Synthetical Applications of the Desulphurisation Reaction. Part I. The Synthesis of Fatty Acids.

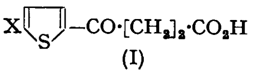
By G. M. BADGER, H. J. RODDA, and W. H. F. SASSE.

[Reprint Order No. 5500.]

Desulphurisation of alkylthienylbutyric acids (III and IV) with Raney nickel gives long-chain fatty acids in excellent yield. Some acylthiophens and thenoylpropionic acids (I and II) have also been desulphurised.

BOUGAULT, CATTELAIN, and CHABRIER (*Bull. Soc. chim.*, 1938, **5**, 1699; 1940, **7**, 780, 781) showed that organo-sulphur compounds are readily desulphurised by Raney nickel and this has since often been confirmed. The reaction has found extensive application in the study of naturally occurring sulphur compounds, such as biotin (du Vigneaud *et al.*, *J. Biol. Chem.*, 1942, **146**, 475; Mozingo *et al.*, *J. Amer. Chem. Soc.*, 1943, **65**, 1013). On the other hand, the potentialities of desulphurisation as a synthetic method seem to have been largely unrecognised. The present paper (for a preliminary report see *Chem. and Ind.*, 1954, 308) records a synthesis of long-chain fatty acids involving desulphurisation of an acidic derivative of an alkylthiophen as the final step; desulphurisation of some acylthiophens and of some thiophen keto-acids has also been examined.

The Raney nickel desulphurisation of 2-acetylthiophen has been reported to yield ethanol, acetaldehyde, and hexan-2-one (Hurd and Rudner, *J. Amer. Chem. Soc.*, 1951, **73**, 5157); but it has now been found that the experimental conditions are critical. Under somewhat different conditions, with W-6 catalyst (Billica and Adkins, *Org. Synth.*, 1949, **29**, 24) acetaldehyde, hexan-2-one, and dodecane-2 : 11-dione were detected among the products. When W-7 catalyst was used, however, no hexan-2-one seemed to be formed and acetaldehyde and dodecane-2 : 11-dione were isolated. The formation of the dione is of interest as it involves dimerisation. The cleavage of carbonyl groups with Raney nickel (in this case yielding acetaldehyde) is by no means unknown (Metayer, *Compt. rend.*, 1948, **226**, 550); but it does not always occur, for 2-ethyl-5-heptanoylthiophen was desulphurised to tridecan-7-one in 90% yield.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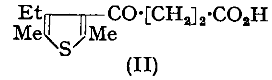
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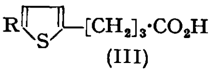
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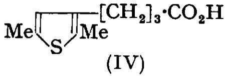
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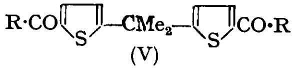
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Desulphurisation of keto-acids has also been shown to proceed without difficulty. For example, β-2-thenoylpropionic acid (I; X = H) gave 4-oxo-octanoic acid,* and β-(4-ethyl-2 : 5-dimethyl-3-thenoyl)propionic acid (II) yielded 5 : 6-diethyl-4-oxo-octanoic acid. However the method has limitations for it was not found possible to desulphurise β-(2-bromo-5-thenoyl)propionic acid (I; X = Br) without removing the bromine. In some circumstances 4-oxo-octanoic acid was obtained; but under other conditions a different acid, probably 4 : 13-dioxohexadecanedioic acid, was isolated. Such a product would be expected if dimerisation occurred following elimination of the bromine to give a free-radical intermediate.

The preparation of long-chain fatty acids by the desulphurisation of alkylthienyl butyric acids (III and IV) proceeds very smoothly, the results being summarised in the Table. As alkylated thiophens are easily synthesised this method may find further application for the synthesis of branched-chain acids which are difficult to obtain by other methods. Dithienylpropanes may also be used, for 2 : 2-di-(5-carboxy-2-thienyl)propane (V; R = OH) was desulphurised in excellent yield.

The alkylthienylbutyric acids required for this investigation were prepared by standard

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* Geneva nomenclature, $CO_2H = 1$.

methods. The reaction of thiophen (or of 2 : 5-dimethylthiophen) with an acyl chloride in the presence of stannic chloride gave an acylthiophen, which was then reduced to an alkylthiophen with hydrazine hydrate. The corresponding β-(2-alkyl-5-thenoyl)propionic acids were prepared from the alkylthiophens by using succinic anhydride and aluminium chloride, and reduction [better by the Huang-Minlon modification of the Wolff–Kishner procedure (*J. Amer. Chem. Soc.*, 1946, **68**, 2487) than by the Clemmensen method] gave the γ-(2-alkyl-5-thienyl)butyric acids (III). However, β-(3-ethyl-2 : 5-dimethyl-4-thenoyl)propionic acid (II) could not be reduced by either method : steric hindrance may be a factor here, for β-(2 : 5-dimethyl-3-thenoyl)propionic acid was reduced without difficulty to γ-(2 : 5-dimethyl-3-thienyl)butyric acid (IV).

