

Studies on Alkylsulfinylcarboxylic Acids

VII. Synthesis of Some (1-Alkylsulfinylalkylidene)-malonic Acids

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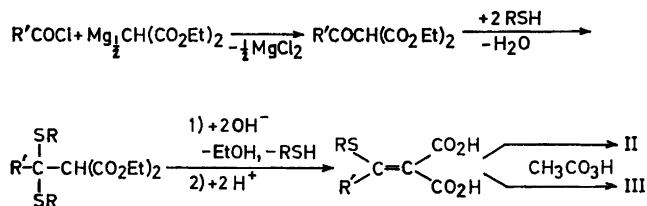
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Some (1-alkylthioalkylidene)-malonic acids have been prepared by the addition of alkyl mercaptans to diethyl acylmalonates and alkaline hydrolysis of the addition products. These sulfide-acids were oxidized to their corresponding sulfoxides and sulfones by means of peracetic acid.

In connection with a study of neighbouring group participation in the reduction of β -alkylsulfinylcarboxylic acids, and in particular α,β -unsaturated acids,^{1,2} a series of sulfur containing alkylidenemalonic acids with the general formula $RS(R')C=C(COOH)_2$ (I) was prepared. This paper will describe the synthesis of such sulfide-acids and their corresponding sulfoxides (II) and sulfones (III).

The preparation of I was carried out by a method analogous to that used by Posner,^{3,4} who obtained 3-alkylthio-2-alkylcrotonic acids from the acid catalyzed addition of alkyl mercaptans to various 2-alkyl substituted acetoacetic esters and subsequent hydrolysis of the mercaptole esters thus formed. A similar method is also described in an American and a British patent⁵ for the synthesis of certain alkylthio alkylidene cyanoacetic esters. The only hitherto reported compound of type I is the ethyl ester of ethylthiomethylidene malonic acid, obtained by condensation of triethyl orthotrithioformate and diethylmalonate in the presence of zinc chloride and acetic anhydride.⁶

The synthetic route for obtaining I, II, and III was the following:



The reaction between a carbonyl compound and a mercaptan sometimes gives an unsaturated sulfide directly,⁷ but this was not observed in our case and the condensation products obtained before alkaline hydrolysis were shown by infrared analysis to consist mainly of mercaptole esters as formulated above. The hemimercaptole first formed in the reaction is obviously more stabilized by mercaptole formation than by water elimination to yield an unsaturated product.^{7,8}

The mercaptole esters could not be purified by vacuum-distillation, because at the temperature required for this operation, a considerable decomposition, probably due to elimination of mercaptan,⁹ was observed and only the lowest homologue in the series could be obtained relatively pure in this way. Therefore, in the other cases the mercaptole esters were hydrolyzed without any preceding purification.

Alkaline hydrolysis caused complete elimination of mercaptan and after acidification I could be isolated in comparatively good yield. No appreciable decarboxylation occurred under the reaction conditions used. The ease with which mercaptan is eliminated in alkaline solution is undoubtedly due to the presence of an activated methine hydrogen in the mercaptole ester. It seems probable that this elimination precedes the hydrolysis of the two ester groups. Posner,^{3,4} on the other hand, found that addition of benzyl mercaptan to ethyl 2-methyl- and 2-ethylacetoacetate gave mercaptole esters which, subjected to alkaline hydrolysis, gave the corresponding acids, *i.e.* no elimination of mercaptan occurred, which is obviously due to the fact that the remaining α -hydrogen is much less activated than in our case.

All sulfide-acids described in this paper were easily purified by recrystallization, but some care had to be taken in order to avoid decarboxylation at higher temperatures. The synthesis of the oxidation products II and III was performed with peracetic acid as the oxidizing agent.

The infrared spectra of the compounds exhibit certain characteristics. The carbon-carbon double bond stretching frequencies in the sulfoxides and sulfones have throughout higher values than in the corresponding sulfides. The magnitude of this shift is 80–90 cm^{-1} . In Table 1 values of some important bands (in KBr) are given. The assignment and positions of the bands given for the sulfide-acids are consistent with values reported by Jones *et al.* for β -alkylthiocrotonic acids.¹⁰

The sulfoxide-acids are all rapidly reduced to the corresponding sulfide-acids in acidic iodide solution which is in agreement with previous observations.^{1,2} A kinetic investigation of this reaction is under progress.

EXPERIMENTAL

For the preparation of the sulfoxides and sulfones a method described earlier was used.³ The acids were purified by recrystallizations from ethyl acetate with a suitable amount of petroleum ether added. The melting points are perhaps of limited value as the acids described here all decarboxylated. This temperature was found to vary with the rate of heating in such a way that the faster the temperature rise, the higher the melting-point, a well-known characteristic of compounds which decompose. In order to obtain as good a reproducibility as possible,¹¹ the melting-point determinations were carried out with the use of a "Kofler Heizbank". The substance was pushed towards the hot

Table 1. Some infrared bands for the compounds $R(R')C=C(CO_2H)_2$ and their probable assignment.

