Pergamon

Tetrahedron Letters, Vol. 36, No. 4, pp. 607-608, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(94)02314-X

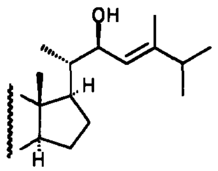
A New Route to Allylic Alcohols: Application to the Construction of Brassinolide Side Chain

Vladimir A. Khripach, Vladimir N. Zhabinskii, Elena V. Zhernosek

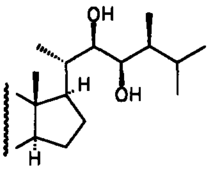
Institute of Bioorganic Chemistry, Byelorussian Academy of Sciences, 220141 Minsk,
Zhodinskaya, 5/2

Abstract: *A new method for the preparation of allylic alcohols is described. It involves the formation of unsaturated sulfons and their reduction with lithium.*

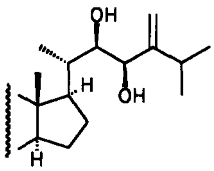
Since the isolation of brassinolide in 1979 a large amount of its syntheses has been described[1]. Those of them are of special interest which include the formation of allilyc alcohols **1**[2] as key intermediates.



1

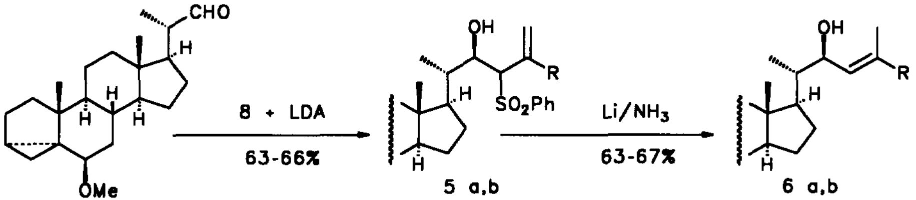


2



3

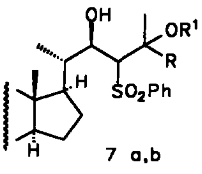
They are convenient synthetic precursors both for brassinolide type side chain containing structures **2** and for other steroids of this series (like **3**, for example). However known methods for preparation of **1** are either multistep[2b-e] or give low yields of the desired product[2a].



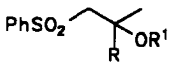
4

5 a,b

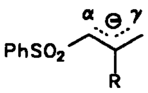
6 a,b



7 a,b



8 a,b



9 a,b

a: R=Me, R^1=Ac
b: R=^{i}Pr, R^1=Bz

Here we report a simple two step approach for the transformation of aldehyde **4** to the allylic alcohols **1**. At the first stage the aldehyde **4**, available from stigmasterol[3], was reacted with anions generated from LDA and β-acyl oxy sulfones **8**. The reaction of sulfones and carbonyl compounds is known to lead to βhydroxy sulfones[4]. In the case of β-acyl oxy sulfones **8** we expected the formation of compounds 7. But instead of them products **5a** and **5b** were isolated from the reaction mixture[5]. Probably the treatment of β-acyl oxy sulfones **8** with 2 eq. of LDA gave the anions **9**, which could react both at α- and at γ-position. The isolation of α-products **5** is in agreement with the literature data. Alkylation of such anions at low temperature was reported to give α-derivatives predominantly[4,6].

At the second stage the sulfone group was removed by reduction of **5** with lithium in liquid ammonia. The reaction proceeded with simultaneous migration of double bond to give the more highly substituted alkenes **6a** and **6b**. It is important to carry out the reduction below -50°C, otherwise a number of by-products with saturated side chain and/or without hydroxyl group are formed.

In addition, the obtained allylic alcohol **6b** was transformed by the known method[2a] *via* 23,24-epoxide into the corresponding 22R,23R-diol in 56% total yield. The spectral data of these compounds are in a good agreement with those previously reported[2a,7].

