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Synthesis of phenyldithioglyoxalic acid and its esters. A route to α-ketodithioacid derivatives

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Abstract. A novel route has been developed for the direct synthesis of the hitherto unknown α-ketodithioacid. Benzaldehyde has been treated with carbon disulphide in the presence of potassium cyanide, thereby making the intermediate carbanion Ph–$\bar{C}$(OH)CN to add on to carbon disulphide eventually leading to the α-ketodithioacid. The methyl and ω-carboxypropyl esters of this acid have also been prepared.

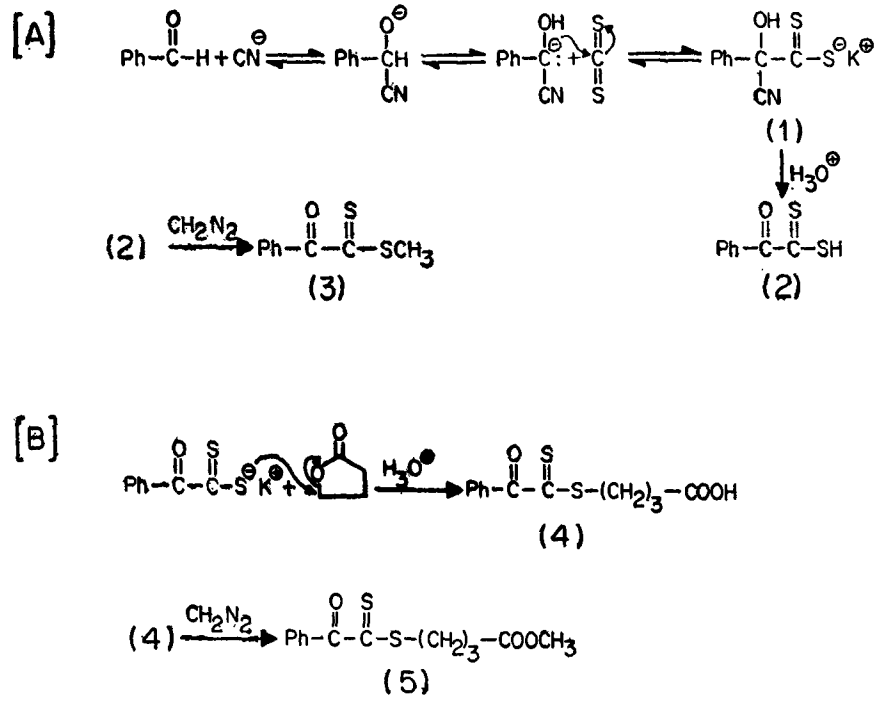
Keywords. Phenylthioglyoxalic acid; esters; α-ketodithioacids; synthesis; benzaldehyde.

1. Introduction

A review of the chemistry of dithioacids and dithioesters (Jansons 1976, 1977) reveals that there has been no report on the synthesis of α-ketodithioacids. We have envisaged a simple route for the direct synthesis of the hitherto unknown α-ketodithioacid viz., phenyldithioglyoxalic acid.

This approach is mainly based on the observation reported by Stetter (1976), according to which the intermediate carbanion in the well-known benzoin condensation could be added on to activated double bonds. The present investigation utilises the above carbonion Ph–$\bar{C}$(OH)CN to interact *in situ* with the electrophile, carbon disulphide, thereby producing the contemplated α-ketodithioacid, as indicated in chart 1. In effect the cyanide ion is used as a catalyst for the addition of a molecule of an aromatic aldehyde across the activated double bond.

Thus the above reaction was carried out with benzaldehyde, in dimethylformamide (*vide* § 2). The isolated dithioacid was found to be quite unstable and could not be distilled even under high vacuum. However, a reasonably pure sample could be obtained by chemical purification followed by a rapid chromatography over silica gel. The benzene eluate furnished an almost pure phenyldithioglyoxalic acid (2) as a viscous dark red liquid in *ca* 35% yield. This sample gave satisfactory IR and NMR spectra, but elemental analysis was unsatisfactory. The mass spectrum could not be taken since the sample tended to decompose and foul up the mass spectrometer inlet.

