

302. *The Use of Thiophen as a Chain-extender. Part I.
Synthetic Oxo- and Hydroxy-alkanoic Acids.*

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The preparation of 6-, 7-, 9-, and 10-oxo- and -hydroxy-octadecanoic acids * and of 13- and 14-oxo- and -hydroxy-docosanoic acid, by desulphurisation of suitably 2,5-disubstituted thiophens with Raney nickel is described. The freezing-point curves of some oxoalkanoic acids have been determined.

THE application of thiophen as a chain-extender has, until recently, not been developed into a general method for the preparation of long-chain compounds. The present work was undertaken because this route is attractive and the products could be used to clarify some inconsistencies in the literature about the physical constants of a number of substituted long-chain acids and their derivatives.

Since the commencement of this work,¹ several papers have appeared on synthetical applications of the desulphurisation of thiophen derivatives, notably the following. Badger, Rodda, and Sasse² prepared a series of aliphatic acids from thienylalkanoic acids, and heptanoic acid has been prepared by Hansen.³ Other acids have been obtained by

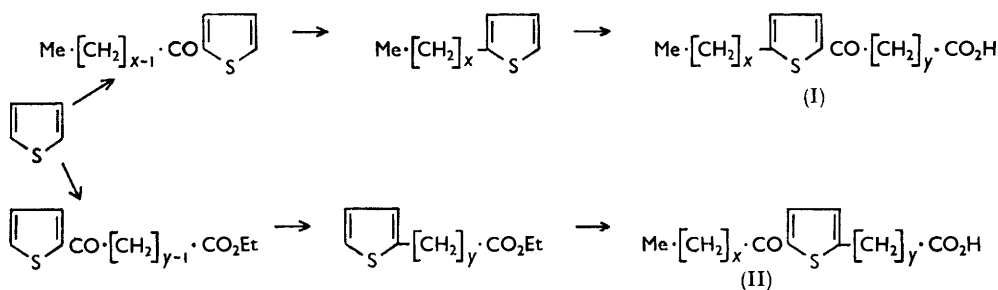
* Geneva nomenclature, CO₂H = 1.

¹ Cf. Grey, McGhie, Pradhan, and Ross, *Chem. and Ind.*, 1954, 578.

² Badger, Rodda, and Sasse, *J.*, 1954, 4162.

³ Hansen, *Acta Chem. Scand.*, 1954, **8**, 695.

Buu-Hoï, Sy, and Xuong⁴ and by Sy,⁵ branched-chain acids by Spaeth and Germain,⁶ and dicarboxylic acids by Buu-Hoï, Sy, and Xuong⁷ and by Wynberg and Logothetis.⁸



2,5-Disubstituted thiophenes have been obtained by the two routes shown. Both sequences involved three main steps; acylation of thiophen with an acid chloride or half-ester chloride, reduction of the keto-group, and a second acylation. The first route was adopted for synthesis of the oxo- and hydroxy-octadecanoic acids, and the second for synthesis of the oxo- and hydroxy-docosanoic acids. The preparation of the thiophen acids, by standard methods, is described in the Experimental section. Depending on the conditions during desulphurisation, either the oxo- or the hydroxy-alkanoic acids could be prepared, as shown in Table 1.

Attention should be drawn to the discrepancies between the melting points reported in this communication for the semicarbazones of 9- and 10-oxo-octadecanoic acid and those in the literature. Our synthetic 9-oxo-acid formed a semicarbazone of m. p. 110–111°. Ross, Gebhardt, and Gerecht¹⁴ report m. p. 118–120°; Jungermann and Spoerri¹⁰ give m. p. 117–119°. The semicarbazone of our synthetic 10-oxo-acid had m. p. 118–119°, in close agreement with Fordyce and Johnson's¹³ value for their synthetic product. Ross *et al.*¹⁴ and Jungermann and Spoerri¹⁰ give m. p. 101–103° and 100.5–102° respectively. The discrepancies are probably due to the methods of preparation employed, which may yield isomeric products not completely separated. Jungermann and Spoerri¹⁰ give m. p. 72° for 10-oxo-octadecanoic acid, whereas the correct value is 82°. A m. p. of 72° corresponds to a ~2 : 3 mixture of the 9- and 10-oxo-acids. The semicarbazone from this acid had a reported m. p. 100.5–102°; this is the m. p. of the semicarbazone of the mixture of 9- and 10-oxo-octadecanoic acids resulting from the hydration of 9,10-stearolic acid.

