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A convenient synthesis of functionalized vinylepoxides

P. Veeraraghavan Ramachandran * and Marek P. Krzeminski

Herbert C. Brown Laboratories of Chemistry, Purdue University, West Lafayette, Indiana 47907-1393, USA

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Abstract

Functionalized vinylepoxides 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.

Keywords: vinylalumination; cyclization; vinylepoxides; 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 vinylepoxides[4] 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 vinylepoxides 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.

* Corresponding author.

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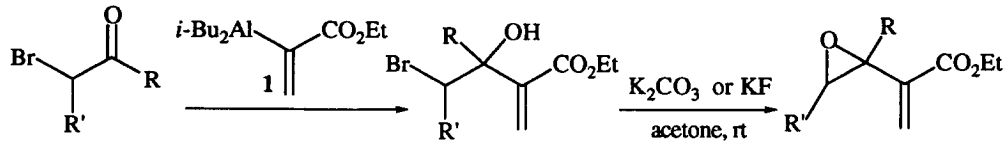


2a: R = H, R' = H
2b: R = H, R' = Me
2c: R = Ph, R' = H
2d: R = CF_3, R' = H

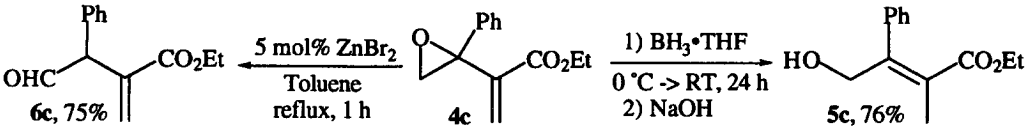
3a: R = H, R' = H, 65%
3b: R = H, R' = Me, 70%
3c: R = Ph, R' = H, 74%
3d: R = CF_3, R' = H, 60%

4a: R = H, R' = H, 75%
4b: R = H, R' = Me, 84%
4c: R = Ph, R' = H, 88%
4d: R = CF_3, R' = H, 82%

(1)

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 vinylepoxides. The epoxidation of **3a–c** was successfully carried out with K_2CO_3 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 K_2CO_3 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% $ZnBr_2$ and obtained the olefinic aldehyde ester **6c** in 75% yield (Eq. 2).



(2)

In conclusion, a convenient synthesis of functionalized vinylepoxides 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 vinylepoxides are in progress.

Acknowledgements

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References

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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.
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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 1*M* 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 Et_2O (3×50 mL). The combined ether layers were washed with $NaHCO_3$ and dried over $MgSO_4$. 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. ^{1}H NMR (300 MHz) δ ($CDCl_3$) (ppm): 1.23 (t, *J*=7.14 Hz, 3H, $\mathbf{CH_3}$), 3.88 (d, *J*=10.9 Hz, 1H, $\mathbf{CH_2}$Br), 4.04 (d, 10.9 Hz, 1H, $\mathbf{CH_2}$Br), 4.15 (qd, *J*=7.14 Hz, 2.8 Hz, 2H, $\mathbf{CH_2}CH_3$), 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). ^{13}C NMR (75 MHz) δ ($CDCl_3$) (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 K_2CO_3 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**. ^{1}H NMR (300 MHz) δ ($CDCl_3$) (ppm): 1.18 (t, *J*=7.1 Hz, 3H, $\mathbf{CH_3}$), 3.14 (d, *J*=5.4 Hz, 1H, $\mathbf{CH_2}$), 3.18 (d, *J*=5.5 Hz, 1H, $\mathbf{CH_2}$), 4.15 (q, *J*=7.1 Hz, 2H, $\mathbf{CH_2}CH_3$), 6.07 (s, 1H, =**CH**), 6.48 (s, 1H, =**CH**), 7.2–7.38 (m, 5H, Ph). ^{13}C NMR (75 MHz) δ ($CDCl_3$) (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).