Synthetic Route to Tricyclic Carbon Compounds by Friedel–Crafts Acylation

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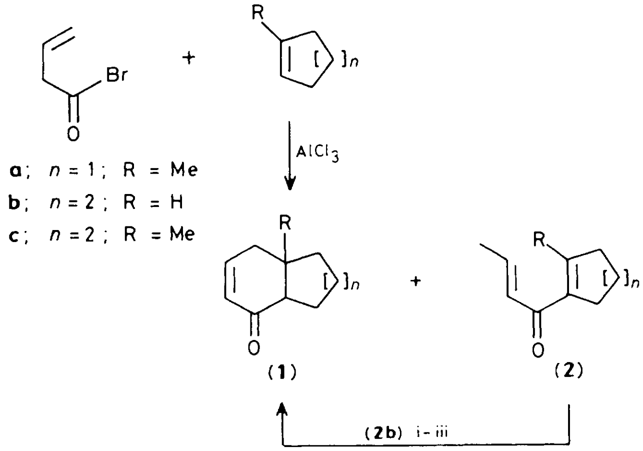
Acylation of cyclohexene by cyclohexenyl- or cyclopentenyl-acetyl chloride gave des-A-11-oxo or des-D-7-oxo steroids.

The total synthesis of steroids remains an active area of research although the aim of the studies and the methods used have changed over the years.[1] Here we propose a one step des-A-11-oxo-steroid (or des-D-7-oxo steroid) synthesis from cyclohexene and cyclopentenylacetyl (or cyclohexenylacetyl) chloride.

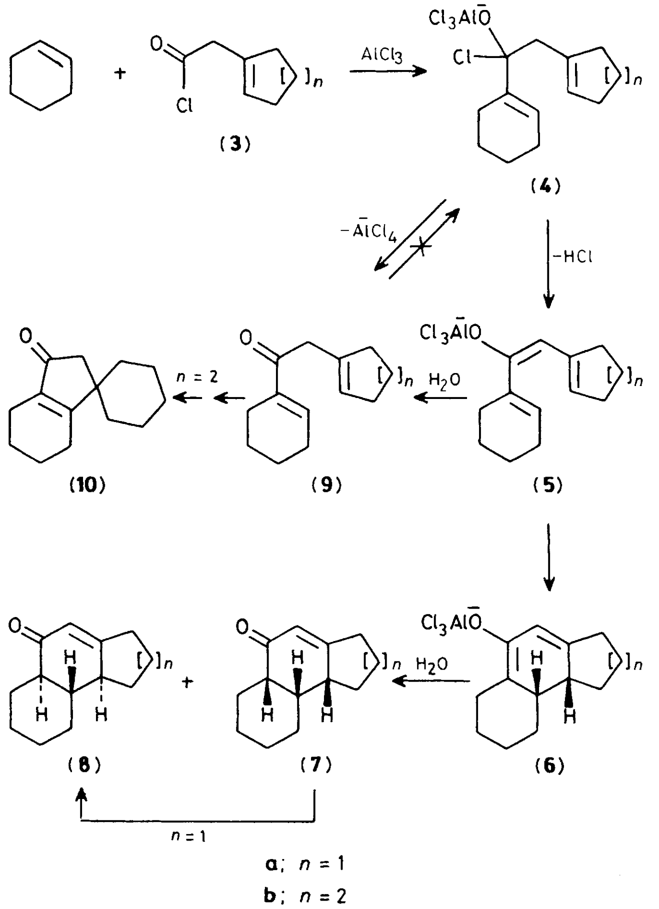
We have previously shown that the Friedel–Crafts acylation of cycloalkenes by vinylacetyl bromide provided a new preparation of octalones (**1b**) and (**1c**) or indanones (**1a**),[2] but the divinyl ketone (**2**) was often the major product. A complementary cyclisation of (**2b**) required trienoxysilane formation followed by heating in toluene[3] (overall yield 45%),[†] Scheme 1.

In contrast, cyclohexene acylation using cyclohexenyl- or cyclopentenyl-acetyl chloride[4] (**3**) gave the tricyclic ketones (**7**) and (**8**) in good yields. In a typical experiment, anhydrous



Scheme 1. *Reagents*: i, Me_3SiCl, Et_3N, dimethylformamide; ii, heat, PhMe; iii, H^+, H_2O.

[†] All new compounds exhibited satisfactory spectroscopic and exact mass spectroscopic data.



Scheme 2

$AlCl_3$ (10 mmol) was stirred at −80 °C with CH_2Cl_2 (25 ml) and (**3**) (10 mmol) for 15 min. Then cyclohexene (10 mmol) in CH_2Cl_2 (5 ml) was added. The mixture was stirred for 2 h at −80 °C and at −20 °C for 16 h and finally hydrolysed [yields: (**7a**) and (**8a**) 80%; (**7b**) and (**8b**) 60%;[5] (**9b**) 30%].

When the condensation of (**3b**) with cyclohexene was stirred at 0 °C for 12 h, the spiro ketone (**10**) was isolated [yields were as follows: (**9b**) 15%; (**7b**) and (**8b**) 60%; (**10**) 25%]. Spiro ketone (**10**) could result from the Nazarov cyclisation of (**9b**).[6]

The cyclisation leading to (**7**) and (**8**) resulted from the thermal disrotatory electrocyclic path involving enolate (**5**) to afford *cis*-enolate (**6**).[7] The enolate (**5**) is likely to have arisen from the tetrahedral intermediate (**4**) and not from the allyl vinyl ketone (**9**). [We observed that (**9**) remained unchanged under the reaction conditions (CH_2Cl_2 and $AlCl_3$), but gave (**10**) at room temperature].

The des-A-11-oxo steroid was a mixture of two separable isomers (**8a**) *anti-trans* (major) and (**7a**) *syn-cis* (minor). By epimerization (by either acid or base catalysis), (**7a**) led only to (**8a**).

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