CHEMISTRY
A European Journal

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Selective Synthesis of Unsymmetrical Aliphatic Acyloins through Oxidation of Iridium Enolates

Authors: Amparo Sanz-Marco, Samuel Martinez Erro, and Belén Martín-Matute

To be cited as: *Chem. Eur. J.* 10.1002/chem.201803117

Link to VoR: http://dx.doi.org/10.1002/chem.201803117

Supported by
ACES

WILEY-VCH

10.1002/chem.201803117

COMMUNICATION

WILEY-VCH

Selective Synthesis of Unsymmetrical Aliphatic Acyloins through Oxidation of Iridium Enolates

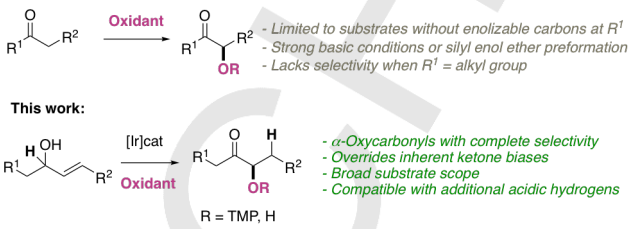
Amparo Sanz-Marco,[a] Samuel Martinez-Erro,[a] and Belén Martín-Matute*[a]

Abstract: The first method to access unsymmetrical aliphatic acyloins is presented. The method relies on a fast 1,3-hydride shift mediated by an Ir(III) complex in allylic alcohols followed by oxidation with TEMPO$^+$. The direct conversion of allylic alcohols into acyloins is achieved in a one-pot procedure. Further functionalization of the Cα´ of the α-aminooxy ketone products gives access to highly functionalized unsymmetrical aliphatic ketones, which further highlights the utility of this transformation.

The selective synthesis of α-oxygenated carbonyl compounds is of paramount importance in organic chemistry.[1,2] These motifs are commonly found in biologically active molecules, and they are versatile building blocks in organic synthesis. Through direct oxidation, α-hydroxy aldehydes,[3] α-hydroxy-β-dicarbonyl compounds,[4] α-hydroxy esters,[5] α-hydroxy *N*-acyl oxazolidinones,[6] and α-hydroxy carboxylic acids[7] can be accessed (Scheme 1a). In a recent contribution, Maulide reported an excellent method for the selective α-oxidation of amides by using triflic anhydride to activate the amide functionality.[8] Similarly, the synthesis of α-hydroxy ketones can be accomplished through the reaction of the parent ketones with different oxidants.[9] However, their selective synthesis (*i.e.*, the formation of single constitutional isomers) is still a rather challenging task. Good results can be obtained when prepared through the oxidation of silyl enol ethers and enolates derived from ketones that *i*) are symmetrical, *ii*) have a single enolizable Cα (e.g., R^1 = aryl), or *iii*) have sterically and/or electronically biased enolizable Cα.[10] Oxidizing agents that have successfully been used include peroxyacids,[11] metal oxides,[12] *N*-sulfonyloxaziridines,[13] and molecular oxygen.[14] Additionally, hypervalent iodine reagents have been used to introduce α-OH , -OAc, or -OTs functionalities.[15] With oxidants such as nitrosobenzene[16] or 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) or its derivatives,[17] the corresponding α-aminooxylated ketones are obtained. These are precursors to the hydroxy ketones upon reduction of the N–O bond. Moreover, they are themselves important as radical initiators in polymerization reactions.[17a,18]

Despite these precedents, a method for the selective synthesis of α-oxygenated carbonyl compounds formally derived from unsymmetrical ketones with unbiased substituents has not been reported. Furthermore, a method that can be used to introduce the α-hydroxy ketone functional group selectively into a molecule with additional carbonyl moieties or acidic hydrogens is still an unresolved challenge.

