JOC The Journal of Organic Chemistry

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# $FeCl_3 \cdot 6H_2O$-Catalyzed Mukaiyama-Aldol Type Reactions of Enolizable Aldehydes and Acetals

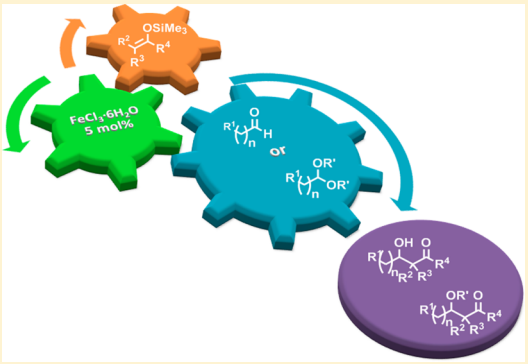
Alejandra Rodríguez-Gimeno,[†] Ana B. Cuenca,[†] Jesús Gil-Tomás,[†] Mercedes Medio-Simón,*[,†] Andrea Olmos,[‡] and Gregorio Asensio[†]

[†]Departamento de Química Orgánica, Universidad de Valencia, Avda. Vicente Andrés Estellés, s/n 46100 Burjassot, Valencia, Spain

[‡]Laboratorio de Catálisis Homogénea, Unidad Asociada al CSIC, CIQSO-Centro de Investigación en Química Sostenible, Universidad de Huelva, Campus El Carmen, 21007 Huelva, Spain

Supporting Information

**ABSTRACT:** Mukaiyama-aldol type reactions of acetals derived from enolizable aldehydes with $FeCl_3 \cdot 6H_2O$, an eco-friendly, low-cost, and stable catalyst, lead to $\beta$-methoxycarbonyl compounds with nearly quantitative yields. The methodology is extended to the parent aldehydes as starting materials, leading to the corresponding aldols with lower yields, but efficiently. Different alkyl and aryl substituted acetals and aldehydes have been tested in the reaction with linear and cyclic silyl enol ethers. Reactions are carried out in an open air atmosphere, and additives are not required. Acetals can be considered activating groups of the carbonyl moiety rather than a protecting group in this type of $FeCl_3 \cdot 6H_2O$-catalyzed condensation.




## INTRODUCTION

Aldol reactions are among the most important procedures for the formation of C−C bonds.[1] Numerous methods have been developed for this reaction, and the Mukaiyama approach emerged as one of the most effective routes in the formation of $\beta$-hydroxyketones, important synthetic intermediates for the preparation of a wide variety of natural products and many other compounds. Since the discovery of the reaction, more than 40 years ago, numerous methods are still being developed to increase its efficiency and stereoselectivity.[1a] Despite all the work done on this transformation, it still suffers from important restrictions. The majority of the methods reported recognized an important reduction of the efficiency of the reaction when enolizable aldehydes are used[2] or even a complete lack of reactivity (Scheme 1).[3] Only a few methods can be used with this type of starting material, but they require complicated noncommercial catalysts[4] or have serious structural and/or functional requirements well on the aldehyde[5] or on the enol[6] counterpart. A typical solution for the preparation of aldols from enolizable aldehydes is the use of acetals as their surrogates (Scheme 1).[7] Acetals are typical carbonyl protecting groups as well as synthetic equivalents of the carbonyl moiety. However, acetals can act as strong electrophiles under acidic conditions by generating an oxonium ion intermediate. Although this method of cleavage gives usually high yields, it requires the use of strong Lewis acids such as TMSOTf, $Bu_2BOTf$, or TMSI and strict anhydrous conditions for the generation of the oxonium ion from the acetal.[8] Another strategy based on $[Ir(COD)(PPh_3)_2]OTf$ as precatalyst has been developed, but it needs to be activated by hydrogen at temperatures of 70 °C.[9] A further possibility is the use of an ester with a reductant instead of the aldehyde.[10] These precedents prompted us to explore alternative methods to allow the use of enolizable aldehydes or their surrogates in Mukaiyama-aldol reactions.

Iron-based catalysts[11] have been discretely used in organic chemistry compared to other transition metals, although they are cheap, easily accessible, nontoxic, and stable. The principal use of iron in organic catalysis is related to oxo and hydride transfer reactions, although carbene, nitrene, and carbanion transfer reactions have also been catalyzed by iron.[12] Another important use of iron as a catalyst profits of its Lewis acid character. In this aspect, iron salts have often been reported as efficient catalysts in Diels−Alder reactions,[13] 1,3-dipolar cyclizations,[14] Friedel−Craft reactions,[15] or Mannich additions.[16] Surprisingly, although the Mukaiyama-aldol reaction is traditionally catalyzed by a Lewis acid, few iron-catalyzed reactions have been described.[17−20] Nevertheless, $FeCl_3$ was already tested in the early stages of the Mukaiyama transformation, although with very low efficiency.[18] Recently, the use of bipyridine,[17a] phosphineoxazoline,[17b] and bisoxazoline[17c,d] $Fe^{II}$ complexes has been successfully reported in the asymmetric version of this process. However, only the bipyridine−iron complexes gave moderated results with enolizable aldehydes, but it required benzoic acid as an additive

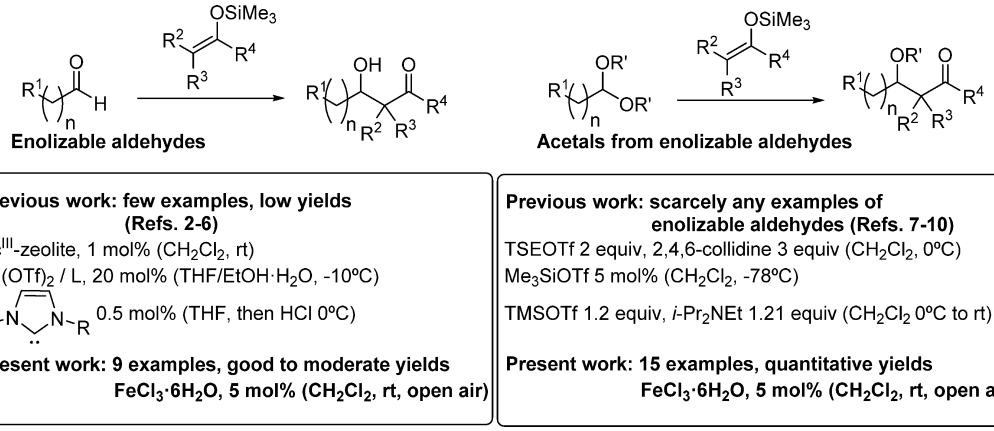
**Received:** July 7, 2014
**Published:** August 7, 2014





dx.doi.org/10.1021/jo501498a | J. Org. Chem. 2014, 79, 8263−8270

**Scheme 1. Mukaiyama-Aldol Reaction with Enolizable Aldehydes and the Use of Their Corresponding Acetals as Surrogates**



