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A five-step formal synthesis of (−)-Jaspine B

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ABSTRACT

A new application of the sequential hydrolysis-oxidation-Wittig olefination (SHOWO) protocol to a D-glucose derivative, and an anomeric deoxygenation reaction of a *xylo*-D-furanose derivative is presented for the five-step formal synthesis of (−)-Jaspine B.

Since the publication of the original report on the isolation of Jaspine B from the Okinawa marine sponge *Pachastrissa* sp. by Higa and coworkers[1] the organic synthetic community has been deeply interested to develop the most concise total synthesis of this anti-tumor compound.[2] Although some asymmetric total syntheses have been reported, in which are included: Sharpless asymmetric epoxidation,[2f] Sharpless asymmetric dihydroxylation,[2k] or Davies conjugate additions of homochiral lithium amides,[2k,m] the chiron approach represents probably the better way for preparing Jaspine B and even other biologically active Jaspines (Fig. 1).[3]

Among the wide repertory of (+)/(−)-Jaspine B and 2-*epi*-(+)/(−)-Jaspine B total syntheses, where the chiron approach is used, we realized that the use of both D-glucose (**1**) and D-xylose offers more advantages than any other carbohydrate. Two of those advantages are: rapid construction of the tetrahydrofuran ring and easy installation of the long chain. In this regard, Chandrasekhar and coworkers obtained the truncated (+)-Jaspine B in 12 steps from L-xylose **2** featuring Wittig olefination of aldehyde **3** for chain elongation, and reductive removal of the methoxy group of **4** with triethylsilane for the formation of the tetrahydrofuranose ring.[4]

In this sense, we realized that it could be feasible to develop a highly efficient and concise formal synthesis of (−)-Jaspine B if we only applied the sequential hydrolysis-oxidation-Wittig olefination (SHOWO) protocol[5] to the DAG derivative **5** for chain elongation, and the Robins anomeric deoxygenation[6] to 1,2-*O*-isopropylidene-α-D-xylofuranose derivative **6** for the construction of the tetrahydrofuran moiety (Scheme 1).

In this sense, we started with the benzylation of the hydroxyl group at C-3 of DAG under standard conditions (BnBr/NaH) to afford **5** in quantitative yield (98%); then **5** was submitted to SHOWO protocol,[7] which consists of one-pot three-step processes: hydrolysis of the 5,6-*O*-isopropylidene group/oxidative cleavage of the formed 5,6-diol and Wittig olefination, to afford compound **6** in only 6 h and 86% yield. It is important to note that, following the traditional procedure for this type of chain elongation (aqueous hydrolysis/$NaIO_4$ 5,6-diol cleavage and Wittig olefination), two days are needed and lower overall yields are obtained. Having the compound **6** in hand (major *Z*-olefine isomer), the formation of the tetrahydrofuran ring (**8**) was achieved in a straightforward manner via nucleophilic substitution reaction at the anomeric position of **6** under Robins conditions ($Et_3SiH/BF_3{\cdot}OEt2$).[6,8] Finally, the (−)-Jaspine B precursor **7** was obtained via the eventual formation of the triflate group with trifluoromethanesulfonic chloride and DMAP followed by a S_N^2 displacement reaction with sodium azide in the presence of tetrabutylammonium fluoride (Scheme 2).[9] It is important to note that this procedure is effective for the azide group introduction and avoids the formation of the elimination products.[4]

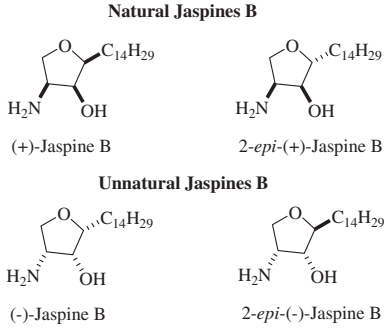

Figure 1. Natural and unnatural Jaspines B with cytotoxic activity.

