Available online at www.sciencedirect.com

SCIENCE DIRECT®

Tetrahedron Letters 45 (2004) 3313–3315

Tetrahedron Letters

Tishchenko reactions and Oppenauer oxidation reactions of aldehydes promoted by diisobutylaluminum hydride

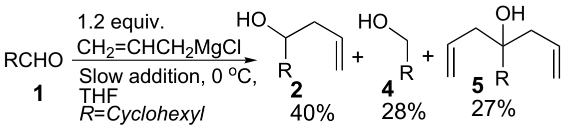
Yung-Son Hon,[a,b,*] Chun-Ping Chang[a] and Ying-Chieh Wong[a]

[a]*Department of Chemistry and Biochemistry, National Chung Cheng University, Chia-Yi 621, Taiwan, ROC*
[b]*Institute of Chemistry, Academia Sinica, Nankang, Taipei 115, Taiwan, ROC*

Received 14 October 2003; revised 9 February 2004; accepted 12 February 2004

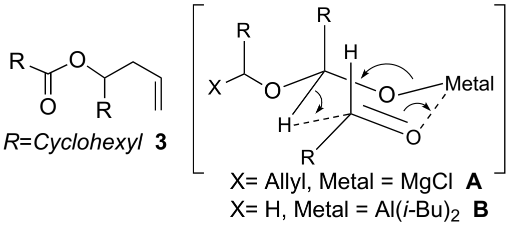
Abstract—The aliphatic aldehydes react with catalytic amount of Dibal-H in *n*-pentane to give the corresponding Tishchenko products in good to excellent yields. Contrary, α-silyloxyaldehydes give α-silyloxyketones via Oppenauer oxidation under similar condition.

The Tishchenko reaction involves the aldehydes dimerization giving the corresponding esters under the influence of aluminum alkoxides.[1] The reaction has been carried out with a number of other catalysts[2] such as alkali metal,[3] alkali earth metal oxide,[4] boric acid,[5] alumina supported KF,[6] Cp_2MH_2 (M=Zr, Hf),[7] EtLnI (Ln=Pr, Nd, Sm),[8] SmI_2,[9] $LiWO_2$,[10] $Fe(CO)_4$,[11] $RuH_2(PPh_3)_4$,[12] $RhH(CO)(PPh_3)_3$,[13] *trans*-ROIr(CO)-$(PPh_3)_2$,[14] nickel complex,[15] and Cu(I).[16] Diisobutylaluminum hydride (Dibal-H) is a useful reducing agent to reduce an aldehyde to the corresponding alcohol. To the best of our knowledge, there is no report on using Dibal-H as catalyst to promote the Tishchenko or Oppenauer reaction of aldehydes. In this report, we will describe our results on such transformations.



(1)

When aldehyde **1** was treated with allylmagnesium chloride in THF by a syringe pump over a period of 1 h at 0 °C, we isolated not only the desired product **2** (40%), but also primary alcohol **4** (28%) and tertiary alcohol **5** (27%) (Eq. 1). Presumably, the alcohol **5** is formed from the reaction of the Grignard reagent with the ester **3**, which is generated from the Tishchenko reaction via an intermediate **A**. Intrigued by this hypothesis, we were curious to know whether the aluminum analogue **B** is applicable to ester formation.



In order to avoid the solvation effect of the etheric solvent with the aluminum reagent, slow addition of Dibal-H to a solution of aldehyde **6a** in anhydrous *n*-pentane was first tried. The typical procedure is described as follows. To a solution of aldehyde **6a** (4.92 mmol) in *n*-pentane (8 mL), a solution of Dibal-H (0.49 mL, 1.0 M solution in hexane) in 1 mL of *n*-pentane was added dropwise by a syringe pump over a period of 1 h at 0 °C. After stirring at ambient temperature for 5 h, ester **7a** was isolated in 77% yield (Table 1, entry 1). The proposed mechanism of this reaction is shown in Figure 1. The reaction of Dibal-H with aldehyde **6a** gives aluminum alkoxide **i**, which undergo nucleophilic addition to aldehyde **6a** to give the corresponding aluminum alkoxide **ii**. The six-membered ring transition state **B′**, which is formed from the reaction of intermediate **ii** with aldehyde **6a**, undergoes Tishchenko reaction to give not only the corresponding ester, but also aluminum

---

Keywords: Tishchenko reaction; Oppenauer oxidation; α-silyloxyaldehyde; α-silyloxyketone.

