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Intramolecular Acryloxypalladation. Stereospecific Synthesis of Ring Fused Unsaturated α-Methylene γ-Butyrolactones.

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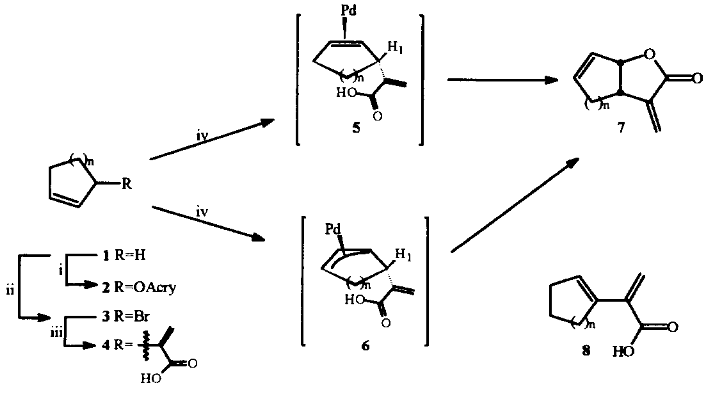
Abstract : The intramolecular carboxypalladation reaction [$Pd(OAc)_2$ 5 mol %, NaOAc 2 eq, O_2, THF, rt] of 2-(2-Cycloalken-1-yle) propenoic acids yields ring fused α-methylene γ-butyrolactones with good yields (75-80%).

Palladium catalyzed acryloxypalladation of double bonds allows a one step synthesis of α–methylene γ–butyrolactones [1], without involving the use of carbon monoxide.[2] However the formation of the lactone depends on the double bond structure : with cycloalkenes **1a, b, c** the π allyl formation competes efficiently with the 1,2 addition of the acrylic carboxylate, so that allylic acrylates **2a, b, c** are the unique reaction products. This behaviour parallels the one observed for acetoxypalladation,[3] but is a drawback for the synthesis of fused ring lactones.



i : in AcryOH Catalyst A; $Pd(OAc)_2$, Benzoquinone, MnO_2.
Catalyst B; $Pd(OAc)_2$, NaOAc, O_2.
ii : NBS, AIBN, CCl_4, reflux, 1 h.
iii : a) Dibal-H, ethylpropynozte, HMPA, THF, 1h 0°c and 16h at 25°C. b) NaOH, H_2O, EtOH,reflux,1h.
iv : in THF Catalyst A; $Pd(OAc)_2$, Benzoquinone, MnO_2.
Catalyst B; $Pd(OAc)_2$, NaOAc, O_2.
a, n=1; **b**, n=2; **c**, n=3.

However ring fused α–methylene γ–butyrolactones such as **7a, b, c** should be obtained from **4a,b,c** whatever mechanism is involved : intramolecular -1,2 carboxypalladation of the double bound of **5a, b, c** or intramolecular attack on carbon-2 of π allyl complex **6a, b, c**.

We have therefore prepared α substituted acrylic acids **4a,b,c** in three steps from the corresponding cycloalkenes **1a,b,c**. Allylic bromination of the latter yields bromides **3a, b, c** which are further reacted with ethylpropynoate in presence of Dibal-H in HMPA.[4, 5] The carboethoxyvinyl intermediate thus obtained are then transformed into the corresponding acids **4a,b,c**.[6]

Preliminary experiments have shown that catalyst **A** [$Pd(OAc)_2$, benzoquinone, MnO_2] used by Bäckvall[7] for acetoxypalladation was efficient in yielding exclusively the lactones **7a,b,c,** with good yields (75-80%). However the work up of the reaction mixture is much more convenient with catalyst **B** [$Pd(OAc)_2$, NaOAc, O_2, THF] which has been previously used by Larock to achieve efficient intramolecular lactonization reactions (with the less practical DMSO solvent).[8] It is interesting to note that we did not observe isomerization products such as **8a, b, c** or derivatives thereof, which should have been observed if a π allyl complex would have formed.

Control experiments with either catalyst **A** or **B**, have shown that intermolecular acryloxypalladation of **1a,b,c** with acrylic acid exclusively yields allylic acrylates **2a, b, c**. It is therefore clear that intramolecular acryloxypalladation of derivatives such as **4a,b,c** provides an efficient entry into fused ring α–methylene γ – butyrolactones.[9] These products are known to present a wide range of biological activities[10] and present an interesting challenge in metal catalyzed synthesis.[11]

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