Tetrahedron Letters 52 (2011) 6118–6121

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Hydroxymethylation of α-substituted nitroacetates

Cong-Bin Ji [a], Yun-Lin Liu [a], Zhong-Yan Cao [a], Yi-Yu Zhang [b], Jian Zhou [a,*]

[a] Shanghai Key Laboratory of Green Chemistry and Chemical Processes, Department of Chemistry, East China Normal University, 3663 N. Zhongshan Road, Shanghai 200062, PR China
[b] College of Chemistry and Material Sciences, Sichuan Normal University, Chengdu, Sichuan 610066, PR China

ARTICLE INFO

Article history:
Received 24 June 2011
Revised 29 August 2011
Accepted 6 September 2011
Available online 10 September 2011

Keywords:
Tetrasubstituted carbon
Hydroxymethylation
α-Substituted nitroacetates

ABSTRACT

Only 1 mol % of K_3PO_4 is efficient enough to catalyze the hydroxymethylation of α-substituted nitroacetates in good to excellent yield. Both aliphatic and aryl substituted nitroacetates work well under this reaction. The first catalytic asymmetric version of this reaction also reported that 10 mol % of cupreidine could catalyze this reaction up to 71% ee and 89% yield. Paraformaldehyde and formalin could both serve as the hydroxymethylation C1 unit. The synthetic application of products is also demonstrated.

The efficient construction of tetrasubstituted carbon centers is a very important task in organic chemistry.[1] In this context, the deprotonative activation of carbon nucleophiles, with three disparate carbon substituents, to react with different electrophiles is a fruitful synthetic strategy.[1,2] For example, α-substituted α-cyanoacetate, β-keto esters,[2a,b] and 3-substituted oxindoles[2c,d] had been widely used for the creation of tetrasubstituted carbon centers. In contrast, the functionalization of α-monosubstituted nitroacetates has been less studied judged by reaction type and substrate scope.[3] For example, although α-aliphatic substituted nitroacetates had been used in Mannich,[3a–f] Michael addition,[3g–m] alkylation,[3n–r] and aldol reaction,[3s] α-aryl substituted nitroacetates were rarely employed for reaction development.[3m]

With our efforts in the preparation of compounds containing a tetrasubstituted carbon center for biological evaluation,[4] we are interested in the hydroxymethylation[5] of α-substituted nitroacetates. The corresponding products are versatile synthons for the synthesis of aziridines, amino alcohols, diamines, and quaternary α-substituted α-amino acids.[6] Surprisingly, this reaction has not been systematically studied. To prepare α-methylene carbonyl compounds, Ono and Kaji found that the hydroxymethylation of α-alkyl nitroacetates and formaldehyde (37% aq) worked well in the presence of 10 mol % of 10% NaOH, with five substrates examined (60–82% yield).[7a] Recently, Chen et al. found that the use of 5 mol % DBU at 70 °C could facilitate the reaction of α-(3-indolyl)methyl nitroacetates and paraformaldehyde to provide α-hydroxymethylated tryptophan precursors.[7b] As far as we know, the hydroxymethylation of α-aryl nitroacetates was not reported, and no asymmetric version was reported. Here, we wish to report a highly efficient hydroxymethylation of both α-aryl and α-alkyl nitroacetates[8] catalyzed by K_3PO_4 and the first example of asymmetric version.