Desulphurisation of acidic derivatives of alkylthiophens.

Thiophen derivative	Product	Method *	Yield (%)
III; R = H	Octanoic acid	C	73
III; R = Et	Decanoic acid	D	51
IV	5-Ethyloctanoic acid	F	93
III; R = *n*-heptyl	Pentadecanoic acid	F	82
II; R = *n*-undecyl	Nonadecanoic acid	F	99
III; R = 5′-ethyloctyl	13-Ethylhexadecanoic acid	F	88
V; R = OH	6 : 6-Dimethylundecanedioic acid	F	93

* See experimental section.

For the preparation of 2 : 2-di-(5-carboxy-2-thienyl)propane (V; R = OH), acetone was condensed with thiophen to give 2 : 2-di-2′-thienylpropane (Schick and Crowley, *J. Amer. Chem. Soc.*, 1951, **73**, 1377), which was then acylated with acetic anhydride in the presence of a trace of iodine to 2 : 2-di-(5-acetyl-2-thienyl)propane (V; R = Me). Oxidation with hypobromite then gave the desired biscarboxythienylpropane.

EXPERIMENTAL

Petroleum X3B is a light petroleum, b. p. 95—135°, containing 33% of aromatic compounds.

Acylthiophens.—A mixture of 2 : 5-dimethylthiophen (110 g.), acetyl chloride (73·2 g.), and carbon disulphide (935 c.c.) was cooled in ice–salt, and finely powdered anhydrous aluminium chloride (163 g.) added in 6 portions during 10 min. The mixture was then carefully warmed until a vigorous reaction occurred. Cooling was necessary to control the reaction. The mixture was worked up in the usual way. Distillation gave 3-acetyl-2 : 5-dimethylthiophen (114 g., 75%), b. p. 119°/16 mm., 128°/39 mm. This method is better than that of Buu-Hoï and Nguyen-Hoán (*Rec. Trav. chim.*, 1948, **67**, 319).

To freshly distilled heptanoyl chloride (22 g.), thiophen (12·5 g.), and anhydrous thiophen-free benzene (150 c.c.) at 0° stannic chloride (16·5 g.) was added dropwise, with stirring, during 40 min. (cf. Johnson and May, *Org. Synth.*, Coll. Vol. 2, p. 8). After 1 hour's stirring at room temperature the mixture was decomposed with 10% hydrochloric acid. The benzene layer was washed with 10% hydrochloric acid, water, 5% sodium carbonate, and water, then dried ($CaCl_2$) and evaporated. 2-Heptanoylthiophen (24·4 g., 84%) had b. p. 170—171°/22 mm. (Cagniant and Deluzarche, *Compt. rend.*, 1947, **225**, 455, give b. p. 152°/13 mm.). The same ketone was prepared (60% yield) from thiophen and heptanoic acid with phosphoric oxide (cf. Hartough and Kosak, *J. Amer. Chem. Soc.*, 1947, **69**, 3098).

In the same way, heptanoyl chloride and 2-ethylthiophen (King and Nord, *J. Org. Chem.*, 1949, **14**, 638), in the presence of stannic chloride, gave 2-ethyl-5-heptanoylthiophen, b. p. 102—104°/0·05 mm. (90%). The oxime had m. p. 39° (Schleicher, *Ber.*, 1886, **19**, 660, gives m. p. 37—38°).

2-Undecanoylthiophen was prepared from thiophen and undecanoyl chloride as above ($SnCl_4$) except that a longer reaction time was beneficial. The stannic chloride was added to the reaction mixture at −5° during 20 min. After a further 30 min. at this temperature the mixture was warmed to 25° during 2 hr. and kept at that temperature for 30 min. 2-Undecanoylthiophen (80% yield) had b. p. 136—137°/0·05 mm. (Cagniant and Deluzarche, *loc. cit.*, give b. p. 205·5°/15·5 mm.).

The acid chloride (b. p. 123°/32 mm.) was prepared from 5-ethyloctanoic acid with thionyl chloride. Stannic chloride was added during ½ hr. with ice-cooling. After a further 4½ hr. at 25°, working up in the usual way gave 2-5′-*ethyloctanoylthiophen* (87%), b. p. 105°/0·04 mm.

