



Pergamon

Tetrahedron Letters 41 (2000) 1959–1962

TETRAHEDRON
LETTERS

Convenient preparation of carbonyl compounds from 1,2-diols utilizing Mitsunobu conditions

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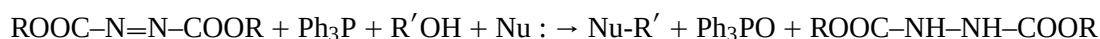
Received 4 August 1999; revised 6 January 2000; accepted 11 January 2000

Abstract

1,1-Disubstituted 1,2-diols are efficiently converted into carbonyl compounds by reaction with triphenylphosphine and diethyl azodicarboxylate. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Mitsunobu reactions; diols; aldehydes.

The Mitsunobu reaction is a useful synthetic tool which allows the conversion of an alcohol function into a wide variety of functional groups.^{1–8}

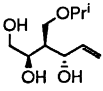
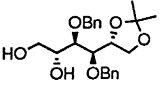
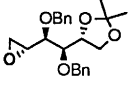
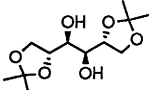
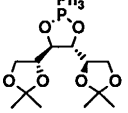
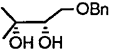
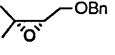
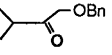
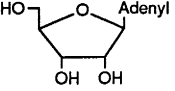
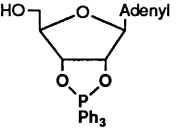
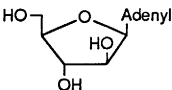
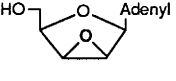
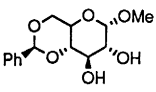
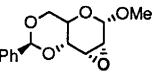


Cyclic compounds are formed when the alcohol molecule contains a suitably placed nucleophile. Epoxides are obtained from acyclic 1,2-diols under the Mitsunobu conditions⁹ and from cyclic *trans*-1,2-diols.^{10–13} Under the same conditions triphenylphosphoranes resulted from cyclic *cis*-1,2-diols.^{11–14} Methyl shikimate (**8a**), having *cis*- and *trans*-diol groups, leads to the corresponding epoxide **8b**, under these conditions.¹⁵

During our research on the synthesis of bioactive compounds from labdane diterpenes we have found that diol **12a** is transformed with excellent yield into drimenal (**12b**)¹⁶ when it is treated with triphenylphosphine (TPP) and diethyl azodicarboxylate (DEAD) in benzene. In order to elucidate the scope and synthetic application of this reaction the behaviour of a variety of 1,2-diols with these reagents has been studied. The results obtained are summarized in Table 1 and compared with those previously reported. As may be seen, monosubstituted and disubstituted 1,2-diols are converted into epoxides or phosphoranes, depending on whether the hydroxyl groups adopt an antiperiplanar (cyclic *trans*-diols and acyclic diols) or an eclipsed conformation (*cis*-diols), respectively. The formation of phosphorane **3b** from diol **3a** can be attributed to the bulky dioxolane groups which prevent the hydroxyl groups from adopting the *anti* disposition. 1,1-Disubstituted-1,2-diols lead to the formation of aldehydes or ketones, depending on whether the less substituted carbon is primary or secondary. Even acyclic 1,1-disubstituted

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Table 1
Reactions of 1,2 diols with the TPP–DEAD system

Diol	Conditions	Product	References
 1a	Benzene, Molecular sieves, 80°C, 14h	 1b (85%)	(9)
 2a	Benzene, rt, 2h	 2b (90%)	
 3a	Benzene, rt, 2h 45 min	 3b (95%)	
 4a	Benzene, rt, 4h	 4b (75%)	 4c (15%)
 5a	Dioxane, 70°C, 40 min	 5b (72%)	(12)
 6a	Dioxane, 70°C, 40 min	 6b (90%)	(12)
 7a	Dioxane, 110°C, 45 min	 7c (87%)	(13)

diols, such as **4a**, yield a significant amount of carbonyl derivative (**4c**), along with the expected epoxide (**4b**); in the case of benzyl derivatives, such as **15a**, the carbonyl compound is favoured.

