Received: 13 February 2018 | Revised: 8 May 2018 | Accepted: 14 May 2018

DOI: 10.1002/aoc.4462

COMMUNICATION

WILEY Applied Organometallic Chemistry

MeZnOMe-mediated reaction of aldehydes with Grignard reagents: A glance into nucleophilic addition/Oppenauer oxidation pathway

Ying Fu[1] | Xian-Zhen Ma[2] | Chun-Zhao Shi[1] | Tong Shen[2] | Zhengyin Du[1]

[1]College of Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou 730070, China

[2]College of Chemistry and Bioengineering, Lanzhou Jiaotong University, Lanzhou 730070, China

Correspondence
Ying Fu and Zhengyin Du, College of Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou, 730070, China.
Email: fuying@iccas.ac.cn; clinton_du@126.com

Funding information
National Natural Science Foundation of China, Grant/Award Number: No.21762040, 21762039 & 21262030

A novel organozincate of RMgX ·MeZnOMe ·LiCl type, formed *in situ* via transmetalation of Grignard reagent RMgBr ·LiCl with MeZnOMe, is shown to be an excellent organometallic species in the nucleophilic addition/Oppenauer oxidation of aldehydes to generate aromatic ketones in high yield. This transformation allows quick access to structurally diverse aryl, heteroaryl, benzyl and alkyl ketones with broad substrate scope and excellent functional group tolerance.

KEYWORDS
aldehyde, Grignard reagent, ketone, Oppenauer oxidation, transmetalation

1 | INTRODUCTION

Organometallic reagents with an oxygen atom instead of a halogen atom as the counterion have quickly been recognized as stable and reactive organometallic species.[1] Early in 1985, Screttas and co-workers[2] observed that the presence of lithium 2-ethoxyethoxide could dramatically improve the solubility of Grignard reagents in aromatic hydrocarbon solvents. Similarly, the presence of magnesium 2-ethoxyethoxide could not only reduce the interaction of alkyl lithium reagents with tetrahydrofuran (THF), allowing their direct preparation in THF solution,[3] but also promote halogen–metal exchange reaction to generate a new Grignard reagent.[4] Remarkably, the presence of aminoalcohol could dramatically improve the nucleophilicity of diorganozinc reagents to realize a quick and asymmetric addition to carbonyls.[5] Recent progresses, especially those from Knochel's group, have demonstrated that organozinc reagents of RZn (OPiv) ·Mg (OPiv) X ·*n*LiCl type[6] are air-stable and always, compared to organozinc halides, exhibit enhanced reactivity.

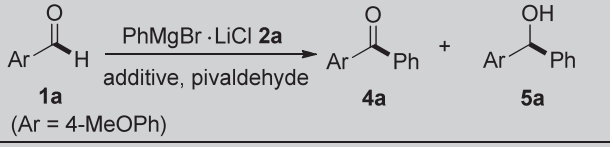
The nucleophilic addition/Oppenauer oxidation of aldehydes (NAOOA)[7] has been demonstrated as a practical and straightforward procedure for ketone synthesis. Grignard reagents[7a–f] are frequently employed as the nucleophiles owing to their high reactivity and easy availability. However, the strong nucleophilicity and basicity of Grignard reagents make some important functional groups, e.g. ester, nitro or nitrile, not compatible with these reaction conditions. Moreover, routes employing Grignard reagents typically involve low temperature. The concentration of the Grignard reagent must be accurately titrated beforehand in case significant side-reactions should occur due to too high or too low a Grignard reagent loading. To circumvent these problems, we[8] and other groups have shown that milder organometallics such as organozinc halides,[7m, o, 8a] organoaluminium reagents,[8b] organotin[7g] and boronic esters[7i] could be employed as nucleophiles in the NAOOA synthesis of ketones. Considering the aforementioned promising properties of alkoxylated organometallic reagents, we thus wondered if alkoxylated organometallic

reagents, generated *in situ* via transmetalation of Grignard reagents with metal alkoxide, could be employed in the one-pot NAOOA synthesis of ketones.

