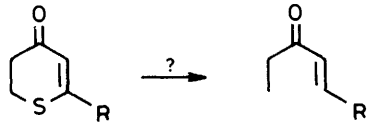
Substituted Thian-4-ones. Part 3.[1] Synthesis and Reactions of 2-Alkyl-5,6-Dihydrothiin-4-ones

Vinod K. Kansal and Richard J. K. Taylor*
School of Chemical Sciences, University of East Anglia, Norwich NR4 7TJ

A number of approaches to the synthesis of 2-alkyl-5,6-dihydrothiin-4-ones (**1**) are described. The treatment of 2-butylthian-4-one (**3**) with *N*-chlorosuccinimide gave a mixture of the alkenes (**1a**) and (**4**) and the corresponding reaction with the dioxolane (**5**) also proved to be non-regioselective. 2-Chlorodihydrothiin-4-one (**6**) was prepared and its reactions with a number of butylcopper reagents studied. The only product isolated from these reactions was 2,2-dibutylthian-4-one (**12**). 3-Chlorodihydrothiin-4-one (**8**) was successfully prepared and converted into 2-butyl-3-chlorothian-4-one (**13**) but dehydrohalogenation could not be achieved. A successful synthesis of the title compounds was achieved based on the generation and alkylation of the β-acylvinyl anion equivalent (**14**). Attempts to desulphurise 2-benzyl-5,6-dihydrothiin-4-one (**1d**) and related compounds in order to produce the α,β-unsaturated ketone (**18**) are discussed.

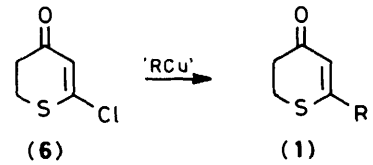
Substituted derivatives of dihydrothiin-4-one are useful synthetic intermediates[2-5] but to our knowledge no one has explored the possibility that these compounds might undergo desulphurisation and thus serve as precursors to α,β-unsaturated ketones. This idea is attractive because polysubstituted dihydrothiin-4-ones are readily available[2-5] and would lead to complex enones not easily prepared by standard procedures. In order to determine the potential of this approach we decided to prepare some simple 2-alkyl-5,6-dihydrothiin-4-ones (**1**) and investigate their desulphurisation reactions to give the enones (**2**). The desulphurisation of related compounds, both saturated[6,7] and unsaturated,[8] is a well-established procedure.



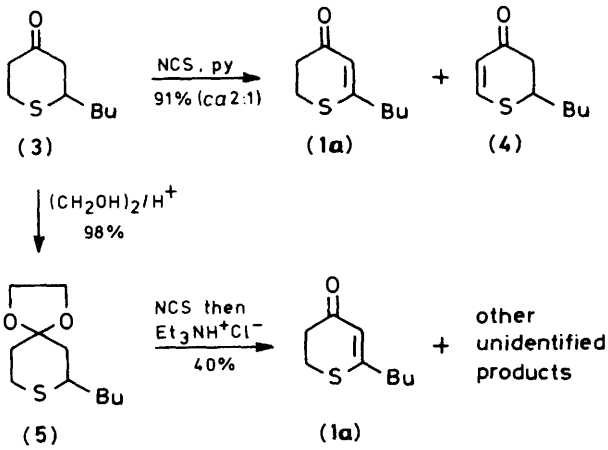
(**1**) (**2**)

An efficient method of preparing compounds (**1**) was sought. Chen *et al.* have shown that symmetrical 2,6-disubstituted thian-4-ones give the corresponding mono-unsaturated derivatives on treatment with *N*-chlorosuccinimide (NCS) and base.[2] 2-Substituted thian-4-ones are readily available[1,6] and so we decided to investigate the regioselectivity of the NCS procedure using 2-butylthian-4-one[1] [(**3**) Scheme 1]. Treatment of (**3**) with NCS/pyridine in dichloromethane gave a mixture of (**1a**; R = Bu) and the regioisomeric alkene (**4**) (91% yield, *ca.* 2:1). The corresponding dioxolane (**5**) was also treated with NCS but hydrolysis/elimination of the crude product gave a complex mixture from which (**1a**) was isolated in only 40% yield after chromatography. These results, summarised in Scheme 1, prompted the search for a regioselective route to 2-substituted 5,6-dihydrothiin-4-ones.

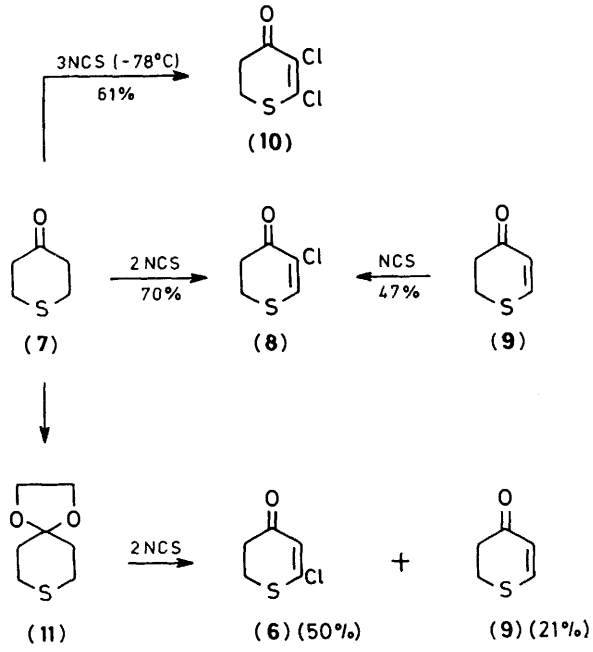
The first approach to come under scrutiny was the reaction of 2-chloro-5,6-dihydrothiin-4-one (**6**) with organocopper reagents:



(**6**) (**1**)



Scheme 1.



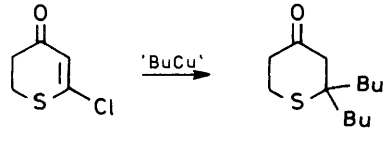
Scheme 2.

