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# THE INTRAMOLECULAR ADDITION OF SULPHENIC ACIDS TO ALKYNES: BICYCLIC ALKENYL SULPHOXIDES

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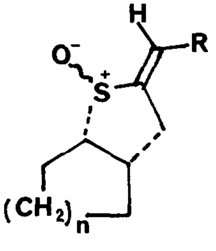
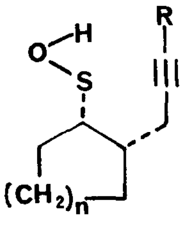
Summary: The preparation of the bicyclic alkenyl sulphoxides 1 (n = 1 and 2; R = $CH_2CH_3$) from the alkynyl sulphenic acids 2 is described.

As part of a programme to prepare novel prostaglandin and prostacyclin analogues we required a method of obtaining bicyclic alkenyl sulphoxides of general structure 1.[1] An attractive synthetic approach appeared to involve the intramolecular cyclisation of the alkynyl sulphenic acids 2.



1

n = 1 and 2

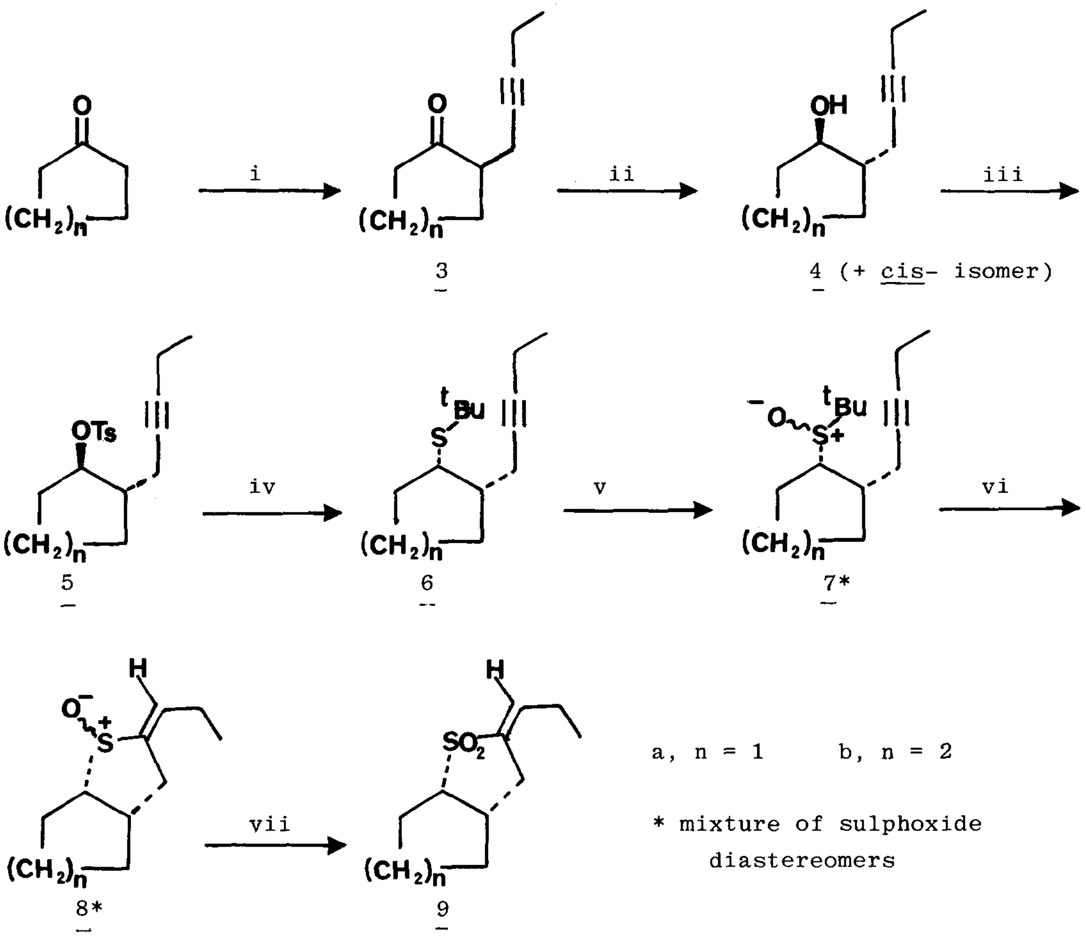


2

Neville Jones and his group have recently shown[2] that the addition of sulphenic acids to unactivated alkynes provides a convenient method of preparing alkenyl sulphoxides. In this paper we demonstrate an application of the intramolecular version of this reaction to the synthesis of the sulphoxides 1 (n = 1 and 2; R = $CH_2CH_3$). Our results are shown in the scheme.

