyclononanone ring in ketones 3 and 4, particularly since earlier ^{13}C -NMR measurements of these two compounds have also suggested such a similarity.^{4a†}

An octant projection shows that the 9-membered ring has quite a different shape in ketones 3 and 4, but the bulk of the other atoms is in a "negative" octant, and nevertheless, the CD is positive for both compounds. The two compounds 3 and 4 also differ in the geometrical



Scheme 2.

1R, 3S- Series:*1S, 3R*- Series:

Scheme 3.

arrangement of the cyclopropane ring with respect to the C=O group, but the magnitudes of the Cotton effects are the same. On the other hand, the torsional angles around

the C(4)-C(5) and C(5)-C(6) bonds are pairwise similar (-46.6° and -45° for the first, $+86^\circ$ and $+60.5^\circ$ for the second of these bonds) along the C-C-C train of bonds.^{4b} Such values characterize a chiral second sphere around the chromophore,⁸ and the signs of the contribution to the CD are opposite to the signs of these angles. A torsional angle of 0° clearly belongs to an achiral situation, and another such will be obtained at an angle somewhat smaller than 90° , because, since the coefficient for the MO-lobe between the two atoms of the perturbing σ -bond is greater than those of the outside lobes, at a torsional angle of 90° this σ -bond will already discriminate between the two possible orbital phase signs.⁸ The signs so obtained are opposite to those for smaller torsional angles, so that the maximum CD-contribution is expected to appear at torsional angles of about 30 – 40° . This is in agreement with the general experience that the greatest CD-values are found for the C_2 -twist cyclohexanone, where this torsional angle is around 30° . For ketones 3 and 4 the contribution from that σ -bond asso-

Table 1. ¹H-NMR signals of H-C(5) in compounds 7, 8, 11 and 12^a

Compound (and configuration)	Chem. shift δ (ppm)	Half-band width $\nu_{1/2}$ (Hz)
7 (<i>1R, 3S</i> -5 α)	5.20	~ 12 (5 β -H)
8 (<i>1R, 3S</i> -5 β)	4.78	~ 22 (5 α -H)
11 (<i>1S, 3R</i> -5 α)	5.18	~ 17 (5 β -H)
12 (<i>1S, 3R</i> -5 β)	4.78	~ 25 (5 α -H)

^a For further NMR data see Experimental.

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