The preparation of the 2-chloro enone (**6**) and related compounds is illustrated in Scheme 2. It is well known[9] that the treatment of dialkyl sulphides with two molar equivalents of chlorinating agent produces α,α- rather than α,α′-dichlorides. We therefore planned to convert thian-4-one (**7**)[10] into the corresponding α,α-dichloride and then dehydrochlorinate it to produce the 2-chloro enone (**6**), but this route did not succeed. Treatment of (**7**) with two equivalents of NCS at room temperature produced just a trace of the required compound (**6**), the major product (70%) being the 3-chloro enone (**8**). Chen *et al.* have shown[2] that substituted 2,3-dihydrothiin-4-ones undergo electrophilic substitution with NCS to produce vinyl chlorides corresponding to (**8**). We presume, therefore, that thian-4-one reacts with the first equivalent of NCS to produce the vinyl sulphide (**9**) (either directly[2] or *via* α-chlorination and spontaneous loss of HCl[9]). The vinyl sulphide (**9**) can then react with the second equivalent of NCS to produce (**8**). To give credence to this hypothesis, (**9**) was prepared[2] and on treatment with NCS produced (**8**) in 47% yield.

Varying the reaction conditions failed to produce a viable synthesis of (**6**) and generally gave complex product mixtures. The exception was when thian-4-one (**7**) was treated with three equivalents of NCS at −78 °C, the reaction then being warmed to room temperature. This protocol gave the 2,3-dichloro enone (**10**) in 61% yield. It seems likely that the required 2-chloro enone (**6**) is an intermediate in the production of (**10**) but we were unable to isolate it from the reaction mixture.

Having decided that the main obstacle to success was the ease with which dehydrochlorination took place we looked at the reaction of the dioxolane (**11**) with 2 equivalents of NCS. The crude product (assumed to be the 2,2-dichloride) was boiled in toluene and the required 2-chloro enone (**6**) was produced in 50% yield along with 21% of the unchlorinated enone (**9**) which presumably arises from monochlorination/dehydrochlorination. The *in situ* dehydrochlorination/acetal hydrolysis observed in this reaction has been described before.[11] After the completion of this part of the project a similar procedure for the conversion of sulphides into 1-chloroalk-1-enyl sulphides was reported.[12]

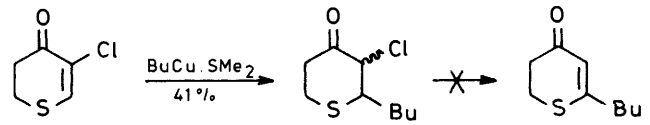
With the 2-chloro enone (**6**) in hand, its reactions with organocopper reagents were investigated. A variety of reagents (Bu_2CuLi, $Bu_2CuLi{\cdot}SMe_2$, Bu(PhS)CuLi, $BuCu{\cdot}SMe_2$, and BuMgBr/catalytic CuCN) were employed but the required 2-butyl enone (**1a**) was not formed. The only identifiable product from these reactions was 2,2-dibutylthian-4-one (**12**). Presumably the β-chloro enone (**6**) is first converted into (**1a**) but this undergoes conjugate addition to give (**12**). After the



(**6**) (**12**)

completion of this work a report was published describing the successful monoaddition of R(PhS)CuLi to enones containing two good leaving groups in the β-position.[13] Similar conditions were unsuccessful in our case but it seems likely that further studies would produce suitable reagents/reaction conditions for carrying out the required transformation.

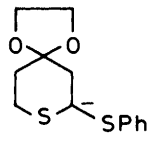
The conjugate addition of the 3-chloro enone (**8**) with $BuCu{\cdot}SMe_2$ was also studied. A mixture of *cis*- and *trans*-2-butyl-3-chlorothian-4-one (**13**) was obtained in 41% combined yield. Unfortunately, the dehydrohalogenation of (**13**) to give (**1a**) could not be achieved using standard conditions (*e.g.*



(**8**) (**13**) (**1a**)

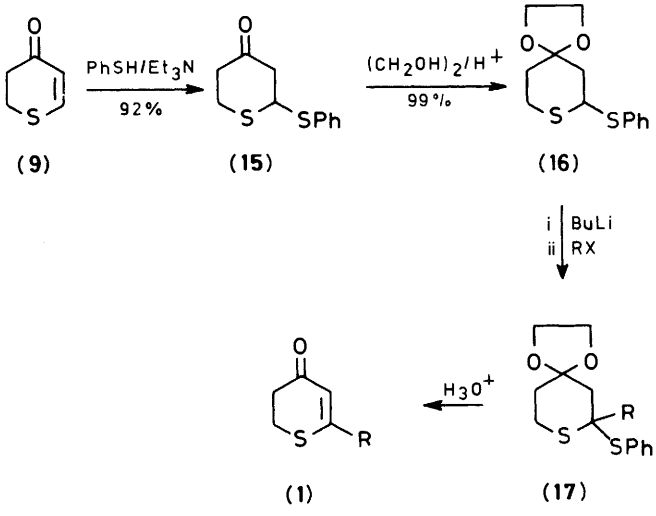
$LiBr/Li_2CO_3/DMF$[14]). Similar problems have been encountered in related systems.[3a]

We next turned our attention to an alternative strategy, the generation and alkylation of the β-acylvinyl anion equivalent (**14**). A number of β-acylvinyl anion equivalents have been



(**14**)

devised.[15] We decided to concentrate our efforts on the preparation of (**14**)[16] since we expected anion generation and alkylation of a dithioacetal system to be straightforward. This proved to be the case (Scheme 3). Treatment of 2,3-dihydrothiin-4-one (**9**)[2] with thiophenol–triethylamine gave the adduct (**15**) which was transformed into the dioxolane (**16**) (91% over 2 steps).[11] This conversion could be carried out in one step ($PhSH–(CH_2OH)_2–H^+$)[11] but the overall yield was lower (70%). The anion (**14**) was generated from (**16**) using BuLi–THF and alkylation occurred readily in the same solvent. The alkylated products (**17**) were hydrolysed (4M-HCl) to give the required products (**1**) in high overall yield (83—91% over 2 steps). Alkylation of (**14**) with allyl bromide also proceeded in high yield (*ca.* 99%) but hydrolysis using hydrochloric acid caused decomposition.



(**9**) (**15**) (**16**)

(**1**) (**17**)

a ; R = Bu (89%)
b ; R = Bu^i (87–90%)
c ; R = Me (83%)
d ; R = CH_2Ph (81–90%)
e ; R = $CH_2CH{=}CH_2$ (see text)

Scheme 3.

