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# Selective Wittig olefination in aqueous media for the rapid preparation of unsaturated 7,3-lactone-α-D-xylofuranose derivatives

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ABSTRACT

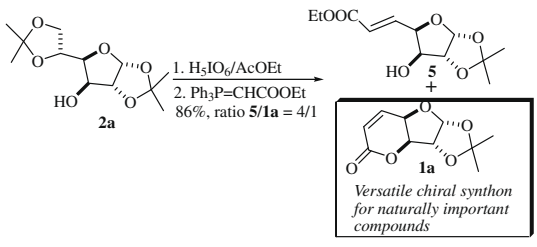
A highly efficient and rapid protocol for the preparation of the title compounds **1a** and **1b** from D-glucose derivatives **2a** and **2b**, respectively, is reported. To this end, highly selective Wittig olefination in aqueous media was developed for the elaboration of α,β-unsaturated acids **5a** and **5b**, which when treated with DCC, lactonization was accomplished and the title compounds **1a** and **1b** were obtained in only three sequential steps with overall yields of 85% and 88%, respectively. Additionally, the Z-selectivity was studied by analyzing conformational models of its corresponding oxophosphorinane intermediaries.



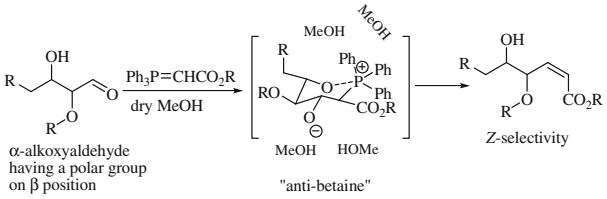
When an organic chemist has the need for the synthesis of unsaturated compounds, always has in mind the very well-known Wittig olefination.[1] There are a number of positive reasons that confer to this reaction the privilege of being the first choice (among other synthetic methods),[2] however, there still are issues for this reaction, such as selectivity[3] and environmental concerns[4] that remain challenging with certain substrates. Under traditional condition reactions, *E*-olefins are the major product for stabilized ylides, whereas *Z*-olefins are preferred for nonstabilized ylides.[3c-e] Although many reaction conditions have been reported to improve the chemoselectivity of the Wittig olefination (such as temperature,[5] pressure,[6] silica gel,[7] additives,[8] and solvents,[4,9]) the ability for full selectivity control is hardly achieved for those α-alkoxyaldehydes.[10] In this sense, some years ago we faced this problem when we reported[11] the sequential hydrolysis-oxidation-Wittig olefination (SHOWO[12]) protocol for the synthesis of α,β-unsaturated esters derived from diacetone-D-glucose (Scheme 1). Although the selectivity was modest, the global yield was good, especially if we take into consideration the synthetic importance of the α,β-unsaturated lactone **1a** as versatile chiral synthon for the preparation of various biologically important compounds.[13] Therefore, we now report the efficient synthesis of **1a** and another lactone analogous **1b** by means of a selective Wittig olefination in aqueous media.[4]

At first glance, we thought that the quest for the Z-selectivity in this kind of substrate would be difficult, since Trouchet and Gentile were first in report poor Z-selectivity in a series of α-alkoxyaldehydes derived from 1,2-*O*-isopropylidene-α-D-furanoses with stabilized ylides,[14] however, Brimacombe et al.,[15] and Shing et al.[16] reported good Z-selectivities for α-alkoxy-β-hydroxyaldehydes with also stabilized ylides in dry methanol. Apparently, two requirements are necessary for achieving high Z-selectivity: (a) a polar or donor group placed at β-position to aldehyde, and, (b) an anhydrous alcoholic solvent.[14,15,3c] It seems that the polar media contribute to stabilize the formation of a chelating 'anti-betaine' leading thus to the preferential occurrence of high Z-selectivities (Scheme 2).[16]

Therefore, if we considered the fact that the anti-betaine structure is stabilized by solvating effect from methanol, then water