During the last few years, our group has developed catalytic methods involving formation of transient transition-metal enolates.[19] These species are produced from allylic alcohol moieties through an internal 1,3-hydrogen shift mediated by Ru, Rh, or Ir catalysts.[20,21] Allylic alcohols are readily available, and by selecting the appropriate allylic alcohol precursor, this versatile approach enables the synthesis of carbonyl compounds functionalized selectively and exclusively at the desired α-carbon in excellent yields. The method has been used in particular for the construction of C–halogen bonds. Our preliminary attempts to apply this strategy to the synthesis of α-oxygenated carbonyl compounds were hampered by oxidative side-reactions of the transition-metal catalysts and the allylic alcohols under the oxidative reaction conditions.[22] After extensive investigations, in this paper we present a versatile strategy that overrides inherent ketone biases, and uses allylic alcohols as synthetic equivalents of enolates for the synthesis of α-oxygenated carbonyl compounds as single constitutional isomers.



Scheme 1. Synthesis of α-oxidized carbonyl compounds.

Initially, we studied the reaction of allylic alcohol **1a** with TEMPO. We observed that decomposition occurred, and allylic alcohol **1a** was only recovered in 33% yield. When 2,2,6,6-tetramethylpiperidine-1-oxoammonium tetrafluoroborate (TEMPO$^+$ BF_4^-, **2**) was used, enone **4** was formed in 58% yield (See SI, Table S1). This is not surprising, as TEMPO$^+$ has been described as an excellent oxidant for alcohols.[22] Thus, it is necessary to use a catalytic system that would mediate the 1,3-hydride shift faster than the background TEMPO-mediated oxidation reaction of the allylic alcohol. Our previous investigations demonstrated that the 1,3-hydride shift can be mediated by complexes of the general formula [Cp*Ir(III)] having at least one halide ligand.[23] The commercially available complex $[Cp^*IrCl_2]_2$ was therefore chosen, and allylic alcohol **1a** as the model substrate. Initial experiments were carried out with TEMPO, aiming to promote its disproportionation[23] into the hydroxylamine (TEMPOH) and TEMPO$^+$ under the inherently acidic reaction conditions used for the Ir-catalyzed isomerization of allylic alcohols.[ψ] α-Aminooxylated ketone **3a** was obtained in a potentially promising 12% yield when TEMPO (2.2 equiv.) was stirred for 30 min before the addition of allylic alcohol **1a**.

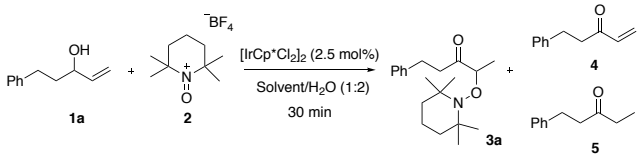
Different single-electron oxidants were evaluated to promote the oxidation of TEMPO, and they gave similar results (see Supporting Information). Satisfactory yields (65%) were obtained when TEMPO (2.2 equiv.) was stirred with HBF_4[24] for 30 min before the addition of **1a** and the catalyst. It can therefore be

[a] Dr. A. Sanz-Marco, S. Martinez-Erro, Prof. B. Martín-Matute
Department of Organic Chemistry
Stockholm University
Stockholm 10691, Sweden
E-mail: belen.martin.matute@su.se

Supporting information for this article is given via a link at the end of the document.

concluded that to obtained α-oxidized ketone **3a**, the efficient generation of TEMPO$^+$ is necessary. It is important to note that in all these instances, **3a** was produced as a single constitutional isomer. This complete selectivity can only be attributed to the oxidation of an enolate intermediate.[19]

Table 1. 1,3-Hydride shift / aminooxylation of **1a**.[a]