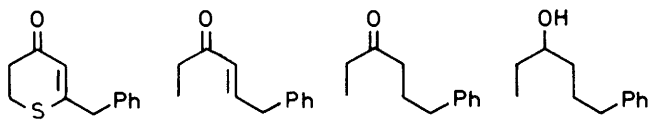
The desulphurisation of the thioenones (**1**) was investigated next. A number of vinyl sulphides have been successfully

Table. Desulphurisation results[a]

Substrate	Reagent	Refluxing solvent (time)	Product (isolated yield)
i (**1d**)	Deactivated W-2 Raney Ni (1 h)[b]	MeOH (6 h)	(**19**) (75%)
ii (**1d**)	Deactivated W-2 Raney Ni (1 h)[b]	4:1 Me_2CO–MeOH (6.5 h)	(**19**) (45%)[c]
iii (**1d**)	Deactivated W-2 Raney Ni (1 h)[b]	5:1 Me_2CO–cyclohexene (96 h)	(**19**) (40%)
iv (**1d**)	Nickel boride[19]	EtOH–H_2O (72 h)	(**21**) (68%)
v (**21**)	Deactivated W-2 Raney Ni (2 h)[b]	Me_2CO (15 h)	(**20**) (96%)
vi (**22**)	Deactivated W-2 Raney Ni (3 h)[b]	8:1 Me_2CO–MeOH (43 h)	No reaction[d]
vii (**23**)	Deactivated W-2 Raney Ni (2.5 h)[b]	8:1 Me_2CO–MeOH (43 h)	No reaction

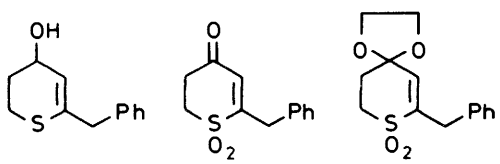
[a] Reaction v was carried out on a 0.75 mmol scale, all others were on 0.5 mmol of substrate. The product mixtures purified by preparative centrifugal chromatography. [b] Excess of W-2 Raney nickel[20] was deactivated by boiling in acetone under reflux[17] for the time indicated. Where necessary the acetone was then decanted and the reaction solvent added (see Experimental section). [c] 20% Starting material recovered. Yield based on consumed starting material = 56%. [d] Additional Raney Ni and prolonged period under reflux gave reduction of the enone system but no desulphurisation.

converted into alkenes[17–19] using W-2 Raney nickel[20] and so our efforts were concentrated on this reagent. The Raney nickel was first deactivated in acetone to avoid carbonyl reduction.[17–19] The 2-benzyl system (**1d**) was chosen as the most suitable substrate for these investigations since the likely reaction products (**18**),[21] (**19**),[22] and (**20**)[22] are known



(**1d**) (**18**) (**19**) (**20**)

compounds with relatively high boiling points. The results of this investigation are shown in the Table. Treatment of (**1d**) with deactivated Raney nickel in methanol[18] or acetone–methanol failed to give the enone (**18**), the only major product being the reduced ketone (**19**) (entries i and ii). Cyclohexene was included in an attempt to minimise over-reduction but to no avail (entry iii). The use of nickel boride[19] in place of Raney nickel gave ketone reduction without desulphurisation (entry iv). The Raney nickel desulphurisation of (**21**), (**22**), and (**23**) was also investigated.



(**21**) (**22**) (**23**)

The alcohol (**21**) underwent desulphurisation with concomitant alkene reduction (entry v) whereas the sulphones (**22**) and (**23**) remained intact even after prolonged exposure to Raney nickel (entries vi and vii).

These studies have produced an efficient procedure for preparing 2-alkyl-5,6-dihydrothiin-4-ones (**1**). The results of the desulphurisation experiments were disappointing, however. A recent publication[23] has shown that substituted 3-alkylthiocyclopent-2-en-1-ones can be desulphurised to substituted cyclopentenones (*i.e.* without reduction of the conjugated double bond) using Raney nickel. It is possible that the over-reduction observed in this study is peculiar to the 2-benzyl-system and that the other 2-alkyl-5,6-dihydrothiin-4-ones will undergo clean desulphurisation. This hypothesis will be tested in future studies and the utility of newly discovered desulphurisation systems will also be investigated.[24]

Experimental

^{1}H N.m.r. spectra were recorded on Jeol PMX 60 or Perkin-Elmer R12 spectrometers. I.r. spectra were obtained on a Perkin-Elmer 297 spectrophotometer and mass spectra on a Kratos MS 25 (low resolution) or Kratos MS 902/DMS 50 SM (high resolution) instrument. A normal work-up procedure consisted of three extractions with the specified solvent, washing of the combined extracts with brine, drying ($MgSO_4$), and removal of the solvent on a rotary evaporator under reduced pressure. Petroleum is the fraction b.p. 40—60 °C. Ether is diethyl ether.

Column chromatography was performed with silica gel 60 (Merck 7734) and preparative centrifugal chromatography was carried out on a Chromatotron Model 7924 using silica gel 60 (Merck 7749).

2-Butyl-4,4-ethylenedioxythiane (**5**).—A mixture of 2-butylthian-4-one (**3**)[1] (0.175 g, 1.02 mmol), ethanediol (0.093 g, 1.5 mmol), and toluene-*p*-sulphonic acid (0.005 g) in benzene (30 ml) was boiled under reflux in a Dean-Stark assembly for 3 h. The reaction mixture was cooled and washed with water, aqueous sodium hydrogencarbonate and then water again. The combined aqueous layers were re-extracted with ether and the ether layer washed once with water. The combined organic fractions were dried and the solvent removed under reduced pressure to give the *acetal* as an analytically pure oil (0.215 g, 98%), R_F 0.46 (CH_2Cl_2); δ(CCl_4) 3.84 (4 H, s), 3.20—2.20 (3 H, m), and 2.00—0.80 (13 H, m); *m/z* 216 (M^+) (Found: C, 61.15; H, 9.3; S, 15.05%. $C_{11}H_{20}SO_2$ requires C, 61.07; H, 9.32; S, 14.82%).

