Pergamon

Tetrahedron Letters, Vol. 38, No. 33, pp. 5885-5886, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)01310-5

Use of a Sulfinyl Tether to Control Diastereofacial Selectivity in [5C + 2C] Pyrone-Alkene Cycloadditions

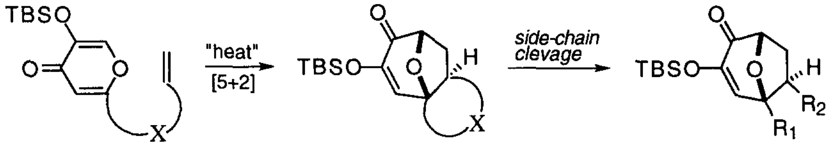
Antonio Rumbo, Luis Castedo, and José L. Mascareñas*

Departamento de Química Orgánica y Unidad Asociada al CSIC. Universidad de Santiago de Compostela, 15706 Santiago de Compostela, Spain.

Abstract. The incorporation of a sulfoxide on the tether connecting an alkene to a 5-silyloxy-4-pyrone diminishes the temperature needed for inducing their thermal [5C+2C] cycloaddition in relation to that required for annulating the homologous sulfide, and allows for attaining modest levels of diastereofacial selectivity. © 1997 Elsevier Science Ltd.

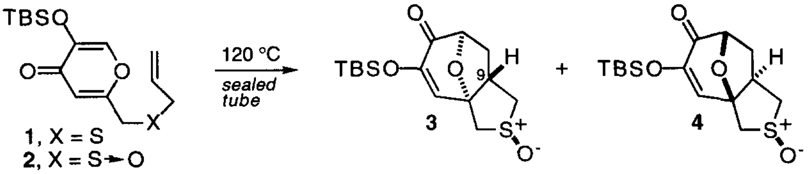
We have previously reported a practical method for the stereoselective synthesis of 8-oxabicyclo[3.2.1]octanes by thermal [5C+2C] cycloaddition between temporarily tethered 5-silyloxy-4-pyrones and alkenes.[1] The chemical versatility and associated utility of the resulting oxabicyclic systems prompted us to explore asymmetric versions of the method.[2] Since the linker connecting the reactants is removed after the cycloaddition, we envisaged that introducing a suitable stereogenic element on that tether (X = chiral auxiliary) could potentially provide a direct route to enantiomerically pure oxabicycles.[3] The constraints imposed by the intramolecularity of the reaction might enable an efficient transfer of asymmetric information to the three newly created stereocenters.

Scheme I



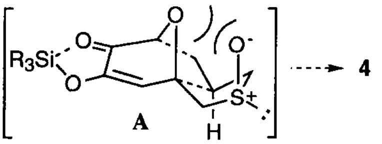
The ready availability of the thioether **1**,[1] prompted us to examine whether the corresponding sulfoxide might induce diastereofacial selectivity in its cycloaddition reaction. Although sulfoxides have been widely used as asymmetric inducers, particularly in intermolecular Diels-Alder reactions,[4] to our knowledge, incorporation of the sulfinyl group in the tether connecting the reacting partners is unprecedented. Thioether **1** was oxidized to **2** by treatment with 1.1 equiv of *m*-chloroperbenzoic acid in dichloromethane at -40°C. Heating of a solution of **2** in 1,2-dichloroethane at 120 °C in a sealed tube for 13 h, gave a 3:1 mixture of the expected racemic diastereoisomers **3** and **4**, in 91% yield.[5] Assignment of the stereochemistry of the cycloadducts was based on their NMR spectra, in particular the remarkable downfield shift (ca. 1 ppm) of the signal for H-9 of **3** with respect to that of diastereoisomer **4** due to a *syn*-axyal effect of the sulfoxide.[6]

Scheme II



A possible explanation for the stereochemical outcome of the annulation is that formation of the minor product (**4**) entails a disfavored interaction between the sulfinyl oxygen and the oxygen bridge of the pyrone (**A**, Fig. 1). In view of the recent reports that the solvent can affect the stereochemical outcome of sulfoxide-directed radical reactions,[7] we carried out the reaction in other solvents. However, we found that changing the solvent had little effect on the diastereoselectivity, and in fact reduced the yield (see table in Fig. 1). We have also examined the cycloaddition reaction of the regioisomeric sulfoxide of **2**, with the tether attached to position 2 of the 3-silyloxy-4-pyrone,[8] and found a similar degree of asymmetric induction.