2-(Pent-2-ynyl)cyclopentan-1-one (3a) was prepared using a published[3] enamine procedure and the substituted cyclohexanone 3b[4] was obtained in a similar manner. Reduction of the ketones 3 gave a mixture of alcohols from which the trans-isomers 4[4] were obtained by preparative centrifugal

## SCHEME



a, n = 1 b, n = 2

* mixture of sulphoxide diastereomers

Reagents

(i) pyrrolidine, benzene, $H^+$ then $BrCH_2C{\equiv}CCH_2CH_3$, dioxane (3a, 38%; 3b, 50%);

(ii) $NaBH_4$, EtOH (4a, 56% + 27% *cis*- ; 4b, 41% + 42% *cis*- );

(iii) $p$-$CH_3C_6H_4SO_2Cl$, pyridine (5a, 97%; 5b, 91%);

(iv) $^tBuSH$, $^iPrONa$, $^iPrOH$ (6a, 30%; 6b, 32%);

(v) 4-Chloroperbenzoic acid, $CH_2Cl_2$ (7a, 86%, major:minor = 78:22; 7b, 100%, major:minor = 82:18);

(vi) xylene, reflux (see Table);

(vii) 4-Chloroperbenzoic acid, $CH_2Cl_2$ (9a, 93% from 8a $\alpha$-oxide, 89% from 8a $\beta$-oxide; 9b, 95% from 8a $\alpha$-oxide, 91% from 8b $\beta$-oxide).

chromatography.[5] Treatment of alcohols 4 with p-toluenesulphonyl chloride gave the trans-tosylates 5[4] which were converted to the cis-t-butylsulphides 6[4] using sodium 2-methylpropane-2-thiolate.[6] Oxidation of sulphides 6 gave diastereomeric mixtures of sulphoxides 7 which were separated by chromatography.[5]

Thermolysis of the sulphoxides 7 in refluxing, degassed, xylene gave the desired bicyclic sulphoxides 8 as mixtures of α- and β-diastereomers. The configuration at sulphur was tentatively assigned by comparison of the $^1$H-NMR and chromatographic properties of 7[7] with those of related compounds.[1a] The product ratios and yields of the thermolyses were found to vary markedly according to which diastereomer of sulphoxide 7 was employed (Table).

TABLE

| Starting Sulphoxide | Product | Yield (α:β ratio) |
|---|---|---|
| 7a (major diastereomer) | 8a | 17% (82:18) |
| 7a (minor diastereomer) | 8a | 72% (61:39) |
| 7b (major diastereomer) | 8b | 97% (30:70) |
| 7b (minor diastereomer) | 8b | 33% (27:73) |

Presumably thermolysis of the sulphoxides 7 gave 2-methylpropene and the sulphenic acids 2 (n = 1 and 2, R = $CH_2CH_3$) by β-elimination. The sulphenic acids 2 could then undergo concerted intramolecular addition to the alkynyl group. This mechanism[2] predicts the stereospecific formation of the E-alkenes 8.

Finally, the α- and β-sulphoxides 8 could be separated chromatographically[5] and individually oxidised to the same sulphone 9 thereby confirming that the products of the thermolysis reactions differed only in configuration at sulphur.

We are currently using the reactions described in this paper to prepare thia-prostacyclin analogues.

## ACKNOWLEDGEMENTS

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## REFERENCES AND NOTES

1. For alternative approaches to systems of this type see:
   (a) K.C. Nicolaou, W.E. Barnette and R.L. Magolda, J. Amer. Chem. Soc., 1981, 103, 3472 and 3486;
   (b) M. Shibasaki and S. Ikegami, Tetrahedron Lett. 1978, 559;
   (c) K. Shimoji, Y. Arai and M. Hayashi, Chem. Lett. 1978, 1375.

2. D.N. Jones, P.D. Cottam and J. Davies, Tetrahedron Lett. 1979, 4977; R. Bell, P.D. Cottam, J. Davies, D.N. Jones and N.A. Meanwell, Ibid, 1980, 4379;
   R. Bell, P.D. Cottam, J. Davies and D.N. Jones, J.C.S. Perkin I, 1981, 2106.

3. E. Demole and M. Winter, Helv. Chim. Acta, 1962, 45, 1256.

4. All new compounds gave satisfactory analyses or high resulution mass spectroscopic data together with consistent $^{1}$H-NMR, $^{13}$C-NMR and IR spectra.

5. Chromatotron Model 7924 (Harrison Research, Palo Alto, California 94306, U.S.A.).

6. Alkenes, resulting from elimination of p-toluenesulphonic acid, were major by-products in these reactions.

7. 8a ($\alpha$-oxide), $R_f$ 0.35 (diethyl ether-ethanol, 98:2); $^{1}$H-NMR ($CDCl_3$) 6.17 (1H,m, vinyl H).

   8a ($\beta$-oxide), $R_f$ 0.16 (diethyl ether-ethanol 98:2); $^{1}$H-NMR ($CDCl_3$) 6.27 (1H,m, vinyl H).

   8b ($\alpha$-oxide), $R_f$ 0.60 (diethyl ether-ethanol, 98:2) $^{1}$H-NMR ($CDCl_3$) 6.12 (1H,m, vinyl H).

   8b ($\beta$-oxide), $R_f$ 0.41 (diethyl ether-ethanol, 98:2); $^{1}$H-NMR ($CDCl_3$) 6.39 (1H,m, vinyl H).

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