The yields in Table 1 are based on the quantity of desulphurisation product obtained, and often a considerable quantity of starting material was isolable. Since direct desulphurisation to the hydroxyalkanoic acids was smooth in all cases, and these compounds are readily oxidised to the oxo-acids (by means of chromium trioxide and acetic acid) this alternative method for the preparation of oxo-acids might be more suitable in some cases.

The freezing-point curve of mixtures of 9- and 10-oxo-octadecanoic acid was determined by Robinson and Robinson⁹ to test their theory on the composition of the hydration product of 9,10-stearolic acid. This determination has been repeated with closely agreeing results. The availability of pure synthetic specimens of 13- and 14-oxodocosanoic acid prompted the application of this method to the investigation of the hydration product of 13,14-behenolic acid, which melts at 84°. The results (Table 3) show that the mixture contains 72.5% of 13-oxodocosanoic acid, in accordance with the prediction made by

⁴ Buu-Hoï, Sy, and Xuong, *Compt. rend.*, 1954, **239**, 1224.

⁵ Sy, *Bull. Soc. chim. France*, 1955, 1175.

⁶ Spaeth and Germain, *J. Amer. Chem. Soc.*, 1955, **77**, 4067.

⁷ Buu-Hoï, Sy, and Xuong, *Compt. rend.*, 1955, 240,442; *Bull. Soc. chim. France*, 1955, 1583; *Rec. Trav. chim.*, 1956, **75**, 463.

⁸ Wynberg and Logothetis, *J. Amer. Chem. Soc.*, 1956, **78**, 1958.

⁹ Robinson and Robinson, *J.*, 1926, 2204.

¹⁰ Jungermann and Spoerri, *J. Amer. Chem. Soc.*, 1953, **75**, 4704.

TABLE I.

| Starting material Acid (I) | Method * | Acid product | M. p. | Lit. | Yield (%) |
|-------------------------------|----------------|-------------------------|------------------|---|-----------|
| $x = 4; y = 7$ | A | 9-Oxo semicarbazone | 81° 110—111 | 83° ⁹ 117—119 ¹⁰ | 84 — |
| | B | 9-Hydroxy | 70—72 | 74—75 ¹¹ | 61 |
| $x = 3; y = 8$ | A | 10-Oxo | 82—82.5 | 82 ¹² | 44 |
| | B | 10-Oxo semicarbazone | 81—82 118—119 | — 121—122 ¹³ ; 100.5—102 ^{10, 14} | 68 — |
| $x = 7; y = 4$ | B | 10-Hydroxy | 78—79 | 84 ¹² ; 81—82 ¹¹ ; 79 ¹⁵ | 61 |
| | C W6 | 6-Oxo semicarbazone | 84 151—152 | 87 ¹² 139—140 ¹⁶ | 38 — |
| $x = 6; y = 5$ | C W7 | 6-Hydroxy | 82—83 | 83 ^{15, 17} | 83 |
| | C W6 | 7-Oxo semicarbazone | 81—82 113—114 | 83 ¹⁵ — | 38 — |
| Acid (II) | C W7 | 7-Hydroxy Docosanoic | 78—79 | 77.6—77.8 ¹⁵ | 63 |
| | $x = 8; y = 7$ | A | 13-Oxo | 91—92 | — |
| B | | 13-Oxo Semicarbazone | 88—90 117—118 | — — | 65 — |
| $x = 7; y = 8$ | C W7 | 13-Hydroxy | 85—86 | 87 ¹⁸ | 70 |
| | A | 14-Oxo | 90—91 | 85 ¹⁸ | 28 |
| | B | 14-Oxo semicarbazone | 90—91 117—118 | — — | 51 — |
| | C W7 | 14-Hydroxy | 83—84 | 87 ¹⁸ | 72 |

* A refers to Raney nickel alloy; B to the catalyst prepared essentially by Brown's¹⁹ method, C W6 and C W7, the catalyst prepared according to the procedure of Billica and Adkins.²⁰

Robinson and Robinson.⁹ Since specimens of pure 6- and 7-oxo-octadecanoic acids were available, a freezing point curve for this mixture was also determined (Table 2) in an attempt to find the composition of the hydration product, m. p. 75°, of 6,7-stearolic (tariric) acid. Unfortunately these results proved inconclusive, as no true eutectic was obtainable.

EXPERIMENTAL

Butyl 2-Thienyl Ketone.—(a) Valeric acid (50 g.) was added slowly to a stirred suspension of phosphoric oxide (71 g.) in anhydrous benzene (250 c.c.) containing thiophen (50 g.). The mixture was stirred for 4 hr. under reflux and then cooled. The benzene layer was decanted and washed with 10% sodium hydroxide solution (5 c.c.) and water (50 c.c.). Removal of the solvent under reduced pressure gave the ketone, which was converted into the *semicarbazone* (55 g.), plates (from ethanol), m. p. 168° (Found: C, 53.7; H, 6.8; N, 19.1. $C_{10}H_{15}ON_3S$ requires C, 53.3; H, 6.7; N, 18.7%).