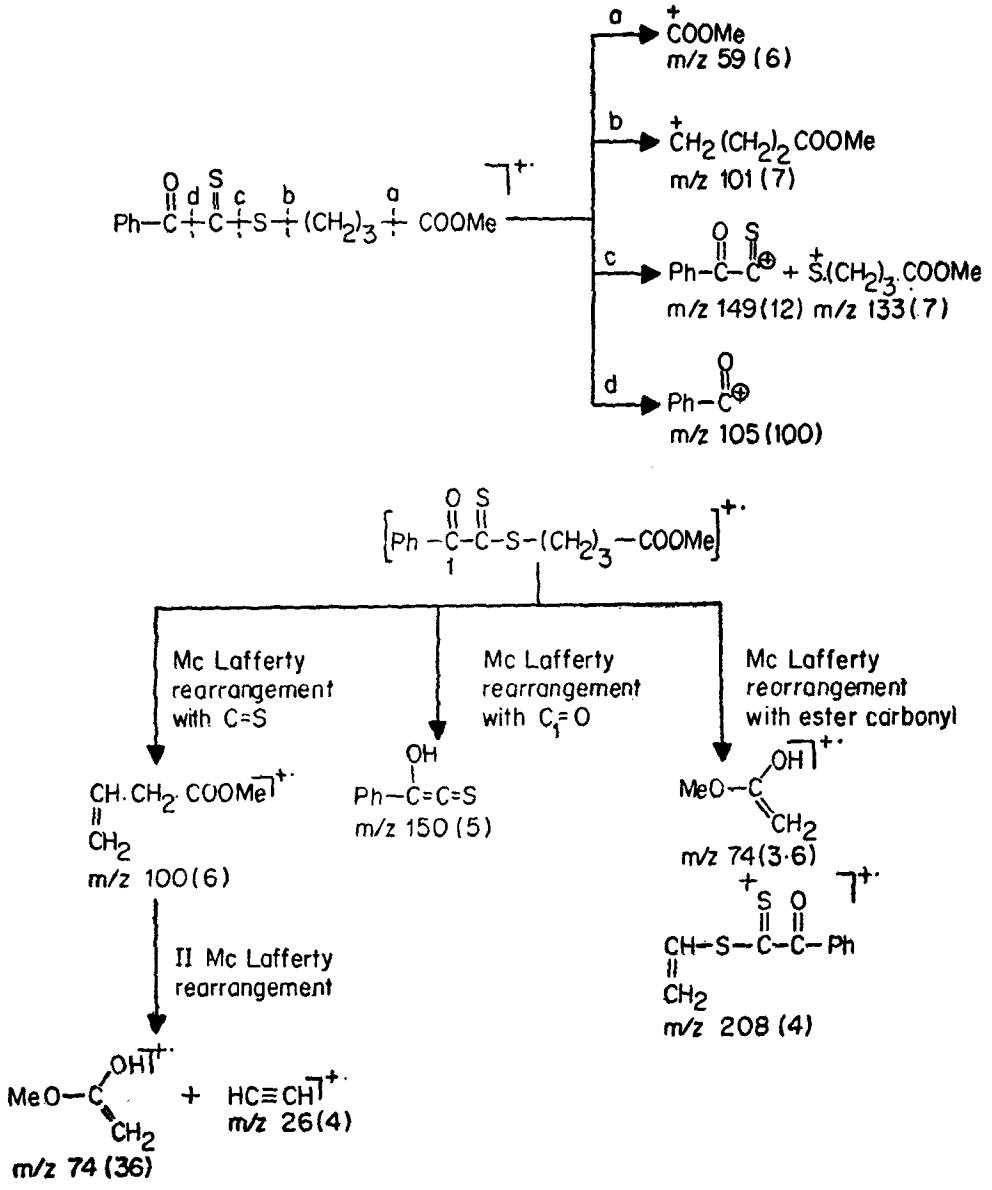


The methyl ester (3) of the above acid could be obtained in a pure state as a pale yellow oily liquid, by employing diazomethane for esterification.