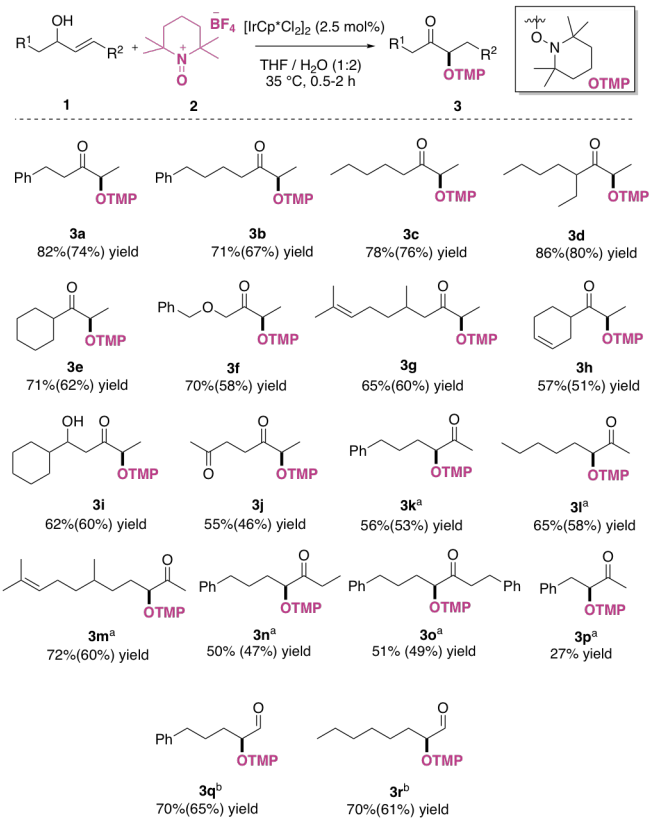


Entry	*T* (°C)	Solvent / H_2O	Yield [%][b]		
			3a	**4**	**5**
1	20	THF	57	7	-
2	35	THF	78	6	5
3	45	THF	63	5	2
4	35	Dioxane	30	4	2
5	35	Dioxolane	60	-	11
6	35	Acetone	51	6	3
7	35	Et_2O	53	4	8
8[c]	35	THF	76	2	-
9[d]	**35**	**THF**	**82**	**4**	**-**
10[e]	35	THF	79	7	-
11[f]	35	THF	53	5	-

[a] **1a** (0.1 mmol, 0.2 M) and **2** (1.2 equiv.) under air. [b] Determined by ^{1}H NMR spectroscopy using an internal standard. [c] 0.1 M. [d] 0.3 M. [e] Under an atmosphere of argon. [f] 1 M.

The alternative pathway, involving isomerization to the ketone followed by oxidation, would result in the formation of a mixture of isomeric products (i.e., oxidation at Cα and at Cα'). An optimization of the reaction conditions using oxoammonium tetrafluoroborate **2** was then carried out (Table 1). The reaction of **1a** with **2** catalyzed by [Cp*IrCl$_2$]$_2$ (2.5 mol%) in THF / H_2O (1:2) at 20 °C gave **3a** in 57% yield (Table 1, entry 1), together with 7% of enone **4**. At higher temperatures, the yield of **3a** increased to 78% at 35 °C (entry 2) after only 15 min. Higher temperatures (45 °C, entry 3) favored the decomposition of allylic alcohol **1a**, resulting in a lower yield of 63% (entry 3). The replacement of THF by other organic solvents proved unsuccessful (entries 4-7). Further tuning of the concentration of the reactants in aqueous THF (entries 8-11) resulted in increased yields (82% at 0.3 M, entry 9). All reactions were run under an atmosphere of air. Similar results were obtained when the reaction was performed under inert atmosphere and with degassed solvents (entry 10). At 1 M (entry 11), the yield was again compromised. Based on these results, the conditions in entry 9 were chosen to study the scope of the reaction. It should be noted that just 1.2 equivalents of oxidant **2** was enough to achieve high yields in a very fast and robust reaction, under an atmosphere of air.

To study the scope of the reaction we mainly chose substrates that would give α-aminooxylated ketones **3** that would be not obtained selectively if synthesized from the corresponding sterically and electronically biased ketone precursors (Scheme 2). Allylic alcohols bearing terminal alkenes provided **3a**-**3j** in high yields. Even allylic alcohols with sterically hindered aliphatic chains (**1d**-**1e**) reacted in yields up to 86%. Remarkably, the reaction conditions were compatible with several functional groups, including ethers (**1f**), alkenes (**1g**-**1h**), *sec*-alcohols (**1i**), and carbonyl groups (**1j**). The presence of some of these functionalities means that some of the substrates have aliphatic methylene groups bearing acidic protons, and even hydroxy functionalities. Nevertheless, this mild, base-free methodology yields complete chemoselectivity and only the allylic alcohol moiety was transformed. The reaction was carried out on allylic alcohols bearing 1,2-disubstituted alkenes (**1k**-**1p**). Here, the Ir-catalyzed 1,3-hydride shift took place more slowly than for terminal allylic alcohols, resulting in the formation of enone by-products. However, when the reactants were added slowly at 45 °C, satisfactory results were obtained (**3k**-**3o**).

