Pergamon

Tetrahedron Letters 40 (1999) 5161–5164

TETRAHEDRON LETTERS

Selective oxidation of primary silyl ethers and its application to the synthesis of natural products

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Received 22 April 1999; accepted 13 May 1999

Abstract

Primary TMS or TES ethers, in the presence of secondary TMS or TES ethers, are selectively oxidized to the corresponding aldehydes under Swern conditions. A short synthesis of key intermediates towards various natural products has been achieved.

The chemoselective oxidation of a primary alcohol function in the presence of a secondary one represents a problem of general interest in organic synthesis.[1,2] The classical approach requires protective group manipulation[3,4] or selective cleavage[5] prior to oxidation. The direct oxidation of primary silyl ethers to aldehydes, in the presence of the same secondary ones, represents one of the possible solutions to this problem.[6] $CrO_3 \cdot 2Py$ has been used for the selective oxidation of primary TMS ethers in the presence of a secondary TMS ether.[7,8] The Swern oxidation[9] has been applied to the synthesis of the trimethylsilylated and triethylsilylated Corey aldehyde showing selectivity due to steric factors.[10–13] However, other reports demonstrated that the Swern reagent can oxidize both primary and secondary TMS and TES ethers.[6,14,15]

In this communication we wish to report that TMS or TES protected 1,2-diols, 1,2,3-triols and polyhydroxy compounds are selectively oxidized to the silyloxy aldehydes by the Swern reagent even if used in excess. As shown in Scheme 1, Swern oxidation produced the silyloxy aldehydes **1a–8a** in good isolated yields (64–86%).[16] These intermediates were used in short syntheses of biologically active compounds such as lipoxins,[17–20] leukotriene B_4,[21] di-HETEs,[17] HETEs[17] and FK-506.[22] Reagents based on CrO_3 were also tested and $CrO_3 \cdot 2Py$ was able to smoothly oxidize TES ethers selectively in the primary position (e.g. Scheme 1, compound **9**). In this particular case $CrO_3 \cdot 2Py$ (64% isolated yield) was superior to the Swern reagent (42% isolated yield containing 27% of ketone). PCC showed selectivity in the case of the TMS or TES protected triols **4**, **5**, **6** and **7**; the silyloxy aldehydes were obtained in up to