* Corresponding author. Tel.: +886-5-2720411x6262; fax: +886-5-27-21040; e-mail: cheysh@ccu.edu.tw

doi:10.1016/j.tetlet.2004.02.145

Table 1. Tishchenko reaction and Oppenauer oxidation of aldehydes promoted by Dibal-H

Entry	Aldehyde	Time (h)	Product	Yield (%)
1	$PhCH_2CH_2CHO$ (**6a**)	5	**7a**	77
2	Cyclohexyl-CHO (**1**)	5	**7b**	93
3	*tert*-Butyl-CHO (**6c**)	5	**7c**	95
4	(*R*)-(+)-Citronellal (**6d**)	5	**7d**	77
5	$H_2C{=}CH(CH_2)_8CHO$ (**6e**)	5	**7e**	97
6	$MeO_2C(CH_2)_6CHO$ (**6f**)	12	**7f**	61
7	$(MeO)_2CH(CH_2)_6CHO$ (**6g**)	12	**7g**	50
8	(*R*)-(−)-Glyceraldehyde acetonide (**6h**)	10	**7h**	60
9	$BnOCH_2CHO$ (**6i**)	8	**7i**	52
10	$TrOCH_2CHO$ (**6j**)	6	**7j**	83
11	$Ph(CH_2)_3CH(OTBS)$-CHO (**6k**)	12	**8k**	78
12	$C_6H_9CH(OTBS)CHO$ (**6l**)	7	**8l**	45
13	*t*-BuCH(OTBS)CHO (**6m**)	12	**8m**	0
14	$Ph(CH_2)_2CH(OTBS)$-CH_2CHO (**6n**)	12	**7n** **8n**	52 29

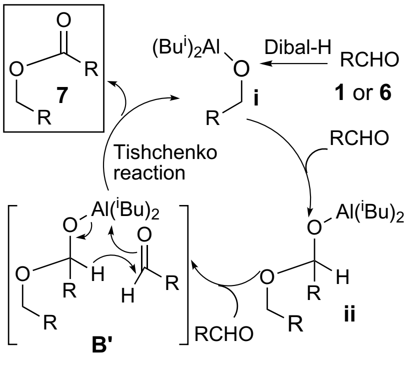


Figure 1. The possible reaction mechanism of aldehydes with Dibal-H via Tishchenko reaction.

alkoxide **i**, which can undergo the second cycle of the Tishchenko reaction. It is worthy to mention that the alkoxy group of intermediate **i** is the only transferable group in the reaction. Therefore, the present reaction mechanism is different from the Tishchenko reaction catalyzed by aluminum trialkoxides.[1]

This reaction conditions have been applied to aldehydes with secondary, tertiary, or quarternary α-carbon in excellent yields (Eq. 2, Table 1, entries 1–3). The aldehydes with isolated alkene moieties **6d** and **6e** gave the corresponding esters in excellent yields (entries 4 and 5). Unfortunately, the α,β-unsaturated aldehydes and aryl aldehydes did not give the desired products and we recovered most of the starting materials. The aldehydes tethered with either methoxycarbonyl **6f**, dimethyl acetal **6g** and acetonide **6h** also underwent Tishchenko reactions in good yields (entries 6–8). The Tishchenko product **7h** is optically pure,[17] indicating that no epimerization occurs during the reaction. Furthermore, α-alkoxyaldehydes **6i** and **6j** underwent Tishchenko reaction in good yields. The bulky trityl group does not

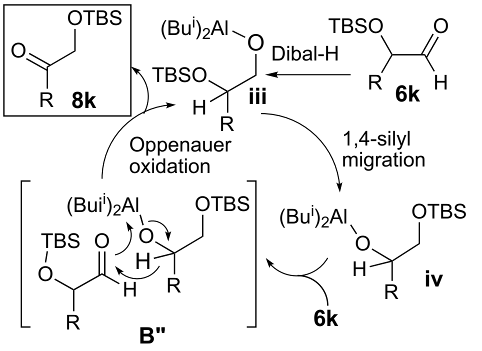
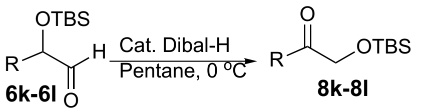


