ACS Catalysis

RESEARCH ARTICLE

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Heterogeneous Catalysis for Tandem Mukaiyama−Michael and Hydrogenation Reactions: One-Pot vs Sequential Processes

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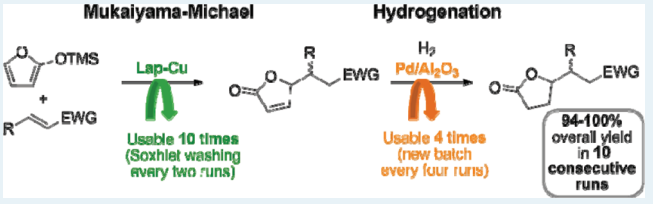
ABSTRACT: Mukaiyama−Michael and hydrogenation reactions can be combined by the use of two heterogeneous catalysts: a copper-exchanged laponite and Pd/Al_2O_3. Although in principle, this combination would be suitable for a one-pot tandem process, it is useful in only two reaction cycles because of irreversible deactivation of the copper catalyst. However, much better results are obtained in a sequential tandem process when the copper catalyst is filtered and the reaction crude is directly used in the hydrogenation reaction without further purification. Under such conditions, it is possible to fully optimize the reuse of each catalyst, up to 10 times the copper catalyst by washing it every two cycles with THF in a Soxhlet extractor, and four times the palladium catalyst that must be renewed every four cycles, whereas the purification steps of the synthetic route are minimized.



KEYWORDS: tandem catalysis, heterogeneous catalysis, Mukaiyama−Michael, hydrogenation

INTRODUCTION

From the point of view of green chemistry, as expressed in its ninth principle, catalytic methods are considered more appropriate than those using stoichiometric reagents.[1] The vast majority of chemical syntheses are still conducted using the traditional paradigm of a single catalytic reaction with either homogeneous or heterogeneous catalysts, followed by costly catalyst separation, product purification steps, or both. On the contrary, biosynthesis in the cells of living organisms goes through multistep enzymatic reactions to convert a starting material into the final product without the separation of intermediates. One of the current trends in organic synthesis is to emulate nature by developing sequential reactions using multiple catalysts in a single reaction vessel using the so-called cascade catalysis[2] or tandem catalysis.[3] The success of these manipulations not only would allow a conceptual advance in the design of new processes, but would also be economically useful by minimizing the use of chemicals, waste production, and processing time.

Soluble chemical catalysts have been employed in tandem catalysis processes,[4,5] but depending on their nature, they can interact with mutual destruction in the so-called "wolf-and-lamb" reactions.[6] For example, acidic catalysts are incompatible with basic catalysts in solution. In this case, heterogeneous catalysis or heterogenized homogeneous catalysts[7] would allow the isolation of the catalytic sites, avoiding their destructive interaction.[8−11] Furthermore, the use of heterogeneous catalysts allows the easy separation and reuse of the catalysts. This methodology should constitute a powerful tool in applied chemistry, allowing extremely complex chemical transformations to take place in a one-pot, cleaner, and more efficient process.

Despite the interest in this strategy, the examples in the literature are rather scarce, including the combination of solid acids and bases,[12−16] different types of heterogeneous catalysts,[17−19] or biocatalysts with chemical catalysts.[20−22] One probable reason for the limited number of examples might be the need for compatibility between catalysts, solvents, reagents, and concomitant products and the general conditions of both reactions. This compatibility would be even more difficult in the synthesis of highly functionalized molecules.

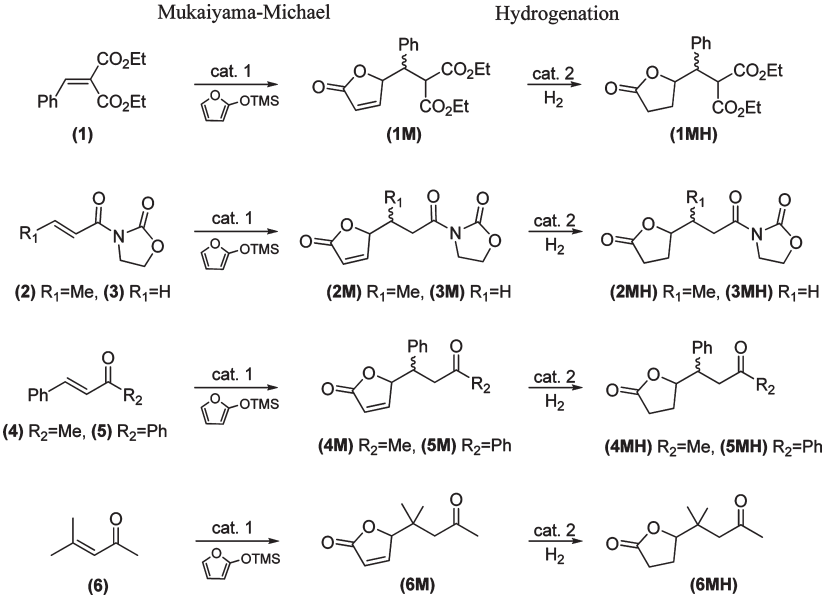
Lactones are frequently encountered as structural motifs within a large variety of natural products and are biologically active compounds. For example they exist in common flavor components,[23,24] and hence, they are employed in the perfumery and food industries. Derivatives of various lactones play an important role as sex attraction pheromones of different insects[25−27] and plant-growth regulators.[28] Lactones (five- and six-member) are important building blocks for the synthesis of natural products such as alkaloids and terpenoids[29−32] and biologically active compounds (e.g., antitumor, antidepressant, and antiviral agents).[33−35] In addition, these products are included in more complex structures used as antibacterial agents or anti-inflammatory and analgesic products.[36] In this paper, the combination of two reactions to obtain γ-butyrolactone derivatives (Scheme 1) will be presented.

The first reaction of this sequence is a Mukaiyama−Michael addition[37−41] of an enolsilane to α,β-unsaturated carbonyl derivatives using a Lewis acid as catalyst. 2-(Trimethylsilyloxy)-furan is a cyclic dienoxy silane d_4 nucleophile that has been largely explored as a reagent in vinylogous Mukaiyama aldol reactions.[42] Hence, the reactions presented in this work are, in fact, vinylogous Mukaiyama−Michael additions.

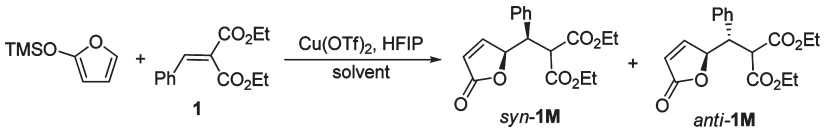
The second reaction is the hydrogenation of the C−C double bond of the obtained furan-2(5*H*)-one. Hydrogenation, using

Received: October 10, 2011
Revised: November 16, 2011
Published: November 21, 2011

Scheme 1. Combination of Mukaiyama−Michael Addition and Hydrogenation



Scheme 2. Benchmark Mukaiyama−Michael Reaction in Homogeneous Phase



either homogeneous[43] or heterogeneous[44,45] catalysts, is, in fact, one of the most studied reactions and probably the most used in the production of fine chemicals.