**Scheme 1.** Sequential hydrolysis-Oxidation-Wittig Olefination protocol (SHOWO).




**Scheme 2.** Putative anti-betaine model that explain Z-selectivities.

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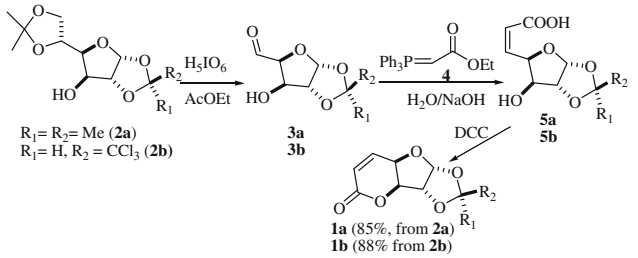
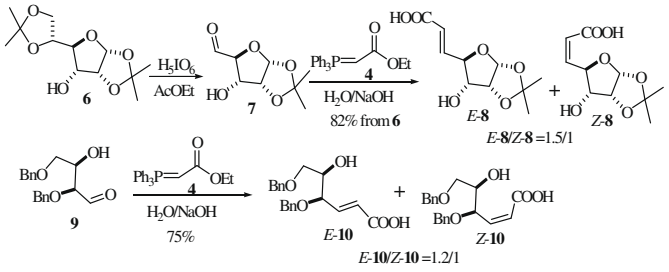



**Scheme 3.** Selective *Z*-olefination and DCC-mediated lactonization to obtain desired unsaturated lactones **1a** and **1b**.




**Scheme 4.** Erosion of the Z-selectivity for D-ribofuranose and D-threose derivatives.

should be also a good medium for the same synthetic purpose, and also it would be partially in accordance with the recent report on the use of water as an efficient medium for selective Wittig olefination.[17] With this in mind, we proceeded to prepare the stabilized ylide **4** in aqueous medium and adding to the corresponding β-hydroxyaldehydes **3a** and **3b**, which were prepared in straightforward manner from D-glucose derivatives **1a** and **1b** and $H_5IO_6$.[18] Results were as we expected, high yield and complete Z-selectivity for the formation of α,β-unsaturated acids **5a** and **5b** was observed. Then, without any purification processes, **5a** and **5b** were treated with *N,N′*-dicyclohexylcarbodiimide (DCC) in $CH_2Cl_2$ to afford the desired α,β-unsaturated lactones **1a** and **1b** in high yields (Scheme 3).

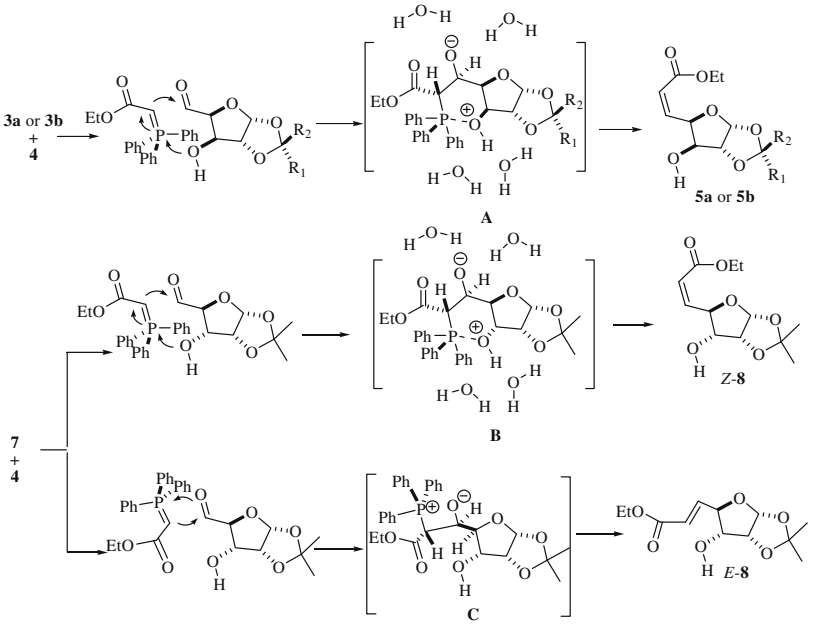
Thus, in an attempt to generalize this methodology by using similar substrate and non-cyclic substrate, we treated D-ribofuranose derivative **7** (which was also generated in straightforward manner from D-allofuranose **6** and $H_5IO_6$) and D-threose derivative **9**[19] under the same Wittig olefination conditions, and complete erosion of the Z-selectivity was observed, giving thus an almost equimolar mixture of α,β-unsaturated acids (Scheme 4).