The successful trapping of the intermediate carbanion in the above mentioned benzoin condensation with the electrophile, carbon disulphide to obtain the desired α-ketodithio acid, led us to study the nucleophilicity of the resulting α-ketodithiocarboxylate anion (1), with other reactive compounds such as γ-butyrolactone. It has already been reported (Ramadas and Srinivasan 1977) that simple dithiocarboxylate anion of the type $R \cdot CSS^{-}M^{+}gX^{-}$, could successfully interact with γ-butyrolactone effecting an alkyl-oxygen cleavage of the lactone, rather than the well-known acyl-oxygen cleavage.

Based on this observation the above ω-carboxypropyl derivative (4) of the above mentioned α-ketodithioacid was prepared by treating the α-ketodithiocarboxylate anion (1) *in situ* with γ-butyrolactone. The resulting ω-carboxypropyl phenyldithiocarboxylate (4) was isolated as a dark red solid in *ca* 80% yield. This acid (4) also exhibited unusual instability and could not be distilled. However, a reasonably pure sample could be obtained by chemical purification.

The methyl ester (5) of the above acid could be obtained in analytically pure state by treating the acid (4) with diazomethane. The anticipated ester, viz. ω-methoxycarbonylpropyl phenyldithiocarboxylate (5) was obtained as a bright red liquid. The mass spectrum of (5) is a good example of competitive and sequential McLafferty rearrangements as shown in chart 2. In the mass spectrum of (5), the fragment ion *m/z* 74 is believed to have been formed through either one or both the routes represented. Detection of fragments, *m/z* 208 as well as 26 suggests that both routes operate. Neither of the dithioesters (3), or (5) gave the molecular ion in the mass spectrum. Studies in these laboratories



with other dithioesters have shown that dithioesters generally do not give the molecular ion (Ramadas and Srinivasan 1977 and unpublished results).

It is noteworthy to mention here that the formation of phenyldithioglyoxalic acid (2) was accompanied by a by-product isolated as a yellow fibre-like solid m.p. 168° in *ca* 20% yield. The structure of this by-product is under investigation.

2. Experimental

2.1. *Synthesis of α-ketodithioacid (phenyldithioglyoxalic acid)*

To a stirred solution of potassium cyanide (4·88 g, 0·075 mol) in dimethylformamide (100 ml) was added dropwise a solution of benzaldehyde (15·3 g, 0·15 mol) in dimethylformamide (25 ml) over a period of 10 min under nitrogen atmosphere. After stirring for 5 more minutes, the reaction mixture was cooled to 0° C and carbon disulphide (2·8 g, 0·375 mol) in dimethylformamide (20 ml) was added dropwise over a period of 15 min. Stirring was continued for 30 min at 0° C. The reaction mixture was gradually raised to room temperature and then stirred at room temperature for 1 hr under nitrogen atmosphere.

The reaction mixture was treated with ice-cold water and then with ice-cold dilute hydrochloric acid (1 : 4) till it became just acidic. It was left at 0° C for a couple of hours. A solid was separated which was filtered and washed quickly with ice-cold ether and finally with a little ice-cold carbon tetrachloride. It was recrystallised from carbon tetrachloride. A lemon yellow fibre-like solid m.p. 168° was obtained in *ca* 20% yield.

The aqueous filtrate (after the removal of the yellow solid) was extracted with ether-ethyl acetate mixture. The combined organic extract was extracted with ice-cold 8% sodium hydroxide solution. The alkaline extract was acidified with ice-cold dilute hydrochloric acid (1 : 4) till it was just acidic. The liberated acid was extracted with ether-ethyl acetate mixture. It was washed with ice-cold water and dried over anhydrous sodium sulphate. The solvent was distilled.

The crude acid was obtained as a viscous red liquid in *ca* 45% yield. It was purified by rapid column chromatography over silica gel. The eluate with benzene furnished a reasonably pure acid as a viscous red liquid in *ca* 35% yield, which exhibited the following spectral characteristics.

IR spectrum (in $CHCl_3$) indicated bands at 3600–2750 (broad), 2650, 2550 (–SH), 1700 (carbonyl), 1620, 1615, 1600 (aromatic C=C) and 1180 cm^{-1} (C=S).