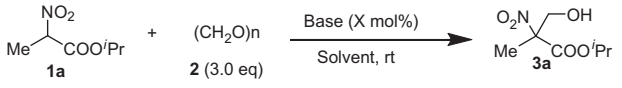
The reaction of α-methyl nitroacetate **1a** and *para*-formaldehyde **2** was chosen to evaluate different bases, using CH_2Cl_2 as the solvent at room temperature. Of all the examined organic bases we first examined, DBU and DBACO could both afford the desired product **3a** in 80% yield (entries 1–4, Table 1). Inorganic bases were then examined (entries 5–9), and K_3PO_4[9] was identified as a powerful catalyst for this reaction, which could promote the reaction to finish within 30 min, affording the product in 81% yield (entry 9). The following evaluation of the solvent effects was carried out using 5 mol % of the catalyst (entries 9–13), and Et_2O turned out to be the best (entry 13). Lowering the catalyst loading to only 1 mol %, the reaction could still finish in 4 h and gave product **3a** in 87% yield (entry 15). We also found that the reaction could proceed very slowly in the absence of catalyst, and product **3a** was obtained in 74% yield after 102 h (entry 16). This result suggested that the use of catalyst was necessary. The employment of K_3PO_4 as the catalyst is remarkable, not only for its high efficiency, but for its environmental benign nature. Because K_3PO_4 is a common fertilizer containing K and P, there is no need to worry about the environmental pollution by the remaining catalyst.

Based on the above results, the evaluation of substrate scope was carried out by running the reaction in Et_2O at room temperature, with 1 mol % of K_3PO_4 as the catalyst (Table 2). The ester group of the nitroacetates was first examined. Isopropyl, methyl, and ethyl esters worked well to afford the corresponding product **3a–c** in high yield (entries 1–3), but isopropyl esters **1a** seemed to be more reactive. Bulky *tert*-butyl ester **1d** could also afford the corresponding product **3d** in 69% yield (entry 4), and the reaction proceeded obviously slowly. The different aliphatic

* Corresponding author. Tel./fax: +86 21 62234560.
E-mail address: jzhou@chem.ecnu.edu.cn (J. Zhou).

0040-4039/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2011.09.020

Table 1
Reaction condition optimization



Entry[a]	Solvent	Base	X	Time	Yield (%)[b]
1	CH_2Cl_2	DBU	10	1.5 h	80
2	CH_2Cl_2	Et_3N	10	3.0 h	59
3	CH_2Cl_2	DMAP	10	3.0 h	76
4	CH_2Cl_2	DBACO	10	3.0 h	80
5	CH_2Cl_2	NaOH	10	0.5 h	48
6	CH_2Cl_2	Na_2CO_3	10	0.5 h	68
7	CH_2Cl_2	K_2CO_3	10	0.5 h	72
8	CH_2Cl_2	KOAc	10	3.0 h	74
9	CH_2Cl_2	K_3PO_4	10	0.5 h	81
10	THF	K_3PO_4	5	50 min	55
11	Acetone	K_3PO_4	5	20 min	59
12	CH_3CN	K_3PO_4	5	20 min	34
13	Et_2O	K_3PO_4	5	70 min	90
14	Et_2O	K_3PO_4	2	2.5 h	91
15	Et_2O	K_3PO_4	1	4.0 h	87
16	Et_2O	–	–	102.0 h	74

[a] 0.5 mmol in 5 mL of solvent under N_2.
[b] Isolated yield.

substituents of the nitroacetates were then checked. It turned out that all the α-aliphatic substituted nitroacetates provided the corresponding product **3e**–**o** in high to excellent yield (entries 5–15). To our delight, α-aryl substituted nitroacetates also worked well under this reaction conditions. The nature of the aryl substituents had no big influence on the yield, and the corresponding products **3p**–**t** were obtained in good to high yield (entries 16–20). However, α-aryl substituted nitroacetates with *ortho* substituent did not work under this reaction condition, possibly because steric hindrance resulting from the *ortho* substituent prevented the approach of base for deprotonative activation. For example, nitroacetate **1u** could not react with paraformaldehyde even in the presence of 100 mol % of K_3PO_4 (entry 21), and no reaction took place even on running the reaction at 40 °C in a screw-capped pressure tube with 20 mol % of K_3PO_4 catalyst.

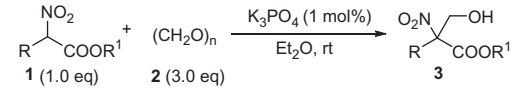
Formalin[5a–m] could also be used as the hydroxymethylation C1 unit (Scheme 1). Four typical substrates **1a**, **1j**, **1p**, and **1q** were examined. α-Aliphatic nitroacetates **1a** and **1j** gave the corresponding product **3a** and **3j** in lower yield than that obtained by using paraformaldehyde (63% vs 87%, 47% vs 99%, respectively). However, α-aryl substituted nitroacetates **1p** and **1q** afforded the corresponding products **3p** and **3q** in high yield, comparable to that obtained by using paraformaldehyde.

