Intramolecular 'Ene' Reactions of Thioaldehydes

Samuel S-M. Choi and Gordon W. Kirby*

Department of Chemistry, University of Glasgow, Glasgow G12 8QQ, U.K.

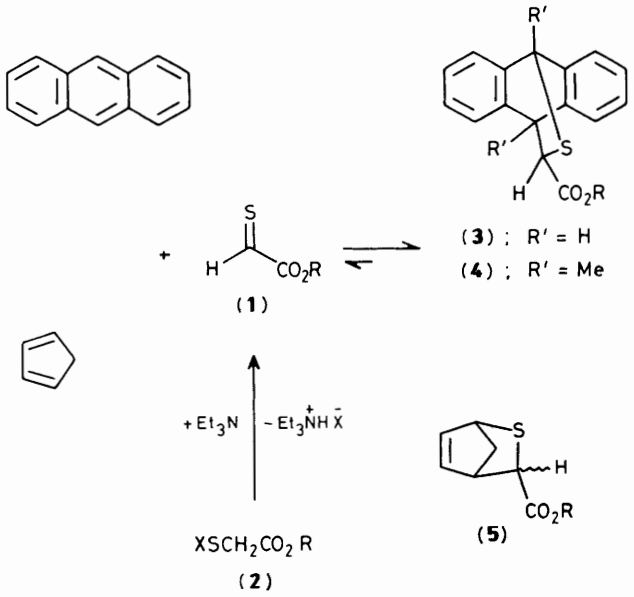
Allylic and homoallylic esters of thioxoacetic acid (**1b**), when generated by thermal cleavage of various Diels–Alder adducts in solution (111 °C) or by flash vacuum pyrolysis (600 °C), undergo intramolecular 'ene' reactions with C–C bond formation.

The labile thioaldehyde, ethyl thioxoacetate (**1a**), formed by 1,2-elimination from sulphenyl derivatives (**2a**), may be trapped *in situ* as Diels–Alder adducts with conjugated dienes (Scheme 1).[1,2] Moreover, the cycloadducts of anthracene (**3a**),[1] 9,10-dimethylanthracene (**4a**),[1] and cyclopentadiene (**5a**)[2] dissociate reversibly at moderate temperatures (80—111 °C) and thereby may serve as convenient, ancillary precursors of the thioaldehyde.

Ethyl thioxoacetate (**1a**)[1] and thiobenzaldehyde[3] undergo intermolecular 'ene' reactions, *e.g.* with β-pinene,[4] by competing pathways (Scheme 2), (a) leading to thiols (**6**), and (b) leading to sulphides (**7**). We expected that the intramolecular 'ene' reaction[5] of thioaldehydes would, for conformational reasons, proceed mainly with C–C bond formation (pathway a) and consequently might be a synthetically valuable complement to the diene reaction. We report here that the crystalline acids (**3b**),[1] (**4b**),[1] and (**5b**)[2] act as 'masked' thioaldehyde units for the synthetic elaboration of allylic (*e.g.* Scheme 3) and homoallylic alcohols[6] *via* the corresponding esters.

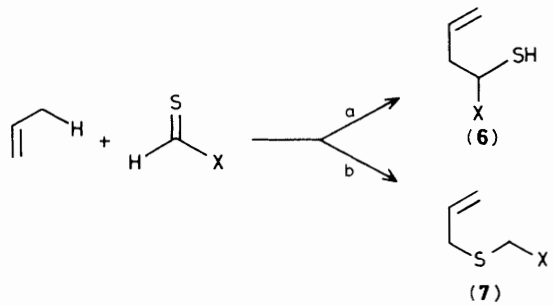
When the prenyl ester (**3c**)† was heated under reflux in

† Esters were prepared from the acids (**3b**), (**4b**), and (**5b**) by treatment in tetrahydrofuran (THF) at room temperature with *N,N'*-carbonyldiimidazole, followed by the appropriate alcohol[6] in THF containing a catalytic amount of alkoxide generated with n-butyl-lithium; all were oils apart from (**3d**), m.p. 97—98 °C.

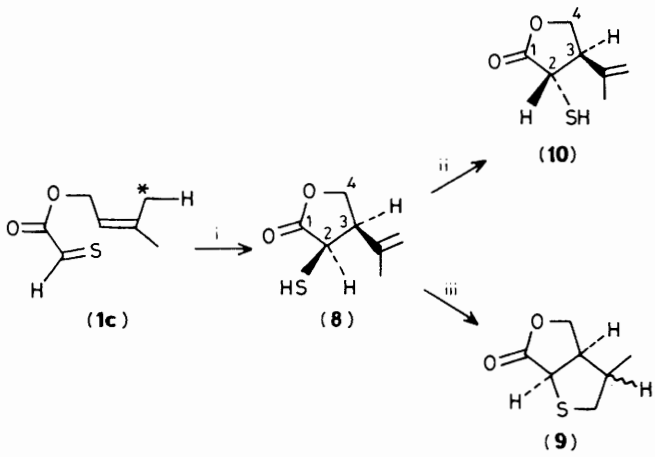


a; R = Et
b; R = H
c; R = $CH_2CH{=}CMe_2$
d; R = $CH_2CH{=}^{Z}CHMe$
e; R = $CH_2CH{=}^{E}CHMe$
f; R = 
g; R = $CH_2CH_2CH{=}CMe_2$