NMR spectrum (in $CDCl_3$) indicated signals at δ 6·85–7·1 (a broad singlet, 1H, due to –SH) which disappeared on exchange with deuterium and 7·25–8·2 (m, 5H, aromatic protons).

2.2. *Conversion of the α-ketodithioacid into its methyl ester* (3)–*(esterification by diazomethane)*

The acid (2) was esterified by an etheral solution of diazomethane (Arndt 1943). The crude ester (3) was obtained as a red liquid. It was purified by column chromatography over silica gel. The eluate with benzene–petroleum ether (2 : 1) furnished the analytical sample of the ester as a pale yellow oily liquid in *ca* 86% yield.

This ester exhibited the following spectral characteristics :

IR spectrum (in CCl_4) indicated bands at 1710 (ester carbonyl), 1600, 1580 (aromatic C=C) and 1115 cm^{-1} (C=S).

NMR spectrum (in $CDCl_3$) exhibited signals at δ 2·96 (s, 3H, $-SCH_3$), 7·2–7·5 and 7·9–8·05 (m, 5H, aromatic protons).

Mass spectrum indicated peaks at *m/z* 150 (5%) ($M-SCH_2$), *m/z* 149 (12%) ($M-SCH_3$), *m/z* 106 (16%) and 105 (100%) ($C_6H_5CO^+$).

Analysis :

	Found	C 54·61%	H 3·50%
$C_9H_8OS_2$	required	C 55·09%	H 4·08%.

2.3. *Conversion of the α-ketodithioacid* (2) *into ω-carboxypropyl phenyldithiocarboxylate* (4)

The α-ketodithiocarboxylate anion (1), obtained by the above method (Experiment 1), was treated *in situ* with γ-butyrolactone (12·9 g, 0·15 mol) in dimethylformamide (30 ml) over a period of 15 min. It was stirred at room temperature for 1 hr and at 55° C for 4 hr.

The reaction mixture was worked up as in experiment 1. The yellow solid was obtained in very low yield (9%). At the end of work-up, the solvent mixture was removed by distillation and the last few millilitres of the solvent were removed at room temperature under reduced pressure using a rotary evaporator. The ω-carboxypropyl phenyldithioester was obtained as a dark red gum. A reasonably pure product was obtained as a red gum in *ca* 80% yield by extraction into alkali and reprecipitation as in experiment 1b. The sample was not pure enough to give satisfactory elemental analysis. Mass spectrum could not be taken for the same reason as for (2). This acid revealed the following spectral characteristics :

IR spectrum : (in CCl_4) indicated bands at 3300–2750 (broad bonded –OH), 1690 (conjugated carbonyl), 1595, 1525 (aromatic C=C) and 1205 cm^{-1} (C=S).

NMR spectrum (in $CDCl_3$) indicated signals at δ 1·7–2·5 (m, 4H, α, β-methylenes), 3·3–3·5 (t, 2H, γ-methylene) and 7·1–8·1 (m, 5H, aromatic protons).

2.4. *Conversion of ω-carboxypropyl phenyldithiocarboxylate* (4) *into ω-methoxycarbonylpropyl phenyldithiocarboxylate* (5) (*esterification of* (4) *by diazomethane*)

Esterification was carried out as in experiment 2. The analytical sample of the ester (5) was obtained as a red liquid in *ca* 84% yield and exhibited the following spectral characteristics :

IR spectrum (in CCl_4) indicated bands at 1715 (ester carbonyl), 1590 (aromatic C=C) and 1250 cm^{-1} (C=S).

NMR spectrum (in $CDCl_3$) indicated signals at δ 1·75–2·60 (m, 4H, α, β-methylenes), 3·2–3·45 (t, 2H, γ-methylene), 3·8 (s, 3H, $-COOCH_3$), and 7·1–8·15 (m, 5H, aromatic protons).

Analysis :

	Found	C 54·84%	H 4·49%
$C_{13}H_{14}O_3S_2$	required	C 55·33%	H 4·97%.

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