Advanced Synthesis & Catalysis

Title: Aldehydes as Carbon Radical Acceptors: Silver Nitrate-Catalyzed Cascade Decarboxylation and Oxidative Cyclization toward Dihydroflavonoid Derivatives

Authors: Wen-Chao Yang, Peng Dai, Kai Luo, Yi-Gang Ji, and Lei Wu

To be cited as: *Adv. Synth. Catal.* 10.1002/adsc.201601407

Link to VoR: http://dx.doi.org/10.1002/adsc.201601407

COMMUNICATION

DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

Aldehydes as Carbon Radical Acceptors: Silver Nitrate Catalyzed Cascade Decarboxylation and Oxidative Cyclization toward Dihydroflavonoid Derivatives

Wen-Chao Yang,[a,c] Peng Dai,[a] Kai Luo,[a,c] Yi-Gang Ji, [a,c] and Lei Wu [a,b,*]

[a] Jiangsu Key Laboratory of Pesticide Science and Department of Chemistry, College of Sciences, Nanjing Agricultural University, Nanjing 210095, P. R. China.
[Tel/Fax: +86-25-84396716; E-mail: rickywu@njau.edu.cn]

[b] Beijing National Laboratory for Molecular Sciences and Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, P. R. China.

[c] College of Plant Protection, Nanjing Agricultural University, Nanjing 210095, P. R. China.

Received: ((will be filled in by the editorial staff))

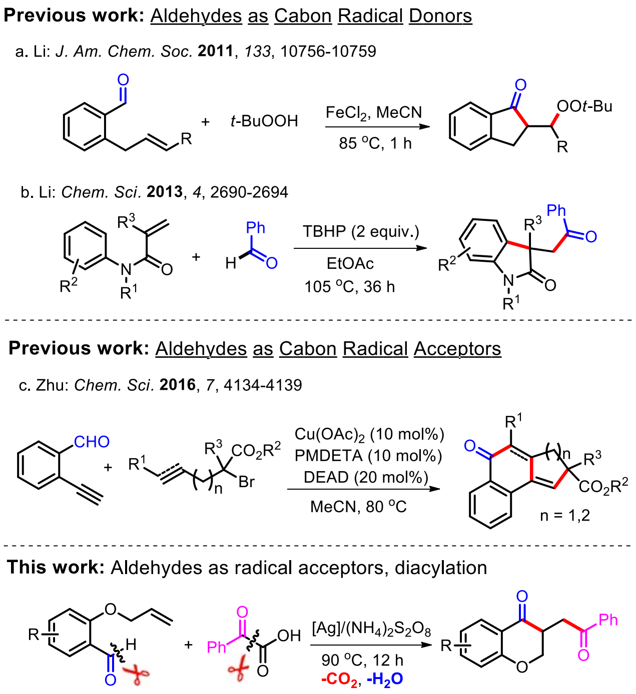
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201######.((Please delete if not appropriate))

Abstract. Silver nitrate-catalyzed cascade decarboxylation and oxidative cyclization of α-oxocarboxylic acids, alkenes, and aldehydes is demonstrated for the first time. With ammonium persulfate as the oxidant, the cascade reactions afford dihydroflavonoid derivatives as products in moderate to good yields, exhibiting a broad substrate tolerance. Control experiments indicated that the mechanism includes a radical pathway with aldehydes as the carbon radical acceptors.

Keywords: Ketones, Decarboxylation, Aldehydic C–H bonds, Oxidative cyclization, Diacylation.

As a chemical skeleton for a range of materials, drugs, and naturally occurring bioactive molecules,[1] ketones are of great importance and have stimulated numerous scientists toward research. Various efficient synthetic approaches have been developed for ketones over the past decades. Recently, transition-metal-catalyzed C-H acylation of aldehydes has become a powerful strategy for preparing ketones *via* the aldehydic C(sp^2)-H bond cleavage.[2,3] Within this regime, the addition of carbonyl radical, which is generated from aldehydes either by transition-metal catalysis or under metal-free conditions, to alkenes or alkynes represents a significant choice for producing ketones.[4] Recent progress on the oxidative tandem coupling of alkenes with aldehydic C–H bonds and other species for the formation of heterocyclic compounds have gained extensive attention owing to its prominent advantage of step-and-atom efficiency.[5] For example, Li's group disclosed a novel iron-catalyzed carbonylation-peroxidation reaction of alkenes with aldehydes and hydroperoxide to obtain 2,3-dihydro-1*H*-inden-1-one derivatives (Scheme 1a).[5a] Lately, Li and co-workers reported a TBHP-mediated oxidative difunctionalization of activated alkenes for the synthesis of 3-(2-oxoethyl) indolin-2-ones using aldehyde as the acylation source (Scheme 1b).[5c] Notably, the aforementioned reactions relied on the generation of acyl radicals from aldehydes, followed by their addition to alkene functionalities. From another point of view, aldehydes as acceptors subjected to free carbon radicals offer an alternative approach to ketone synthesis. However, owing to their dissociation energy differentiation, the addition intermediates (alkoxy radicals) preferably undergo C-C β-scission reverting to the original aldehydes, instead of undergoing C-H β-scission to form ketones.[6] Consequently, this strategy is not only challenging, but is also extremely underdeveloped. In an elegant study, Zhu *et al.* reported the only example of aldehydes as radical acceptors, in which a Cu-catalyzed cascade annulation of enynals with alkenyl or alkynyl α-bromocarbonyls was described for the synthesis of various cyclohexenone-fused polycyclic compounds (Scheme 1c).[6] Therefore, a milder, direct and convenient approach such as the oxidative cyclization of alkenes using aldehydes as radical acceptors to achieve carbonyl-containing heterocyclic compounds is still highly desirable.