(Found: C, 71·0; H, 9·5; S, 13·3. $C_{14}H_{22}OS$ requires C, 70·7; H, 9·3; S, 13·5%). The 2 : 4-*dinitrophenylhydrazone* separated from ethanol as orange-red plates, m. p. 96° (Found: C, 57·7; H, 6·4; N, 13·1. $C_{20}H_{26}O_4N_4S$ requires C, 57·4; H, 6·3; N, 13·4%). The *semicarbazone* crystallised from ethanol as colourless plates, m. p. 143° (Found: N, 14·4. $C_{15}H_{25}ON_3S$ requires N, 14·2%).

Alkylthiophens.—3-Acetyl-2 : 5-dimethylthiophen (77 g.) and 50% aqueous hydrazine (170 c.c.) in ethylene glycol (400 c.c.) were heated at 170° (cf. King and Nord, *loc. cit.*). When no more water and hydrazine hydrate distilled, the mixture was cooled to 80° and potassium hydroxide (100 g.) added. On slow heating the evolution of nitrogen began at 110° and was fast at 135—145°. At this temperature most of the reduced product distilled as a yellow oil, and after 1 hr. at 145° no further distillation took place. After purification in the usual way, 3-ethyl-2 : 5-dimethylthiophen (59 g., 85%) had b. p. 80°/28 mm. (Buu-Hoï and Nguyen-Hoân report b. p. 182—184°/760 mm. for the compound prepared in 44% yield by Clemmensen reduction of the ketone).

Preparation of 2-*n*-heptylthiophen required use of diethylene glycol for the reduction. When 2-heptanoylthiophen (10 g.), 60% aqueous hydrazine hydrate (18 c.c.), and diethylene glycol (155 c.c.) were heated to 180°, all the water and excess of hydrazine hydrate distilled off in 2 hr. The mixture was cooled below 100°, potassium hydroxide (9·7 g.) was added, and the temperature was then kept at 180° for 2 hr. When isolated in the usual way, 2-n-*heptylthiophen* (9 g., 97%) had b. p. 120°/20 mm. (Found: C, 72·7; H, 10·05; S, 17·7. $C_{11}H_{18}S$ requires C, 72·5; H, 9·95; S, 17·6%).

2-Undecanoylthiophen (44 g.), 60% aqueous hydrazine hydrate (68·5 c.c.), and diethylene glycol (580 c.c.) were heated at 195° for 2 hr. After cooling, potassium hydroxide (36·6 g.) was added, and the reaction was completed at 155° (2 hr.). 2-n-*Undecylthiophen* (37·5 g., 91%) had b. p. 104°/0·06 mm. (Found: C, 75·8; H, 11·1; S, 13·3. $C_{15}H_{26}S$ requires C, 75·6; H, 10·9; S, 13·5%).

Reduction of 2-5′-ethyloctanoylthiophen was effected with hydrazine hydrate as described for 2-heptylthiophen. 2-5′-*Ethyloctylthiophen*, obtained in 88% yield, had b. p. 78—79°/0·05 mm. (Found: C, 75·2; H, 11·0; S, 14·0. $C_{14}H_{24}S$ requires C, 74·9; H, 10·8; S, 14·3%).

Preparation of β-2-*Thenoylpropionic Acids.*—Succinic anhydride (1 mol.) and anhydrous aluminium chloride (2·2 mol.) were dissolved in nitrobenzene (1 l.) and the solution cooled in ice. A solution of the thiophen derivative (1 mol.) in nitrobenzene (500 c.c.) was then added dropwise, with stirring, during ½ hr. Cooling was continued for a further ½ hr., and the mixture was then stirred at room temperature for 5 hr. After decomposition with 20% hydrochloric acid and ice, the solvent was removed in steam. The supernatant liquid was decanted and 10% aqueous sodium carbonate (1500 c.c.) added to the residue, and the resulting solution treated with steam to remove the last traces of volatile matter. The alkaline solution was then treated with charcoal and the crude acids were precipitated with hydrochloric acid. The yield of purified product was between 55 and 63%.

(i) After recrystallisation from water (charcoal), β-2-thenoylpropionic acid had m. p. 118—119° (Fieser and Kennelly, *J. Amer. Chem. Soc.*, 1935, **57**, 1615, give m. p. 119—120°).

(ii) After recrystallisation from petroleum X3B, and from toluene, β-(2-ethyl-5-thenoyl)-propionic acid had m. p. 95° (Buu-Hoï, Hoân, and Khoi, *J. Org. Chem.*, 1950, **15**, 959, give m. p. 96°).

(iii) After recrystallisation from water, and then from petroleum X3B, β-(2 : 5-dimethyl-3-thenoyl)propionic acid had m. p. 111° in agreement with Steinkopf, Poulsson, and Herdey (*Annalen*, 1938, **536**, 132).