2 | RESULTS AND DISCUSSION

Pivaldehyde[9] was selected as the oxidant as being non-enolizable, having high oxidative potency[10] (E_0 = 211 mV) and high steric hindrance around the carbonyl functionality. Additionally, pivaldehyde and neopentanol are both volatile, allowing removal by laboratory distillation. Then, various kinds of metallic alkoxides were screened to evaluate their effects on phenylmagnesium bromide (**1a**) (Table 1). At first, Al $(O^iPr)_3$[11] was introduced because it is a traditional catalyst in Oppenauer oxidation of alcohols. However, in our reaction system, secondary alcohol **5a** was formed as the main product. The desired ketone product **4a** was obtained in 16% yield (entry 1). When one equivalent of Et_2Zn was introduced as the additive, ethyl and phenyl groups were simultaneously transferred to *p*-anisaldehyde **2a**, delivering the desired secondary alcohol **5a** and 1-(4-methoxyphenyl)-1-propanol in roughly equal proportion. In this case, ketone **4a** was produced in a yield of only 2.4% according to GC–MS analysis (entry 2). To avoid Et transference, Zn $(O^iPr)_2$ was used and the organozincate PhMgBr ·Zn $(O^iPr)_2$·LiCl thus formed did not show any nucleophilicity towards *p*-anisaldehyde that, apart from 30% of *p*-anisaldehyde remaining in the reaction system, a 56% yield of *p*-anisyl alcohol was produced.[12] Adducts of secondary alcohol **5a** and ketone **4a** were not detected (entry 3). When Zn $(OMe)_2$ was employed, the ketone adduct **4a** and alcohol **5a** were again not formed. Nevertheless, a roughly 1:1 mixture of Tishchenko esters[13] (21% in all), derived from *p*-anisaldehyde **2a** and pivaldehyde, were formed as the main byproducts, with roughly 70% of **2a** remaining in the reaction system (entry 4). From these experiments, we recognized that mixed organozincates of PhMgBr ·Et_2Zn ·LiCl[14] type are strong nucleophiles whereas organozincates of PhMgBr ·Zn $(OR)_2$·LiCl species are not, presumably because of the strong acidity of PhMgBr ·Zn $(OR)_2$·LiCl which inhibits the nucleophilic transference of phenyl anion from organozincate to aldehydes. To further modulate the nucleophilicity and Lewis acidity of organozincates, $EtZnO^iPr$ was introduced that resulted in a marked increase in molar ratio of ketone **4a** to alcohol **5a** from 1/10 (Et_2Zn; entry 2) to 2/1 (entry 5). Notably, the employment of EtZnOMe instead of $EtZnO^iPr$ markedly improved the molar ratio of **4a** to **5a** up to 150/1. Ketone **4a** was obtained in 78% isolated yield (GC–MS, 89%; entry 6). The best outcome was achieved by the employment of MeZnOMe as additive whereby *p*-anisaldehyde **2a** was totally consumed and ketone **4a** was isolated in 86% yield (GC–MS, 91% yield; entry 7). Most noteworthy is that the transfer of methyl or ethyl groups from PhMgBr ·EtZnOMe ·LiCl or PhMgBr ·MeZnOMe ·LiCl to aldehyde **2a** was completely suppressed. To examine the halide effect of Grignard reagent PhMgX, PhMgCl ·LiCl and PhMgI ·LiCl were then employed instead of PhMgBr ·LiCl. Reaction with PhMgCl ·LiCl proceeded quite well and roughly equal yield of ketone **4a** was obtained (entry 8). PhMgI ·LiCl exhibited similar reactivity, albeit the yield of **4a** and chemical selectivity being not as good as that of PhMgBr (entry 9).

TABLE 1 Evaluation of additives[a]



1a (Ar = 4-MeOPh) 4a 5a

Entry	Additive	4a/5a[b]	4a (%)[b]
1	Al $(O^iPr)_3$	1/3	16[c]
2	Et_2Zn	1/10	2.4
3	Zn $(O^iPr)_2$	0/0	0
4	Zn $(OMe)_2$	0/0	0
5	$EtZnO^iPr$	2/1	26
6	EtZnOMe	150/1	89/78[c]
7	MeZnOMe	1/0	91/86[c]
8	MeZnOMe	1/0	84[c,d]
9	MeZnOMe	12/1	78[c,e]

[a]Reaction conditions: PhMgBr ·LiCl (2.5 mmol) was treated with the additive (2.0 mmol) at 0 °C for 10 min; then a mixture of pivaldehyde (4.0 mmol) and *p*-anisaldehyde (2.0 mmol) in THF (10 ml) was added. The reaction mixture was stirred at ambient temperature for 2 h.

