

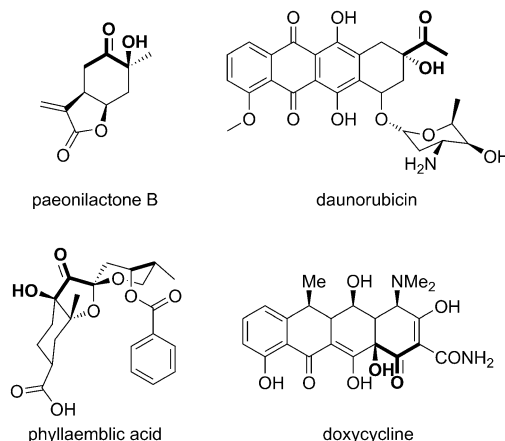
Highly Efficient C–H Hydroxylation of Carbonyl Compounds with Oxygen under Mild Conditions**

Yu-Feng Liang and Ning Jiao*

Abstract: A transition-metal-free Cs_2CO_3 -catalyzed α -hydroxylation of carbonyl compounds with O_2 as the oxygen source is described. This reaction provides an efficient approach to tertiary α -hydroxycarbonyl compounds, which are highly valued chemicals and widely used in the chemical and pharmaceutical industry. The simple conditions and the use of molecular oxygen as both the oxidant and the oxygen source make this protocol very environmentally friendly and practical. This transformation is highly efficient and highly selective for tertiary $\text{C}(\text{sp}^3)\text{--H}$ bond cleavage.

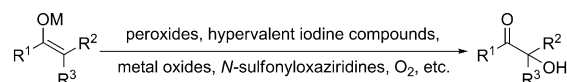
Tertiary α -hydroxycarbonyl groups are ubiquitous structural motifs in organic chemistry. They serve as valuable building blocks and are present in many biologically active compounds and synthetic drugs,^[1] such as paeonilactone B,^[1a] daunorubicin,^[1b] phyllaemblic acid,^[1c] and doxycycline^[1d] (Scheme 1). Furthermore, they have been widely used as efficient photo-initiators for ultraviolet-light-cured coatings in the coating industry for the surface protection of various materials.^[2] Therefore, the preparation of tertiary α -hydroxycarbonyl compounds has received considerable attention.^[3] In the past decades, oxidation of the corresponding enolates or silyl enol ethers with peroxides, hypervalent iodine compounds, metal oxides, *N*-sulfonyloxaziridines, oxygen, and other oxidants has been described (Scheme 2a).^[3]

The use of molecular oxygen as an oxidant and oxygen-atom source for oxygen incorporation in organic synthesis has attracted considerable attention owing to its inexpensive, abundant, and environmentally benign nature.^[4,5] Although a significant number of transition-metal-catalyzed C–H hydroxylation reactions have been developed,^[6,7] practical and efficient C–H hydroxylation reactions with molecular

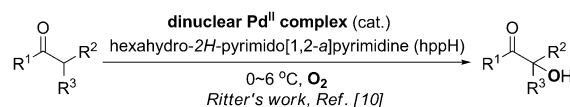


Scheme 1. Biologically active molecules and drugs.

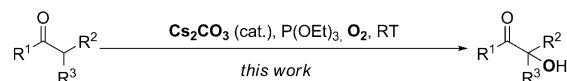
a) Oxidation of enolates or silyl enol ethers



b) Pd-catalyzed hydroxylation of carbonyl compounds with O_2



c) **Transition-metal-free** hydroxylation of carbonyl compounds with O_2



Scheme 2. Transformation of carbonyl compounds into tertiary α -hydroxycarbonyl compounds.

[*] Y.-F. Liang, Dr. N. Jiao

State Key Laboratory of Natural and Biomimetic Drugs
School of Pharmaceutical Sciences, Peking University
Xue Yuan Road 38, Beijing 100191 (China)
E-mail: jiaoning@bjmu.edu.cn
Homepage: <http://sklnbd.bjmu.edu.cn/nj/>

Dr. N. Jiao

State Key Laboratory of Organometallic Chemistry
Chinese Academy of Sciences
Shanghai 200032 (China)

[**] Financial support from the National Basic Research Program of China (973 Program; Grant No. 2009CB825300), the National Science Foundation of China (No. 21172006), and the National Young Top-Notch Talent Support Program are greatly appreciated. We thank Xiaoyang Wang of this research group for reproducing the results for **2h** and **2i**.



Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.201308698>.

oxygen as the oxidant and oxygen source are still desirable. Whereas previous autooxidation^[8] and metal-mediated aerobic oxidative hydroxylation^[9] reactions of carbonyl compounds had shown limited scope in terms of possible substrates, a milestone was set by Ritter and co-workers in the form of a transformation catalyzed by a bimetallic palladium complex with O_2 as the oxidant and oxygen source as the first practical, efficient, and general approach based on aerobic C–H hydroxylation for the synthesis of tertiary α -hydroxycarbonyl compounds (Scheme 2b).^[10] Despite the significance of the reaction, it is not without disadvantages: The expensive and complex Pd catalyst used has to be completely removed from the product, especially in the synthesis of pharmaceutical compounds. Therefore, a practical and efficient method for the direct C–H hydroxylation of carbonyl compounds with molecular oxygen under mild conditions is still required.

Herein, we present a transition-metal-free Cs_2CO_3 -catalyzed direct α -hydroxylation of carbonyl compounds with O_2 for the synthesis of tertiary α -hydroxycarbonyl compounds at room temperature (Scheme 2c). The significance of the present finding is fourfold: 1) The reaction shows broad generality: various carbonyl compounds, including ketones, esters, amides, aldehydes, and β -dicarbonyl compounds, could be efficiently converted into the desired tertiary α -hydroxycarbonyl compounds. Bioactive compounds and drugs could be modified by this procedure. 2) Molecular oxygen is employed as a reagent and the sole oxidant, thus making this method very environmentally friendly. 3) Simple and readily available Cs_2CO_3 emerges as an efficient catalyst, rather than a transition-metal catalyst, which is often expensive and is required to be completely removed from products, especially in the synthesis of pharmaceutical compounds. 4) The $\text{Cs}_2\text{CO}_3/\text{P}(\text{OEt})_3/\text{O}_2$ system is inexpensive, mild, and readily handled with high catalytic efficiency and safety.

Recently, copper-catalyzed aerobic oxidative C–H functionalization reactions have been significantly improved.^[11,12] Inspired by these results, we initially investigated the copper-catalyzed aerobic oxidation of 2-methyl-1-phenylpropan-1-one (**1a**) under O_2 in the presence of Cs_2CO_3 as a base at room temperature. To our delight, the expected hydroxylation product **2a** was obtained; however, the yield was very low (Table 1, entry 1). The efficiency of the reaction was significantly improved by the addition of inexpensive and readily available $\text{P}(\text{OEt})_3$ (Table 1, entry 2). We were surprised to find that the hydroxylation reaction also took place efficiently

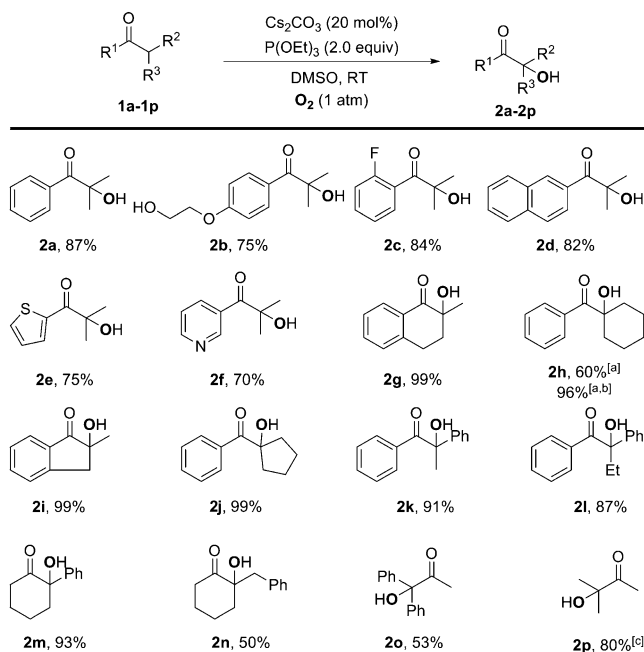
with just a catalytic amount of Cs_2CO_3 (Table 1, entry 3). The Pd, Cu, Fe, Ru, Ir, Ni, and Ag content in the Cs_2CO_3 , $\text{P}(\text{OEt})_3$, and DMSO used was less than $\delta = 0.1$ ppm in each case (ICPMS analysis; see the Supporting Information), which indicated that this hydroxylation reaction is promoted by Cs_2CO_3 itself rather than catalyzed by trace metal impurities. Reactions in the presence of other bases as potential catalysts, such as K_2CO_3 , Na_2CO_3 , CsOAc , and CsNO_3 , did not proceed (Table 1, entries 4–7; see also the Supporting Information). Product **2a** was observed in trace amounts when CsOH was employed (Table 1, entry 8). The yield decreased slightly when PPh_3 was used instead of $\text{P}(\text{OEt})_3$ (Table 1, entry 9); in contrast, the reaction did not proceed in the presence of $\text{Na}_2\text{S}_2\text{O}_3$ (entry 10). The use of other solvents, such as DMF, NMP, and toluene, led to the formation of **2a** in very low yields (see the Supporting Information). Notably, a reaction in the absence of Cs_2CO_3 did not proceed, and only a trace amount of **2a** was formed without $\text{P}(\text{OEt})_3$ (Table 1, entries 11 and 12). This transformation also proceeded well in air, but the yield of **2a** was slightly lower (Table 1, entry 13). In contrast, the reaction did not occur under argon (Table 1, entry 14).

