

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

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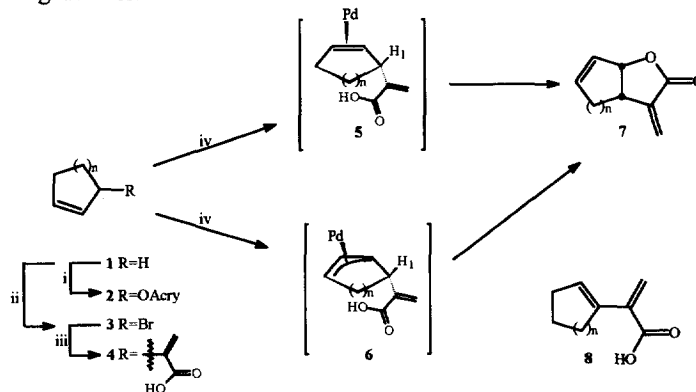
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Abstract : The intramolecular carboxypalladation reaction [Pd(OAc)₂ 5 mol %, NaOAc 2 eq, O₂, THF, rt] of 2-(2-Cycloalken-1-yl) propenoic acids yields ring fused α -methylene γ -butyrolactones with good yields (75-80%).

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Palladium catalyzed acryloxypalladation of double bonds allows a one step synthesis of α -methylene γ -butyrolactones¹, 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, MnO₂.
Catalyst B; Pd(OAc)₂, NaOAc, O₂.

ii : NBS, AIBN, CCl₄, reflux, 1 h.

iii : a) Dibal-H, ethylpropynoate, HMPA, THF, 1h 0°C and 16h at 25°C. b) NaOH, H₂O, EtOH, reflux, 1h.

iv : in THF Catalyst A; Pd(OAc)₂, Benzoquinone, MnO₂.

Catalyst B; Pd(OAc)₂, NaOAc, O₂.

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 bond 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** [$\text{Pd}(\text{OAc})_2$, benzoquinone, MnO_2] used by Bäckvall⁷ for acetoxy-palladation 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** [$\text{Pd}(\text{OAc})_2$, 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 acryloxy-palladation of **1a,b,c** with acrylic acid exclusively yields allylic acrylates **2a, b, c**. It is therefore clear that intramolecular acryloxy-palladation 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 activities¹⁰ and present an interesting challenge in metal catalyzed synthesis.¹¹

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