Tetrahedron Letters 49 (2008) 5090–5093

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Solvent-free hydroalkylation of olefins with 1,3-diketones catalyzed by phosphotungstic acid

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ARTICLE INFO

Article history:
Received 3 April 2008
Revised 31 May 2008
Accepted 6 June 2008
Available online 12 June 2008

Keywords:
Solvent-free
Hydroalkylation
Olefin
1,3-Diketone
Phosphotungstic acid

ABSTRACT

An efficient and convenient method for the direct hydroalkylation of styrene and norborene with 1,3-diketones has been developed by using 12-phosphotungstic acid as an eco-friendly, and air- and moisture-tolerable catalyst. Reactions proceeded without any solvent, providing a clean access to alkylated 1,3-diketones.

The construction of carbon–carbon bonds is among the most important concerns in modern organic chemistry.[1] The alkylation of 1,3-dicarbonyl compounds is one of the most common methods for carbon–carbon bond formation. Traditionally, however, organic halides are employed as typical electrophiles in these reactions, and a stoichiometric amount of bases, which would generate undesired byproducts and decrease the atom economy, is required.[2] Nowadays, an emphasis in green chemistry is to develop environmentally benign routes, which hold significant potential for reduction of byproduct and waste, and lowering of energy cost.[3] Therefore, the catalytic direct alkylation of 1,3-dicarbonyl compounds with alkenes would provide a greener alternative.

In 1993, a pioneer work on ruthenium-catalyzed hydroarylation of alkenes was accomplished by Murai and co-workers.[4] After that, extensive studies have been focused on the exploration of efficient catalytic system to promote the addition of active methylene compounds to alkenes. Widenhoefer and co-workers reported an elegant palladium-catalyzed intramolecular hydroalkylation of alkenyl 1,3-diketones to form 2-acylcyclohexanones,[5] which was later improved by employing lanthanide triflates as additives.[6] Che and co-workers described a Au(I) complexes-catalyzed intramolecular addition of β-ketoamide to unactivated alkenes.[7] Furthermore, platinum- or palladium-catalyzed intermolecular additions of ethylene and propylene with 1,3-diketones has also been realized.[8] Hartwig and co-workers disclosed the palladium-catalyzed addition of the α-C–H bond of monocarbonyl and 1,3-dicarbonyl compounds to conjugated dienes.[9] Trost and co-workers reported an elegant asymmetric hydroalkylation reaction of allenes with pronucleophiles.[10] Very recently, Li and co-workers developed a new system for the highly effective intermolecular addition of active methylene compounds to alkenes by using gold and silver as the catalysts.[11] Since then, various Lewis acids such as bismuth triflate,[12] ferric chloride,[13] indium chloride,[14] Lewis acidic ruthenium complex,[15] a combination of gallium triflate and triflic acid,[16] as well as Brønsted acid such as proton-exchanged montmorillonite[17] have been employed to facilitate this transformation.

On the other hand, heteropoly acids (HPAs) such as 12-phosphotungstic acid (PWA) and 12-phosphomolybdic acid (PMA), which are often regarded as green catalysts for their commercial availability, stability, reutilization, and clean reaction processes,[18] are promising and highly active solid acids as an alternative to traditional metal catalysts.[19]

Moreover, solvent-free reactions have been paid more and more attentions recently, often providing clean, efficient, and high-yielding organic processes in modern synthetic chemistry.[20] Recently, we reported a highly efficient C–N bond formation reaction promoted by PWA.[21] In our continuous interest in solvent-free organic reactions,[22] herein, we demonstrate a convenient hydroalkylation reaction of styrene and norbornene with 1,3-dicarbonyl compounds mediated by PWA without any solvent.

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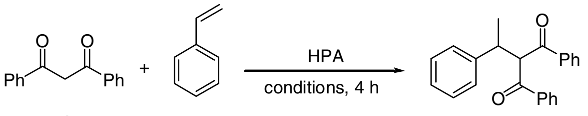
doi:10.1016/j.tetlet.2008.06.029

Table 1
Optimizing reaction conditions of direct hydroalkylation reaction of styrene with 1,3-diphenylpropane-1,3-dione[a]



1a **2a** **3a**

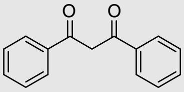
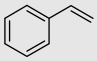
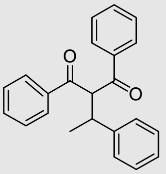
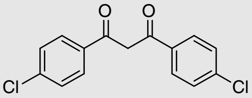
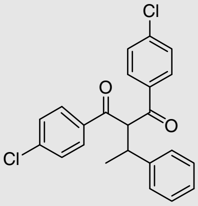
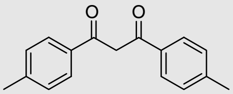
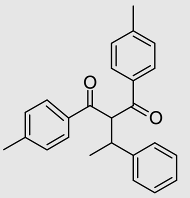
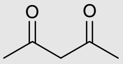
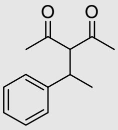
Entry	Solvent	T/°C	Yield[b] (%)
1	Neat	20	Trace
2	Neat	40	48
3	Neat	60	65
4	Neat	70	87
5	Neat	80	94
6	Neat	100	90
7[d]	Neat	80	60
8	CH_3NO_2	80	Trace
9	DCE	Reflux	42
10	TCE	80	20
11	CH_3CN	Reflux	Trace
12	*n*-Heptane	80	Trace
13	Toluene	80	Complex
14	THF	Reflux	NR[c]
15	EtOAc	Reflux	NR[c]
16	DMF	80	NR[c]
17	DMSO	80	NR[c]
18	PEG-400	80	NR[c]
19	H_2O	80	NR[c]