The above results indicate that Cs_2CO_3 is a competent catalyst for the α -hydroxylation of carbonyl compounds. The scope of the transformation was then investigated under the standard conditions (Table 1, entry 3; Scheme 3). Hydroxy and fluoride groups were compatible with this protocol (products **2b,c**). Naphthyl and heteroaryl substrates could also participate in the reaction (products **2d–f**), and a variety of tertiary $\text{C}(\text{sp}^3)\text{--H}$ bonds at the α -position of ketones could be hydroxylated in excellent yields (products **2g–p**). The

Table 1: Screening of different parameters.^[a]

Entry	Catalyst	Base	Additive	Yield [%] ^[b]
1	CuBr_2	Cs_2CO_3	–	5
2	CuBr_2	Cs_2CO_3	$\text{P}(\text{OEt})_3$	91 (87)
3	Cs_2CO_3	–	$\text{P}(\text{OEt})_3$	91 (87)
4	K_2CO_3	–	$\text{P}(\text{OEt})_3$	0
5	Na_2CO_3	–	$\text{P}(\text{OEt})_3$	0
6	CsOAc	–	$\text{P}(\text{OEt})_3$	0
7	CsNO_3	–	$\text{P}(\text{OEt})_3$	0
8	CsOH	–	$\text{P}(\text{OEt})_3$	trace
9	Cs_2CO_3	–	PPh_3	78 (74)
10	Cs_2CO_3	–	$\text{Na}_2\text{S}_2\text{O}_3$	trace
11	–	–	$\text{P}(\text{OEt})_3$	0
12	Cs_2CO_3	–	–	trace
13 ^[c]	Cs_2CO_3	–	$\text{P}(\text{OEt})_3$	76 (73)
14 ^[d]	Cs_2CO_3	–	$\text{P}(\text{OEt})_3$	0
15 ^[e]	Cs_2CO_3	–	$\text{P}(\text{OEt})_3$	79 (75)

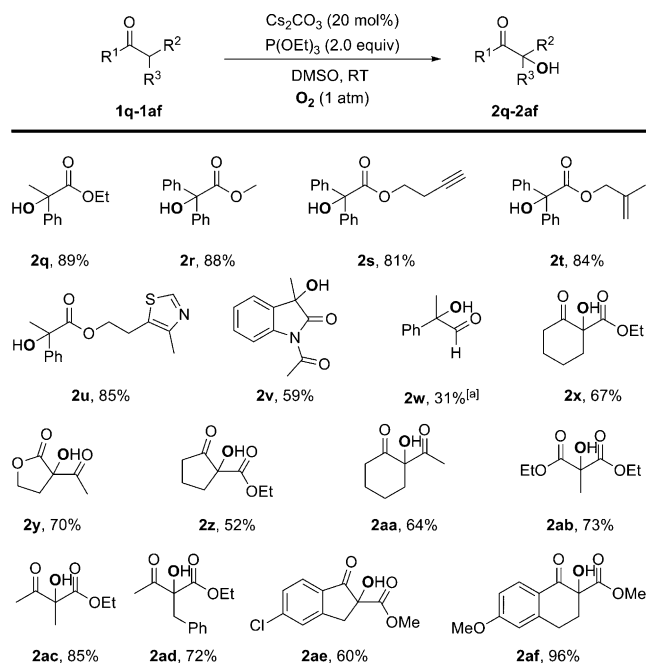
[a] Reaction conditions: **1a** (0.5 mmol), catalyst (0.1 mmol), base (1.0 mmol), additive (1.0 mmol), DMSO (2 mL); the mixture was stirred at room temperature under O_2 (1 atm) for 24 h. [b] The yield was determined by GC with biphenyl as an internal standard. The value in parentheses is the yield of the isolated product. [c] The reaction was carried out in air (1 atm) for 48 h. [d] The reaction was carried out under Ar (1 atm). [e] The reaction was carried out in the dark. DMSO = dimethyl sulfoxide.



