Stereospecific *cis*-Reduction of Hexahydro-3-oxophenanthrene Derivatives. Total Synthesis of a New Class of Ring-C Aromatic Steroid

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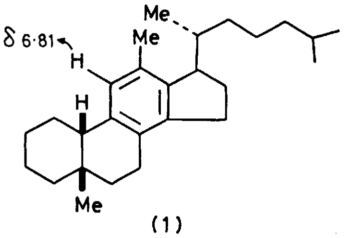
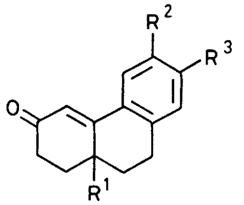
Catalytic hydrogenation (Pd/C, 10%) of the hexahydro-3-oxophenanthrene (**2a**) in acidic medium gave the *trans*-fused octahydrophenanthrene ring system (**5b**) predominantly, whereas reduction of (**2a**—**c**) with $LiAlH_4$ followed by oxidation gave exclusively the *cis*-fused systems (**4a**), (**4c**), and (**4e**), respectively; the products (**4a**) and (**5b**) have been elaborated to the 10βH and 10αH isomers, respectively, of 5,12-dimethyl-5β-gonane-8,11,13-triene-17-one.

The presence of partially aromatised hydrocarbons related to steroids in geological samples has been noticed by several authors,[1] and the first identification of one type, *e.g.* (**1**) has recently been reported by Ourisson and his associates.[1]

In connection with the total synthesis of (**1**) and related compounds,[1] we searched for a method for the exclusive *cis*-reduction of the hexahydrophenanthrene derivative (**2a**). We report here a general and efficient stereospecific *cis*-reduction procedure for (**2a**) and analogous compounds, leading to a total synthesis of the title compounds.

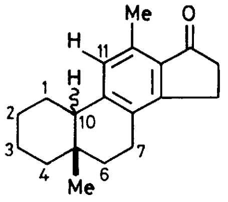


(1)



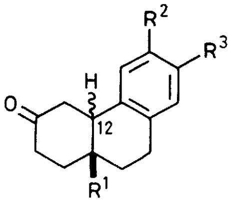
(2)

a; $R^1=R^2=Me, R^3=H$
b; $R^1=Me, R^2=H, R^3=OMe$
c, $R^1=R^2=H$, $R^3=OMe$



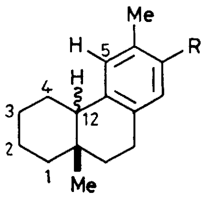
(3)

a; 10βH
b; 10αH



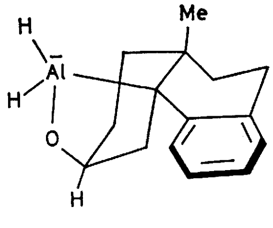
(4)

a; 12βH ; $R^1=R^2=Me, R^3=H$
b; 12αH ; $R^1=R^2=Me, R^3=H$
c ; 12βH ; $R^1=Me, R^2=H$, $R^3=OMe$
d ; 12αH ; $R^1=Me, R^2=H$, $R^3=OMe$
e ; 12βH; $R^1=R^2=H$, $R^3=OMe$



(5)

a; 12βH, R = H
b; 12αH, R = H
c ; 12βH, R = COMe
d; 12αH, R = COMe
e; 12βH, R = $\underset{\underset{O}{\|}}{C}-CH=CH_2$



(6)

Catalytic reduction (Pd–C, 10%) of (**2a**)† under neutral conditions afforded 50% (isolated yield)‡ of a 7:93 mixture (g.l.c.) of the saturated hydrocarbons (**5a**) and (**5b**); and 40% of 42:58 mixture of the saturated ketones (**4a**) and (**4b**), respectively. Similar reduction of (**2a**) in pyridine solution was encouraging as it provided 90% of a 85:15 mixture of the *cis*- (**4a**) and the *trans*-ketone (**4b**). Hydrogenation of (**2a**) in acetic acid containing perchloric acid afforded directly 78% of a 10:90 mixture of *cis*- (**5a**) and the *trans*-hydrocarbon (**5b**), respectively. Lithium–liquid ammonia reduction of (**2a**), using ammonium chloride as the proton donor, furnished 73% of a 65:35 mixture of (**4a**) and (**4b**). The methoxy-ketone (**2b**)[2] on similar reduction provided the same mixture of the *cis*- (**4c**) and the *trans*-ketone (**4d**), indicating thereby that the electronic effect of the *p*-methoxy-group has nothing to do with stereochemical outcome of this reduction.