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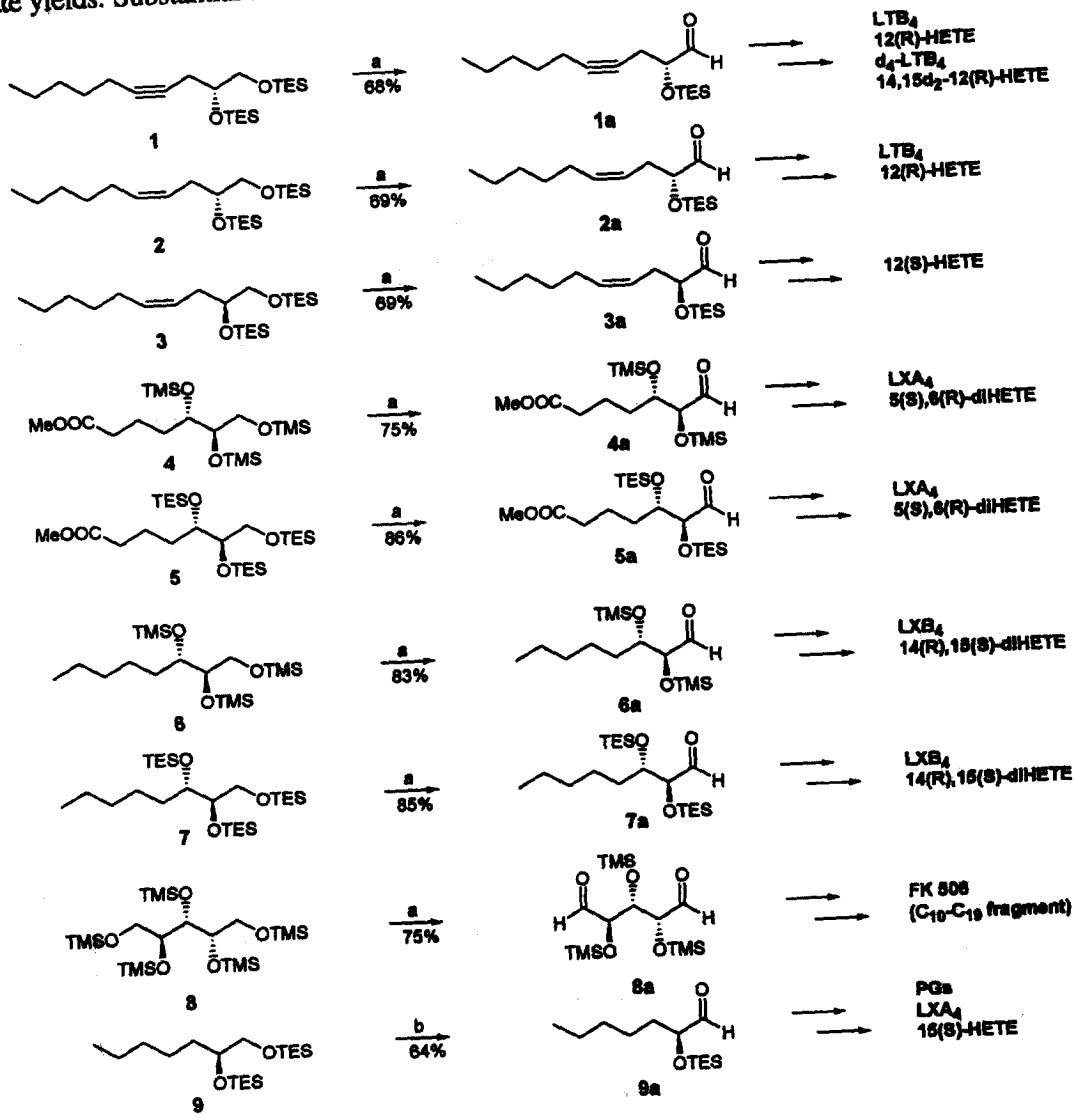
0040-4039/99/$ - see front matter
PII: S0040-4039(99)00956-9

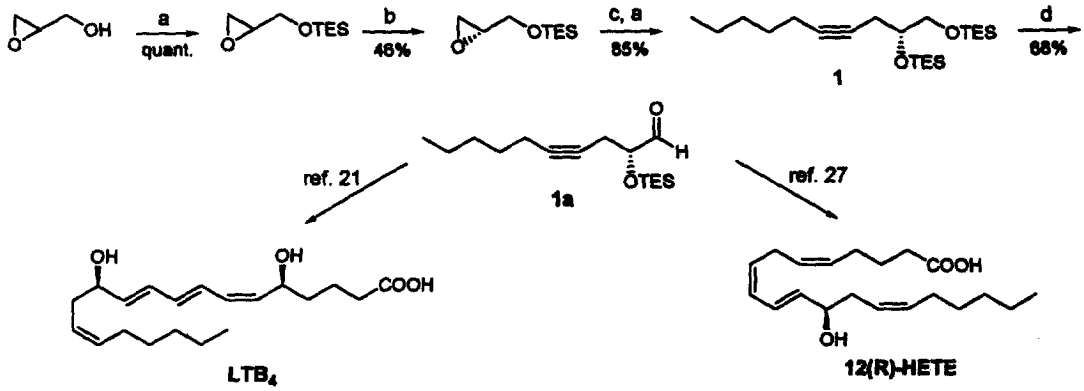
70% isolated yield. However, the di-TES ethers **1** and **9** gave with PCC or PDC the aldehydes in only moderate yields. Substantial amounts of ketone (~35% versus aldehyde) were co-produced.



