Thiazanones are six-membered heterocyclic compounds containing one nitrogen and one sulphur atom with a carbonyl function. Fatty acids possessing a chain-substituted thiazanone ring have not yet been reported in the literature. Only a few methods are available for the synthesis of thiazanones: 2-aminooximino-4-oxo-5,6-dihydro-1,3-thiazinum bromide was prepared by heating β-bromopropionyl chloride [Br(CH₂)₃COCl] and ammonium thiocyanate followed by reaction with ammonia (1), 2-p-chlorophenyl-3-alkyl-4-m-thiazanones were obtained by treatment of mercaptals with p-chlorobenzaldehyde (2), and benzothiazinones were synthesized by condensation of o-mercaptobenzamide with methyl acetylenedicarboxylate (3). A number of 1,3- and 1,4-benzothiazinones have been evaluated for their central nervous system (CNS) depressant activity (4). Incorporation of the thiazanone ring in fatty acid chain is expected to enhance the application of these derivatives. Recently, we have reported the synthesis of fatty chain-substituted 4-thiazolidinones (5). In continuation of our work on derivatization of keto fatty acids (6), we synthesized chain-substituted thiazanone derivatives by condensing keto fatty esters and a long chain aldehyde with β-mercaptopropionopropionic acid in the presence of ammonium carbonate.

Long chain oxo compounds, having a carbonyl function at penultimate (methyl 10-oxoundecanoate, I), internal (methyl 9-oxooctadecanoate, II), vicinal dioxo (9,10-diooxo-octadecanoate, III) and terminal (1-octadecanal, IV) positions were used for the synthesis of thiazanone derivatives.

MATERIALS AND METHODS

All mp were observed on Koffler apparatus and were uncorrected. The spectroscopic and chromatographic methods were the same as detailed in our previous paper (5) except where specified. Lithium aluminium hydride (LiAlH₄, >98%), chromic anhydride, methylene chloride and pyridine were supplied by E. Merck (Darmstadt, FRG) and β-mercaptopropionopropionic acid by Sigma Chemical Co. (St. Louis, MO). The methyl esters of long chain oxo acids were prepared by refluxing them with absolute methanol and a few drops of sulphuric acid. The abbreviations s, t, m, and br denote singlet, triplet, multiplet and broad, respectively. Petroleum ether refers to a fraction of bp 40–60 °C, and ether refers to diethyl ether.

Preparation of oxo fatty acids (I–III). 10-Oxoundecanoic (I, mp 58–59 °C) and 9,10-diooxo-octadecanoic (III, mp 86 °C) acids were prepared according to the methods discussed in an earlier paper (5). 9-Oxooctadecanoic acid (II) was obtained from pure Wrightia tinctoria seed oil (7) using Gunstone’s partitioning procedure (8). 9-Hydroxy-12-octadecenoic acid isolated from this seed oil was hydrogenated by palladium on charcoal in ethyl acetate to give 9-hydroxyoctadecanoic acid (mp 80–81 °C) which, on Jones’ oxidation (10), afforded 9-octadecenoic acid [mp 79–80 °C; lit. (8) 79.5 °C]. IR (CCl₄): 1710 (acid carbonyl), 1720 cm⁻¹ (chain carbonyl).

Preparation of octadecanal (IV). Methyl stearate (10 g) was dissolved in dry ether (500 ml) and slowly added to a stirred suspension of LiAlH₄ (2 g) in dry ether (200 ml). After stirring for a further 10 min at room temperature, excess of LiAlH₄, was destroyed by the cautious addition of wet ether and then water. Dilute H₂SO₄ (2 l, 2M) was added to the cooled mixture (5). A vigorous reaction took place. The contents were refluxed, and the progress of reaction was monitored by thin layer chromatography (TLC). At the end of the reaction, the solvent was removed under reduced pressure. The residue was extracted with ether, washed with 10% NaHCO₃ solution and dried over anhydrous sodium sulphate. The product thus obtained was crystallized from petroleum ether/benzene (4:1, v/v).
The experimental and spectral data of respective thiaza-
rones are summarized in Table 1.

RESULTS AND DISCUSSION

The oxo compounds (I-IV) on treatment with β-
mercaptocarboxylic acid in the presence of ammonium car-
bonate following the procedure of Paryzek et al. (13) yield-
ed the corresponding 4-m-thiazanones (Ia–IVa) as shown
in Scheme 1.