The ultimate aim of this work was the combination of the reactions in the same reaction flask using different starting substrates (Scheme 1), but the study of the conditions for each individual reaction and the compatibility between the different components of both reactions has been previously performed.

RESULTS AND DISCUSSION

Mukaiyama−Michael Reaction. The study of the reaction conditions (solvent, catalyst, temperature, etc.) was carried out using diethyl benzylidenemalonate (**1**) as Michael acceptor (Scheme 2). Two products are obtained in this reaction using $Cu(OTf)_2$ as Lewis acid in homogeneous phase:[46] *syn*-**1M** and *anti*-**1M**, with the major product having syn stereochemistry as shown by X-ray diffraction (Figure 1).

The yield under such conditions was low (Table 1, entry 1), presumably as a result of the high stability of the Cu(II)-malonyl enolate complex. On the basis of a previous work,[47,48] hexafluoroisopropyl alcohol (HFIP) was added as a coreagent up to a HFIP/**1** molar ratio of 1.5:1. The presence of HFIP improved the conversion from 58% to quantitative (Table 1, entries 1−4), over a 4 h reaction time and with no effect on the stereoselectivity. The variation in the amount of HFIP had an impact in the kinetics of the process, but amounts as low as HFIP/**1** = 0.1 were able to promote the total conversion of the substrate, albeit in longer reaction times. Dichloromethane was also tested as solvent, with only a small negative influence both in yield and diastereoselectivity (Table 1, entry 5).

To prevent any interaction with the hydrogenation catalyst and to recover and reuse the Lewis acid in subsequent reaction cycles, it was necessary to develop a heterogeneous catalyst. Lap-Cu catalyst was prepared by cation exchange of laponite synthetic clay[49] with copper(II) triflate in methanol. The copper content of the catalyst was 0.48 mmol per gram of solid.[50] The results of the Mukaiyama−Michael reaction with this catalyst are also gathered in Table 1.

The heterogeneous catalyst showed lower activity than the homogeneous one, and reaction times had to be increased up to 24 h to achieve high conversions. In this case, HFIP was also necessary as an additive (Table 1, entries 6−7), and the laponite support itself has no catalytic activity (entry 8). It is worth noting that diastereoselectivity was modified by the use of the heterogeneous catalyst, up to a syn/anti ratio around 75/25, with only a minor effect of the reaction solvent (Table 1, entries 7−10). This result indicates that it is a genuine immobilization effect due to the orientation of the box-Cu-benzylidenemalonate intermediate with respect to the clay surface that takes part in the stereochemical outcome of the reaction. In fact, modifications of the diastereoselectivity[51] and also of the enantioselectivity[52] in asymmetric reactions have also been detected for other reactions using clays as supports. Finally, to achieve total conversion, it was necessary to increase the amount of copper catalyst from 10 to 15% (Table 1, entry 11).

Under such conditions, the heterogeneous catalyst could be recovered with only a slight loss of activity after one reaction cycle.

dx.doi.org/10.1021/cs200518s |*ACS Catal.* 2012, 2, 56–64

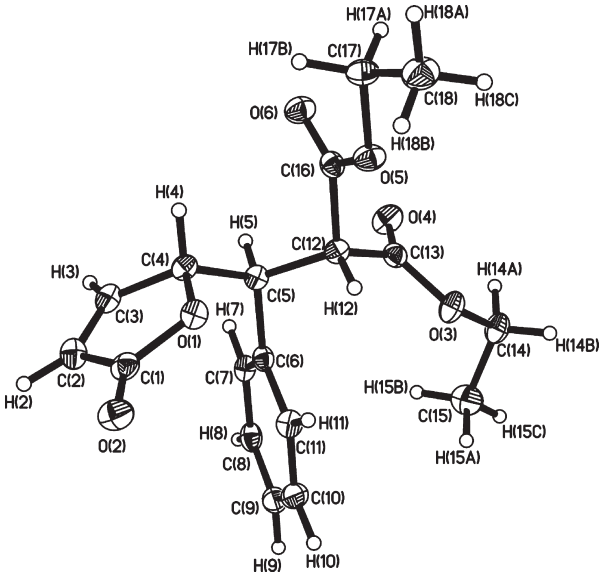


Figure 1. X-ray crystal structure of compound *syn*-**1M**. For the ORTEP diagram, the thermal ellipsoids are shown at 50% probability. Selected bond distances (Å) and angles (°): O(1)−C(1) 1.3714(13), O(1)−C(4) 1.4519(12), C(1)−C(2) 1.4695(16), C(1)−O(2) 1.2065(13), C(2)−C(3) 1.3237(16), C(3)−C(4) 1.4944(15), C(4)−C(5) 1.5359(14), C(5)−C(12) 1.5527(15), C(3)−C(4)−C(5) 113.94(9), C(4)−C(5)−C(6) 113.28(9).

The absence of leaching was checked by filtration experiments after complete addition of 2-(trimethylsilyloxy)furan (5 h), in which the filtrate showed a total absence of activity. In contrast, the activity dropped more dramatically after the second run (Table 1, entries 12−13 and Figure 2). Lewis acid catalysts are usually deactivated by the adsorption of products or byproducts, and this is one of the reasons for the need for a high amount of catalyst. This effect was demonstrated by the recovery of part of the activity after washing with THF in a Soxhlet extractor (Table 1, entry 14 and Figure 2). Thus, the optimized recovery method included the Soxhlet extraction every two reaction cycles, in this way obtaining a recovered catalyst even more active than the original one (Table 1, entry 15). With this operating system, more than 10 cycles could be carried out with the same catalyst without copper leaching and keeping high activity, both in the kinetic behavior of the catalyst and the final yield (Figure 2). Hence, the total productivity of the catalyst, TON = 65 after 10 cycles, is greatly enhanced from the result in homogeneous phase, TON = 10.

After tuning the reaction conditions, other Michael acceptors were tested in this reaction, including *N*-acyl-oxazolidinones **2** and **3** as well as α,β-unsaturated ketones **4**−**6**. The results are shown in Table 2. Almost quantitative yields were obtained with all the substrates. Conversions at short reaction times were very similar to those obtained with **1** (Table 1), showing the similar reactivity of all the substrates tested. In the cases in which diastereomers are formed, the anti isomer was the major one (Scheme 3), in both the homogeneous and heterogeneous phases, in agreement with most of reports for analogous reactions,[53−56] and even direct Michael additions on α,β-unsaturated ketones.[57] The selectivity was not significantly changed by the nature of the catalyst, except in the case of **4M**. Recovery was tested with substrates **2** and **5**. In both cases, a drop of yield was also observed in the recovery of the catalyst after the second cycle. That drop was worked out by washing the catalyst in a Soxhlet extractor with THF before the third cycle.