Scheme 3. Cs_2CO_3 -initiated α -hydroxylation of ketones with O_2 . For the standard reaction conditions, see Table 1, entry 3. Yields shown are for the isolated products. [a] Reaction time: 72 h. [b] The reaction was carried out with 1.0 equiv of Cs_2CO_3 . [c] The yield was determined by ^1H NMR spectroscopy.

hydroxylation reaction is highly chemo- and regioselective. Only tertiary C(sp³)–H bonds can be hydroxylated to form tertiary alcohols (products **2m–p**). Secondary C(sp³)–H bonds (for example, in propiophenone) or primary C(sp³)–H bonds (for example, in acetophenone) were unreactive in this reaction. In the case of product **2n**, this alcohol was the only product observed in the reaction, even though an active benzyl position was present in the substrate. The transformation of the simple alkyl ketone **1p** proceeded well to produce **2p** in good yield.

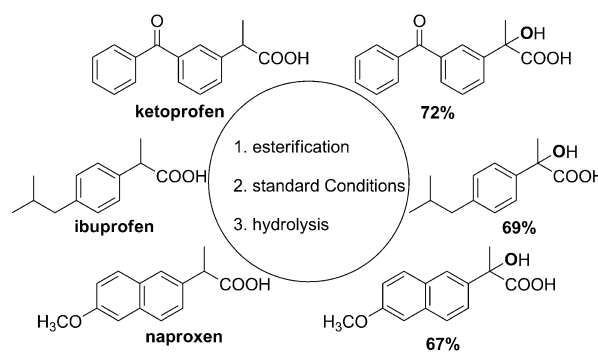
To our delight, the hydroxylation of esters and amides also occurred smoothly (Scheme 4). Products containing an alkynyl (product **2s**), alkenyl (product **2t**), or heteroaryl



Scheme 4. Cs₂CO₃-initiated α -hydroxylation of esters, amides, aldehydes, and β -dicarbonyl compounds with O₂. For the standard reaction conditions, see Table 1, entry 3. Yields shown are for the isolated products. [a] Morpholine (1.0 equiv) was added.

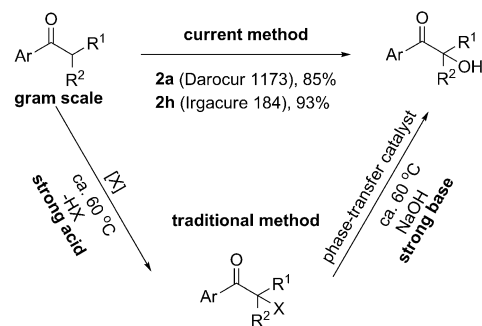
group (product **2u**) could be obtained in high yields. The hydroxylation of amide **1v** produced **2v**, the core structure of several natural products,^[13] in good yield. The reaction of aldehydes gave a messy reaction mixture under the standard conditions. A little of the corresponding C₁-shortened ketone was obtained along with several unidentified products. We found that the addition of morpholine (1.0 equiv) could improve the selectivity of the reaction to produce the α -hydroxylation product **2w** in 31% yield. Significantly, the present strategy was also applicable to an array of β -dicarbonyl compounds (products **2x–af**).^[14] Notably, the compatibility of the reaction with alkyne (product **2s**), alkene (product **2t**), and chloride substituents on the aromatic ring (product **2ae**) offers an opportunity for further transformations.

Significantly, several drug substrates, such as ketoprofen, ibuprofen, and naproxen, could be modified by this method to



Scheme 5. Drug diversification.

afford the respective hydroxylated products in moderate yields in three steps (Scheme 5). Thus, this method has potential for drug diversification. Notably, products **2a** (Darocur 1173), **2b** (Irgacure 2959), and **2h** (Irgacure 184), which are widely used as photoinitiators for clear coating under UV light,^[15] were also efficiently prepared (Scheme 3). In the traditional method for their preparation, halogenation is followed by hydrolysis (Scheme 6),^[16] and in the two-step

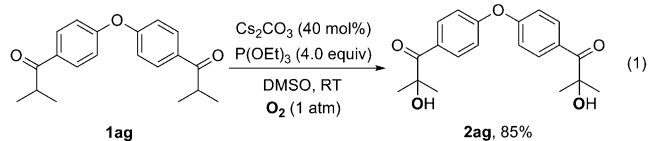


Scheme 6. Gram-scale synthesis of **2a** and **2h**.