R	R'	Stretching frequencies cm^{-1}			
		C=O	C=C	S=O	SO ₂ symm.
Me-	EtS-	1710 ^a	1563		
»	EtSO-	1742 ^a	1656	943?	
»	EtSO ₂ -	1724 ^a	1637		1110
Et-	EtS-	1727, 1701	1553		
»	EtSO-	1727 ^a	1642	1011	
»	EtSO ₂ -	1754 ^a	1647		1136
Me-	BzS-	1704 ^a	1563		
»	BzSO-	1724 ^a	1645	982	
»	BzSO ₂ -	1754, 1695	1650		1134
Et-	BzS-	1727, 1701	1548		
»	BzSO-	1730, 1718	1637	987	
»	BzSO ₂ -	1761, 1724	1642		1126

^a No distinct doublet.

part of the bar and the temperature at which the substance immediately began to melt and decompose was taken as the m.p. The values obtained with the conventional technique, using capillary tubes and a rate of heating of about 1°/min are given within parenthesis for comparison. For the sulfoxide compounds the latter method gave in general bad reproducibility.

Some of the acids were found to contain water of crystallization which was removed by drying the finely ground substance in a vacuum-desiccator over phosphorus pentoxide. The equivalent weight determinations were carried out by titration with 0.1 M sodium hydroxide using phenolphthalein as indicator.

Diethyl acetylmalonate (I) was prepared according to Lund.¹² From 320.3 g (2 mole) of diethyl malonate 327.7 g (81 %) of I with b.p. 114–117°/12 mm, $n_D^{24} = 1.4451$ was obtained. (Ref. 13: B.p. 115–117°/13 mm, $n_D^{20} = 1.4477$).

Diethyl propionylmalonate (II) could be prepared analogously to I, with the exception that the step involving isolation of the cupric enolate was omitted because of the bad crystallization properties of the latter. Starting with 480.5 g (3 mole) of diethyl malonate the yield was 397.5 g (61 %) of II. B.p. 122–124°/8 mm, $n_D^{21} = 1.4422$. (Ref. 14: B.p. 137°/14 mm, $n_D^{20} = 1.4420$).

Diethyl [1,1-(diethylthio)-ethyl]-malonate (III). An ice-cooled mixture of 20.3 g (0.1 mole) of I, 14.9 g (0.24 mole) of ethyl mercaptan and 6.8 g (0.05 mole) of anhydrous zinc chloride was saturated with dry hydrogen chloride. The solution was then allowed to attain room temperature. After standing over night two separate layers had formed. The whole was poured into cold water and extracted three times with chloroform. The chloroform solution was washed with water, dried with calcium chloride, filtered and evaporated. The residue was vacuum-distilled yielding 13.2 g (42 %) of fairly pure mercaptole ester with b.p. 154.5–157°/0.25 mm and $n_D^{22} = 1.4908$. (Found: C 50.7; H 7.81; S 20.3. Calc. for C₁₃H₂₄O₄S₂: C 50.6; H 7.84; S 20.8). The sulfur analysis and an infrared spectrum indicate that the product might be contaminated with a small amount of unsaturated ester.

(1-Ethylthioethylidene)-malonic acid (IV). A mixture of 13.2 g (0.043 mole) of III, 5.2 g (0.13 mole) of sodium hydroxide dissolved in 30 ml water, and 15 ml ethanol was refluxed until it was completely homogeneous and then for a further 2 h. The ethanol was then removed by distillation, the residue filtered hot after the addition of some

decolourizing carbon, cooled, and acidified with dilute hydrochloric acid. The sulfide-acid only partially precipitated from the solution and it was therefore extracted with ether. The ether solution was dried with anhydrous magnesium sulfate, filtered and evaporated. After recrystallization of the product 6.4 g (34 % calc. from I) with m.p. 144° (132°) was obtained. (Found: C 44.0; H 5.32; S 16.9; equiv. wt. 94.7. Calc. for $C_7H_{10}O_2S$: C 44.2; H 5.30; S 16.9; equiv. wt. 95.1.)

(1-Ethylsulfinylolethylidene)-malonic acid (V). Oxidation of IV with an equivalent amount of peracetic acid yielded a substance which, after two recrystallizations, had a m.p. of 146° (116°). (Found: C 40.6; H 4.90; S 15.7; equiv. wt. 104.4. Calc. for $C_7H_{10}O_5S$: C 40.8; H 4.89; S 15.55; equiv. wt. 103.1.)

