378. *The Orientation of Substitution in the Isomeric Thiophthens. The Synthesis of Solid Thiophthen [Thiopheno(3′ : 2′-2 : 3)thiophen].*

By Frederick Challenger and John L. Holmes.

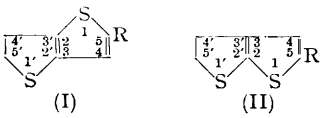
The structure of the solid thiophthen [thiopheno(3′ : 2′-2 : 3)thiophen] (I; R = H), previously determined by *X*-ray and (zero) dipole measurements, has been established by synthesis from (3-thienylthio)acetic acid by ring closure and reduction; α-(3-thienylthio)-propionic and -*n*-butyric acid similarly yield the 5-methyl and the 5-ethyl homologue. Raney nickel reduction of the methyl ketones from (I; R = H) and liquid thiophthen (II; R = H) yields octan-2-one and 5-methylheptan-2-ol respectively, thus confirming the structure of (I) and (II) and showing that substitution in the Friedel–Crafts reaction occurs in position 5.

The two isomeric thiophthens (I; R = H) and (II; R = H) produced in the reaction between acetylene and boiling sulphur have been extensively studied during the last twenty years by one of us and his co-workers [(*a*) Challenger and Harrison, *J. Inst. Pet. Tech.*, 1935, **21**, 135; (*b*) Challenger and G. M. Gibson, *J.*, 1940, 305; (*c*) Bruce, Challenger, H. B. Gibson, and Allenby, *J. Inst. Pet.*, 1948, **34**, 226; (*d*) Challenger, Clapham, and Emmott, *ibid.*, p. 922; (*e*) Challenger and Emmott, *ibid.*, 1951, **37**, 396; (*f*) Challenger and Fishwick, *ibid.*, 1953, **39**, 320]. In (*a*) it was reported that a preliminary *X*-ray analysis kindly carried out by Dr. Bernal showed that the solid isomer possesses a plane of symmetry and is therefore represented by (I; R = H), a conclusion confirmed by Dr. F. R. Goss, who showed that it has a zero dipole moment. This physical evidence being accepted for structure (I; R = H), it was shown (*e*) that the liquid isomer must be (II; R = H) as was already almost certain from other considerations (*a*, *e*). Since then it has been found (*b*, *d*, *e*) that, for numerous electrophilic substituents, the position entered in the solid isomer is always the same. A similar conclusion was reached for liquid thiophthen. In neither case was the position determined, but later (*f*) it was shown that for the liquid isomer the position is 5, *i.e.*, adjacent to the sulphur atom. This conclusion is confirmed by further work now to be described.

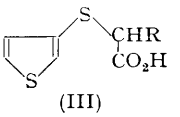
The solid isomer has been synthesised. (3-Thienylthio)acetic acid (III; R = H) (Challenger, Miller, and Gibson, *J.*, 1948, 769) with hot sulphuric acid yields 4 : 5-dihydro-4-oxothiopheno(3′ : 2′-2 : 3)thiophen (IV; R = H). This compound, which was first prepared but not analysed by G. M. Gibson (Thesis, Univ. Leeds, 1939), forms a benzylidene derivative and on reduction with lithium aluminium hydride in ether yields solid thiophthen, identified by m. p. and mixed m. p. and by those of the picrate and styphnate. The corresponding 5-methyl and 5-ethyl derivatives of solid thiophthen were synthesised in a similar manner from α-(3-thienylthio)propionic acid (a liquid characterised as the amide) and α-(3-thienylthio)-*n*-butyric acid (a liquid characterised as the ethyl ester and the amide) by cyclisation to the liquids, 4 : 5-dihydro-5-methyl- and -5-ethyl-4-oxothio-

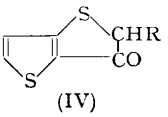
pheno(3′ : 2′-2 : 3)thiophen (IV; R = Me or Et), followed by reduction as before. The 5-methylthiophthen (I; R = Me) is a liquid forming a picrate, styphnate, and 1 : 3 : 5-trinitrobenzene derivative. The 5-ethylthiophthen (I; R = Et) is also an oil. Its picrate and 1 : 3 : 5-trinitrobenzene compound did not depress the m. p. of the corresponding derivatives of the 5-ethylthiophthen obtained (*f*) by Wolff–Kishner reduction of the corresponding 5-acetyl derivative (I; R = COMe). Reduction of this ketone with Raney nickel yields nickel sulphide and octan-2-one, characterised as semicarbazone and *p*-nitrophenylhydrazone by comparison with authentic specimens (Henderson, Henderson, and Heilbron, *Ber.*, 1914, **47**, 887). This reaction confirms the structure of (I; R = COMe), and hence of solid thiophthen itself, and also the position of substitution in the Friedel–Crafts reaction.