(b) A solution of valeryl chloride (36 g.) and thiophen (25 g.) in dry benzene (300 c.c.) was cooled to 0°. Freshly distilled stannic chloride (77 g.) was added in small portions ($\frac{1}{2}$ hr.) at 0—10°. The cooling-bath was removed and the mixture stirred at room temperature for 1 hr. N-Hydrochloric acid (200 c.c.) was added with cooling, and, after separation, the benzene layer was washed with water and evaporated. Distillation of the residue gave butyl 2-thienyl ketone (43 g.), b. p. 130—133°/12 mm. (Spurlock²¹ gives b. p. 258°/760 mm.).

Propyl 2-Thienyl Ketone.—Procedure (b) gave the product as a colourless oil (78%), b. p. 106—111°/8 mm., rapidly becoming pale yellow (Hartough and Kosak²² give b. p. 87—92°/3 mm.).

¹¹ Tomecko and Adams, *J. Amer. Chem. Soc.*, 1927, **49**, 524.

¹² Robinson and Robinson, *J.*, 1925, 179.

¹³ Fordyce and Johnson, *J. Amer. Chem. Soc.*, 1933, **55**, 3368.

¹⁴ Ross, Gebhardt, and Gerecht, *J. Amer. Chem. Soc.*, 1949, **71**, 284.

¹⁵ Bergström, Aulin-Erdtman, Rolander, Stenhagen and Ostling, *Acta Chem. Scand.*, 1952, **6**, 1157.

¹⁶ Fieser and Szmuskovicz, *J. Amer. Chem. Soc.*, 1948, **70**, 3352.

¹⁷ Bougault and Charaux, *Compt. rend.*, 1911, **153**, 573.

¹⁸ Bowman, *J.*, 1950, 177.

¹⁹ Brown, *J. Soc. Chem. Ind.*, 1950, **69**, 353.

²⁰ Billica and Adkins, *Org. Synth.*, 1949, **29**, 25.

²¹ Spurlock, *J. Amer. Chem. Soc.*, 1953, **75**, 1115.

²² Hartough and Kosak, *J. Amer. Chem. Soc.*, 1947, **69**, 3095.

Alternatively, syrupy phosphoric acid (1.0 c.c.) was added dropwise to a stirred mixture of thiophen (33.6 g.) and butyric anhydride (63 g.) at 70°, and the mixture was stirred under reflux for 1 hr. More phosphoric acid (0.5 c.c.) was added and stirring continued for 1 hr. Water (50 c.c.) and ether (100 c.c.) were added successively to the cooled mixture, and the separated organic layer was washed with 5% sodium carbonate solution and dried (Na₂SO₄). After removal of the solvent, the ketone (41.4 g.) was distilled (b. p. 121°/15 mm.).

Heptyl 2-Thienyl Ketone.—Prepared by method (b), the ketone (74%) had b. p. 172—175°/10 mm. (Campaigne and Diedrich²³ give b. p. 140—143°/1 mm.).

Hexyl 2-Thienyl Ketone.—Prepared by method (b), the ketone (61%) had b. p. 150°/10 mm. (Cagniant and Deluzarche²⁴ give b. p. 152°/13 mm.).

2-Pentylthiophen.—(a) Potassium hydroxide (45 g.) in triethylene glycol (100 c.c.) was added to a solution of butyl 2-thienyl ketone semicarbazone (55 g.) in triethylene glycol (400 c.c.) at 70°. The mixture was heated with stirring, until the internal temperature reached 135°, refluxing then beginning. After 20 min. at this temperature, the product was allowed to distil until the distillation temperature reached 260°. The distillate was dissolved in ether (200 c.c.) and washed with water (50 c.c.), 2N-hydrochloric acid (50 c.c.), and water (50 c.c.). The dried (Na₂SO₄) solution was evaporated and distillation yielded 2-pentylthiophen (16.3 g.), b. p. 202—205°/769 mm.

(b) A solution of butyl 2-thienyl ketone (43 g.) in diethylene glycol (400 c.c.) containing hydrazine hydrate (44 c.c.) was stirred at 120° for $\frac{1}{2}$ hr. After the mixture had cooled to 40°, potassium hydroxide (40 g.) in hot diethylene glycol (150 c.c.) was added, and the solution was stirred at 150° for $\frac{1}{2}$ hr. The product was then allowed to distil until the distillation temperature reached 250°. Working up as before gave 2-pentylthiophen (33 g.), b. p. 202—204°/769 mm. (Picon²⁵ gives b. p. 80—98°/10 mm.).