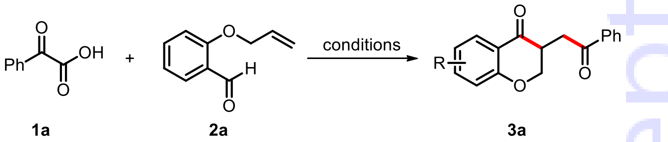
Decarboxylative cross-coupling reactions for the construction of C-C and C-X bonds have currently attracted a great deal of interest due to their potential advantage, such as using readily available, stable, and low-cost carboxylic acids, extruding nontoxic CO_2 gas as the byproduct, and high selectivity.[7] The catalytic decarboxylative coupling reactions were achieved with transition-metal complexes, including those of palladium,[8] rhodium,[9] nickel,[10] copper,[11] silver,[12] and other metals,[13] or by photoredox catalysis.[14] Of these, the high efficiency of decarboxylative functionalization of alkenes with tandem cyclization makes this most appealing to synthetic scientists.[15] For instance, Mai *et al.* described a $AgNO_3/K_2S_2O_8$ promoted decarboxylative tandem alkyl-arylation of *N*-aryl-cinnamamides with aliphatic carboxylic acids to access a variety of 3,4-disubstituted dihydroquinolin-2(1*H*)-ones in aqueous solution.[15c] Later on, Wang’s group developed a direct decarboxylative carbonyl-arylation of alkenes with *α*-oxocarboxylic acids. The reaction was catalyzed by mild hypervalent iodine reagents (HIRs) under visible-light irradiation to give carbonyl-containing oxindoles.[15e] Mechanistically, these reactions were initiated by acyl radicals through decarboxylation. We thus envisioned that, with intramolecular alkenes and aldehydes as successive acceptors, the radical propagation might undergo cyclization to afford dihydroflavonoid skeletons.[16] However, to the best of our knowledge, apart from the pioneering works mentioned above, cascade oxidative difunctionalization of alkenes with aldehydic C(sp^2)-H bonds and decarboxylation has never been reported so far. Inspired by these works and our ongoing interest in transition-metal catalysis and radical chemistry,[17] we herein report the first silver nitrate-catalyzed cascade decarboxylative radical addition/cyclization of alkenes and *α*-oxocarboxylic acids with aldehydes as radical acceptors to furnish dihydroflavonoid derivatives (Scheme 1).



Scheme 1. Representative studies of aldehydes as carbon radical donors in difunctionalization of alkenes (a, b), aldehydes as carbon radical acceptor (c), and this work.

To investigate the $AgNO_3$-catalyzed oxidative tandem diacylation of alkenes, initially, a solution of 2-oxo-2-phenylacetic acid (**1a**) and 2-(allyloxy)-benzaldehyde (**2a**) in DMF was treated with $AgNO_3/K_2S_2O_8$ at 90 °C under air for 12 h. To our delight, the reaction gave the desired cyclization product **3a**, albeit with only 10% isolated yield (entry 1, Table 1). Subsequently, solvent effects were investigated, and we found that the conversion efficiency strongly depended on the solvents used. No product was detected in dichloroethane, H_2O, or acetonitrile (entries 2-4). Nevertheless, the reaction proceeded quite smoothly in aqueous solution, providing the cyclization product in acceptable yields ranging from 27% to 47% (entries 5-8). Further investigations revealed that acetone/H_2O (1:1) is the most appropriate medium, which afforded **3a** in 52% yield (entry 9). Various oxidants were used to improve the efficiency, among which oxone, TBHP, and DTBP gave no conversion at all (entries 10-12). Utilizing ammonium persulfate as the oxidant slightly improved the yield of **3a** to 57% (entry 13). Other metal precursors such as silver oxide, silver carbonate, cuprous chloride, and copper acetate proved to be less effective (entries 14-17). The cascade reaction exhibited higher efficiency when the loading of silver nitrate was increased to 10 mol% and 20 mol%, giving comparably higher yields of isolated **3a** (entry 18-19). Delightfully, when the ratio of **1a**/**2a** was changed to 2:1, the adduct formed in 73% yield (entry 20). It was noticed that further increasing the amount of $(NH_4)_2S_2O_8$ to 4.0 equiv gave only a moderate yield of 45% (entry 21). Eventually, no diacylation product was obtained in the control experiments in the absence of silver catalysts or oxidants (entries 22-23). These investigations revealed that the amount of catalyst/oxidant, the ratio of the substrates, and solvents are essential to the feasibility and efficiency of the reaction.

