Pergamon

Tetrahedron Letters, Vol. 38, No. 13, pp. 2235-2236, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00325-0

Novel Wagner-Meerwein Rearrangement of a Bicyclo[3.1.1]heptanol under Mitsunobu Conditions

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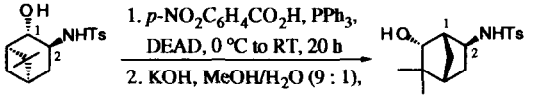
Abstract: *Treatment of bicyclo[3.1.1]heptanol* **1** *under standard Mitsunobu conditions afforded after hydrolysis the rearranged bicyclo[2.2.1]heptanol* **2** *in 80% overall yield.* © 1997 Elsevier Science Ltd.

The skeletal rearrangement of naturally derived terpenes, such as β-pinene, has intrigued synthetic chemists for many years.[1] Indeed, this has prompted detailed mechanistic and theoretical studies into the factors that are responsible for these important rearrangements. Electrophilic, photochemical, radical and thermal methods have been employed to effect the structural reorganization of β-pinene type skeletons *via* a series of complementary rearrangement pathways.[1,2] In this paper, we report a novel Wagner-Meerwein rearrangement[3] of the bicyclo[3.1.1]heptanol **1** skeleton, under Mitsunobu conditions for the synthesis of a new rigid enantiomerically pure scaffold (**Scheme 1**).[4,5]

Scheme 1

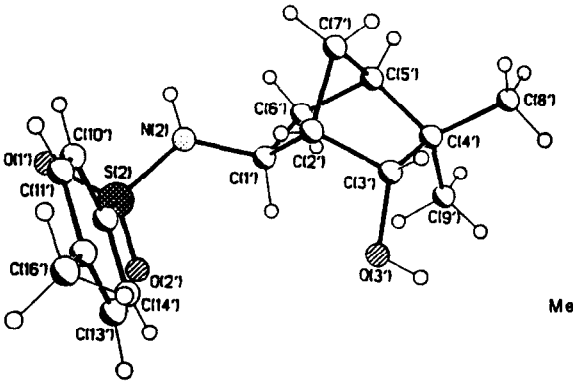


1 **2**

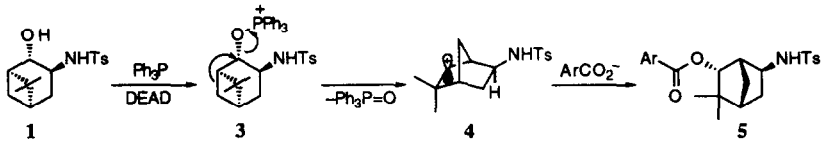
In the course of our synthetic studies aimed at the *de novo* synthesis of new ligands for asymmetric catalysis, we required the inversion of the secondary alcohol at C-1 of **1**. Treatment of the bicyclo[3.1.1]heptanol **1** under standard Mitsunobu conditions, followed by hydrolysis, furnished the rearranged bicyclo[2.2.1]heptanol **2** in 80% overall yield. This is the first example, to our knowledge, of a Mitsunobu-induced Wagner-Meerwein rearrangement. The structure of **2** was confirmed by *X*-ray crystallography[6] and a series of two-dimensional NMR experiments (**Fig. 1**).

The proposed mechanism for this transformation is outlined in **Scheme 2**. The initial step presumably involves the formation of a phosphonium ion **3** which induces a stereospecific migration of the methylene bridge antiperiplanar to the departing triphenylphosphine oxide resulting in the formation of carbocation **4**. The initial formation of a carbocation seems unlikely, since the alternative Wagner-Meerwein rearrangement of the geminally substituted bridge or Ene-type fragmentation would have been expected.[1] Endo trapping of the resulting carbocation **4** results in the carboxylate **5**, which is then hydrolyzed to the alcohol **2**. E1 type elimination of the carbocation **4** is avoided due to the α-geminal methyl groups or the formation of an *anti*-Bredt alkene.

Figure 1



Scheme 2



In conclusion, we have discovered a novel and mild method for inducing a Wagner-Meerwein rearrangement of the bicyclo[3.1.1]heptanol **1** to the bicyclo[2.2.1]heptanol **2**.

Acknowledgments

We would like to thank the University of Delaware Research Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society for generous financial support.

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† To whom correspondence regarding the *X*-ray crystal structure should be addressed.

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6. Crystal structure data for **2** ($C_{16}H_{23}NO_3S$): monoclinic, $P2_1$, a = 8.496(5) Å, b = 20.394(3) Å, c = 9.834(2) Å, β = 92.65(3)°, Z = 4 (two ind. mol.), $R(F)$ = 4.02%. $R(wF^2)$ = 10.88%.

(*Received in USA* 14 *January* 1997; *revised* 12 *February* 1997; *accepted* 13 *February* 1997)