This unexpected result suggests that: the presence of a hydroxyl group (or related functional group) in β-position is insufficient to lead Z-selectivity, but stereochemistry and conformational restriction are also key factors. Therefore, in such cases to get higher Z-selectivities, anhydrous methanolic conditions are mandatory.[15,16]

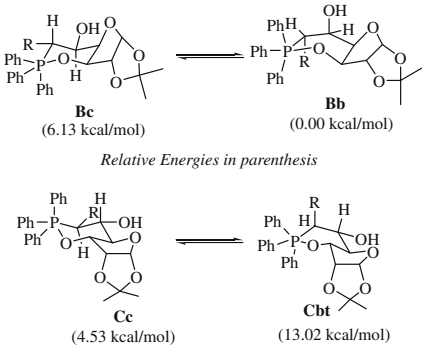
In order to give a rational explanation for Z-selectivity in the cases of **5a** and **5b**, anti-betaine **A** (derived from the reaction between **3a** or **3b** plus **4**) is proposed, and anti-betaine **B** along with its normal syn-betaine **C** (derived from **7** plus **4**) are also proposed (Scheme 5). Thus, the apparent dependence of Z-selectivity with respect to stereochemistry of β-hydroxy group was investigated by theoretical conformational study for oxaphosphorinane structures **A** and **B** (as anti-betaine models). In fact, by taking into consideration the aqueous (protic) conditions, it seems logical to postulate the existence of oxaphosphorinanes as intermediaries for Wittig olefinations. Besides, in a similar manner, γ-oxido ylides afford oxaphospholanes (five-membered ring P-heterocyclic) as stable intermediaries during the Wittig reaction.[20] Investigating conformational studies reported in the literature for that six-membered ring P-heterocyclic xylo and ribofuranoses,[21] we found that, chair-boat equilibrium operates in xylofuranose derivatives[22] meanwhile chair–boat-twisted equilibrium for those ribofuranose derivatives.[23]

The geometry of oxaphosphorinane conformers **Bc** and **Bb** derived from xylofuranose derivatives, and **Cc** and **Cbt** from ribofuranose derivatives were fully optimized by using GAUSSIAN 03 software package with the Density Functional Theory (DFT) in combination with the 6-31G(d) basis set.[24] All The structures were characterized as true minima by calculating their respective vibrational frequencies at the same level of theory (Scheme 6).

By analyzing their relative energies we found that boat conformation (**Bb**), corresponding to xylo derivative, is 6.13 kcal/mol more stable than its chair conformer (**Bc**), meanwhile chair




**Scheme 5.** Proposed intermediaries in Wittig olefination of xylo and ribofuranose derivatives.




**Scheme 6.** Conformer energy values for proposed oxaphosphorinanes present in Wittig olefination of xylo and ribofuranose derivatives.

conformer (**Cc**) for the ribo derivative is 8.49 kcal/mol more stable than its boat-twisted conformer (**Cbt**). Furthermore, key finding of this study comes from the energy gap of 4.53 kcal/mol among the lowest conformers of both diastereoisomer oxaphosphorinanes (**Bb** and **Cc**), being **Bc** the most stable oxaphosphorinanes.[25] This energy difference should be attributed to the energy strain caused by the trans-fusion for ribofuranose derivative, as Gerlt et al. previously found,[26] by thermodynamic experiments in trans-fused six-membered ring phosphates (cAMP), that 5 kcal/mol of thermodynamic instability is regarded to geometry strain resulting from the trans-fusion. Therefore, on the basis of the above-mentioned theoretical results, we can assume that the trans-fusion strain energy of ribofuranose derivative **7** destabilize the formation of the anti-betaine (**B**) leading to the preferential formation of normal betaine **C** and thus to produce higher E-selectivity than Z-selectivity. This result is actually interesting, because pointed out that the conformation of the anti-betaine plays a key role in the Z-selectivity of α-alkoxy-β-hydroxyaldehydes with stabilized ylides.

In summary, we have developed a highly efficient sequential protocol for the synthesis of α,β-unsaturated-7,3-lactone-α-D-xylofuranoses from D-glucose derivatives, which are versatile chiral synthons for the preparation of biologically important compounds. The key step of the synthesis is the development of a highly Z-selective Wittig olefination reaction in aqueous media. Additionally, the anti-betaine model, which presumably provides a rational explanation for Z-selectivities was studied by theoretical methods and demonstrated that boat conformation of the cyclic anti-betaine is crucial for the Z-selectivity.