2-Butylthiophen.—2-Butyrylthiophen (30 g.) and hydrazine hydrate (33 c.c.) in ethylene glycol (400 c.c.) were stirred at 120° for 1 $\frac{1}{2}$ hr., then cooled to 30°. Potassium hydroxide (30 g.) in hot ethylene glycol (100 c.c.) was added, and the stirred mixture was heated at 150—155° for 1 hr. The distilled product was dissolved in ether (150 c.c.), and the ethereal solution was washed with water (30 c.c.), 2N-hydrochloric acid (30 c.c.), and water (30 c.c.). Evaporation of the dried (Na₂SO₄) ethereal solution followed by distillation gave 2-butylthiophen (20 g.), b. p. 182—190°/770 mm., $n_D^{18.5}$ 1.5015 (Hartough²⁶ gives b. p. 181°/770 mm., n_D^{20} 1.5014).

2-Octylthiophen.—2-Octanoylthiophen (35 g.) and 90% hydrazine hydrate (40 c.c.) in diethylene glycol (400 c.c.) were kept at 130° for $\frac{1}{2}$ hr. Next day potassium hydroxide (60 g.) in hot diethylene glycol (200 c.c.) was added, and the mixture was stirred at 140° for $\frac{1}{2}$ hr. Liquid was distilled off, until the internal temperature reached 160°, and stirring was continued at this temperature for 1 hr. The solution was poured on ice (600 g.), acidified by hydrochloric acid (200 c.c.), and extracted with chloroform (2 × 50 c.c.). Evaporation of the washed (water; 30 c.c.) and dried (MgSO₄) solution gave on distillation 2-octylthiophen (24 g.), b. p. 123—125°/10 mm. (Campaigne and Diedrich²³ give b. p. 106—108°/1 mm.).

2-Heptylthiophen.—Reduction of 2-heptanoylthiophen by the previous method gave 2-heptylthiophen, b. p. 125°/20 mm. (Found: C, 72.3; H, 9.8. C₁₁H₁₈S requires C, 72.5; H, 10.0%).

8-(5-Pentyl-2-thienyl)octanoic Acid.—Freshly distilled stannic chloride (36 g.) was added with stirring during 45 min. at 0—10° to 2-pentylthiophen (21 g.) and 8-ethoxycarbonyloctanoyl chloride (32 g.) in benzene (250 c.c.), and the whole was stirred at room temperature for 1 hr. 10% Hydrochloric acid (100 c.c.) was then added, with stirring and ice-cooling. The benzene layer was washed with water (25 c.c.) and evaporated. Potassium hydroxide (20 g.) in 77% aqueous ethanol (300 c.c.) was added, and the mixture heated under reflux for 1 $\frac{1}{2}$ hr. The filtrate was poured into water (400 c.c.) and acidified with hydrochloric acid (40 c.c.). The solid was filtered off and dissolved in potassium hydroxide (20 g.) in water (250 c.c.). After ether-extraction (to remove neutral material) and re-acidification with hydrochloric acid (50 c.c.), an oil separated. Crystallisation from chloroform–light petroleum (b. p. 60—80°), followed by recrystallisation from aqueous acetone, gave prismatic needles of the *octanoic acid*

²³ Campaigne and Diedrich, *J. Amer. Chem. Soc.*, 1948, **70**, 391.

²⁴ Cagniant and Deluzarche, *Compt. rend.*, 1947, **22**, 455.

²⁵ Picon, F.P. 958,232/1950.

²⁶ Hartough, "Thiophene and its Derivatives," Interscience Publishers Inc., New York, 1952, p. 68.

(30 g.), m. p. 67—68° (Found: C, 66.7; H, 8.7. $C_{18}H_{28}O_3S$ requires C, 66.6; H, 8.7%). After 14 days' storage with an excess of Brady's reagent, the 2,4-dinitrophenylhydrazone was obtained as red needles, m. p. 111—112° (from ethanol) (Found: C, 56.8; H, 6.2; N, 11.2. $C_{24}H_{32}O_6N_4S$ requires C, 57.1; H, 6.4; N, 11.1%).

