Thialactones formed by Intramolecular 'Ene' Reactions of Thioaldehydes

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ω-Vinylalkyl esters (**3**) of thioxoacetic acid, generated by retro-Diels–Alder cleavage of their cyclopentadiene cycloadducts (**2**), underwent Type III intramolecular 'ene' reactions during flash vacuum pyrolysis at 500 °C to give 3-thialactones† having 6- to 11-membered rings.

The labile thioaldehyde, ethyl thioxoacetate ($EtO_2C{\cdot}CHS$),[1] formed conveniently from the Bunte salt[2] ($EtO_2C{\cdot}CH_2$-SSO_3Na), may be trapped efficiently as the *endo* and *exo* cyclopentadiene adducts (**1**; R = Et). These adducts dissociate[2,3] at moderate temperatures (*ca.* 100 °C) and thereby serve as auxiliary precursors for the thioaldehyde. We showed recently[4] that various allylic and homoallylic thioxoacetates, formed thermally from the corresponding precursors (**1**), underwent Type I[5] intramolecular 'ene' reactions, with C–C bond formation, to give cyclic thiols. We now report a homologous series of Type III[5] intramolecular 'ene' reactions, giving, with C–S bond formation, thialactones as the only significant products (Scheme 1).

The esters (**2**), prepared in the usual way[4] as oily mixtures of stereoisomers from the *endo* and *exo* acids (**1**; R = H), were evaporated at 50—150 °C, generally from thin films deposited on Celite powder, through a silica flash vacuum pyrolysis (FVP) tube at 500 °C and *ca.* 10^{-2}—10^{-4} mbar (bar = 10^5 Pa). The products were collected, along with cyclopentadiene, in a trap cooled in liquid nitrogen. The yields after purification are given in Scheme 1 (reaction conditions and yields were not optimised).

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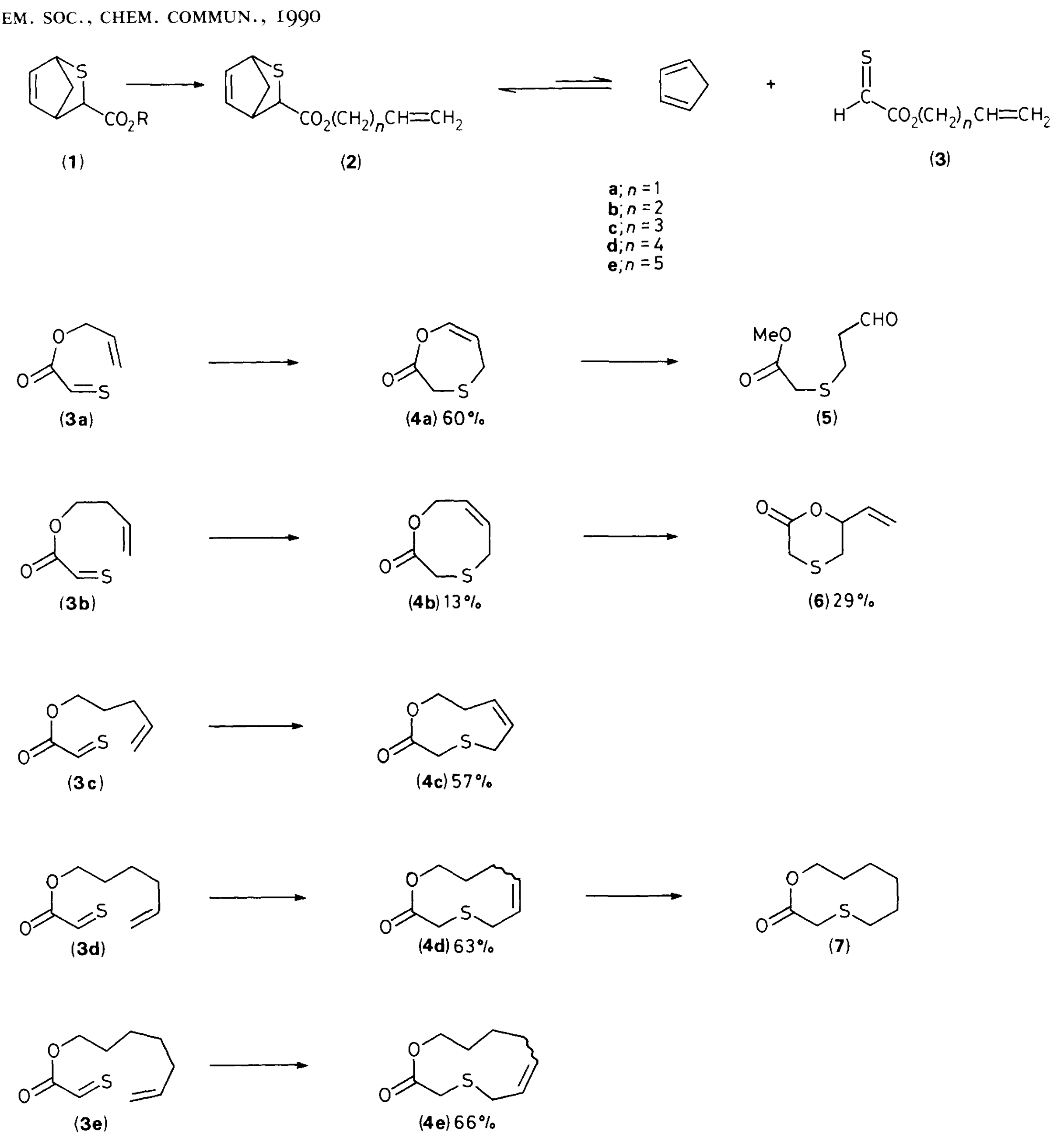
† *Spectral data* for the thialactones: ^{13}C NMR, δ ($CDCl_3$; 50.4 MHz): (**4a**), 22.9(t), 29.4(t), 111.1(d), 141.5(d), and 167.8(s); (**4b**), 29.3(t), 32.0(t), 63.6(t), 127.1(d), 128.2(d), and 169.8(s); (**4c**), 28.0(t), 28.3(t), 31.5(t), 59.9(t), 123.7(d), 132.0(d), and 170.2(s); (**4d**) (major isomer), 28.4(t), 31.4(t), 34.6(t), 37.0(t), 65.4(t), 125.6(d), 135.5(d), and 173.1(s); (**4d**) (minor isomer), 22.6(t), 25.0(t), 29.4(t), 34.2(t), 63.1(t), 128.2(d), 129.3(d), and 170.9(s); (**4e**) (major isomer), 25.7(t), 27.2(t), 33.9(t), 35.4(t), 37.3(t), 67.1(t), 126.3(d), 135.0(d), and 172.4(s); (**4e**) (minor isomer), 25.3(t), 25.5(t), 27.9(t), 30.3(t), 35.1(t), 66.8(t), 127.4(d), 131.4(d), and 170.9(s); (**6**), 26.0(t), 29.4(t), 79.1(d), 118.7(t), 133.6(d), and 167.3(s).



