Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters 45 (2004) 8165–8168
Tetrahedron Letters

Diisobutylaluminium hydride (DIBAL-H) as a molecular scalpel: a new mechanistic proposal for a spiroketal rearrangement

Xiangbao Meng, Yongmin Zhang, Matthieu Sollogoub* and Pierre Sinaÿ

Ecole Normale Supérieure, Département de Chimie, UMR 8642: CNRS-ENS-Université Pierre et Marie Curie Paris 6, 24, rue Lhomond, 75231 Paris Cedex 05, France

Received 11 June 2004; revised 6 September 2004; accepted 6 September 2004
Available online 21 September 2004

Abstract—Taking advantage of our knowledge of the capacity of DIBAL-H to de-*O*-alkylate, we propose an alternative mechanism for a spiroketal rearrangement described by E. Suàrez. We also show that this proposal can account for the formation of the secondary product, whose original structure we propose to correct.

In our ongoing interest in de-*O*-benzylation reactions mediated by aluminium reagents,[1–4] we were stimulated by a rearrangement described by Suàrez and co-workers.[5] This reaction, depicted in Scheme 1, is a DIBAL-H mediated transformation of the spiroketal **1** into a major bicyclic product **2**. It is, overall, a reductive ring opening and a nucleophilic substitution to form a dioxadecalin, and is interestingly accompanied by a de-*O*-benzylation reaction. A secondary product is formed; its supposed structure **3** is shown in Scheme 1.

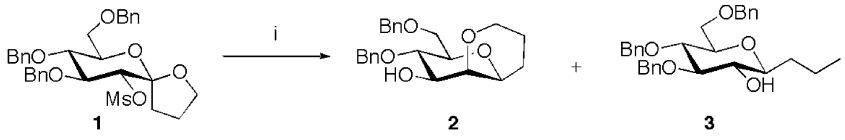
The mechanism proposed by the Spanish group for the formation of **2** is depicted in Scheme 2, the opening and reduction of the spiroketal being followed by a reductive debenzylation, which is promoted by a hydride ion and assisted by the neighbouring methanesulfonyl group. The alkoxy anion would finally attack the cyclic adduct to form **2**.

To explain the formation of the minor product **3**, Suàrez et al. proposed that the spiroketal opening and reduction would be followed by a *trans*-esterification of the mesyl and a reduction of the formed primary methanesulfonyl group, as shown in Scheme 3. A distinctive feature of both proposed mechanisms is that the methanesulfonate is not chosen as the leaving group in the presence of an alcoholate on the molecule.

We have recently demonstrated[1] that perbenzylated methyl α-D-mannopyranoside is de-*O*-benzylated on positions 2 and 3 with TIBAL (Scheme 4). DIBAL-H having similar de-*O*-benzylating properties, we wondered whether the formation of compound **2**, having a *manno*-type configuration, could be explained in this way.

In the present paper, we would like to propose an alternative mechanism accounting for the formation of the two products, based on our experience on de-*O*-benzylation reactions mediated by DIBAL-H.

To this purpose we synthesised the bicyclic compound **8**, that we anticipated to be the precursor of **2**. Indeed, it seemed reasonable to think that the first step of the

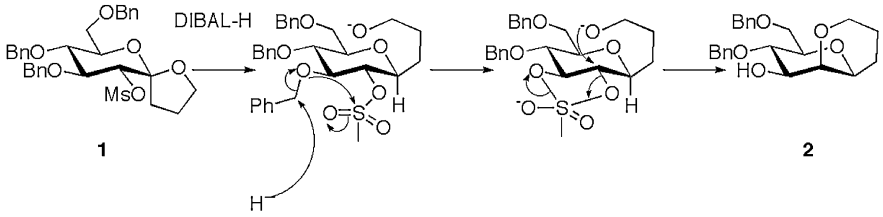


1 2 3

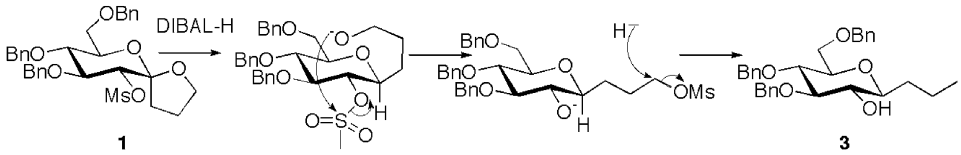
Scheme 1. E. Suàrez's rearrangement of spiroketal **1**. Reagents and conditions: (i) DIBAL-H (10 equiv), CH_2Cl_2, reflux, 72 h, 72%, **2**:**3**, 3:1.