Scheme 1. [23] (a) DMSO/$(COCl)_2$, CH_2Cl_2, Et_3N, –70°C; (b) $CrO_3 \cdot 2Py$, CH_2Cl_2, 0°C → rt

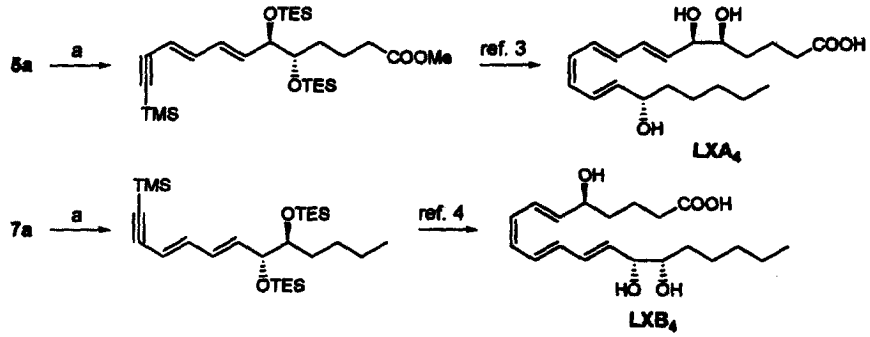
Scheme 2 outlines a short synthesis of leukotriene B_4 and 12(*R*)-HETE from **1a**. The starting chiral TES-glycidol[24] was obtained with >99% ee using Jacobsen's hydrolytic kinetic resolution with 1% (*S,S*)-salen-Co catalyst.[25] Nucleophilic addition of 1-heptynyllithium in the presence of $BF_3 \cdot Et_2O$ followed by silylation gave **1** that was converted to **1a** by Swern oxidation. Wittig reaction with the chiral C_1–C_{10} phosphonate, according to Nicolaou, followed by Lindlar hydrogenation and deprotection gave LTB_4.[21] 12(*R*)-HETE was obtained from **1a** in a similar way as reported in the literature.[26,27] The same intermediate **1a** was used for the preparation of the deuterated analogues. 12(*S*)-HETE was synthesized using the (*R,R*)-salen-Co catalyst.

Scheme 3 outlines the short synthesis of LXA_4 and LXB_4 from **5a** and **7a**. The chiral triols were obtained in high yield (90%) from 2-deoxy-D-ribose as described earlier.[28,29] Wittig reaction and



Scheme 2. [23] (a) TESCl, imidazole, Et_3N, DMF; (b) (*S,S*)-(salen)Co(III)(AcO) catalyst, H_2O, ether; (c) 1-heptyne, *n*-BuLi, $BF_3 \cdot Et_2O$, THF, –78°C; (d) DMSO/$(COCl)_2$, CH_2Cl_2, Et_3N, –70°C

Pd(0)/Cu(I) coupling, according to Nicolaou, followed by Lindlar reduction and deprotection, gave lipoxin A_4[3,29,30] or B_4.[4]



Scheme 3. [23] (a) TMS–C≡C–CH=CH–CH_2PPh_3Br, *n*-BuLi, THF, –78°C

The di-aldehyde **8a**, obtained from the TMS protected D-arabitol **8**, was converted to the C_{10}–C_{19} fragment of FK 506 using simultaneous homologation in two directions.[22] Compound **9a** was transformed to the TES ether of (*S*)-1-octyn-3-ol via: (a) CBr_4/PPh_3, (b) *n*-BuLi sequence,[31] a key intermediate in the synthesis of PGs, LXA_4 and 15(*S*)-HETE.[17]

In summary, the direct oxidation of primary TMS and TES ethers, in the presence of secondary ones, has been achieved and applied to the synthesis of biologically active compounds. The combination of Jacobsen's hydrolytic kinetic resolution, as described for TES-glycidol, with this method provides an easy access to optically pure building blocks. Further applications will be reported in due course.

Acknowledgements

Financial support of this research in part by Laboratorios Lasa S.A., Barcelona (Spain), and the Department of Cell Biology UMDNJ-SOM is gratefully acknowledged.