Table 1. Results of Mukaiyama−Michael Reaction with Diethyl Benzylidenemalonate[a]

entry	solvent	cat. (mol %)	run	HFIP/**1**	time (h)	yield (%)[b]	syn/anti[b]
1	toluene	$Cu(OTf)_2$ (10)	1	0	4	58	98/2
2	toluene	$Cu(OTf)_2$ (10)	1	0.1	4	83	97/3
3	toluene	$Cu(OTf)_2$ (10)	1	0.75	4	91	98/2
4	toluene	$Cu(OTf)_2$ (10)	1	1.5	4	100	98/2
5	CH_2Cl_2	$Cu(OTf)_2$ (10)	1	1.5	4	91	84/16
6	toluene	Lap-Cu (10)	1	0	24	52	78/22
7	toluene	Lap-Cu (10)	1	1.5	24	87	74/26
8	toluene	laponite[d]	1	1.5	24	1	n.d.
9	CH_2Cl_2	Lap-Cu (10)	1	1.5	24	89	68/32
10	DCE[c]	Lap-Cu (10)	1	1.5	24	71	70/30
11	toluene	Lap-Cu (15)	1	1.5	5[e]	39	77/23
					9[f]	54	76/24
					24	100	77/23
12			2	1.5	5[e]	36	77/23
					9[f]	49	76/24
					24	91	76/24
13			3	1.5	24	35	77/23
14			4[g]	1.5	24	67	75/25
15			3[g]	1.5	5[e]	42	76/24
					9[f]	84	77/23
					24	100	77/23

[a] Reaction conditions: 1 mmol of diethyl benzylidenemalonate, HFIP (HFIP/**1** ratio shown in table), 5 mL of solvent and catalyst (amount in table) at r.t. Slow addition (5 h) of 2 mmol of 2-(trimethylsilyloxy)furan in 10 mL of solvent. [b] Determined by gas chromatography. [c] 1,2-Dichloroethane. [d] Blank reaction with the same amount of laponite without copper. [e] Addition of 2-(trimethylsilyloxy)furan just finished. [f] 5 h addition + 4 h reaction. [g] The solid was washed with THF using a Soxhlet extractor.

Hydrogenation. The hydrogenation reaction was first tested using the Mukaiyama−Michael product from benzylidenemalonate (**1M**) as starting reagent (Scheme 4). Given the wide variety of commercially available hydrogenation catalysts, only a limited number of them were tested. We looked for activity under mild conditions, room temperature, and atmospheric pressure, if possible, as well as compatibility with the first reaction in one pot. Toluene was chosen as the reaction solvent because it yielded the best results in the precedent Mukaiyama−Michael reaction. The results obtained with different catalysts are showed in Table 3.

Both supported palladium catalysts, either on carbon or on alumina (Table 3, entries 1−2), were highly active under those mild conditions. The analogous rhodium catalyst on alumina was poorly active (Table 3, entry 3). With regard to homogeneous catalysts, the cationic $[Rh(NBD)_2]BF_4$ was much more active than the neutral $(Ph_3P)_3RhCl$ (Table 3, entries 4−5). This result opened the way to the preparation of a supported catalyst by immobilization on laponite by cationic exchange, analogously to the copper catalyst; however, the solid catalyst prepared in this way was not active at all (Table 3, entry 6). In addition, some recovery experiments were carried out, and both Pd catalysts could be used in four reaction cycles without loss of activity. Hence, both catalysts were chosen to carry out the study of compatibility between both reactions.

With regard to the rest of the products obtained in the Mukaiyama−Michael reactions (**2M**-**6M**), the hydrogenation

dx.doi.org/10.1021/cs200518s |*ACS Catal.* 2012, 2, 56–64

reaction under the same conditions also led to quantitative conversions, obtaining the corresponding products **2MH**−**6MH**.

Compatibility Studies. In the combination of two reactions in one pot with the simultaneous presence of both catalysts, a high number of reaction parameters must be compatible, such as solvent, temperature, reagents, and byproducts. Thus, before coupling both reactions, several compatibility studies were carried out using the transformation of **1** as a model process (Scheme 5).

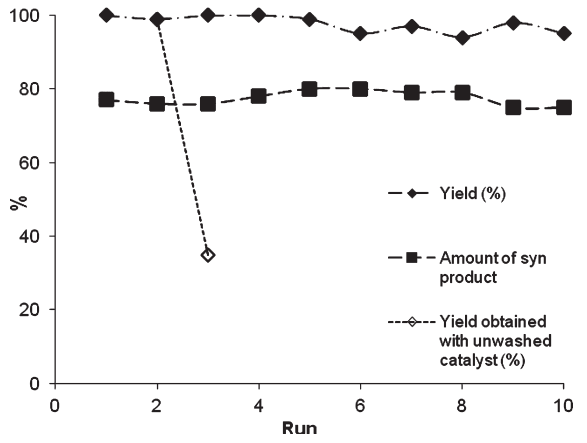
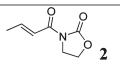
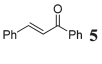


Figure 2. Recovery of Lap-Cu in the Mukaiyama−Michael reaction with catalyst washing with THF in a Soxhlet apparatus every two runs.

Table 2. Mukaiyama−Michael with Different Substrates[a]

entry	Michael acceptor	homogeneous		heterogeneous	
		yield (%)[b]	*syn*/*anti*[b]	yield (%)[b]	*syn*/*anti*[b]
1	 **2**	100	7/93	100	6/94
2	 **3**	100	-	99	-
3	 **4**	98	27/73	100	47/53
4	 **5**	100	29/71	100	27/73
5	 **6**	100	-	99	-

[a] Reaction conditions: 1 mmol of Michael acceptor, 1.5 mmol of HFIP, 5 mL of toluene and catalyst (homogeneous: 10 mol %; heterogeneous: 15 mol %) at r.t.; slow addition (5 h) of 2 mmol of 2-(trimethylsilyloxy)furan in 10 mL of toluene. [b] Determined by ^{1}H NMR.

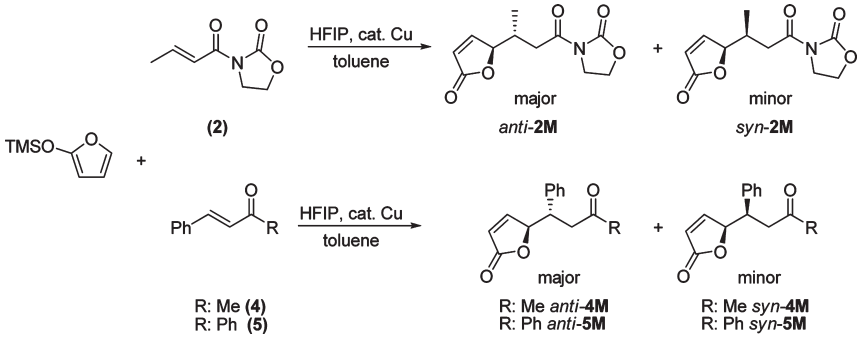
In the first compatibility study, the Mukaiyama−Michael addition was carried out in the presence of each Pd catalyst, keeping the same reaction conditions previously optimized (Scheme 5A). In the case of Pd/C, the yield of **1M** greatly decreased, up to only 10%, whereas the presence of Pd/Al_2O_3 did not have any negative effect. An adsorption study showed that both diethyl benzylidenemalonate (**1**) and 2-(trimethylsilyloxy)furan can be adsorbed in great amounts on Pd/C or even only on activated carbon, although in the case of a competitive adsorption, the furan derivative is selectively adsorbed due to its aromatic nature. The capture of the reagents from the reaction medium through a presumably fast adsorption process should prevent the reaction on the copper catalyst, accounting for the yield drop. To confirm this hypothesis, the adsorption capacity of Pd/C was saturated by addition of 16 mmol of 2-(trimethylsilyloxy)furan, and then Lap-Cu, diethyl benzylidenemalonate (**1**), and HFIP were added. Under such conditions, the reaction proceeds with high yield, demonstrating the role played by the adsorption on Pd/C and the unsuitability of this catalyst for a tandem process.

