

## Triphenylphosphine–iodine: an efficient reagent for the regioselective dehydration of tertiary alcohols

E. J. Alvarez-Manzaneda,<sup>a,\*</sup> R. Chahboun,<sup>a</sup> E. Cabrera Torres,<sup>a</sup> E. Alvarez,<sup>a</sup>  
R. Alvarez-Manzaneda,<sup>b</sup> A. Haidour<sup>a</sup> and J. Ramos<sup>a</sup>

<sup>a</sup>Departamento de Química Orgánica, Facultad de Ciencias e Instituto de Biotecnología, Universidad de Granada, 18071 Granada, Spain

<sup>b</sup>Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Almería, 04120 Almería, Spain

Received 4 March 2004; revised 12 April 2004; accepted 13 April 2004

**Abstract**—Tertiary alcohols react under mild conditions with triphenylphosphine and iodine to give the most stable alkene in good yield.

© 2004 Elsevier Ltd. All rights reserved.

The conversion of alcohols to olefins constitutes a very useful functional group interconversion in organic synthesis. Although several methods have been reported to effect this transformation,<sup>1</sup> they involve the use of strong acids, high temperatures or transformation to their ester derivatives, which, in some cases, preclude their use with sensitive molecules.

Iodine has long been utilized to dehydrate some tertiary alcohols. However, this method suffers from low reproducibility and many other drawbacks, such as low regioselectivity and poor yield.<sup>2</sup>

The triphenylphosphine–tetrachloromethane system has been reported for dehydrating some 14 $\beta$ -hydroxy steroids.<sup>3</sup>

More recently, the dehydration of secondary and tertiary alcohols by treatment with triphenylbismuth dibromide–iodine under an inert atmosphere has been described.<sup>4</sup>

Continuing research into the development of new synthetic methodologies,<sup>5</sup> as part of our investigation of the synthesis of bioactive compounds from diterpenes, we studied the triphenylphosphine–iodine system to achieve the regioselective dehydration of tertiary alcohols. Sev-

eral alcohols bearing different functional groups, and having methyl, methylene and methyne groups in the  $\beta$  position, were treated with  $\text{PhP}_3\text{-I}_2$  in  $\text{CH}_2\text{Cl}_2$ . The results and conditions are summarized in the Table 1.

The treatment of alcohols **1** and **3** with the reagent afforded exclusively the tetrasubstituted regioisomers **2** and **4** in high yield.

The dehydration of **5** gave alkene **6**, whereas ketoalcohol **7** led to the more stable  $\alpha,\beta$ -unsaturated ketone **8**.

Ketone, ester and amide groups remained unaltered under the reaction conditions. Thus, hydroxyesters **9** and **11** and hydroxyamide **13** afforded the corresponding unsaturated compounds **10**, **12** and **14**.

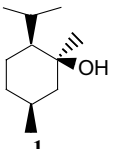
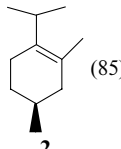
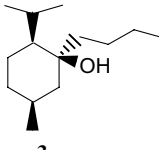
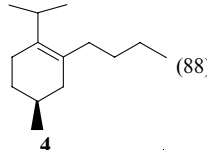
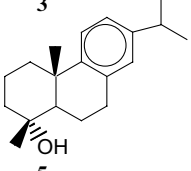
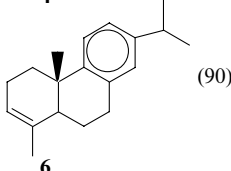
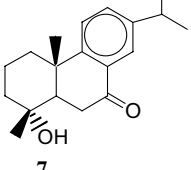
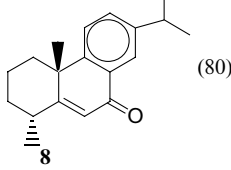
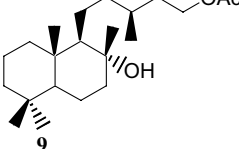
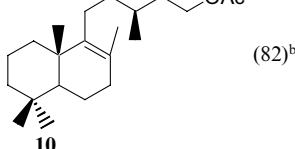
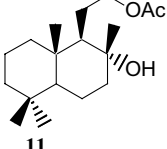
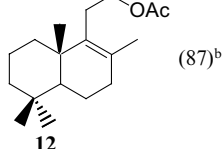
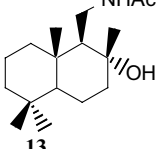
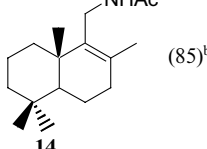
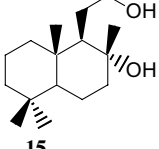
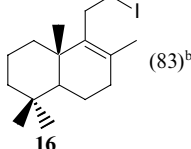
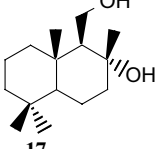
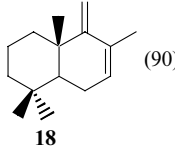
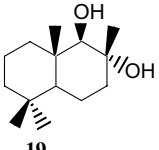
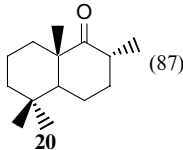
The 1,4-dihydroxyderivative **15** was converted into the homoallylic iodide **16**.<sup>6</sup> However, the 1,3-dihydroxyderivative **17** underwent elimination to give the stable conjugated diene **18**. Dehydration of the 1,2-diol **19** yielded, as would be expected, the ketone **20**.<sup>7,9</sup>

Compound **16** is the key intermediate in the total synthesis of the *seco*-labdane chapecoderin A.<sup>7</sup> The conversion of diol **15**, which was obtained in high yield in a two-step sequence from the natural diterpene (–)-sclareol by the present authors,<sup>8</sup> into **16** (entry 8) involves the formal synthesis of the above *seco*-labdane from (–)-sclareol.