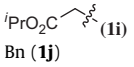
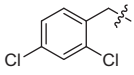
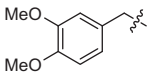
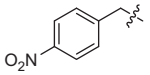
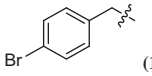
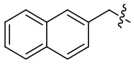
It should be noted that this hydroxymethylation reaction could be carried out in air without erosion of the yield. For example, the hydroxymethylation of nitroacetate **1a** and **1r** under atmosphere afforded almost the same reactivity and the yield of products **3a** and **3r** as those reactions that ran under an atmosphere of N_2 (entries 1 and 18).

Thus the synthetic application of the obtained products was demonstrated by the following transformations (Scheme 2). For example, α-phenyl substituted product **3p** could be readily reduced to the corresponding amino alcohol **4p** in 76% yield by Zn/HCl, which was further converted to oxazolidinone **5** in 89% yield. α-Methyl substituted product **3a** was reduced to amino alcohol **4a** in 57% yield by hydrogenation. Aziridine **6** could be prepared from **4a** in 24% yield in two steps. Triazole **7** was easily obtained from product **3a** in three steps with 32% yield, which was further converted to a novel quaternary α-substituted α-amino acid derivative **8** in 90% yield.

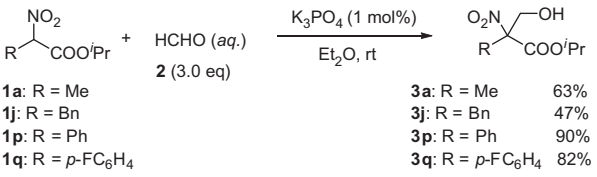
We next tried to develop an enantioselective version of this reaction. Because the background reaction could slowly take place at

Table 2
Substrate scope for hydroxymethylation of α-substituted nitroacetates



Entry[a]	R	R^1	3	Time (h)	Yield (%)[b]
1	Me (**1a**)	*i*-Pr	**3a**	4.0	87 (86)[c]
2	Me (**1b**)	Me	**3b**	36.0	82
3	Me (**1c**)	Et	**3c**	9.0	86
4	Me (**1d**)	*t*-Bu	**3d**	23.0	69
5	Et (**1e**)	*i*-Pr	**3e**	8.0	88
6	*n*-Bu (**1f**)	*i*-Pr	**3f**	4.0	95
7	*i*-Bu (**1g**)	*i*-Pr	**3g**	7.0	98
8	 (**1h**)	*i*-Pr	**3h**	20.0	94
9	 (**1i**)	*i*-Pr	**3i**	10.0	78
10	Bn (**1j**)	*i*-Pr	**3j**	2.5	99
11	 (**1k**)	*i*-Pr	**3k**	8.0	97
12	 (**1l**)	*i*-Pr	**3l**	20.0	92
13	 (**1m**)	*i*-Pr	**3m**	20.0	62
14	 (**1n**)	*i*-Pr	**3n**	3.0	93
15	 (**1o**)	*i*-Pr	**3o**	6.0	96
16	Ph (**1p**)	*i*-Pr	**3p**	8.0	85
17	*p*-FC_6H_4 (**1q**)	*i*-Pr	**3q**	12.0	89
18	*p*-$MeOC_6H_4$ (**1r**)	*i*-Pr	**3r**	40.0	77 (78)[c]
19	*p*-ClC_6H_4 (**1s**)	*i*-Pr	**3s**	15.0	85
20	*m*-BrC_6H_4 (**1t**)	*i*-Pr	**3t**	15.0	87
21	*o*-ClC_6H_4 (**1u**)	*i*-Pr	**3u**	16.0	–