Table 1. Reaction conditions optimization.[a]



entry	catalyst	oxidant	solvent	yield (3a,%)[b]
1	$AgNO_3$	$K_2S_2O_8$	DMF	10
2	$AgNO_3$	$K_2S_2O_8$	dichloroethane	N.R.
3	$AgNO_3$	$K_2S_2O_8$	H_2O	N.R.
4	$AgNO_3$	$K_2S_2O_8$	CH_3CN	N.R.
5	$AgNO_3$	$K_2S_2O_8$	DMF/H_2O (1:1)	43
6	$AgNO_3$	$K_2S_2O_8$	THF/H_2O (1:1)	31
7	$AgNO_3$	$K_2S_2O_8$	dioxane/H_2O (1:1)	27
8	$AgNO_3$	$K_2S_2O_8$	CH_3CN/H_2O (1:1)	47
9	$AgNO_3$	$K_2S_2O_8$	acetone/H_2O (1:1)	52
10	$AgNO_3$	Oxone	acetone/H_2O (1:1)	N.R.
11	$AgNO_3$	TBHP	acetone/H_2O (1:1)	N.R.
12	$AgNO_3$	DTBP	acetone/H_2O (1:1)	N.R.
13	$AgNO_3$	$(NH_4)_2S_2O_8$	acetone/H_2O (1:1)	57
14	Ag_2O	$(NH_4)_2S_2O_8$	acetone/H_2O (1:1)	48

15	Ag_2CO_3	$(NH_4)_2S_2O_8$	acetone/H_2O (1:1)	51
16	CuCl	$(NH_4)_2S_2O_8$	acetone/H_2O (1:1)	N.R.
17	$Cu(OAc)_2$	$(NH_4)_2S_2O_8$	acetone/H_2O (1:1)	N.R.
18[c]	$AgNO_3$	$(NH_4)_2S_2O_8$	acetone/H_2O (1:1)	61
19[d]	$AgNO_3$	$(NH_4)_2S_2O_8$	acetone/H_2O (1:1)	60
20[e]	**$AgNO_3$**	**$(NH_4)_2S_2O_8$**	**acetone/H_2O (1:1)**	**73**
21[f]	$AgNO_3$	$(NH_4)_2S_2O_8$	acetone/H_2O (1:1)	45
22	-	$(NH_4)_2S_2O_8$	acetone/H_2O (1:1)	0
23	$AgNO_3$	-	acetone/H_2O (1:1)	0

[a] Reaction conditions: 2-oxo-2-phenylacetic acid (**1a**, 0.30 mmol), 2-(allyloxy)benzaldehyde (**2a**, 0.60 mmol), catalyst (5 mol%), oxidant (2.0 equiv.), solvent (2.0 mL) at 90 ºC for 12 h.

[b] Isolated yields, N.R.=no reaction.

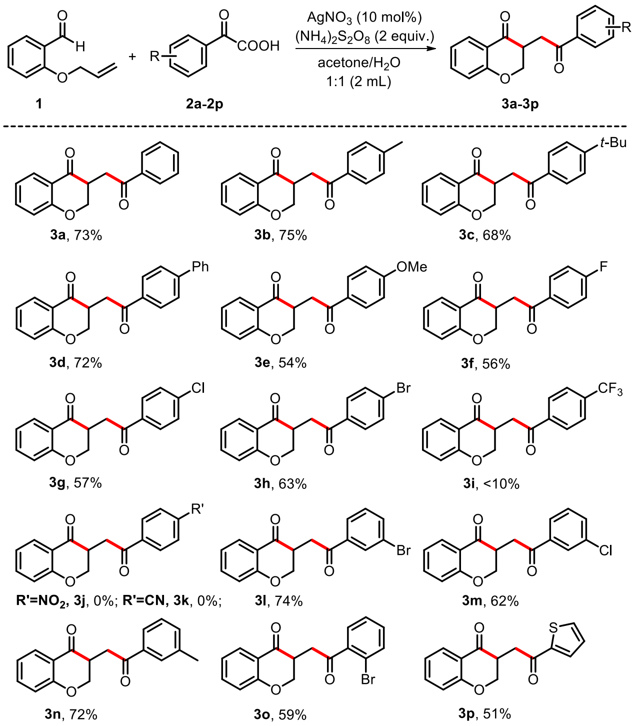
[c] 10% mmol $AgNO_3$.

[d] 20% mmol $AgNO_3$.

[e] 10% mmol $AgNO_3$ was used, **1a** : **2a** (2:1).

[f] 4.0 equiv oxidant.

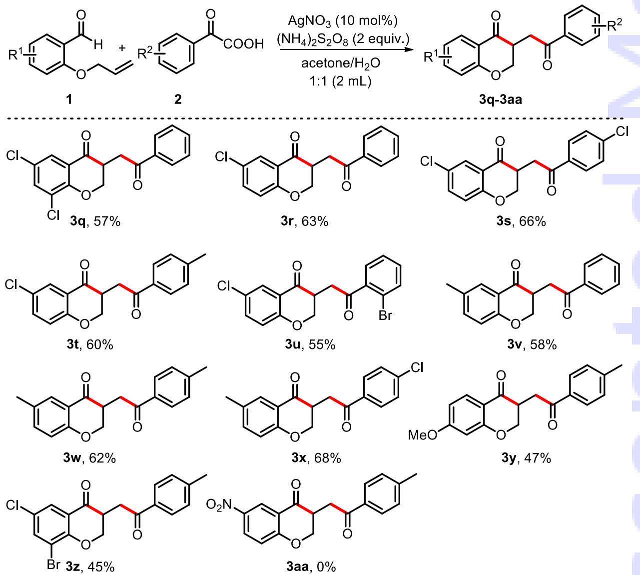
Table 2. Substrate scopes of α-oxocarboxylic acids.[a]



[a]Reaction conditions: 2-(allyloxy)benzaldehyde (0.30 mmol), 2-oxo-2-phenylacetic acid (0.60 mmol), $AgNO_3$ (10 mol%), $(NH_4)_2S_2O_8$ (2.0 equiv.), acetone/H_2O (1:1, 2.0 mL) at 90 ºC for 12 h. Isolated yields.