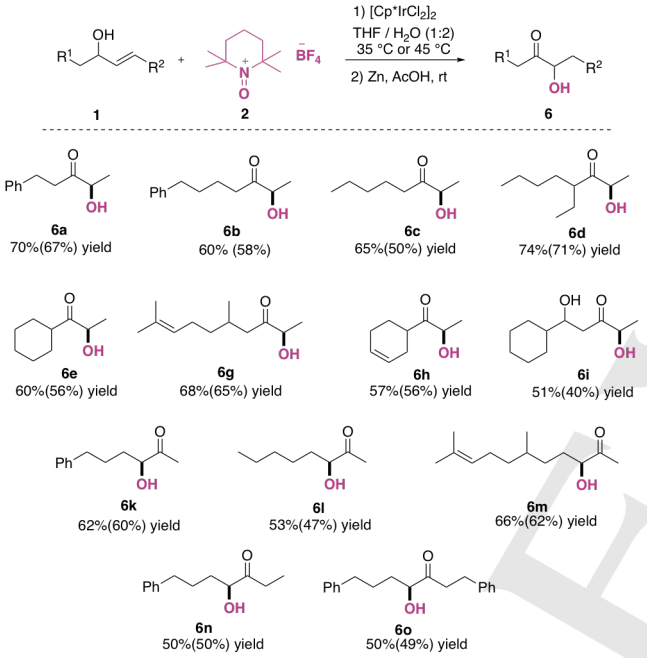


Scheme 2. Isomerization / aminooxylation of allylic alcohols. Yields by ^{1}H NMR spectroscopy (isolated yields in parentheses). [a] By slow addition of the reactants at 45 °C. [b] By slow addition of the reactants.

When the allylic system was conjugated, as in **1p**, the oxidation of the alcohol moiety was faster than the isomerization / aminooxylation process, resulting in a low yield of 27%. Primary allylic alcohols were also transformed into the corresponding α-aminooxylated aldehydes (**3q**-**3r**) in good yields.

10.1002/chem.201803117

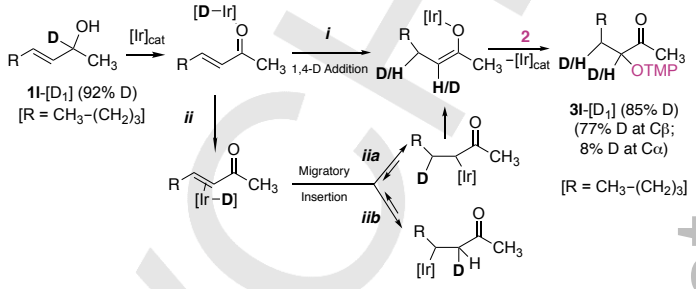
α-Aminooxylated ketones **3** can easily be converted into acyloins **6** by reductive cleavage of the N–O bond. Current available methods rely on isolating the α-aminooxylated ketones and carrying out the reduction in a separate step.[5,25] One-pot reactions have numerous benefits, including decreasing the amounts of solvent, effort, and energy used, and the amount of waste produced.[26] The tandem 1,3-hydride shift / aminoxylation reaction reported here takes place under essentially neutral and additive-free conditions, thus we decided to investigate the synthesis of acyloins **6** from allylic alcohols in a one-pot procedure. The reduction step was carried out with zinc metal in AcOH at rt.[25] After a short optimization of the one-pot procedure (see Supporting Information), the optimal conditions were applied to several allylic alcohols (Scheme 3).



Scheme 3. One-pot synthesis of unsymmetric acyloins from allylic alcohols. Yields by ^{1}H NMR spectroscopy (isolated yields in parentheses).

