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Tetrahedron Letters

Tetrahedron Letters 46 (2005) 285–287

Platinum(II)/europium(III)-catalyzed intramolecular hydroalkylation of 4-pentenyl β-dicarbonyl compounds

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Received 11 October 2004; revised 9 November 2004; accepted 10 November 2004
Available online 26 November 2004

Dedicated to Professor Iwao Ojima on the occasion of his 60th birthday in honor of his contributions to synthetic organic, organometallic, and medicinal chemistry

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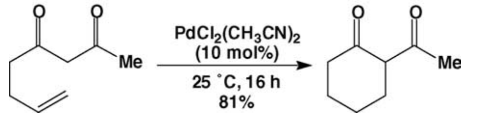
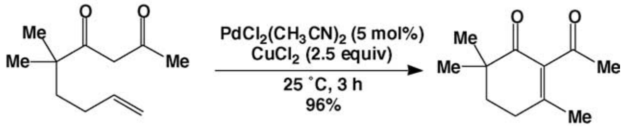
Abstract—Reaction of 5,5-dimethyl-8-nonene-2,4-dione with a catalytic mixture of $[PtCl_2(CH_2{=}CH_2)]_2$ (**2**) (1 mol%), and $EuCl_3$ (2 mol%) in dioxane that contained HCl (1.0 equiv) at 90 °C for 18 h led to the isolation of 2-acetyl-3,6,6-trimethyl-2-cyclohexanone in 85% yield. A number of 4-pentenyl β-dicarbonyl compounds underwent intramolecular hydroalkylation to form cyclohexanones in moderate to excellent yield.

We recently reported the Pd(II)-catalyzed intramolecular hydroalkylation of 3-butenyl β-dicarbonyl compounds and related substrates (Eq. 1), which represent the first examples of the catalytic hydroalkylation of an unactivated olefin with a stabilized carbon nucleophile.[1–3] However, efforts to extend this protocol to the hydroalkylation of 4-pentenyl β-dicarbonyl compounds have not been successful as 4-pentenyl β-dicarbonyl compounds instead tend to undergo oxidative alkylation in the presence of Pd(II) to form cyclohexenones (Eq. 2).[3,4] The difficulty in extending palladium-catalyzed hydroalkylation to 4-pentenyl β-dicarbonyl compounds can be traced to the mechanism of hydroalkylation. Specifically, the initially formed palladium alkyl complex **I** does not react with HCl to release the cyclohexanone but instead undergoes isomerization via iterative β-hydride elimination/addition to form palladium enolate complex **II** that undergoes protonolysis (Scheme 1).[2,3] Therefore, palladium-catalyzed olefin hydroalkylation can be achieved only when the requisite palladium enolate complex is formed prior to olefin displacement from a palladium olefin intermediate.



(1)



(2)

For the reasons noted above, we sought to identify a transition metal complex that would catalyze the hydroalkylation of alkenyl β-dicarbonyl compounds through a pathway involving nucleophilic attack on a metal–olefin complex followed by protonolysis of the resulting metal-alkyl species prior to β-hydride elimination. The olefin ligand of Pt(II)–olefin complexes are readily attacked by carbon[5] and heteroatom[6] nucleophiles to form Pt(II)–alkyl complexes that, in sharp contrast to a Pd(II)–alkyl complex, are stable with respect to β-hydride elimination but reactive toward protonolysis. On the basis of this reactivity, we began to investigate the application of simple Pt(II) complexes as catalysts for the addition of carbon and heteroatom nucleophiles to unactivated olefins. These efforts have led to the development of effective Pt(II)-catalyzed protocols for the intermolecular hydroalkylation[7] and hydroamination[8] of ethylene with β-diketones and carboxamides, respectively, the intramolecular hydroarylation of alkenyl indoles,[9] and the intramolecular hydroalkoxylation of hydroxy olefins.[10] These results, in particular the hydroalkylation of ethylene with β-diketones, suggested that

