



Pergamon

Tetrahedron Letters 40 (1999) 7879–7881

TETRAHEDRON
LETTERS

A convenient synthesis of functionalized vinyloxydes

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Received 6 July 1999; revised 24 August 1999; accepted 25 August 1999

Abstract

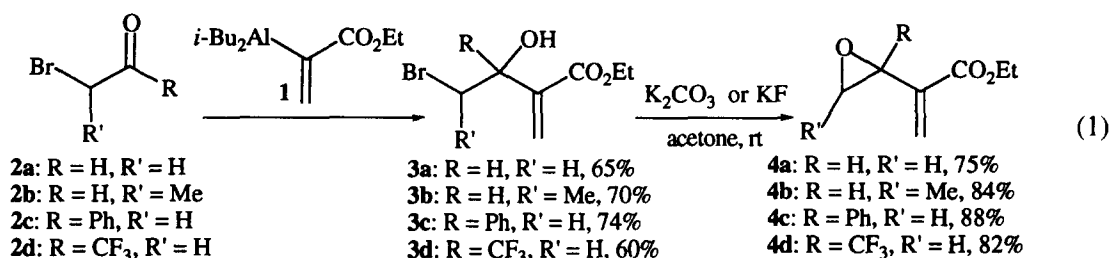
Functionalized vinyloxydes were synthesized, in high yields, from α -bromoaldehydes and -ketones via vinylalumination, followed by cyclization with K_2CO_3 or KF under non-aqueous conditions. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: vinylalumination; cyclization; vinyloxydes; borane.

A decade ago, Tsuda and co-workers reported the conjugate reduction of α -acetylenic ketones and esters by DIBAL-H-HMPA complex.¹ They also observed that the [α -(ethoxycarbonyl)vinyl]aluminum intermediate (**1**) can be trapped with allyl bromides.¹ Later they extended the scope of **1** by carrying out the nucleophilic addition of the vinyl moiety to aldehydes and ketones, the latter in the presence of Lewis acids, providing an easy access to functionalized allyl alcohols.² We recently showed that the vinylalumination of activated ketones, such as fluoroketones, α -keto esters, α -acyl cyanides, and α -acetylenic ketones does not require Lewis acid catalysis.³ The importance of vinyloxydes⁴ in organic syntheses prompted us to examine the preparation of the vinyl halohydrin precursors from α -haloaldehydes and -ketones. Our study of the vinylalumination of α -bromocarbonyls has shown that addition to the carbonyl proceeds without Lewis acid catalysis. The successful preparation of a series of functionalized vinyloxydes and their reactions are reported herein.

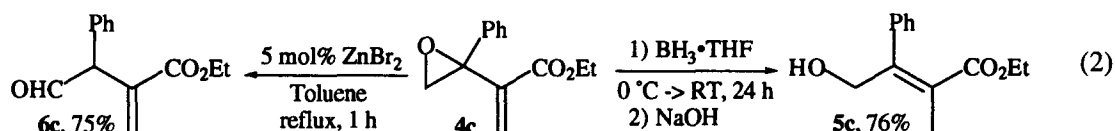
Vinylalumination of bromoacetaldehyde **2a** was complete in 15 h at room temperature (rt). Dilute HCl workup provided 65% yield of the product bromohydrin **3a** (Eq. 1). A similar result was obtained with a branched bromoaldehyde, 2-bromopropionaldehyde **2b** and the product **3b** was isolated in 70% yield.⁵ The reaction was then extended to representative bromo ketones. Phenacyl bromide **2c** and 1-bromo-3,3,3-trifluoro-2-propanone **2d** provided the corresponding bromohydrins **3c** and **3d** in 74% and 60% yields, respectively.

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We avoided aqueous alkaline conditions for the epoxidation of these bromohydrins due to the presence of the ester moiety. We conducted the cyclizations in dry acetone and obtained 75–88% yields of the vinyl epoxides. The epoxidation of **3a–c** was successfully carried out with K₂CO₃ as base (Eq. 1). However, the trifluoromethyl bromohydrin **3d** afforded only 65% yield of the corresponding epoxide **4d**, and we improved the yield to 82% by replacing K₂CO₃ with KF.⁶

Having achieved the synthesis of the vinyl epoxides, we carried out two representative reactions characteristic of these oxiranes. Zaidlewicz and co-workers has reported a stereoselective synthesis of allylic alcohols via the reduction of vinyl epoxides.⁷ We examined such a reduction with **4c**. We were interested in observing whether the reducible ester moiety is compatible under the reaction conditions. Indeed, treatment of **4c** with borane–THF opened the epoxide with stereoselective migration of the double bond without affecting the ester. The *E*-hydroxy ester **5c** was isolated in 76% yield (Eq. 2). We then attempted a Lewis-acid catalyzed isomerization of **4c** with 5 mol% ZnBr₂ and obtained the olefinic aldehyde ester **6c** in 75% yield (Eq. 2).