Figure 2. The possible reaction mechanism of α-silyloxyaldehydes with Dibal-H via Oppenauer oxidation (R=$PhCH_2)_3$–).

retard the reaction at all (entries 9 and 10). Interestingly, α-silyloxyaldehyde **6k** reacted with Dibal-H afforded α-silyloxyketone **8k** instead of the corresponding Tishchenko product (Eq. 3, entry 11). The proposed mechanism of this reaction is shown in Figure 2. The reaction of Dibal-H with aldehyde **6k** gives the aluminum alkoxide **iii**, which undergoes 1,4-silyl group migration to give the corresponding aluminum alkoxide **iv**. The six-membered ring transition state **B″**, which is formed from the reaction of intermediate **iv** with aldehyde **6k**, undergoes Oppenauer oxidation[18] to give not only the corresponding α-silyloxyketone **8k**, but also aluminum alkoxide **iii**, which can undergo the second cycle of the reaction. The failure of secondary aluminum alkoxide **iv** to proceed the Tishchenko pathway may be due to the steric reason. α-Silyloxyaldehydes **6l** also gave the Oppenauer oxidation product **8l** in good yields (entry 12). These results indicate that the migration of the silyl group from secondary alkoxysilyl ether **iii** to the primary alkoxysilyl ether **iv** is a favorable process. However, there is no reaction for α-silyloxyaldehyde **6m** probably due to the steric effect (entry 13). Interestingly, Dibal-H reacts with β-silyloxyaldehyde **6n** to give both Tishchenko product **7n** (52%) and Oppenauer oxidation product **8n** (29%) (entry 14). The formation of product **8n** results from the 1,5-silyl group migration, which is not a facile process, and hence the Tishchenko pathway becomes a predominant one.

$$\underset{\mathbf{6}}{RCHO} \xrightarrow[\text{Pentane, 0 °C}]{\text{Cat. Dibal-H}} \underset{\mathbf{7}}{RCO_2CH_2R} \qquad (2)$$



6k-6l **8k-8l** (3)

In conclusion, the slow addition of the catalytic amount of Dibal-H to the aldehydes in *n*-pentane gives the corresponding Tishchenko products in good yields. The reactions work quite well for aldehydes bearing 2°-, 3°-, and 4°-α-carbon. However, α-silyloxyaldehyde affords the Oppenauer oxidation product in good yield under similar condition.

Acknowledgements

We are grateful to the National Science Council, National Chung Cheng University and Academia Sinica for the financial support.