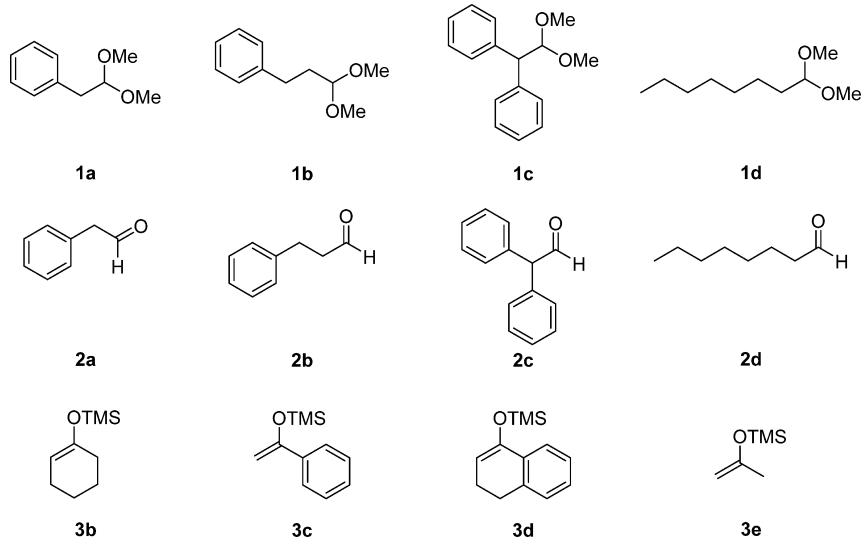




**Figure 1.** Dimethyl acetals **1**, enolizable aldehydes **2**, and silyl enol ethers **3**.

in combination with the catalyst. The other two methods reported gave poor results with saturated aldehydes. In addition, all three catalysts need the use of anoxic conditions to avoid the oxidation of $Fe^{II}$ to $Fe^{III}$ with subsequent loss of the catalytic activity. The development of aldol reactions in water[19] has brought about the possibility of using water-compatible catalysts such as, for instance, $FeCl_3$ or $FeCl_3 \cdot 6H_2O$,[20] although the reaction was mostly applied to aromatic or nonenolizable aldehydes.

On the basis of the above precedents, we decided to assay $FeCl_3 \cdot 6H_2O$ to catalyze the Mukaiyama-aldol reaction of enolizable aldehydes due to the moderated Lewis acid character and the high air and water stability of this cheap, environmentally friendly, stable, and easy to handle salt.

## RESULTS AND DISCUSSION

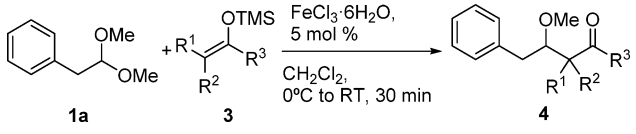
Several $Fe^{III}$ salts were assayed to optimize the catalytic system (see the Supporting Information), and $FeCl_3 \cdot 6H_2O$ was selected to perform the Mukaiyama-aldol reaction of acetals **1** derived from enolizable aldehydes or their precursor aldehydes **2** with silyl enol ethers **3**. 2-Phenylaldehyde dimethylacetal (**1a**), selected as a representative starting material, was treated with different silyl enol ethers **3** (Figure 1) in the presence of 5 mol % $FeCl_3 \cdot 6H_2O$. The formation of the corresponding $\beta$-methoxycarbonyl compounds **4** was efficiently promoted under these conditions (Table 1). Reactions were performed by adding the catalyst over a solution of **1a** and the silyl enol ethers **3a**−**3f** in dichloromethane at 0 °C. The resulting solution was stirred for 30 min at room temperature to yield the corresponding products **4aa**−**4af** after evaporation of the residue and purification through silica column chromatography. Reactions were performed in an open atmosphere without any special care to exclude the presence of moisture or air. Nearly quantitative isolated yields were obtained in most cases for the silyl enol ethers **3** used, independently of their structure or electronic character. The yield was slightly lower in the case of the less reactive ketene silyl acetal **3f**.[8a] Acetone silyl enol ether **3e** gave a lower yield due to partial desilylation.

The influence of the structure of **1** in the reaction efficiency was explored. Acetals **1b**−**1e** (Figure 1) were subjected to react with a selection of silyl enol ethers **3a**−**3c** to give the corresponding compounds **4** with satisfactory to quantitative yields (Table 2). $\alpha$-Substituted acetals **1e** and **1c** did not experience a decrease in the reaction efficiency. Completely saturated octanal dimethyl acetal (**1d**) gave also quantitative conversion into the desired product with all the silyl enol ethers tested.

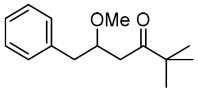
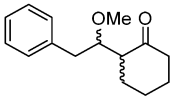
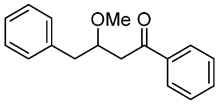
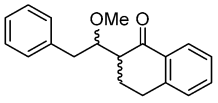
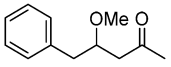
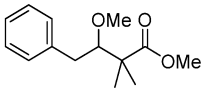
It is remarkable that only compounds **4** containing a completely methylated hydroxy group were obtained in all cases, thus allowing their direct use for future transformations.


dx.doi.org/10.1021/jo501498a | J. Org. Chem. 2014, 79, 8263−8270

**Table 1. $FeCl_3·6H_2O$-Catalyzed Mukaiyama-Aldol Type Reaction of Acetal 1a with Silyl Enol Ethers 3**[a,b,c,d,e]




1a 3 4

| Run | 3 | 4 | Yield (%)[b] |
|---|---|---|---|
| 1 | 3a |  4aa | >99 |
| 2 | 3b |  4ab | >99[c] |
| 3 | 3c |  4ac | 97 |
| 4 | 3d |  4ad | >99[d] |
| 5 | 3e |  4ae | 44[e] |
| 6 | 3f |  4af | 71 |

[a]Reaction conditions: 1.0 equiv of **1a**, 1.1 equiv of **3a**–**3f**, 0.05 equiv of $FeCl_3·6H_2O$, 0.29 M $CH_2Cl_2$, 30 min, rt. [b]Isolated yields. [c]Relation *syn*:*anti* 55:45. [d]Relation *syn*:*anti* 60:40. [e]Desilylation of the ketone was found.

This behavior is quite common, but not general in Mukaiyama-aldol reactions that afford in some occasions to free aldols or their mixtures with methylated products.[8c,9] Compounds **4** were also stable under our reaction conditions and did not lead to $\alpha,\beta$-unsaturated carbonyl compounds even in the presence of $FeCl_3·6H_2O$, an acid catalyst.[8a,21]

The *syn* diastereoisomer always predominated, and the value of the *syn*:*anti* ratio ranged from 55:45 to 70:30 when two diastereoisomers could be obtained. With the aim of increasing the diastereoselection, a number of reactions were performed at temperatures between −78 and 25 °C (Table 3), but the *syn*:*anti* ratio remained unchanged. This observation and the fact that the diastereoselectivity found was in all cases similar to that reported in reactions catalyzed by other Lewis acids[22] have been interpreted previously based on dipolar, inductive, and steric effects.[23]

Encouraged by the excellent results obtained with acetals **1** derived from enolizable aldehydes, we decided to explore the reactivity of the parent free aldehydes. Nonprotected enolizable aldehydes **2a**–**2d** (Figure 1), selected by their poor results under typical Mukaiyama reaction conditions, were exposed to react with representative silyl enol ethers **3a**–**3c** in the same conditions as previously employed by us in the condensation of acetals **1** (Table 4). The direct condensation of enolizable aldehydes is known to afford poor results in the Mukaiyama-aldol condensation according to previous reports in the literature.[2,3] Accordingly, we observed a decrease in the efficiency of the reaction, but satisfactory yields (see Table 4) were still obtained under our reaction conditions in the majority of the cases. Notably, our reactions proceeded in 1–4 h, a reaction time shorter than that reported for typical aldol reactions, which require 12–24 h or even some days.[24] Compounds **5** were less stable than their corresponding acetal derivatives **4**, giving rise in some cases to partial elimination of water in the chromatographic purification process. In the reaction with unprotected aldehydes, the formation of the *syn* diastereoisomer was also prevalent.