Encouraged by the optimal results, we further evaluated the generality and scope of the substrates for this cascade reaction. Initially, a variety of substituted α-oxocarboxylic acids, with both electron-donating and electron-withdrawing substituents on the phenyl moiety, was investigated. As summarized in Table 2, it was found that most of the substrates exhibited good group tolerance, producing the corresponding adducts in moderate to good yields. Electron-donating substituents such as methyl-, *t*-butyl-, and phenyl performed well in the system affording the desired products (**3b**-**3d**) with 68-75% yields. In general, the reactions exhibited remarkable sensitivity to the electron density of the substituents. For instance, the *para*-methoxy substituent, which is a representative strong electron-donating group, led to an apparent drop in efficiency with 54% yield of isolated **3e**. Likewise, strong electron-withdrawing groups such as trifluoromethyl, nitro, and nitrile substantially impaired the cascade reactions (**3i, 3j,** and **3k)** resulting in sluggish conversions. Delightfully, substrates with *para*-halogen-substituents were applicable with moderate yields ranging from 56-74% (**3f**-**3h**). In addition, α-oxocarboxylic acids with *meta*-Br-, Cl-, and methyl-substituents (**3l**-**3n**) underwent smoothly to afford comparable or higher yields to *para*-substituted ones. When it came to *ortho*-substitution, substrate **2o** gave the diacylation product **3o** in 59% yield, which indicated that the cascade reaction was relatively insensitive to steric effect. Moreover, heteroaromatic thiophene substituted α-oxocarboxylic acid proved a reliable substrate, furnishing **3p** in 51% yield. The reactions were also extended to other potential acyl radical precursors, including methyl 2-oxo-2-phenylacetate and 1,3-dioxoisoindolin-2-yl benzoate, in which no target adducts were isolated (see SI for details).

Table 3. Reactivity of 2-(allyloxy)benzaldehyde derivatives. [a]



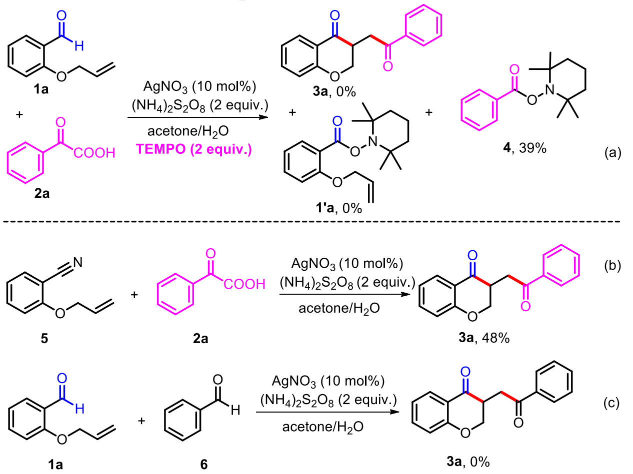
[a] Reaction conditions: 2-(allyloxy)benzaldehyde (0.30 mmol), 2-oxo-2-phenylacetic acid (0.60 mmol), $AgNO_3$ (10 mol%), $(NH_4)_2S_2O_8$ (2.0 equiv.), acetone/H_2O (1:1, 2.0 mL) at 90 ºC for 12 h. Isolated yields.

Next, the scope of 2-(allyloxy)benzaldehyde derivatives was investigated. Quite interestingly, the electron density effect of the substituents in this case was similar to that of the aforementioned results. As depicted in Table 3, the substrates containing weak electron effect groups, whether withdrawing or donating, reacted quite well with the α-oxocarboxylic acid derivatives. Even for the dichloro-substituted substrate, 6,8-dichloro-3-(2-oxo-2-phenylethyl)-chromen-4-one (**3q**) was obtained in a moderate yield

10.1002/adsc.201601407

of 57%. In addition, the efficiency remained unchanged when different *α*-oxo-carboxylic acid derivatives were used, producing the target adducts (**3r-3x**) with medium yields. It was observed that 4-methoxy substitution retarded the reaction with a comparatively lower yield of **3y**. Moreover, nitro substitution on 2-(allyloxy)-benzaldehyde inhibited the reaction, just as **2j** and **2k** did, as shown in Table 2. Considering that the reaction might follow a radical pathway, we reasoned that the distinct electron effects shown in Table 2 and Table 3 could be attributed to two aspects: 1) strong electron-donating groups reduce the susceptibility of aldehyde to radical attack; and 2) strong electron-withdrawing groups, especially the nitro group, are notorious for inhibiting radical attack. These observations prompted us to verify the validity of aldehydes as radical acceptors.