[b]Product ratios and yields of **4a** were determined by GC–MS analysis.

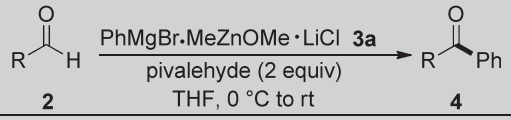
[c]Isolated yield.

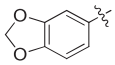
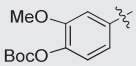
[d]PhMgCl ·LiCl (2.5 mmol) was used.

[e]PhMgI ·LiCl (2.5 mmol) was used.

With these optimized reaction conditions in hand, we then screened the substrate scope of aromatic aldehydes using PhMgBr ·MeZnOMe ·LiCl (**3a**) as the nucleophile. As summarized in Table 2, a wide range of aromatic or heteroaromatic aldehydes were successfully converted into phenyl ketones in good to excellent yields. Neither electron-donating nor electron-accepting substituents appeared to influence the reaction course. Heteroaromatic ketones **4p–4r** were prepared in good yields from 2-thenaldehyde, furfural and 3-pyridinecarboxaldehyde, respectively. *Ortho*-substituted aromatic aldehydes were applicable to the optimized reaction conditions, implying that steric hindrance does not have a key role in these

TABLE 2 MeZnOMe-mediated reactions of PhMgBr ·LiCl with aldehydes[a]

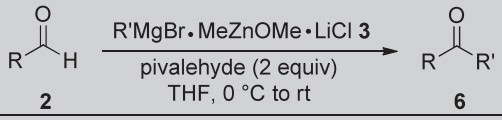


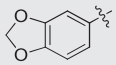
Entry	R	4	Yield (%)[b]
1	4-$MeOC_6H_4$	**4a**	86
2	4-$Me_2NC_6H_4$	**4b**	63
3	2-$MeOC_6H_4$	**4c**	72
4	2-MeC_6H_4	**4d**	76
5	4-ClC_6H_4	**4e**	91
6	3-ClC_6H_4	**4f**	82
7	2-ClC_6H_4	**4g**	76
8	4-FC_6H_4	**4h**	84
9	4-CNC_6H_4	**4i**	62
10	4-$NO_2C_6H_4$	**4j**	57
11	3-$NO_2C_6H_4$	**4k**	51
12	4-$CO_2MeC_6H_4$	**4l**	71
13		**4m**	88
14		**4n**	74
15	2,4-$Cl_2C_6H_3$	**4o**	76
16	2-Thienyl	**4p**	84
17	2-Furyl	**4q**	61
18	3-Pyridyl	**4r**	65

[a]Reaction conditions: PhMgBr ·LiCl (2.5 mmol) was treated with MeZnOMe (2.0 mmol) at 0 °C for 10 min; then a mixture of pivaldehyde (4.0 mmol) and aldehyde **2** (2.0 mmol) in THF (10 ml) was added and stirred at room temperature for 2 h.

[b]Isolated yield.

TABLE 3 MeZnOMe-mediated reactions of Grignard reagents with aldehydes[a]



Entry	R	R′	6	Yield (%)[b]
1	4-ClC_6H_4	4-ClC_6H_4	**6a**	71
2	4-FC_6H_4	4-FC_6H_4	**6b**	56
3	4-$CO_2MeC_6H_4$	3-$CF_3C_6H_4$	**6c**	75
4	3,4,5-$(MeO)_3C_6H_2$	3-$CF_3C_6H_4$	**6d**	74
5	3,4,5-$(MeO)_3C_6H_2$	4-CNC_6H_4	**6e**	68
6	4-$CO_2EtC_6H_4$	4-$CO_2MeC_6H_4$	**6f**	72
7	4-$NO_2C_6H_4$	Biphenyl	**6g**	62
8	4-MeC_6H_4	3-Thienyl	**6h**	63
9	4-ClC_6H_4	3-Thienyl	**6i**	58
10	4-$NO_2C_6H_4$	3-Thienyl	**6j**	49
11	4-$MeOC_6H_4$	Et[c]	**6k**	84
12		Et[c]	**6l**	82
13	4-$MeOC_6H_4$	4-ClBn	**6m**	76
14	4-ClC_6H_4	4-ClBn	**6n**	73

[a]Reaction conditions: R ′MgBr ·LiCl (**3**) (2.5 mmol) was treated with MeZnOMe (2.0 mmol) at 0 °C for 10 min; then a mixture of pivaldehyde (4.0 mmol) and substrate aldehyde (2.0 mmol) in THF (10 ml) was added and the reaction mixtures was stirred at room temperature for 2 h.

