Pergamon

Tetrahedron Letters 39 (1998) 2335–2338

TETRAHEDRON LETTERS

Stereocontrolled Access to Polyenol Ethers by Conjugate Elimination/Ring Fission Reactions.

David Lançois and Jacques Maddaluno.*

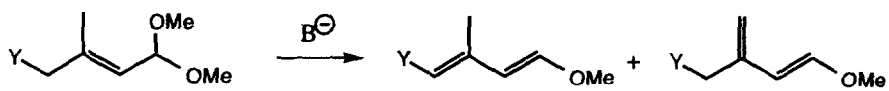
Laboratoire des Fonctions Azotées et Oxygénées Complexes de l'IRCOF

Université de Rouen, F-76821 Mont St Aignan (France)

Received 10 December 1997; accepted 19 January 1998

Abstract: Conjugate elimination reactions are able to transform dienic acetals into the corresponding trienol diethers and efficiently convert γ-alkoxy α,β-unsaturated epoxides into hydroxy dienol ethers.

Their occurence in many natural products of biological interest[1] as well as in organic conductors exhibiting non-linear optical properties[2] places trienic compounds at the heart of converging attentions. Functionalizing these compounds with such sensitive groups as enol ethers or enamines remains however a challenging goal in synthesis because of the extreme fragility of the polyenic systems obtained. The long-lasting interest of our laboratory in terpenoid and polyethylenic chemistry[3] has led us to propose a general method relying on a base-triggered conjugate elimination reaction[4] on α,β-unsaturated γ-functionalized acetals to prepare 1,4-disubstituted 1,3-dienes (Scheme 1).[5]



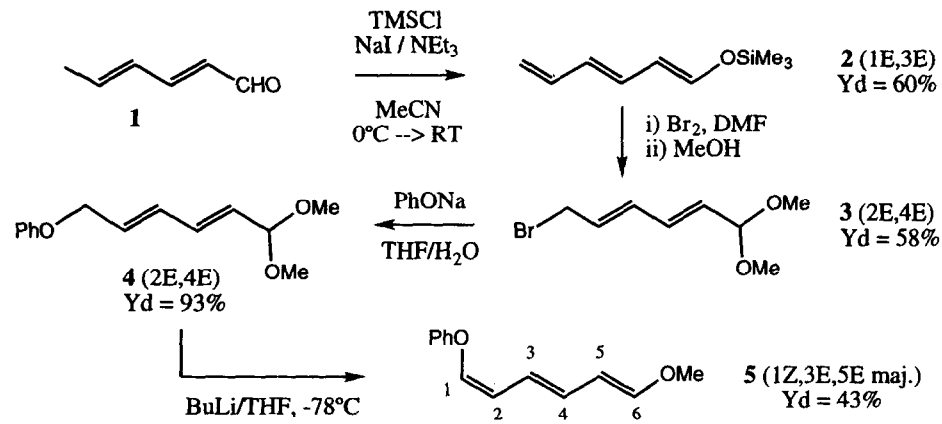
Y = OAr, SAr, NR^1R^2 Y = OAr, SAr, NR^1R^2 Y = NR^1R^2

Scheme 1.

Since this reaction increases the number of double bonds in a rather simple way, its application to a diene-triene conversion could constitute an attractive route to these compounds. We have thus first considered extensions of this reaction to ω-eliminations, that would allow, through the switch of two double bonds, a direct transformation of functionalized dienic acetals into corresponding trienol ethers. A linear and a branched dienic substrates have been prepared according to Schemes 2 and 3. The linear one has been obtained converting commercial EE-sorbaldehyde **1** into its EE silyl enol ether **2**.[6] Bromination[6c,7] of this triene in dry DMF at -30°C followed by methanol quenching then aqueous basic work-up provides in a fair 58% yield the expected EE dienic bromoacetal **3**. The allylic bromine is easily substituted by sodium phenoxide in biphasic conditions at room temperature to give dienic acetal **4**, the first substrate for our study. Its low-temperature deprotonation by

