

THIOPHENOL ADDITIONS TO ALKENYLIDENECYCLOPROPANES.

A NOVEL SYNTHESIS OF KARAHANAENONE

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Summary: The additions of thiophenol to alkenylidenecyclopropanes (e.g. 3, 14) are found to be highly regioselective and stereoselective leading to endo- (or cis-) vinyl sulphide adducts (e.g. 4, 15) resulting from additions to the 1,4-double bonds in the starting materials. Thiophenol addition to (1) leads to a mixture of the vinyl sulphides (16) and (17) which undergo Cope rearrangement producing the cycloheptadiene (18); hydrolysis of (18) then gives karahanaenone (19) an odoriferous constituent of Japanese hop and Cypress oil.

In previous studies we have shown that C<sub>10</sub>- alkenylidenecyclopropanes, derived from the addition of 3,3-dimethylallene carbene to appropriate alkenes [e.g. (1), from isoprene], provide useful substrates for the synthesis of novel acyclic monoterpenes through acid- and base-catalysed rearrangements e.g. (1) → (2).<sup>1</sup> We have now extended these studies to an investigation of the selectivity of thiophenol additions to substrates of the type (1).<sup>2</sup> In this Letter, we summarise the outcome of this investigation, and the development of the findings into a novel and facile synthesis of the 7-ring monoterpene karahanaenone (19), an odoriferous constituent of Japanese hop and Cypress oil Cupressus sempervirens.<sup>3</sup>

Treatment of the alkenylidenecyclopropane (3) with thiophenol (1 equiv; benzene, 25°, 4 h.) resulted in highly regioselective and stereoselective addition to the 1,4-double bond in (3) leading to the endo-sulphide (4; 80%) (9:1 endo:exo), b.p. 100 - 105°/0.1 mm.,  $\delta_{\text{H}}$  0.84 - 1.96 (m, 11H), 1.99 (CMe<sub>2</sub>). 6.95 - 7.3 (m, 5H);  $\delta_{\text{C}}$  0.0d, 14.9 d, 20.6 t, 22.2 t, 22.5, 23.1, 23.5, 123.7, 124.6 d, 127.4 d, 128.5 d, 138.3, 145.3 p.p.m.<sup>4</sup> The structure of the adduct followed from these spectral data, and also from the observation that ozonisation led to the expected thioester (5),  $\nu_{\text{max}}$  1710 cm<sup>-1</sup>. The data are not consistent with the structure (6) put forward by Gompper and Lach for the adduct.<sup>5</sup> In some experiments we were able to isolate the minor products (7; ~1%) and (8; ~1%) by chromatography, but no evidence for the co-formation of (6) was obtained. Reductive cleavage of the vinyl sulphide (4), using

lithium in ammonia,<sup>6</sup> led to the vinyl cyclopropane (9) as a 9:1 mixture of endo-[ $\delta_{\text{H}}$  5.0 (d,  $\underline{J}$  6)] and exo-[ $\delta_{\text{H}}$  4.6 (d,  $\underline{J}$  8)] isomers, showing identical chromatographic and closely similar spectral data to those of the authentic endo-vinylcyclopropane obtained by catalytic semi-hydrogenation of (3).<sup>7</sup>

In a similar manner, the alkenylidenecyclopropanes (10) and (11) produced from reaction of 3,3-dimethylallene carbene with cyclopentene and  $\alpha$ -pinene respectively, led to the corresponding vinyl sulphide adducts (12) (79%) 4:1 endo:exo) and (13) (66%), on treatment with thiophenol. Reaction between thiophenol and the acetylenic alkenylidenecyclopropane (14) also proceeded in a regioselective manner, producing the vinyl sulphide (15; 46%) (3:1 cis:trans),  $\delta_{\text{H}}$  1.14 (Me, trans), 1.34 (Me, cis), 1.84 ( $\text{:CH}$ , trans), 1.89 ( $\text{:CH}$ , cis);  $\delta_{\text{C}}$  18.7q (Me, trans), 22.1q (Me, cis), 91.0 ( $\text{C:CH}$ , trans), 87.2 ( $\text{C:CH}$ , cis). No products resulting from the addition of thiophenol to the acetylenic group in (14) were found.