[b]Isolated yield.

[c]EtZnOMe was used instead of MeZnOMe.

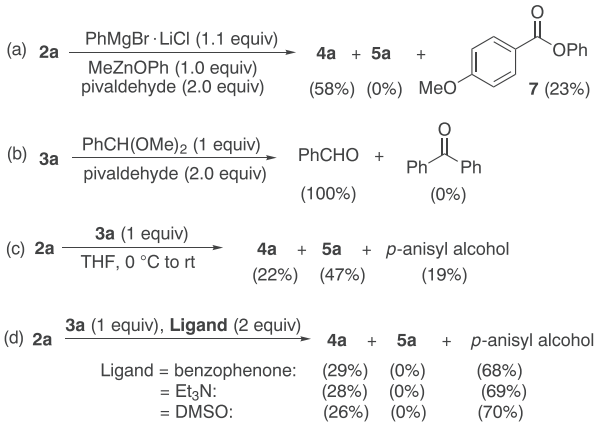
reactions (**4c**, **4d**, **4 g** and **4o**). Sensitive functional groups, such as ester (**4 l**), nitro (**4j** and **4 k**) and cyano (**4i**), are well tolerated on the rings of aromatic aldehydes.

Encouraged by these promising results for organozincate **3a**, we subsequently set out to explore the applicability of RMgBr ·MeZnOMe ·LiCl (**3**), derived from Grignard reagents other than PhMgBr ·LiCl (Table 3). In this respect, organozincates derived from *meta*- and *para*-substituted arylmagnesium bromides and 3-thienylmagnesium bromide reacted smoothly with aromatic aldehydes to give diaryl ketones **6a**–**6j** in good yields. Again, functional groups such as CF_3 (**6c** and **6d**), nitro (**6 g** and **6j**), cyano (**6e**) and ester (**6c** and **6f**) are tolerated on the rings of both aromatic aldehydes and organozincates. Alkylzincates reacted readily with aromatic aldehydes to furnish the corresponding mixed ketones in high yields (**6 k** and **6 l**). Highly enolizable benzylic ketones (**6 m** and **6n**) could be obtained in good yields from benzylmagnesium chloride without apparent formation of aldol condensation byproducts.

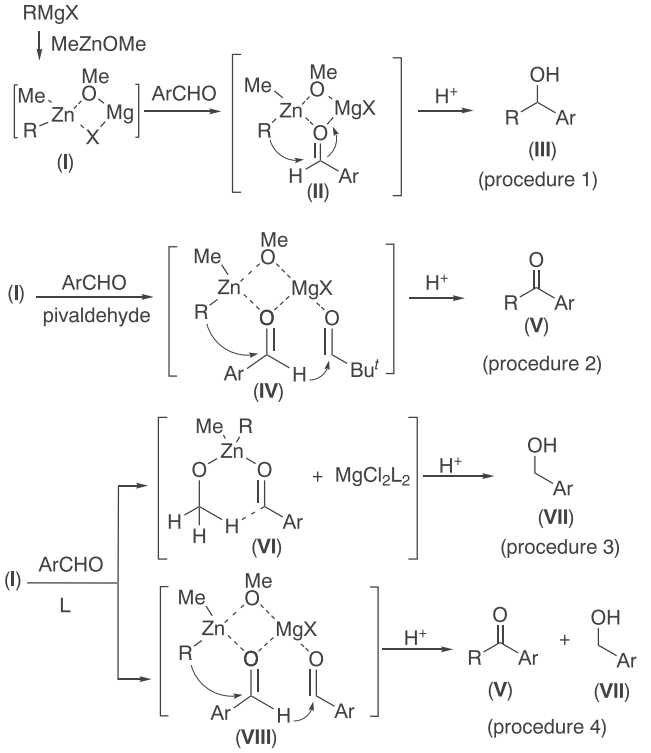
Mechanistically, it is widely accepted that these types of reactions proceed via nucleophilic addition of organometallics to aldehydes to yield the secondary alcoholates, which then coordinate with pivaldehyde to induce hydride transfer to produce the ketone products. However, another possibility must be considered in MeZnOMe-participating reactions. It is known that aldehydes can form hemiacetal intermediates when they are treated with metallic alkoxide such as in Tishchenko reaction[15] or Cannizzaro reaction.[16] Previously, during our research on the reaction of organozinc reagents with sulfonyl chlorides,[17] we observed that when sulfonyl chloride was treated with phenylzinc phenoxide (PhZnOPh), the phenoxide anion transferred preferentially over the phenyl anion to the sulfonyl group. Data from Table 1 clearly show that the employment of a less bulky zinc alkoxide favors the ketone product which is exactly contrary to the common recognition that a bulky metal alkoxide

