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A Convergent Strategy Toward Linear *Cis*-Skipped Polyenes

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Abstract: An easy preparation of symmetric Cis-skipped polyenic hydrocarbons **1** to **5** combining the controlled classical Wittig reaction or the oxidative dimerization of phosphoranes is described.
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Cis-skipped double bonds are the main feature of polyunsaturated fatty acids (PUFA's). To study the ^{13}C NMR of ethylenic carbon atoms of PUFA's and related compounds[1] we elaborated a complete data base of *cis*-skipped functionalized polyenic compounds. This synthetic work generated several efficient procedures that are of general interest in this field.

A recent paper from Noiret and *Coll*[2] devoted to the preparation of symmetric *Z* olefins by ylids autoxidation, prompts us to report herein our own results on the topic. The selective syntheses of unsaturated hydrocarbons **1** to **5**[3] show the usefulness of the oxidative dimerization of phosphonium salts when combined with the stereoselective Wittig reaction that forms the base of our strategy to build up *cis* double bonds. We used the C3 and C6 homologating agents **A** and **B**,[4] which respectively were condensed onto hexanal and ylids **8**. The resulting ethylenic acetals **6** and **9** were converted to aldehyde **7**, precursor of phosphorane **8a**, and to aldehyde **10**.[5] Final Wittig reaction of the aldehydes with phosphorane **11** led to polyenes **2** and **4**, while condensation of **10** with **8a** allowed to synthesize the pentaene **5** in good yields (Scheme 1).

Cis-6-dodecene **1** and trienes **3** were prepared by oxidative dimerization of phosphorane **11** and mono-unsaturated phosphoranes **8a** and **8b**. This dimerization allowed the general strategy to converge toward the full set of polyenes. During previous work on the synthesis of PUFA's using the Wittig reaction,[6] we observed that autoxidation of ylids occurred under the reaction conditions, leading to symmetric olefins as by-products. This side reaction is due to the presence of minute amount of O_2 contained either in the solvent, the phosphonium salt or the base.[7] Condensation of the ylid and O_2 gives a dioxaphosphetane which undergoes a *syn* ring cleavage that leads to an aldehyde and triphenylphosphine oxide. The aldehyde further reacts with a second ylid molecule, through a classical Wittig reaction, to furnish the symmetric Z-alkene.

Under controlled reaction conditions the oxidative dimerization of phosphoranes can be synthetically useful and we took advantage of this feature to prepare the key C6 homologating agent **B** from **A**.[4b] Then high dilution (0.05 M) and low temperature (-80°C) while bubbling oxygen into solutions of **11** or **8** stereoselectively led to *cis* olefins **1** and **3**, obtained in good yields.[8] No trace of trans or conjugated compounds could be found by ^{13}C and ^{1}H NMR analysis even of the crude reaction mixture.[9]

Both Wittig reaction and ylid autoxidation can lead to quite pure Z-olefins with NaNMDS as the base,[10] providing that they are run at low temperature (-80°C) and high dilution (0.05 M). The stereochemical

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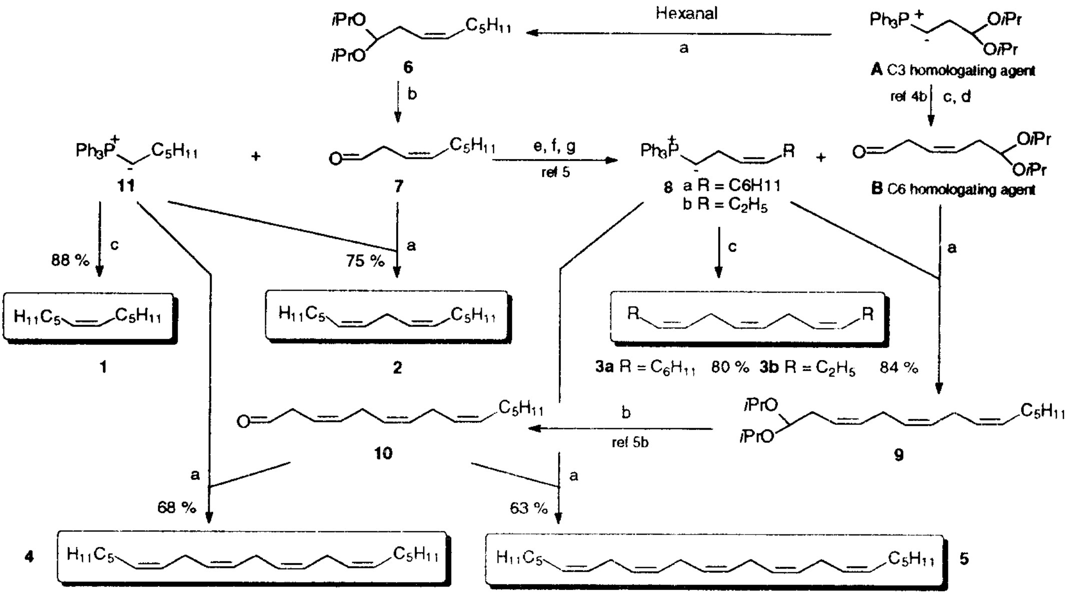
outcome of the Wittig reaction has been bound to these factors,[11] and we found that the autoxidation process is totally stereoselective under the same conditions, with bubbling O_2 rather than by contact with air.