The relative reactivity of compounds **1** and **2** was investigated in a competition experiment between **1a** and **2a** in their condensation with **3a** (Scheme 2). Acetal **1a** reacted faster than the parent aldehyde **2a** to afford a 2.3:1 mixture of compounds **4aa** and **5aa**. Consequently, acetals can be considered activating groups of the carbonyl moiety rather than a protecting group in the Mukaiyama-aldol type condensation.

## CONCLUSIONS

A robust and general method for the Mukaiyama type condensation of dimethylacetals derived from enolizable aldehydes catalyzed by $FeCl_3·6H_2O$ has been developed, leading to $\beta$-methoxy ketones with excellent yields. This methodology has been extended also to the parent enolizable aldehydes as starting materials with fair results, although their reactivity was remarkably lower if compared to that of their acetal surrogates. Because of the eco-friendly character, low-cost, and stability of the $FeCl_3·6H_2O$ catalyst and the fact that reactions are performed in an open air atmosphere in the absence of additives, our approach becomes a method of choice for the C–C bond formation using Mukaiyama type reactions.

## EXPERIMENTAL SECTION

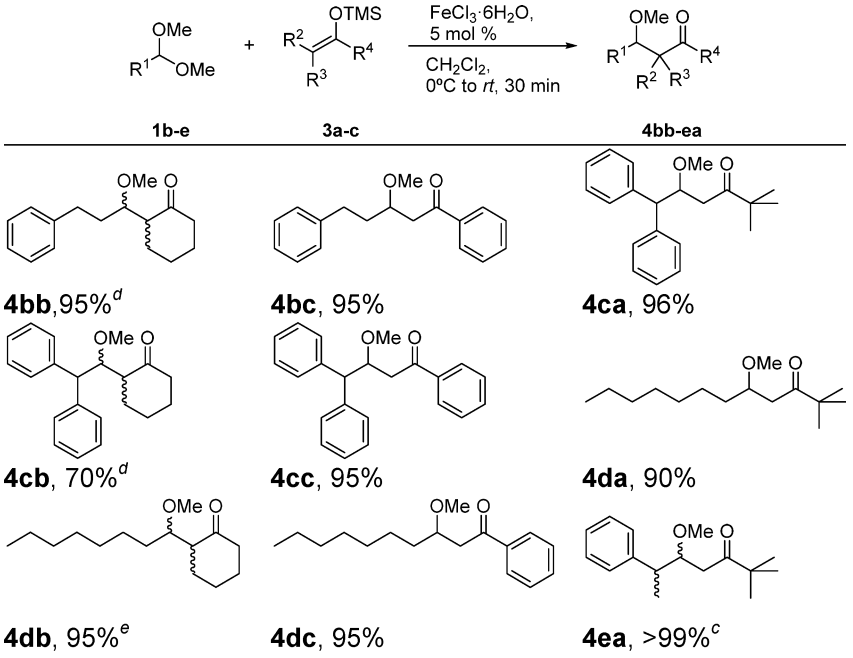
**General Methods.** Chemicals were purchased from commercial suppliers and used as delivered. All reactions were carried out in test tubes or Schlenk tubes. Deuterated solvents were purchased and used without further purification. NMR spectra were recorded at room temperature on 300, 400, or 500 MHz spectrometers. Chemical shifts are given in parts per million (ppm) and coupling constants in Hz. In the $^1H$ and $^{13}C$ spectra, chemical shifts are reported relative to deuterated solvents ($CDCl_3$: 7.26/77.2 ppm; $CD_2Cl_2$: 5.32/54.0 ppm). The following abbreviations were used for $^1H$ NMR to indicate the signal multiplicity: s (singlet), d (doublet), t (triplet), m (multiplet), br s (broad singlet). High-resolution mass spectra were obtained with ESI-TOF analyzer equipment. Analytical thin-layer chromatography was carried out using commercial aluminum sheets precoated (0.2 mm layer thickness) with silica gel 60 F254, and visualization was effected with short wavelength UV light (254 nm). Product purification by flash chromatography was performed using 230–400 mesh silica gel.

**Materials.** Acetals (**1a**, **1d**, and **1e**), aldehydes **2**, silyl enol ethers **3**, all the commercial reagents, and $FeCl_3·6H_2O$ catalyst were commercially available and were used without further purification.

**Synthesis of Acetals. General Procedure.** To a magnetically stirred mixture of the corresponding aldehyde (1 equiv, 5 mmol) and trimethyl orthoformate (1.2 equiv, 6 mmol) in methanol (1 M) was added *p*-TsOH·$H_2O$ (0.01 equiv, 1 mol %), and the mixture was

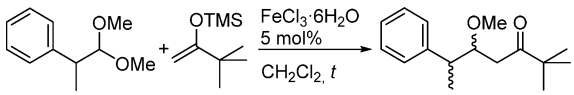

dx.doi.org/10.1021/jo501498a | J. Org. Chem. 2014, 79, 8263–8270

**Table 2. Acetals 1 in $FeCl_3·6H_2O$-Catalyzed Mukaiyama-Aldol Type Reaction with Silyl Enol Ethers 3**[a,b,c,d,e]




[a]Reaction conditions: 1.0 equiv of **1b**–**1e**, 1.1 equiv of **3a**–**3c**, 0.05 equiv of $FeCl_3·6H_2O$, 0.29 M $CH_2Cl_2$, 30 min, rt. [b]Isolated yields. [c]Relation *syn*:*anti* 70:30. [d]Relation *syn*:*anti* 57:43. [e]Relation *syn*:*anti* 60:40.

**Table 3. Effect of Temperature on the Reaction Diastereoselectivity**[a]




| run | temperature (°C) | yield (%)[b] | *syn*:*anti*[c] |
|---|---|---|---|
| 1 | 25[d] | >99 | 70:30 |
| 2 | 0[e] | >99 | 70:30 |
| 3 | −40[f] | >99 | 70:30 |
| 4 | −78[f] | >99 | 71:29 |

[a]Reaction conditions: 1.0 equiv of **1e**, 1.1 equiv of **3a**, 0.05 equiv of $FeCl_3·6H_2O$, 0.29 M $CH_2Cl_2$, *t*. [b]Isolated yields. [c]Relation *syn*:*anti* determined by $^1H$ NMR. [d]30 min. [e]1.15 h. [f]2 h.

stirred at room temperature until completion of the reaction (12–24 h, TLC). The mixture was extracted with $H_2O/Et_2O$. The combined $Et_2O$ extracts were dried ($Na_2SO_4$) and concentrated under reduced pressure, and the product was obtained as a colorless oil and used without purification

*(3,3-Dimethoxypropyl)benzene (**1b**).* Compound **1b** was prepared according to the general procedure and was obtained in >99% yield (0.9013 g, 5 mmol) as a colorless oil. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.28–7.02 (m, 5H), 4.30 (t, $J$ = 5.7 Hz, 1H), 3.26 (s, 6H), 2.60 (dd, $J$ = 9.0, 7.0 Hz, 2H), 1.85 (ddd, $J$ = 10.0, 8.0, 5.9 Hz, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 141.8, 128.5, 126.0, 103.9, 52.9, 34.2, 31.0.The spectral data match with those reported in the literature.[25]