In the second compatibility study, the effect of the presence of Lap-Cu and HFIP on the hydrogenation reaction with Pd catalysts was tested (Scheme 5B). It was shown that the hydrogenation reaction with any Pd catalyst proceeded in the same way as in the absence of copper catalyst; however, given the incompatibility result with Pd/C in the previous test, Pd/Al_2O_3 was chosen for the tandem system.

Apart from the compatibility between catalysts, it was also necessary to check the compatibility between the hydrogenation reaction and the reagents and byproduct of the Mukaiyama−Michael addition. In fact, 2-(trimethylsilyloxy)furan is used in a slight excess over the Michael acceptor, and the main byproduct, furan-2(5*H*)-one, comes from its hydrolysis, with moisture traces present in the hydrophilic heterogeneous catalyst. None of these products negatively affects the hydrogenation reaction, but the hydrogenated product of furan-2(5*H*)-one, γ-butyrolactone, was obtained as a byproduct, together with the main product, **1MH**, in the global process shown in Scheme 6.

One-Pot and Sequential Reactions. Because both reagents of the Mukaiyama−Michael reaction are susceptible to hydrogenation, in the one-pot tandem process, hydrogen atmosphere was introduced in the reaction vessel after the time required for completion of the Mukaiyama−Michael step. The results obtained in the tandem Mukaiyama−Michael and hydrogenation under appropriate conditions and in the recovery and reuse of the mixture of catalysts are shown in Table 4.

Scheme 3. Diastereomers Obtained in the Mukaiyama−Michael Reaction of 2, 4, and 5



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Scheme 4. Hydrogenation Reaction Using 1M As Substrate

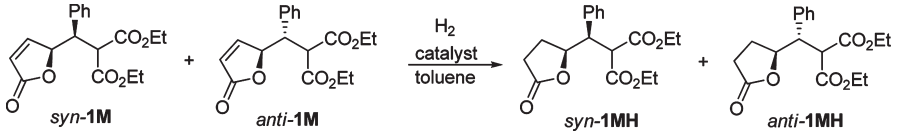


Table 3. Hydrogenation of 1M with Different Catalysts.[a]

entry	catalyst	yield (%)
1	Pd/C	99
2	Pd/Al_2O_3	100
3	Rh/Al_2O_3	13
4	$(Ph_3P)_3RhCl$	30
5	$[Rh(NBD)_2]BF_4$	100
6	$[Rh(NBD)_2]$-lap	<5

[a] Reaction conditions: 1 mmol of **1M**, 0.024 mmol of catalyst, 2 mL of toluene at r.t.; 1 atm of H_2, 12 h. NBD: norbornadiene.

As can be seen, the global yield was very high in the first two cycles (Table 4, runs 1 and 2) but significantly dropped in the third cycle. This is due to the deactivation of the Lewis acid catalyst, despite the fact that the mixture of catalysts was washed with THF in a Soxhlet before the third cycle. One possible explanation for this effect is that deactivation of the Lewis acid catalyst is more effective with the hydrogenated products than with the non-hydrogenated products. However, a control test of the Mukaiyama−Michael reaction in the presence of the hydrogenated products led to the same catalytic activity, pointing to the role of hydrogenated byproducts as the main source responsible for deactivation. The NMR study of the products extracted from deactivated Lap-Cu in the Soxhlet treatment showed the presence of γ-butyrolactone together with signals compatible with polymerization products, even in the absence of H_2 and Pd catalyst. This might be due to the simultaneous presence of a Lewis acid and a secondary alcohol (HFIP), producing a hydrogen transfer process similar to the Meerwein−Ponndorf−Verley reduction.[58] This deactivating effect of γ-butyrolactone and its byproducts would be enhanced in the case of the tandem process involving hydrogenation of furan-2(5*H*)-one generated by the use of an excess of 2-(trimethylsilyloxy)furan.

In view of that result and taking advantage of the heterogeneous nature of the catalysts, a sequential process was envisaged. The catalysts were separated after each reaction by filtration, and the reaction crude was used in the following reaction without further purification. Under such conditions, the copper catalyst could be reused up to 10 times if the solid was washed every two cycles with THF in a Soxhlet extractor (Table 5). The palladium was deactivated after four cycles. The attempts to regenerate the catalyst by washing were unsuccessful, and it was renewed every four cycles. This system preserves some of the advantages of the one-pot tandem reactions, such as the reduction in purification steps, but it is operationally more complicated. On the other hand, the separation of the catalysts allows the optimization of the use of each solid by reaching their maximum productivity, whereas in the mixture of catalysts, the less recoverable one limits the recoverability of the mixture.

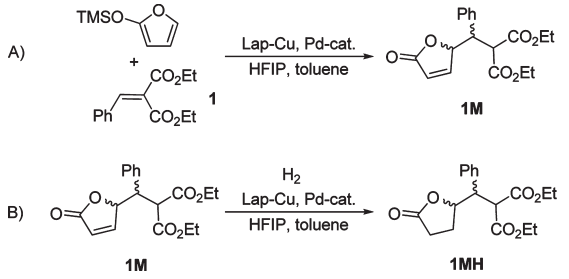
The Mukaiyama−Michael−hydrogenation combination was also studied using compounds **2** and **5** as representative of the other two families of substrates. In the one-pot processes, the global yield of **2MH** and **5MH** was found to be very high in the first two cycles but significantly dropped in the third cycle (98−87−52% for **2MH** and 100−98−20% for **5MH**) due to deactivation of the copper catalyst, as happened with **1** (Table 4). On the contrary, the sequential tandem Mukaiyama−Michael−hydrogenation process, filtration of the copper catalyst before hydrogenation, allowed obtaining results similar to those shown in Table 5 (over 95% overall yield).

Table 4. Tandem Mukaiyama−Michael Hydrogenation.[a]

	yield (%)		
run	Mukaiyama−Michael	hydrogenation	global
1	100	100	98
2	96	100	96
3	45	100	45

[a] Reaction conditions: 1 mmol of diethyl benzylidenemalonate, 1.5 mmol of HFIP, 15 mol % of Lap-Cu, 2.5 mol % of Pd/Al_2O_3, 5 mL of toluene, and 2 mmol of 2-(trimethylsilyloxy)furan in 10 mL of solvent added over 5 h at r.t. After 24 h, hydrogen (1 atm) was added.