9-(5-Butyl-2-thenoyl)nonanoic Acid.—2-Butylthiophen (28 g.) was treated with 9-ethoxycarbonylnonanoyl chloride (55 g.) as above. The crude ethyl ester (68 g.) was distilled (b. p. 194°/0.3 mm.). After hydrolysis and purification, the thenoylnonanoic acid (35 g.) had m. p. 63—64° [plates from light petroleum (b. p. 60—80°)] (Found: C, 66.4; H, 8.8; S, 9.3. $C_{18}H_{28}O_3S$ requires C, 66.7; H, 8.7; S, 9.9%). The 2,4-dinitrophenylhydrazone crystallised from ethanol as red needles, m. p. 109—110° (Found: C, 57.0; H, 6.2; N, 11.1. $C_{24}H_{32}O_6N_4S$ requires C, 57.1; H, 6.4; N, 11.1%).

5-(5-Octyl-2-thenoyl)pentanoic Acid.—2-Octylthiophen (24 g.) was treated with 5-ethoxycarbonylpentanoyl chloride (24 g.) as above. Distillation gave ethyl 5-(5-octyl-2-thenoyl)pentanoate (35 g.), b. p. 211—212°/0.4 mm., which on saponification yielded the pentanoic acid (30 g.), m. p. 64—65° (from aqueous ethanol) (Found: C, 67.0; H, 8.8. $C_{18}H_{28}O_3S$ requires C, 66.7; H, 8.7%). The 2,4-dinitrophenylhydrazone crystallised from aqueous ethanol as red needles, m. p. 129—130° (Found: C, 57.1; H, 6.4; N, 10.8. $C_{24}H_{32}O_6N_4S$ requires C, 57.1; H, 6.4; N, 11.1%).

6-(5-Heptyl-2-thenoyl)hexanoic Acid.—Freshly distilled stannic chloride (16 c.c.) was added with stirring during 45 min. at 0—5° to 2-heptylthiophen (25 g.) and 6-cyanohexanoyl chloride (20 g.) in benzene (250 c.c.). Working up as usual and distillation gave 2-(6-cyanohexanoyl)-5-heptylthiophen (33 g.), b. p. 210°/0.4 mm. (Found: C, 70.3; H, 8.8; N, 4.1. $C_{18}H_{27}ONS$ requires C, 70.8; H, 8.9; N, 4.6%). Potassium hydroxide (20 g.) in water (50 c.c.) was added to the cyanohexanoylheptylthiophen (30 g.) in ethanol (300 c.c.), and the mixture was heated under reflux for 36 hr. Some ethanol (150 c.c.) was distilled off, ethylene glycol (150 c.c.) was added, and the whole was heated to 160° for 3 hr. After cooling, the product was poured into ice-cold 2N-hydrochloric acid (750 c.c.) with stirring. The crude product was filtered off; recrystallisation from aqueous ethanol gave 6-(5-heptyl-2-thenoyl)hexanoic acid (26 g.), plates, m. p. 73—74° (Found: C, 66.6; H, 8.6. $C_{18}H_{28}O_3S$ requires C, 66.7; H, 8.7%). The 2,4-dinitrophenylhydrazone crystallised from ethanol as red needles, m. p. 106—108° (Found: C, 58.0; H, 6.5; N, 10.6. $C_{24}H_{32}O_6N_4S$ requires C, 57.1; H, 6.4; N, 11.1%).

9-Oxo-octadecanoic Acid.—Nickel-aluminium alloy (15 g.) was added during 1 hr. to 8-(5-pentyl-2-thenoyl)octanoic acid (1.1 g.) in 17% sodium hydroxide solution (150 c.c.), which was stirred vigorously and heated under reflux. Stirring and heating were continued for 4 hr. Next day 50% hydrochloric acid (200 c.c.) was slowly added, and the product was extracted with chloroform. Evaporation and crystallisation from light petroleum (b. p. 60—80°) and then from ethyl acetate gave 9-oxo-octadecanoic acid (0.6 g.), m. p. 81° (Robinson and Robinson⁹ give m. p. 83°). The semicarbazone, crystallised from ethanol, had m. p. 110—111° (Jungermann and Spoerri¹⁰ give m. p. 117—119°) (Found: C, 64.4; H, 10.4; N, 11.8. Calc. for $C_{19}H_{37}O_3N_3$: C, 64.2; H, 10.5; N, 11.8%).

9-Hydroxyoctadecanoic Acid.—A solution of the thenoyloctanoic acid (0.8 g.) in ethanol (100 c.c.) was heated under reflux for 28 hr. with Raney nickel (4 g.) prepared as described by Brown¹⁹ but washed with 3 l. of water. The filtered catalyst was dissolved in 50% hydrochloric acid (200 c.c.), and the solution was extracted with ether. The washed (water) and dried ($MgSO_4$) extract was mixed with the ethanolic filtrate, and the whole was evaporated under reduced pressure. The hydroxy-acid (0.45 g.), crystallised from ethyl acetate, had m. p. 70—72° (Tomecko and Adams¹¹ give m. p. 74—75°).