*(2,2-Dimethoxyethane-1,1-diyl)dibenzene (**1c**).* Compound **1c** was prepared according to the general procedure and was obtained in >99% yield (1.2116 g, 5 mmol) as a colorless oil. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.44–7.21 (m, 10H), 5.08 (d, $J$ = 7.7 Hz, 1H), 4.32 (d, $J$ = 7.7 Hz, 1H), 3.38 (s, 6H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 141.2, 128.8, 128.5, 126.5, 106.6, 54.7, 54.1. The spectral data match with those reported in the literature.[26]

**General Procedure for $FeCl_3·6H_2O$-Catalyzed Mukaiyama Type Reaction.** A Schlenk with a Teflon stirring bar was charged with the corresponding acetal **1** or aldehyde **2** (1 equiv, 0.5 mmol) and silyl enol ether **3** (1.1 equiv, 0.55 mmol) in $CH_2Cl_2$ (0.29 M) at 0 °C. Subsequently, $FeCl_3·6H_2O$ (0.05 equiv, 5 mol %) was added. The reaction was stirred at room temperature until consumption of the starting material (monitored by TLC). Next, the reaction was diluted with dichloromethane (2–3 mL) and filtered over activated aluminum oxide. The solvent was removed under reduced pressure, and the corresponding products (**4** or **5**) were isolated by silica gel column chromatography.

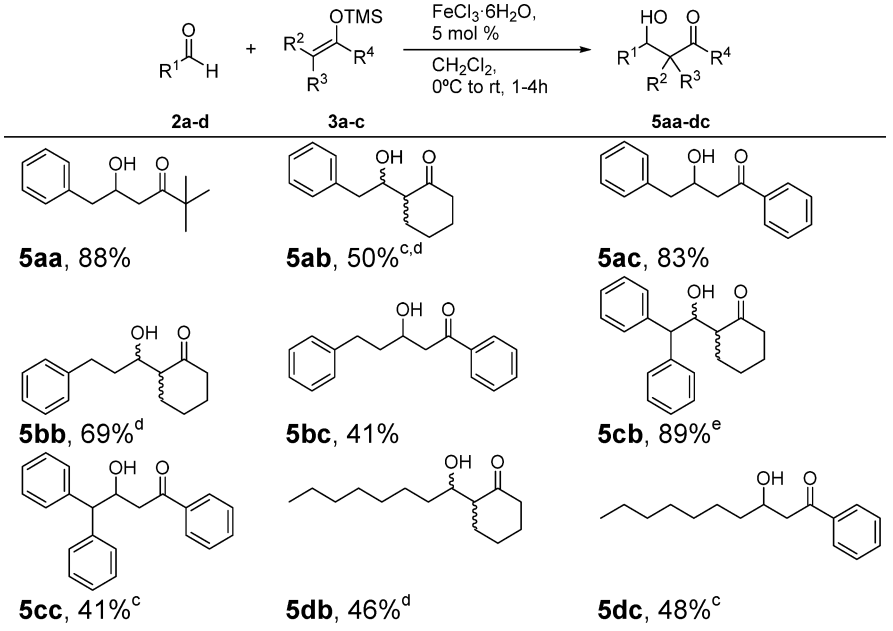
*5-Methoxy-2,2-dimethyl-6-phenylhexan-3-one (**4aa**).* Compound **4aa** was prepared according to the general procedure and was obtained in >99% yield (117.2 mg, 0.5 mmol) as a yellow oil. Eluents: hexane/ethyl acetate = 100:1. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.41–7.33 (m, 2H), 7.29–7.27 (m, 3H), 4.13–4.00 (m, 1H), 3.38 (s, 3H), 2.96 (dd, $J$ = 14.0, 6.5 Hz, 1H), 2.91–2.80 (m, 2H), 2.50 (dd, $J$ = 17.2, 5.0 Hz, 1H), 1.19 (s, 9H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 214.2, 138.5, 129.6, 128.4, 126.3, 78.3, 57.7, 44.3, 41.1, 40.1, 26.2. HRMS (ESI-TOF) $m/z$: $[M + Na]^+$ Calcd for $C_{15}H_{22}O_2Na$ 257.1517; found 257.1515.

*2-(1-Methoxy-2-phenylethyl)cyclohexan-1-one (**4ab**).* Compound **4ab** was prepared according to the general procedure and was obtained in >99% yield (116.2 mg, 0.5 mmol) as a mixture of diastereoisomers in a 55:45 proportion (*syn*/*anti*). *Syn* diastereoisomer: Eluents: hexane/ethyl acetate = 100:1. Yellow oil. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.23–7.18 (m, 2H), 7.16–7.08 (m, 3H), 3.86 (td, $J$ = 6.5, 4.3 Hz, 1H), 3.22 (s, 3H), 2.81 (dd, $J$ = 13.7, 6.3 Hz, 1H), 2.67 (dd, $J$ = 13.7, 6.7 Hz, 1H), 2.36–2.25 (m, 1H), 2.21–2.05 (m, 3H), 1.98–1.91 (m, 1H), 1.89–1.78 (m, 1H), 1.68–1.45 (m, 3H). $^{13}C$ NMR (75 MHz,) $\delta$ 211.8, 138.8, 129.5, 128.5, 126.3, 79.5, 58.5, 53.4, 42.5, 37.9, 27.5, 27.3, 24.9. HRMS (ESI-TOF) $m/z$: $[M + H]^+$ Calcd for $C_{15}H_{21}O_2$ 233.1542; found 233.1537. *Anti* diastereoisomer: Eluents: hexane/ethyl acetate = 100:1. Yellow oil. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.23–7.11 (m, 5H), 3.74 (ddd, $J$ = 8.2, 4.6, 3.4 Hz, 1H), 3.10 (s, 3H), 2.79 (dd, $J$ = 13.8, 3.3 Hz, 1H), 2.61–2.49 (m, 2H), 2.39–2.23 (m, 2H), 2.08 (ddd, $J$ = 12.1, 6.9, 3.8 Hz, 1H), 2.02–1.91 (m, 1H), 1.88–1.81 (m, 1H), 1.66–1.50 (m, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 212.0, 139.9, 129.5, 128.3, 126.1, 81.7, 58.2, 53.2, 42.6, 37.9, 28.4, 27.6, 24.8. HRMS (ESI-TOF) $m/z$: $[M + H]^+$ Calcd for $C_{15}H_{21}O_2$ 233.1542; found 233.1537.