The relative stereochemistry of compounds **9a–b**, **10a–b**, **11a–b** and **14a–b** was established on the

basis of spectroscopic evidence and through NOE experiments.¹⁸ The ¹H NMR spectrum of **9b** showed overlapped signals, making analysis of the NOE experiments difficult. This compound undergoes easy oxidation by air to the corresponding acid **9c**, whose spectrum was unequivocally assigned. Diols **11a–13a** are intermediates of our synthetic research and were chemically correlated. Compounds **12b** and **13b** showed identical properties to those reported in the literature.^{16,17}

In summary, this reaction, which takes place under neutral conditions, constitutes a mild alternative for preparing carbonyl derivatives from alkenes.

Acknowledgements

The authors thank the CYCYT (Project PB98-1365) for financial support.

References

1. Mitsunobu, O.; Yamada, M. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2380–2382.
2. Mitsunobu, O. *Synthesis* **1981**, 1–28.
3. Camp, D.; Jenkins, I. A. *Aust. J. Chem.* **1988**, *41*, 1835–1840.
4. Manna, S.; Falck, J. R. *Synth. Commun.* **1985**, *15*, 663–665.
5. Edwards, M. L.; Stermerick, D. M.; McCarthy, J. R. *Tetrahedron Lett.* **1990**, *31*, 3417–3420.
6. Hoffman, W. A. *J. Org. Chem.* **1982**, *47*, 5209–5210.
7. Miller, M. J.; Mattingly, P. G.; Morrison, M. A.; Kerwin Jr., J. F. *J. Am. Chem. Soc.* **1980**, *102*, 7026–7032.
8. Kolasa, T.; Miller, M. J. *J. Org. Chem.* **1987**, *52*, 4978–4984.
9. Mitsunobu, O.; Keido, T.; Nishida, M. *Chem. Lett.* **1980**, 1613–1615.
10. Guthrie, R. D.; Jenkins, I. D.; Yamasaki, R. *J. Chem. Soc., Chem. Commun.* **1980**, 784–785.
11. Mitsunobu, O.; Kimura, J.; Inzuma, K.; Yanagida, N. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 510–513.
12. Mengel, R.; Bartke, M. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 697–780.
13. Kinoshita, M.; Taniguchi, M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2147–2156.
14. Kimura, J.; Fujisawa, Y.; Sawada, T.; Mitsunobu, O. *Chem. Lett.* **1974**, 691–692.
15. McGowan, D. A.; Berchtold, G. A. *J. Org. Chem.* **1981**, *46*, 2381–2383.
16. Razmilic, I.; Sierra, J. R.; Cortés, M. *Chem. Lett.* **1985**, 1113.
17. Simmons, D. P.; Reichlin, D.; Skuy, D. *Helv. Chim. Acta* **1988**, *71*, 1000–1006.