(iv) After recrystallisation from benzene–light petroleum (b. p. <40°) β-(4-*ethyl*-2 : 5-*dimethyl*-3-*thenoyl*)*propionic acid* formed plates, m. p. 92°. An analytical specimen of the same m. p. was prepared by sublimation at 80°/0·01 mm. (Found: C, 59·9; H, 6·7; S, 13·5. $C_{12}H_{16}O_3S$ requires C, 60·0; H, 6·7; S, 13·3%). Its p-*bromophenacyl ester* crystallised from petroleum X3B in blades, m. p. 89° (Found: C, 55·3; H, 5·1; Br, 18·3. $C_{20}H_{21}BrO_4S$ requires C, 55·2; H, 4·9; Br, 18·4%).

(v) After recrystallisation from petroleum X3B, and from benzene, β-(5-*heptyl*-2-*thenoyl*)-*propionic acid* formed plates, m. p. 102° (Found: C, 63·8; H, 7·9; S, 11·5. $C_{15}H_{22}O_3S$ requires C, 63·8; H, 7·9; S, 11·4%).

(vi) After recrystallisation from benzene, β-(5-*undecyl*-2-*thenoyl*)*propionic acid* formed plates, m. p. 108—109° (Found: C, 67·7; H, 8·9; S, 9·7. $C_{19}H_{30}O_3S$ requires C, 67·4; H, 8·9; S, 9·5%). The sodium salt was sparingly soluble in water.

(vii) Recrystallisation from light petroleum (b. p. 40—100°) gave β-(5-5′-*ethyloctyl*-2-

thenoyl)propionic acid as plates, m. p. 70° (Found: C, 66·8; H, 8·7; S, 9·5. $C_{18}H_{28}O_3S$ requires C, 66·8; H, 8·7; S, 9·9%).

(viii) Crude β-(5-bromo-2-thenoyl)propionic acid was extracted with boiling water (Soxhlet), and the resulting product recrystallised from xylene. The acid had m. p. 141° (Buu-Hoï, Hoán, and Xuong, *Rec. Trav. chim.*, 1950, **69**, 1108, give m. p. 142°).

Reduction of the β-*Thenoylpropionic Acids.*—Reduction of the keto-acids was effected by the Huang-Minlon procedure (*J. Amer. Chem. Soc.*, 1946, **68**, 2487), the following relative quantities being used: keto-acid (1 mol.), hydrazine hydrate (3·62 mols., as 50 or 60% aqueous solution), potassium hydroxide (3·38 mols.), and diethylene glycol (2130 c.c.). The mixture was heated at 180—190° for 3—4 hr., excess of hydrazine hydrate and water being allowed to distil. When worked up in the usual way the reduced acids were obtained by distillation and purified by crystallisation (when possible). β-(4-Ethyl-2 : 5-dimethyl-3-thenoyl)propionic acid was not reduced by this method, and the Clemmensen method likewise failed with this acid.

(i) γ-2-Thienylbutyric acid, obtained in 95% yield, had b. p. 120°/0·5 mm. (Fieser and Kennelly, *loc. cit.*, give b. p. 130—134°/1·5 mm.). Its *p*-bromophenacyl ester had m. p. 57—58° (Papa, Schwenk, and Ginsberg, *J. Org. Chem.*, 1949, **14**, 723, give m. p. 58—59°).

(ii) γ-(5-Ethyl-2-thienyl)butyric acid, obtained in 80% yield, had b. p. 150°/0·5 mm. (Buu-Hoï, Hoán, and Khoi, *loc. cit.*, report b. p. 190—192°/18 mm.).

(iii) γ-(2 : 5-Dimethyl-3-thienyl)butyric acid, b. p. 124°/0·04 mm., was obtained in 88% yield. It was recrystallised from light petroleum (b. p. <40°) and then had m. p. 55—56°, in agreement with Steinkopf, Poulsson, and Herdey (*loc. cit.*). The same acid was also obtained (in 50% yield) by Clemmensen reduction of the keto-acid.

(iv) γ-(5-n-*Heptyl-2-thienyl)butyric acid*, obtained in 88% yield, had b. p. 152°/0·04 mm. and formed blades, m. p. 39—40°, from light petroleum (b. p. <40°) (Found: C, 67·2; H, 9·0; S, 11·9. $C_{15}H_{24}O_2S$ requries C, 67·1; H, 9·0; S, 11·95%).

(v) γ-(5-n-*Undecyl-2-thienyl)butyric acid*, obtained in 83% yield, had b. p. 200°/0·07 mm. After recrystallisation from light petroleum (b. p. <40°) (using solid carbon dioxide), it formed blades, m. p. 32° (Found: C, 70·6; H, 9·9; S, 9·9. $C_{19}H_{32}O_2S$ requires C, 70·3; H, 9·9; S, 9·9%).