*3-Methoxy-1,4-diphenylbutan-1-one (**4ac**).* Compound **4ac** was prepared according to the general procedure and was obtained in 97% yield (123.4 mg, 0.5 mmol) as a colorless solid (mp 54–56 °C). $^1H$

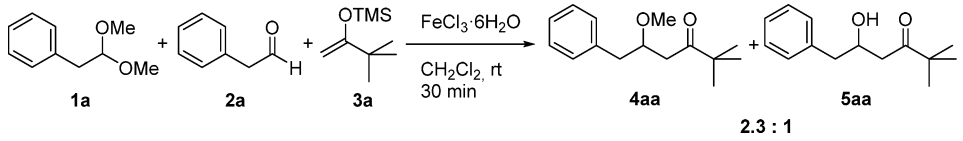

dx.doi.org/10.1021/jo501498a | J. Org. Chem. 2014, 79, 8263–8270

**Table 4. Enolizable Aldehydes 2 in $FeCl_3·6H_2O$-Catalyzed Mukaiyama-Aldol Type Reaction with Silyl Enol Ethers 3**[a,b,c,d,e]




[a]Reaction conditions: 1.0 equiv of **2a−2d**, 1.1 equiv of **3a−3c**, 0.05 equiv of $FeCl_3·6H_2O$, 0.29 M $CH_2Cl_2$, rt. [b]Isolated yields. [c]Reaction carried out with 0.1 equiv of $FeCl_3·6H_2O$. [d]Relation *syn:anti* 55:45. [e]Purification by flash chromatography gave the elimination product.

**Scheme 2. Competition Experiment between Acetal 1a, Aldehyde 2a, and Silyl Enol Ether 3a**




NMR (300 MHz, $CDCl_3$) $\delta$ 8.09−8.04 (m, 2H), 7.76−7.67 (m, 1H), 7.63−7.58 (m, 2H), 7.51−7.38 (m, 5H), 4.31 (dtd, $J$ = 7.3, 6.1, 4.9 Hz, 1H), 3.52 (s, 3H), 3.41 (dd, $J$ = 16.6, 7.3 Hz, 1H), 3.18−3.00 (m, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 198.9, 138.3, 137.3, 133.2, 129.7, 128.7, 128.5, 128.2, 126.5, 78.7, 57.7, 42.9, 40.3. The spectral data match with those reported in the literature.[27]

*2-(1-Methoxy-2-phenylethyl)-3,4-dihydronaphthalen-1(2H)-one (**4ad**).* Compound **4ad** was prepared according to the general procedure and was obtained in >99% yield (140.2 mg, 0.5 mmol) as a mixture of diastereoisomers in a 60:40 proportion (*syn*/*anti*). *Syn* diastereoisomer: Yellow solid (mp 61−63 °C). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.05 (dd, $J$ = 7.8, 1.3 Hz, 1H), 7.48 (td, $J$ = 7.5, 1.5 Hz, 1H), 7.39−7.19 (m, 7H), 4.47 (ddd, $J$ = 8.6, 6.5, 2.5 Hz, 1H), 3.33 (s, 3H), 3.18−3.09 (m, 1H), 3.09−2.88 (m, 2H), 2.80 (dd, $J$ = 13.6, 8.1 Hz, 1H), 2.42 (ddd, $J$ = 12.7, 4.5, 2.5 Hz, 1H), 2.33 (dt, $J$ = 12.6, 4.1 Hz, 1H), 2.26−2.09 (m, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 198.6, 144.2, 138.7, 133.7, 133.0, 129.4, 128.7, 128.6, 127.6, 126.6, 126.5, 79.8, 58.7, 50.4, 38.0, 29.1, 22.2. *Anti* diastereoisomer: Yellow solid (mp 62−63 °C). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.05 (dd, $J$ = 7.9, 1.2 Hz, 1H), 7.48 (td, $J$ = 7.5, 1.5 Hz, 1H), 7.36−7.27 (m, 5H), 7.25−7.17 (m, 2H), 4.20 (dt, $J$ = 8.9, 3.4 Hz, 1H), 3.22 (s, 3H), 3.11−2.99 (m, 2H), 2.99−2.90 (m, 1H), 2.81−2.66 (m, 2H), 2.34 (dq, $J$ = 12.6, 4.1 Hz, 1H), 2.12−1.98 (m, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 199.0, 144.4, 140.1, 133.5, 133.2, 129.5, 128.9, 128.3, 127.4, 126.8, 126.2, 82.5, 58.1, 50.0, 38.1, 29.3, 23.6. The spectral data match with those reported in the literature.[28]

*4-Methoxy-5-phenylpentan-2-one (**4ae**).* Compound **4ae** was prepared according to the general procedure and was obtained in 44% yield (42.3 mg, 0.22 mmol) as a yellow oil. Eluents: hexane/ethyl acetate = 50:1. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.26−7.07 (m, 5H), 3.91−3.77 (m, 1H), 3.27 (s, 3H), 2.84 (dd, $J$ = 13.7, 5.8 Hz, 1H), 2.68−2.51 (m, 2H), 2.34 (dd, $J$ = 16.3, 4.4 Hz, 1H), 2.04 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 207.6, 138.1, 129.6, 128.5, 126.5, 78.4, 57.5, 47.9, 39.9, 31.2. HRMS (ESI-TOF) $m/z$: $[M + H]^+$ Calcd for $C_{12}H_{17}O_2$ 193.1223; found 193.1214.

*Methyl 3-Methoxy-2,2-dimethyl-4-phenylbutanoate (**4af**).* Compound **4af** was prepared according to the general procedure and was obtained in 71% yield (83.9 mg, 0.36 mmol) as a yellow oil. Eluents: hexane/ethyl acetate = 50:1. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.24−7.14 (m, 5H), 3.60 (s, 3H), 3.55 (dd, $J$ = 8.7, 3.5 Hz, 1H), 2.94 (s, 3H), 2.68−2.51 (m, 2H), 1.19 (s, 3H), 1.13 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 177.4, 139.9, 129.5, 128.4, 126.2, 88.1, 61.0, 51.9, 48.0, 38.0, 21.4, 20.8. HRMS (ESI-TOF) $m/z$: $[M + Na]^+$ Calcd for $C_{14}H_{20}O_3Na$ 259.1310; found 259.1310.

*2-(1-Methoxy-3-phenylpropyl)cyclohexan-1-one (**4bb**).* Compound **4bb** was prepared according to the general procedure and was obtained in 95% yield (117.0 mg, 0.48 mmol) as a mixture of diastereoisomers in a 57:43 proportion (*syn*/*anti*). *Syn* diastereoisomer: Eluents: hexane/ethyl acetate = 30:1.Colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.39−7.32 (m, 2H), 7.31−7.25 (m, 3H), 3.83 (dt, $J$ = 7.2, 5.1 Hz, 1H), 3.47 (s, 3H), 2.86−2.66 (m, 2H), 2.52−2.21 (m, 5H), 2.05−1.77 (m, 4H), 1.78−1.68 (m, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 211.9, 142.2, 128.5, 125.9, 77.9, 58.5, 54.6, 42.4, 34.4, 32.0, 27.9, 27.4, 24.7. HRMS (ESI-TOF) $m/z$: $[M + Na]^+$ Calcd for $C_{16}H_{22}O_2Na$ 269.1512; found 269.1511. *Anti* diastereoisomer: Eluents: hexane/ethyl acetate = 30:1. Colorless oil. $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.29−7.26 (m, 1H), 7.23−7.21 (m, 2H), 7.19−7.16 (m, 1H), 3.70 (ddd, $J$ = 8.0, 4.8, 2.9 Hz, 1H), 3.36 (s, 3H), 2.83−2.80 (m, 1H), 2.71−2.62 (m, 2H), 2.43−2.36 (m, 1H), 2.34−2.28 (m, 1H), 2.10−2.10 (m, 1H), 2.05−1.98 (m, 1H), 1.93−1.86 (m, 1H), 1.85−1.79 (m, 1H), 1.70−1.61 (m, 4H). $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 212.2, 142.5, 128.6, 128.4, 125.9, 79.2, 57.6, 52.7, 42.5, 33.1, 32.3, 27.9, 27.6, 24.8. HRMS (ESI-TOF) $m/z$: $[M + Na]^+$ Calcd for $C_{16}H_{22}O_2Na$ 269.1512; found 269.1511.