2-Butyl-5,6-dihydrothiin-4-one (**1a**) via *NCS Reactions*.—(i) *From 2-butylthian-4-one* (**3**). NCS (0.157 g, 1.17 mmol) was added portionwise to a solution of 2-butylthian-4-one (**3**)[1] (0.178 g, 1.03 mmol) in dichloromethane (10 ml), containing pyridine (0.086 g, 1.1 mmol) and the reaction was stirred at room temperature for 1 h under nitrogen. The reaction mixture was diluted with dichloromethane and then washed with water, 10% hydrochloric acid, water again, and then finally dried. Removal of the solvent under reduced pressure furnished a mixture of (**1a**) and (**4**) (0.16 g, 91%) in the ratio of *ca.* 2:1 according to ^{1}H n.m.r. spectroscopy. Separation of this mixture by column chromatography on silica (5:1 ⟶ 2:1 petroleum–ether) gave 2-butyl-2,3-dihydrothiin-4-one (**4**), R_F 0.39 (petroleum–ether, 1:1), $\nu_{max.}$(liquid) 1 657 and 1 546 cm^{-1}; δ($CDCl_3$) 7.4 (1 H, d, *J* 10 Hz), 6.1 (1 H, d, *J* 10 Hz), 3.9—3.0 (1 H, m), 3.0—2.5 (2 H, m), and 2.0—0.6 (9H, m) (Found: *M*, 170.0769. $C_9H_{14}OS$ requires *M*, 170.0765). This was followed by *2-butyl-5,6-dihydrothiin-4-one* (**1a**) R_F 0.30 (petroleum–ether, 1:1), $\nu_{max.}$(liquid) 1 652 and 1 565 cm^{-1}; δ(CCl_4) 5.78 (1 H, s), 3.10 (2 H, m), 2.46 (4 H, m), 1.50 (4 H, m), and 0.9 (3 H, m); *m/z* 170 (M^+) (Found: C, 63.25; H, 8.45; S, 19.05. $C_9H_{14}OS$ requires C, 63.48; H, 8.29; S, 18.83).

(ii) *From 2-butyl-4,4-ethylenedioxythiane* (**5**). NCS (0.56 g, 4.1 mmol) was added to a stirred, cooled (0 °C) solution of the title compound (**5**) (0.846 g, 3.9 mmol) in carbon tetrachloride (25 ml) under a nitrogen atmosphere. The reaction was stirred at 0 °C for 2 h, after which the precipitated succinimide was removed by

filtration and washed well with ether. The organic filtrates were combined and the solvent removed under reduced pressure. Toluene (20 ml) and triethylamine (1 ml) were added to the resulting oil and the mixture was boiled under reflux for 2 h. After cooling, the solution was washed with water, 2M-hydrochloric acid, and water again, and then dried. Removal of the solvent under reduced pressure gave an oil. Purification by preparative centrifugal chromatography (petroleum–ethyl ether, 1 : 1) gave 2-*butyl*-5,6-*dihydrothiin*-4-*one* (**1a**) as a colourless oil (0.265 g, 40%) which was identical with the sample obtained in (i).

3-*Chloro*-5,6-*dihydrothiin*-4-*one* (**8**).—(i) *From thian*-4-*one* (**7**). NCS (2.97 g, 0.022 mol) was added portionwise to a stirred solution of thian-4-one (**7**)[10] (1.16 g, 0.01 mol) in CCl_4 (20 ml) under N_2 at room temperature. The reaction was stirred at room temperature for 30 min and then boiled under reflux for 2 h. The reaction was cooled, the black precipitate was removed by filtration, and the precipitate was washed several times with ether. The organic filtrates were combined and the solvent removed under reduced pressure. The crude product was filtered through a short alumina column using dichloromethane and then ether as eluant. Removal of the solvent under reduced pressure and trituration of the product with petroleum gave a solid. Recrystallisation from ether–petroleum gave the *vinyl chloride* (**8**) (1.03 g, 70%) as white crystals, m.p. 80—81 °C; R_F 0.57 (CH_2Cl_2); $\nu_{max.}$(CCl_4) 1 685 cm^{-1}; δ(CCl_4) 7.40 (1 H, s), 3.30 (2 H, m), and 2.90 (2 H, m); *m/z* 150, 148 (M^+) (Found: C, 40.4; H, 3.2; Cl, 23.95; S, 21.55%. C_5H_5ClOS requires C, 40.41; H, 3.39; Cl, 23.86, S, 21.57%). T.l.c. of the crude reaction mixture indicated that a trace of the 2-chloro isomer (**6**) was also formed in this reaction.

(ii) *From* 2,3-*dihydrothiin*-4-*one* (**9**). NCS (0.162 g, 1.2 mmol) was added to a stirred solution of 2,3-dihydrothiin-4-one (**9**)[2] (0.114 g, 1 mmol) in dichloromethane (20 ml) under nitrogen at room temperature. The reaction was then stirred at room temperature for 12 h. The solution was concentrated under reduced pressure and then filtered through a short alumina column using dichloromethane as eluant. Further purification using preparative centrifugal chromatography (CH_2Cl_2) gave the *vinyl chloride* (**8**) (0.07 g, 47%) which was identical with the sample obtained in (i).

2,3-*Dichloro*-5,6-*dihydrothiin*-4-*one* (**10**).—NCS (3.20 g, 0.024 mol) was added portionwise to a stirred solution of thian-4-one (**7**)[10] (1.16 g, 0.01 mol) in dichloromethane (20 ml) at −78 °C under nitrogen. Stirring was continued at −78 °C for 4.5 h and t.l.c. analysis then indicated that the reaction was incomplete. A further batch of NCS (0.6675 g, 0.005 mol) was added and stirring at −78 °C continued for 4.5 h. The reaction was then stirred at room temperature for 12 h; the precipitated succinimide was removed by filtration and washed well with ether. The organic filtrates were combined and the solvent removed under reduced pressure. The resulting solid was filtered through a short alumina column using dichloromethane as eluant. Removal of the solvent under reduced pressure and recrystallisation of the product from dichloromethane–petrolem gave the 2,3-*dichloride* (**10**) (1.2 g, 61%) as white crystals, m.p. 68—70 °C; R_F 0.47 (CH_2Cl_2); $\nu_{max.}$(CCl_4) 1 688 cm^{-1}; δ(CCl_4) 3.20 (2 H, m) and 2.78 (2 H, m); *m/z* 186, 184, 182 (M^+) (Found: C, 33.05; H, 2.01; Cl, 38.7; S, 17.55. $C_5H_4Cl_2OS$ requires C, 32.80; H, 2.20; Cl, 38.74; S, 17.51%).