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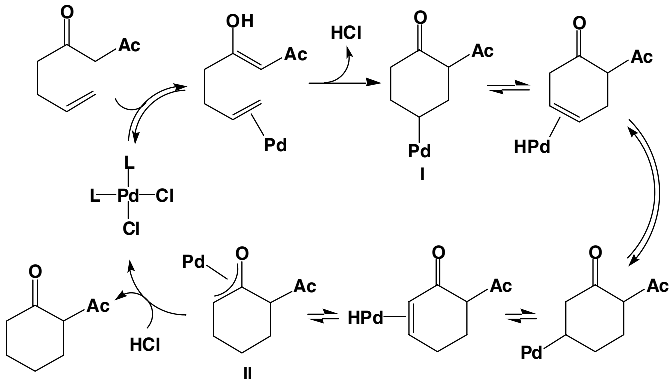
doi:10.1016/j.tetlet.2004.11.060



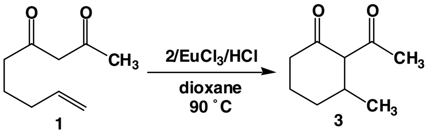
Scheme 1.

Pt(II) complexes might also catalyze the intramolecular hydroalkylation of 4-pentenyl β-dicarbonyl compounds. Here we report the Pt(II)/Eu(III)-catalyzed hydroalkylation of 4-pentenyl β-dicarbonyl compounds to form substituted cyclohexanones.

In an initial experiment, treatment of 8-nonene-2,4-dione (**1**) with a catalytic amount of $[PtCl_2(CH_2{=}CH_2)]_2$ (**2**) (2.5 mol%) in dioxane at 90 °C for 19 h led to 66% conversion to form **3** in 13% GC yield (Table 1, entry 1). On the assumption that protonolysis of the Pt–C bond of the initially formed platinum alkyl species was slow under these conditions, we explored the effect of acid on the platinum-catalyzed conversion of **1** to **3**. In support of our hypothesis, treatment of **1** with a catalytic amount of **2** (2.5 mol%) in dioxane that contained HCl at 90 °C for 22 h formed **3** in 63% GC yield and 45% isolated yield (Table 1, entry 2). Because both lanthanide[11] and transition metal[12] Lewis acids catalyze the addition of β-dicarbonyl compounds to Michael acceptors, we considered that a Lewis acid might also facilitate the platinum-catalyzed cyclization of **1**.[13] We focused on the use of $EuCl_3$ as a Lewis acid co-catalyst for platinum-catalyzed olefin hydroalkylation because we had previously employed $EuCl_3$ to good effect in the Pd-catalyzed oxidative alkylation of propene with β-dicarbonyl compounds.[7] Treatment of **1** with a mixture of **2** (2.5 mol%) and $EuCl_3$ (5 mol%) in dioxane that contained HCl formed **3** in 76% GC yield and 64% isolated yield (Table 1, entry 3). Employing this procedure, catalyst loading was dropped to 1% of **2** and 2% of $EuCl_3$ without decrease in the isolated yield of **3**, although longer reaction time was required (Table 1, entry 4). Platinum(II) was required for cyclization and treatment of **1** with $EuCl_3$ (2 mol%) and HCl (1 equiv) in dioxane at 90 °C for 21 h formed no detectable amounts of **3** by GC analysis of the crude reaction mixture (Table 1, entry 5).

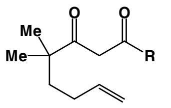
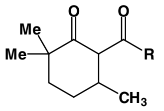
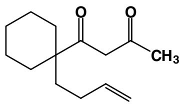
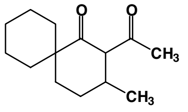
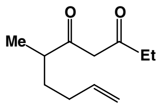
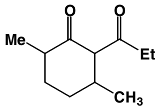
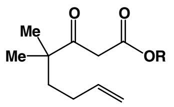
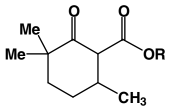
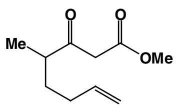
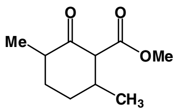
A number of 4-pentenyl β-diketones underwent Pt/Eu-catalyzed hydroalkylation to form the corresponding cyclohexanones in moderate to excellent yield (Table 2).