10-Oxo-octadecanoic Acid.—Neutral Raney nickel (4 g.), prepared as described by Brown,¹⁹ but washed with 20 l. of water, was added to 9-(5-butyl-2-thenoyl)nonanoic acid (1.6 g.) in ethanol (150 c.c.), and the mixture was heated under reflux for 4 hr. Working up as above gave the acid (1.0 g.), m. p. 81—82° (from ethyl acetate). The semicarbazone, crystallised from ethanol, had m. p. 118—119° (Found: C, 64.2; H, 10.6; N, 11.7. Calc. for $C_{19}H_{37}O_3N_3$: C, 64.2; H, 10.5; N, 11.8%) (Fordyce and Johnson¹³ give m. p. 121—122°; Jungermann and Spoerri¹⁰ and Ross, Gebhart and Gerecht¹⁴ give m. p. 100.5—102°). The methyl ester, prepared with ethereal diazomethane, crystallised from methanol in leaflets, m. p. 45—46° (Bergström *et al.*¹⁵ give m. p. 45.8—46.1°).

10-Hydroxyoctadecanoic Acid.—(A) The thenoylnonanoic acid (0.8 g.), on reduction by the method used for the octanoic acid, yielded 10-hydroxyoctadecanoic acid (0.45 g.), m. p. 78—79°

(from ethyl acetate) (Robinson and Robinson¹² give m. p. 84°; Tomecko and Adams¹¹ give m. p. 81—82°; Bergström *et al.*¹⁵ give m. p. 79°).

(B) Potassium borohydride (0.1 g.) was added to the oxo-acid (0.2 g.) in *n*-sodium hydroxide (10 c.c.) containing ethanol (10 c.c.). Next day the product was poured into *n*-hydrochloric acid (110 c.c.), and the precipitated solid was filtered off. Recrystallisation from ethyl acetate gave 10-hydroxyoctadecanoic acid, m. p. 79—80°.

6-Oxo-octadecanoic Acid.—Raney nickel catalyst (W6)²⁰ (from 100 g. of alloy) was added to the thenoylpentanoic acid (10 g.) in ethanol (500 c.c.), and the mixture was heated under reflux for 4½ hr. Working up as usual gave the oxo-acid (3.5 g.), m. p. 78—81° (from ethyl acetate). Several recrystallisations from the same solvent raised the m. p. to 84° (Robinson and Robinson¹² give m. p. 87°). The *semicarbazone* crystallised from ethanol in plates, m. p. 151—152° (Found: C, 64.7; H, 10.5; N, 11.6. C₁₉H₃₇O₃N₃ requires C, 64.2; H, 10.5; N, 11.8%) (Fieser and Szmuskovicz¹⁶ give m. p. 139—140°).

6-Hydroxyoctadecanoic Acid.—Raney nickel catalyst (W7)²⁰ (from 200 g. of alloy) was added to the thenoylpentanoic acid (10 g.) in ethanol (1 l.), and the mixture was heated under reflux for 3 hr. Next day heating was resumed for 1 hr. The usual procedure, after crystallisation from 80% ethanol, gave the 6-hydroxy-acid (7.7 g.), m. p. 77—80°. Two recrystallisations from the same solvent gave m. p. 82—83° (Bougault and Charaux¹⁷ and Bergström *et al.*¹⁵ give m. p. 83°).

7-Oxo-octadecanoic Acid.—Reduction of the thenoylhexanoic acid (10 g.) by the method used for the pentanoic acid, gave, after crystallisation from 80% ethanol, 7-oxo-octadecanoic acid (3.5 g.), m. p. 76—77°, m. p. 81—82° after repeated recrystallisation (Bergström *et al.*¹⁵ give m. p. 83°). The *semicarbazone* crystallised from ethanol in prismatic needles, m. p. 113—114° (Found: C, 64.1; H, 10.2; N, 11.3. C₁₉H₃₇O₃N₃ requires C, 64.2; H, 10.5; N, 11.8%).

7-Hydroxyoctadecanoic Acid.—Thenoylhexanoic acid (10 g.), on reduction by the method used for the pentanoic acid and crystallisation of the product from 80% ethanol, gave 7-hydroxyoctadecanoic acid (5.8 g.), m. p. 72—75°, m. p. 78—79° after repeated recrystallisation (Bergström *et al.*¹⁵ give m. p. 77.6—77.8°).