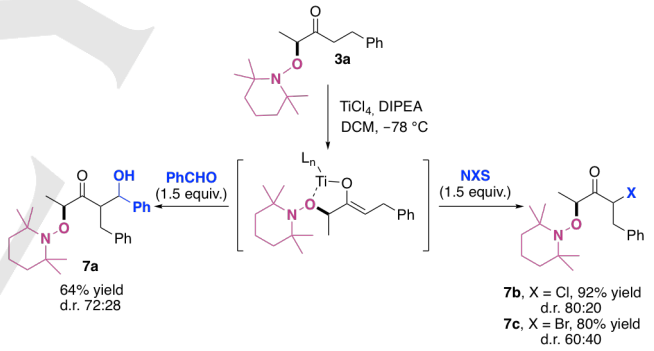
A wide range of allylic alcohols with terminal alkenes **1a-1i** were successfully transformed into the corresponding α-hydroxy ketones in good to moderate isolated yields. Even allylic alcohols with internal alkenes **1k-1o** were converted into the desired acyloins with complete selectivity and in satisfactory isolated yields. The yields of the one-pot reactions were comparable to those obtained for the synthesis of α-aminooxylated ketones **3**, indicating full conversion in the reduction process. Notably, functional groups sensitive to oxidation are tolerated in the reaction, and α-hydroxy ketones **6g-6i** and **6m** were synthesized with complete chemoselectivity.

The reaction of **1l**-[D_1] (92% D) (Scheme 4) afforded α-aminooxylated ketone **3l**-[D_1] (85% D) with a deuterium distribution of 77% D at Cβ and 8% D at Cα . The deuterium distribution in the oxidized ketone agrees well with our previous investigation. [23] Thus, the 1,3-H(D) shift occurs *via* formation of enone intermediates,[19,20,23] which then undergo reduction of the double bond *via* a 1,4-hydride/deuteride addition (path *i*) or a migratory insertion / β-hydride/deuteride elimination pathway (*iia* and *iib*). The latter (*iib*) is responsible for the introduction of D at Cα. Upon reaction of the resulting enolate with oxoammonium tetrafluoroborate salt **2**, the corresponding acyloin is obtained (Scheme 4).



Scheme 4. Proposed mechanism for the iridium-catalyzed isomerization / aminooxylation / reduction of allylic alcohols

To further demonstrate the synthetic importance of our method, the remaining Cα´ of **3a** was functionalized following a method developed by Romea and Urpí.[27] Thus, a Ti-enolate was formed upon coordination to **3a** (Scheme 5). Subsequent addition of benzaldehyde, *N*-chlorosuccinimide (NCS) or N-bromosuccinimide (NBS) gave selectively functionalized ketones **7a**, **7b**, and **7c**.



Scheme 5. Synthesis of carbonyl compounds with both Cα and Cα' selectively functionalized. Isolated yields.

In conclusion, the first method for the synthesis of aliphatic unsymmetrical acyloins as single constitutional isomers is reported. The method relies on fast Ir(III)-catalyzed 1,3-hydride shift in allylic alcohols in the presence of the oxidant. Only when a fast hydride shift takes place are unwanted oxidative side-reactions avoided**.** A wide range of allylic alcohols bearing several functional groups were successfully transformed. Also, in a one-pot procedure, allylic alcohols could be directly transformed into acyloins. As the conditions are base-free, acidic functionalities or enolizable methylenes are tolerated. The synthetic utility of this selective method was further demonstrated through selective further functionalization at the α'-carbon.

Acknowledgements

This project was supported by the Swedish Research Council through Vetenskapsrådet and Formas, and by the Knut and Alice Wallenberg Foundation. A. S.-M. thanks Universitat de València, the Generalitat Valenciana and the European Social Fund for a post-doctoral grant.

Keywords: oxidation • iridium • hydride shift • α-hydroxy ketones • allylic alcohols

Notes

ψ HCl is formed in catalytic amounts in the 1,3-H shift by $[Cp^*IrCl_2]_2$.

[1] M. J. Bouma, B. Olofsson in *Comprehensive Organic Synthesis* (2nd Edition, Eds.: P. Knochel and G. A. Molander), Elsevier Ltd., **2014**, *7*, pp. 213–241.