Keywords: Aluminium; Diisobutylaluminium hydride (DIBAL-H); Carbohydrates; Spiroketal.
* Corresponding author. Tel.: +33 1 4432 3335; fax: +33 1 4432 3397; e-mail: matthieu.sollogoub@ens.fr

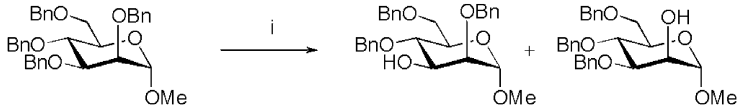
0040-4039/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2004.09.030



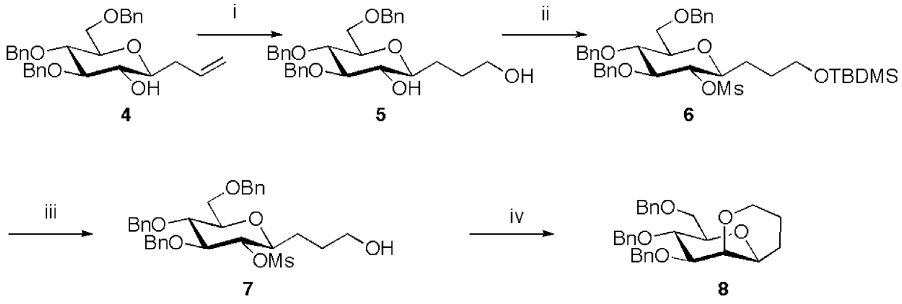
Scheme 2. E. Suàrez's mechanism proposal for the formation of **2**.



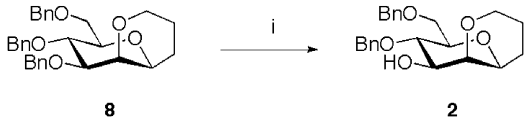
Scheme 3. E. Suàrez's mechanism proposal for the formation of **3**.



Scheme 4. De-*O*-benzylation of perbenzylated methyl α-D-mannopyranoside. Reagents and conditions: (i) TIBAL (5 equiv), toluene, 50 °C, 3 h, 89%, 1:1.



Scheme 5. Synthesis of bicyclic compound **8**. Reagents and conditions: (i) (a) BH_3·THF (2.8 equiv), THF, 0 °C, 2 h; (b) H_2O_2, NaOH (3 N), rt, 30 min, 63%. (ii) (a) TBDMSCl (1.2 equiv), imidazole (1.5 equiv), DMF, rt, 6 h; (b) MsCl (12 equiv), pyridine, rt, 12 h, 73%. (iii) TBAF (1.5 equiv), THF, rt, 4 h, 96%. (iv) NaH (10 equiv), DMF, 60 °C, 20 h, 67%.

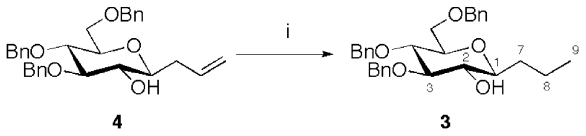


Scheme 6. Action of DIBAL-H on compound **8**. Reagents and conditions: (i) DIBAL-H (10 equiv), CH_2Cl_2, reflux, 72 h, 72%.

rearrangement consisted in the reductive spiroketal ring opening followed by an intramolecular nucleophilic substitution of the mesylate to form the bicyclic compound **8**. The synthesis of this compound is shown in Scheme 5. The known *C*-allyl glucoside **4**[6] is transformed into the diol **5**[7] thanks to a hydroboration, subsequent selective silylation of the primary alcohol on **5** followed by mesylation of the remaining hydroxyl group afforded **6**. Desilylation of **6** and treatment of the resulting alcohol **7** by sodium hydride in DMF at 60 °C gave the desired bicyclic benzylated compound **8** in 67% yield.

Bicyclic compound **8** was now submitted to the action of DIBAL-H for 72 h at 50 °C and the product of the reaction showed the same spectral and analytical data as the major compound **2** obtained by Suàrez's (Scheme 6). No other product being observed in the reaction, we then supposed that minor product **3** of the rearrangement reaction might be formed through a different intermediate than **8**.