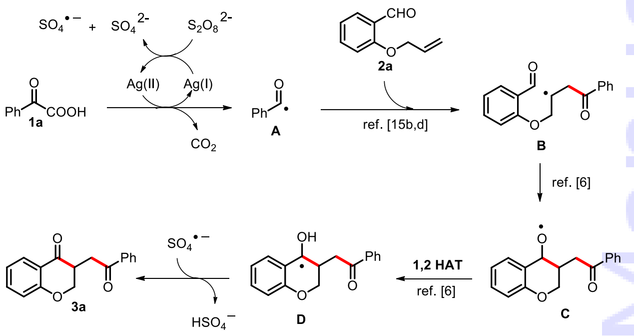
Scheme 2. Control Experiments



To gain further insight into the reaction mechanism, several control experiments were designed and conducted. Firstly, 2 equiv of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy), a well-known radical scavenger, was added to the reaction of **1a** with **2a** under the standard conditions, which completely inhibited the cascade reaction. Notably, only the acyl radical generated from 2-oxo-2-phenylacetic acid (**2a**) was trapped successfully by TEMPO, affording the corresponding adduct (**4**) in 39% yields (Scheme 2, eq. a). The results implied that the reactions might have occurred through a radical pathway and ruled out radical initiation from aldehyde. As a comparison, when 2-(allyloxy)benzonitrile (**5**) was employed instead of 2-(allyloxy)benzaldehyde (**1a**), the cascade reaction proceeded to give cyclized product **3a** in 48% yield (Scheme 2, eq. b). This observation indicated that the generation of acyl radical from *α*-oxo-carboxylic acids occurred first, followed by hydrolysis to yield ketones,[18] since the cyano group could serve as an ideal carbon radical acceptor. Finally, benzaldehyde (**6**) was reacted with **1a**, which did not yield the desired product **3a**; this further revealed that the carbonyl radical could not be generated from either of the aldehydic groups under the experimental conditions (Scheme 2, eq. c). Overall, the control experiments collectively demonstrated that aldehydes serve as carbon radical acceptors.

On the basis of the experimental results and some previous reports, [12d,15d] a plausible mechanism is proposed in Scheme 3. Initially, Ag(I) is oxidized by the persulfate anion to generate the Ag(II) intermediate, which then abstracts a single electron from the carboxylate to produce the carboxyl radical.[12g] A quick decarboxylation of the carboxyl radical yields the corresponding acyl radical **A**.[15b,d] The nucleophilic acyl radical then attacks the carbon-carbon double bond of **2a**, leading to the formation of a radical intermediate **B**.[15b,d] Sequential radical attack on the aldehyde moiety affords an alkoxyl radical **C**, followed by a formal 1,2-H shift to deliver the benzyl radical **D**.[6] Finally, the sulfate radical anion abstracted a hydrogen from **D**, giving product **3a**.[15b]

Scheme 3. Plausible mechanism



In conclusion, we have developed, for the first time, a silver nitrate-catalyzed cascade decarboxylation and oxidative cyclization reaction of *α*-oxocarboxylic acids, alkenes, and aldehydes. With ammonium persulfate as the oxidant, the cascade reactions afforded dihydroflavonoid derivatives with moderate to good yields, exhibiting a broad substrate tolerance. The reaction mechanism was exemplified *via* a radical pathway with aldehydes as the carbon radical acceptors. Various carbonyl-incorporated dihydroflavonoid derivatives were accessed by this new methodology featuring simple operation and mild conditions.

Experimental Section

Typical Procedures for the Silver Nitrate Catalyzed Cascade Decarboxylation and Oxidative Cyclization of *α*-Oxocarboxylic Acid, Alkene and Aldehyde:

A reaction tube equipped with a magnetic stir bar was charged with 2-(allyloxy)benzaldehyde (**1a**, 48.6 mg, 0.30 mmol), 2-oxo-2-phenylacetic acid (**2a**, 90.0 mg, 0.60 mmol), AgNO$_3$ (5.1 mg, 0.03mmol), (NH$_4$)$_2$S$_2$O$_8$ (136.8 mg, 0.60 mmol), and acetone/H$_2$O (1:1, 2.0 mL), respectively. The mixtures were allowed to react at 90 °C for 12 h. When the reaction was complete, the solution was concentrated under reduced pressure before further purification by flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 10:1 to 5:1, v/v) to furnish the desired product **3a** (58.3 mg, 73%).

Acknowledgements

This project is supported by the Foundation Research Project of Jiangsu Province (The Natural Science Found No. BK20141359), the Fundamental Research Funds for the Central Universities (Grant No. KYTZ201604), and “333 High Level Talent Project” of JiangSu Province.

References

[1] a) M. A. Kienzler, S. Suseno, D. Trauner, *J. Am. Chem. Soc.* **2008**, *130*, 8604-8605; b) A. Obase, A. Kageyama, Y. Manabe, T. Ozawa, T. Araki, H. Yokoec, M. Kanematsu, M. Yoshida, K. Shishido, *Org. Lett.* **2013**, *15*, 3666-3669; c) L. Gyermek, L. F. Soyka, *Anesthesiology*, **1975**, *42*, 331-344.