Table 1. Effect of HCl, $EuCl_3$, and catalyst loading on the conversion of **1** to **3** catalyzed by $[PtCl_2\ (CH_2{=}CH_2)]_2$ (**2**)



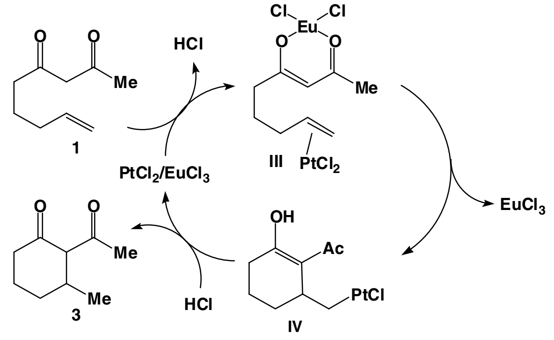
Entry	**2** (mol%)	HCl (equiv)	$EuCl_3$ (mol%)	Time (h)	GC yield(%)	Isolated yield (%)
1	2.5	—	—	19	13	—
2	2.5	1	—	22	63	45
3	2.5	1	5	22	76	64
4	1	1	2	41	—	64
5	—	1	2	21	0	—

Table 2. Hydroalkylation of 4-pentenyl β-dicarbonyl compounds catalyzed by $[PtCl_2(CH_2{=}CH_2)]_2$ (**2**) (1 mol%), and $EuCl_3$ (2 mol%) in dioxane that contained HCl (1.0 equiv) at 90 °C for 18–22 h

Entry	Substrate	Cyclohexanone	Yield (%)[a]
			
1	R = Me		85
2	R = Et		87
3	R = *i*-Pr		91
4	R = *t*-Bu		55[b]
5	R = Cy		89
6			93
7			31
			
8	R = Me		66
9	R = Et		77
10	R = *i*-Pr		80
11			40

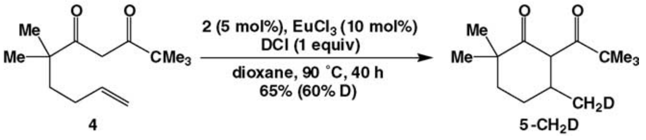
[a] Isolated yields of >95% purity.

[b] Reaction run with 2.5 mol% of **2** for 63 h.



Scheme 2.

4-Pentenyl β-diketones that possessed *gem*-dimethyl groups on the alkenyl chain were particularly effective substrates for Pt/Eu-catalyzed hydroalkylation, presumably due to the Thorpe–Ingold effect on cyclization (Table 2, entries 1–6).[14] 4-Pentenyl β-keto esters also underwent Pt/Eu-catalyzed hydroalkylation to form the corresponding 2-carboalkoxycyclohexanones in moderate to good yield (Table 2, entries 8–11). Substitution of DCl for HCl in the Pt/Eu-catalyzed cyclization of β-diketone **4** led to isolation of **5**-CH_2D in 65% yield as the exclusive deuterated isotopomer (Eq. 3).



(3)

On the basis of the mechanisms of the palladium[2,3] and platinum-catalyzed[9] addition of carbon nucleophiles to unactivated olefins and the mechanisms of the stoichiometric addition of carbon and nitrogen nucleophiles to platinum olefin complexes,[5,6] we propose a mechanism for the Pt/Eu-catalyzed intramolecular hydroalkylation of **1** involving outer-sphere attack of a europium enolate on the platinum-complexed olefin of **III** to form the platinum cyclohexylmethyl species **IV** (Scheme 2). Protonolysis of the Pt–C bond of **IV** with HCl would release **3** and regenerate the Pt(II) catalyst. Direct protonolysis of the Pt–C bond of **IV** is supported by the formation of **5** –CH_2D as the exclusive deuterated isotopomer in the Pt/Eu-catalyzed hydroalkylation of **4** (Eq. 3).

In summary, we have developed an effective Pt/Eu-catalyzed protocol for the intramolecular hydroalkylation of 4-pentenyl β-dicarbonyl compounds to form substituted cyclohexanones.

Acknowledgements

Acknowledgement is made to the NSF (CHE-03-04994) for support of this research. R.W. thanks the Camille and Henry Dreyfus Foundation and GlaxoSmithKline for additional unrestricted financial assistance.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2004.11.060. Experimental procedures and spectroscopic data for new compounds (4 pages).

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