Scheme 5. Compatibility Studies



CONCLUSIONS

The combination of Mukaiyama−Michael reaction and hydrogenation is possible by the use of a copper-exchanged laponite and Pd/Al_2O_3, respectively, as catalyst. This combination leads to very high yields in two reaction cycles when both catalysts are added at the beginning, in a one-pot tandem process. However, the best results are obtained in a sequential tandem process, when the copper catalyst is filtered and the reaction crude is used in the next reaction without further purification. Under such conditions, the copper catalyst can then be reused up to 10 times if the solid is washed every two cycles with THF in a Soxhlet extractor and the palladium catalyst is renewed every four cycles. In this way, the use of each catalyst can be optimized, whereas the use of the crude in the next reaction minimizes the purification steps of the synthetic route.

dx.doi.org/10.1021/cs200518s |*ACS Catal.* 2012, 2, 56–64

Scheme 6. Tandem Mukaiyama−Michael and Hydrogenation with Lap-Cu and Pd/Al_2O_3 As Catalysts

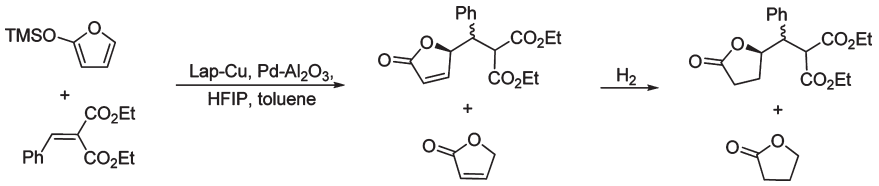


Table 5. Sequential Tandem Mukaiyama−Michael Hydrogenation Reactions[a]

	Mukaiyama−Michael		hydrogenation		
run	Lap-Cu	yield (%)	Pd/Al_2O_3	yield (%)	overall yield (%)
1	new	100	new	100	100
2	recov.1	99	recov.1	100	99
	Soxhlet Extraction[b]				
3	recov.2	100	recov.2	100	100
4	recov.3	100	recov.3	100	100
	Soxhlet Extraction[b]		New Batch[c]		
5	recov.4	99	new	100	99
6	recov.5	95	recov.1	100	95
	Soxhlet Extraction[b]				
7	recov.6	97	recov.2	100	97
8	recov.7	94	recov.3	100	94
	Soxhlet Extraction[b]		New Batch[c]		
9	recov.8	98	new	100	98
10	recov.9	95	recov.1	100	95

[a] Reaction conditions: 1 mmol of diethyl benzylidenemalonate, 1.5 mmol of HFIP, 15 mol % of Lap-Cu, 5 mL of toluene at r.t.; slow addition (5 h) of 2 mmol of 2-(trimethylsilyloxy)furan in 10 mL of toluene. Cu catalyst filtered after 24 h, and addition of 2.5 mol % of Pd/Al_2O_3 and hydrogen (1 atm). [b] The Cu catalyst was washed with THF using a Soxhlet extractor. [c] A new batch of Pd catalyst was used.

Further research is currently ongoing to include this methodology in longer sequences of reaction.

EXPERIMENTAL SECTION

The hydrogenation catalysts (Table 3) and all reagents were purchased from Aldrich and used as received without further purification, except (*E*)-3-(but-2-enoyl)oxazolidin-2-one (**2**) and 3-acryloyloxazolidin-2-one (**3**), which were prepared according to the literature.[59]

Preparation of (*E*)-3-butyl-2-enoyloxazolidin-2-one (2). To a solution of oxazolidin-2-one (34.4 mmol) in anhydrous THF (115 mL) at −78 °C under argon atmosphere, a solution of BuLi (1.6 M in diethyl ether, 21.6 mL) was slowly added. After 15 min, (*E*)-but-2-enoyl chloride (38 mmol) was added, and the mixture was stirred for 30 min at −78 °C and other 15 min at 0 °C. The reaction was stopped by adding an excess of a saturated solution of NH_4Cl (∼30 mL), and the resulting mixture was concentrated under vacuum. The residue was diluted with ether and washed successively with saturated solutions of $NaHCO_3$ and NaCl. The organic phase was dried over anhydrous $MgSO_4$, filtered, and concentrated under vacuum to obtain an orange oil. The product was purified by column chromatography on silica (hexane/ethyl acetate = 3:2). The pure product was a white solid. Yield: 80%. ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.18 (m, 2H), 4.39 (t, J = 7.9 Hz, 2H), 4.04 (t, J = 7.9 Hz, 2H), 1.94 (d, J = 6.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 195.5, 165.2, 146.8, 121.4, 62.0, 42.6, 18.5.

Preparation of 3-Acryloyloxazolidin-2-one (3). The procedure is similar to that described above except that acryloyl chloride (38 mmol) was used as substrate. The pure product was obtained as white crystals. Yield: 42%. ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.47 (dd, J_1 = 17 Hz, J_2 = 10.5 Hz, 1H), 6.54 (dd, J_1 = 17 Hz, J_2 = 1.8 Hz, 1H;), 5.85 (dd, J_1 = 10.5 Hz, J_2 = 1.8 Hz, 1H), 4.42 (t, J = 8.1 Hz, 2H), 4.06 (t, J = 8.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 165.1, 153.4, 131.8, 127.0, 62.2, 42.6.

Copper(II)-Exchanged Laponite (Lap-Cu). To a solution of $Cu(OTf)_2$ (180 mg, 0.5 mmol) in methanol (6 mL), laponite (1 g) was slowly added, and the suspension was stirred at room temperature for 24 h under argon atmosphere. The solid was filtered off and thoroughly washed with methanol (10 mL) and then with dichloromethane (20 mL) and, finally, dried under vacuum. The copper content (0.48 mmol/g) was determined by plasma emission spectroscopy on a Perkin-Elmer Plasma 40 emission spectrometer.

CATALYTIC TESTS

Mukaiyama−Michael Addition with Lap-Cu. Dried copper-laponite catalyst (143 mg) was added to a mixture of the corresponding α,β-unsaturated carbonyl compound (1 mmol) and hexafluoroisopropanol (1.5 mmol) in 5 mL of solvent under argon. Then, a solution of 2-(trimethylsilyloxy)furan (2 mmol) in 10 mL of solvent was slowly added to the suspension over 5 h. The mixture was stirred at room temperature for 24 h. In the case of **1M**, the reaction was monitored by GC (FID from Hewlett-Packard 5890 II) using a cross-linked methyl silicone column (30 m × 0.25 mm × 0.35 μm), helium as carrier gas (20 psi), injector temperature 230 °C, detector temperature 250 °C, and oven temperature program 45 °C (4 min)−25 °C/min−200 °C (0 min)−40 °C/min−250 °C (5 min). The yield of the other products was determined by ^{1}H NMR using mesitylene as stardard. At the end of the reaction, the catalyst was removed by filtration and washed with dry dichloromethane. The solid was dried under vacuum for 12 h prior to reuse. The mixtures of products were purified by column chromatography on silica. Isolated yields: **1M**, 96% (319.1 mg); **2M**, 95% (227.3 mg); **3M**, 93% (209.4 mg); **4M**, 94% (216.4 mg); **5M**, 94% (274.8 mg); and **6M**, 91% (165.8 mg). The diastereomers ***syn*-1M** and ***anti*-2M** could be crystallized from the anti/syn mixture using hexane and ethyl acetate. In the leaching tests, the solid catalyst was filtered after complete addition of 2-(trimethylsilyloxy)furan

dx.doi.org/10.1021/cs200518s |*ACS Catal.* 2012, 2, 56–64

(5 h), with a conversion in the range of 36−42%. The reaction was allowed to proceed in the filtrate, with no additional conversion after 24 h.