(vi) γ-(5-5′-*Ethyloctyl-2-thienyl)butyric acid*, obtained in 89% yield, had b. p. 192°/0·1 mm., 180°/0·04 mm. (Found: C, 69·8; H, 9·7; S, 10·5. $C_{18}H_{30}O_2S$ requires C, 69·6; H, 9·7; S, 10·3%).

2 : 2-*Di-2′-thienylpropane.*—The following procedure was superior to that of Schick and Crowley (*J. Amer. Chem. Soc.*, 1951, **73**, 1377). Acetone (19·5 g.) was added dropwise to a well-stirred mixture of thiophen (42 g.) and sulphuric acid (72%; 63 g.) during 5 min., at 60—65°, but when the addition was complete the temperature was raised to 70° for 4 hr. Water was added and the organic material extracted with chloroform. The combined extracts were washed with 10% aqueous sodium carbonate, then water, and dried ($CaCl_2$). Distillation gave 2 : 2-di-2′-thienylpropane (29·5 g., 57%), b. p. 74—76°/0·05 mm. (Schick and Crowley, *loc. cit.*, give b. p. 86°/0·3 mm., and 47% yield).

2 : 2-*Di-(5-acetyl-2-thienyl)propane.*—To 2 : 2-di-2′-thienylpropane (10·4 g.) and acetic anhydride (25·6 g.) at 100° a solution of iodine (0·2 g.) in ether (20 c.c.) was added dropwise during 5 min. (cf. Cairns, McKusick, and Weinmayr, *J. Amer. Chem. Soc.*, 1951, **73**, 1270). Heating was continued for 2 hr., the reaction then being stopped by the addition of sodium hydrogen sulphite (0·25 g.) in water (20 c.c.). The organic material was extracted with chloroform, and the extract washed with 7·5% aqueous sodium hydroxide, 5% hydrochloric acid, 5% aqueous sodium carbonate, and water. The chloroform was evaporated, and the residue purified by chromatography on alumina in petroleum X3B. A yellow band was eluted with petroleum X3B, benzene then being used to elute the main product. Concentration of the benzene solution, followed by addition of a little petroleum X3B, gave the desired ketone (8·8 g., 60%). After recrystallisation from petroleum X3B and then from ethanol 2 : 2-*di-(5-acetyl-2-thienyl)propane* was obtained as plates, m. p. 75—75·5° (Found: C, 62·0; H, 5·6; S, 22·0. $C_{15}H_{16}O_2S_2$ requires C, 61·6; H, 5·5; S, 21·9%).

2 : 2-*Di-(5-carboxy-2-thienyl)propane.*—Bromine (4·6 g.) was added slowly to an ice-cold solution of sodium hydroxide (3·17 g.) in water (27 c.c.). 2 : 2-Di-(5-acetyl-2-thienyl)propane (1·4 g.) was then added and the mixture stirred for 10 hr., the temperature being allowed to rise gradually to 15°. The reaction was completed by heating on a water-bath for 30 min. Excess of hypobromite was removed with sulphur dioxdie, and the mixture was steam-distilled to remove carbon tetrabromide and bromoform. [The residue was extracted with ether, whereby some ketone (0·11 g.) was recovered.] The desired product was obtained by acidifi-

cation of the alkaline solution, and after re-solution in sodium hydrogen carbonate solution and precipitation with hydrochloric acid 2 : *2-di-(5-carboxy-2-thienyl)propane* (0·88 g., 62%) was obtained as a colourless powder which darkened at 260° and had m. p. 275—277° (decomp.) (Found: C, 52·8; H, 4·3; S, 21·5. $C_{13}H_{12}O_4S_2$ requires C, 52·7; H, 4·1; S, 21·6%). It could not be recrystallised.

Desulphurisation of 2-*Acetylthiophen.*—(i) 2-Acetylthiophen (20 g.) was added to W-7 Raney nickel catalyst (prepared from 125 g. of nickel–aluminium alloy; Billica and Adkins, *loc. cit.*) in toluene (500 c.c.) which had previously been refluxed over W-7 catalyst. Nitrogen was passed through the apparatus while the mixture was refluxed, with vigorous stirring, for 8½ hr. The escaping gases were passed through 2 flasks containing ice-cold water, and the resulting solution was shown to contain acetaldehyde. It was identified by preparation of the 2 : 4-dinitrophenylhydrazone, m. p. 167—168°, the dimedone derivative, m. p. 141°, and the anhydride of the latter, m. p. 173—174°, and comparison with authentic specimens.