References and notes

1. (a) Villani, F. J.; Nord, F. F. *J. Am. Chem. Soc.* **1947**, *69*, 2605–2607, and references cited therein; (b) Ogata, Y.; Kawasaki, A.; Kishi, I. *Tetrahedron* **1967**, *23*, 825–830; (c) Lin, I.; Day, A. R. *J. Am. Chem. Soc.* **1952**, *74*, 5133–5135; (d) Saegusa, T.; Ueshima, T. *J. Org. Chem.* **1968**, *33*, 3310–3311; (e) Baidossi, W.; Rosenfeld, A.; Wassermann, B. C.; Schutte, S.; Schumann, H.; Blum, J. *Synthesis* **1996**, 1127–1130; (f) Ooi, T.; Miura, T.; Takaya, K.; Marouka, K. *Tetrahedron Lett.* **1999**, *40*, 7695–7698; (g) Ooi, T.; Ohmatsu, K.; Sasaki, K.; Miura, T.; Marouka, K. *Tetrahedron Lett.* **2003**, *44*, 3191–3193; (h) Shirakawa, S.; Takai, J.; Sasaki, K.; Miura, T.; Maruoka, K. *Hetreocycles* **2003**, *59*, 57–61.
2. For a review, see: Chang, C. P.; Hon, Y. S. *Chemistry (The Chinese Chem. Soc., Taipei)* **2002**, *60*, 561–572.
3. (a) Bunce, R. A.; Shellhammer, A., Jr. *J. Org. Prep. Proc. Int.* **1987**, *19*, 161–166; (b) Törmäkangas, O. P.; Koskinen, A. M. P. *Tetrahedron Lett.* **2001**, *42*, 2743–2746.
4. (a) Tanabe, K.; Saito, K. *J. Catal.* **1974**, *35*, 247–253; (b) Tsuji, H.; Yagi, F.; Hattori, H.; Kita, H. *J. Catal.* **1994**, *148*, 759–770; (c) Seki, T.; Akutu, K.; Hattori, H. *Chem. Commun.* **2001**, 1000–1001; (d) Törmäkangas, O. P.; Saarenketo, P.; Koskinen, A. M. P. *Org. Process Res. Dev.* **2002**, *6*, 125–131.
5. (a) Stapp, P. R. *J. Org. Chem.* **1973**, *38*, 1433–1434; (b) Jedlinski, Z.; Kowalczuk, M. *J. Org. Chem.* **1979**, *44*, 222–224.
6. Kabashima, H.; Tsuji, H.; Nakata, S.; Tanaka, Y.; Hattori, H. *Appl. Catal. A: Gen.* **2000**, *194/195*, 227–240.
7. (a) Morita, K. I.; Nishiyama, Y.; Ishii, Y. *Organometallics* **1993**, *12*, 3748–3752; (b) Umekawa, Y.; Sakaguchi, S.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.* **1997**, *62*, 3409–3412.
8. (a) Yokoo, K.; Mine, N.; Taniguchi, H.; Fujiwara, Y. *J. Organomet. Chem.* **1985**, *279*, C19–C21; (b) Onozawa, S. Y.; Sakakura, T.; Tanaka, M.; Shiro, M. *Tetrahedron* **1996**, *52*, 4291–4302; (c) Berberich, H.; Roesky, P. W. *Angew. Chem., Int. Ed.* **1998**, *37*, 1569–1571; (d) Gillespie, K. M.; Munslow, I. J.; Scott, P. *Tetrahedron Lett.* **1999**, *40*, 9371–9374.
9. (a) Evans, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1990**, *112*, 6447–6449; (b) Curran, D. P.; Wolin, R. L. *Synlett* **1991**, 317–318; (c) Takeno, M.; Kikuchi, S.; Morita, K.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.* **1995**, *60*, 4974–4975; (d) Uenishi, J.-I.; Masuda, S.; Wakabayashi, S. *Tetrahedron Lett.* **1991**, *32*, 5097–5100; (e) Hsu, J.-L.; Fang, J.-M. *J. Org. Chem.* **2001**, *66*, 8573–8584; (f) Smith, A. B., III; Lee, D.; Adams, C. M.; Kozlowski, M. C. *Org. Lett.* **2002**, *4*, 4539–4541.
10. Villacorta, G. M.; Filippo, J. S., Jr. *J. Org. Chem.* **1983**, *48*, 1151–1154.
11. (a) Yamashita, M.; Watanabe, Y.; Mitsudo, T. A.; Takegami, Y. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 3597–3600; (b) Bankston, D. *J. Org. Chem.* **1989**, *54*, 2003–2005.
12. (a) Morino, H.; Ito, T.; Yamamoto, A. *Chem. Lett.* **1978**, 17–20; (b) Ito, T.; Horino, H.; Koshino, Y.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 504–512; (c) Grushin, V. V.; Alper, H. *J. Org. Chem.* **1991**, *56*, 5159–5161.
13. (a) Grigg, R.; Mitchell, T. R. B.; Suthivaiyakit, S. *Tetrahedron* **1981**, *37*, 4313–4319; (b) Maussoui, M.; Beaupere, D.; Nadjo, L.; Uzan, R. *J. Organomet. Chem.* **1983**, *259*, 345–353; (c) Bergens, S. H.; Fairlie, D. P.; Bosnich, B. *Organometallics* **1990**, *9*, 566–571.
14. Bernard, K. A.; Atwood, J. D. *Organometallics* **1988**, *7*, 235–236.
15. Burkhardt, E. R.; Bergman, R. G.; Heathcock, C. H. *Organometallics* **1990**, *9*, 30–44.
16. Tsuda, T.; Habu, H.; Saegusa, T. *Chem. Commun.* **1974**, 620–620.
17. Ermolenko, L.; Sasaki, N. A.; Potier, P. *Synlett* **2001**, 1565–1566.
18. Djerrassi, C. *Org. React.* **1951**, *6*, 207–272.