[2] a) S. Tang, L. Zeng, Y. Liu, A. Lei, *Angew. Chem., Int. Ed.* **2015**, *54*, 15850-15853; b) B.-X. Tang, R.-J. Song, C.-Y. Wu, Y. Liu, M.-B. Zhou, W.-T. Wei, G.-B. Deng, D.-L. Yin, J.-H. Li, *J. Am. Chem. Soc.* **2010**, *132*, 8900-8902; c) H. Li, P, Li, L. Wang, *Org. Lett.* **2013**, *15*, 620-623; d) C. Li, L. Wang, P, Li, W. Zhou, *Chem.–Eur. J.* **2011**, *17*, 10208-10212; e) Z. Shi, N. Schrŏder, F. Glorius, *Angew. Chem., Int. Ed.* **2012**, *51*, 8092-8096; f) V. Chudasama, R. J. Fitzmaurice, J. M. Ahern, S. Caddick, *Chem. Commun.* **2010**, *46*, 133-135; g) X, Jia, S. Zhang, W. Wang, F. Luo, J. Cheng, *Org. Lett.* **2009**, *11*, 3120-3123; h) C.-W. Chan, Z. Zhou, A. S. C. Chan, W.-Y. Yu, *Org. Lett.* **2010**, *12*, 3926-3929; i) B. Mu, J. Li, D. Zou, Y. Wu, Y. Wu, *Org. Lett.* **2016**, *18*, 5260-5263.

[3] For reviews, see: a) M. C. Willis, *Chem. Rev.* **2010**, *110*, 725-748; b) C. Pan, X. Jia, J. Cheng, *Synthesis*, **2012**, 677-685.

[4] a) C. Liu, D. Liu, A. Lei, *Acc. Chem. Res.* **2014**, *47*, 3459-3470; b) S. Tsujimoto, T. Iwahama, S. Sakaguchi and Y. Ishii, *Chem. Commun.* **2001**, 2352-2353; c) X. Mi, C. Wang, M. Huang, Y. Wu, Y. Wu, *J. Org. Chem.* **2015**, *80*, 148-155; d) Z. Zheng, L. Dian, Y. Yuan, D. Zhang-Negrerie, Y. Du, K. Zhao, *J. Org. Chem.* **2014**, *79*, 7451-7458; e) X.-H. Ouyang, R.-J. Song, Y. Li, B. Liu, J.-H. Li, *J. Org. Chem.* **2014**, *79*, 4582-4589.

[5] a) W. Liu, Y. Li, K. Liu, Z. Li, *J. Am. Chem. Soc.* **2011**, *133*, 10756-10759; b) J. Wang, C. Liu, J. Yuan, A. Lei, *Angew. Chem., Int. Ed.* **2013**, *52*, 2256-2259; c) M.-B. Zhou, R.-J. Song, X.-H. Ouyang, Y. Liu, W.-T. Wei, G.-B. Deng, J.-H. Li, *Chem. Sci.* **2013**, *4*, 2690–2694; d) Q. Ke, B. Zhang, B. Hu, Y. Jin, G. Lu, *Chem. Commun.* **2015**, *51*, 1012-1015; e) J. Zhao, P. Li, X. Li, C. Xia, F. Li, *Chem. Commun.* **2016**, *52*, 3661-3664; f) L. Lv, S. Lu, Q. Guo, B. Shen, Z. Li, *J. Org. Chem.* **2015**, *80*, 698-704; g) L. Lv, L. Qi, Q. Guo, B. Shen, Z. Li, *J. Org. Chem.* **2015**, *80*, 12562-12571.

[6] C. Che, Q. Huang, H. Zheng, G. Zhu, *Chem. Sci.* **2016**, *7*, 4134-4139.

[7] For selected reviews, see: a) N. Rodíguez, L. J. Goossen, *Chem. Soc. Rev.* **2011**, *40*, 5030-5048; b) J. D. Weaver, A. Recio, A. J. Grenning, J. A. Tunge, *Chem. Rev.* **2011**, *111*, 1846-1913; c) L.-N. Guo, H. Wang, X.-H. Duan, *Org. Biomol. Chem.* **2016**, *14*, 7380-7391; d) H. Li, T. Miao, M. Wang, P. Li, L. Wang, *Synlett*, **2016**, *27*, 1635-1648; e) H. Huang, K. Jia, Y. Chen, *ACS Catal.* **2016**, *6*, 4983-4988; f) R. Shang, L. Liu, *Sci. China Chem.* **2011**, *54*, 1670-1687.

[8] a) A. G. Myers, D. Tanaka, M. R. Mannion, *J. Am. Chem. Soc.* **2002**, *124*, 11250-11251; b) L. J. Goossen, N. Rodriguez, K. Goossen, *Angew. Chem. Int. Ed.* **2008**, *47*, 3100-3120; *Angew. Chem.* **2008**, *120*, 3144-3164; c) C. Wang, I. Piel, F. Glorius, *J. Am. Chem. Soc.* **2009**, *131*, 4194-4195; d) S. Guin, S. K. Rout, A. Gogoi, W. Ali, B. K. Patela, *Adv. Synth. Catal.* **2014**, *356*, 2559-2565; e) P. Hu, Y. Shang, W. Su, *Angew. Chem. Int. Ed.* **2012**, *51*, 5945-5949; *Angew. Chem.* **2012**, *124*, 6047-6051; f) R. Shang, Z.-W. Yang, Y. Wang, S.-L. Zhang, L. Liu, *J. Am. Chem. Soc.* **2010**, *132*, 14391-14393; g) Z. Ma, H. Liu, C. Zhang, X. Zheng, M. Yuan, H. Fu, R. Li, H. Chen, *Adv. Synth. Catal.* **2015**, *357*, 1143-1148; h) W. H. Fields, J. J. Chruma, *Org. Lett.* **2010**, *12*, 316-319; i) F. Zhang, M. F. Greaney, *Org. Lett.* **2010**, *12*, 4745–4747; j) S. Messaoudi, J.-D. Brion, M. Alami, *Org. Lett.* **2012**, *14*, 1496–1499; k) J. Luo, Y. Lu, S. Liu, J. Liu, G.-J. Deng, *Adv. Synth. Catal.* **2011**, *353*, 2604-2608.