Scheme 1. *Conditions*: flash vacuum pyrolysis at 500 °C, evaporation temperatures 50—150 °C, initial pressures *ca.* 10^{-4} mbar.

The structure of the enol thialactone (**4a**) was confirmed by its cleavage at room temperature in methanol containing silica gel to give the aldehyde (**5**). The thiaheptenolide (**4b**) was accompanied by (**2b**) (11%) and the thiapentanolide (**6**), which presumably arose by sigmatropic rearrangement of the initial 'ene' product (**4b**), the sole allylic lactone of the series. Indeed, pyrolysis of (**2b**) at 400 °C gave (**4b**) but not (**6**). The thianonenolide (**4d**) was obtained as a *ca.* 2 : 1 mixture of geometrical isomers, which did not separate on silica TLC plates. The mixture formed well-defined crystals, m.p. 34 °C (from light petroleum), having essentially the same composition. Reduction with an excess of diimide (from dipotassium azodicarboxylate) gave a separable mixture of the saturated lactone (**7**) and a small quantity of the major isomer (**4d**), believed to be the *trans* geometrical isomer. The thiadecenolide (**4e**) was likewise obtained as a *ca.* 2 : 1 mixture of geometrical isomers.

Type III intramolecular 'ene' reactions,[5,6] which must proceed through bridged bicyclic transition states, are infrequently observed, in contrast with the common, Type I reactions involving fused bicyclic transition states. The efficient, Type III cyclisation of the thioaldehydes (**3**), especially to give medium-ring (8- to 11-membered) products, no doubt depends, *inter alia*, upon the high enophilic character of α-oxothials and the essentially unimolecular FVP reaction conditions. This procedure might, in principle, be applied to the synthesis of other cyclic carbonyl compounds. Sulphur extrusion with ring contraction[7] should also extend the synthetic utility of the products. Recently, Motoki *et al.* reported[8] the analogous cyclisation of *o*-(alkenyloxy)thiobenzophenones to give benzo-oxathiocines and a benzo-oxathiecine, apparently[8] the first known examples of Type III, thiocarbonyl 'ene' reactions.

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