Concise Synthesis of 1,4a-Bifunctionalised Decalin Building Blocks by C-H Activation of Decalin

Mario Uosis-Martin, Mary F. Mahon, Maksims Yevglevskis and Simon E. Lewis*

Department of Chemistry, University of Bath, Bath, BA2 7AY, UK.
Fax: +44 (0)1225 386231
E-mail: s.e.lewis@bath.ac.uk

Received: The date will be inserted once the manuscript is accepted.

Abstract: Friedel–Crafts acylation of decalin introduces functionality at C1 and C4a, which may be elaborated to novel building blocks possessing a methyl ketone, methyl carbinol or vinyl group at the ring junction.

Key words: hydrocarbons, acylation, bicyclic compounds, alkenes, Wittig reaction.

Functionalised decalins occur widely in steroid1 and terpenoid2 natural products. As such, great efforts have been expended on developing synthetic routes to both cis-3 and trans-decalins.4 There has been particular interest in decalins bearing functionality both at C1 and at C4a, as these have found diverse applications in the pharmaceutical and fragrance industries.5 In the course of ongoing studies in total synthesis, we required access to vinyl trans-decalin bearing an axially disposed substituent at C1. Access to this vinyl alcohol 1 may be envisaged by means of a one-carbon homologation of 4a-vinyltrans-1-decalone (Scheme 1). Vinyl alcohol 1 has not been reported to date; surprisingly, nor has vinyl ketone 2. We therefore sought a concise, scalable route to these potentially useful building blocks from inexpensive starting materials.

Scheme 1

Baddeley and co-workers have reported an unusual Friedel–Crafts acylation of decalin 3 with aluminium trichloride and acetyl chloride.6 The reaction is believed to proceed by acylium ion-mediated hydride abstraction.7 Although such acylations have been reported for a variety of saturated hydrocarbon substrates,8 the decalin case is of particular synthetic utility, since careful control of the reaction conditions allows for formation of tricylic enol ether 4 as the major product (Scheme 2). Furthermore, the boiling point of 4 is distinct from that of the starting material (which accounts for most of the mass balance) or byproducts, allowing for large scale non-chromatographic purification by distillation. It has been shown5,9 that cis-decalin is much more reactive than trans-decalin under these reaction conditions; if a commercial mixture of cis- and trans-decalin is used, unreacted starting material is recovered that is enriched in the trans isomer. We have repeated this reaction on a large scale and disclose NMR data for 4 for the first time. Despite the apparent synthetic utility of this access to a selectively functionalised decalin, 4 has been exploited in synthesis only infrequently thus far.10

Scheme 2

Enol ether 4 serves as a useful entry to 2, as it possesses functionality in the desired positions, including the quaternary centre. Conditions have been established for the acidic hydrolysis of 4 and it is reported6c,d that both epimeric alcohols 5 and 6 may be accessed depending on the reaction conditions. We undertook hydrolysis of 4 under mild reaction conditions, obtaining 6 in 51% yield (Scheme 3). Unreacted 4 persisted regardless of reaction times, suggesting the ready reversibility of the ring opening; when 6 was resubjected to reaction conditions, 4 was observed to form. Hydroxyketone 6 may be isolated in pure form by crystallisation from the reaction mixture, as 4 is liquid at room temperature. The structures of 5 and 6 had been assigned initially by chemical correlation and on the basis of their IR spectra.6c,d Crystalline 6 was subjected to x-ray crystallographic analysis (Figure 1), confirming the original structural assignment.

Scheme 3
Conversion of the methyl ketone functionality in 6 to a vinyl group is formally a reductive transformation. Accordingly, the alcohol in 6 was protected as a silyl ether, followed by reduction with DIBAL-H to furnish 8 as a single diastereomer. In order to assign the relative configuration of the newly-installed stereocentre in 8, precursor 7 was also reduced with LiAlH₄, which was not entirely diastereoselective. An acidic workup of this latter reaction served to remove the protecting group in situ, furnishing diastereomeric diols 11 and 12 (Scheme 4). The major epimer was diol 11, identical to material formed by desilylation of 8. The relative configuration of 11 was confirmed by x-ray crystallography (Figure 2). Attempts at sulfonylation of 8 in order to effect elimination to the desired vinyldecalin 10 were unsuccessful, which we ascribe to steric hindrance of the neopentyl hydroxyl group.

As an alternative approach to 1 and 2, we opted to elaborate 6 by means of a Shapiro reaction. Treatment with 2-mesitylenesulfonylhydrazide gave hydrazone 13, which could also be accessed directly from enol ether 4 (in a yield of 66%). When 13 was exposed to 3 equivalents of butyllithium (required due to the presence of the free hydroxyl group) followed by protic quench, vinyl alcohol 14 was accessed in good yield (Scheme 5).

From vinyl alcohol 14, vinyl ketone 2 was accessed by Swern oxidation. A subsequent serendipitous observation was that the vinyl group in 2 is inert to hydroboration with 9-BBN, this reagent instead effecting unexpected ketone reduction back to 14 and its epimer 15; no other products were recovered (Scheme 6).

The inertness of the vinyl group in fact permits access to the desired target 1 in a simple two-step sequence. Wittig methylenation of the ketone in 2 (best achieved with KO²Bu as base) provides bis(alkene) 16 without epimerisation at the ring junction. In a remarkable transformation, hydroboration of 16 with 9-BBN displays total regio- and diastereoselectivity; treatment of the hydroboration product with basic peroxide furnishes 1 as the sole isomer and in good yield (Scheme 7).
The relative configuration of 1 was established by Swern oxidation to the corresponding aldehyde 17. In the NOESY spectrum of 17, correlation was observed between the aldehyde proton and the vinyl group methine (Scheme 8).

In summary, we have demonstrated concise access to a range of 1,4a-bifunctionalised decalin derivatives which are likely to find diverse applications in synthesis. Our studies in total synthesis employing these building blocks are ongoing and results will be reported in due course.

Supporting Information for this article is available online at http://www.thieme-connect.de/ejournals/toe/synlett.

Acknowledgment

We thank EPSRC for funding (DTA studentship to M.U.M.). We also thank Prof. J. Grant Buchanan and Dr. Andrew Silvanus (Bath) for helpful discussions.

References


(11) 6: CCDC #824429. 11: CCDC #824430.
1,4a-Bifunctionalised Decalins

R^1, R^2 = H, OH, OTBDMS, =O, =CH_2, CH_2OH, CHO
R^3 = COCH_3, CH(OH)CH_3, CH=CH_2