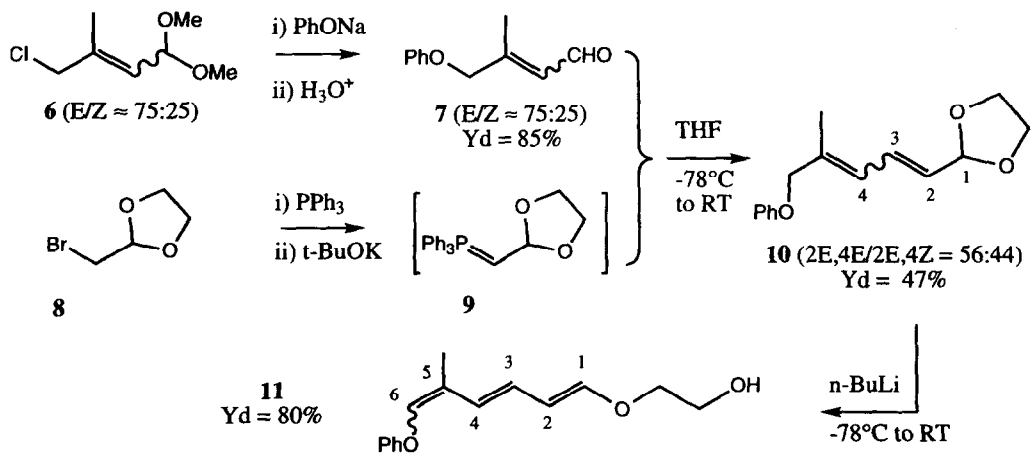
0040-4039/98/$19.00
PII: S0040-4039(98)00195-6

n-BuLi[5] followed by a rapid aqueous work-up yields trienol diether **5** as a mixture of isomers in which the 1Z,3E,5E one is by far dominant.[8]



Scheme 2.

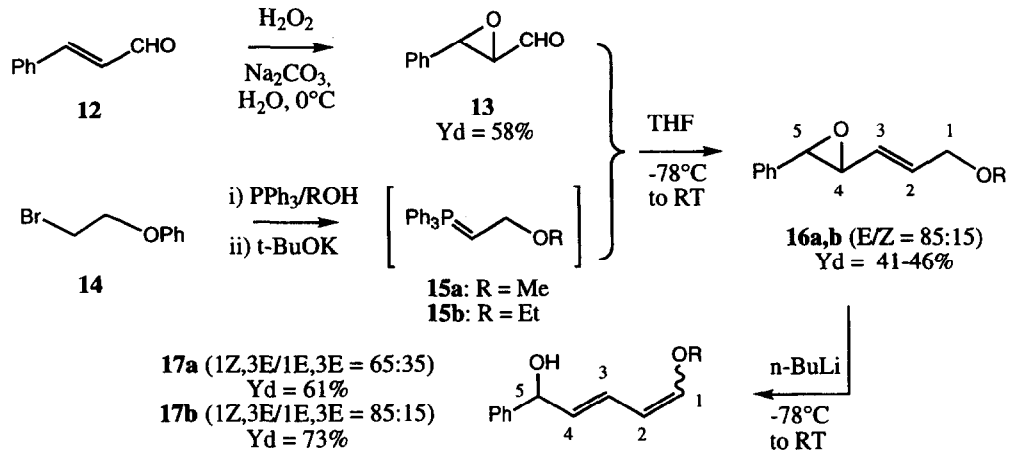
The branched acetal **10** was prepared from chloroacetal **6**[9] by allylic chlorine substitution followed by acidic hydrolysis (Scheme 3). The phenoxy aldehyde **7** was obtained with 85% yield in a 75:25 E/Z ratio, identical to that in **6**. A Wittig reaction involving ylid **9** derived from potassium t-butylate deprotonation of corresponding functionalized phosphonium bromide[10] gives access to dienic acetal **10**. While the newly created double bond is of pure E configuration, the 4Z relative abundance is increased with respect to that in **7**. The n-BuLi induced deprotonation in THF gives access to the branched trienolether **11** in excellent yield. A ^{1}H NMR analysis on this product indicates that the major isomer (≥ 80%) is 1E,3E[11], the 5,6 double bond configuration remaining to be determined.



Scheme 3.