The IR spectrum of Ia (Table 1) revealed characteristic
bands at 3170 (NH stretching), 1735 and 1660 (ester and
lactam carbonyl), 1405 (C-N stretch), 1225 (C-S wagging),
720 (NH wag.) and 670 cm⁻¹ (C-S stretch). These values
are in agreement with the structure of Ia. The ¹H NMR
spectrum of Ia exhibited two sharp singlets at δ 1.55 for
terminal α-methyl protons and at δ 3.68 for ester methyl
protons. The ring protons gave triplet signals at δ 2.85
(CH₂-S) and 2.55 (CH~CONH) while NH proton appeared
at δ 8.6 as a broad singlet. The methylene protons alpha
to ring and ester carbonyl appeared at δ 1.75 and 2.30,
respectively. The chain methylene protons absorbed at
δ 1.30 as a broad singlet. On the basis of these data, the
product Ia was formulated as 2-8'-carbomethoxyoctyl-
2-methyl-4-m-thiazanone.

Thiazanone IIa gave similar IR and ¹H NMR char-
acteristics as Ia except for the appearance of terminal
methyl and four methylene protons (α- to ring) at δ 0.88
and 1.65, respectively. The product IIa was characterized
as 2-7'-carbomethoxyheptyl-2-nonyl-4-m-thiazanone.

Similarly, the thiazanone (IVa) located at a terminal
position displayed almost the same diagnostic peaks in
IR and ¹H NMR spectra as observed in Ia and IIa. The
only characteristic ¹H NMR peak observed was at δ 4.52
for the methine proton attached to C-2 position of
the ring. The product IVa was identified as 2-heptadecyl-4-
m-thiazanone.

Thiazanone (IIIa) obtained from the vicinal dioxo
ester (III) exhibited a clear single spot on the TLC plate.
It showed IR absorption bands at 3185 (NH stretch), 1740
and 1660 (ester and lactam carbonyl), 1405 (C-N stretch),
770 (NH Wag.) 1230 and 640 (C-S wag. and stretch), along
with a free carbonyl band at 1715 cm⁻¹. The ¹H NMR spec-
trum exhibited a multiplet at δ 2.27 integrating for four
methylene protons α- to chain and ester carbonyls. The
two methylene protons alpha to the ring appeared at δ 1.30
as a broad singlet. On the basis of these data, the product
IIIa was formulated as 2-heptadecyl-4-m-thiazanone.

The experimental and spectral data of respective thiaza-
nones are summarized in Table 1.

<table>
<thead>
<tr>
<th>Thiazanone</th>
<th>Rxn time (hr)</th>
<th>Yield (%)</th>
<th>m.p. (°C)</th>
<th>IR (cm⁻¹)</th>
<th>¹H NMR in CDCl₃ (δ, ppm)</th>
<th>Combustion analysis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>24</td>
<td>48</td>
<td>53</td>
<td>(CCL): 3170,1735,1660,1405,1225,720,670</td>
<td>1.30,1.55,1.75,2.30,2.55,2.85,3.68,8.60</td>
<td>calcd. for C₉,H₁₄,O₇,N,S: C,59.01;H,9.04;N,4.65; S,7.07 found: C,59.79;H,8.86;N,4.70</td>
</tr>
<tr>
<td>IIa</td>
<td>30</td>
<td>86</td>
<td>—</td>
<td>(film):3170,1730,1665,1225,710,690,1410</td>
<td>0.88,1.30,1.65,2.30,2.60,2.82,3.65,8.60</td>
<td>calcd. for C₂₂,H₄₂,O₃,N,S: C,66.06;H,10.53;N,3.30 found: C,66.15;H,10.27;N,3.48</td>
</tr>
<tr>
<td>IIIa</td>
<td>50</td>
<td>96</td>
<td>—</td>
<td>(film):3185,1740,1715,1660,1405,1230,770,640</td>
<td>0.88,1.30,1.65,2.27,2.57,2.88,3.70,8.40</td>
<td>calcd. for C₂₂,H₃₉O₄,N,S: C,63.89;H,9.51;N,3.39 found: C,63.92;H,9.49;N,3.38</td>
</tr>
<tr>
<td>IVa</td>
<td>10</td>
<td>91</td>
<td>67</td>
<td>(CCL):3160,1670,1410,1230,780,690</td>
<td>0.88,1.30,1.80,2.53,2.82,4.52,8.50</td>
<td>calcd. for C₂₃,H₄₂,O₉,N,S: C,70.80;H,11.61;N,3.94 found: C,70.90;H,11.59;N,3.90</td>
</tr>
</tbody>
</table>

Scheme 1. Synthesis of fatty thiazanones.