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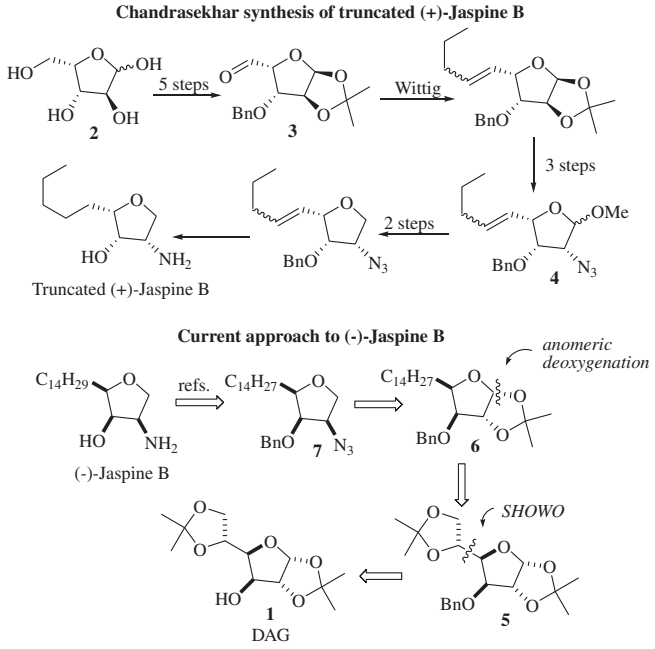
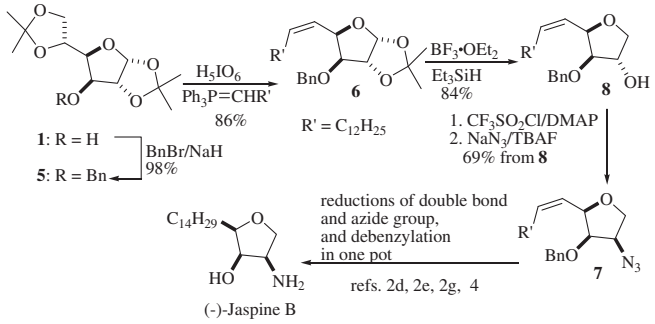


Scheme 1. Chandrasekhar synthesis of truncated (+)-Jaspine B (12 steps) and current approach for (−)-Jaspine B.



Scheme 2. Five-steps formal synthesis of (−)-Jaspine B.

In summary, we have described here, a five-step formal synthesis of (−)-Jaspine B (six-step total synthesis if we used the general one-pot reduction and deprotection protocol widely reported), which represents the most concise route to (−)-Jaspine B. Additionally, in this Letter it has been shown (once again) that the SHOWO protocol is an effective and powerful tool in the synthetic scenario for chain elongation processes.