2-*Chloro*-5,6-*dihydrothiin*-4-*one* (**6**).—NCS (6.70 g, 0.05 mol) was added portionwise to a stirred solution of 4,4-ethylenedioxythiane (**11**)[6] (3.83 g, 0.024 mol) in benzene under nitrogen at 0 °C. The orange reaction mixture was stirred at 0 °C for 1 h, and then at room temperature for 4 h. The precipitated succinimide was removed by filtration and washed well with benzene. The combined organic filtrates were combined and the solvent removed under reduced pressure. Toluene (60 ml) was added to the crude reaction product and the mixture boiled under reflux for 5 h. Removal of the solvent under reduced pressure gave an oil which was purified by preparative centrifugal chromatography (petroleum–ether, 86:14). The major product was the 2-*chloride* (**6**) (1.78 g, 50%) as an oil, R_F 0.29 (petroleum–ether, 1 : 1); $\nu_{max.}$(liquid film) 1 676 cm^{-1}; δ(CCl_4) 6.28 (1 H, s), 3.34 (2 H, m), and 2.50 (2 H, m); *m/z* 150, 148 (M^+) (Found: C, 40.2; H, 3.55; Cl, 24.2; S, 21.55. C_5H_5ClOS requires C, 40.41; H, 3.39; Cl, 23.86; S, 21.57%). Continued elution with the same solvent gave 2,3-dihydrothiin-4-one (**9**) (0.6 g, 21%) which was identical with an authentic[2] sample.

Reactions of 2-*Chloro*-5,6-*dihydrothiin*-4-*one* (**6**) *with Organocopper Reagents*.—(i) *With* Bu_2CuLi. Butyl-lithium in hexane (1.36 ml, 2.2 mmol) was added to a stirred suspension of purified[25] copper(I) iodide (0.209 g, 1.1 mmol) in dry ether (5 ml) at −50 °C under nitrogen. After 5 min dimethyl sulphide (1 ml) was added and the solution stirred at −78 °C for 30 min. Vinyl chloride 6 (0.148 g, 1 mmol) in ether (0.5 ml) was then added and the reaction stirred at −78 °C for 1 h. The reaction was then warmed to −20 °C and 2M-hydrochloric acid (2 ml) added. The reaction mixture was diluted with ether and the precipitated copper salts removed by filtration. The ether extracts were washed with water, dried, and the solvent removed under reduced pressure. The resulting oil was purified by preparative centrifugal chromatography (petroleum–ether, 4:1) to give, as the major product, 2,2-*dibutylthian*-4-*one* (**12**) (0.12 g, 55%) as an oil, R_F 0.5 (petroleum–ether, 3:2), $\nu_{max.}$(liquid film) 1 720 cm^{-1}; δ(CCl_4) 2.80 (2 H, m), 2.40 (4 H, m), and 1.70—0.80 (18 H, m); *m/z* 228 (M^+) (Found: C, 68.3; H, 10.6; S, 14.25%. $C_{13}H_{24}OS$ requires C, 68.36; H, 10.59; S, 14.04%).

(ii) *Other organocopper reagents*. Reactions with the following reagents were carried out using standard procedures: (*a*) Bu_2CuLi (1.1 mmol) with (**6**) (1 mmol) gave (**12**) (*ca.* 30%). (*b*) BuCu (1.1 mmol) and Me_2S (1 ml) with (**6**) (1 mmol) gave (**12**) (*ca.* 32%). (*c*) Bu(PhS)CuLi (1.1 mmol) in THF with (**6**) (1 mmol) gave a complex mixture of products. (*d*)BuMgBr (1.2 mmol)/CuCN (0.12 mmol) on addition to (**6**) (1 mmol) gave a complex mixture of products.

cis- *and* trans-2-*Butyl*-3-*chlorothian*-4-*one* (**13**).—Butyl-lithium in hexane (2 ml, 3.3 mmol) was added to a stirred solution of copper(I) iodide (0.629 g, 3.3 mmol) in dry ether (5 ml) and dimethyl sulphide (2 ml) at −50 °C under nitrogen. After 5 min at −50 °C the solution was cooled to −78 °C and stirred at this temperature for 1 h. A solution of 3-chloro-5,6-dihydrothiin-4-one (0.455 g, 3 mmol) in dry THF (2 ml) was then added and the reaction stirred at −78 °C for 1 h. After the mixture had warmed to −10 °C, 5% hydrochloric acid (5 ml) was added and the whole treated to a normal ether work-up. Trituration of the resultant semisolid with petroleum, filtration to remove the remaining copper salts, and removal of the solvent from the filtrate under reduced pressure gave an oil which was purified by preparative centrifugal chromatography (petroleum–ether, 9:1). The major products were a mixture of cis- and trans-2-*butyl*-3-*chlorothian*-4-*one* (0.254 g, 41%), as an oil, R_F 0.72 and 0.81 (petroleum–ether, 2.5:1); $\nu_{max.}$(liquid film) 1 715 cm^{-1}; δ 4.46 (*ca.* 0.3 H, d, *J* 3 Hz), 4.10 (1 H, m), 3.68 (1 H, d, *J* 4 Hz), 3.40—2.40 (*ca.* 5 H, m), and 2.00—0.60 (*ca.* 12 H, m); *m/z* 208 and 206 (M^+) (Found: C, 52.45; H, 7.2; Cl, 17.05; S, 15.3. $C_9H_{15}ClOS$ requires C, 52.29; H, 7.31; Cl, 17.15; S, 15.51%).

Attempted Dehydrochlorination of cis- *and* trans-(**13**).—The *cis*/*trans*-(**13**) mixture (0.05 g, 0.25 mmol), lithium carbonate (0.033 g, 0.5 mmol), and lithium bromide (0.041 g, 0.5 mmol) in

dry DMF (5 ml) were stirred and heated at 140—150 °C under nitrogen for 36 h.

Analysis by t.l.c. indicated that little if any dehydrochlorination had taken place.