favors the Oppenauer oxidation. To verify whether the methoxyl anion participates in the reaction sequence, a series of control reactions were performed (Scheme 1). First, when MeZnOPh was introduced as the additive, phenyl ester **7** (23%) was generated according to GC–MS analysis, implying that phenoxide anion did attack aldehyde carbonyl to form a hemiacetal intermediate (Scheme 1a). However, ^{1}H NMR analysis showed that the addition of an equimolar amount of MeZnOMe and LiCl to a *p*-anisaldehyde solution in THF-d_8 did not influence the chemical shift of aldehyde hydrogen, indicating that a stable hemiacetal intermediate, derived from reaction of MeZnOMe/LiCl with aldehyde **2a**, was not formed. Furthermore, treatment of benzaldehyde dimethyl acetal with **3a** under optimal reaction conditions did not give benzophenone (Scheme 1b), thus precluding the possibility that ketones are formed through nucleophilic substitution of a hemiacetal hydride with organozinc methoxide.

To get further information on the reaction approach, aldehyde **2a** was treated with an equimolar amount of **3a**, which yielded, besides the desired secondary alcohol **5a** (47%), a roughly equal amount of ketone **4a** (22%) and *p*-anisyl alcohol (19%, GC–Ms analysis), indicating that ketone **4a** was formed via *in situ* Oppenauer oxidation of secondary alcohol **5a** with aldehyde **2a** (Scheme 1c). Interestingly, in the presence of two equivalents of benzophenone (an non-reductive ketone and an inert carbonyl to organozincate **3a**), equimolar reaction of **2a** and **3a** gave ketone **4a** (29%) and *p*-anisyl alcohol (69%)[12] products according to GC–MS analysis. Similar results were observed when two equivalents of Et_3N[18] or DMSO[19] were employed as the additive. Secondary alcohol **5a** was not detected in these cases (Scheme 1d). All these empirical results strongly supported that ketones were formed through a self-promoted nucleophilic addition/Oppenauer oxidation reaction of organometallics to aromatic aldehydes (Scheme 2). That is,



SCHEME 1 Control reactions



SCHEME 2 Proposed reaction mechanism

Grignard reagent RMgX (for clarity, LiCl was omitted) was transmetalated by MeZnOMe into a methoxyl organozincate (**I**) in which the nucleophilic R, with enhanced nuclephilicity compared with RZnX species, attacked the aromatic aldehydes to yield the alcohol **III** (procedure 1). In the presence of pivaldehyde, organozincate **I** coordinated simultaneously with pivaldehyde and aldehyde substrate ArCHO to form a complex (**IV**) in which the nucleophilic R moiety preferentially attacked aromatic aldehyde rather than the sterically hindered pivaldehyde. Concomitantly, hydride transfer from the *in situ* formed secondary alcoholate to pivaldehyde was induced and that produced the ketone product **V** (procedure 2). When a poor hydride acceptor or just a ligand (e.g. benzophenone, Et_3N or DMSO) was used, bimetallic complex **I** was fractured and complex **VI** was generated to induce a Meerwein–Ponndorf–Verley type hydride transfer from methoxide to ArCHO to produce benzylic alcohol **VII** as the main product. In these cases, ketone **V** could be generated via a minor complex (**VIII**) (procedure 4).