On careful analysis of NMR data, it appeared to us that the proposed structure **3** could hardly be a pyranose ring. To confirm our thought, we reduced the double bond of **4**[6] into the saturated *C*-propyl-glucoside **3** and showed that the NMR[8] was clearly different from the one given by Suàrez (Scheme 7).

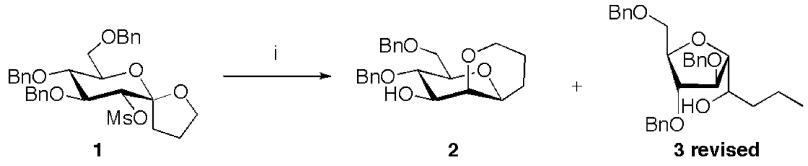


Scheme 7. Synthesis of *C*-propyl-glucoside **3**. Reagents and conditions: (i) H_2, PtO_2, AcOEt, rt, 30 min, 75%.

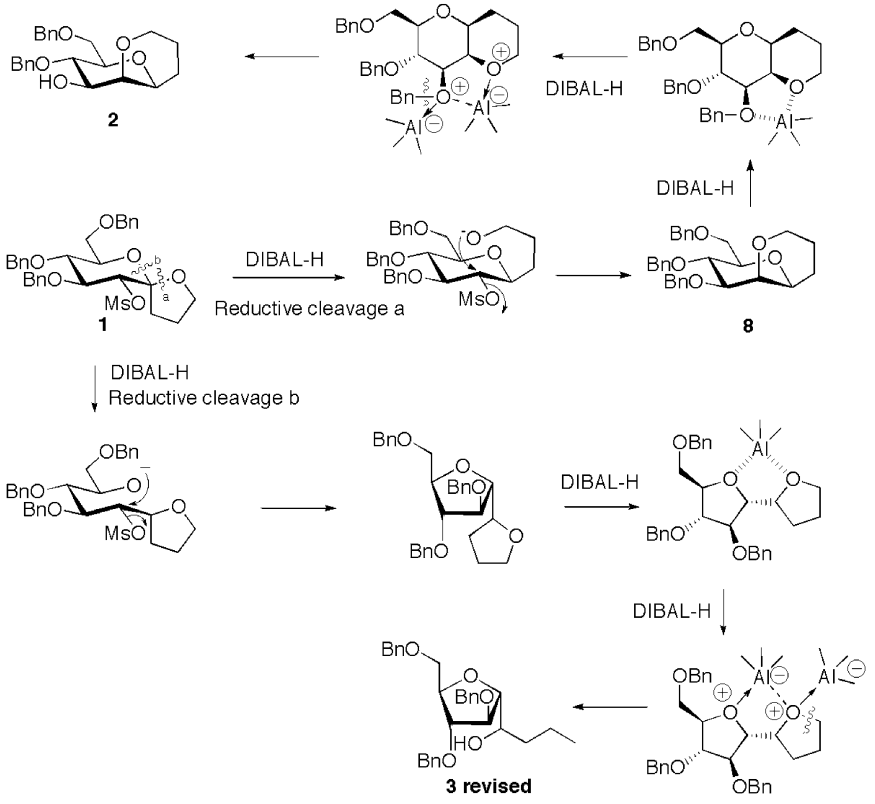
In fact, we also reproduced the rearrangement reaction as described by Suàrez et al. and isolated the two same products that we analysed by NMR. Hence, we propose another structure for the minor product,[9] whose NMR compares very well to closely related furanosidic compound.[10] (Scheme 8 and supporting information).

In conclusion, we propose that the mechanisms accounting for the formation of **2** and **3 revised** are both composed, as shown in Scheme 9, of two independent reactions. The first step would consist in the spiroketal reductive opening of either the pyranose (path a) or the furanose (path b) rings, next followed by recyclisation through S_N2 type displacement of the mesylate by the formed alcoholate. E. Suàrez himself already reported about this possibility elsewhere.[11] The second step would therefore be a de-*O*-alkylation reaction promoted by excess of DIBAL-H. As recently proposed by us,[4] this de-*O*-alkylation would start with the formation of a penta-coordinated complex between the aluminium reagent and the 1,2-*cis* oxygen pattern of the sugar. A second aluminium atom selects the less hindered oxygen and directs the dealkylation. In the case of product **2**, the benzyl on position 3 is cleaved, in the case of **3 revised** the less substituted tetrahydrofuranic ring is opened (Scheme 9).

