



Amberlyst-15-catalyzed intramolecular S_N2' oxaspirocyclization of tertiary allylic alcohols

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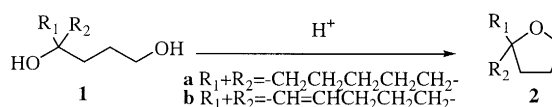
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Abstract

A variety of substituted 1-oxaspiro[4.5]dec-6-ene and 1-oxaspiro[5.5]undec-7-ene systems have been prepared by utilizing Amberlyst-15-catalyzed S_N2' oxaspirocyclizations under mild reaction conditions (-20°C) in quantitative yields. In this process, a tertiary allylic alcohol serves as the precursor of π -allylic carbocation and the primary, secondary or tertiary alcohol within the same molecule serves as the nucleophile. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Amberlyst-15; S_N2' oxaspirocyclization; tertiary allylic alcohols; allylic oxaspirocycles.

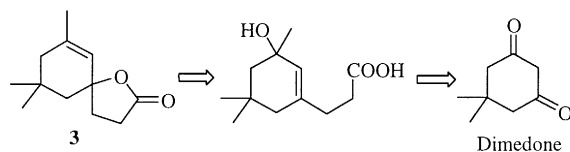
The syntheses of oxaspirocycles **2** are available from the tertiary alcohols **1** that can form stabilized carbocations under acid treatment, and internal capture by the second hydroxy group to form oxaspirocycles^{1,2} (Scheme 1). Sometimes the same strategy cannot be extended to the preparation of allylic oxaspirocycles such as **2b** since the precursor **1b** has a marked tendency towards elimination³ of the tertiary and allylic alcohol. In view of this difficulty, Constantino et al.³ developed a circuitous route for the synthesis of allylic spiro- α -lactone **3** starting from dimedone in an overall yield of 8.8% (Scheme 2).



Scheme 1.

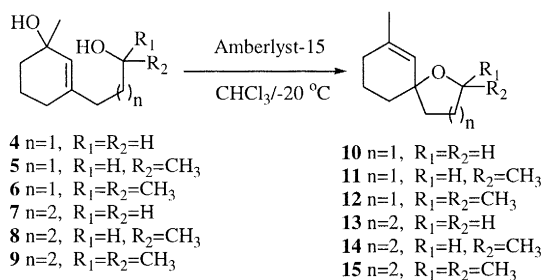
Palladium-catalyzed oxaspirocyclization of conjugated diene⁴ or allylic ester⁵ by using alkoxides as nucleophiles has also emerged as a synthetically versatile method for constructing allylic oxaspirocycle systems. But tertiary alkoxides have not been widely used as nucleophiles in π -allyl palladium chemistry.

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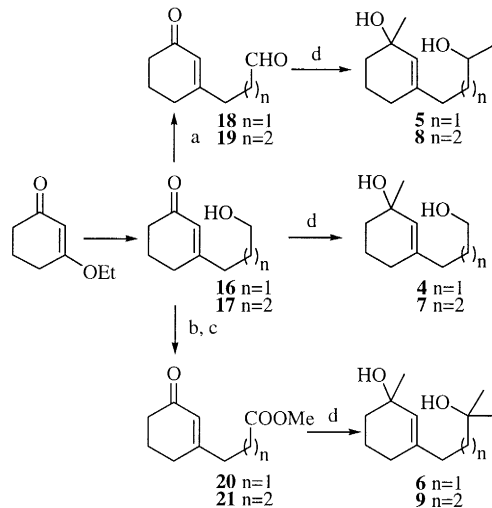
Scheme 2.

In this report, we demonstrate that the route for Amberlyst-15-catalyzed intramolecular S_N2' oxaspirocyclizations of tertiary allylic alcohols **4–9**, even in the case of sterically hindered tertiary nucleophile, can be applied to the syntheses of allylic oxaspirocycles in quantitative yields (Scheme 3).



Scheme 3.

The syntheses of tertiary allylic alcohols **4–9** were accomplished as outlined in Scheme 4. The sequence was initiated by the reaction of the Normant Grignard reagent⁶ with the vinylogous ester 3-ethoxy-2-cyclohexen-1-one. The resulting ketoalcohols **16** and **17** were oxidized to the aldehydes **18** and **19**⁷ (PCC, CH_2Cl_2 , room temperature) and methyl esters **20** and **21** (Jones reagent, acetone, $0^\circ C$ then CH_2N_2 , diethyl ether, $0^\circ C$). The alcohols, aldehydes and esters were converted to their corresponding tertiary allylic alcohols **4–9** by treatment with methylolithium in THF at $-40^\circ C$ in quantitative yields without any purification.

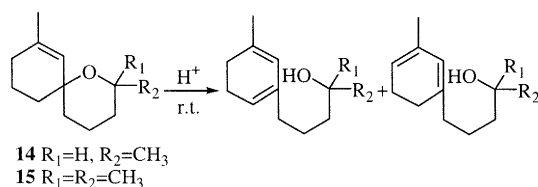


Scheme 4. (a) PCC, CH_2Cl_2 , room temperature; (b) Jones reagent, acetone, $0^\circ C$; (c) CH_2N_2 , diethyl ether, $0^\circ C$; (d) CH_3Li /diethyl ether, THF, $-40^\circ C$

All the tertiary allylic alcohols **4–9** underwent S_N2' oxaspirocyclization on treatment with Amberlyst-15 ($CHCl_3$, $-20^\circ C$) to produce the corresponding 1-oxaspiro[4.5]dec-6-enes **10–12** and 1-oxaspiro[5.5]undec-7-enes **13–15** in quantitative yields. Amberlyst-15 is a macroreticular sulfonic

acid-based polystyrene cationic exchange resin, and thus the work-up procedure⁸ is very simple, involving only filtration of the resin and removal of the solvent to obtain the product in a high state of purity.

The competing elimination reaction (Scheme 5) was only observed in the case of 2-substituted 1-oxaspiro[5.5]undec-7-ene systems at room temperature. Lowering the reaction temperature to -20°C can prevent the elimination reaction from occurring.



Scheme 5.

In summary, allylic oxaspirocycles are readily accessible by Amberlyst-15-catalyzed intramolecular $\text{S}_{\text{N}}2'$ oxaspirocyclization of tertiary allylic alcohols from simple starting materials with high yields and easy work-up features. They can be further functionalized and should provide useful entries to the total synthesis of oxaspirocyclic natural products (such as: thespirane, thespirone, vetispirane, dactyloxene B, etc.).

General experimental procedure: Preparation of 7-methyl-1-oxaspiro[4.5]dec-6-ene (**10**): Amberlyst-15 resin (20 mg) was added to a solution of tertiary allylic alcohol **4** (73 mg, 0.429 mmol) in 5 ml of chloroform (stabilized with 2-methyl-2-butene, Merck cat. No. 2444). The mixture was then stirred at -20°C for 1 h under nitrogen. The reaction mixture was filtered through KHCO_3 , and concentrated under rotary evaporator/aspirator system to give **10** (65 mg, 0.427 mmol, 99.5%) in a high state of purity without a purification procedure.

Acknowledgements

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