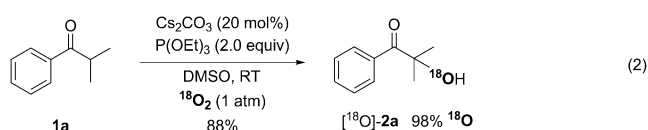
procedure, a strong acid is produced, and a strong base is consumed. In comparison, the current method is environmentally friendly and practical. To investigate the practical application of this transformation in organic synthesis, we conducted gram-scale reactions of **1a** and **1h**. The desired products were produced without any significant decrease in efficiency (85 versus 87% for the reaction on a 0.5 mmol scale for **2a**, 93 versus 96% for the reaction on a 0.5 mmol scale for **2h**; Scheme 3 and Scheme 6).

Furthermore, both potentially reactive C–H bonds in substrate **1ag** could be hydroxylated to form the difunctional product **2ag** in 85% yield [Eq. (1)]. Such products present more advantages than monofunctional products as photoinitiators.^[17]

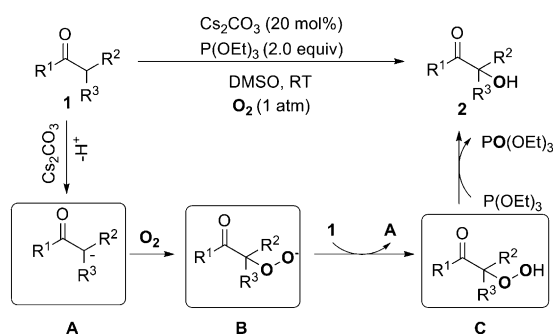
To gain an understanding of the mechanism, we investigated some control experiments. The results of ¹⁸O labeling



proved that the oxygen atom in the hydroxy group originates from molecular oxygen [Eq. (2)]. Moreover, $P^{18}O(OEt)_3$ was also obtained in this case [Eq. (2); see the Supporting Information]. The reaction proceeded well in the presence of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) or 1,1-diphenylethylene to produce the desired product **2a** in 88 and 86% yield, respectively; these reactions indicate that a radical process might not be involved in the present transformation. When the singlet oxygen inhibitor 1,4-diazabicyclo[2,2,2]octane (DABCO) was added to the model reaction,^[18] the reaction was not inhibited, and **2a** was isolated in 81% yield. Furthermore, the reaction also proceeded well in the dark (Table 1, entry 15), which may exclude the participation of singlet molecular oxygen in this transformation.



On the basis of these preliminary results, a possible mechanism is proposed (Scheme 7). Initially, substrate **1** undergoes a Cs_2CO_3 -initiated deprotonation to produce



Scheme 7. Proposed mechanism.

the corresponding carbanion **A**. Subsequently, carbanion **A** reacts with O_2 to generate a superoxide anion **B**, which could obtain a proton from substrate **1** to form a superoxide **C** and regenerate carbanion **A**. Intermediate **C** would then undergo reduction by $P(OEt)_3$ ^[19] to give the desired product **2**.

In summary, we have demonstrated a Cs_2CO_3 -initiated α -hydroxylation of carbonyl compounds to give tertiary α -hydroxycarbonyl compounds, which are highly valued chemicals and widely used in the chemical and pharmaceutical industries. The reaction is not only applicable to ketones, but also to esters, amides, aldehydes, and β -dicarbonyl compounds. Notably, molecular oxygen or air, the most environmentally friendly oxidant, was employed at a pressure of 1 atmosphere at room temperature without any transition-metal catalysts. Studies to elucidate the detailed mechanism and synthetic applications of this efficient and practical hydroxylation are under way in our laboratory.

Received: October 6, 2013

Published online: November 26, 2013

Keywords: cesium · C–H functionalization · dioxygen · hydroxylation · oxygenation