[9] a) J. M. Neely, T. Rovis, *J. Am. Chem. Soc.* **2014**, *136*, 2735-2738; b) Z. Sun, J. Zhang, P. Zhao, *Org. Lett.* **2010**, *12*, 992-995; c) Y. Zhang, H. Zhao, M. Zhang, W. Su, *Angew. Chem. Int. Ed.* **2015**, *54*, 3817-3821; *Angew. Chem.* **2015**, *127*, 3888-3892; d) R. Qiu, L. Zhang, C. Xu, Y. Pan, H. Pang, L. Xu, H. Li, *Adv. Synth. Catal.* **2015**, *357*, 1229-1236.

[10] a) K. Yang, C. Zhang, P. Wang, Y. Zhang, H. Ge, *Chem. Eur. J.* **2014**, *20*, 7241-7244; b) G. Li, T. Wang, F. Fan, Y.-M. Su, Y. Li, Q. Lan, X.-S. Wang, *Angew. Chem. Int. Ed.* **2016**, *55*, 3491-3495; *Angew. Chem.* **2016**, *128*, 3552-3556; c) L. W. Sardzinski, W. C. Wertjes, A. M. Schnaith, D. Kalyani, *Org. Lett.* **2015**, *17*, 1256-1259.

[11] a) Q. Feng, Q. Song, *Adv. Synth. Catal.* **2014**, *356*, 1697-1702; b) L. Yin, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2009**, *131*, 9610-9611; c) J. Hu, N. Zhao, B. Yang, G. Wang, L. Guo, Y. Liang, S. Yang, *Chem. Eur. J.* **2011**, *17*, 5516-5521; d) Z. Cui, X. Shang, X.-F. Shao, Z.-Q. Liu, *Chem. Sci.* **2012**, *3*, 2853-2858; e) G. Hu, Y. Gao, Y. Zhao, *Org. Lett.* **2014**, *16*, 4464-4467; f) Y. Zhang, S. Patel, N. Mainolfi, *Chem. Sci.* **2012**, *3*, 3196-3199; g) J. Zhang, D. Li, H. Chen, B. Wang, Z. Liu, Y. Zhang, *Adv. Synth. Catal.* **2016**, *358*, 792-807; h) B. R. Ambler, R. A. Altman, *Org. Lett.* **2013**, *15*, 5578-5581; i) A. Joshi, D. C. Mohan, S. Adimurthy, *Org. Lett.* **2016**, *18*, 464–467.

[12] a) S. Bhadra, W. I. Dzik, L. J. Goossen, *J. Am. Chem. Soc.* **2012**, *134*, 9938-9941; b) F. Yin, Z. Wang, Z. Li, C. Li, *J. Am. Chem. Soc.* **2012**, *134*, 10401-10404; c) F. Chen, A. S. K. Hashmi, *Org. Lett.* **2016**, *18*, 2880-2882; d) Y. Zhu, X. Li, X. Wang, X. Huang, T. Shen, Y. Zhang, X. Sun, M. Zou, S. Song, N. Jiao, *Org. Lett.* **2015**, *17*, 4702-4705; e) P.-F. Wang, X.-Q. Wang, J.-J. Dai, Y.-S. Feng, H.-J. Xu, *Org. Lett.* **2014**, *16*, 4586-4589; f) J. Liu, C. Fan, H. Yin, C. Qin, G. Zhang, X. Zhang, H. Yi, A. Lei, *Chem. Commun.* **2014**, *50*, 2145-2147; g) H. Wang, L.-N. Guo, X.-H. Duan, *Chem. Commun.* **2014**, *50*, 7382-7384.

[13] a) K. Yang, X. Chen, Y. Wang, W. Li, A. A. Kadi, H.-K. Fun, H. Sun, Y. Zhang, G. Li, H. Lu, *J. Org. Chem.* **2015**, *80*, 11065-11072; b) K. Xu, Z. Wang, J. Zhang, L. Yu, J. Tan, *Org. Lett.* **2015**, *17*, 4476-4478; c) H. Tan, H. Li, J. Wang, L. Wang, *Chem. Eur. J.* **2015**, *21*, 1904-1907; d) R. Trivedi, J. A. Tunge, *Org. Lett.* **2009**, *11*, 5650-5652; e) C. Wang, J. A.

Tunge, *Org. Lett.* **2005**, *7*, 2137-2139.