The catalyst was filtered off and washed with boiling toluene (3 × 100 c.c.). The filtrate and washings were combined, the toluene removed by fractionation, and the residue fractionated under reduced pressure. Three fractions were collected: (*a*) b. p. 58—60°/20 mm. (0·1 g.); (*b*) b. p. 48—50°/0·1 mm. (8 g.); and (*c*) b. p. 98—100°/0·1 mm. (1·0 g.). Fractions (*a*) and (*b*) consisted essentially of 2-acetylthiophen (identified as the 2 : 4-dinitrophenylhydrazone, m. p. 244°). After several recrystallisations from light petroleum fraction (*c*) gave dodecane-2 : 11-dione as blades, m. p. 66—67° (lit., m. p. 67·4—67·8°) (Found: : C, 73·0; H, 11·0. Calc. for $C_{12}H_{22}O_2$: C, 72·7; H, 11·1%). A haloform reaction (Hawkins and Young, *J.*, 1950, 2804) gave sebacic acid, identified by comparison with an authentic specimen.

(ii) 2-Acetylthiophen (20 g.) was added to W-6 Raney nickel catalyst (prepared from 125 g. of nickel–aluminium alloy; Billica and Adkins, *loc. cit.*) in ethanol (350 c.c.) which had been distilled from potassium hydroxide and previously refluxed over W-6 catalyst. Other experimental details were as above. The ice-water absorbed acetaldehyde (1·2 g.), isolated as the dimedone derivative, corresponding to 3·34 g. of 2-acetylthiophen.

After separation of the catalyst the alcohol was removed by distillation through a jacketed fractionating column (2 × 60 cm.) filled with multi-turn glass helices and carrying a variable take-off head. A reflux ratio of 1 : 15 was used. The residue was fractionated through a Vigreux column and yielded 5 fractions: (*a*) b. p. 60—128° (2 g.); (*b*) b. p. 129° (4 g.); (*c*) b. p. 90°/10 mm. (5·4 g.); (*d*) b. p. <84°/0·03 mm. (0·2 g.); (*e*) b. p. 84°/0·03 mm. (1·2 g.). Fraction (*a*) was a mixture of ethanol and 2-hexanone [2 : 4-dinitrophenylhydrazone (3 g., corresponding to 0·94 g. of ketone)]. Fraction (*b*) was hexan-2-one [2 : 4-dinitrophenylhydrazone, orange-red rods, m. p. 105° (lit., 104—105°); semicarbazone had m. p. 121° (lit., 121—122·5°)]. Fraction (*c*) was 2-acetylthiophen, and fraction (*e*) dodecane-2 : 11-dione.

Desulphurisation of 2-*Ethyl*-5-*heptanoylthiophen.*—2-Ethyl-5-heptanoylthiophen (20 g.) was desulphurised with W-6 Raney nickel (from 125 g. of nickel–aluminium alloy) in ethanol, for 6 hr. The mixture was worked up as described above. Distillation gave tridecan-7-one (15·8 g., 90%), m. p. 31—32° (lit., 31°) (Found: C, 78·9; H, 13·4; O, 8·2. Calc. for $C_{13}H_{26}O$: C, 78·7; H, 13·2; O, 8·1%). The *p*-nitrophenylhydrazone (from ethanol) had m. p. 96° (lit., 97°).

Desulphurisations of Acidic Derivatives of Thiophen.—(*A*) Desulphurisation of γ-2-thienylbutyric acid according to the method of Papa, Schwenk, and Ginsberg (*loc. cit.*) gave octanoic acid (39%), 44% of the starting material being recovered. After two distillations the octanoic acid had m. p. 15—16° (lit., 16°), and the *p*-bromophenacyl ester (from aqueous ethanol) had m. p. 66—67° (lit., 67°).

(*B*) Raney nickel alloy (63 g.) was dissolved in aqueous sodium hydroxide, and digested at 50° ± 2° as described by Billica and Adkins (*loc. cit.*). The supernatant liquid was then decanted and γ-2-thienylbutyric acid (12·4 g.) in 10% aqueous sodium hydroxide (40 c.c.) added. The total volume was adjusted to 200—250 c.c. and the mixture kept at 80—110° for 4 hr., with stirring. The nickel was filtered off and washed with hot 10% sodium hydroxide solution. The combined washings and filtrate were added to concentrated hydrochloric acid (150 c.c.) and water (150 c.c.) with stirring. After extraction with ether (dried with $MgSO_4$), the product was distilled and yielded starting material (2·5 g., b. p. 120°/0·5 mm.) and octanoic acid (4·8 g., 48%; b. p. 86°/0·5 mm.). After two further distillations the octanoic acid had m. p. 16°.

(*C*) Raney nickel alloy (125 g.) was dissolved and digested at 50° ± 2° as described by Billica and Adkins (*loc. cit.*). The catalyst was then carefully washed by decantation with distilled water (6 × 500 c.c.). γ-2-Thienylbutyric acid (8 g.) in 10% aqueous sodium carbonate was added to a suspension of the catalyst in distilled water (600 c.c.). After 1·75 hours' stirring on a steam-bath the catalyst was filtered off and washed with hot sodium carbonate solution. The filtrate and washings were then worked up as in method *B*. Distillation gave octanoic acid (5·0 g., 73%; b. p. 78°/0·05 mm.), m. p. 16°.