(1-Ethylsulfonylolethylidene)-malonic acid (VI) was obtained by oxidation of IV with peracetic acid in excess and had after purification a m.p. of 150° (146°). (Found: C 37.8; H 4.51; S 14.3; equiv. wt. 112.7. Calc. for $C_7H_{10}O_6S$: C 37.8; H 4.54; S 14.4; equiv. wt. 111.1.)

(1-Ethylthiopropylidene)-malonic acid (VII). In analogy with the preparation of III, 74.5 g (1.2 mole) of ethyl mercaptan and 108.5 g (0.5 mole) of II were mixed, zinc chloride (34 g) added, the mixture cooled in ice and saturated with dry hydrogen chloride. After a few hours a water layer began to separate. The rest of the synthesis was performed as described above. The mercaptole ester was not distilled in this case, only an initial fraction for the removal of unreacted II was taken. The residue was then hydrolyzed directly. The isolated product was recrystallized and in this way 22.0 g (22 %) with m.p. 154° (119°) was obtained. (Found: C 47.1; H 5.86; S 15.6; equiv. wt. 102.7. Calc. for $C_8H_{12}O_2S$: C 47.1; H 5.92; S 15.7; equiv. wt. 102.1.)

(1-Ethylsulfanylpropylidene)-malonic acid (VIII). Oxidation of VII gave, after several recrystallizations from acetone-petroleum ether, a substance melting at 167° (130°). (Found: C 43.9; H 5.50; S 14.4; equiv. wt. 111.8. Calc. for $C_8H_{12}O_3S$: C 43.6; H 5.49; S 14.6; equiv. wt. 110.1.)

(1-Ethylsulfonylpropylidene)-malonic acid (IX). With peracetic acid in excess the oxidation of VII yielded a product which, after several recrystallizations, had m.p. 125° (123°). (Found: C 40.8; H 5.28; S 13.5; equiv. wt. 118.7. Calc. for $C_8H_{12}O_5S$: C 40.7; H 5.12; S 13.6; equiv. wt. 118.1.)

(1-Benzylthioethylidene)-malonic acid (X). This compound was prepared in the same way as VII. Starting with 20.3 g (0.1 mole) of I, 24.8 g (0.2 mole) of benzyl mercaptan, and 6.8 g of zinc chloride, 10.4 g (41 %) of X with m.p. 163° (147°) was obtained. (Found: C 57.0; H 4.74; S 12.8; equiv. wt. 125.8. Calc. for $C_{12}H_{12}O_4S$: C 57.1; H 4.79; S 12.7; equiv. wt. 126.15.)

(1-Benzylsulfinylolethylidene)-malonic acid (XI). One recrystallization from acetone-petroleum ether and another from ethyl acetate-petroleum ether gave a product with m.p. 175° (127°). (Found: C 53.7; H 4.50; S 11.8; equiv. wt. 135.5. Calc. for $C_{12}H_{12}O_5S$: C 53.7; H 4.51; S 11.95; equiv. wt. 134.15.)

(1-Benzylsulfonylolethylidene)-malonic acid (XII). Recrystallizations from ether-petroleum ether and from ethyl acetate-petroleum ether were made. M.p. 196° (175°). (Found: C 50.7; H 4.24; S 10.9; equiv. wt. 145.4. Calc. for $C_{12}H_{12}O_6S$: C 50.7; H 4.25; S 11.3; equiv. wt. 142.15.)

(1-Benzylthiopropylidene)-malonic acid (XIII). For the synthesis of this compound a longer reaction time was necessary, otherwise the method was the same as described for VII. 108.5 g (0.5 mole) of II, 124 g (1.0 mole) of benzyl mercaptan, and 40.8 g of zinc chloride were mixed, saturated with dry hydrogen chloride at 0°C and then allowed to stand at room temperature for 40 h. The yield finally obtained after several recrystallizations was 37.7 g (28 %) with m.p. 143° (113°). (Found: C 58.7; H 5.22; S 12.1; equiv. wt. 134.1. Calc. for $C_{13}H_{14}O_4S$: C 58.6; H 5.30; S 12.0; equiv. wt. 133.2.)

(1-Benzylsulfanylpropylidene)-malonic acid (XIV) was purified as described for XI. M.p. 156° (129°). (Found: C 55.05; H 5.02; S 11.4; equiv. wt. 143.1. Calc. for $C_{13}H_{14}O_5S$: C 55.3; H 5.00; S 11.4; equiv. wt. 141.2.)

(1-Benzylsulfonylpropylidene)-malonic acid (XV) was purified as described for XII. M.p. 166° (152°). (Found: C 52.3; H 4.73; S 10.9; equiv. wt. 149.8. Calc. for $C_{13}H_{14}O_6S$: C 52.3; H 4.73; S 10.75; equiv. wt. 149.2.)

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