[2] a) K. C. Nicolaou, G. Vassilikogiannakis, K. B. Simonsen, P. S. Baran, Y.-L. Zhong, V. P. Vidali, E. N. Pitsinos, E. A. Couladouros, *J. Am. Chem. Soc.* **2000**, *122*, 3071–3079; b) X. Liao, Y. Wu, J. D. De Brabander, *Angew. Chem. Int. Ed.* **2003**, *42*, 1648–1652; *Angew. Chem.* **2003**, *115*, 1686-1690; c) M. B. Andrus, E. J. Hicken, J. C. Stephens, D. K. Bedke, *J. Org. Chem.* **2006**, *71*, 8651–8654; d) A. Brackovic, J. E. Harvey, *Chem. Commun.* **2015**, *51*, 4750–4765.

[3] a) S. P. Brown, M. P. Brochu, C. J. Sinz, D. W. C. MacMillan *J. Am. Chem. Soc.* **2003**, *125*, 10808–10809; b) P. Merino, T. Tejero, *Angew. Chem. Int. Ed.* **2004**, *43*, 2995–2997; *Angew. Chem.* **2004**, 116, 3055–3058; c) C. S. Beshara, A. Hall, R. L. Jenkins, T. C. Jones, R. T. Parry, S. P. Thomasa, N. C. O. Tomkinson, *Chem. Commun.* **2005**, *41*, 1478–1480.

[4] a) M. Uyanik, D. Suzuki, T. Yasui, K. Ishihara, *Angew. Chem. Int. Ed.* **2011**, *50*, 5331–5334; *Angew. Chem.* **2011**, *123*, 5443–5446; b) H. Asahara, N. Nishiwaki, *J. Org. Chem.* **2014**, *79*, 11735–11739; c) Z. Li, T. Li, J. Li, L. He, X. Jia, J. Yang, *Synlett*, **2015**, *26*, 2863–2865; d) A. O. Terent'ev, V. A. Vil', E. S. Gorlov, G. I. Nikishin, K. K. Pivnitsky, W. Adam, *J. Org. Chem.* **2016**, *81*, 810–823.

[5] a) U. Jahn, *J. Org. Chem.* **1998**, *63*, 7130–7131; b) S. Dayan, Y. Bareket, S. Rozen, *Tetrahedron* **1999**, *55*, 3657–3664; c) E. Dinca, P. Hartmann, J. Smrček, I. Dix, P. G. Jones, U. Jahn, *Eur. J. Org. Chem.* **2012**, 4461–4482.

[6] a) P. J. Mabe, A. Zakarian, *Org. Lett.* **2014**, *16*, 516–519; b) A. Pinto, D. Kaiser, B. Maryasin, G. Di Mauro, L. Gónzalez, N. Maulide, *Chem. Eur. J.* **2018**, *24*, 2515–2519.

[7] a) W. Adam, W. Boland, J. Hartmann-Schreier, H.-U. Humpf, M. Lazarus, A. Saffert, C. R. Saha-Möller, P. Schreier, *J. Am. Chem. Soc.* **1998**, *120*, 11044–11048; b) Y. Masuda, K. Mori, *Eur. J. Org. Chem.* **2005**, 4789–4800.

[8] a) J. Shao, X. Huang, S. Wang, B. Liu, B. Xu, *Tetrahedron* **2012**, *68*, 573–579; b) A. De la Torre, D. Kaiser, N. Maulide, *J. Am. Chem. Soc.* **2017**, *139*, 6578–6581; c) X. Li, F. Lin, K. Huang, J. Wei, X. Li, X. Wang, X. Geng, N. Jiao, *Angew. Chem. Int. Ed.* **2017**, *56*, 12307-12311; *Angew. Chem.* **2017**, *129*,12475-12479.

[9] Other methods to synthesize acyloins: a) P. Hoyos, J.-V. Sinisterra, F. Molinari, A. R. Alcántara, P. Domínguez de María, *Acc. Chem. Res.* **2010**, *43*, 288–299. b) S. M. Langdon, M. M. D. Wilde, K. Thai, M. Gravel, *J. Am. Chem. Soc.* **2014**, *136*, 7539-7542. c) M. Beigi, E. Gauchenova, L. Walter, S. Waltzer, F. Bonina, T. Stillger, D. Rother, M. Pohl, M. Müller, *Chem. Eur. J.* **2016**, *22*, 13999–14005.