In conclusion, a convenient synthesis of functionalized vinyl epoxides via the vinylalumination of α -bromocarbonyls has been developed.⁸ The epoxides undergo typical reactions without affecting the functional group attached. Further transformations of these vinyl epoxides are in progress.

Acknowledgements

Financial assistance from the Purdue Borane Research Fund is gratefully acknowledged. Helpful discussions with Dr. M. Venkat Ram Reddy are also acknowledged.

References

1. Tsuda, T.; Yoshida, T.; Kawamoto, T.; Saegusa, T. *J. Org. Chem.* **1987**, *52*, 1624.
2. Tsuda, T.; Yoshida, T.; Saegusa, T. *J. Org. Chem.* **1988**, *53*, 1037.
3. (a) Ramachandran, P. V.; Reddy, M. V. R.; Rudd, M. T.; de Alaniz, J. R. *Tetrahedron Lett.* **1998**, *39*, 8791. (b) Ramachandran, P. V.; Reddy, M. V. R.; Rudd, M. T. *Tetrahedron Lett.* **1999**, *40*, 627.
4. Lindstroem, U. M.; Francko, R.; Pinault, N.; Somfai, P. *Tetrahedron Lett.* **1997**, *38*, 2027.
5. Surprisingly, the crude ¹H NMR of the bromohydrin **3b** and the epoxide **4b** suggest the presence of only the *anti*-isomer. This is being studied carefully.
6. Lundt, I.; Pedersen, C. *Synthesis* **1992**, 669.
7. Zaidlewicz, M.; Uzarewicz, A.; Sarnowski, R. *Synthesis* **1979**, 62.

8. The experimental procedure for the synthesis of **4c** is as follows: To a stirred solution of HMPA (3.88 g, 20 mmol) in anhydrous THF (55 mL), 15 mL of 1M DIBAL-H (15 mmol) in hexanes was added at 0°C and stirred for 0.5 h. Ethyl propiolate (0.98 g, 1.01 mL, 10 mmol) was added and the mixture was stirred at 0°C for 1 h, followed by the addition of **2c** (3.98 g, 20 mmol). The mixture was warmed to rt and stirred for 15 h, quenched with 50 mL of 0.5 M HCl at 0°C, and extracted with Et₂O (3×50 mL). The combined ether layers were washed with NaHCO₃ and dried over MgSO₄. Removal of the solvents and purification by column chromatography over silica gel (hexane:ethyl acetate: 95:5) provided 2.21 g (7.4 mmol, 74%) of **3c** as a thick liquid. ¹H NMR (300 MHz) δ (CDCl₃) (ppm): 1.23 (t, *J*=7.14 Hz, 3H, CH₃), 3.88 (d, *J*=10.9 Hz, 1H, CH₂Br), 4.04 (d, 10.9 Hz, 1H, CH₂Br), 4.15 (qd, *J*=7.14 Hz, 2.8 Hz, 2H, CH₂CH₃), 4.47 (s, 1H, OH), 6.09 (s, 1H, =CH), 6.53 (s, 1H, =CH), 7.32 (m, 3H, Ph), 7.48 (m, 2H, Ph). ¹³C NMR (75 MHz) δ (CDCl₃) (ppm): 13.99, 40.71, 61.40, 76.56, 125.83, 127.28, 128.08, 128.41, 128.71, 133.40, 141.19 (C=C), 142.00 (C=C), 166.68 (C=O). 13.8 g (100 mmol) of K₂CO₃ was added to 3.0 g (10 mmol) of **3c** dissolved in acetone (40 mL) and stirred vigorously for 6 h. The mixture was filtered, concentrated, and purified by column chromatography over silica to provide 1.92 g (88%) of **4c**. ¹H NMR (300 MHz) δ (CDCl₃) (ppm): 1.18 (t, *J*=7.1 Hz, 3H, CH₃), 3.14 (d, *J*=5.4 Hz, 1H, CH₂), 3.18 (d, *J*=5.5 Hz, 1H, CH₂), 4.15 (q, *J*=7.1 Hz, 2H, CH₂CH₃), 6.07 (s, 1H, =CH), 6.48 (s, 1H, =CH), 7.2–7.38 (m, 5H, Ph). ¹³C NMR (75 MHz) δ (CDCl₃) (ppm): 14.01, 55.81, 59.90, 60.97, 126.43, 128.01, 128.29, 128.71, 138.44 (C=C), 140.04 (C=C), 165.25 (C=O).