- [1] a) M. G. Edwards, M. N. Kenworthy, R. R. A. Kitson, M. S. Scott, R. J. K. Taylor, *Angew. Chem.* **2008**, *120*, 1961; *Angew. Chem. Int. Ed.* **2008**, *47*, 1935; b) G. Minotti, P. Menna, E. Salvatorelli, G. Cairo, L. Gianni, *Pharmacol. Rev.* **2004**, *56*, 185; c) Y.-J. Zhang, T. Tanaka, T. Iwamoto, C.-R. Yang, I. Kouno, *Tetrahedron Lett.* **2000**, *41*, 1781; d) G. Olack, H. Morrison, *J. Org. Chem.* **1991**, *56*, 4969.
- [2] a) C. Decker, *Macromol. Rapid Commun.* **2002**, *23*, 1067; b) K. Dietliker, P. Murer, R. Hüsler, T. Jung, PCT Int. Appl. US 20100104979, **2010**; c) J. P. Fouassier, X. Allonas, J. Lalevée, C. Dietlin, *Photochemistry and Photophysics of Polymer Materials*, Wiley, Hoboken, **2010**, p. 351.
- [3] B.-C. Chen, P. Zhou, F. A. Davis, E. Ciganek, *Organic Reactions*, Vol. 62 (Ed.: L. E. Overman), Wiley, New York, **2003**, p. 1.
- [4] For reviews, see: a) S. S. Stahl, *Angew. Chem.* **2004**, *116*, 3480; *Angew. Chem. Int. Ed.* **2004**, *43*, 3400; b) B. M. Stoltz, *Chem. Lett.* **2004**, *33*, 362; c) T. Punniyamurthy, S. Velusamy, J. Iqbal, *Chem. Rev.* **2005**, *105*, 2329; d) K. M. Gligorich, M. S. Sigman, *Angew. Chem.* **2006**, *118*, 6764; *Angew. Chem. Int. Ed.* **2006**, *45*, 6612; e) M. S. Sigman, D. R. Jensen, *Acc. Chem. Res.* **2006**, *39*, 221; f) J. Muzart, *Chem. Asian J.* **2006**, *1*, 508; g) E. M. Beccalli, G. Brogini, M. Martinelli, S. Sottocornola, *Chem. Rev.* **2007**, *107*, 5318; h) J. Piera, J. E. Bäckvall, *Angew. Chem.* **2008**, *120*, 3558; *Angew. Chem. Int. Ed.* **2008**, *47*, 3506; i) S. S. Stahl, *Science* **2005**, *309*, 1824; j) M. J. Schultz, M. S. Sigman, *Tetrahedron* **2006**, *62*, 8227; k) W. Wu, H. Jiang, *Acc. Chem. Res.* **2012**, *45*, 1736; l) Z. Shi, C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3381.
- [5] For some recent examples from our research group, see: a) T. Wang, N. Jiao, *J. Am. Chem. Soc.* **2013**, *135*, 11692; b) Z. Xu, C. Zhang, N. Jiao, *Angew. Chem.* **2012**, *124*, 11529; *Angew. Chem. Int. Ed.* **2012**, *51*, 11367; c) Y. Su, X. Sun, G. Wu, N. Jiao, *Angew. Chem.* **2013**, *125*, 9990; *Angew. Chem. Int. Ed.* **2013**, *52*, 9808; d) Y. Su, L. Zhang, N. Jiao, *Org. Lett.* **2011**, *13*, 2168; e) R. Lin, F. Chen, N. Jiao, *Org. Lett.* **2012**, *14*, 4058; f) C. Zhang, P. Feng, N. Jiao, *J. Am. Chem. Soc.* **2013**, *135*, 15257.
- [6] For some examples of the hydroxylation of $C(sp^3)$ –H bonds, see: a) L. V. Desai, K. L. Hull, M. S. Sanford, *J. Am. Chem. Soc.* **2004**, *126*, 9542; b) R. Giri, J. Liang, J. G. Lei, J. J. Li, D. H. Wang, X. Chen, I. C. Naggar, C. Y. Guo, B. M. Foxman, J.-Q. Yu, *Angew. Chem.* **2005**, *117*, 7586; *Angew. Chem. Int. Ed.* **2005**, *44*, 7420; c) M. S. Chen, M. C. White, *Science* **2007**, *318*, 783; d) K. Chen, J. M. Richter, P. S. Baran, *J. Am. Chem. Soc.* **2008**, *130*, 7247; e) K. Kamata, K. Yonehara, Y. Nakagawa, K. Uehara, N. Mizuno, *Nat. Chem.* **2010**, *2*, 478; f) Y. Yang, F. Moinodeen, W. Chin, T. Ma, Z. Jiang, C.-H. Tan, *Org. Lett.* **2012**, *14*, 4762; g) M. A. Bigi, S. A. Reed, M. C. White, *J. Am. Chem. Soc.* **2012**, *134*, 9721; h) E. M. Simmons, J. F. Hartwig, *Nature* **2012**, *483*, 70; i) Z. Ren, F. Mo, G. Dong, *J. Am. Chem. Soc.* **2012**, *134*, 16991; j) L. Gómez, I. Garcia-Bosch, A. Company, J. Benet-Buchholz, A. Polo, X. Sala, X. Ribas, M. Costas, *Angew. Chem.* **2009**, *121*, 5830; *Angew. Chem. Int. Ed.* **2009**, *48*, 5720; k) I. Prat, J. S. Mathieson, M. Güell, X. Ribas, J. M. Luis, L. Cronin, M. Costas, *Nat. Chem.* **2011**, *3*, 788; l) I. Prat, L. Gómez, M. Canta, X. Ribas, M. Costas, *Chem. Eur. J.* **2013**, *19*, 1908; m) E. McNeill, J. Du Bois, *J. Am. Chem. Soc.* **2010**, *132*, 10202; n) B. H. Brodsky, J. Du Bois, *J. Am. Chem. Soc.* **2005**, *127*, 15391; o) N. D. Litvinas, B. H. Brodsky, J. Du Bois, *Angew. Chem.* **2009**, *121*, 4583; *Angew. Chem. Int. Ed.* **2009**, *48*, 4513; p) M. A. Bigi, S. A. Reed,