[10] B.-C. Chen, P. Zhou, F. A. Davis, E. Ciganek, **2004**. α-Hydroxylation of Enolates and Silyl Enol Ethers. *Organic Reactions*. 62:1:1–356.

[11] a) G. M. Rubottom, M. A. Vazquez, D.R. Pelegrina, *Tetrahedron Lett.* **1974**, *15*, 4319–4322; b) G. M. Rubottom, J. M. Gruber, *J. Org. Chem.* **1978**, *43*, 1599–1602; c) H. M. Lee, C. Nieto-Oberhuber, M. D. Shair, *J. Am. Chem. Soc.* **2008**, *130*, 16864-16866.

[12] a) E. Vedejs, *J. Am. Chem. Soc.* **1974**, *96*, 5944–5946; b) W. Adam, R. T. Fell, V. R. Stegmann, C. R. Saha-Möller, *J. Am. Chem. Soc.* **1998**, *120*, 708–714; c) A. K. El-Qisairi, H. A. Qaseer, *J. Organomet. Chem.* **2002**, *659*, 50-55.

[13] a) F. A. Davis, A. C. Sheppard, *J. Org. Chem.* **1987**, *52*, 954–955; b) F. A. Davis, B.-C. Chen, *Chem. Rev.* **1992**, *92*, 919–934.

[14] a) H.-J. Li, J.-L. Zhao, Y.-J. Chen, L. Liu, D. Wang, C.-J. Li *Green. Chem.* **2005**, *7*, 61–63; b) Y.-F. Liang, N. Jiao, *Angew. Chem. Int. Ed.* **2014**, *53*, 548–552; *Angew. Chem.* **2014**, *126*, 558–562.

[15] a) K. C. Nicolaou, T. Montagnon, T. Ulven, P. S. Baran, Y.-L. Zhong, F. Sarabia, *J. Am. Chem. Soc.* **2002**, *124*, 5718–5728; b) S. F. Kirsch, *J. Org. Chem.* **2005**, *70*, 10210–10212; c) M. Ochiai, Y. Takeuchi, T. Katayama, T. Sueda, K. Miyamoto *J. Am. Chem. Soc.* **2005**, *127*, 12244–12245; d) P. Mizar, T. Wirth, *Angew. Chem. Int. Ed.* **2014**, *53*, 5993–5997; *Angew. Chem.* **2014**, *126*, 6103–6107; e) S. Beaulieu, C. Y. Legault, *Chem. Eur. J.* **2015**, *21*, 11206–11211.

[16] a) N. Momiyama, H. Yamamoto, *J. Am. Chem. Soc.* **2003**, *125*, 6038–6039; b) D. B. Ramachary; C. F. Barbas, III *Org Lett.* **2005**, *7*, 1577–1580; c) A. Yanagisawa, Y. Lin, A. Takeishi, K. Yoshida, *Eur. J. Org. Chem.* **2016**, 5355-5359.

[17] a) M. Schämann, H. J. Schäfer, *Synlett* **2004**, *9*, 1601–1603; b) M. Pouliot, P. Renaud, K. Schenk, A. Studer, T. Vogler, *Angew. Chem. Int. Ed.* **2009**, *48*, 6037–6040; *Angew. Chem.* **2009**, *121*, 6153-6156; c) M. Hayashi, M. Shibuya, Y. Iwabuchi, *Org. Lett.* **2012**, *14*, 154–157; d) Y.-X. Xie, R.-J. Song, Y. Liu, Y.-Y. Liu, J.-N. Xiang, J.-H. Lia, *Adv. Synth. Catal.* **2013**, *355*, 3387–3390; e) P. Feng, S. Song, L.-H. Zhang, N. Jiao, *Synlett* **2014**, *25*, 2717–2720; f) P. Schroll, B. König, *Eur. J. Org. Chem.* **2015**, 309–313.

[18] C. J. Hawker, A. W. Bosman, E. Harth, *Chem. Rev.* **2001**, *101*, 3661–3688.