[14] a) A. Noble, S. J. McCarver, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2015**, *137*, 624-627; b) C. Zhou, P. Li, X. Zhu, L. Wang, *Org. Lett.* **2015**, *17*, 6198-6201; c) N. Xu, P. Li, Z. Xie, L. Wang, *Chem. Eur. J.* **2016**, *22*, 2236-2242; d) W.-T. Xu, B. Huang, J.-J. Dai, J. Xu, H.-J. Xu, *Org. Lett.* **2016**, *18*, 3114-3117; d) H. Huang, G. Zhang, Y. Chen, *Angew. Chem., Int. Ed.* **2015**, *54*, 7872−7876, *Angew. Chem.* **2015**, *127*, 7983-7987; e) G. H. Lovett, B. A. Sparling, *Org. Lett.* **2016**, 18, 3494–3497.

[15] a) X.-F. Xia, S.-L. Zhu, C. Chen, H. Wang, Y.-M. Liang, *J. Org. Chem.* **2016**, *81*, 1277-1284; b) W.-P. Mai, G.-C. Sun, J.-T. Wang, G. Song, P. Mao, L.-Y. Yang, J.-W, Yuan, Y.-M. Xiao, L.-B. Qu, *J. Org. Chem.* **2014**, *79*, 8094-8102; c) W.-P. Mai, J.-T. Wang, L.-Y. Yang, J.-W, Yuan, Y.-M. Xiao, P. Mao, L.-B. Qu, *Org. Lett.* **2014**, *16*, 204-207; d) H. Wang, L.-N. Guo and X.-H. Duan, *Adv. Synth. Catal.* **2013**, *355*, 2222-2226; e) W. Ji, H. Tan, M. Wang, P. Li, L. Wang, *Chem. Commun.* **2016**, *52*, 1462-1465; f) S. Tang, X. Gao, A. Lei, *Adv. Synth. Catal.* **2016**, *358*, 2878-2882.

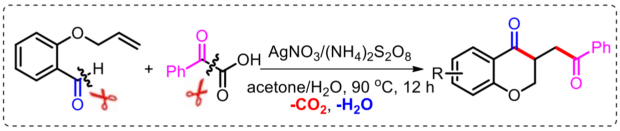
[16] For the synthesis of dihydroflavonoid derivatives, see: a) M. Fridén-Saxin, T. Seifert, M. R. Landergren, T. Suuronen, M. Lahtela-Kakkonen, E. M. Jarho, K. Luthman, *J. Med. Chem.* **2012**, *55*, 7104-7113; b) T. Seifert, M. Malo, T. Kokkola, K. Engen, M. Fridén-Saxin, E. A. A. Wallén, M. Lahtela-Kakkonen, E. M. Jarho, K. Luthman, *J. Med. Chem.* **2014**, *57*, 9870-9888; c) W.-D. Z. Li, B.-C. Ma, *Org. Lett.* **2005**, *7*, 271-274; d) J. R. de Alaniz, M. S. Kerr, J. L. Moore, T. Rovis, *J. Org. Chem.* **2008**, *73*, 2033-2040; e) A. T. Biju, N. E. Wurz, F. Glorius, *J. Am. Chem. Soc.* **2010**, *132*, 5970-5971; f) M. S. Kerr, T. Rovis, *J. Am. Chem. Soc.* **2004**, *126*, 8876-8877; g) H. Takikawa, K. Suzuki, *Org. Lett.* **2007**, *9*, 2713-2716.

[17] a) M. Mao, L. Zhang, Y.-Z. Chen, J. Zhu, L. Wu, *ACS Catal.* **2017**, 7, 181-185; b) K. Luo, Y.-Z. Chen, L.-X. Chen, L. Wu, *J. Org. Chem.* **2016**, *81*, 4682-4689; c) K. Luo, Y.-Z. Chen, W.-C. Yang, J. Zhu, L. Wu, *Org. Lett.* **2016**, *18*, 452-455; d) W.-C. Yang, P. Dai, K. Luo, L. Wu, *Adv. Synth. Catal.* **2016**, *358*, 3184-3190; e) J. Zhu, M. Mao, H.-J. Ji, J.-Y. Xu, L. Wu, *Org. Lett.* **2017**, DOI:10.1021/acs.orglett.7b00213.

[18] a) Y. Yamamoto, D. Matsumi, R. Hattori, K. Itoh, *J. Org. Chem.* **1999**, *64*, 3224-3229; b) J. Streuff, M. Feurer, P. Bichovski, G. Frey, U. Gellrich, *Angew. Chem. Int. Ed.* **2012**, *51*, 8661-8664; *Angew. Chem.* **2012**, *124*, 8789-8792; c) J. Zheng, Y. Zhang, D. Wang, S. Cui, *Org. Lett.* **2016**, *18*, 1768-1771; d) Y.-Y. Han, H. Jiang, R. Wang, S. Yu, *J. Org. Chem.* **2016**, *81*, 7276-7281.

COMMUNICATION

Aldehydes as Carbon Radical Acceptors: Silver Nitrate Catalyzed Cascade Decarboxylation and Oxidative Cyclization toward Dihydroflavonoid Derivatives



- ☐ **Cascade decarboxylation and oxidative cyclization**
- ☐ **Aldehydes as radical acceptors**
- ☐ **Diacylation to dihydroflavonoids with broad substrate scopes**

Adv. Synth. Catal. **2017**, *Volume*, Page – Page

Wen-Chao Yang, Peng Dai, Kai Luo, Yi-Gang Ji and Lei Wu*