*3-Methoxy-1,5-diphenylpentan-1-one (**4bc**).* Compound **4bc** was prepared according to the general procedure and was obtained in 95%


dx.doi.org/10.1021/jo501498a | J. Org. Chem. 2014, 79, 8263−8270

yield (127.5 mg, 0.48 mmol) as a yellow oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.06−8.00 (m, 2H), 7.66−7.59 (m, 1H), 7.56−7.49 (m, 2H), 7.38−7.25 (m, 5H), 4.06−3.96 (m, 1H), 3.45 (s, 3H), 3.44−3.35 (m, 1H), 3.05 (dd, $J$ = 16.2, 5.7 Hz, 1H), 3.02−3.09 (m, 2H), 2.04−1.94 (m, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 198.8, 142.0, 137.3, 133.2, 128.6, 128.6, 128.6, 128.4, 128.4, 128.3, 128.3, 128.2, 125.9, 77.1, 57.3, 43.2, 36.3, 31.5. The spectral data match with those reported in the literature.[29]

*5-Methoxy-2,2-dimethyl-6,6-diphenylhexan-3-one (**4ca**).* Compound **4ca** was prepared according to the general procedure and was obtained in 96% yield (149.0 mg, 0.48 mmol) as a white solid (mp 68−70 °C). Eluents: hexane/ethyl acetate = 50:1. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.25−7.21 (m, 2H), 7.17−7.08 (m, 6H), 7.07−6.99 (m, 2H), 4.38 (ddd, $J$ = 8.1, 7.2, 4.0 Hz, 1H), 3.86 (d, $J$ = 8.1 Hz, 1H), 2.91 (s, 3H), 2.64 (dd, $J$ = 17.5, 7.2 Hz, 1H), 2.34 (dd, $J$ = 17.5, 4.0 Hz, 1H), 0.87 (s, 9H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 214.7, 142.5, 142.0, 129.1, 128.7, 128.6, 128.4, 126.6, 126.6, 80.2, 59.3, 56.9, 44.4, 41.3, 26.2. HRMS (ESI-TOF) $m/z$: $[M + Na]^+$ Calcd for $C_{21}H_{26}O_2Na$ 333.1830; found 333.1834.

*2-(1-Methoxy-2,2-diphenylethyl)cyclohexan-1-one (**4cb**).* Compound **4cb** was prepared according to the general procedure and was obtained in 70% yield (107.9 mg, 0.35 mmol) as a mixture of diastereoisomers in a 57:43 proportion (*syn*/*anti*). *Syn* diastereoisomer: Eluents: hexane/ethyl acetate = 30:1. Pale yellow solid. (mp 124−126 °C). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.32−7.31 (m, 2H), 7.22−7.17 (m, 6H), 7.11−7.08 (m, 2H), 4.58 (dd, $J$ = 9.6, 2.8 Hz, 1H), 3.95 (d, $J$ = 9.6 Hz, 1H), 2.94 (s, 3H), 2.35−2.28 (m, 1H), 2.22−2.15 (m, 1H), 2.09−1.98 (m, 2H), 1.87 (m, 1H), 1.84−1.77 (m, 1H), 1.68−1.63 (m, 1H), 1.59−1.49 (m, 1H), 1.41−1.30 (m, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 212.0, 142.5, 142.4, 129.0, 128.8, 128.4, 126.7, 126.5, 80.5, 60.5, 55.1, 52.7, 42.1, 26.5, 26.0, 24.7. HRMS (ESI-TOF) $m/z$: $[M + Na]^+$ Calcd for $C_{21}H_{24}O_2Na$ 331.1669; found 331.1668. *Anti* diastereoisomer: Eluents: hexane/ethyl acetate = 30:1. White solid. (mp 122−125 °C). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.53−7.49 (m, 2H), 7.31−7.27 (m, 2H), 7.27−7.19 (m, 5H), 7.18−7.15 (m, 1H), 4.29 (d, $J$ = 6.3 Hz, 1H), 4.02 (t, $J$ = 6.3 Hz, 1H), 2.97 (s, 3H), 2.58−2.47 (m, 1H), 2.35−2.25 (m, 1H), 2.25−2.13 (m, 1H), 1.97−1.90 (m, 2H), 1.83−1.73 (m, 1H), 1.68−1.52 (m, 2H), 1.48−1.40 (m, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 212.0, 142.7, 141.3, 129.8, 129.0, 128.5, 128.4, 126.6, 126.5, 85.1, 61.0, 54.6, 53.9, 42.8, 31.1, 27.9, 24.9. HRMS (ESI-TOF) $m/z$: $[M + Na]^+$ Calcd for $C_{21}H_{24}O_2Na$ 331.1669; found 331.1668.

*3-Methoxy-1,4,4-triphenylbutan-1-one (**4cc**).* Compound **4cc** was prepared according to the general procedure and was obtained in 95% yield (156.9 mg, 0.48 mmol) as a yellow solid (mp 98−100 °C). Eluents: hexane/ethyl acetate = 30:1. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.78−7.75 (m, 2H), 7.48−7.40 (m, 1H), 7.37−7.31 (m, 4H), 7.31−7.26 (m, 1H), 7.25−7.17 (m, 5H), 7.14−7.05 (m, 2H), 4.62 (td, $J$ = 7.6, 3.9 Hz, 1H), 4.04 (d, $J$ = 7.9 Hz, 1H), 3.19 (dd, $J$ = 16.8, 7.4 Hz, 1H), 3.05 (s, 3H), 2.90 (dd, $J$ = 16.8, 3.9 Hz, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 199.2, 142.4, 141.8, 137.3, 133.2, 129.2, 128.7, 128.7, 128.6, 128.5, 128.3, 126.7, 126.6, 80.5, 59.1, 57.0, 43.1. HRMS (ESI-TOF) $m/z$: $[M + Na]^+$ Calcd for $C_{23}H_{22}O_2Na$ 353.1512; found 353.1509.

*5-Methoxy-2,2-dimethyldodecan-3-one (**4da**).* Compound **4da** was prepared according to the general procedure and was obtained in 90% yield (109.1 mg, 0.45 mmol) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.69 (ddd, $J$ = 11.9, 8.7, 5.3 Hz, 1H), 3.29 (s, 3H), 2.78 (dd, $J$ = 17.0, 6.9 Hz, 1H), 2.42 (dd, $J$ = 17.0, 5.4 Hz, 1H), 1.36−1.17 (m, 12H), 1.12 (s, 9H), 0.90−0.80 (m, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 214.6, 77.3, 57.4, 44.5, 41.5, 34.3, 31.9, 29.8, 29.4, 26.3, 26.3, 25.4, 22.8, 14.2. The spectral data match with those reported in the literature.[30]