2-*Phenylthio*-4,4-*ethylenedioxythiane* (**16**).—(i) *Two-step procedure.* Freshly distilled thiophenol (11 g, 0.1 mol) and triethylamine (11.44 g, 0.1 mol) were added to a stirred solution of 2,3-dihydrothiin-4-one (**9**)[2] (7.98 g, 0.07 mol) in dry toluene (100 ml) under nitrogen and the reaction was stirred at room temperature for 19 h. The reaction was then washed with water, 10% aqueous potassium hydroxide, and water again. The aqueous washings were extracted with ether and the combined organic fractions were dried and the solvent removed under reduced pressure. Trituration of the resulting oil with petroleum gave the *thioacetal* (**15**) as white crystals (14.42 g, 92%) which were recrystallised from ether–petroleum, m.p. 70—71 °C; R_F 0.57 (CH_2Cl_2); $\nu_{max.}$($CHBr_3$) 1 705 cm^{-1}; δ 7.60—7.00 (5 H, m), 4.48 (1 H, t, *J* 7 Hz), and 2.20—3.40 (6 H, m); *m/z* 224 (M^+) (Found: C, 58.94; H, 5.47; S, 28.51%. $C_{11}H_{12}OS_2$ requires C, 58.89; H, 5.39; S, 28.58%).

A mixture of (**16**) (4.67 g, 0.021 mol), ethylene glycol (1.93 g, 0.031 mol), and toluene-*p*-sulphonic acid (20 mg) in dry benzene (60 ml) was boiled under reflux in a Dean-Stark assembly for 2 h. After cooling, the reaction mixture was washed with water, aqueous sodium hydrogencarbonate, and water again. The combined aqueous layers were re-extracted with ether, the organic layers combined, dried, and the solvent removed under reduced pressure. Trituration of the resulting oil with petroleum gave the *dioxolane* (**16**) as white crystals (5.50 g, 99%) which were recrystallised from ether–petroleum, m.p. 58—59 °C; R_F 0.37 (petroleum–ether, 1:1); δ 7.24 (5 H, m), 4.20 (1 H, dd, *J* 3, 4 Hz), 3.88 (4 H, s), 2.90 (2 H, m), and 2.00 (4 H, m); *m/z* 268 (M^+) (Found: C, 58.4; H, 6.0; S, 24.0. $C_{13}H_{16}S_2O_2$ requires C, 58.175; H, 6.01; S, 23.89%).

(ii) *One-step procedure.* Thiophenol (1.65 g, 0.015 mol) was added to a stirred solution of 2,3-dihydrothiin-4-one (**9**)[2] (1.14 g, 0.01 mol) in benzene (40 ml). After 15 min at room temperature ethanediol (1.24 g, 0.02 mol) and toluene-*p*-sulphonic acid (50 mg) were added. The reaction mixture was then boiled under reflux for 6 h in a Dean-Stark assembly. Work-up as in the acetalisation step of (i) gave an oil which was purified by column chromatography on silica (CH_2Cl_2) giving the *dioxalane* (**16**) (1.80 g, 70%) identical with the sample obtained in (i).

Alkylation and Hydrolysis of the Thioacetal (**16**).—(a) *Two-pot procedure.* Butyl-lithium in hexane (1.2 mmol) was added dropwise to a stirred solution of the thioacetal (**16**) (0.27 g, 1 mmol) in dry THF (4 ml) at −30 to −35 °C under nitrogen. The yellow reaction mixture was stirred at −35 °C for 30 min and then cooled to −78 °C. The alkyl halide (1.8 mmol) was then added and stirring continued until t.l.c. indicated that the reaction was complete: (**17a**), 90 min; (**17b**), 70 min; (**17c**), 60 min; (**17d**), 120 min; (**17e**), 60 min. Saturated ammonium chloride solution was then added and the reaction given a normal ether work-up. The products (**17**), which were pure according to ^1H n.m.r. spectroscopy, were obtained in high yield: (**17a**), 99%; (**17b**), 95%; (**17c**), 98%; (**17d**), 99%; (**17e**), 99%. All were oils apart from 2-benzyl-2-phenylthio-4,4-ethylenedioxythiane (**17d**) which was recrystallised from methanol as white crystals, m.p. 84—86 °C.

The alkylation products (**17**) were hydrolysed without further purification. A mixture of the thioacetal (**17**) (1 mmol) and 4M-hydrochloric acid (2 ml) in acetone (10 ml) was boiled under reflux under nitrogen for the following times: (**17a**), 6 h; (**17b**), 8 h; (**17c**), 6 h; (**17d**), 18 h. When (**17e**) was subjected to these conditions extensive decomposition occurred according to t.l.c. The reaction mixtures were cooled, diluted with water, and extracted with ether (3 × 25 ml). The combined ether layers were washed with 10% aqueous potassium hydroxide and then with water. The aqueous washings were re-extracted with ether and the ether washed with water. The combined organic layers were dried and the solvent removed under reduced pressure. Purification of the resulting oils by preparative centrifugal chromatography (petroleum–ether, 7:3) gave the following 2-alkyl-5,6-dihydrothiin-4-ones (**1**):

2-Butyl-5,6-dihydrothiin-4-one (**1a**) [89% from (**16**)] which was identical with the material obtained earlier.

2-*Isobutyl*-5,6-*dihydrothiin*-4-*one* (**1b**) [87% from (**16**)], R_F 0.34 (CH_2Cl_2); $\nu_{max.}$(CCl_4) 1 650 cm^{-1}; δ($CDCl_4$) 5.80 (1 H, s), 3.20 (2 H, m), 2.60 (2 H, m), 2.00 (3 H, m), and 0.96 (6 H, d, *J* 6 Hz); *m/z* 170 (M^+) (Found: C, 63.65; H, 8.5; S, 18.95. $C_9H_{14}OS$ requires C, 63.485; H, 8.29; S, 18.83%).

2-*Methyl*-5,6-*dehydrothiin*-4-*one* (**1c**) [83% from (**16**)]; R_F 0.22 (petroleum–ether, 1:1); $\nu_{max.}$(CCl_4) 1 650 cm^{-1}; δ(CCl_4) 5.84 (1 H, s), 3.15 (2 H, m), 2.50 (2 H, m), and 2.10 (3 H, s); *m/z* 128 (M^+) (Found: C, 56.15; H, 6.45; S, 24.85. C_6H_8SO requires C, 56.22; H, 6.29; S, 25.01%).