Diethyl (S,R*)-2-[(5-Oxo-2,5-dihydrofuran-2-yl)(phenyl)-methyl]malonate (**syn-1M**).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.30−7.09 (m, 6H), 5.78 (dd, J_1 = 5.7 Hz, J_2 = 2.1 Hz, 1H), 5.54−5.53 (m, 1H), 4.27 (q, J = 7.1 Hz, 2H), 4.22 (d, J = 11.8 Hz, 1H), 3.89−3.83 (m, 3H), 1.30 (t, J = 7.1 Hz, 3H), 0.87 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 172.5, 168.0, 167.1, 154.8, 133.6, 128.9, 128.4, 128.1, 122.1, 82.2, 62.1, 61.5, 53.6, 47.3, 14.0, 13.5. HR-MS (ESI$^+$): m/z = 333.1335 [MH$^+$]. Calcd. for $C_{18}H_{21}O_6$: 333.1333. mp (°C): 71−72.

Diethyl (R,R*)-2-[(5-Oxo-2,5-dihydrofuran-2-yl)(phenyl)-methyl]malonate (**anti-1M**) (from the Spectrum of an Anti/Syn Mixture).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.30−7.09 (m, 6H), 6.05 (dd, J_1 = 5.8 Hz, J_2 = 2.0 Hz, 1H), 5.39 (dt, J_1 = 8.0 Hz, J_2=1.8 Hz, 1H), 4.23−4.18 (m, 3H), 3.94−3.82 (m, 2H), 3.70 (dd, J_1 = 9.6 Hz, J_2 = 8.0 Hz, 1H), 1.28 (t, J = 7.1 Hz, 3H), 0.98 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 171.9, 167.8, 166.9, 154.7, 136.0, 128.9, 128.8, 128.3, 121.9, 84.2, 62.0, 61.5, 54.4, 48.8, 13.8, 13.6.

Structural Analysis of *syn*-1M. X-ray data were collected at 100.0(2) K on a Bruker SMART APEX CCD diffractometer equipped with a normal focus, 2.4 kW sealed tube source (molybdenum radiation, λ = 0.71073 Å) operating at 50 kV and 30 mA. Each frame exposure time was 10 s, covering 0.3° in ω. Data were collected over the complete sphere by a combination of three sets, and corrected for absorption by using a multiscan method applied with the SADABS program.[60] The structure was solved by the direct method and refined by full-matrix least-squares on F^2 using Bruker SHELXTL program package,[61] including isotropic and subsequently anisotropic displacement parameters for all non-hydrogen atoms. Weighted R factors (R_w) and goodness of fit (S) are based on F^2, and conventional R factors are based on F. All hydrogen atoms were included in observed positions and refined freely.

Data for *syn*-1M. $C_{18}H_{20}O_6$, M = 332.34; colorless irregular block, 0.26 × 0.24 × 0.24 mm^3; monoclinic, $P2(1)/n$; a = 11.2495(8) Å, b = 8.9424(6) Å, c = 16.7491(12) Å; β = 102.0430(10) (°); Z = 4; V = 1647.8(2) Å^3; D_c = 1.340 g/cm^3; μ = 0.101 mm^{-1}, minimum and maximum transmission factors 0.822 and 1.000; $2\theta_{max}$ = 57.48; 14315 reflections collected, 3987 unique [R(int) = 0.0260]; number of data/restrains/parameters 3987/0/297; final GoF 1.047, R_1 = 0.0366 [3231 reflections $I > 2\sigma(I)$], wR_2 = 0.0999 for all data; largest peak and hole 0.323 and −0.258e Å^{-3}.

(R,R*)-3-(2′,5′-Dihydro-5′-oxo-2′-furyl)butanoyl-1,3-oxazolidin-2-one (**anti-2M**).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.53 (dd, J_1 = 5.6 Hz, J_2 = 1.3 Hz, 1H), 6.16 (dd, J_1 = 5.6 Hz, J_2 = 2.0 Hz, 1H), 5.02 (ddd, J_1 = 6.2, J_2 = 2.0 Hz, J_3 = 1.3 Hz, 1H), 4.48−4.41 (m, 2H), 4.07−4.01 (m, 2H), 3.16 (dd, J_1 = 16.8 Hz, J_2 = 5.9 Hz, 1H), 2.86 (dd, J = 16.8 Hz, J_2 = 7.6 Hz, 1H), 2.59−2.44 (m, 1H), 1.10 (d, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 172.5, 171.5, 154.56, 153.5, 122.4, 86.1, 62.1, 42.5, 37.5, 33.3, 16.0. HR-MS (ESI$^+$): m/z = 240.0869 [MH$^+$]. Calcd. for $C_{10}H_{14}NO_5$: 240.0872. mp (°C): 88−90 (lit.[53] = 88−89).

(R,S*)-3-(2′,5′-Dihydro-5′-oxo-2′-furyl)butanoyl-1,3-oxazolidin-2-one (**syn-2M**) (from the Spectrum of an Anti/Syn Mixture).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.45 (dd, J_1 = 5.8 Hz, J_2 = 1.5 Hz, 1H), 6.17 (dd, J_1 = 5.8 Hz, J_2 = 2.1 Hz, 1H), 5.20−5.18 (m, 1H), 4.45−4.41 (m, 2H), 4.05−4.01 (m, 2H), 3.15 (dd, J_1 = 17.4 Hz, J_2 = 7.3 Hz, 1H), 2.90 (dd, J_1 = 17.5 Hz, J_2 = 6.4 Hz, 1H), 2.68−2.58 (m, 1H), 0.94 (d, J = 7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 172.9, 171.6, 155.7, 153.4, 122.6, 85.3, 62.1, 42.5, 38.0, 32.0, 13.9.

*3-(2′,5′-Dihydro-5′-oxo-2′-furyl)propanoyl-1,3-oxazolidin-2-one (**3M**).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.48 (dd, J_1 = 5.7 Hz, J_2 = 1.4, 1H), 6.13 (dd, J_1 = 5.7 Hz, J_2 = 2.0 Hz, 1H), 5.19−5.15 (m, 1H), 4.44 (t, J = 8.1 Hz, 2H), 4.03 (t, J = 8.1 Hz, 2H), 3.14−3.10 (m, 2H), 2.30−2.22 (m, 1H), 1.99−1.90 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 172.6, 172.0, 155.7, 153.4, 121.9, 82.0, 62.2, 42.5, 30.6, 27.7. HR-MS (ESI$^+$): m/z = 226.0712 [MH$^+$]. Calcd. for $C_{10}H_{12}NO_5$: 226.0715. Colorless oil.