3 | CONCLUSIONS

In the presence of two equivalents of pivaldehyde, methylorganozinc methoxide RMgX ·MeZnOMe ·LiCl, formed *in situ* by transmetalation of Grignard reagents

RMgX ·LiCl with MeZnOMe, is able to convert aldehydes into ketones at ambient temperature in high yields. The key distinguishing feature of these reactions is that bimetallic alkoxyl organozincate intermediates were formed which coordinated simultaneously with aldehyde substrates and pivaldehyde, enabling the nucleophilic transfer of R to aldehyde substrates and Oppenauer-type transfer of hydride to pivaldehyde in 'one step'. This transformation allows quick access to structurally diverse aryl as well as heteroaryl, benzyl and alkyl ketones with broad substrate scope and excellent functional group tolerance.

4 | EXPERIMENTAL

4.1 | General Remarks

All the reactions were carried out under argon or nitrogen atmosphere. ^{1}H NMR and ^{13}C NMR spectra were recorded using a Varian-Mercury Plus (400 MHz) spectrometer or Bruker 600 MHz AVANCE II spectrometer using $CDCl_3$ as a solvent. Chemical shifts of ^{1}H NMR and ^{13}C NMR spectra were recorded in parts per million (ppm) with tetramethylsilane as an internal standard.

4.2 | General Procedure for Preparation of Organozinc Alkoxides

Under argon or nitrogen atmosphere, alcohol (2.0 mmol) in THF (4.0 ml) was added dropwise to 2.0 ml of dialkylzinc reagent in toluene (1.0 M) in 30 min at 0 °C and the reaction mixture was then stirred for another 30 min under the same conditions. Then Grignard reagent RMgBr ·LiCl (2.5 mmol) in THF (5 ml) was added carefully via a syringe and the reaction mixture was further stirred at this temperature for 10 min.

4.3 | General Procedure for Reaction of Organozinc Alkoxides with Aldehydes

To the organozinc alkoxide prepared as described in Section 4.2 was added a solution of substrate aldehyde (2.0 mmol) and pivaldehyde (0.34 g, 4.0 mmol, 0.43 ml) in THF (10 ml) in an ice–water bath. After the reaction mixture was stirred at room temperature for 2 h, the reaction mixture was quenched by aqueous NH_4Cl (10 ml). Ethyl acetate (10 ml) was then added and the organic phase was separated, washed with water (10 ml) and then with brine (10 ml). The water phase was extracted with ethyl acetate (2 × 10 ml). The organic phase was combined, dried (Na_2SO_4) and concentrated under reduced pressure. Ketones were obtained by column chromatography on silica gel using petroleum–ethyl acetate as an eluent.

ACKNOWLEDGMENTS

We are grateful for financial support from the National Natural Science Foundation of China (nos. 21762040, 21762039 and 21262030).

ORCID

Ying Fu http://orcid.org/0000-0002-7312-1570
Zhengyin Du http://orcid.org/0000-0002-7124-8754

REFERENCES

[1] a) L. Lochmann, M. Janata, *Cent. Eur. J. Chem.* **2014**, *12*, 537; b) D. Tilly, F. Chevallier, F. Mongin, P. C. Gros, *Chem. Rev.* **2014**, *114*, 1207; c) F. Mongin, A. Harrison-Marchand, *Chem. Rev.* **2013**, *113*, 7563; d) Y. Fu, X. Zhao, H. Hugel, B. Hou, D. Huang, Z. Du, *Curr. Org. Chem.* **2015**, *19*, 2324.

[2] a) C. G. Screttas, M. Micha-Screttas, *J. Organomet. Chem.* **1985**, *290*, 1; b) B. R. Steele, M. Micha-Screttas, C. G. Screttas, *Appl. Organomet. Chem.* **2002**, *16*, 501.

[3] a) C. G. Screttas, B. R. Steele, *J. Organomet. Chem.* **1989**, *54*, 1013; b) I. D. Kostas, C. G. Screttas, *J. Organomet. Chem.* **1997**, *62*, 5575.

[4] A. Boudin, G. Cerveau, C. Chuit, R. J. P. Corriu, C. Reye, *Tetrahedron* **1989**, *45*, 171.