- M. C. White, *Nat. Chem.* **2011**, 3, 216; q) P. E. Gormisky, M. C. White, *J. Am. Chem. Soc.* **2013**, 135, 14052.
- [7] For some examples of the hydroxylation of C(sp²)–H bonds, see: a) T. Jintoku, K. Nishimura, K. Takaki, Y. Fujiwara, *Chem. Lett.* **1991**, 193; b) Q. Liu, P. Wu, Y. Yang, Z. Zeng, J. Liu, H. Yi, A. Lei, *Angew. Chem.* **2012**, 124, 4744; *Angew. Chem. Int. Ed.* **2012**, 51, 4666; c) I. Garcia-Bosch, A. Company, J. R. Frisch, M. Torrent-Sucarrat, M. Cardellach, I. Gamba, M. Güell, L. Casella, L. Que, Jr., X. Ribas, J. M. Luis, M. Costas, *Angew. Chem.* **2010**, 122, 2456; *Angew. Chem. Int. Ed.* **2010**, 49, 2406; d) Y. H. Zhang, J.-Q. Yu, *J. Am. Chem. Soc.* **2009**, 131, 14654; e) F. Mo, L. J. Trzpekowski, G. Dong, *Angew. Chem.* **2012**, 124, 13252; *Angew. Chem. Int. Ed.* **2012**, 51, 13075; f) G. Shan, X. Yang, L. Ma, Y. Rao, *Angew. Chem.* **2012**, 124, 13247; *Angew. Chem. Int. Ed.* **2012**, 51, 13070; g) V. S. Thirunavukkarasu, L. Ackermann, *Org. Lett.* **2012**, 14, 4210; h) F. Yang, L. Ackermann, *Org. Lett.* **2012**, 14, 6206; i) P. Y. Choy, F. Y. Kwong, *Org. Lett.* **2013**, 15, 270; j) Y. Yan, P. Feng, Q.-Z. Zheng, Y.-F. Liang, J.-F. Lu, Y. Cui, N. Jiao, *Angew. Chem.* **2013**, 125, 5939; *Angew. Chem. Int. Ed.* **2013**, 52, 5827.
- [8] a) C. E. Frank, *Chem. Rev.* **1950**, 46, 155; b) K. U. Ingold, *Acc. Chem. Res.* **1969**, 2, 1; c) I. Hermans, J. Peeters, P. A. Jacobs, *Top. Catal.* **2008**, 50, 124.
- [9] a) T. Arai, T. Sato, H. Noguchi, H. Kanoh, K. Kaneko, A. Yanagisawa, *Chem. Lett.* **2006**, 35, 1094; b) H. Sakurai, I. Kamiya, H. Kitahara, H. Tsunoyama, T. Tsukuda, *Synlett* **2009**, 245; c) Y. Monguchi, T. Takahashi, Y. Iida, Y. Fujiwara, Y. Inagaki, T. Maegawa, H. Sajiki, *Synlett* **2008**, 2291.
- [10] G. J. Chuang, W. Wang, E. Lee, T. Ritter, *J. Am. Chem. Soc.* **2011**, 133, 1760.
- [11] For reviews, see: a) O. Daugulis, *Top. Curr. Chem.* **2010**, 292, 57; b) A. E. Wendlandt, A. M. Suess, S. S. Stahl, *Angew. Chem.* **2011**, 123, 11256; *Angew. Chem. Int. Ed.* **2011**, 50, 11062; c) C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, 41, 3464.
- [12] For some recent examples of copper-catalyzed oxygenation with O₂, see: a) L. Zhang, X. Bi, X. Guan, X. Li, Q. Liu, B.-D. Barry, P. Liao, *Angew. Chem.* **2013**, 125, 11513; *Angew. Chem. Int. Ed.* **2013**, 52, 11303; b) J. M. Hoover, B. L. Ryland, S. S. Stahl, *J. Am. Chem. Soc.* **2013**, 135, 2357; c) A. N. Campbell, S. S. Stahl, *Acc. Chem. Res.* **2012**, 45, 851; d) E. Boess, C. Schmitz, M. Klusmann, *J. Am. Chem. Soc.* **2012**, 134, 5317; e) Y.-F. Wang, X. Zhu, S. Chiba, *J. Am. Chem. Soc.