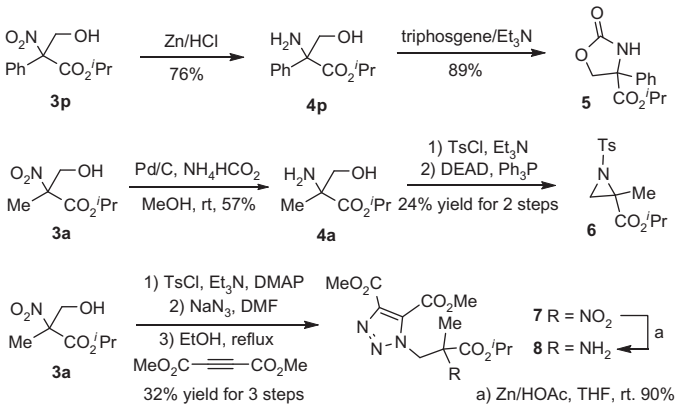
[a] Reaction scale: 0.5 mmol.
[b] Isolated yield.
[c] Reaction run in air.



Scheme 1. Formalin as the hydroxymethylation C1 unit.

room temperature, the model reaction of nitroacetate **1a** with paraformaldehyde was carried out at 0 °C, in the presence of 5 mol % of chiral catalyst with CH_2Cl_2 as the solvent. Since K_3PO_4 was an efficient base for this reaction, we first tried using chiral phase transfer catalysts in combination with K_3PO_4 for reaction development. To our great disappointment, when two commercially available chiral phase transfer catalysts **9a** and **9b** were used, product **3a** was obtained in racemic form (entries 1 and 2, Table 3). Because nitrogen based organobase could efficiently catalyze this reaction, we next examined cinchona alkaloid derivatives,[10] and some typical results were given below. Moderate ee was obtained for product **3a** when using $(QD)_2PYR$ **10** (entry 3). After intensive screening, bifunctional catalyst **13**, which Deng developed for the Michael addition of malonates to nitroalkenes,[10a] was found to be the most enantioselective, affording product **3a** in 38% ee (entry 6).

We initially examined the influence of the catalyst structure on the enantioselectivity. Without the phenol hydroxy group,



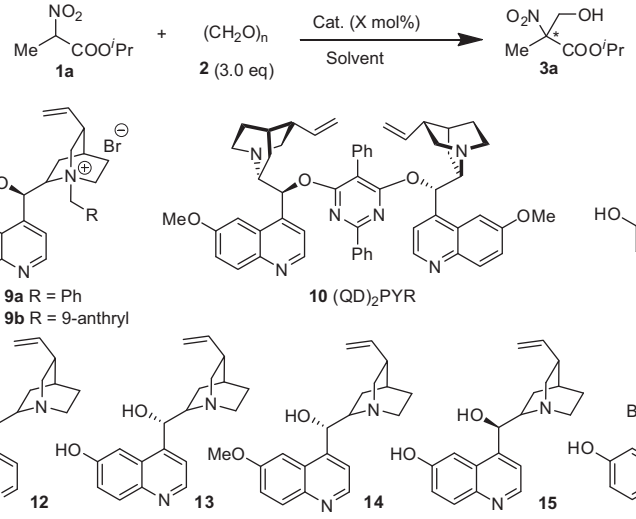
Scheme 2. Product elaboration.

cinchonine **12** afforded product **3a** in 23% ee (entry 5), and quinidine provided product **3a** in 26% ee (entry 7). Both results suggested the importance of the phenol group in an enantiofacial control. We next tried cupreidine derived catalyst **16**, and only 23% ee was obtained for product **3a** (entry 9), suggesting the importance of the alcoholic hydroxyl group. These results were useful for the development of new chiral bifunctional Brønsted acid–base catalysts for further improving the ee. The quinine derived catalyst **15** could give the opposite enantiomer of product **3a** in 37% ee (entry 8). We next used catalyst **13** to examine the solvent effects at −10 °C (entries 10–15), and toluene turned out to be more suitable which afforded product in 44% ee (entry 15). Improving the catalyst loading to 10 mol % and lowering the temperature to −25 °C, the ee of product **3a** could be improved to 60% (entry 16), but it took 6 days for the reaction to complete.