18. All new compounds were fully characterized spectroscopically and had satisfactory high resolution mass spectroscopy data. Compound **9a**: ¹H NMR (400 MHz, CDCl₃): δ 0.90 (s, 3H, Me-C₂), 0.99 (s, 3H, Me-C₂), 1.10 (bd, J=10.1 Hz, H-7), 1.22–1.46 (m, 3H, H-5, H-6), 1.54 (m, 1H, H-5), 1.72 (bs, 1H, H-1), 2.01 (bd, J=10.1 Hz, 1H, H-7), 2.09 (dd, J=4.7, 1.3 Hz, 1H, H-4), 2.55 (bs, 2H, OH), 3.56 (d, J=11.2 Hz, 1H, CH₂OH), 3.68 (d, J=11.2 Hz, 1H, CH₂OH). Observed NOEs: 3.56 and 3.68 with 0.90; 0.99 with 2.01. Compound **9b**: ¹H NMR (400 MHz, CDCl₃): δ 1.10 (s, 3H, Me-C₂), 1.13 (s, 3H, Me-C₂), 1.28 (dt, J=9.9, 1.5 Hz, 1H, H-7), 1.34–1.51 (m, 2H, H-5, H-6), 1.59–1.74 (m, 3H, H-5, H-6, H-7), 1.89 (dd, J=3.2, 1.5 Hz, 1H, H-4), 2.09 (ddd, J=3.8, 2.3, 2.3 Hz, 1H, H-3), 2.53 (t, J=4.2 Hz, 1H, H-1), 9.84 (d, J=2.3 Hz, 1H, CHO). Compound **9c**: ¹H NMR (400 MHz, CDCl₃): δ 1.03 (s, 3H, Me-C₂), 1.12 (s, 3H, Me-C₂), 1.25 (bd, J=10.1 Hz, 1H, H-7), 1.33 (m, 1H, H-5), 1.41 (m, 1H, H-6), 1.63 (d, J=10.1 Hz, 1H, H-7), 1.68 (m, 1H, H-5), 1.86 (bs, 1H, H-4), 1.97 (m, 1H, H-6), 2.38 (bs, 1H, H-3), 2.44 (bs, 1H, H-1), 10.32 (s, 1H, COOH). Observed NOE: 2.38 with 1.25. Compound **10b**: ¹H NMR (400 MHz, CDCl₃): δ 0.70 (s, 3H, Me-C₆), 1.20 (s, 3H, Me-C₆), 1.25 (m, 1H, H-5), 1.80–1.95 (m, 3H, H-3, H-4, H-5), 2.10 (m, 1H, H-3), 2.25 (m, 1H, H-5), 2.38 (m, 1H, H-7), 2.53 (m, 1H, H-1), 2.74 (m, 1H, H-2), 9.75 (s, 1H, CHO). Observed NOEs: 9.75 with 0.70 and 1.20. Compound **11b**: ¹H NMR (300 MHz, CDCl₃): δ 0.74 (s, 3H, Me-16), 0.79 (s, 3H, Me-15), 0.86 (s, 3H, Me-14), 1.20–1.60 (m, 10H, H-2, H-2', H-6, H-6', H-7, H-1, H-3, H-9, H-11), 1.71 (m, 2H, H-3, H-11), 1.95 (m, 1H, H-7), 2.33 (m, 1H, H-2), 2.43 (bt, J=5.0 Hz, 1H, H-8), 3.62 (t, J=6.4 Hz, 2H, H-12), 4.48 (d, J=12.0 Hz, 1H, OCH₂Ph), 4.55 (d, J=12.0 Hz, 1H, OCH₂Ph), 7.38 (m, 5H, Bn), 10.01 (s, 1H, H-13). Observed NOE: 10.01 with 0.74. Compound **14b**: ¹H NMR (400 MHz, CDCl₃): δ 0.03 (s, 3H, Me-Si), 0.04 (s, 3H, Me-Si), 0.83 (s, 3H, Me-13), 0.85 (s, 3H, Me-14), 0.87 (s, 9H, *t*-Bu-Si), 0.94 (dt, J=13.0, 3.9 Hz, 1H, H-1α), 1.04 (d, J=6.4 Hz, 3H, Me-12), 1.12 (m, 1H, H-9), 1.14 (s, 3H, Me-15), 1.17 (dd, J=13.5, 3.9 Hz, 1H, H-3α), 1.19 (d, J=3.8 Hz, H-5), 1.42 (bd, J=12.6 Hz, 1H, H-3β), 1.47 (dq, J=13.1 Hz, 1H, H-2α), 1.64 (dt, J=13.7, 10.4, 3.4 Hz, 1H, H-2β), 1.86 (bd, J=13.1 Hz, 1H, H-1β), 2.31 (d, J=13.9 Hz, 1H, H-6), 2.36 (dd, J=13.9, 3.8 Hz, 1H, H-6), 2.65 (dq, J=12.2, 6.4 Hz, 1H, H-8), 3.59 (dd, J=11.0, 4.1 Hz, 1H, H-11), 3.85 (dd, J=11.0, 1.7 Hz, 1H, H-11).