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THIA-ANALOGUES OF TROPANE ALKALOIDS.
SYNTHESIS OF INTERMEDIATES FROM MONOCYCLIC PRECURSORS.

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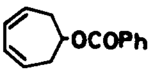
The trans addition of SCl_2 to double bonds has been applied to unsubstituted cyclic polyenes for the preparation of sulphur-bridged bicyclic systems.[1,2] SCl_2 also reacts with active methylene compounds with elimination of HCl to form acyclic thioethers (1:2 adduct)[3] and thioketones (1:1 adduct)[4].

To achieve a general synthesis of 8-thiabicyclo[3.2.1]octanes, as precursors to 8-thia-analogues of tropane alkaloids, we have investigated the condensation of SCl_2 with substituted cycloheptadienes,[5] two of which contain an enolisable carbonyl group.

Diene (1) reacted predictably with SCl_2 in CH_2Cl_2 at -70° producing, in quantitative yield, dichlorobenzoate (2) [m.p. 160-161°; m/e 316, 318, 320 (M^+)]. In contrast, dienone (3) behaved as an active methylene compound and reacted in CH_2Cl_2 at -5° with evolution of HCl giving an unstable pale yellow oil as major product (80%). This material, which possessed two distinct bridgehead resonances (δ 3.57 and 3.86) and a non-conjugated carbonyl group (ν^{CCl_4} 1749 cm^{-1}), was identified as allylic chloride (4) on the basis of double resonance experiments. During chromatography on alumina or on heating in vacuum 4 underwent partial decomposition ($<$ 10%) with further loss of HCl forming the canary-yellow, photolabile enone (5) (ν^{KBr} 1696 cm^{-1}) by a skeletal rearrangement similar to that observed in 9-thiabicyclo[3.3.1]nonyl systems.[6]

In condensation with SCl_2 diene acetal (6) and dienone (7) offer more than one possible mode of addition. Surprisingly, each furnished one major adduct (> 90%) viz. 8 [m.p. 112-114°; m/e 254, 256, 258 (M^+)] and 9 [m.p. 139-141°; m/e 210, 212, 214 (M^+); ν^{CCl_4} 1761 cm^{-1}]. The structural assignment of 8 and 9 followed from their PMR spectra, each of which possessed two non-coincident $\underline{H}\text{-}\overset{|}{\underset{|}{C}}\text{-}Cl$ resonances in the δ 4.5-5.0 region, inconsistent with more symmetrical systems such as 11 and 12. Moreover, dilute aqueous acid selectively hydrolysed 8, with retention of the acetal function, to chloroalcohol (10) [m.p. 85-87°, m/e 236, 238 (M^+) ; ν^{CHCl_3} 3559 cm^{-1}], reflecting the difference in reactivity of the two chlorine substituents of 8.

From the limited number of examples studied, the highly regio- and stereoselective addition of SCl_2 to substituted cycloheptadienes represents a convenient entry to the synthesis of the thio-ether relatives of the tropanes and furnishes intermediates with useful functionality. By comparison, a synthesis[7] of the 8-thiabicyclo[3.2.1]octane ring system using expensive 8-aza analogues as precursors proved to be unsuccessful for certain substrates.



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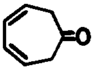

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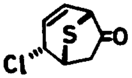

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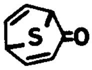

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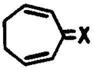
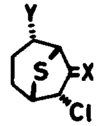


6 $X=OCH_2CH_2O$

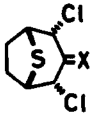
7 $X=O$



8 $X=OCH_2CH_2O$, $Y=Cl$

9 $X=O$, $Y=Cl$

10 $X=OCH_2CH_2O$, $Y=OH$



11 $X=OCH_2CH_2O$

12 $X=O$

Satisfactory analytical data have been obtained for 2, 8, 9 and 10 (microanalysis) and 4 (mass measurement) but not for the unstable enone (5).

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