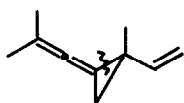
The addition of thiophenol to the alkenylidenecyclopropane (1) produced from isoprene and dimethylallene carbene, led to a 2:1 mixture of cis and trans-isomers of the vinyl sulphides (16) and (17) (ca. 25%). Although the trans-isomer (17),  $\delta_{\text{H}}$  0.7 - 1.15 (m,  $\text{CH}_2$ ), 1.04 (Me), 1.54 - 1.86 (m,  $\text{CH}$ ), 1.9 ( $\text{:CMe}$ ), 2.07 ( $\text{:CMe}$ ), 4.75 - 5.05 (m,  $\text{:CH}_2$ ), 5.47 (dd,  $\underline{J}$  14 and 9,  $\text{HC:CH}_2$ ), 7.1 (5H), could be separated by chromatography, the cis-isomer (16) instead underwent spontaneous Cope rearrangement, in situ at 25°, leading to the 1,4-cycloheptadiene (18),  $\delta_{\text{H}}$  1.14 ( $\text{CMe}_2$ ), 1.78 ( $\text{:CMe}$ ), 2.23 (d,  $\underline{J}$  7,  $\text{CH}_2\text{CH:}$ ), 2.81 (d,  $\underline{J}$  6,  $\text{:CHCH}_2\text{CMe}$ ), 5.4 (t,  $\underline{J}$  7,  $\text{:CHCH}_2$ ), 6.01 (t,  $\underline{J}$  6,  $\text{HC:CSPH}$ ), 7.04 - 7.42 (m, 5H). The same 1,4-cycloheptadiene was also produced (70%) when the trans-vinyl sulphide (17) was heated at 160° for 3 h. in a sealed tube.<sup>8</sup>

Hydrolysis of the vinyl sulphide moiety in (18) ( $\text{HgCl}_2$ -MeCN- $\text{H}_2\text{O}$ , reflux 12 h.),<sup>9</sup> followed by chromatography, then led to karahanaenone (19) (45%), a pleasant smelling oil,  $\nu_{\text{max}}$  1705  $\text{cm}^{-1}$ ,  $\delta_{\text{H}}$  1.09 ( $\text{CMe}_2$ ), 1.66 ( $\text{:CMe}$ ), 2.25 (br, 4H), 2.71 (br. t,  $\underline{J}$   $\sim$  7,  $\text{COCH}_2$ ), 5.43 (br,  $\text{:CH}$ ), (semicarbazone, m.p. 164 - 168°) showing spectral data closely similar to those reported for the natural product.<sup>10</sup>

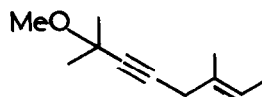
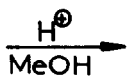
We thank Dr. E. Demole (Firmenich) for providing spectral data of their synthetic karahanaenone. We also thank the S.E.R.C. for a studentship (to P.M.C) and Proprietary Perfumes Ltd. for financial support (C.A.S.E. award to P.M.C).

#### References

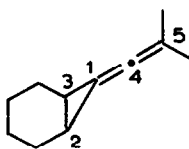
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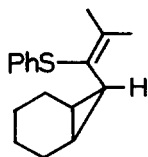
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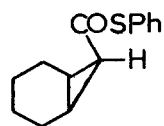
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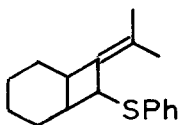
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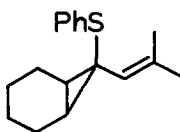
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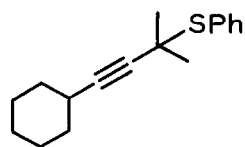
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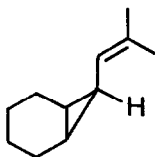
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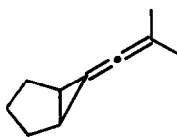
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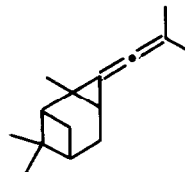
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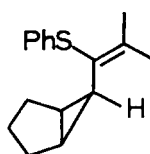
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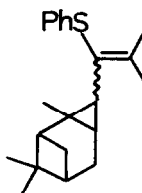
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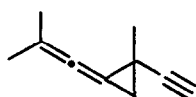
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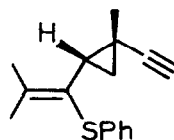
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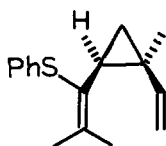
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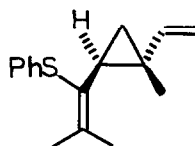
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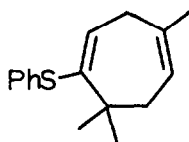
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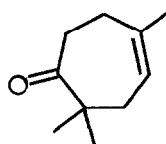
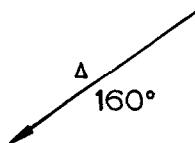
(16)



(17)



(18)



(19)

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