The substrate scope with respect to different α-substituted nitroacetate was then examined by running the reaction in toluene at −25 °C in the presence of 10 mol % of **13**. As shown in Table 4, five α-aliphatic substituted nitroacetates worked well to afford the corresponding products in 51–71% ee with good to high yield (entries 1–5). However, when α-phenyl nitroacetate **1p** was used, the enantioselectivity decreased to 25%. Although there is ample room for further improvement in the enantioselectivity, our results represented the first example of this useful hydroxymethylation.

In conclusion, we have developed a highly efficient hydroxymethylation of both α-alkyl and aryl substituted nitroacetates catalyzed by only 1 mol % of K_3PO_4. Ether paraformaldehyde or formalin can serve as the electrophilic reaction partner. We also

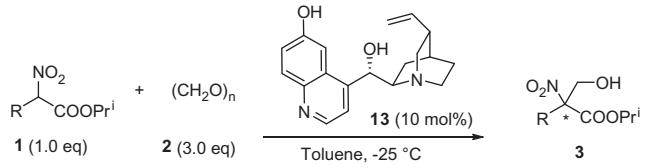
Table 3
Condition optimization for asymmetric version



Entry[a]	Cat.	X	Solvent	*T* (°C)	Yield (%)[b]	ee (%)[c]
1[d]	**9a** K_3PO_4	5	CH_2Cl_2	0	51	0
2[d]	**9b** K_3PO_4	5	CH_2Cl_2	0	63	0
3	**10**	5	CH_2Cl_2	0	74	14
4	**11**	5	CH_2Cl_2	0	89	2[e]
5	**12**	5	CH_2Cl_2	0	92	23[e]
6	**13**	5	CH_2Cl_2	0	84	38
7	**14**	5	CH_2Cl_2	0	89	26
8	**15**	5	CH_2Cl_2	0	95	37[e]
9	**16**	5	CH_2Cl_2	0	79	23
10	**13**	5	CH_2Cl_2	−10	89	40
11	**13**	5	$ClCH_2CH_2Cl$	−10	87	18
12	**13**	5	Et_2O	−10	68	28
13	**13**	5	MeOBu-*t*	−10	87	11
14	**13**	5	THF	−10	Trace	–
15	**13**	5	Toluene	−10	97	44
16	**13**	10	Toluene	−25	83	60

[a] On a 0.20 mmol scale.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis.
[d] **9a** or **9b** (5 mol %) and K_3PO_4 (5 mol %).
[e] Opposite enantiomer.

Table 4
Substrate scope of asymmetric version



Entry[a]	R	3	Time (d)	Yield (%)[b]	ee (%)[c]
1	Me (**1a**)	**3a**	6	83	60
2	Et (**1e**)	**3e**	6	80	64
3	*n*-Bu (**1f**)	**3f**	6	77	71
4	*i*-Bu (**1g**)	**3g**	6	72	51
5	 (**1h**)	**3h**	6	89	52
6	Ph (**1p**)	**3p**	7	82	25

[a] 0.2 mmol sacle.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis.

developed the first example of asymmetric catalytic version, and up to 71% ee was achieved by now. The synthetic versatility of the products was also demonstrated. The development of new chiral bifunctional Brønsted acid–base catalysts to improve both the reactivity and enantioselectivity of this hydroxymethylation reaction is now in progress in our lab.

Acknowledgments

The financial support from the National Natural Science Foundation of China (20902025), Shanghai Pujiang Program (10PJ1403100), and the Fundamental Research Funds for the Central Universities (East China Normal University 11043) are highly appreciated.

Supplementary data

Supplementary data associated (experimental details, IR, MS, and NMR spectra) with this Letter can be found, in the online version, at doi:10.1016/j.tetlet.2011.09.020.