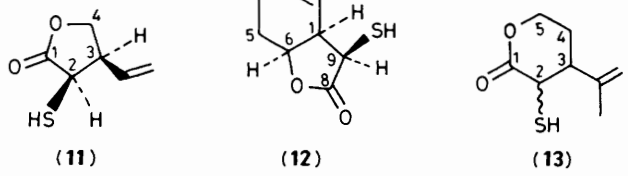
Scheme 1



Scheme 2



Scheme 3. *Reagents*: i, 111 °C in PhMe or 600 °C at 0.008 mmHg; ii, Et_3N in CH_2Cl_2, 20 °C; iii, O_2 in PhMe, 111 °C, or azoisobutyronitrile in C_6H_6, 80 °C.



toluene (32 mM)‡ under nitrogen for 4 h, efficient conversion into a mixture of anthracene and the thiol (**8**)§ was observed (Scheme 3); traces of air caused a by-product (**9**) to form. The corresponding cycloadduct (**4c**) of 9,10-dimethylanthracene similarly gave the thiol (**8**). Treatment of this *cis*-thiol (**8**) with triethylamine in dichloromethane at room temperature gave, essentially quantitatively, the *trans*-thiol (**10**). This epimerisation demonstrated the *cis*-stereochemistry (**8**); confirmation came from the ^{1}H n.m.r. spectra§ of the thiols and from nuclear Overhauser enhancement (n.O.e.) experiments. The high, *cis* stereoselectivity of the cyclisation (**1c**) → (**8**) indicates a concerted 'ene' reaction.[5] Further examples of stereochemical control, and evidence for selective attack at the '*cis*' methyl group of (**1c**) (asterisk in Scheme 3), came from experiments with the crotyl esters (**3d**) and (**3e**) and the cyclohexenyl ester (**3f**).

The (*Z*)-ester (**3d**) gave, under the foregoing conditions, anthracene and the *cis*-thiol (**11**) in high yield. The thermolysis of (**3d**) (11 mM) was slower than that of (**3c**) (32 mM),‡ requiring *ca.* 8 rather than 4 h for completion. In contrast, the (*E*)-ester (**3e**) gave no isolable amounts of any 'ene' product under the same conditions, even after 12 h. Both stereo- and regio-chemical control were observed in the 'ene' reaction of the cyclohexenyl derivative (**1f**). The precursor (**3f**) was converted cleanly in 7 h, in refluxing toluene as before, into anthracene and the bicyclic thiol (**12**); no isomer of (**12**) was detected by ^{1}H n.m.r. spectroscopy (90 MHz). Again, hydrogen had been abstracted from the allylic site '*cis*' to the pendant thial group, and the *cis–cis* stereochemistry (**12**) implies a concerted process. The 1,9-*cis* configuration (**12**) was established by epimerisation at C(9) with triethylamine in dichloromethane.

Thermolysis of the cyclopentadiene adducts (**5c**) proceeded much more slowly than that of the corresponding anthracene adduct (**3c**). Faster conversion into (**8**) was observed in xylene at 110 °C when nitrogen was passed *through* the solution to expel cyclopentadiene as it was formed.‡ However, thermolysis of cyclopentadiene adducts was inconveniently slow for preparative purposes. Flash vacuum pyrolysis (F.V.P.) was chosen as an alternative procedure, since unimolecular dissociation and 'ene' cyclisation could occur consecutively without competition from the bimolecular recapture of the thioaldehyde by cyclopentadiene. Dr. I. Gosney (University of Edinburgh) kindly lent his F.V.P. apparatus[7] for the

‡ The overall conversion (**3c**) → (**8**) was slower for more concentrated solutions. Anthracene, liberated in the reaction, retards the first-order formation of the 'ene' product by second-order recapture of the thioaldehyde (**1c**) (Scheme 1) (*cf.* ref. 6).

§ The 'ene' reaction products were all obtained as oils, apart from (**12**), m.p. 58—61 °C. Selected spectroscopic data, submitted with the manuscript, are available from the authors upon request.

following experiments. The *exo*-ester (**5c**) was evaporated slowly at 80 °C through a silica tube at 600 °C and 0.008 mmHg; the products were collected in a trap cooled in liquid nitrogen, then were dissolved in dichloromethane at room temperature. Evaporation of the solvent and cyclopentadiene gave the pure thiol (**8**) (95%) as a mixture of the *cis*-(**8**) and *trans*-isomer (**10**) (*ca.* 1 : 3). Presumably, partial epimerisation of the *cis*-thiol had occurred in the hot tube. Similarly, evaporation of the homoallylic ester (**5g**) at 100 °C, and pyrolysis as before, gave the δ-lactone (**13**) (62%), again as a mixture of *cis*- and *trans*-isomers (*ca.* 1 : 9).

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