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

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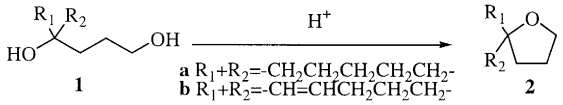
**Abstract**

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. 

*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 elimination[3] 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 diene[4] or allylic ester[5] 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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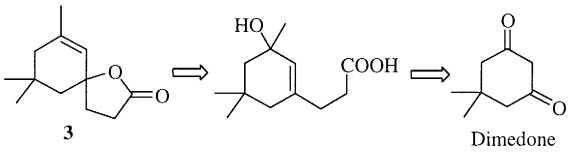
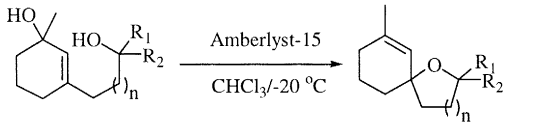



Scheme 2.

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).

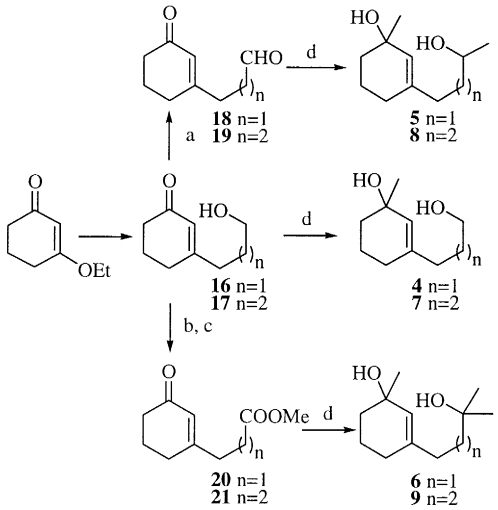



**4** n=1, $R_1$=$R_2$=H
**5** n=1, $R_1$=H, $R_2$=$CH_3$
**6** n=1, $R_1$=$R_2$=$CH_3$
**7** n=2, $R_1$=$R_2$=H
**8** n=2, $R_1$=H, $R_2$=$CH_3$
**9** n=2, $R_1$=$R_2$=$CH_3$

**10** n=1, $R_1$=$R_2$=H
**11** n=1, $R_1$=H, $R_2$=$CH_3$
**12** n=1, $R_1$=$R_2$=$CH_3$
**13** n=2, $R_1$=$R_2$=H
**14** n=2, $R_1$=H, $R_2$=$CH_3$
**15** n=2, $R_1$=$R_2$=$CH_3$

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 reagent[6] 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°C then $CH_2N_2$, diethyl ether, 0°C). The alcohols, aldehydes and esters were converted to their corresponding tertiary allylic alcohols **4**–**9** by treatment with methyllithium in THF at −40°C in quantitative yields without any purification.

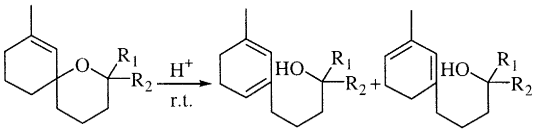



Scheme 4. (a) PCC, $CH_2Cl_2$, room temperature; (b) Jones reagent, acetone, 0°C; (c) $CH_2N_2$, diethyl ether, 0°C; (d) $CH_3Li$/diethyl ether, THF, −40°C

All the tertiary allylic alcohols **4**–**9** underwent $S_N2'$ oxaspirocyclization on treatment with Amberlyst-15 ($CHCl_3$, −20°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 procedure[8] 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.




**14** $R_1$=H, $R_2$=$CH_3$
**15** $R_1$=$R_2$=$CH_3$

Scheme 5.

In summary, allylic oxaspirocycles are readily accessible by Amberlyst-15-catalyzed intramolecular $S_N2'$ 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: theaspirane, theaspirone, 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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## References

1. Eaton, P. E.; Cooper, G. F.; Johnson, R. C.; Mueller, R. H. *J. Org. Chem.* **1972**, *37*, 1947–1950.
2. Mudryk, B.; Cohen, T. *J. Org. Chem.* **1989**, *54*, 5657–5659.
3. Constantino, M. G.; Beltrame Jr., M.; de Medeiros, E. F.; da Silva, G.-V. J. *Synth. Commun*. **1992**, 22, 2859–2864.
4. Andersson, P. G.; Nilsson,Y. I. M.; Bäckvall, J.-E. *Tetrahedron* **1994**, *50*, 559–572.
5. Stanton, S. A.; Felman, S. W.; Parkhurst, C. S.; Godleski, S. A. *J. Am. Chem. Soc.* **1983**, *105*, 1964–1969.
6. Cahiez, G.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1978**, 3013–3014.
7. Godleski, S. A.; Valpey, R. S. *J. Org. Chem.* **1982**, *47*, 381–383.
8. Coppola, G. M. *Synthesis* **1984**, 1021–1023.