The reduction of the double bond of α,β-unsaturated carbonyl compounds with $LiAlH_4$ is well documented in the literature,[3] and the reduction proceeds through the alkoxy-aluminium hydride. Reductions of the unsaturated ketones (**2a, b**) with $LiAlH_4$ in refluxing tetrahydrofuran, and subsequent oxidation of the resulting alcohols with pyridinium dichromate afforded in 76 and 52% yield, respectively, the saturated *cis*-ketones (**4a**) and (**4c**), homogeneous by g.l.c. and ^1H n.m.r. spectroscopy. The methoxy-ketone (**2c**),[4] lacking the angular methyl group, after a similar reduction–oxidation sequence also provided, in comparable yield,§ (50%) the *cis*-ketone (**4e**), identical to an authentic sample.[4] Not a trace of the *trans*-ketones could be detected in these hydride reductions.

Stereochemical evidence for the above hydride reduction suggests that the reaction is intramolecular, and the formation of a carbon–aluminium bond[3b,5] as shown in (**6**) (Al not tetrahedral) is probably necessary. The results so far obtained indicate that the generation of the intermediate (**6**) may not be totally dependent on the presence or absence of the angular methyl group.

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† All new compounds described herein are racemic and provided the expected spectral data and elemental analyses.

‡ The percentage yields mentioned in other cases are all isolated ones.

§ The lower yield of the saturated *cis*-ketones (**4c**) and (**4e**) may possibly be due to the resonance effect of the *p*-OMe which impedes conventional 5-centre hydride transfer to the styrene double bond, and destabilises to a certain extent the intermediate benzylic carbanion.

Huang–Minlon reduction of the *cis*-ketone (**4a**) afforded in 80% yield the *cis*-hydrocarbon (**5a**). Friedel–Crafts acetylation¶ of this in the presence of tin(IV) chloride in methylene chloride provided regiospecifically the acetyl derivative (**5c**) (70%). The crude vinyl ketone (**5e**), prepared from (**5c**) by a recently developed procedure,[6] was directly cyclised with conc. H_2SO_4 to afford the key tetracyclic *cis*-ketone (**3a**) [42% based on (**5c**)], a potential intermediate for the synthesis of (**1**) and related compounds.[1]

The mixture of (**5a**) and (**5b**), obtained directly from (**2a**) through hydrogenation in acid medium, afforded the tetracyclic *trans*-ketone (**3b**) in comparable yield (42%) following the sequence used for (**5a**) → (**3a**).

The yields of (**3a, b**) were slightly improved (52%) when vinyl ketones were prepared from the acetyl derivatives through a Mannich base procedure.

Careful ^1H n.m.r. study of the octahydrophenanthrene system related to (**5a, b**) revealed[7] that the aromatic C-5 proton in the *trans*-isomer shows a signal at lower field than does the corresponding hydrogen in the *cis*-isomer; we observed this also in the present study. The aromatic C-5 protons in our *cis*- (**5c**) and *trans*-acetyl derivative (**5d**) show slightly broad singlets at δ 6·75 and 7·07, respectively. The aromatic C-11 proton of the crystalline *cis*- (**3a**) and the *trans*-tetracyclic ketone (**3b**) also showed singlets at δ 6·80 and 7·00, respectively.

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¶ This reaction in the presence of anhydrous $AlCl_3$ gave a mixture which showed no characteristic singlet for the angular methyl group.