[a] Unless otherwise specified, all the reactions were performed with 0.25 mmol (56.1 mg) of **1a**, 0.87 mmol (90.6 mg) of **2**, and 5 mg of PWA in neat or the presence of 2 mL of indicated solvent.
[b] Isolated yield.
[c] No reaction.
[d] PMA was used as the catalyst.

Initial studies were conducted using 1,3-diphenylpropane-1,3-dione (**1a**) and styrene (**2**) as a prototype reaction. Various reaction conditions of this transformation were extensively investigated with the results summarized in Table 1. The PWA-catalyzed solvent-free reaction at 20 °C only afforded trace product (entry 1). Elevating the reaction temperature increased the yields obviously (entries 2–5). When the reaction was performed under neat condition at 80 °C, to our delight, it proceeded mildly and rapidly, delivering the final adduct in excellent yield (94%) within 4 h (entry 5). Further elevating the temperature was not beneficial, affording the product in a slightly decreased yield (entry 6). When PMA was employed as catalyst, a lower yield was obtained (entry 7). Then various solvents were examined to facilitate this transformation. Only trace product (entry 8) was detected when the reaction was performed in CH_3NO_2, which was used as a privileged solvent in intermolecular hydroalkylation reactions.[11a,12,14] 1,2-Dichloroethane, another common solvent, afforded the adduct in 42% after refluxing for 4 h (entry 9). When 1,1,2,2-tetrachloroethane was employed, the yield decreased dramatically (entry 10). While CH_3CN and *n*-heptane gave only trace product, a complex mixture was observed in toluene (entries 11–13). Other solvents were also investigated, including THF, EtOAc, DMF, DMSO, PEG-400, and H_2O. However, no reaction was observed in all these cases (entries 14–19).

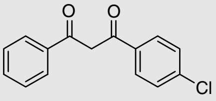
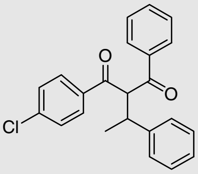
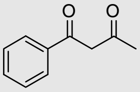
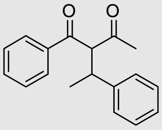
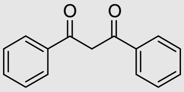
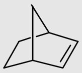
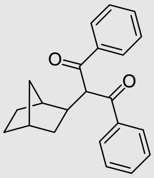
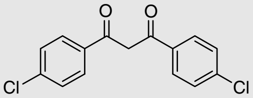
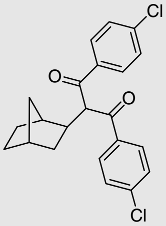
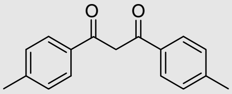
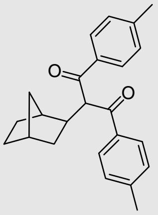
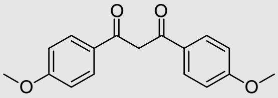
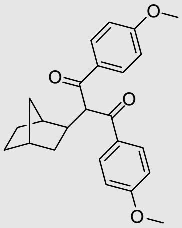
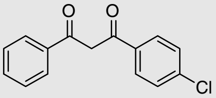
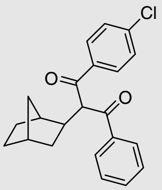
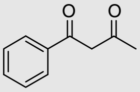
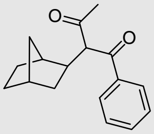
With the optimized conditions in hand, next we investigated the scope of 1,3-diketone substrates in the hydroalkylation reaction of styrene and norbornene.[23] The results are summarized in Table 2. The reaction of symmetric 1,3-diarylpropane-1,3-diones with *para*-substituents on the phenyl moiety (**1b**, **1c**) with styrene at 80 °C was investigated, furnishing the final adducts in slightly decreased yields compared with 1,3-diphenylpropane-1,3-dione

Table 2
PWA-catalyzed hydroalkylation reactions of styrene and norbornene with 1,3-diketones[a]

Entry	1,3-Diketone	Alkenes	Time (h)	Product	Yield[b] (%)
1	 **1a**	 **2a**	4	 **3a**	94
2	 **1b**	**2a**	2.5	 **3b**	92
3	 **1c**	**2a**	3.5	 **3c**	89
4[c]	 **1d**	**2a**	3	 **3d**	75