References and notes

1. For recent reviews, see: (a) Riant, O.; Hannedouche, J. *Org. Biomol. Chem.* **2007**, *5*, 873–888; (b) Shibasaki, M.; Kanai, M. *Chem. Rev.* **2008**, *108*, 2853–2873; (c) Bella, M.; Gasperi, T. *Synthesis* **2009**, 1583.
2. For reviews, see: (a) Palomo, C.; Oiarbide, M.; López, R. *Chem. Soc. Rev.* **2009**, *38*, 632–653; (b) Erkkil, A.; Majander, I.; Pihko, P. M. *Chem. Rev.* **2007**, *107*, 5416–5470; (c) Trost, B. M.; Brennan, M. K. *Synthesis* **2009**, 3003–3025; (d) Zhou, F.; Liu, Y.-L.; Zhou, J. *Adv. Synth. Catal.* **2010**, *352*, 1381–1407; (e) Bella, M.; Gasperi, T. *Synthesis* **2009**, 1583–1614.
3. For Mannich reaction, see: (a) Knudsen, K. R.; Jørgensen, K. A. *Org. Biomol. Chem.* **2005**, *3*, 1362–1364; (b) Han, B.; Liu, Q.-P.; Li, R.; Tian, X.; Xiong, X.-F.; Deng, J.-G.; Chen, Y.-C. *Chem. Eur. J.* **2008**, *14*, 8094–8097; (c) Singh, A.; Johnston, J. N. *J. Am. Chem. Soc.* **2008**, *130*, 5866–5867; (d) Chen, Z.; Morimoto, H.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2008**, *130*, 2170–2171; (e) Uraguchi, D.; Koshimoto, K.; Ooi, T. *J. Am. Chem. Soc.* **2008**, *130*, 10878–10879; (f) Puglisi, A.; Raimondi, L.; Benaglia, M.; Bonsignore, M.; Rossi, S. *Tetrahedron Lett.* **2009**, *50*, 4340–4342; For Michael addition, see: (g) Halland, N.; Hazell, R. G.; Jørgensen, K. A. *J. Org. Chem.* **2002**, *67*, 8331–8338; (h) Li, H.; Wang, Y.; Tang, L.; Wu, F.; Liu, X.; Guo, C.; Foxman, B. M.; Deng, L. *Angew. Chem., Int. Ed.* **2005**, *44*, 105–108; (i) Duvall, J. R.; Wu, F.; Snider, B. B. *J. Org. Chem.* **2006**, *71*, 8579–8590; (j) Linton, B. R.; Reutershan, M. H.; Aderman, C. M.; Richardson, E. A.; Brownell, K. R.; Ashley, C. W.; Evans, C. A.; Miller, S. J. *Tetrahedron Lett.* **2007**, *48*, 1993–1997; (k) Lu, H.-H.; Wang, X.-F.; Yao, C.-J.; Zhang, J.-M.; Wu, H.; Xiao, W.-J. *Chem. Commun.* **2009**, 4251–4253; (l) Chen, L.; Zhou, G. *Chin. J. Synth. Chem.* **2009**, *17*, 146–150; (m) Cui, H.-F.; Li, P.; Wang, X.-W.; Chai, Z.; Yang, Y.-Q.; Cai, Y.-P.; Zhu, S.-Z.; Zhao, G. *Tetrahedron* **2011**, *67*, 312–317; For alkylation reaction, see: (n) Alvarez-Ibarra, G.; Csákÿ, A. G.; de la Oliva, C. G. *J. Org. Chem.* **2000**, *65*, 3544–3547; (o) Manabe, K.; Kobayashi, S. *Org. Lett.* **2003**, *5*, 3241–3244; (p) Soengas, R. G.; Estévez, J. C.; Estévez, R. J.; Maestro, M. A. *Tetrahedron: Asymmetry* **2003**, *14*, 1653–1658; (q) Kieltsch, I.; Eisenberger, P.; Togni, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 754–757; (r) Maki, K.; Kanai, M.; Shibasaki, M. *Tetrahedron* **2007**, *63*, 4250–4257; (s) Harel, T.; Rozen, S. *J. Org. Chem.* **2007**, *72*, 6500–6503.