References

1. Tomioka, H.; Takai, K.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 1605–1608.

2. de Nooy, A. E. J.; Besemer, A. C.; Bekkum H. v. *Synthesis* **1996**, 1153–1174.
3. Nicolaou, K. C.; Veale, C. A.; Webber, S. E.; Katerinopoulos. *J. Am. Chem. Soc.* **1985**, *107*, 7515–7518.
4. Nicolaou, K. C.; Webber, S. E. *Synthesis* **1986**, 453–461.
5. Lee, A. S.-Y.; Yeh, H.-C.; Shie, J.-J. *Tetrahedron Lett.* **1998**, *39*, 5249–5252.
6. Muzart, J. *Synthesis* **1993**, 11–27.
7. Mahrwald, R.; Theil, F.; Schick, H.; Schwarz, S.; Palme, H.-J.; Weber, G. *J. Prakt. Chem.* **1986**, *328*, 777–783.
8. Mahrwald, R.; Theil, F.; Schick, H.; Palme, H.-J.; Nowak, H.; Weber, G.; Schwarz, S. *Synthesis* **1987**, 1012–1013.
9. Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165–185.
10. Tolstikov, G. A.; Miftakhov, M. S.; Adler, M. E.; Komissarova, N. G.; Kuznetsov, O. M.; Vostrikov, N. S. *Synthesis* **1989**, 940–942.
11. Tolstikov, G. A.; Miftakhov, M. S.; Alde, M. E.; Valeev, F. A.; Vostrikov, N. S. *Zh. Org. Khim.* **1987**, *23*, 1564–1565.
12. Mahrwald, R.; Schick, H.; Vasil'eva, L. L.; Pivnitsky, K. K.; Weber, G.; Schwarz, S. *J. Prakt. Chem.* **1990**, *332*, 169–175.
13. Tidwell, T. T. *Synthesis* **1990**, 857–870.
14. Tolstikov, G. A.; Miftakhov, M. S.; Vostrikov, N. S.; Komissarova, N. G.; Adler, M. E.; Kuznetsov, O. M. *Zh. Org. Khim.* **1988**, *24*, 224–225.
15. Afonso, C. M.; Barros, M. T.; Maycock, C. D. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1221–1223.
16. A representative experimental procedure is as follows: a solution of oxalyl chloride (1.1 ml, 2.0 M in dichloromethane, 2.2 mmol) was added dropwise to dimethyl sulfoxide (0.31 ml, 4.4 mmol) in dichloromethane (2 ml) at –70°C. After 15 min, 1 (0.2 g, 0.5 mmol) in dichloromethane (2 ml) was added and stirring was continued for 20 min at –70°C followed by 20 min at –40°C. Triethylamine (1.05 ml, 7.5 mmol) was added at –70°C and the reaction was allowed to reach rt. The mixture was diluted with water, extracted with dichloromethane and the organic layer was separated, washed with brine and dried (Na_2SO_4). The product was purified by flash chromatography in the presence of 5% triethylamine. The TMS ethers were oxidized with 1.2 equiv. of oxalyl chloride and 2.4 equiv. of dimethyl sulfoxide at –70°C.
17. Nicolaou, K. C.; Ramphal, J. Y.; Petasis, N. A.; Serhan, C. N. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1100–1116.
18. Lee, T. H.; Crea, A. E. G.; Gant, V.; Spur, B. W.; Marron, B. E.; Nicolaou, K. C.; Reardon, E.; Brezinski, M.; Serhan, C. N. *Am. Rev. Resp. Dis.* **1990**, *141*, 1453–1458.
19. Christie, P. E.; Spur, B. W.; Lee, T. H. *Am. Rev. Respir. Dis.* **1992**, *145*, 1281–1284.
20. Corey, E. J.; Su, W.; Cleaver, M. B. *Tetrahedron Lett.* **1989**, *32*, 4181–4184.