(*D*) Raney nickel catalyst was prepared as described in method *B* and washed by decantation with distilled water (5 × 120 c.c.). γ-(5-Ethyl-2-thienyl)butyric acid (10 g.) in 10% aqueous sodium carbonate was added to the catalyst, the total volume being adjusted to *ca.* 300 c.c. The mixture was then heated on a steam-bath, with stirring, for 3 hr. Fractionation of the product gave decanoic acid (4·5 g., 51%; b. p. 116—120°/0·1 mm.) and starting material (1·3 g., 13%; b. p. 143°/0·1 mm.). After two distillations the decanoic acid had m. p. 30° (lit., 31°). The *p*-bromophenacyl ester had m. p. 67° (Found: C, 58·6; H, 6·9; Br, 21·4. Calc. for $C_{18}H_{25}O_3Br$: C, 58·7; H, 6·8; Br, 21·6%).

(*E*) γ-(5-Ethyl-2-thienyl)butyric acid (7·9 g.) was desulphurised by W-6 Raney nickel (*ca.* 63 g.) in boiling toluene, for 4 hr. Excessive frothing occurred. The catalyst was filtered off and washed with hot toluene, the filtrate and washings being combined. After removal of the solvent the product was distilled and gave decanoic acid (2·6 g., 38%; b. p. 120°/0·1 mm., m. p. 31°).

Desulphurisation of γ-(2 : 5-dimethyl-3-thienyl)butyric acid was effected similarly but with benzene instead of toluene. 5-*Ethyloctanoic acid* was obtained, in 41% yield, having b. p. 83—84°/1·05 mm. (Found: C, 69·9; H, 11·75; O, 18·4. $C_{10}H_{20}O_2$ requires C, 69·7; H, 11·7; O, 18·6%). The p-*bromobenzylthiuronium salt* (cf. Dewey and Shashy, *J. Amer. Chem. Soc.*, 1941, **63**, 3526), recrystallised from aqueous ethanol and then from toluene, formed plates, m. p. 142—143° (Found: C, 52·1; H, 7·1; N, 6·4. $C_{18}H_{29}O_2N_2SBr$ requires C, 51·8; H, 7·0; N, 6·7%).

(*F*) Desulphurisation of γ-(2 : 5-dimethyl-3-thienyl)butyric acid was also effected by method *C* except that a volume of 900 c.c. was used instead of 600 c.c. Under these conditions, 5-ethyloctanoic acid was obtained in 93% yield.

In some experiments the products were strongly adsorbed on the catalyst and were recovered by extraction with boiling ethanol or by dissolution of the nickel in hydrochloric acid.

Pentadecanoic Acid.—Desulphurisation of γ-(5-heptyl-2-thienyl)butyric acid by method *F* gave pentadecanoic acid, b. p. 138—139°/0·05 mm., m. p. 52—53° (lit., 52·5—53·5°), in 55% yield. However, after the catalyst had been washed with several lots of boiling ethanol, a further 27% yield of pentadecanoic acid was obtained. The *p*-bromophenacyl ester (from ethanol) had m. p. 77·5° (Found: C, 63·1; H, 8·0; Br, 18·5. Calc. for $C_{23}H_{35}O_3Br$: C, 62·9; H, 8·0; Br, 18·2%). The *p*-bromophenacyl ester (from ethanol) had m. p. 91—91·5° (lit., 91·3—91·8°).

Nonadecanoic Acid.—Desulphurisation of γ-(5-undecyl-2-thienyl)butyric acid was carried out according to method *F*, but to avoid excessive frothing, the temperature was kept at 80°. The catalyst was dissolved in hydrochloric acid and the product extracted with ether and added to that obtained from the alkaline filtrates. In this way nonadecanoic acid, m. p. 67—68·5° (lit., 66·5°; 69—70°) was obtained in 99% yield. The p-*phenylphenacyl ester*, recrystallised from ethanol and from acetone, formed leaflets, m. p. 98—98·5° (Found: C, 80·7; H, 10·0; O, 9·5. $C_{33}H_{48}O_3$ requires C, 80·6; H, 9·7; O, 9·7%). The p-*bromophenacyl ester* separated from ethanol in leaflets, m. p. 87—87·5° (Found: C, 65·2; H, 8·4; Br, 16·0. $C_{27}H_{43}O_3Br$ requires C, 65·4; H, 8·75; Br, 16·1%).