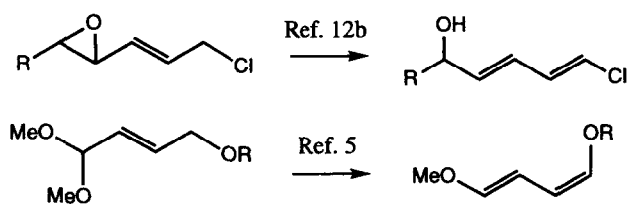
This class of reactions could also be extended to the conjugate opening of α,β-unsaturated heterocycles. The rapid ring fission undergone by homoallyl (or homobenzyl) cyclic ethers has been described[12a] and has

been very recently applied to unsaturated epoxides and 1,3-dioxolanes.[12b] We have decided to prepare α,β-unsaturated epoxides **16** following a strategy relying once again on a Wittig-type coupling between cinnamaldehyde epoxide[13] **13** and phosphonium ylids **15** (Scheme 4). Those have been prepared from commercial bromophenetol **14** and triphenylphosphine at reflux of methanol or ethanol.[14] The phosphonium bromides thus obtained, that bear a methoxy or an ethoxy group, respectively, can be deprotonated by potassium terbutylate at -78°C in THF, providing the unsaturated epoxides **16** in fair yields and with a good E control of the newly formed 2,3 double bond. When treated by n-butyllithium in conditions identical to those mentionned above, **16** yield dienes **17** in good yields and stereocontrols depending on the nature of the alkoxy group.



Scheme 4.

Interestingly, the 3,4 double bond is pure E in both cases; but while the methoxy ether **16a** affords a relatively mediocre control of the 1,2 double bond (1Z,3E/1E,3E ≈ 65:35), its ethoxy counterpart **16b** improves the 1Z,3E/1E,3E ratio up to 85:15.[15] The Z control of the 1,2 double bond is noteworthy as i) it is opposite to the total E selectivity reported by Yadav et al.[12b] for a comparable reaction applied to a set of allylic chlorides; ii) it matches our own observations on deprotonation-elimination reactions on γ-alkoxy and aryloxy unsaturated acetals[5] (Scheme 5).



Scheme 5.

The allylic ether function thus seems to play a key role in the determination of the newly created double bond configuration. Possible origins of this phenomenon will be discussed in a full paper to come.[16]

Acknowledgments. The authors thank Dr Lucette Duhamel for helpful discussions. We also thank Rhône-Poulenc Chimie for generous samples of chloroacetal **6**.

REFERENCES AND NOTES:

1. Recent exemples: a) Crousse, B.; Alami, M.; Linstrumelle, G. *Tetrahedron Lett.* **1997**, *38*, 5297-5300. b) Solladié, G.; Somny, F.; Colobert, F. *Tetrahedron: Asymm.* **1997**, *8*, 801-810. c) Soullez, D.; Plé, G.; Duhamel, L. *J. Chem. Soc. Perkin Trans. I* **1997**, 1639-1645.
2. a) Spangler, C. W.; Mc Coy, R. K.; Dembek, A. A.; Sapochak, L. S.; Gates, B. D. *J. Chem. Soc. Perkin Trans. I* **1989**, 151-154. b) Spangler, C. W.; Rathunde, A. *J. Chem. Soc. Chem. Commun.* **1989**, 26-27. c) Knoll, K.; Schrock, R.R. *J. Am. Chem. Soc.* **1989**, *111*, 7989-8004. d) Spangler, C. W.; Liu, P. K.; Dembek, A. A.; Havelka, K. O. *J. Chem. Soc. Perkin Trans. 1*, **1991**, 799-802. e) Bublitz, G. U.; Ortiz, R.; Marder, S. R.; Boxer, S. G. *J. Am. Chem. Soc.* **1997**, *119*, 3365-3376.
3. *See inter alia:* a) Duhamel, L.; Duhamel, P.; Lecouvé, J. P. *Tetrahedron* **1987**, *43*, 4349-4358. b) Duhamel, L.; Ancel, J.E. *Tetrahedron* **1992**, *48*, 9237-9240. c) Duhamel, L.; Duhamel, P.; Plé, G.; Ramondenc, Y. *Tetrahedron Lett.* **1993**, *34*, 7399-7400.
4. Mioskowski, C.; Manna, S. ; Falck, J. R. *Tetrahedron Lett.* **1984**, *25*, 519-522.
5. a) Maddaluno, J.; Gaonac'h, O.; Marcual, A.; Toupet, L.; Giessner-Prettre, C. *J. Org. Chem.* **1996**, *61*, 5290. b) Guillam, A.; Maddaluno, J.; Duhamel, L. *J. Chem. Soc. Chem. Commun.* **1996**, 1295-1296. c) Martin, C.; Maddaluno, J.; Duhamel, L. *Tetrahedron Lett.* **1996**, *37*, 8169-8172.
6. a) Cazeau, P.; Duboudin, F.; Moulines, F.; Babot, O.; Dunogues, J. *Tetrahedron* **1987**, *43*, 2075-2088. b) Poirier, J. M.; Hennequin, L. *Synth. Commun.* **1985**, *15*, 217. c) Ramondenc, Y. Ph.D. Thesis, Université de Rouen, 1992.
7. Rhône-Poulenc Industries, French Patent no. 7700855 (1977).
8. Triene **5** is very prone to hydrolysis. The precise amounts and configurations of the other isomers have not be determined yet.
9. Acetal **6** is an industrial intermediate (Rhône-Poulenc Chimie) available as a ≈ 75:25 E/Z mixture.
10. The phosphonium bromide precursor of **9** was prepared from bromodioxolane **8** according to Cresp, T. M.; Sargent, M. V.; Vogel, P. *J. Chem. Soc. Perkin Trans. 1*, **1974**, 37-41.
11. ^{1}H NMR (200MHz, $CDCl_3$) for **11**: δ (ppm) 1.80 (3H, s), 3.85 (4H, s), 5.71 ($1H^2$, dd, J = 12.3, 10.8Hz), 6.10 ($1H^3$, dd, J = 10.8, 15.2Hz), 6.27 ($1H^6$, s), 6.64 ($1H^1$, d, J = 12.3Hz), 6.68 ($1H^4$, d, J = 15.2Hz), 7.02 (3H, m), 7.23 (2H, m).
12. a) Margot, C.; Rizzolio, M.; Schlosser, M. *Tetrahedron* **1990**, *46*, 2411-2424. b) Yadav, J. S.; Barma, D. K.; Dutta, D. *Tetrahedron Lett.* **1997**, *38*, 4479-4482.
13. Hu, Y.; Harada, A.; Takahashi, S. *Synth.Commun.* **1988**, *18*, 1607-1610.
14. Schweiser, E. E.; Bach, R. D. *J. Org. Chem.* **1964**, *29*, 1746-1751.
15. ^{1}H NMR (200MHz, $CDCl_3$) for **17a**: 1Z,3E isomer: δ (ppm) 3.65 (3H, MeO, s), 5.05 ($1H^2$, dd, J = 5.8, 12.5Hz), 5.22 ($1H^5$, d, J = 4.0Hz), 5.62 ($1H^4$, dd, J= 4.5, 15.0Hz), 5.93 ($1H^1$, d, J = 5.8Hz), 6.64 ($1H^3$, dd, J = 12.5, 15.0Hz), 7.35 ($5H_{Ar}$, m). 1E,3E isomer: δ (ppm) 3.57 (3H, MeO, s), 5.19 ($1H^5$, m), 5.49 ($1H^2$, dd, J = 11.7, 12.0Hz), 5.66 ($1H^4$, m), 6.15 ($1H^3$, dd, J = 11.7, 12.0Hz), 6.61 ($1H^1$, d, J = 12.0Hz), 7.35 ($5H_{Ar}$, m). **17b**: 1Z,3E isomer: δ (ppm) 1.26 ($3H_{Et}$, t, J = 6.3Hz), 3.85 ($2H_{Et}$, q, J = 6.3Hz), 5.04 ($1H^2$, dd, J = 6.0, 10.4Hz), 5.24 ($1H^5$, d, J = 7.1Hz), 5.68 ($1H^4$, dd, J = 7.1, 15.5Hz), 5.99 ($1H^1$, d, J = 6.0Hz), 6.65 ($1H^3$, dd, J = 15.5, 10.4Hz), 7.30 ($5H_{Ar}$, m).
16. Guillam, A.; Maddaluno, J.; Toupet, L. *in preparation.*