21. Nicolaou, K. C.; Zipkin, R. E.; Dolle, R. E.; Harris, B. D. *J. Am. Chem. Soc.* **1984**, *106*, 3548–3551.
22. Nakatsuka, M.; Ragan, J. A.; Sammakia, T.; Smith, D. B.; Uehling, D. E.; Schreiber, S. L. *J. Am. Chem. Soc.* **1990**, *112*, 5583–5601.
23. Satisfactory spectroscopic data were obtained for all compounds. Selected spectra: **1a**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.6 (d, *J*=1.8 Hz, 1H), 4.0 (m, 1H), 2.6–2.4 (m, 2H), 2.2–2.0 (m, 2H), 1.5–1.4 (m, 2H), 1.4–1.2 (m, 4H), 1.0 (t, *J*=7.8 Hz, 9H), 0.9 (t, *J*=6.9 Hz, 3H), 0.6 (q, *J*=7.8 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 202.2, 83.0, 76.0, 74.4, 30.9, 28.3, 23.4, 22.0, 18.5, 13.7, 6.4, 4.6; **5a**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.6 (dd, *J*=2.1, 0.4 Hz, 1H), 3.9–3.8 (m, 1H), 3.8 (dd, *J*=3.3, 2.1 Hz, 1H), 3.6 (s, 3H), 2.3 (t, *J*=7.2 Hz, 2H), 1.8–1.4 (m, 4H), 0.9 (2 t, *J*=7.8 Hz, 18H), 0.6 (2 q, *J*=7.8 Hz, 12H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 203.8, 173.7, 80.5, 75.2, 51.4, 33.9, 32.9, 20.8, 6.7, 6.5, 4.9, 4.6; **6a**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.6 (dd, *J*=1.7, 0.8 Hz, 1H), 3.7 (m, 2H), 1.6–1.2 (m, 8H), 0.9 (t, *J*=6.9 Hz, 3H), 0.1 (2 s, 18H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 203.6, 80.7, 75.0, 33.1, 31.7, 25.0, 22.5, 13.9, 0.2, 0.04; **7a**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.6 (dd, *J*=2.1, 0.6 Hz, 1H), 3.9–3.8 (m, 1H), 3.8 (dd, *J*=3.3, 2.1 Hz, 1H), 1.6–1.4 (m, 2H), 1.3–1.2 (m, 6H), 0.9 (t, *J*=7.9 Hz, 3H), 0.9 (t, *J*=8.0 Hz, 18H), 0.5 (q, *J*=8.0 Hz, 12H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 204.0, 80.6, 75.8, 33.6, 31.8, 24.9, 22.5, 13.8, 6.7, 6.5, 4.9, 4.7; **9a**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.6 (d, *J*=1.8 Hz, 1H), 3.9 (dt, *J*=6.1, 1.8 Hz, 1H), 1.7–1.5 (m, 2H), 1.4–1.2 (m, 6H), 1.0 (t, *J*=7.8 Hz, 9H), 0.9 (t, *J*=6.9 Hz, 3H), 0.6 (q, *J*=7.8 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 204.6, 77.0, 32.7, 31.6, 24.1, 22.4, 13.8, 6.7, 4.7.
24. Mori, Y.; Asai, M.; Okumura, A.; Furukawa, H. *Tetrahedron* **1995**, *51*, 5299–5314.
25. Furrow, M. E.; Schaus, S. E.; Jacobsen, E. N. *J. Org. Chem.* **1998**, *63*, 6776–6777.
26. Leblanc, Y.; Fitzsimmons, B. J.; Adams, J.; Perez, F.; Rokach, J. *J. Org. Chem.* **1986**, *51*, 789–793.
27. Taffer, I. M.; Zipkin, R. E. *Tetrahedron Lett.* **1987**, *28*, 6543–6544.
28. Corey, E. J.; Marfat, A.; Munroe, J. E.; Kim, K. S.; Hopkins, P. B.; Brion, F. *Tetrahedron Lett.* **1981**, *22*, 1077–1080.
29. Lee, T. H.; Lympany, P.; Crea, A. E. G.; Spur, B. W. *Biochem. Biophys. Res. Commun.* **1991**, *180*, 1416–1421.
30. Yadav, J. S.; Barma, D. K.; Dutta, D. *Tetrahedron Lett.* **1998**, *39*, 143–146.
31. Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769–3772.