4. (a) Qian, Z.-Q.; Zhou, F.; Du, T.-P.; Wang, B.-L.; Ding, M.; Zhao, X.-L.; Zhou, J. *Chem. Commun.* **2009**, 6753–6755; (b) Ding, M.; Zhou, F.; Qian, Z.-Q.; Zhou, J. *Org. Biomol. Chem.* **2010**, *8*, 2912–2914; (c) Liu, Y.-L.; Zhou, F.; Cao, J.-J.; Ji, C.-B.; Ding, M.; Zhou, J. *Org. Biomol. Chem.* **2010**, *8*, 3847–3850; (d) Liu, Y.-L.; Wang, B.-L.; Cao, J.-J.; Chen, L.; Zhang, Y.-X.; Wang, C.; Zhou, J. *J. Am. Chem. Soc.* **2010**, *132*, 15176–15178; (e) Cao, J.-J.; Zhou, F.; Zhou, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 4976–4980; (f) Ding, M.; Zhou, F.; Liu, Y.-L.; Wang, C.-H.; Zhao, X.-L.; Zhou, J. *Chem. Sci.* **2011**, *2*, 2035–2039; (g) Liu, Y.-L.; Shi, T.-D.; Zhou, F.; Zhao, X.-L.; Wang, X.; Zhou, J. *Org. Lett.* **2011**, *13*, 3826–3829.
5. For selected examples of hydroxymethylation reaction: (a) Ozasa, N.; Wadamoto, M.; Ishihara, K.; Yamamoto, H. *Synlett* **2003**, 2219–2221; (b) Ishikawa, S.; Hamada, T.; Manabe, K.; Kobayashi, S. *J. Am. Chem. Soc.* **2004**, *126*, 12236–12237; (c) Casas, J.; Sundén, H.; Córdova, A. *Tetrahedron Lett.* **2004**, *45*, 61176119; (d) Torii, H.; Nakadai, M.; Ishihara, K.; Saito, S.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 1983–1986; (e) Kobayashi, S.; Ogino, T.; Shimizu, H.; Ishikawa, S.; Hamada, T.; Manabe, K. *Org. Lett.* **2005**, *7*, 4729–4731; (f) Kokubo, M.; Kobayashi, S. *Synlett* **2008**, 1562–1564; (g) Bica, K.; Gaertner, P. *Eur. J. Org. Chem.* **2008**, 3453–3456; (h) Kan, T.; Kawamoto, Y.; Asakawa, T.; Furuta, T.; Fukuyama, T. *Org. Lett.* **2008**, *10*, 169–171; (i) Kokubo, M.; Ogawa, C.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 6909–6911; (j) Mouri, S.; Chen, Z.; Matsunaga, S.; Shibasaki, M. *Chem. Commun.* **2009**, 5138–5140; (k) Shen, K.; Liu, X.; Wang, W.; Wang, G.; Cao, W.; Li, W.; Hu, X.; Lin, L.; Feng, X. *Chem. Sci.* **2010**, *1*, 590–595; (l) Kobayashi, S.; Kokubo, M.; Kawasumi, K.; Nagano, T. *Chem. Asian J.* **2010**, *5*, 490–492; (m) Pasternak, M.; Paradowska, J.; Rogazińska, M.; Mlynarski, J. *Tetrahedron Lett.* **2010**, *51*, 4088–4090; (n) Fukuchi, I.; Hamashima, Y.; Sodeoka, M. *Adv. Synth. Catal.* **2007**, *349*, 509–512; (o) Srinivas, N.; Bhandari, K. *Tetrahedron Lett.* **2008**, *49*, 7070–7073; (p) Srinivas, N.; Marrapu, V. K.; Bhandari, K. *Synlett* **2009**, 1346–1350; (q) Liu, X.-L.; Liao, Y.-H.; Wu, Z.-J.; Cun, L.-F.; Zhang, X.-M.; Yuan, W.-C. *J. Org. Chem.* **2010**, *75*, 4872–4875; (r) Kuhl, N.; Glorius, F. *Chem. Commun.* **2011**, 573–575.