2-*Benzyl*-5,6-*dihydrothiin*-4-*one* (**1d**) [81% from (**16**)]; R_F 0.18 (petroleum–ether, 1:1); $\nu_{max.}$(CCl_4) 1 650 cm^{-1}; δ(CCl_4) 7.16 (5 H, s), 5.92 (1 H, s), 3.56 (2 H, s), 3.04 (2 H, m), and 2.44 (2 H, m); *m/z* 204 (M^+) (Found: C, 70.3; H, 6.05; S, 15.8. $C_{12}H_{12}OS$ requires C, 70.55; H, 5.92; S, 15.69%).

(b) *One-pot procedure.* The *in situ* hydrolysis of (**17b**) and (**17d**) to (**1b**) and (**1d**) was successful and this procedure would presumably be applicable to (**17a**) and (**17c**) as well. After alkylation as in (*a*) 4M-hydrochloric acid (4 ml) was added and the reaction was boiled under reflux [(**17b**), 8 h; (**17d**), 14 h] under nitrogen. The isolation procedure described in (*a*) gave (**1b**) [90% from (**16**)] and (**1d**) [91% from (**16**)].

2-*Benzyl*-5,6-*dihydrothiin*-4-*ol* (**21**).—Sodium borohydride (0.05 g, 1.3 mmol) was added portionwise to a stirred solution of 2-benzyl-5,6-dihydrothiin-4-one (**1d**) (0.204 g, 1 mmol) in methanol (10 ml) at 0 °C. The reaction was stirred at 0 °C for 2 h and then water was added. A normal dichloromethane work-up gave the *alcohol* (**21**) (0.187 g, 91%) as an oil, which was pure by t.l.c., R_F 0.20 (CH_2Cl_2); $\nu_{max.}$(CCl_4) 3 365 cm^{-1}; δ(CCl_4) 7.10 (5 H, s), 5.50 (1 H, d, *J* 5 Hz), 4.04 (1 H, m), 3.32 (2 H, s), 2.70 (2 H + OH, m), and 1.80 (2 H, m); *m/z* 206 (M^+) (Found: C, 69.8; H, 6.75; S, 15.35. $C_{12}H_{14}SO$ requires C, 69.86; H, 6.84; S, 15.54%).

2-*Benzyl*-5,6-*dehydrothiin*-4-*one* 1,1-*Dioxide* (**22**).—*m*-Chloroperbenzoic acid (80%; 0.215 g, 1 mmol) was added portionwise to a stirred solution of 2-benzyl-5,6-dihydrothiin-4-one (**1d**) (0.204 g, 1 mmol) in dichloromethane (20 ml) at 0 °C. After 15 min a further portion of the peracid (80%; 0.215 g, 1 mmol) was added and the mixture stirred for 4 h at 4 °C and 5 h at room temperature. The solvent was removed under reduced pressure and the solid obtained purified by preparative centrifugal chromatography (CH_2Cl_2) giving (after the *m*-chlorobenzoic acid) the *sulphone* (**22**) (0.23 g, 97%) as white crystals which were recrystallised from dichloromethane–petroleum, m.p. 110—112 °C; R_F 0.30 (CH_2Cl_2); $\nu_{max.}$($CHCl_3$) 1 685, 1 325, and 1 130 cm^{-1}; δ 7.18 (5 H, m), 5.72 (1 H, d, *J* 2 Hz), 3.88 (2 H, d, *J* 2 Hz), 3.60 (2 H, m), and 3.12 (2 H, m); *m/z* 236 (M^+) (Found: C, 60.75; H, 5.0; S, 13.6. $C_{12}H_{12}O_3S$ requires C, 61.00; H, 5.12; S, 13.57%).

2-*Benzyl*-4,4-*ethylenedioxy*-5,6-*dihydrothiin* (**23**).—A mixture of 2-benzyl-5,6-dihydrothiin-4-one 1,1-dioxide (**22**) (0.13 g, 0.55 mmol), ethanediol (0.062 g, 1 mmol), and toluene-*p*-sulphonic acid (5 mg) in benzene (40 ml) was boiled under reflux in a Dean-Stark assembly for 42 h. Additional ethanediol (0.062 mg, 1 mmol) and toluene-*p*-sulphonic acid (10 mg) were then added

and the mixture refluxed for a further 6 h. After the reaction mixture had cooled, anhydrous potassium carbonate (*ca.* 1 g) was added and the whole stirred for 15 min. The mixture was then filtered, the solid washed with dichloromethane, and the solvent removed from the combined filtrates under reduced pressure. Trituration with a little ether gave the *dioxolane* (**23**) (0.147 g, 96%) as white crystals which were recrystallised from ether, m.p. 136—137 °C; R_F 0.27 (CH_2Cl_2); $\nu_{max.}$($CHCl_3$) 1 315 and 1 112 cm^{-1}; δ 7.28 (5 H, s), 5.40 (1 H, d, J < 1 Hz), 3.92 (4 H, s), 3.72 (2 H, d, J < 1 Hz), 3.44 (2 H, m), and 2.46 (2 H, m); m/z 280 (M^+) (Found: C, 59.9; H, 5.6. $C_{14}H_{16}O_4S$ requires C, 59.98; H, 5.75%).

Raney Nickel Desulphurisations.—W-2 Raney nickel[20] was deactivated by boiling in acetone for the time indicated in the Table. The acetone was then decanted and the reaction solvent added together with the substrate (0.5 mmol). The reactions were monitored by t.l.c. The following two procedures are illustrative.

(i) *Reaction of 2-benzyl-5,6-dihydrothiin-4-one* (**1d**) *with Raney nickel in methanol.* W-2 Raney nickel[20] (3 g) was washed with acetone (4 × 5 ml) and then boiled under reflux with acetone (15 ml) for 3 h. The mixture was cooled, the solvent decanted, and the Raney nickel washed with distilled water (2 × 10 ml), 95% ethanol (3 × 15 ml), and then methanol (25 ml), the solvents being decanted after each washing. A solution of the title compound (0.102 g, 0.5 mmol) in methanol (15 ml) was added to the Raney nickel and the solution was boiled under reflux for 6 h. The reaction mixture was cooled, filtered through Celite, and the solvent removed under reduced pressure. The crude product was purified by preparative centrifugal chromatography (petroleum–ether, 7:3) to give 6-phenylhexan-3-one (**19**) (0.66 g, 75%) as a colourless oil with i.r. and n.m.r. spectra consistent with the structural assignment. The semicarbazone of (**19**) was prepared, m.p. 150—152 °C (lit.,[22] m.p. 150—151 °C).