Mixed m. p. data for the 6- and 7-oxo-acids are in Table 2.

TABLE 2. *M. p. of mixtures of 6- and 7-oxo-octadecanoic acid.*

| 6-Oxo (%) | 7-Oxo (%) | F. p. | 6-Oxo (%) | 7-Oxo (%) | F. p. | 6-Oxo (%) | 7-Oxo (%) | F. p. |
|-----------|-----------|-------|-----------|-----------|-------|-----------|-----------|-------|
| 100 | 0 | 83.1° | 84.3 | 45.7 | 69.0° | 25.0 | 75.0 | 67.9° |
| 87.0 | 13.0 | 79.2 | 50.3 | 49.7 | 68.8 | 20.6 | 79.4 | 68.0 |
| 77.0 | 23.0 | 75.7 | 45.9 | 54.1 | 68.4 | 15.7 | 84.3 | 68.4 |
| 69.1 | 30.9 | 72.7 | 41.4 | 58.6 | 68.2 | 11.7 | 88.3 | 69.2 |
| 63.6 | 36.4 | 70.2 | 35.8 | 64.2 | 68.0 | 5.2 | 94.8 | 71.1 |
| 58.7 | 41.3 | 69.3 | 29.3 | 70.7 | 67.9 | 0 | 100 | 72.1 |

13-Oxodocosanoic Acid.—Thiophen (15 c.c.) and 7-ethoxycarbonylheptanoyl chloride (25 g.) in benzene (150 c.c.) were treated with stannic chloride (20 c.c.) in the usual way. Distillation furnished *ethyl 7-2'-thenoylheptanoate* (26 g.), b. p. 145—150°/0.1 mm. (Found: C, 62.4; H, 7.65. C₁₄H₂₀O₃S requires C, 62.7; H, 7.5%). The *2,4-dinitrophenylhydrazone*, red needles from ethanol, had m. p. 92° (Found: C, 53.0; H, 5.1; N, 12.6. C₂₀H₂₄O₆N₄S requires C, 53.6; H, 5.4; N, 12.5%). The keto-ester (24 g.) and hydrazine hydrate (15 c.c.) in ethylene glycol (250 c.c.) were stirred at 120° for ½ hr., and then allowed to cool to 40°. Potassium hydroxide (30 g.) in ethylene glycol (120 c.c.) was added, and the mixture was stirred at 155° for 1 hr. The water formed was distilled off during 1 hr. until the internal temperature reached 190°. The cooled product was poured into water (450 c.c.), acidified with hydrochloric acid (150 c.c.), and extracted with ether. The combined extracts were washed with water, dried (Na₂SO₄), and evaporated. The acid was heated with ethanol (150 c.c.), benzene (75 c.c.), and sulphuric acid (0.5 c.c.), under a water separator (Dean and Stark) and a 24-inch Fenske column. The usual procedure gave, on distillation, *ethyl 8-thienyloctanoate* (19 g.), b. p. 162°/4 mm. (Found: C, 65.9; H, 8.9. C₁₄H₂₂O₂S requires C, 66.1; H, 8.7%). The ester (18 g.) and decanoyl chloride (14.6 g.) in benzene (100 c.c.) were treated with stannic chloride (9 c.c.) in the usual way. A portion of the product was distilled, giving *ethyl 8-(5-decanoyl-2-thienyl)octanoate*, b. p. 220°/0.3 mm. The bulk was saponified, to yield *8-(5-decanoyl-2-thienyl)octanoic acid*

(23 g.), m. p. 67—68° (from ethanol) (Found: C, 69.4; H, 9.7. $C_{22}H_{36}O_3S$ requires C, 69.4; H, 9.5%). The 2,4-dinitrophenylhydrazone crystallised from ethanol as red needles, m. p. 103—104° (Found: C, 60.3; H, 7.1; N, 10.2. $C_{28}H_{40}O_6N_4S$ requires C, 60.0; H, 7.2; N, 10.0%).

The acid (1.9 g.) in ethanol (150 c.c.) was treated with Raney nickel catalyst (*ca.* 5 g.) (prepared by Brown's¹⁹ method but washed with 20 l. of water). The product (62%) had m. p. 88—89° after recrystallisation from ethyl acetate. The semicarbazone, m. p. 117—118°, crystallised in needles from ethanol (Found: C, 67.4; H, 11.0; N, 9.9. $C_{23}H_{45}O_3N_3$ requires C, 67.1; H, 11.0; N, 10.2%).