Scheme 1: a: $NaN(SiMe_3)_2$, THF, -80°C; b: TsOH, THF, Δ; c: $NaN(SiMe_3)_2$, THF, -80°C, O_2; d: HCOOH, Acetone, Δ; e: $LiAlH_4$, THF, -30°C; f: Ph_3PBr_2, CH_3CN, rt; g: Ph_3P, CH_3CN, reflux.

The convergent strategy combining Wittig reaction and autoxidation of phosphoranes enabled us to prepare a complete set of unsaturated hydrocarbons, some of them new,[12] featuring one to five *Z* double bonds. It can be easily expanded to functionalized compounds to afford a general method in this field.

References and notes

1 Sandri, J.; Soto, T.; Gras, J-L.; Viala, J. *Magnetic Resonance in Chemistry*, under the press.

2 Poulain, S.; Noiret, N.; Patin, H. *Tetrahedron Lett.* **1996**, *37*, 7703-06.

3 Other preparation of **1**: ref 2. Matsuda, H.; Schlosser, M. Tetrahedron **1988**, *44*, 2875-82. Compound **2**: Jeffery, T.; Gueugnot, S.; Linstrumelle, G. *Tetrahedron Lett* **1992**, *33*, 5757-60.

4 a) Viala, J.; Santelli, M. *Synthesis* **1988**, 395-397. b) Sandri, J.; Viala, J. *Synthesis* **1995**, 271-275

5 a) Compounds **7** and **8a**: Pons, J-M.; Pommier, A.; Lerpiniere, J.; Kocienski, P. *J. Chem. Soc. Perkin Trans 1* **1993**, 1549-1551. b) Compounds **8b** and **10**: Sandri, J.; Viala, J. *J. Org. Chem.* **1995**, *60*, 6627-30.

6 Viala, J.; Sandri, J. *Tetrahedron Lett.* **1992**, *33*, 4897-90. Viala, J.; Labaudinière, R. *J. Org. Chem.* **1993**, *58*, 1280. and ref 3 and 4b.

7 Bestmann, H.J. *Angew. Chem.* **1960**, *72*, 34. Bestmann, H.J.; Kratzer, O. *Chem. Ber.* **1963**, *96*, 1899-1906. Bestmann, H.J. *Pure Appl. Chem.* **1979**, *51*, 515.

8 Typical procedure: A 0.6 M solution of $NaN(Me_3Si)_2$ in toluene (2.56 mL) is added to a suspension of 3-hexenyltriphenylphosphium bromide (658 mg) in THF (14 mL) at -30°C, then stirred 30 min at 0°C then 30 min at rt. After cooling at -80°C, oxygen was bubbled into the ylide solution for few minutes, then warming up to rt and classical work-up led to the unsaturated hydrocarbon **3b** (107 mg, 84%). ^1H NMR (200 MHz, δ ppm) (5.55-5.25 (6H, m), 2.83-2.78 (4H, br t, $J = 5$ Hz), 2.15-2.00 (4H, br quint, $J = 7.5$ Hz), 0.97 (6H, t, $J = 7$ Hz). ^{13}C NMR (52.32 MHz, δ ppm) 132.04 (2C), 128.35 (2C), 127.18 (2C), 25.58 (2C), 20.61 (2C), 14.34 (2C).

9 All compounds gave satisfactory analytical and spectral data.

10 Bestmann, H.J.; Werner, S.; Vostrowsky, O. *Chem. Ber.* **1979**, *109*, 1694-700.

11 Schlosser, M.; Schaub, B.; de Oliveira-Neto, J.; Jeganathan, S. *Chimia* **1986**, *40*, 244-45. Reitz, A.; Nortey, S.; Jordan, A.; Mutter, M.; Maryanoff, B. *J.Org.Chem. 51*, **1986**, 3302-08

12 **3a** and **4** have been described in literature: Gunstone, F.D.; Pollard, M.R.; Scrimgeour, C.M.; Vedenayagam, H.S. Chem. Phys. Lipids **1977**, *18*, 115-29. Nissinen, R.; Sewon, P. *Phytochemistry* **1994**, *37*, 179-182.

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