*2-(1-Methoxyoctyl)cyclohexan-1-one (**4db**).* Compound **4db** was prepared according to the general procedure and was obtained in 95% yield (114.2 mg, 0.48 mmol) as a mixture of diastereoisomers in a 60:40 proportion (*syn*/*anti*). *Syn* diastereoisomer: Colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.67 (dt, $J$ = 10.4, 5.1 Hz, 1H), 3.32 (s, 3H), 2.43−2.17 (m, 3H), 2.15−1.58 (m, 7H), 1.33−1.16 (m, 11H), 0.85 (t, $J$ = 6.7 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 212.0, 78.1, 58.3, 54.3, 42.4, 32.2, 31.9, 29.8, 29.4, 27.4, 27.2, 25.7, 24.7, 22.7, 14.2. *Anti* diastereoisomer: Colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.62 (m, 1H), 3.31 (s, 3H), 2.65−2.52 (m, 1H), 2.45−2.21 (m, 2H), 2.09−1.94 (m, 2H), 1.94−1.81 (m, 1H), 1.69−1.19 (m, 15H), 0.87 (t, $J$ = 6.7 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 212.3, 79.7, 57.6, 53.1, 42.4, 32.0, 31.1, 29.9, 29.4, 28.1, 27.6, 25.9, 24.7, 22.8, 14.2. The spectral data match with those reported in the literature.[31]

*3-Methoxy-1-phenyldecan-1-one (**4dc**).* Compound **4dc** was prepared according to the general procedure and was obtained in 95% yield (125.9 mg, 0.48 mmol) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.04−7.95 (m, 2H), 7.59 (ddd, $J$ = 6.4, 3.8, 1.3 Hz, 1H), 7.54−7.44 (m, 2H), 3.98−3.82 (m, 1H), 3.38 (s, 3H), 3.32 (dd, $J$ = 16.1, 6.9 Hz, 1H), 2.97 (dd, $J$ = 16.1, 5.3 Hz, 1H), 1.66−1.24 (m, 12H), 0.92 (t, $J$ = 6.7 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 199.2, 137.5, 133.1, 128.7, 128.3, 77.7, 57.3, 43.4, 34.5, 31.9, 29.8, 29.4, 25.3, 22.7, 14.2.The spectral data match with those reported in the literature.[26]

*5-Methoxy-2,2-dimethyl-6-phenylheptan-3-one (**4ea**).* Compound **4ea** was prepared according to the general procedure and was obtained in >99% yield (124.2 mg, 0.5 mmol) as a colorless oil mixture of diastereoisomers. Spectra of the inseparable mixture of diastereoisomers in a 71:29 proportion (*syn*/*anti*). The *syn*/*anti* assignment was determined in comparison with the spectra reported in the literature.[32] *Syn* diastereoisomer: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.34−7.15 (m, 5H), 3.91 (td, $J$ = 7.3, 3.6 Hz,1H,), 3.34 (s, 3H), 2.91−2.82 (m, 1H), 2.79−2.59 (m, 1H), 2.37−2.23 (m, 1H), 1.34−1.29 (m, 3H), 1.07−1.04 (m, 9H). *Anti* diastereoisomer: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.34−7.15 (m, 5H), 3.91 (td, $J$ = 7.3, 3.6 Hz, 1H,), 3.27 (s, 1H), 3.05−2.99 (m, 1H), 2.79−2.59 (m, 1H), 2.37−2.23 (m, 1H), 1.34−1.29 (m, 3H), 1.07−1.04 (m, 9H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 214.6, 214.5, 144.3, 143.4, 128.5, 128.4, 128.3, 128.0, 126.5, 126.4, 81.9, 81.7, 59.3, 58.7, 44.5, 44.4, 42.6, 40.4, 38.7, 26.3, 26.2, 17.3, 16.2.

*5-Hydroxy-2,2-dimethyl-6-phenylhexan-3-one (**5aa**).* Compound **5aa** was prepared according to the general procedure and was obtained in 88% yield (96.9 mg, 0.44 mmol) as a white dense oil in 1.5 h. Eluents: hexane/ethyl acetate = 50:1. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.49−7.19 (m, 5H), 4.62−4.27 (m, 1H), 3.03−2.50 (m, 4H), 1.21 (s, 9H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 217.3, 138.2, 129.4, 128.5, 126.5, 68.9, 44.2, 42.9, 42.3, 26.3. The spectral data match with those reported in the literature.[33]

*2-(1-Hydroxy-2-phenylethyl)cyclohexan-1-one (**5ab**).* Compound **5ab** was prepared according to the general procedure and was obtained in 50% yield (54.6 mg, 0.25 mmol) as a white solid (mp 58−60 °C) in 1 h. (eluents: Hexane/ethyl acetate = 5:1). Spectra of the inseparable mixture of diastereoisomers in a 55:45 proportion (*syn*/*anti*). *Syn* diastereoisomer: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.37−7.29 (m, 5H), 4.45−4.37 (m, 1H), 3.35 (br s, 1H,), 2.86 (dd, $J$ = 13.7, 8.0 Hz,1H), 2.71 (dd, $J$ = 13.7, 6.3 Hz, 1H), 2.47−2.25 (m, 3H), 2.21−1.96 (m, 4H), 1.85−1.62 (m, 2H). *Anti* diastereoisomer: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.28−7.22 (m, 5H), 3.99 (br s, 1H), 2.96 (dd, $J$ = 13.8, 4.5 Hz, 1H), 2.78 (dd, $J$ = 13.8, 8.1 Hz, 1H), 2.55 (s, 1H), 2.47−2.25 (m, 3H), 2.21−1.96 (m, 4H), 1.85−1.62 (m, 2H). $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 215.5, 214.7, 138.9, 138.7, 129.6, 129.3, 128.7, 128.5, 126.6, 126.5, 73.0, 70.3, 55.0, 54.2, 43.1, 42.8, 40.5, 39.6, 31.2, 28.1, 27.9, 26.8, 25.1, 25.0. HRMS (ESI-TOF) $m/z$: $[M + H]^+$ Calcd for $C_{14}H_{19}O_2$ 219.1380; found 219.1380.

*3-Hydroxy-1,4-diphenylbutan-1-one (**5ac**).* Compound **5ac** was prepared according to the general procedure and was obtained in 83% yield (99.7 mg, 0.42 mmol) as a yellow solid (mp 75−77 °C) in 1 h. Eluents: hexane/ethyl acetate = 5:1. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.95−7.93 (m, 2H), 7.62−7.58 (m, 1H), 7.50−7.45 (m, 2H), 7.38−7.34 (m, 2H), 7.33−7.24 (m, 3H), 4.55−4.49 (m, 1H), 3.26 (br s, 1H), 3.22−3.08 (m, 2H), 3.01 (dd, $J$ = 13.6, 7.1 Hz, 1H), 2.88 (dd, $J$ = 13.6, 6.4 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 200.6, 138.2, 136.9, 133.6, 129.6, 128.8, 128.7, 128.2, 126.7, 69.1, 44.2, 43.1. The spectral data match with those reported in the literature.[34]

*2-(1-Hydroxy-3-phenylpropyl)cyclohexan-1-one (**5bb**).* Compound **5bb** was prepared according to the general procedure and was obtained in 69% yield (80.2 mg, 0.35 mmol) as a colorless oil in 3.5 h. Eluents: hexane/ethyl acetate = 5:1. Spectra of the inseparable


dx.doi.org/10.1021/jo501498a | J. Org. Chem. 2014, 79, 8263−8270

mixture of diastereoisomers in a 55:45 proportion (*syn*/*anti*). *Syn* diastereoisomer: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.19−7.22 (m, 1H), 7.17−7.07 (m, 5H), 3.74−3.63 (m, 1H), 2.67−2.53 (m, 1H), 2.34−2.19 (m, 2H), 2.01 (dd, $J$ = 9.5, 3.9 Hz, 2H), 1.90−1.44 (m, 8H). *Anti* diastereoisomer: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.19−7.22 (m, 1H), 7.17−7.07 (m, 5H), 4.05 (dt, $J$ = 9.6, 3.0 Hz, 1H), 2.84−2.74 (m, 1H), 2.34−2.19 (m, 2H), 2.01 (dd, $J$ = 9.5, 3.9 Hz, 2H), 1.90−1.44 (m, 8H). $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 215.9, 215.0, 142.5, 142.2, 128.6, 128.6, 128.5, 128.5, 126.0, 125.9, 71.1, 68.7, 56.2, 55.4, 43.0, 42.8, 35.6, 34.9, 32.6, 31.7, 31.1, 30.9, 27.9, 27.8, 26.7, 25.1, 25.1. HRMS (ESI-TOF) $m/z$: $[M + H]^+$ Calcd for $C_{15}H_{21}O_2$ 233.1536; found 233.1541.