[5] L. Pu, H.-B. Yu, *Chem. Rev.* **2001**, *101*, 757.

[6] a) S. Bernhardt, G. Manolikakes, T. Kunz, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50*, 9205. *Angew. Chem.* **2011**, *123*, 9372; b) C. I. Stathakis, S. Bernhardt, V. Quint, P. Knochel, *Angew. Chem. Int. Ed.* **2012**, *51*, 9428. *Angew. Chem.* **2011**, *123*, 9372; c) S. M. Manolikakes, M. Ellwart, C. I. Stathakis, P. Knochel, *Chem. Eur. J.* **2014**, *20*, 12289; d) C. I. Stathakis, S. M. Manolikakes, P. Knochel, *Org. Lett.* **2013**, *15*, 1302; e) A. Hernán-Gómez, E. Herd, E. Hevia, A. R. Kennedy, P. Knochel, K. Koszinowski, S. M. Manolikakes, R. E. Mulvey, C. Schnegelsberg, *Angew. Chem. Int. Ed.* **2014**, *53*, 2706. *Angew. Chem.* **2014**, *126*, 2744; f) M. Ellwart, P. Knochel P, *Angew. Chem. Int. Ed.* **2015**, *54*, 10662. *Angew. Chem.* **2015**, *127*, 10808; g) T. J. Greshock, K. P. Moore, R. T. McClain, A. Bellomo, C. K. Chung, S. D. Dreher, P. S. Kutchukian, Z. Peng, I. W. Davies, P. Vachal, M. Ellwart, S. M. Manolikakes, P. Knochel, P. G. Nantermet, *Angew. Chem. Int. Ed.* **2016**, *55*, 13714. *Angew. Chem.* 2016, *128*, 13918; h) Y.-H. Chen, M. Ellwart, V. Malakhov, P. Knochel, *Synthesis* **2017**, *49*, 3215.

[7] a) B. Byrne, M. Karras, *Tetrahedron Lett.* **1987**, *28*, 769; b) B. K. Wilk, J. L. Helom, C. W. Coughlin, *Org. Process. Res. Dev.* **1998**, *2*, 407; c) M. Schroeter, *Synth. Commun.* **2005**, *35*, 2203; d) J. L. Namy, J. Souppe, J. Collin, H. B. Kagan, *J. Organomet. Chem.* **1984**, *49*, 2045; e) V. Schulze, P. G. Nell, A. Burton, R. W. Hoffmann, *J. Organomet. Chem.* **2003**, *68*, 4546; f) R. J. Kloetzing, A. Krasovskiy, P. Knochel, *Chem. Eur. J.* **2007**, *13*, 215; g) A. S. Levashov, N. A. Aksenov, I. V. Aksenova, V. V. Konshin, *New J. Chem.* **2017**, *41*, 8297; h) J. Yuan, J. Wang, G. Zhang, C. Liu, X. Qi, Y. Lan, J. T. Miller, A. J. Kropf, E. E. Bunel, A. Lei, *Chem. Commun.* **2015**, *51*, 576; i) L.-J. Gu, C. Jin, H.-T. Zhang, *Chem. Eur. J.* **2015**, *21*, 8741; j) X. Liu, L. Yu, M. Luo,

J. Zhu, W. Wei, *Chem. Eur. J.* **2015**, *21*, 8745; k) C. Zhao, J. Yan, Z. Xi, *J. Organomet. Chem.* **2003**, *68*, 4355; l) F. S. Melkonyan, D. E. Kuznetsov, M. A. Yurovskaya, A. V. Karchava, *RSC Adv.* **2013**, *3*, 8388; m) C. Jin, L. Gu, M. Yuan, *Catal. Sci. Technol.* **2015**, *5*, 4341; n) S. Tang, L. Zeng, Y. Liu, A. Lei, *Angew. Chem. Int. Ed.* **2015**, *54*, 15850; o) X. Yue, X. Qi, R. Bai, A. Lei, Y. Lan, *Chem. Eur. J.* **2017**, *23*, 6419; p) J.-J. Wu, Y. Li, H.-Y. Zhou, A.-H. Wen, C.-C. Lun, S.-Y. Yao, Z. Ke, B.-H. Ye, *ACS Catal.* **2016**, *6*, 1263.