References and Notes

1. (a) McMorris, T.C.; Donaubauer, J.R.; Silveria, M.H.; Molinski, T.F. *ACS symposium series.* **1991**, *474*, 36-42. (b) Khripach, V.A.; Zhabinskii, V.N.; Litvinovskaya, R.P. *ibid.* **1991**, *474*, 43-55. (c) Khripach, V.A.; Zhabinskii, V.N.; Lakhvich, F.A. *Brassinosteroids;* Science and Technic: Minsk. 1993; pp. 140-159.
2. (a) Fung, S.; Siddal, I.B. *J. Am. Chem. Soc.* **1980**, *102*, 6580-6581. (b) Anastasia, M; Allevi, P.; Ciuffreda, P.; Fiecchi, A.; Scala, A. *J. Org. Chem.* **1984**, *49*, 4297-4300. (c) Khripach, V.A.; Litvinovskaya, R.P.; Baranovskii, A.V.; Ermolenko, E.A. *Khimiya heterocycl. soed.* **1990**, 1073-1076. (d) Back, T.G.; Brunner, K.; Krihsna, M.V.; Lai, E.K.Y. *Can. J. Chem.* **1989**, *67*, 1032-1037. (e) Takahashi, T.; Ootahe, A.; Yamada, H.; Tsuji, J. *Tetrahedron Lett.* **1985**, *26*, 69-72.
3. (a) Steele, J.A.; Mosettig, E. *J. Org. Chem.* **1963**, *28*, 571-572. (b) Pappas, J.J.; Keaveney, W.P.; Gancher, E.; Berger, M. *Tetrahedron Lett.* **1966**, 4273-4278.
4. Simpkins, N.S. *Sulfones in Organic Synthesis;* Pergamon Press, 1993.
5. All compounds have been completely characterized by analytical and spectroscopic methods; NMR ($CDCl_3$, 200 MHz) data are given for:

   5a: δ 0.65 (s, 18-Me, 3H), 1.00 (s, 19-Me, 3H), 1.74 (s, 25-Me, 3H), 2.77 (t, J=3 Hz, C_6-H, 1H), 3.33 (s, 6-OMe, 3H), 3.70 (s, 22-OH, 1H), 3.78 (d, J=12 Hz, C_{23}-H, 1H), 4.51 (d, J=12 Hz, C_{22}-H, 1H), 4.60 (s, C_{28}-H, 1H), 4.97 (s, C_{28}-H, 1H), 7.5-7.9 (m, Ph, 5H);

   5b: δ 0.61 (s, 18-Me, 3H), 1.03 (s, 19-Me, 3H), 2.79 (s, C_6-H, 1H), 3.33 (s, 6-OMe, 3H), 3.58 (br.s, 22-OH, 1H), 3.78 (d, J=10 Hz, C_{23}-H, 1H), 4.34 (d, J=10 Hz, C_{22}-H, 1H), 5.01 (s, C_{28}-H, 1H), 5.20 (s, C_{28}-H, 1H), 7.5-7.9 (m, Ph, 5H);

   6a: δ 0.84 (s, 18-Me, 3H), 1.04 (s, 19-Me, 3H), 2.68 (t, J=2.4 Hz, C_6-H, 1H), 3.32 (s, 6-OMe, 3H), 4.46 (d, J=10 Hz, C_{22}-H, 1H), 5.36 (s, 22-OH, 1H);

   6b: δ 0.73 (s, 18-Me, 3H), 1.03 (s, 19-Me, 3H), 1.62 (s, 28-Me, 3H), 2.78 (t, J=2.4 Hz, C_6-H, 1H), 3.34 (s, 6-OMe, 3H), 4.48 (d, J=9.6 Hz, C_{22}-H, 1H), 5.32 (d, J=9.6 Hz, C_{23}-H, 1H).
6. (a) Hirama, M. *Tetrahedron Lett.* **1981**, *22*, 1905-1908. (b) Binns, M.R.; Haynes, R.K.; Katsifis, A.G.; Schober, P.A.; Vonwiller, S.C. *J. Org. Chem.* **1989**, *54*, 1960-1968.
7. Hayami, H.; Sato, M.; Kanemoto, S.; Morizawa, Y.; Oshima, K.; Nozaki, H. *J. Am. Chem. Soc.* **1983**, *105*, 4491-4492.

(*Received in UK* 5 *August* 1994; *revised* 24 *November* 1994; *accepted* 25 *November* 1994)