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SYNTHESIS OF A POTENTIAL STEROID INTERMEDIATE BY ANIONIC OXY-COPE REARRANGEMENT

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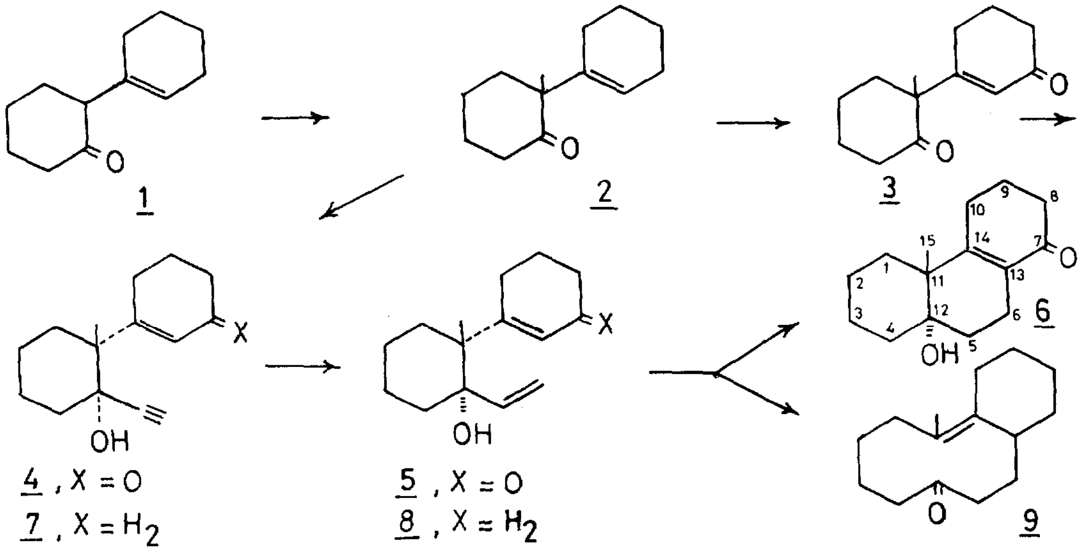
Abstract:

The synthesis of the tricyclic ketol 6 which is a potential intermediate for non-aromatic steroids has been achieved via an anionic oxy-Cope rearrangement.

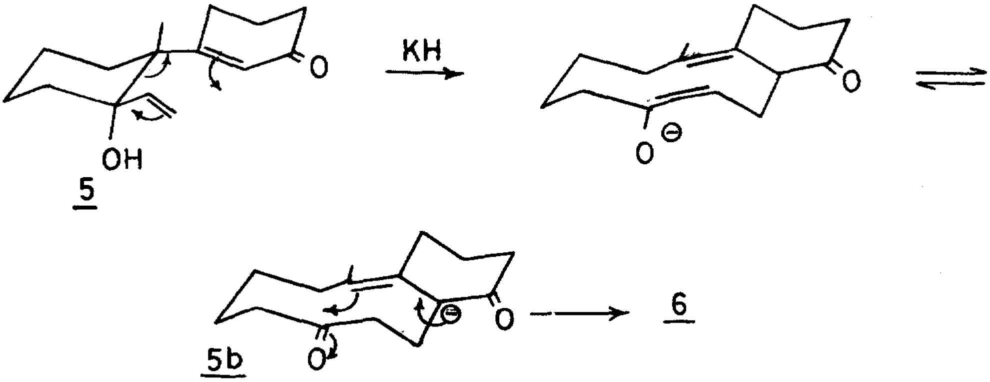
Previously we have reported[1] a new synthesis of angularly substituted octalins via an anionic oxy-Cope rearrangement. We report here an extension of the above methodology to the synthesis of the tricyclic hydroxy ketone 6 - a potential steroid intermediate. Scheme 1 outlines the steps involved:



Scheme 1

Methylation of the readily[2] available enone 1 (t-BuOK, MeI, RT, 14 h) gave[3] the ketone 2 (bp. 95-98°/0.7 mm, 65%). Oxidation of the ketone 2 (t-butylchromate t-BuOK, 40°C 40 h) gave the diketone 3 (mp. 45-46°, 52%). Direct ethynylation of diketone 3 occurrred at the enone carbonyl group. However selective ketalization (72%) of the enone carbonyl by Paquett's method[4] [CPTS $(CH_2\ OH)_2$ ØH, 14 h] followed by ethynylation (LiC≡CH, THF, - 78°, 2.5 h) furnished the desired ethynyl carbinol 4 (mp. 135-6°, 51%) after chromatography (SiO_2). Partial reduction of the carbinol 4 (Py, $Pd/CaCO_3$) gave the vinyl carbinol 5 (mp. 116-117°, 85%). Ethynylation of ketone 2 gave the carbinol 7 (mp. 110-112°, 86%) which upon partial reduction gave the vinyl carbinol 8 (75%) as a liquid after chromatography (SiO_2). X-ray analysis[5] of the crystalline carbinol 7 showed that the olefinic and acetylenic moieties are diequatorial. The vinyl carbinol 8 underwent rearrangement with KH in refluxing DME (1 h) to give the cyclodecaenone 9 (mp. 55-56°, 50%). The carbinol 5 however proved more reactive and rearranged under milder conditions (KH, DME, 0°, 1 h) followed by a transannular reaction to give the tricyclic ketol 6 as a viscous liquid (45%) after chromatography (SiO_2)[3].

The difference in the course of rearrangement of carbinols 5 and 8 must be due to the generation of a stabilized carbanion 5b due to the presence of an adjacent carbonyl group; this species (Scheme II) has the right stereoelectronic requirement for a nucleophilic attack on the carbonyl group to give the trans carbinol 6.



Scheme II

Acknowledgement:

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References:

1. K. Thangaraj, P.C. Srinivasan and S. Swaminathan, Tet. Lett. 23, 4983 (1982).
2. J. Plesk, Coll. Czech. Chem. Comm., 21,902(1956), C.A. 50, 7732(1956).
3. Spectral data for compound 6: IR($CHCl_3$) νmax 3600 (OH), 1670 (Conj C=O), 1610 cm^{-1}. (C=C). PMR ($CDCl_3$/TMS),δ 1.2 (s. 3H), 1.5-2.3 (m, 19H), CMR : in ppm; 200.12 (s. C_7), 170.48 (s, C_{14}), 127.20 (s, C_{13}), 73.85 (s, C_{12}) 47.82 (s, C_{11}), 19.82 (q, C_{15}) and other carbons at 42.45, 34.82, 37.24, 31.32, 28.88, 26.72, 24.50, 22.58, 20.72 as triplets respectively. Analysis $C_{15}H_{22}O_2$ calculated C = 76.88, H = 9.46, found C = 76.86, H = 9.47%. Satisfactory spectral and analytical data were obtained for all other compounds.
4. L.A. Paquette and T.J. Nitz. Tet. Lett. 25, 3047 (1984).
5. We thank Mr. V. Krishnaswamy, Department of Physics, I.I.T., Bombay for doing this X-ray analysis.

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