6. For reviews, see: (a) Cativiela, C.; Díaz-de-Villegas, M. D. *Tetrahedron: Asymmetry* **1998**, *9*, 3517–3599; (b) Lucet, D.; Gall, T. L.; Mioskowski, C. *Angew. Chem., Int. Ed.* **1998**, *37*, 2580–2627; (c) Atkison, R. S. *Tetrahedron* **1999**, *55*, 1519–1559; (d) Reetz, M. T. *Chem. Rev.* **1999**, *99*, 1121–1162; (e) Bergmeier, S. C. *Tetrahedron* **2000**, *56*, 2561–2576; (f) Sweeney, J. B. *Chem. Soc. Rev.* **2002**, *31*, 247–258; (g) Gröger, H. *Chem. Rev.* **2003**, *103*, 2795–2827; (h) Hu, X. E. *Tetrahedron* **2004**, *60*, 2701–2743.
7. (a) Ono, N.; Miyake, H.; Fujii, M.; Kaji, A. *Tetrahedron Lett.* **1983**, *24*, 3477–3480; (b) Sui, Y.; Liu, L.; Zhao, J.-L.; Wang, D.; Chen, Y.-J. *Tetrahedron Lett.* **2007**, *48*, 3779–3782.
8. Both α-aryl and α-aliphatic substituted nitroacetates can be easily synthesized according to literature methods: (a) Kornblum, N.; Blackwood, R. K.; Powers, J. W. *J. Am. Chem. Soc.* **1957**, *79*, 2507–2509; (b) Berry, J. P.; Isbell, A. F.; Hunt, G. E. *J. Org. Chem.* **1972**, *37*, 4396–4399; (c) Mattingly, P. G.; Miller, M. J. *J. Org. Chem.* **1981**, *46*, 1557–1564; (d) Nakamura, S.; Sugimoto, H.; Ohwada, T. *J. Am. Chem. Soc.* **2007**, *129*, 1724–1732.
9. For K_3PO_4 catalyzed reactions, see for examples: (a) Prakash, G. K. S.; Vaghoo, H.; Panja, C.; Surampudi, V.; Kultyshev, R.; Mathew, T.; Olah, G. A. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 3026–3030; (b) Dandepally, S. R.; Williams, A. L. *Tetrahedron Lett.* **2009**, *50*, 1071–1074; (c) Ren, H.; Ye, S.; Liu, F.; Wu, J. *Tetrahedron* **2010**, *66*, 8242–8246; (d) Cleary, T.; Brice, J.; Kennedy, N.; Chavez, F. *Tetrahedron Lett.* **2010**, *51*, 625–628; (e) Chen, Z.-G.; Wang, Y.; Wei, J.-F.; Zhao, P.-F.; Shi, X.-Y. *J. Org. Chem.* **2010**, *75*, 2085–2088.
10. (a) Li, H.; Wang, Y.; Tang, L.; Deng, L. *J. Am. Chem. Soc.* **2004**, *126*, 9906–9907; (b) Yeboah, E. M. O.; Yeboah, S. O.; Singh, G. S. *Tetrahedron* **2011**, *67*, 1725–1762; (c) Marcelli, T.; Hiemstra, H. *Synthesis* **2010**, 1229–1279; (d) Palomo, C.; Oiarbide, M.; López, R. *Chem. Soc. Rev.* **2009**, *38*, 632–653; (e) Connon, S. J. *Chem. Commun.* **2008**, 2499–2510; (f) Enders, D.; Grondal, C.; Hüttl, M. R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 1570–1581; (g) Tian, S. K.; Chen, Y.; Huang, J.; Tang, L.; McDaid, P.; Deng, L. *Acc. Chem. Res.* **2004**, *37*, 621–631; (h) Seayad, J.; List, B. *Org. Biomol. Chem.* **2005**, *3*, 719–724; (i) Dalko, P. I.; Moisan, L. *Angew. Chem., Int. Ed.* **2004**, *43*, 5138–5175.