13-*Ethylhexadecanoic Acid.*—γ-(5-5′-Ethyloctyl-2-thienyl)butyric acid (10 g.) was desulphurised by method *F*. After being washed with three lots of boiling ethanol the catalyst was found (by dissolution in hydrochloric acid) to be virtually free from adsorbed fatty acid. Worked up in the usual way, 13-*ethylhexadecanoic acid* was obtained, in 88% yield, as a colourless oil, b. p. 156°/0·1 mm. (Found: C, 76·3; H, 12·45; O, 11·2. $C_{18}H_{36}O_2$ requires C, 76·0; H, 12·8; O, 11·25%). The p-*phenylphenacyl ester*, recrystallised from ethanol, had m. p. 70° after softening at 35° (Found: C, 80·45; H, 9·75. $C_{32}H_{46}O_2$ requires C, 80·3; H, 9·7%). The p-*bromophenacyl ester* had m. p. 40·5° (from aqueous ethanol) (Found: C, 64·7; H, 8·3; O, 10·0. $C_{26}H_{41}O_3Br$ requires C, 64·85; H, 8·6; O, 10·0%).

6 : 6-*Dimethylundecanedioic Acid.*—Desulphurisation of 2 : 2-di-(5-carboxy-2-thienyl)propane (10 g.) was carried out by method *F*. After recrystallisation from benzene–light petroleum, 6 : 6-*dimethylundecanedioic acid* (93%) was obtained as leaflets, m. p. 71° (Found: C, 64·2; H, 9·7; O, 26·0. $C_{13}H_{24}O_4$ requires C, 63·9; H, 9·9; O, 26·2%). Its *bis*-p-*bromophenacyl ester* separated from ethanol in leaflets, m. p. 136° (Found: C, 54·7; H, 5·3; Br, 25·3.

$C_{29}H_{34}O_6Br_2$ requires C, 54·6; H, 5·4; Br, 25·0%). Its *bis*-p-*phenylphenacyl ester* crystallised from ethanol in plates, m. p. 100° (Found: C, 77·8; H, 6·8. $C_{41}H_{44}O_6$ requires C, 77·8; H, 7·0%).

4-*Oxo-octanoic Acid*.—β-2-Thenoylpropionic acid was desulphurised according to method *F* except that only half the quantity of catalyst was used. 4-Oxo-octanoic acid (57% yield) had b. p. 168—170°/15 mm., m. p. 53·5—54° (Papa, Schwenk, and Ginsberg, *loc. cit.*, give m. p. 54—54·5°).

5 : 6-*Diethyl-4-oxo-octanoic Acid*.—Method *C* was used to desulphurise β-(4-ethyl-2 : 5-dimethyl-3-thenoyl)propionic acid. 5 : 6-*Diethyl-4-oxo-octanoic acid* was obtained as a colourless oil, b. p. 120—121°/0·06 mm., which became brown in light and air (Found: C, 67·65; H, 10·1; O, 22·8. $C_{12}H_{22}O_3$ requires C, 67·25; H, 10·35; O, 22·4%). The thermally unstable p-*bromobenzylthiuronium* salt separated from aqueous ethanol in plates, m. p. 138—139° (Found: C, 52·7; H, 6·6; Br, 17·9. $C_{20}H_{31}O_3N_2BrS$ requires C, 52·3; H, 6·8; Br, 17·4%). This acid could not be reduced by the Wolff–Kishner method under conditions described above for the reduction of thenoylpropionic acids.

Desulphurisation of β-(5-*Bromo-2-thenoyl*)*propionic Acid*.—Desulphurisation by method *C* gave 4-oxo-octanoic acid in 25% yield. In another experiment the catalyst was prepared and washed by decantation as usual and kept suspended in water (300 c.c.) on a steam-bath for 1 hr. before addition of the bromothenoylpropionic acid in sodium carbonate solution. The total volume was kept at 500 c.c. No immediate precipitate was formed, but a white solid separated after strong cooling. After recrystallisation from ethanol this product, which seems to be 4 : 13-*dioxohexadecanedioic acid*, was obtained in prisms, m. p. 152—153° (yield 3·5%) (Found: C, 61·1; H, 8·2; O, 30·1. $C_{16}H_{26}O_6$ requires C, 61·1; H, 8·3; O, 30·5%).

Attempts to desulphurise the bromothenoylpropionic acid without elimination of the bromine, by using deactivated catalyst (Spero, McIntosh, and Levin, *J. Amer. Chem. Soc.*, 1948, **70**, 1907), were unsuccessful.

Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory, Melbourne. We also thank the Socony-Vacuum Laboratories, New Jersey, for a generous gift of thiophen.

UNIVERSITY OF ADELAIDE, SOUTH AUSTRALIA. [*Received, June 28th*, 1954.]