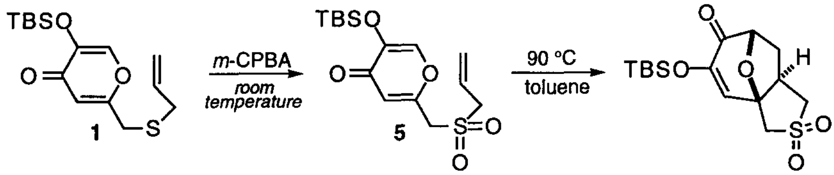
Figure 1



solvent	yield	**3/4**
$(CH_2)_2Cl_2$	91%	3:1
toluene	40%	3.5:1
THF	53%	4:1
CH_3CN	45%	4.3:1

An interesting feature of the above results is the substantial decrease in the temperature needed to induce the cycloaddition of **2** as compared to sulfide **1**, complete reaction of which requires heating at 145 °C for two days.[1] This result, which can be explained in terms of a Thorpe-Ingold effect,[9] suggested that increasing the substitution at the sulfur might further decrease the thermal requirements for the cycloaddition. Accordingly, we found that cycloaddition of sulfone **5** can be carried out by heating at 90 °C (18 h, 91% yield), while at that temperature sulfoxide **2** (and of course sulfide **1**) remained practically unchanged after three days.

Scheme III



To conclude, although the degree of stereochemical induction achieved was modest, it is likely that moving the sulfinyl group to a different position in the tether, or altering the electronic or steric features of the disposable stereocenter may provide better results. Work in under way to investigate these alternatives and thus to confirm the practical validity of the above approach for asymmetric induction.

Acknowledgments. Support of this research by the spanish M.E.C. and the Xunta de Galicia, under Grants SAF-95-0878 and XUGA 20901A94, respectively, is gratefully acknowledged. A. R. thanks the Xunta de Galicia for a predoctoral fellowship. We also thank Prof. Paul Wender for helpful initial suggestions.

References and Notes

(1) Rumbo, A.; Castedo, L.; Mouriño, A.; Mascareñas, J. L. *J. Org. Chem.* **1993**, *58*, 5585.

(2) For recent asymmetric approaches to 8-oxabicyclo[3.2.1]octane units, see: (a) Davies, H. M. L.; Ahmed, G.; Churchill, M. R. *J. Am. Chem. Soc.* **1996**, *118*, 10774. (b) Lautens, M.; Aspiotis, R.; Colucci, J. *J. Am. Chem. Soc.* **1996**, *118*, 10930.

(3) Asymmetric temporary tethers have been used in other cycloaddition reactions, see : (a) Shea, K. J.; Gauthier, D. R. Jr. *Tetrahedron Lett.* **1994**, *35*, 7311. (b) Craig, D.; Ford, M. J.; Stones, J. A. *Tetrahedron Lett.* **1996**, *37*, 535.

(4) García Ruano, J. L.; Carretero, J. C.; Carreño, M. C.; Martín, L. M.; Urbano, A. *Pure & Appl. Chem.* **1996**, *68*, 925.

(5) These compounds were separated by flash chromathography. ^1H NMR (250 MHz, $CDCl_3$): **3**, δ= 0.16 (s, 6H), 0.94 (s, 9H), 2.10 (ddd, *J* = 1.5, 8.2 and 14.4 Hz, 1H), 2.30 (ddd, *J* = 2.6, 8.2 and 14.0 Hz, 1H), 2.59 (dd, *J* = 11.8 and 13.4 Hz, 1H), 3.14 (dd, *J* = 1.3 and 15.3 Hz, 1H), 3.38 (dd, *J* = 7.0 and 13.4 Hz, 1H), 3.57 (d, *J* = 15.4 Hz, 1H), 3.74 (m, 1H, *H-9*), 4.78 (d, *J* = 8.3 Hz, 1H), 6.42 (s, 1H). **4**: δ= 0.16 (s, 6H), 0.92 (s, 9H), 2.12 (ddd, *J* = 1.4, 8.0 and 13.7 Hz, 1H), 2.44 (ddd, *J* = 2.7, 8.3 and 14.2 Hz, 1H), 2.81 (m, 1H, *H-9*), 2.91 (t, *J* = 12 Hz, 1H), 3.41 (AB, *J* = 14.6 Hz, 2H), 3.77 (dd, *J* = 7.0 and 11.2 Hz, 1H), 4.85 (dd, *J* = 1.2 and 8.3 Hz, 1H), 6.19 (s, 1H).

(6) Lett, R.; Marquet, A. *Tetrahedron* **1974**, *30*, 3379.

(7) Renaud, P.; Bourquard, T.; Gerster, M.; Moufid, N. *Angew. Chem. Int. Ed. Eng.*. **1994**, *33*, 1601 and references cited therein.

(8) This compound was obtained by oxidation of the corresponding thioether, which was prepared as described previously (ref. 1).

(9) (a) Parril, A. L.; Dolata, D. P. *Tetrahedron Lett.* **1994**, *35*, 7319. (b) Jung, M. E.; Gervay, J. *J. Am. Chem. Soc.* **1991**, *113*, 224.

(*Received in UK* 9 *June* 1997; *accepted* 27 *June* 1997)