(ii) *Reaction of 2-benzyl-5,6-dihydrothiin-4-ol* (**21**) *with Raney nickel in acetone.* W-2 Raney nickel[20] (5.0 g) was washed with acetone (4 × 20 ml) and then boiled under reflux with acetone (40 ml) for 2 h. A solution of the alcohol (**21**) (0.156 g, 0.75 mmol) in acetone (10 ml) was then added and the reaction was boiled under reflux for 15 h. After cooling, the reaction mixture was filtered through Celite and the filtrate concentrated under reduced pressure. The resulting oil was dissolved in ether and flash chromatographed on silica/$MgSO_4$ to furnish 1-phenylhexan-1-ol (**20**) (0.13 g, 96%) as an oil, $\nu_{max.}$(liquid) 3 350 cm^{-1}; δ(CCl_4) 7.10 (5 H, br s), 3.80—3.00 (1 H, m), 2.86—1.30 (8 H + OH, m), and 1.00 (3 H, t, J 7 Hz).

Nickel Boride Reduction of 2-Benzyl-5,6-dihydrothiin-4-one (**1d**).—Sodium borohydride (1.89 g, 50 mmol) in water (20 ml) was added dropwise to a well-stirred solution of nickel(II) chloride hexahydrate (5.93 g, 25 mmol) and the title compound (**1d**) (0.102 g, 0.5 mmol) in ethanol (150 ml) under nitrogen. A black precipitate formed and the reaction was then boiled under reflux for 72 h. The reaction mixture was filtered through Celite and the Celite washed thoroughly with ethanol. The filtrate was concentrated under reduced pressure and then given a normal dichloromethane work-up. The resulting oil was purified by column chromatography on silica (ether as eluant) giving 2-benzyl-5,6-dihydrothiin-4-ol (**21**) (0.07 g, 68%) as an oil identical in all respects with the sample prepared earlier.

Acknowledgements

We thank the S.E.R.C. for a Post-doctoral Research Assistantship (V. K. K.).

References

1 Part 1, R. J. Batten, J. D. Coyle, and R. J. K. Taylor, *Synthesis*, 1980, 910; Part 2, R. J. Batten, J. D. Coyle, R. J. K. Taylor, and S. Vassiliou, *J. Chem. Soc., Perkin Trans 1*, 1982, 1177.
2 C. H. Chen, G. A. Reynolds, and J. A. Van Allan, *J. Org. Chem.*, 1977, **42**, 2777.
3(*a*) C. H. Chen, G. A. Reynolds, and B. C. Cossar, *J. Org. Chem.*, 1981, **46**, 2752; (*b*) C. H. Chen, J. J. Doney, and G. A. Reynolds, *J. Org. Chem.*, 1981, **46**, 4604.
4 G. A. Reynolds, *J. Heterocycl. Chem.*, 1975, **12**, 755.
5 S. Ohuchida, N. Hamanaka, and M. Hayashi, *J. Am. Chem. Soc.*, 1981, **103**, 4597.
6 J. Davies and J. B. Jones, *J. Am. Chem. Soc.*, 1979, **101**, 5405.
7 R. W. Hoffmann, W. Helbig, and W. Ladner, *Tetrahedron Lett.*, 1982, **23**, 3479.
8 K. Kondo, A. Negishi, K. Matsui, D. Tunemoto, and S. Masamune, *J. Chem. Soc., Chem. Commun.*, 1972, 1311; P. L. Stotter and R. E. Hornish, *J. Am. Chem. Soc.*, 1973, **95**, 4444; J. P. Demoute, D. Hainault, and E. Toromanoff, *C. R. Acad. Sci., Ser. C*, 1973, **277**, 49.
9 D. L. Tuleen and T. B. Stephens, *J. Org. Chem.*, 1969, **34**, 31.
10 C. Barkenbus, V. C. Midkiff, and R. M. Newman, *J. Org. Chem.*, 1951, **16**, 232.
11 P. Bakuzis and M. L. F. Bakuzis, *J. Org. Chem.*, 1981, **46**, 235.
12 C. C. Fortes, H. C. Fortes, and D. C. R. G. Goncalves. *J. Chem Soc., Chem. Commun.*, 1982, 857.
13 R. K. Dieter, J. R. Fishpaugh, and L. A. Silks, *Tetrahedron Lett.*, 1982, **23**, 3751.
14 J. Grimshaw, J. T. Grimshaw, and H. R. Juneja, *J. Chem. Soc., Perkin Trans 1*, 1972, 50.
15 C. Shih and J. S. Swenton, *J. Org. Chem.*, 1982, **47**, 2825 and references therein.
16 For related approaches see G. K. Cooper and L. J. Dolby, *J. Org. Chem.*, 1979, **44**, 3414; T. Cohen, D. A. Bennett, and A. J. Mura, *ibid.*, 1976, **41**, 2506.
17 G. Rosenkranz, S. Kaufmann, and J. Romo, *J. Am. Chem. Soc.*, 1949, **71**, 3689.
18 R. L. Autrey and P. W. Scullard, *J. Am. Chem. Soc.*, 1968, **90**, 4917.
19 R. B. Boar, D. W. Hawkins, J. F. McGhie, and D. H. R. Barton, *J. Chem. Soc., Perkin Trans. 1*, 1973, 654.
20 R. Mozingo, *Org. Synth.*, Coll. Vol. 3, 1955, 181.
21 S. Tatsuya, N. Ikuzo, and D. Hiroshi, *Chem. Lett.*, 1977, 1021.
22 F. C. Montgomery and W. H. Saunders, *J. Org. Chem.*, 1976, **41**, 2368.
23 R. Danieli, G. Martelli, G. Spunta, and S. Rossini, *J. Org. Chem.*, 1983, **48**, 123.
24 B. M. Trost and P. L. Ornstein, *Tetrahedron Lett.*, 1981, **22**, 3463.
25 G. H. Posner and C. E. Whitten, *Org. Synth.*, 1976, **55**, 122.

Received 31*st August* 1983; *Paper* 3/1509