(S,S*)-5-(3-Oxo-1-phenylbutyl)furan-2(5H)-one (**anti-4M**) (from the Spectrum of an Anti/Syn Mixture).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.35−7.09 (m, 6H), 6.09 (dd, J_1 = 5.7 Hz, J_2 = 1.9 Hz, 1H), 5.15 (dt, J_1 = 7.5 Hz, J_2 = 1.8 Hz, 1H), 3.48−3.41 (m, 1H), 3.03 (dd, J_1 = 17.5 Hz, J_2 = 5.3 Hz, 1H), 2.90 (dd, J_1 = 17.5 Hz, J_2 = 8.1 Hz,1H), 2.06 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 205.8, 172.6, 155.4, 139.4, 129.0, 128.1, 127.8, 122.0, 85.7, 45.0, 44.3, 30.5. HR-MS (ESI$^+$, of the anti/syn mixture): m/z = 231.1016 [MH$^+$]. Calcd. for $C_{14}H_{15}O_3$: 231.1013.

(R,S*)-5-(3-Oxo-1-phenylbutyl)furan-2(5H)-one (**syn-4M**) (from the Spectrum of an Anti/Syn Mixture).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.35−7.09 (m,6H), 5.34 (q, J = 1.9 Hz, 1H), 3.69−3.76 (m, 1H), 3.23 (dd, J_1 = 18.2 Hz, J_2 = 8.3 Hz, 1H), 2.96−2.86 (m, 1H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 206.5, 172.8, 155.1, 137.0, 128.7, 128.3, 127.7, 122.2, 84.2, 44.8, 42.7, 30.5.

(S,S*)-5-(3-Oxo-1,3-diphenylpropyl)furan-2(5H)-one (**anti-5M**) (from the Spectrum of an Anti/Syn Mixture).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.81−7.78 (m, 2H), 7.52−7.11 (m, 9H), 6.00 (dd, J_1 = 5.7 Hz, J_2 = 2.1 Hz, 1H), 5.20−5.17 (m, 1H), 3.64−3.59 (m, 1H), 3.49 (dd, J_1 = 17.7 Hz, J_2 = 5.0 Hz, 1H), 3.39 (dd, J_1 = 17.6 Hz, J_2 = 8.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 197.3, 172.7, 155.6, 139.6, 136.6, 133.3, 128.9, 128.6, 128.1, 128.0, 127.7, 122.1, 85.8, 44.3, 40.1. HR-MS (ESI$^+$, of the anti/syn mixture): m/z = 293.1176 [MH$^+$]. Calcd. for $C_{19}H_{17}O_3$: 293.1172.

(R,S*)-5-(3-Oxo-1,3-diphenylpropyl)furan-2(5H)-one (**syn-5M**) (from the Spectrum of an Anti/Syn Mixture).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.91−7.88 (m, 2H), 7.52−7.11 (m, 9H), 5.77 (dd, J_1 = 5.7 Hz, J_2 = 2.1 Hz, 1H), 5.38−5.36 (m, 1H), 3.90−3.86 (m, 1H), 3.73 (dd, J_1 = 18.0 Hz, J_2 = 8.3 Hz, 1H), 3.37 (dd, J_1 = 13.1 Hz, J_2 = 5.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 197.8, 172.8, 155.2, 139.7, 137.2, 133.5, 128.9, 128.7, 128.3, 128.0, 127.6, 122.0, 84.3, 42.9, 40.1.

*5-(1,1-Dimethyl-3-oxobutyl)furan-2(5H)-one (**6M**).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.48 (dd, J_1 = 5.8 Hz, J_2 = 1.5 Hz, 1H), 6.15 (dd, J_1 = 5.8 Hz, J_2 = 2.1 Hz, 1H), 5.30−5.28 (m, 1H), 2.69 (d, J = 17.1 Hz, 1H), 2.40 (d, J = 17.1 Hz, 1H), 2.15 (s, 3H), 1.17 (s, 3H), 0.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 207.3, 172.8, 154.0, 122.4, 87.9, 50.3, 36.7, 31.7, 23.0, 22.3. HR-MS (ESI$^+$): m/z = 183.1030 [MH$^+$]. Calcd. for $C_{10}H_{15}O_3$: 183.1016. Colorless oil.

Hydrogenation of the Mukaiyama−Michael addition Products. Pd catalyst (0.24 mmol) was added to a solution of the product obtained in the Mukaiyama−Michael reaction (1 mmol) in 5 mL of toluene, then a complete atmosphere of hydrogen was guaranteed by several cycles of vacuum and hydrogen. The substrate was hydrogenated in 12 h at room temperature.

Products were isolated by filtration and solvent elimination under vacuum. The purity was confirmed by ^{1}H NMR. Isolated yields: **1MH**, 98% (327.4 mg); **2MH**, 99% (238.8 mg); **3MH**, 97% (220.4 mg); **4MH**, 99% (229.9 mg); **5MH**, 95% (279.6 mg); **6MH**, 98% (180.5 mg).

Diethyl (R,R*)-2-[(5-Oxotetrahydrofuran-2-yl)(phenyl)-methyl]malonate (**anti-1MH**) (from the Spectrum of an Anti/Syn Mixture).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.21−7.12 (m, 5H), 4.87−4.82 (m, 1H), 4.25−4.20 (m, 3H), 3.94−3.88 (m, 2H), 3.68 (t, J = 9.6 Hz, 1H), 2.49−2.35 (m, 1H), 2.30−2.17 (m, 1H), 2.06−1.97 (m, 1H), 1.88−1.77 (m, 1H), 1.28 (t, J = 7.13 Hz, 3H), 0.96 (t, J = 7.13 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 175.9, 167.8, 167.0, 136.0, 130.0, 128.9, 128.6, 81.3, 61.8, 61.3, 55.4, 50.1, 29.5, 26.2, 13.8, 13.5.

Diethyl (S,R*)-2-[(5-Oxotetrahydro-2-furanyl)(phenyl)-methyl]malonate (**syn-1MH**).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.21−7.12 (m, 5H), 5.00−4.96 (m, 1H), 4.26 (q, J = 7.1 Hz, 2H), 4.18 (d, J = 11.8 Hz, 1H), 3.85 (q, J = 7.1 Hz, 2H), 3.57 (dd, J_1 = 11.8 Hz, J_2 = 2.4 Hz, 1H), 2.30−2.17 (m, 2H), 1.88−1.77 (m, 1H), 1.66−1.57 (m, 1H), 1.30 (t, J = 7.1 Hz, 3H), 0.88 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 177.0, 167.4, 167.0, 134.3, 130.1, 128.6, 127.6, 79.2, 61.9, 61.4, 53.9, 49.1, 27.8, 24.9, 14.0, 13.5. HR-MS (ESI$^+$): m/z = 335.1481 [MH$^+$]. Calcd. for $C_{18}H_{23}O_6$: 335.1489. Colorless oil.

(R,R*)-3-(5′-Oxotetrahydro-2′-furyl)butanoyl)-1,3-oxazolidin-2-one (**anti-2MH**).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 4.46−4.30 (m, 3H), 4.09−3.99 (m, 2H), 3.25 (dd, J_1 = 16.4 Hz, J_2 = 6.1 Hz, 1H), 2.82 (dd, J_1 = 16.8 Hz, J_2 = 7.2 Hz, 1H), 2.57−2.51 (m, 2H), 2.44−2.26 (m, 2H), 2.12−1.87 (m, 1H), 1.02 (d, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 176.6, 172.0, 153.7, 83.7, 62.1, 42.6, 38.5, 35.0, 28.7, 26.1, 15.3. HR-MS (ESI$^+$): m/z = 242.1030 [MH$^+$]. Calcd. for $C_{11}H_{16}NO_5$: 242.1028. mp (°C) = 110−112 (lit.[53] = 110−111).