**Keywords:** Tertiary alcohols; Regioselective dehydration; Alkenes; Triphenylphosphine; Iodine.

\* Corresponding author. Tel./fax: +34-958-24-80-89; e-mail: [eamr@ugr.es](mailto:eamr@ugr.es)

**Table 1.** Dehydration of tertiary alcohols with the  $\text{Ph}_3\text{P-I}_2$  system

Entry	Substrate	Time (h)	Product (%) <sup>a</sup>
1		2	
2		2.5	
3		4	
4		3.5	
5		3	
6		2.5	
7		2	
8		3.5	
9		3	
10		2.5	

<sup>a</sup> All new compounds were fully characterized.<sup>b</sup> Minor regioisomers were obtained in less than 10%.

**Experimental procedure:** Iodine (1.2 mmol) was added to a solution of Ph<sub>3</sub>P (1.2 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) and the mixture was stirred at room temperature for 10 min. A solution of the alcohol (1.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL) was then added and the mixture was further stirred at room temperature, the reaction being monitored by TLC. Aq 5% NaHSO<sub>3</sub> was added and the mixture was stirred for 10 min. It was then diluted with CH<sub>2</sub>Cl<sub>2</sub> and the organic phase washed with H<sub>2</sub>O and brine successively, after which it was dried and evaporated to give a crude. This, after flash column chromatography on silicagel (hexane/ether), gave the alkene.

In conclusion, the Ph<sub>3</sub>P–iodine system is an inexpensive reagent, which transforms tertiary alcohols into the most stable alkene, under mild and easily-implemented experimental conditions. Some functional groups, such as ketone, ester and amide, remain unaltered under these conditions.

#### Acknowledgements

Financial support was received from Ministerio de Ciencia y Tecnologia (Project PPQ 2002-03308).

#### References and notes

- (a) Buehler, C. A.; Pearson, D. E. In *Survey of Organic Synthesis*; Wiley Interscience: New York, 1970; Vol. I, pp 71–76, Vol. II, pp 78–84; (b) Barton, D.; Ollis, W. D. In *Comprehensive Organic Chemistry*; Pergamon: Oxford, 1979; Vol. I, pp 640–644; (c) March, J. A. *Advanced Organic Chemistry: Reactions, Mechanisms and Structures*. 5th ed.; Wiley Interscience: New York, 2001, pp 1326–1328; (d) Larock, R. C. *Comprehensive Organic Transformations*; VCH, 1989, pp 151–154.
- (a) Fieser, L. F.; Fieser, M. In *Reagents for Organic Synthesis*; John Wiley: New York, 1967; Vol. I, pp 498–504; (b) Reeve, W.; Reichel, D. M. *J. Org. Chem.* **1972**, *37*, 68–72; (c) Elsner, B. B.; Strauss, H. E. *J. Chem. Soc.* **1957**, 288–292; (d) Hibbert, H. *J. Am. Chem. Soc.* **1915**, *37*, 1748–1752.
- Theil, F.; Linding, C.; Repke, K. *Zeitschrift fuer Chemie* **1980**, *20*, 372–373.
- Dorta, R. L.; Suarez, E.; Betancor, C. *Tetrahedron Lett.* **1994**, *35*, 5035–5038.
- (a) Barrero, A. F.; Alvarez-Manzaneda, E.; Chahboun, R.; Meneses, R. *Synlett* **1999**, 1663–1666; (b) Barrero, A. F.; Alvarez-Manzaneda, E.; Chahboun, R.; Meneses, R. *Synlett* **2000**, 197–200; (c) Barrero, A. F.; Alvarez-Manzaneda, E.; Chahboun, R. *Tetrahedron Lett.* **2000**, *41*, 1959–1962; (d) Barrero, A. F.; Alvarez-Manzaneda, E.; Chahboun, R.; Cuerva, J. M.; Segovia, A. *Synlett* **2000**, 1269–1272; (e) Barrero, A. F.; Alvarez-Manzaneda, E.; Chahboun, R.; Meneses, R.; Romera, J. L. *Synlett* **2001**, 485–488.
- Corey's iodination procedure involves the transformation of primary and secondary alcohols into the corresponding iodides by treatment with a mixture of triphenylphosphine–iodine–imidazole in acetonitrile–ether; Corey, E. J.; Pyne, S. G.; Su, W. *Tetrahedron Lett.* **1983**, *24*, 4883–4886, The tertiary hydroxy groups remained unaltered under these conditions.
- Hagiwara, H.; Takeuchi, F.; Hoshi, T.; Suzuki, T.; Ando, M. *Tetrahedron Lett.* **2001**, *42*, 7629–7631.
- Barrero, A. F.; Alvarez-Manzaneda, E.; Altarejos, J.; Salido, S.; Ramos, J. M. *Tetrahedron* **1993**, *49*, 10405–10412.
- Hagiwara, H.; Nagatomo, H.; Kazayama, S.; Sakai, H.; Hoshi, T.; Suzuki, T.; Ando, M. *J. Chem. Soc., Perkin Trans. I* **1999**, 457–459.