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## Supplementary data

Supplementary data (general procedure for the preparation of **1a** and **1b** and Cartesian coordinates for conformers **Bc**, **Bb**, **Cc**, and **Cbt**) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.02.094.

## References and notes

1. (a) Wittig, G.; Geissler, G. *Liebigs Ann. Chem.* **1953**, *580*, 44–68; (b) Wittig, G. *Science* **1980**, *210*, 600–604.
2. (a) Kolodiazhnyi, O. I. *Phosphorus Ylides: Chemistry and Applications in Organic Chemistry*; Wiley-VCH: New York, 1999; (b) Takeda, T. In *Modern Carbonyl Olefination*; Wiley-VCH: Weinheim, Germany, 2004.
3. (a) Guo, X.; Wang, J.; Li, C.-H. *J. Am. Chem. Soc.* **2009**, *131*, 15092–15093; (b) Nicolaou, K. C.; Härter, M. W.; Gunzner, J. L.; Nadin, A. *Liebigs Ann. Recl.* **1997**, 1283–1301; (c) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863–927; (d) Vedejs, E.; Peterson, M. J. *Top. Stereochem.* **1994**, *21*, 1–57; (e) Walker, B. J. *Organophosphorus Chem.* **1996**, *27*, 264–307.
4. (a) El-Batta, A. M.; Jiang, C.; Zhao, W.; Anness, R.; Cooksy, A. L.; Bergdahl, M. *J. Org. Chem.* **2007**, *72*, 5244–5259; (b) Dambacher, J.; Zhao, W.; El-Batta, A.; Anness, R.; Jiang, C.; Bergdahl, M. *Tetrahedron Lett.* **2005**, *46*, 4473–4477.
5. Fodor, G.; Tömösközi, I. *Tetrahedron Lett.* **1961**, *2*, 579–582.
6. (a) Nonnenmacher, A.; Mayer, R.; Plieninger, H. *Liebigs Ann. Chem.* **1983**, 2135–2140; (b) Isaacs, N. S.; El-Din, G. N. *Tetrahedron Lett.* **1987**, *28*, 2191–2192.
7. Patil, V. J.; Mävers, U. *Tetrahedron Lett.* **1996**, *37*, 1281–1284.
8. (a) House, H. O.; Jones, V. K.; Frank, G. A. *J. Org. Chem.* **1964**, *29*, 3327–3333; (b) Fliszár, S.; Hudson, R. F.; Salvadori, G. *Helv. Chim. Acta* **1964**, *47*, 159–162; (c) Rüchardt, C.; Panse, P.; Eichler, S. *Chem. Ber.* **1967**, *100*, 1144–1164; (d) Corey, E. J.; Clark, D. A.; Goto, G.; Marfat, A.; Mioskowski, C.; Samuelsson, B.; Hammarström, S. *J. Am. Chem. Soc.* **1980**, *102*, 1436–1439; (e) Marriott, D. P.; Bantick, J. R. *Tetrahedron Lett.* **1981**, *22*, 3657–3658; (f) Stafford, J. A.; McMurry, J. E. *Tetrahedron Lett.* **1988**, *29*, 2531–2534; (g) Westman, G.; Wennerström, O.; Raston, I. *Tetrahedron* **1993**, *49*, 483–488; (h) Hooper, D. L.; Garagan, S.; Kayser, M. M. *J. Org. Chem.* **1994**, *59*, 1126–1128; (i) Thiemann, T.; Thiemann, C.; Sasaki, S.; Vill, V.; Mataka, S.; Tashiro, M. *J. Chem. Res. Synop.* **1997**, 248–249.
9. Boulaire, V. L.; Grée, R. *Chem. Commun.* **2000**, 2195–2196.
10. Harcken, C.; Martin, S. F. *Org. Lett.* **2001**, *3*, 3591–3593.
11. Sartillo-Piscil, F.; Vargas, M.; Anaya de Parrodi, C.; Quintero, L. *Tetrahedron Lett.* **2003**, *44*, 3919–3921.
12. Dr. Shaw has also used the term SHOWO for the same synthetic purpose: Reddy, L. V. R.; Reddy, P. V.; Shaw, A. K. *Tetrahedron: Asymmetry* **2007**, *18*, 542–546.