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References and notes

1. (a) Kuruda, I.; Musman, M.; Ohtani, I. I.; Ichibata, T.; Tanaka, J.; Gravalos, D. G.; Higa, T. *J. Nat. Prod.* **2002**, *65*, 1505; (b) Ledroit, V.; Debitus, C.; Lavaud, C.; Massiot, G. *Tetrahedron Lett.* **2003**, *44*, 225.
2. (a) Sudhakar, N.; Kumar, A. R.; Prabhakar, A.; Jagadeesh, B.; Rao, B. V. *Tetrahedron Lett.* **2005**, *46*, 325; (b) Bhaket, P.; Morris, K.; Stauffer, C. S.; Datta, A. *Org. Lett.* **2005**, *7*, 875; (c) van den Berg, R.; Boltje, T.; Verhagen, C.; Litjens, R.; Vander Marel, G.; Overkleeft, H. *J. Org. Chem.* **2006**, *71*, 836; (d) Du, Y.; Liu, J.; Linhardt, R. J. *J. Org. Chem.* **2006**, *71*, 1251; (e) Liu, J.; Du, Y.; Dong, X.; Meng, S.; Xiao, J.; Cheng, L. *Carbohydr. Res.* **2006**, *341*, 2653; (f) Ribes, C.; Falomir, E.; Carda, M.; Marco, J. A. *Tetrahedron* **2006**, *62*, 5421; (g) Lee, T.; Lee, S.; Kwak, Y. S.; Kim, D.; Kim, S. *Org. Lett.* **2007**, *9*, 429; (h) Reddy, L. V. R.; Reddy, P. V.; Shaw, A. K. *Tetrahedron: Asymmetry* **2007**, *18*, 542; (i) Ramana, C. V.; Giri, A. G.; Suryawanshi, S. B.; Gonnade, R. G. *Tetrahedron Lett.* **2007**, *48*, 265; (j) Prasad, K. R.; Chandrakumar, A. *J. Org. Chem.* **2007**, *72*, 6312; k Abraham, E.; Candela-Lena, J. I.; Davies, S. G.; Georgiou, M.; Nicholson, R. L.; Roberts, P. M.; Russell, A. J.; Sanchez-Fernandez, E. M.; Smith, A. D.; Thomson, J. E. *Tetrahedron: Asymmetry* **2007**, *18*, 2510; (l) Yakura, T.; Sato, S.; Yoshimoto, Y. *Chem. Pharm. Bull.* **2007**, *55*, 1284; (m) Abraham, E.; Brock, E. A.; Candela-Lena, J. I.; Davies, S. G.; Georgiou, M.; Nicholson, R. L.; Perkins, J. H.; Roberts, P. M.; Russell, A. J.; Sanchez-Fernandez, E. M.; Scott, P. M.; Smith, A. D.; Thomson, J. E. *Org. Biomol. Chem.* **2008**, *6*, 1665; (n) Passiniemi, M.; Koskinen, A. M. P. *Tetrahedron Lett.* **2008**, *49*, 980; (o) Venkatesan, K.; Srinivasan, K. V. *Tetrahedron: Asymmetry* **2008**, *19*, 209; (p) Enders, D.; Terteryan, V.; Palecek, J. *Synthesis* **2008**, 2278; (q) Ichikawa, Y.; Matsunaga, K.; Masuda, T.; Kotsuki, H.; Nakano, K. *Tetrahedron* **2008**, *64*, 11313; (r) Reddipalli, G. S.; Venkataiah, M.; Mishra, M. K.; Fadnavis, N. W. *Tetrahedron: Asymmetry* **2009**, *20*, 1802; (s) Inuki, S.; Yoshimitsu, Y.; Oishi, S.; Fujii, N.; Ohno, H. *Org. Lett.* **2009**, *11*, 4478; (t) Inuki, S.; Yoshimitsu, Y.; Oishi, S.; Fujii, N.; Ohno, H. *J. Org Chem.* **2010**, *75*, 3831; (u) Yoshimitsu, Y.; Inuki, S.; Oishi, S.; Fujii, N.; Ohno, H. *J. Org. Chem.* **2010**, *75*, 3843; (v) Urano, H.; Enomoto, M.; Kuwahara, S. *Biosci., Biotechnol., Biochem.* **2010**, *74*, 152; (w) Salma, Y.; Ballereau, S.; Maaliki, C.; Ladeira, S.; Andrieu-Abadie, N.; Genison, Y. *Org. Biomol. Chem.* **2010**, *8*, 3227; (x) Passiniemi, M.; Koskinen, A. M. P. *Org. Biomol. Chem.* **2011**, *9*, 1774; (y) Llaveria, J.; Diaz, Y.; Matheu, M. I.; Castillon, S. *Eur. J. Org. Chem.* **2011**, 1514; (z) Sanchez-Eleuterio, A.; Quintero, L.; Sartillo-Piscil, F. *J. Org. Chem.* **2011**, *76*, 5466; For a review, see: (aa) Abraham, E.; Davies, S. G.; Roberts, P. M.; Russell, A. J.; Thomson, J. E. *Tetrahedron: Asymmetry* **2008**, *19*, 1027.
3. Twenty seven synthesis of Jaspine B and diastereoisomers, and 22 synthesis involved the use of the Chiral Pool.
4. Chandrasekhar, S.; Tiwari, B.; Prakash, S. J. *ARKIVOK* **2006**, 155.
5. For examples of the SHOWO protocol in synthesis: (a) Sartillo-Piscil, F.; Vargas, M.; Anaya de Parrodi, C.; Quintero, L. *Tetrahedron Lett.* **2003**, *44*, 3919; (b) Reddy, L. V. R.; Swamy, G. N.; Shaw, A. K. *Tetrahedron: Asymmetry* **2008**, *19*, 1372; (c) Ramirez, E.; Meza-Leon, R.; Quintero, L.; Sartillo-Piscil, F. *Tetrahedron Lett.* **2010**, *51*, 2178; (d) Sidnei, M.; Ligeour, T. C.; Caroline, L.; Christine, G.; Delphine, J.; Emanuelle, D.; Francoise, D. *Green Chem.* **2011**, *13*, 1812; (e) Venkat, R. P.; Vikas, B.; Brijesh, K.; Shaw, A. K. *Eur. J. Org. Chem.* **2011**, 1575.