In summary, it is worth noting that DIBAL-H is a powerful agent of de-*O*-alkylation, provided that a suitable 1,2-*cis* deoxygenated pattern is available on the molecule. This work offers two more examples of DIBAL-H acting so-to-say as molecular scalpel.[12]



Scheme 8. E. Suàrez's rearrangement of spiroketal **1** with the revised structure for the minor product. Reagents and conditions: (i) DIBAL-H (10 equiv), CH_2Cl_2, reflux, 72 h, 72%, **2**:**3 revised**, 3:1.



Scheme 9. New proposal for the formation of **2** and **3 revised** from **1**.

Acknowledgements

The authors would like to thank the French Ministry of Research and Technology for post-doctoral fellowship to XM (No. 2003-375).

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2004.09.030.

References and notes

1. Sollogoub, M.; Das, S. K.; Mallet, J.-M.; Sina, P. *C. R. Acad. Sci. Paris, t.2, Série IIc* **1999**, *22*, 441–448.
2. Chevalier-du Roizel, B.; Cabianca, E.; Rollin, P.; Sinaÿ, P. *Tetrahedron* **2002**, *58*, 9579–9583.
3. Pearce, A. J.; Sinaÿ, P. *Angew. Chem.* **2000**, *112*, 3756–3758; *Angew. Chem., Int. Ed.* **2000**, *39*, 3610–3612.
4. Lecourt, T.; Hérault, A.; Pearce, A. J.; Sollogoub, M.; Sina, P. *Chem. Eur. J.* **2004**, *12*, 2960–2971.
5. Betancor, C.; Dorta, R. L.; Freire, R.; Prangé, T.; Suàrez, E. *J. Org. Chem.* **2000**, *65*, 8822–8825.
6. Cipolla, L.; Lay, L.; Nicotra, F. *J. Org. Chem.* **1997**, *62*, 6678–6681.
7. Shuto, S.; Terauchi, M.; Yahiro, Y.; Abe, H.; Ichikawa, S.; Matsuda, A. *Tetrahedron Lett.* **2000**, *41*, 4151–4155.
8. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.20 (m, 15H, H-arom.), 5.02 (d, 1H, $J = 11.5$ Hz, CH_2Ph), 4.85 (d, 1H, $J = 10.8$ Hz, CH_2Ph), 4.77 (d, 1H, $J = 11.5$ Hz, CH_2Ph), 4.69 (d, 1H, $J = 12.3$ Hz, CH_2Ph), 4.64 (d, 1H, $J = 10.5$ Hz, CH_2Ph), 4.61 (d, 1H, $J = 12.1$ Hz, CH_2Ph), 3.78 (dd, 1H, $J_{5,6} = 2.3$, $J_{6,6'} = 11$ Hz, H-6), 3.74 (dd, 1H, $J_{5,6'} = 4$ Hz, H-6′), 3.66 (t, 1H, $J_{4,3} = J_{4,5} = 9.3$ Hz, H-4), 3.52 (t, 1H, $J_{3,2} = 9$ Hz, H-3), 3.46 (ddd, 1H, H-5), 3.35 (t, 1H, $J_{2,1} = 9.1$ Hz, H-2), 3.22 (dt, 1H, $J_{1,2} = J_{1,7} = 9.1$, $J_{1,7'} = 2.5$ Hz, H-1), 2.11 (br s, 1H, OH), 1.82 (dddd, 1H, $J = 2.5$, $J = 4.4$, $J = 10.3$ Hz, H-7), 1.68–1.37 (m, 3H, H-7′, H-8), 0.97 (t, 3H, $J_{9,8} = 7.3$ Hz, H-9); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.6, 138.2, 138.0 (3C arom. quat.), 128.7–127.5 (C arom.), 86.9 (C-3), 79.2 (C-1), 79.0 (C-5), 78.6 (C-4), 75.1, 74.7, 73.4 ($3CH_2Ph$), 73.9 (C-2), 69.0 (C-6), 33.8 (C-7), 18.5 (C-8), 14.1 (C-9).
9. The absolute configuration of the exocyclic stereocenter has not been determined in this work.
10. Persky, R.; Albeck, A. *J. Org. Chem.* **2000**, *65*, 5632–5638.
11. Betancor, C.; Dorta, R. L.; Freire, R.; Martin, A.; Prangé, T.; Suàrez, E. *J. Org. Chem.* **1998**, *63*, 6355–6362.
12. "Cyclodextrins unterm Messer", *Nachrichten aus der Chemie* **2001**; *49*, 6.