13-Hydroxydocosanoic Acid.—The thenoyloctanoic acid (1.9 g.) was reduced with Raney nickel catalyst (W7)²⁰ (from 46 g. of alloy). After recrystallisation from ethyl acetate, the product (1.25 g.) had m. p. 85—86° (Bowman¹⁸ gives m. p. 87°).

14-Oxodocosanoic Acid.—Thiophen (20 c.c.) and 8-ethoxycarbonyloctanoyl chloride (42 g.) in benzene (200 c.c.) were treated with stannic chloride (20 c.c.). Distillation of the product gave ethyl 8-2'-thenoyloctanoate (40 g.), b. p. 175—185°/0.5 mm. (Found: C, 63.5; H, 8.0. $C_{18}H_{22}O_3S$ requires C, 63.8; H, 7.9%). On reduction of this ester (40 g.) with hydrazine hydrate followed by distillation, ethyl 9-2'-thienylnonanoate (27 g.) was obtained as a colourless oil, b. p. 167—171°/2 mm. (Found: C, 66.9; H, 9.2. $C_{15}H_{24}O_2S$ requires C, 67.1; H, 9.0%). This product (27 g.) and nonanoyl chloride (17.7 g.) in benzene (150 c.c.) were treated with stannic chloride (26 g.) in the usual way. Distillation of a portion of the product gave ethyl 9-(5-nonanoyl-2-thienyl)nonanoate, b. p. 202—206°/0.5 mm. (Found: C, 70.1; H, 9.8. $C_{24}H_{40}O_3S$ requires C, 70.6; H, 9.9%). Saponification of the remainder gave, after recrystallisation from aqueous ethanol, 9-(5-nonanoyl-2-thienyl)nonanoic acid (18.5 g.), m. p. 67—68°. The 2,4-dinitrophenylhydrazone crystallised from ethanol as red needles, m. p. 101—102° (Found: C, 60.1; H, 7.2; N, 10.0. $C_{28}H_{40}O_6N_4S$ requires C, 60.0; H, 7.2; N, 10.0%). Raney nickel (*ca.* 5 g.; prepared by Brown's¹⁹ method, but washed with 20 l. of water) was added to the thienylnonanoic acid (1.9 g.) in ethanol (150 c.c.), and the mixture was heated under reflux for 4 hr. Evaporation of the filtrate left no residue. The nickel residue was dissolved in 18% hydrochloric acid (500 c.c.), and the solution was extracted with ether. The ethereal solution was washed with water, dried (Na_2SO_4), and evaporated. Recrystallisation of the residue from ethyl acetate gave 14-oxodocosanoic acid (0.9 g.), m. p. 90—91° (Bowman¹⁸ gives m. p. 85°) (Found: C, 74.9; H, 11.9. Calc. for $C_{22}H_{42}O_3$: C, 74.5; H, 11.9%). The semicarbazone, m. p. 117—118°, crystallised in needles from ethanol (Found: C, 66.9; H, 11.0; N, 10.1. $C_{23}H_{45}O_3N_3$ requires C, 67.1; H, 11.0; N, 10.2%). For m. p. data see Table 3.

TABLE 3. *M. p. of mixtures of 13- and 14-oxodocosanoic acid.*

| 13-Oxo (%) | 14-Oxo (%) | M. p. | 13-Oxo (%) | 14-Oxo (%) | M. p. | 13-Oxo (%) | 14-Oxo (%) | M. p. |
|------------|------------|-------|------------|------------|-------|------------|------------|-------|
| 0 | 100 | 88.5° | 48.7 | 51.3 | 80.0° | 67.0 | 33.0 | 82.8° |
| 20.8 | 79.2 | 86.6 | 50.0 | 50.0 | 79.1 | 75.4 | 24.6 | 84.2 |
| 34.4 | 65.6 | 84.5 | 52.0 | 48.0 | 79.3 | 87.5 | 12.5 | 86.6 |
| 38.6 | 61.4 | 83.6 | 52.9 | 47.1 | 79.5 | 100.0 | 0 | 87.5 |
| 41.6 | 58.4 | 82.8 | 59.2 | 40.8 | 80.8 | | | |
| 46.5 | 53.5 | 80.2 | | | | | | |

14-Hydroxydocosanoic Acid.—Reduction of the thienylnonanoic acid (1.9 g.) with Raney nickel catalyst (W7)²⁰ under the conditions used for reduction of the octanoic acid and recrystallisation of the product from ethyl acetate gave 14-hydroxydocosanoic acid (1.28 g.), m. p. 83—84° (Bowman¹⁸ gives m. p. 87°) (Found: C, 73.8; H, 12.2. Calc. for $C_{22}H_{44}O_3$: C, 74.1; H, 12.4%).