* **2012**, 134, 3679; f) H. Wang, Y. Wang, D. Liang, L. Liu, J. Zhang, Q. Zhu, *Angew. Chem.* **2011**, 123, 5796; *Angew. Chem. Int. Ed.* **2011**, 50, 5678; g) Z.-Q. Wang, W.-W. Zhang, L.-B. Gong, R.-Y. Tang, X.-H. Yang, Y. Liu, J.-H. Li, *Angew. Chem.* **2011**, 123, 9130; *Angew. Chem. Int. Ed.* **2011**, 50, 8968; h) C. Zhang, N. Jiao, *J. Am. Chem. Soc.* **2010**, 132, 28; i) C. Zhang, Z. Xu, L. Zhang, N. Jiao, *Angew. Chem.* **2011**, 123, 11284; *Angew. Chem. Int. Ed.* **2011**, 50, 11088.
- [13] a) T. Teruhisa, W. E. Hume, U. Takashi, O. Kazuhiko, U. Yasuyuki, K. Kazuo, H. Shinji, N. Jun, S. Hitoshi, T. Mutsuo, N. Hiroshi, N. Ryu, *J. Med. Chem.* **2001**, 44, 4641; b) H. Piyasena, E. Matthew, L. M. Sandra, K. Jay, W. Harvey, G. B. Christopher, J. P. Debra, Q. Gao, H. Stella, K. G. Valentin, A. M. Nicholas, *J. Med. Chem.* **2002**, 45, 1487; c) M. L. Eugenia, P. H. Raquel, C. Mathias, *Nat. Prod. Rep.* **2010**, 27, 1138.
- [14] For reviews on the α -hydroxylation of β -dicarbonyl compounds, see: a) F. A. Davis, B. C. Chen, *Chem. Rev.* **1992**, 92, 919; b) J. Christoffers, A. Baro, T. Werner, *Adv. Synth. Catal.* **2004**, 346, 143; c) A. M. R. Smith, K. K. Hii, *Chem. Rev.* **2011**, 111, 1637; d) A. Russo, C. De Fusco, A. Lattanzi, *RSC Adv.* **2012**, 2, 385; for an example involving cesium-salt catalysis, see: e) T. Watanabe, T. Ishikawa, *Tetrahedron Lett.* **1999**, 40, 7795.
- [15] a) S. Jockusch, M. S. Landis, B. Freiermuth, N. J. Turro, *Macromolecules* **2001**, 34, 1619; b) J. Eichler, C. P. Herz, I. Naito, W. Schnabel, *J. Photochem.* **1980**, 12, 225.
- [16] a) R. Hüsler, A. Fuchs, PCT Int. Appl. WO 2004009651, **2004**; b) E. Meneguzzo, G. Norcini, G. L. Bassi, PCT Int. Appl. US 20110065962, **2011**.
- [17] a) M. Visconti in *Photochemistry and UV Curing: New Trends* (Ed.: J. P. Fouassier), Research Signpost, Trivandrum, **2006**, pp. 153; b) A. Fuchs, R. Hüsler, C. Schregenerberger, M. Kunz, PCT Int. Appl. WO 03040076, **2003**; c) C. Dietlin, J. Lalevee, X. Allonas, J. P. Fouassier, M. Visconti, G. L. Bassi, G. Norcini, *J. Appl. Polym. Sci.* **2008**, 107, 246.
- [18] a) W. Ando, T. Saiki, T. Migita, *J. Am. Chem. Soc.* **1975**, 97, 5028; b) T. Christ, F. Kulzer, P. Bordat, T. Basché, *Angew. Chem.* **2001**, 113, 4323; *Angew. Chem. Int. Ed.* **2001**, 40, 4192; c) J. Sivaguru, M. R. Solomon, T. Poon, S. Jockusch, S. G. Bosio, W. Adam, N. J. Turro, *Acc. Chem. Res.* **2008**, 41, 387.
- [19] a) E. J. Bailey, J. Elks, D. H. R. Barton, *Proc. Chem. Soc. London* **1960**, 214; b) E. J. Bailey, D. H. R. Barton, J. Elks, J. F. Templeton, *J. Chem. Soc.* **1962**, 1578.