6. Ewing, G. J.; Robins, M. J. *Org. Lett.* **1999**, *1*, 635.
7. A solution of **5** (2.0 g, 5.7 mmol) and periodic acid (1.55 g, 6.8 mol) in 80 mL of dry ethyl acetate was stirred for 2 h, whereby a solid formed that was separated by filtration. Evaporation under reduced pressure afforded a colorless syrup, which was dissolved in 50 mL of THF. This solution was added dropwise to the solution of phosphorus ylide previously prepared [tridecyltriphenylphosphonium bromide (3.6 g, 6.84 mmol) in 150 mL of dried THF under an atmosphere of argon, the mixture was cooled at 0 °C and *n*-butyllithium was added dropwise (5.13 mL, 8.2 mmol of THF solution 1.6 M); the reaction mixture was stirred for 30 min]. The resulting reaction mixture was stirred at for 4 h 0 °C. The reaction was stopped by the addition of 50 mL of water. Extracted with ethyl acetate (3 × 50 mL), dried the combined organic phase over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography to yield 2.18 g of **6** (86% yield) as a *Z*/*E* mixture (9:1, respectively). $[\alpha]_D = -68.3$ (*c* 1.0, $CHCl_3$), ^1H NMR (400 MHz, $CDCl_3$) δ: 0.89 (t, *J* = 7.2 Hz, 3H), 1.25 (m, 20H), 1.32 (s, 3H), 1.52 (s, 3H), 2.07 (m, 2H), 3.83 (d, *J* = 2.8 Hz 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.62 (d, *J* = 3.6 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.94 (dd, *J* = 7.6, 3.2 Hz, 1H), 5.69 (m, 2H), 5.95 (d, *J* = 3.6 Hz, 1H), 7.31 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 22.6, 23.2, 26.1, 26.2, 26.8, 26.9, 28.0, 29.1, 29.3, 29.4, 29.43, 29.5, 29.6, 31.9, 41.5, 71.9, 75.8, 83.0, 83.3, 104.6, 111.3, 123.4, 127.4, 127.7, 128.3, 135.2, 137.6. HRMS-FAB mode, calcd for $C_{28}H_{44}O_4$: 444.3240; found 444.3244.
8. To a solution of **6** (0.5 g, 1.12 mmol) in CH_2Cl_2 (50 mL) at 0 °C were added trietyl silane (0.71 mL, 4.48 mmol) and $BF_3{\cdot}Et_2O$ (0.16 mL, 1.34 mmol). The reaction mixture was stirred at ambient temperature for 2 h, before to add an aqueous saturated solution of $NaHCO_3$ (15 mL) and CH_2Cl_2 (40 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by flash chromatography to afford 0.37 g of **8** in (84% yield), as a white solid, mp = 45 °C; $[\alpha]_D = -64.2$ (*c* = 1.0, $CHCl_3$) ^1H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, *J* = 6.8 Hz, 3H), 1.25 (m, 20H), 2.10 (m, 2H), 3.67 (dd, *J* = 10.0, 1.6 Hz, 1H), 3.78 (dd, *J* = 4, 1.2 Hz, 1H), 4.20 (dd, *J* = 10.0, 4.4 Hz, 1H), 4.40 (b, 1H), 4.60 (s, 2H), 4.83 (dd, *J* = 8.0, 4.0 Hz, 1H), 5.68 (m, 2H), 7.31 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 22.7, 27.9, 29.3, 29.4, 29.5, 29.6, 29.7, 31.9, 72.2, 73.4, 75.8, 75.9, 85.6, 124.5, 127.4, 127.7 128.4, 134.9, 137.9. HRMS-FAB mode, calcd for $C_{25}H_{40}O_3$: 388.2977; found 388.3010.
9. Trifluoromethanesulfonyl chloride (0.68 mL, 6.45 mmol) was added dropwise to a stirred solution of **8** (0.5 g, 1.29 mmol) dissolved in CH_2Cl_2 (6 mL) at 0 °C. After 10 min, DMAP (0.18 g, 1.5 mmol) was added to the stirred solution at the same temperature and allowed to react for 24 h. The reaction mixture was concentrated under reduced pressure and washed successively with hexane (3 × 5 mL). The organic layer was concentrated and the residue was dissolved in DMF (2.5 mL), and NaN_3 (0.168 g, 2.58 mmol) and tetrabutylammonium fluoride 1.0 M (1.29 mL, 1.29 mmol) were added. The resulting reaction mixture was stirred at rt for 24 h. The reaction mixture was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel to obtain 0.37 g of **7** (69% yield) as a syrup. $[\alpha]_D = -80.1$ (*c* = $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, *J* = 6.8 Hz, 3H), 1.25 (m, 20H), 2.08 (m, 2H), 3.95 (m, 3H), 4.10 (t, *J* = 4.8 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.69 (d, *J* = 12.0 Hz, 1H), 4.70 (m, 1H), 5.70 (m, 2H), 7.35 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.11, 22.7, 27.8, 29.3, 29.34, 29.5, 29.7, 31.9, 61.6, 68.7, 73.3 75.8, 80.4, 124.9, 127.8, 127.9, 128.4, 135.2, 137.4.