*3-Hydroxy-1,5-diphenylpentan-1-one (**5bc**).* Compound **5bc** was prepared according to the general procedure and was obtained in 41% yield (52.1 mg, 0.21 mmol) as a yellow oil in 4 h. Eluents: hexane/ethyl acetate = 5:1. $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.04−7.92 (m, 2H), 7.67−7.57 (m, 1H), 7.55−7.45 (m, 2H), 7.36−7.30 (m, 2H), 7.29−7.27 (m, 2H), 7.25−7.20 (m, 1H), 4.30−4.26 (m, 1H), 3.40 (d, $J$ = 2.9 Hz, 1H), 3.20 (dd, $J$ = 17.7, 2.8 Hz, 1H), 3.11 (dd, $J$ = 17.7, 8.9 Hz, 1H), 2.93 (ddd, $J$ = 14.7, 9.7, 5.3 Hz, 1H), 2.80 (ddd, $J$ = 13.8, 9.5, 6.9 Hz, 1H), 2.05−1.93 (m, 1H), 1.93−1.79 (m, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 201.0, 142.0, 136.8, 133.7, 128.8, 128.6, 128.5, 128.2, 126.0, 67.2, 45.2, 38.3, 32.0. The spectral data match with those reported in the literature.[9,35]

*(E)-2-(2,2-Diphenylethylidene)cyclohexan-1-one (**5cb**).* Compound **5cb** was prepared according to the general procedure and was obtained in 89% yield (123.0 mg, 0.45 mmol) as a white solid (mp 78−81 °C) in 2 h. Eluents: hexane/ethyl acetate = 100:1. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.35−7.19 (m, 10H), 7.13 (dt, $J$ = 10.0, 2.2 Hz, 1H), 4.94 (d, $J$ = 10.0 Hz, 1H), 2.63 (td, $J$ = 6.5, 2.2 Hz, 2H), 2.49 (t, $J$ = 6.7 Hz, 2H), 1.93−1.84 (m, 2H), 1.83−1.72 (m, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 201.1, 143.0, 140.1, 136.2, 128.8, 128.4, 126.8, 48.9, 40.4, 27.1, 23.6, 23.3. HRMS (ESI-TOF) $m/z$: $[M + H]^+$ Calcd for $C_{20}H_{21}O$ 277.1587; found 277.1584.

*3-Hydroxy-1,4,4-triphenylbutan-1-one (**5cc**).* Compound **5cc** was prepared according to the general procedure and was obtained in 41% yield (64.9 mg, 0.21 mmol) as a pale yellow solid (mp 126−128 °C) in 1.5 h. Eluents: hexane/ethyl acetate = 50:1. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.94−7.85 (m, 2H), 7.63−7.22 (m, 13H), 5.13 (ddd, $J$ = 11.6, 7.4, 3.3 Hz, 1H), 4.13 (d, $J$ = 9.1 Hz, 1H), 3.20−3.13 (m, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 200.5, 142.2, 141.6, 136.9, 133.5, 128.9, 128.8, 128.7, 128.7, 128.4, 128.2, 126.9, 126.8, 70.1, 57.8, 43.6. The spectral data match with those reported in the literature.[36]

*2-(1-Hydroxyoctyl)cyclohexan-1-one (**5db**).* Compound **5db** was prepared according to the general procedure and was obtained in 46% yield (52.1 mg, 0.23 mmol) as a colorless oil in 2 h. Eluents: hexane/ethyl acetate = 20:1. Spectra of the inseparable mixture of diastereoisomers in a 55:45 proportion (*syn*/*anti*). *Syn* diastereoisomer: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.72 (t, $J$ = 7.2 Hz, 1H), 2.45−2.26 (m, 3H), 2.14−2.04 (m, 2H), 2.00−1.85 (m, 1H), 1.74−1.58 (m, 2H), 1.56−1.38 (m, 3H), 1.37−1.20 (m, 11H), 0.87 (t, $J$ = 6.9 Hz, 3H). *Anti* diastereoisomer: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.13−4.03 (m, 1H), 2.45−2.26 (m, 3H), 2.14−2.04 (m, 2H), 2.00−1.85 (m,1H), 1.74−1.58 (m, 2H), 1.56−1.38 (m, 3H), 1.37−1.20 (m, 11H), 0.87 (t, $J$ = 6.9 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 216.0, 215.2, 71.7, 69.2, 56.1, 55.1, 43.0, 42.8, 33.7, 33.0, 32.0, 32.0, 30.9, 29.8, 29.7, 29.4, 29.4, 28.0, 27.8, 26.5, 26.3, 25.3, 25.1, 25.1, 22.8, 14.2. HRMS (ESI-TOF) $m/z$: $[M + H]^+$ Calcd for $C_{14}H_{27}O_2$ 227.2006; found 227.2009.

*3-Hydroxy-1-phenyldecan-1-one (**5dc**).* Compound **5dc** was prepared according to the general procedure and was obtained in 48% yield (59.6 mg, 0.24 mmol) as a white solid (mp 40−43 °C) in 1.5 h. Eluents: hexane/ethyl acetate = 20:1. $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.97−7.95 (m, 2H), 7.60−7.57 (m, 1H), 7.52−7.43 (m, 2H), 4.22 (br s, 1H), 3.26−3.12 (m, 2H), 3.04 (dd, $J$ = 17.6, 9.1 Hz, 2H), 1.67−1.56 (m, 2H), 1.53−1.47 (m, 2H), 1.42−1.21 (m, 9H), 0.88 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 201.2, 137.0, 133.7, 128.8, 128.2, 67.9, 45.2, 36.7, 32.0, 29.7, 29.4, 25.7, 22.8, 14.2. The spectral data match with those reported in the literature.[37] HRMS (ESI-TOF) $m/z$: $[M + H]^+$ Calcd for $C_{16}H_{25}O_2$ 249.1849; found 249.1849.

## ■ ASSOCIATED CONTENT

### Supporting Information

Optimization table and copies of $^1$H and $^{13}$C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

## ■ AUTHOR INFORMATION


### Corresponding Author

*E-mail: mercedes.medio@uv.es.


### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

This work was supported by the Spanish Ministerio de Ciencia e Innovación, European Community Founds (FEDER), CTQ 2010-19999 and CTQ2011-28942-C02-02 grants. A.O. thanks the Spanish government for a Juan de la Cierva contract. We thank the SCSIE (Universidad de Valencia) for access to instrumental facilities.

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