Preparation of Bicyclic Compounds from the Products of Conjugate Addition of Allylic Sulphoxide and Phosphine Oxide Carbanions to Cyclopent-2-enones

Richard K. Haynes* and Andrew G. Katsifis

Department of Organic Chemistry, University of Sydney, Sydney 2006, Australia

The conversion of the compounds obtained from the conjugate addition of the carbanions of allylic sulphoxides and phosphine oxides into bicyclo[3.3.0]octanes, bicyclo[2.2.1]heptanes, and bicyclo[3.2.1]octanes whose configurations reflect those of the starting compounds is described.

The respective formation of the products (**5**) and (**6**), and (**7**) and (**8**), from cyclopentenone and the carbanions of the (*E*)-but-2-enyl sulphoxide (**1**) and phosphine oxide (**2**), and the (*Z*)-but-2-enyl sulphoxide (**3**) and phosphine oxide (**4**), has been explained in terms of 'trans-fused chair–chair'-like transition states.[1] As the reactions appear to be general for a number of allylic carbanions bearing polar, charge-stabilizing groups, they have an obvious application in synthesis. One use for the reaction products would be to generate bicyclic systems through ring-closure of the three-carbon allylic chain with the cyclopentanone such that the configuration at the allylic centre is retained in the process. We describe here three modes of ring-closure which lead to bicyclic products whose configurations reflect those of the starting compound.

As attempts to form bicyclo[3.3.0]octanes from the model substrate (**10**) or the derived sulphide (**11**) by cationic cyclization were unsuccessful, we sought to enhance the enolic character of these compounds prior to ring-closure. Thus, the enolate (**9**) generated in tetrahydrofuran (THF) from the carbanion of dimethylallyl phenyl sulphoxide and cyclopentenone was treated with methyl cyanoformate[2] at −60 °C to give the cyclopentanone (**12**)† in 83% yield from the carbanion.‡ As attempted ring-closure of the product under Pummerer conditions failed, it was reduced by Bu_3PI_2[1] to the sulphide (**13**) (90%), which with $SnCl_4$ (1 equiv.) in dichloromethane at 0 °C gave the bicyclo-octanone (**14**) (73%) as a 3 : 1 mixture of diastereoisomers epimeric at C-8. In similar fashion the bicyclo-octanone (**16**) (7 : 1 mixture of diastereoisomers epimeric at C-8) was prepared from the carbanion of butyl (*E*)-but-2-enyl sulphoxide (**15**) [54% from (**15**)], and its isomer (**18**) (7 : 1 mixture of diastereoisomers epimeric at C-8) from the carbanion of butyl (*Z*)-but-2-enyl sulphoxide (**17**)§ [56% from (**17**)].

With potassium t-butoxide (1 equiv.) in THF at room temperature during 24 h, the sulphoxide (**10**) yielded the bicycloheptanone (**19**) (60%) as two diastereoisomers in the ratio of 5 : 1. Similarly, the phosphine oxide (**6**) gave the bicycloheptanone (**20**) (90%) as a single diastereoisomer. The configuration at C-5 in (**20**) corresponds to that at C-1′ in compound (**6**). H-6 was shown to be *cis* to the methyl group by ^1H n.m.r. nuclear Overhauser effect (n.O.e) difference experiments involving preirradiation of the methyl protons; this is also indicated by the coupling constants of 4.0 Hz between H-6 and H-5.[4] From compound (**8**), the bicycloheptanone (**21**) was obtained in over 90% yield. Again, H-5 and H-6 were shown to be *trans* by n.O.e. experiments, and by the small coupling constant (*ca.* 1.1 Hz) between H-6 and H-7_{anti}.[3] Thus, the intramolecular addition of the enolate to the vinylic phosphine oxide in (**6**) and (**8**) which leads to the bicycloheptanes (**20**) and (**21**) is controlled by a conformational effect

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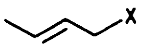
† All new compounds have been fully characterized by high field ^1H n.m.r. and other spectroscopic techniques, and by microanalyses. Yields refer to compounds purified by chromatography. Where mixtures of diastereoisomers were obtained, these were separated by h.p.l.c. and characterised.

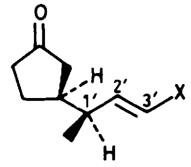
‡ Although enol esters could be prepared from the enolate and acetic or pivalic anhydrides, their yields (50—60%) were less satisfactory than in the above case.

§ The use of the n-butyl rather than phenyl as the non-allylic substituent in the starting sulphoxides was dictated by our inability to prevent the isomerisation of the (*Z*)-isomer of but-2-enylphenyl sulphoxide producing substantial quantities of the (*E*)-isomer prior to use. A t-butyl group could not be used in the sequence as this was lost during cyclization.