[8] a) Y. Fu, X. L. Zhao, H. Hügel, H. Huang, Z. Du, K. Wang, Y. Hu, *Org. Biomol. Chem.* **2016**, *14*, 9720; b) Y. Fu, Y. Yang, H. M. Hügel, Z. Du, K. Wang, D. Huang, Y. Hu, *Org. Biomol. Chem.* **2013**, *11*, 4429.

[9] T. Ooi, H. Otshuka, T. Miura, H. Ichikawa, K. Maruoka, *Org. Lett.* **2002**, *4*, 2669.

[10] a) H. Adkins, R. M. Elofson, A. G. Rossow, C. C. Robinson, *J. Am. Chem. Soc.* **1949**, *71*, 3622; b) R. H. Baker, C. C. Robinson, *J. Am. Chem. Soc.* **1940**, *62*, 3305.

[11] a) J. F. Eastham, R. Teranishi, *Org. Synth.* **1955**, *35*, 39; b) K. Ishihara, H. Yamamoto, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley, New York **2001**.

[12] *p*-Anisyl alcohol was formed probably partly due to the high reductivity of organozincates and partially due to magnesium salt- or lithium salt-induced Cannizzaro reaction between p-anisaldehyde and pivaldehyde. a) M. S. Abaee, R. Sharifi, M. M. Mojtahedi, *Org. Lett.* **2005**, *7*, 5893; b) L. Zhang, S. Wang, S. Zhou, G. Yang, E. Sheng, *J. Organomet. Chem.* **2006**, *71*, 3149; c) M. M. Mojtahedi, E. Akbarzadeh, R. Sharifi, M. S. Abaee, *Org. Lett.* **2007**, *9*, 2791.

[13] a) K. J. Ralston, A. N. Hulme, *Synthesis* **2012**, *44*, 2310; b) S. P. Curran, S. J. Connon, *Org. Lett.* **2012**, *14*, 1074; c) M. M. Mojtahedi, E. Akbarzadeh, R. Sharifi, M. S. Abaee, *Org. Lett.* **2007**, *9*, 2791; d) S. P. Curran, S. J. Connon, *Angew. Chem. Int. Ed.* **2012**, *51*, 10866 *Angew. Chem.* 2012, 124, 11024.

[14] a) M. Uchiyama, S. Nakamura, T. Ohwada, M. Nakamura, E. Nakamura, *J. Am. Chem. Soc.* **2004**, *126*, 10897; b) J. E. Fleckenstein, K. Koszinowski, *Organometallics* **2011**, *30*, 5018; c) C. A. Musser, H. G. Richey, *J. Organomet. Chem.* **2000**, *65*, 7750; d) M. Hatano, S. Suzuki, K. Ishihara, *J. Am. Chem. Soc.* **2006**, *128*, 9998.

[15] For Grignard reagent- and magnesium aryloxide-promoted Tishchenko reactions, see: a) L. Cronin, F. Manoni, C. J. O'Connor, S. J. Connon, *Angew. Chem. Int. Ed.* **2010**, *49*, 3045; b) B. M. Day, W. Knowelden, M. P. Coles, *Dalton Trans.* **2012**, *41*, 10930.

[16] M. B. Smith, J. March, *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 6th ed., Wiley-Interscience, New York **2007**.

[17] Y. Fu, W. Zhu, X. Zhao, H. Hügel, Z. Wu, Y. Su, Z. Du, D. Huang, Y. Hu, *Org. Biomol. Chem.* **2014**, *12*, 4295.

[18] Et^3N was employed as an efficient ligand in Cannizzaro, Tishchenko and Meerwein–Ponndorf–Verley reactions.[12c]

[19] DMSO is an oxidant used in Swern oxidation; see: K. Omura, A. K. Sharma, D. Swern, *J. Organomet. Chem.* **1976**, *41*, 957.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Fu Y, Ma X-Z, Shi C-Z, Shen T, Du Z. MeZnOMe-mediated reaction of aldehydes with Grignard reagents: A glance into nucleophilic addition/Oppenauer oxidation pathway. *Appl Organometal Chem*. 2018;e4462. https://doi.org/10.1002/aoc.4462