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Synthesis of Tetrahydrofurans and Pyrans *via* Palladium(0)-Mediated Cyclisation

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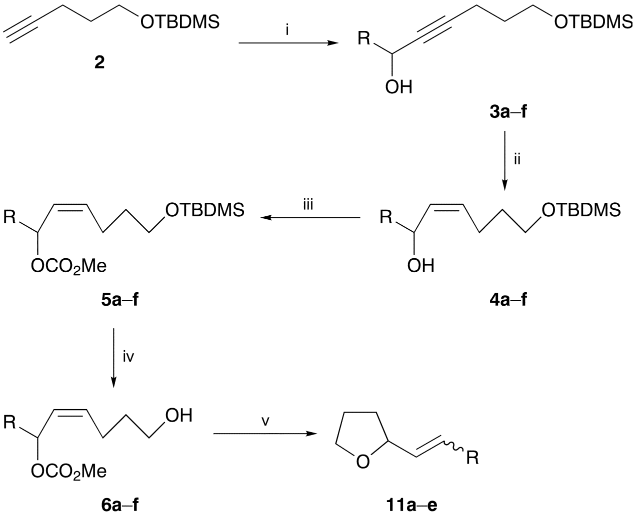
Palladium(0)-catalysed cyclisation of the appropriate hydroxy allylic carbonates in THF allowed the formation of tetrahydrofurans and pyrans *via* a 5-*exo-trig* or a 6-*exo-trig* mechanism; preliminary experiments in the presence of palladium complexes associated with chiral ligands gave the expected substituted tetrahydrofurans with low enantioselectivities.

The regio- and stereo-selective synthesis of tetrahydrofurans and pyrans is an important challenge as they are key structures of natural compounds such as ionophores. Following our work concerning the palladium(0) catalysed formation of the carbon–oxygen bond,[29–35] we report a palladium(0) based cyclisation of an appropriate hydroxy allylic carbonate leading to substituted tetrahydrofurans and pyrans.

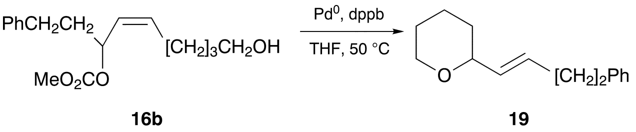


a R = Ph; **b** R = 2-MeC$_6$H$_4$; **c** R = PhCH$_2$CH$_2$; **d** R = *c*-C$_6$H$_{11}$
e R = *n*-C$_6$H$_{13}$; **f** R = *tert*-butyl

Scheme 1 *Reagents and conditions:* i, BuLi, RCHO, THF, DMPU, −40 °C then −10 °C; ii, H_2, Lindlar Pd, MeOH, 25 °C; iii, $ClCO_2Me$, C_5H_5N, DMAP, CH_2Cl_2, 25 °C; iv, $Bu_4NF.3H_2O$, THF, 25 °C; v, Pd^0–dppb, THF, 50 °C

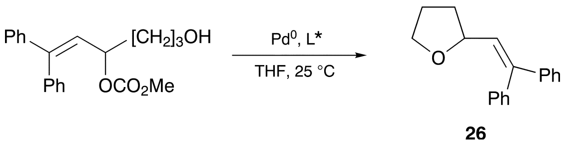
Condensation of the lithio derivative of protected pent-1-yn-5-ol **2** with various aldehydes (Scheme 1) gave the prop-2-ynylic alcohols **3** in good yields whose hydrogenation with hydrogen in the presence of Lindlar palladium led to the (*Z*) allylic alcohols **4**. Reaction of alcohols **4** with methyl chloroformate in the presence of pyridine and DMAP gave the expected protected allylic carbonates **5**. The desired hydroxy allylic carbonates **6** were obtained by deprotection of the hydroxy function of **5**. When these compounds **6** were treated with a catalytic amount of palladium(0) associated with 1,4-bis(diphenylphosphino)butane in THF at 50 °C, the corresponding unsaturated tetrahydrofurans **11** were obtained in good yields, *via* a 5-*exo-trig* mechanism.

The use of hex-1-yn-6-ol instead of pent-1-yn-5-ol in this sequence led to the formation of the unsaturated tetrahydropyran **19** *via* the same mechanism (Scheme 2), although the use of but-1-yn-4-ol gave only dienes **17** and **18** resulting from *β*-elimination.



Scheme 2

Preliminary experiments concerning the cyclisation of the prochiral allylic carbonate **24** in the presence of palladium(0) associated with chiral ligands led to the expected unsaturated tetrahydrofuran **26**, but with low enantioselectivities (Scheme 3).



Scheme 3

Techniques used: ^{1}H and ^{13}C NMR and chiral HPLC

References: 38

Schemes: 9

Tables: 2 (yields for products of condensation, hydrogenation, methoxycarbonylation and deprotection; enantioselectivities in the cyclisation reaction)

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