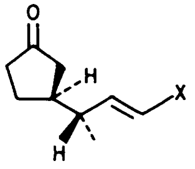


(1) X = S(O)Bu^t
(2) X = P(O)Ph$_2$
(15) X = S(O)Bu^n

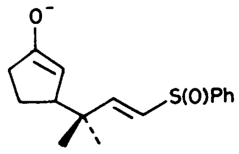
(3) X = S(O)Bu^t
(4) X = P(O)Ph$_2$
(17) X = S(O)Bu^n



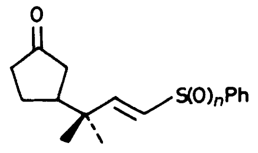
(5) X = S(O)Bu^t
(6) X = P(O)Ph$_2$



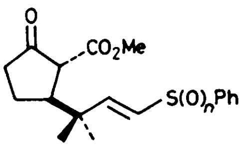
(7) X = S(O)Bu^t
(8) X = P(O)Ph$_2$



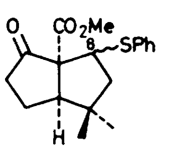
(9)



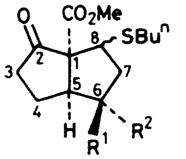
(10) n = 1
(11) n = 0



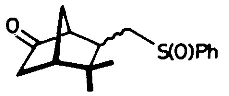
(12) n = 1
(13) n = 0



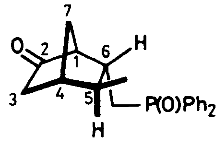
(14)



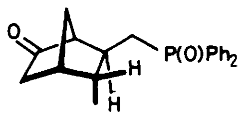
(16) R^1 = Me, R^2 = H
(18) R^1 = H, R^2 = Me



(19)



(20)



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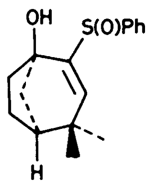

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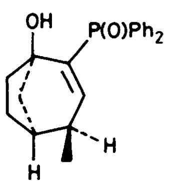
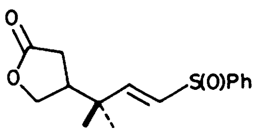
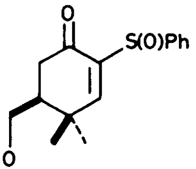


(23)

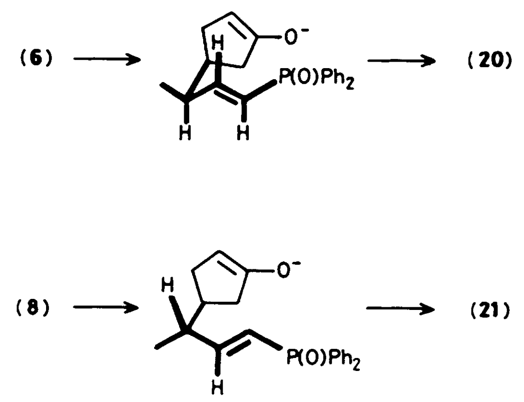


(24)



(25)

For structures (5)—(25), only one enantiomer is shown.



Scheme 1

involving the allylic system in the starting compounds. H-1′ and H-2′ in each of (6) and (8), with coupling constants of 8.0 Hz, are approximately antiperiplanar,[4] as A^{1,3}-strain[5] causes the allylic system to adopt a preferred conformation in which the methyl group is approximately antiperiplanar to the double bond. Hence, cyclisation will proceed as depicted in Scheme 1. A brief report on the formation of a bicycloheptanone from a sulphone provides the only other example of these reactions.[6]

With lithium di-isopropylamide (LDA) (2.5 equiv.) in THF at −78 °C, the sulphoxide (10) during 5 min gave the bicyclo[3.2.1]octanol (22) (55%). A reaction of this kind has been reported previously.[7] The product does not arise from the enolate (9) which in the presence of excess of LDA forms a dianion resulting from deprotonation of the vinylic sulphoxide.[1] Thus, deprotonation of the vinylic sulphoxide is kinetically favoured over enolate formation when the neutral starting material (10) is treated with LDA. Similarly, the phosphine oxide (6) gave the bicyclo-octanol (23) (60%), a reaction which involves the hitherto unreported deprotonation of a vinylic phosphine oxide. When the lactone (24)[1] is treated with excess of LDA, the initial adduct formed by the addition of the vinyl carbanion to the carbonyl group undergoes ring-opening to yield the cyclohexenone (25) (58%).

The facile preparation of the bicyclic systems described herein considerably extends the usefulness of the conjugate addition reactions. Another mode of ring-closure of an adduct derived by the conjugate addition of a carbanion of an allylic sulphoxide has been very recently described.[8] The conceptual basis for the latter work was clearly reliant upon the model we have proposed for these reactions.

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