[19] Characterization of a C–bound Ru-enolate from an allylic alcohol: Bartoszewicz, A.; Jeżowska, M. M.; Laymand, K.; Möbus, J.; Martín-Matute, B. *Eur. J. Inorg. Chem.* **2012**, 1517.

[20] a) N. Ahlsten, B. Martín-Matute, *Chem. Commun.* **2011**, *47*, 8331–8333; b) N. Ahlsten, A. Bermejo Gómez, B. Martín-Matute, *Angew. Chem. Int. Ed.* **2013**, *52*, 6273–6276; *Angew. Chem.* **2013**, *125*, 6393–6396; c) A. Bermejo Gómez, E. Erbing, M. Batuecas, A. Vázquez-Romero, B. Martín-Matute, *Chem. Eur. J.* **2014**, *20*, 10703–10709; d) A. Vázquez-Romero, A. Bermejo Gómez, B. Martín-Matute, *ACS Catal.* **2015**, *5*, 708–714.

[21] Base-catalyzed isomerization: S. Martinez-Erro, A. Sanz-Marco, A. Bermejo Gómez, A. Vázquez-Romero, M. S. G. Ahlquist, B. Martín-Matute, *J. Am. Chem. Soc.* **2016**, *138*, 13408–13414.

[22] a) W. F. Bailey, J. M. Bobbitt, *J. Org. Chem.* **2007**, *72*, 4504–4509; b) M. A. Mercadante, C. B. Lelly, J. M. Bobbitt, L. J. Tilley, N. E. Leadbeater, *Nature Protocols* **2013**, *8*, 666–676; c) J. M. Bobbitt, A. L. Bartelson, W. F. Bailey, T. A. Hamlin, C. B. Kelly, *J. Org. Chem.* **2014**, *79*, 1055–1067.

[23] E. Erbing, A. Vázquez-Romero, A. Bermejo Gómez, A. E. Platero-Prats, F. Carson, X. Zou, P. Tolstoy, B. Martín-Matute, *Chem. Eur. J.* **2016**, *22*, 15659–15663.

[24] M. Schaemann, H. J. Schaefer, *Synlett*, **2004**, *9*, 1601–1603.

[25] a) D. L. Boger, R. M. Garbaccio, Q. Jin, *J. Org. Chem.* **1997**, *62*, 8875–8891; b) M. Hartmann, Y. Li, A. Studer, *J. Am. Chem. Soc.* **2012**, *134*, 16516–16519; c) Y. Li, M. Hartmann, C. G. Daniliuc, A. Studer, *Chem. Commun.* **2015**, *51*, 5706–5709.

[26] D. E. Fogg, E. N. dos Santos, *Coord. Chem. Rev.* **2004**, *248*, 2365–2379.

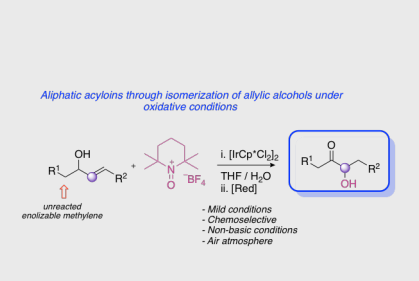
[27] a) J. G. Solsona, P. Romea, F. Urpí, J. Vilarrasa, *Org. Lett.* **2003**, *5*, 519–522; b) M. Fàbregas, A. Gómez-Palomino, M. Pellicena, D. F. Reina, P. Romea, F. Urpí, M. Font-Bardia, *Org. Lett.* **2014**, *16*, 6220–6223.

10.1002/chem.201803117

WILEY-VCH

COMMUNICATION

Selective Oxidation. A selective method to synthesize unsymmetrical acyloins as single constitutional isomers is presented. From allylic alcohols, a fast iridium-catalyzed 1,3-hydride followed by an oxidation affords α-hydroxy carbonyls with outstanding selectivity.



*Amparo Sanz-Marco, Samuel Martinez-Erro, Belén Martín-Matute**

Page No. – Page No.

Selective Synthesis of Unsymmetrical Aliphatic Acyloins through Oxidation of Iridium Enolates