13. (a) Gesson, J. P.; Jacquesy, J. C.; Mondon, M. *Tetrahedron Lett.* **1987**, *28*, 3945–3948; (b) Gesson, J. P.; Jacquesy, J. C.; Mondon, M. *Tetrahedron* **1989**, *45*, 2627–2640; (c) Bessodes, M.; Benamghar, R.; Antonakis, K. *Carbohydr. Res.* **1990**, *200*, 493–496; (d) Dongsoo, K. *Agric. Chem. Biotechnol.* **2005**, *49*, 62–64; See also: (e) Baskaran, S.; Vasu, J.; Kodukulla, R. P. K.; Trivedi, G. K. *Tetrahedron* **1996**, *52*, 4515–4526; (f) Subramanian, B.; Griski, K. T. *J. Chem. Res.* **1995**, 308–309; (g) Tadano, K.-i.; Shimada, K.-i.; Miyake, A.; Ishihara, J.; Ogawa, S. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 3978–3986.
14. Tronchet, J. M.; Gentile, B. *Helv. Chim. Acta* **1979**, *62*, 2091–2098.
15. (a) Brimacombe, J. S.; Hanna, R.; Kabir, A. K. M. S.; Bennett, F.; Taylor, I. D. *J. Chem. Soc., Perkin Trans. 1* **1986**, 815–821; (b) Brimacombe, J. S.; Kabir, A. K. M. S. *Carbohydr. Res.* **1986**, *150*, 35–51.
16. Shing, T. K. M.; Tsui, H.-Ch.; Zhou, Z.-H. *J. Org. Chem.* **1995**, *60*, 3121–3130.
17. We mean 'partially' because in those reports E-selectivities are observed: see Ref. 4.
18. Wu, W.; Wu, Y. *J. Org. Chem.* **1993**, *58*, 3586–3588.
19. Bisseret, P.; Boiteau, J.-G.; Eustache, J. *Tetrahedron Lett.* **2003**, *44*, 2351–2354.
20. Maryanoff, B. E.; Reitz, A. B.; Duhl-Emswiler, B. A. *J. Am. Chem. Soc.* **1985**, *107*, 217–226.
21. (a) Gallagher, M. J. In *Phosphorus-31 NMR Spectroscopy in Stereochemical Analysis*; Verkade, J. G., Quin, L., Eds.; VCH: Deerfield Beach, FL, 1987. Chapter 9; (b) Bentrude, W. G. Steric and Stereoelectronic Effects in 1,3,2-Dioxaphosphorinanes. In *Methods in Stereochemical Analysis*; Juaristi, E., Ed.; VCH: New York, 1995; (c) Frank, É.; Wolfling, J. *Curr. Org. Chem.* **2007**, *11*, 1610.
22. (a) Sartillo-Piscil, S.; Cruz-Gregorio, S.; Sánchez, M.; Höpfl, H.; Anaya de Parrodi, C.; Quintero, L. *Tetrahedron* **2003**, *59*, 4077–4083; (b) Cruz-Gregorio, S.; Sánchez, M.; Clara-Sosa, A.; Bérnes, S.; Quintero, L.; Sartillo-Piscil, F. *J. Org. Chem.* **2005**, *70*, 7107–7113; (c) Hermans, R. J. M.; Buck, H. M. *J. Org. Chem.* **1988**, *53*, 2077–2084; (d) Neeser, J.-T.; Tronchet, J. M. J.; Charollais, E. J. *Can. J. Chem.* **1983**, *61*, 1387–1396.
23. Nelson, K. A.; Bentrude, W. G.; Setzer, W. N.; Hutchinson, J. P. *J. Am. Chem. Soc.* **1987**, *109*, 4058–4064.
24. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. GAUSSIAN 03, Revision E.01, Gaussian Inc., Wallingford CT, 2004.
25. Other phosphorinane conformations were found close in energy, however the ones showed in Scheme 6 represent the conformation that either controlling or destabilizing Z-selectivity.
26. (a) Gerlt, J. A.; Gutterson, N. I.; Datta, P.; Belleau, B.; Penney, C. I. *J. Am. Chem. Soc.* **1980**, *102*, 1655–1665; (b) Gerlt, J. A.; Gutterson, N. I.; Drews, R. E.; Sokolow, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 1655–1670.