(R,S*)-3-(5′-Oxotetrahydro-2′-furyl)butanoyl)-1,3-oxazolidin-2-one (**syn-2MH**) (from the Spectrum of an Anti/Syn Mixture).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 4.50 (m, 1H), 4.43−4.38 (m, 2H), 4.04−3.99 (m, 2H), 3.08 (dd, J_1 = 16.4 Hz, J_2 = 6.1 Hz, 1H), 2.79 (dd, J_1 = 16.4 Hz, J_2 = 7.6 Hz, 1H), 2.54−2.49 (m, 2H), 2.48−2.39 (m, 1H), 2.32−2.19 (m, 1H), 2.08−1.97 (m, 1H), 1.03 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 177.0, 171.7, 153.5, 83.2, 62.1, 42.5, 37.3, 33.7, 28.7, 24.6, 14.8.

*3-(5′-Oxotetrahydro-2′-furyl)propanoyl)-1,3-oxazolidin-2-one (**3MH**).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 4.63−4.56 (m, 1H), 4.45−4.40 (m, 2H), 4.04−4.00 (m, 2H), 3.10 (t, J = 7.2 Hz, 2H), 2.56−2.52 (m, 2H), 2.41−2.33 (m, 1H), 2.07−2.01 (m, 2H), 1.93−1.83 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 176.8, 172.3, 153.5, 79.6, 62.2, 42.5, 31.2, 30.0, 28.7, 27.8. HR-MS (ESI$^+$): m/z = 228.0875 [MH$^+$]. Calcd. for $C_{10}H_{14}NO_5$: 228.0872. Colorless oil.

(S,S*)-5-(3-Oxo-1-phenylbutyl)dihydrofuran-2(3H)-one (**anti-4MH**) (from the Spectrum of an Anti/Syn Mixture).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.34−7.22 (m, 5H), 4.62−4.57 (m, 1H), 3.41−3.36 (m, 1H), 3.13 (dd, J_1 = 17.2 Hz, J_2 = 4.6 Hz, 1H), 2.90 (dd, J_1 = 17.2 Hz, J_2 = 9.0 Hz, 1H), 2.48−2.44 (m, 2H), 2.07 (s, 3H), 2.03−1.95 (m, 1H), 1.88−1.77 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 206.1, 176.6, 139.1, 128.8, 128.2, 127.5, 82.8, 46.5, 46.0, 30.5, 28.4, 26.4. HR-MS (ESI$^+$, of the anti/syn mixture): m/z = 233.1177 [MH$^+$]. Calcd. for $C_{14}H_{17}O_3$: 233.1172.

(R,S*)-5-(3-Oxo-1-phenylbutyl)dihydrofuran-2(3H)-one (**syn-4MH**) (from the Spectrum of an Anti/Syn Mixture).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.34−7.22 (m, 5H), 4.83−4.79 (m, 1H), 3.41−3.36 (m, 1H), 3.17 (dd, J_1 = 17.2 Hz, J_2 = 4.6 Hz, 1H), 2.95 (dd, J_1 = 17.2 Hz, J_2 = 9.0 Hz, 1H), 2.30−2.18 (m, 2H), 2.13 (s, 3H), 2.03−1.95 (m, 1H), 1.88−1.77 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 206.7, 177.2, 137.8, 129.2, 128.7, 127.5, 81.5, 45.7, 44.3, 30.6, 28.8, 25.0.

(S,S*)-5-(3-Oxo-1,3-diphenylpropyl)dihydrofuran-2(3H)-one (**anti-5MH**) (from the Spectrum of an Anti/Syn Mixture).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.31−7.00 (m, 10H), 4.53−4.47 (m, 1H), 2.70−2.60 (m, 1H), 2.45−2.39 (m, 1H), 2.37−2.24 (m, 2H), 1.99−1.89 (m, 1H), 1.87−1.77 (m, 1H), 1.73−1.64 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 177.1, 141.3, 139.2, 128.8, 128.4, 128.3, 128.2, 127.4, 125.8, 83.9, 50.7, 33.0, 28.7, 26.6. HR-MS (ESI$^+$, of the anti/syn mixture): m/z = 295.1328 [MH$^+$]. Calcd. for $C_{19}H_{19}O_3$: 295.1329.

(R,S*)-5-(3-Oxo-1,3-diphenylpropyl)dihydrofuran-2(3H)-one (**syn-5MH**) (from the Spectrum of an Anti/Syn Mixture).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.31−7.07 (m, 10H), 4.66−4.61 (m, 1H), 2.70−3.60 (m, 1H), 2.53−2.39 (m, 1H), 2.37−2.09 (m, 2H), 2.08−1.89 (m, 1H), 1.87−1.77 (m, 1H), 1.73−1.64 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 177.2, 141.5, 138.2, 129.2, 128.7, 128.4, 128.2, 127.3, 125.9, 83.2, 49.5, 33.1, 28.4, 25.5.

*5-(1,1-Dimethyl-3-oxobutyl)dihydrofuran-2(3H)-one (**6MH**).* ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 4.60 (dd, J_1 = 9.1 Hz, J_2 = 6.8 Hz, 1H), 2.61−2.46 (m, 2H), 2.60 (d, J = 16.3 Hz, 1H), 2.40 (d, J = 16.3 Hz, 1H), 2.17−2.09 (m, 1H), 2.13 (s, 3H), 2.03−1.92 (m, 1H), 1.04 (s, 3H), 1.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 207.8, 177.0, 85.5, 50.6, 36.4, 32.2, 29.3, 22.5, 22.1, 21.7. HR-MS (ESI$^+$): m/z = 185.1172 [MH$^+$]. Calcd. for $C_{10}H_{17}O_3$: 185.1170. Colorless oil.

One-Pot Reactions. Copper-laponite (143 mg) and palladium catalyst (0.24 mmol) were added to a solution of the corresponding α,β-unsaturated carbonyl compound (1 mmol) and hexafluoroisopropyl alcohol (1.5 mmol) in 5 mL of solvent, then a solution of 2-(trimethylsilyloxy)furan (2 mmol) in 10 mL of solvent was slowly added to the suspension over 5 h. The reaction was monitored by ^{1}H NMR, and at the end of the Mukaiyama−Michael reaction, hydrogen was added, and the mixture was stirred for 12 h. After this time, the mixture of catalysts was filtered off and washed with dry dichloromethane. The solids were dried under vacuum for 12 h prior to reuse. The global yield was determined by ^{1}H NMR using mesitylene as standard.

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ACKNOWLEDGMENT

Financial support from the Spanish Ministerio de Ciencia e Innovación (Projects CTQ2008-05138 and Consolider Ingenio 2010 CSD2006-0003), and the Diputación General de Aragón (E11 Group cofinanced by the European Regional Development Funds) is gratefully acknowledged.

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