(*continued on next page*)

Table 2 (*continued*)

Entry	1,3-Diketone	Alkenes	Time (h)	Product	Yield[b] (%)
5	 **1e**	**2a**	3	 **3e**	90 (60:40)[d]
6	 **1f**	**2a**	3	 **3f**	91 (55:45)[d]
7	 **1a**	 **2b**	4	 **3g**	96
8	 **1b**	**2b**	2.5	 **3h**	92
9	 **1c**	**2b**	2.5	 **3i**	93
10	 **1g**	**2b**	4	 **3j**	85
11	 **1e**	**2b**	2.5	 **3k**	94 (50:50)[d]
12	 **1f**	**2b**	3	 **3l**	90 (65:35)[d]

[a] Unless otherwise specified, all the reactions were performed with 0.25 mmol of **1**, alkene **2** (0.87 mmol of **2a** or 0.32 mmol of **2b**), and 5 mg of PWA at 80 °C without any solvent. Only the *exo* product could be formed in the reaction of **2b**.

[b] Isolated yield.

[c] Reaction was performed at 120 °C.

[d] The ratio of diastereoisomers was determined by ^{1}H NMR spectroscopy.

Table 3
The reusability of PWA in the hydroalkylation of styrene with 1,3-diphenylpropane-1,3-dione[a]

Cycle	1	2	3
Time (h)	4	4	4
Yield[b] (%)	92	90	87

[a] All the reactions were performed with 0.25 mmol of **1a**, 0.87 mmol of styrene **2a**, and 5 mg of PWA at 80 °C.
[b] Isolated yield.

1a (entries 2 and 3 vs entry 1). The electronic factor of the substituents exhibited an insignificant influence on the reactivity of 1,3-diketones (entries 2 and 3). When acetylacetone was heated with styrene at 80 °C, the corresponding product was isolated in low yield. Elevating the temperature to 120 °C proved helpful, the reaction completed in 2 h, affording product **3d** in 75% yield (entry 4). Two asymmetric 1,3-diketones were employed, both of them gave the corresponding adducts in high yields as mixtures of inseparable diastereoisomers (entries 5 and 6).

Norbornene was usually employed as an active alkene in the Lewis acid-promoted hydroalkylation reactions. Its feasibility of hydroalkylation with 1,3-dicarbonyl compounds under the present reaction conditions was investigated subsequently (entries 7–12). As the reaction with styrene, symmetric 1,3-diphenylpropane-1,3-diones with different substituents gave the alkylated products in high yields, ranging from 85% to 96% after heating at 80 °C for several hours (entries 7–10). The hydroalkylation of norbornene with asymmetric 1,3-diphenylpropane-1,3-dione **1e** afforded the product in 94% yield as a 50:50 mixture of diastereoisomers (entry 11). When 1-phenylbutane-1,3-dione **1f** was employed as the substrate, a similar reactivity was observed and the product was isolated in 90% yield with 65:35 diastereoisomer ratio (entry 12).

The advantage of PWA could be further demonstrated by its reutilization in this transformation. Upon completion of the hydroalkylation of styrene with 1,3-diketone **1a**, dichloromethane was added to the reaction mixture, and the thus precipitated PWA was collected by filtration. The recovered PWA was reused to catalyze the reaction with the results listed in Table 3. Gratifyingly, the recovered PWA could be reused for at least three times without the loss of activity apparently.

In conclusion, we have demonstrated an efficient methodology for the solvent-free direct hydroalkylation reactions of styrene and norbornene with 1,3-dicarbonyl compounds catalyzed by PWA. The reactions proceeded in excellent yields, could be performed in air, and avoided the usage of toxic organic solvent. Moreover, the short reaction time, simplicity, practicability, simple workup, as well as the use of a small amount and recycling of readily available, reactive, non-moisture-sensitive, and non-toxic PWA as the catalyst in an environmentally benign process make the current protocol more attractive.

Acknowledgments

The authors are grateful for the financial support from National Natural Science Foundation of China (No. 20772117) and Anhui Provincial Bureau of Education.

Supplementary data

Spectroscopic and analytical data for compounds **3b**, **3c**, **3e**, **3h**, **3i**, and **3j**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.06.029.

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23. *General procedure for the PWA-catalyzed direct hydroalkylation of alkenes with 1,3-diketones:* To a small vial were added 1,3-diketone **1** (0.25 mmol), alkene **2** (0.87 mmol for styrene; 0.32 mmol for norbornene), and 12-phosphotungstic acid (5 mg). The vial was sealed and the reaction mixture was allowed to heat at 80 °C for the indicated time (monitored by TLC). Upon completion, 5 mL of CH_2Cl_2 was added, then the reaction mixture was filtered to recover PWA and the organic solution was evaporated to dryness in vacuo. The residue was separated on a silica gel column with petroleum ether/ethyl acetate 4:1 as the eluent to afford the desired product **3**.