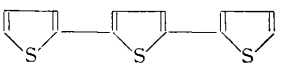
The methyl ketone from liquid thiophthen, *viz.*, (II; R = COMe), on reduction with Raney nickel yields 5-methylheptan-2-ol (Welt, *Ann. Chim. Phys.*, 1895, **6**, 135). No ketone could be isolated in this reaction. The alcohol was characterised as the α-naphthylamine addition product of the 3 : 5-dinitrobenzoate. No other solid derivative could be obtained. On oxidation, 5-methylheptan-2-one (Wild, *Annalen*, 1917, **414**, 118) was obtained (semicarbazone and 2 : 4-dinitrophenylhydrazone).

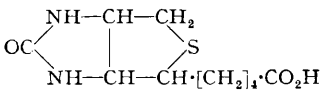

(I)

(II)


(III)


(IV)


(V)


(VI)

The 5-methylheptan-2-ol required for reference was synthesised from *sec.*-butylmagnesium chloride; with gaseous formaldehyde this gave 2-methylbutan-1-ol, and the corresponding bromide by the ethyl acetoacetate synthesis gave 5-methylheptan-2-one which was then reduced with Raney nickel to the required alcohol. From the reaction with formaldehyde a high-boiling liquid, $C_{11}H_{24}O_2$, was also obtained which had no alcoholic properties but gave 2-methylbutyl bromide with aqueous hydrobromic acid. It appeared to be di-(2-methylbutyl)formal, $CH_2(O{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2Me)_2$. Pantony (Thesis, Univ. Leeds, 1948) obtained dinonylformal from the reaction between formaldehyde and octylmagnesium bromide. These formals may arise thus: $R{\cdot}MgX + CH_2O \longrightarrow R{\cdot}CH_2{\cdot}O{\cdot}MgX$; $2R{\cdot}CH_2{\cdot}OMgX + CH_2O \longrightarrow (R{\cdot}CH_2{\cdot}O)_2CH_2 + MgO + MgX_2$. A similar by-product was obtained from gaseous formaldehyde and hexylmagnesium bromide.

Challenger *et al.* (*c*) found isomeric dithienyls in the purified distillate from the interaction of acetylene and boiling sulphur. Lease and Zechmeister later (*J. Amer. Chem. Soc.*, 1947, **69**, 270, 273) isolated α-terthienyl (V) from the flowers of the Indian marigold, *Tagetus erecta* (Nat. Order *Compositæ*). Many members of this natural order contain polyacetylene derivatives; *e.g.*, Sörensen and Stene (*Annalen*, 1941, **549**, 80) isolated the diolefinic diacetylene $Me{\cdot}CH{:}CH{\cdot}C{:}C{\cdot}C{:}C{\cdot}CH{:}CH{\cdot}CO_2Me$ from *Matricaria inodora*, a plant closely allied to the common camomile. The corresponding dihydro-derivative $Me{\cdot}CH_2{\cdot}CH_2{\cdot}C{:}C{\cdot}C{:}C{\cdot}CH{:}CH{\cdot}CO_2Me$ occurs in *Lachnophyllum gossypinum* (Wiljams, Smirnow, and Goljmow, *J. Gen. Chem. Russia, A*, 1935, **5**, 1195). Carlina oxide (benzyl-2-furylacetylene) occurs in the oil obtained from the roots of *Carlina acaulis* [*Cirsium acaule* (L.) Scop.].

It may be more than a coincidence that the only instance so far recorded of the occurrence of a true thiophen derivative in plants should be found in a family so many members of which contain polyacetylenes. The α-terthienyl may arise by interaction of hydrogen sulphide with a straight-chain compound containing an acetylenic–olefinic system, possibly also some methylene groups, as in the second compound cited above. Other reactions such as oxidation, decarboxylation, or dehydrogenation might be involved. It could be argued that a long-chain paraffin or fatty acid might serve equally well as the

starting point. Ring closure would, however, undoubtedly be facilitated by the presence of olefinic and acetylenic linkages.

A natural product with a modified thiophen nucleus is β-biotin (VI) which contains a tetrahydrothiophen ring with a $[CH_2]_4$·C side chain. Many natural unsaturated fatty acids, including the acetylenic derivatives erythrogenic acid CH_2:CH·C:C·$[CH_2]_4$·C:C·$[CH_2]_7$·CO_2H or CH_2:CH·$[CH_2]_4$·C:C·C:C·$[CH_2]_7$·CO_2H and tariric acid Me·$[CH_2]_{10}$·C:C·$[CH_2]_4$·CO_2H, contain this grouping and it is possible that both the heterocyclic ring and the side chain of biotin may arise from an acid of this type.

Experimental

Reductive Fission of 5-Acetylthiopheno(3′ : 2′-2 : 3)thiophen.—The ketone (3 g.) in ethyl alcohol (80 c.c.) was refluxed with an alcoholic suspension (25 c.c.) of Raney nickel for 3 hr. The solution slowly became red and finally colourless again. Next day the solid was separated and shown to evolve hydrogen sulphide with dilute acid. On removal of alcohol from the filtrate an orange oil remained which had a ketonic odour. It distilled at 70°/17 mm. (1·5 g.) and was purified *via* its sodium hydrogen sulphite compound. Decomposition with sodium carbonate and redistillation gave *n*-hexyl methyl ketone (Found : C, 74·6; H, 12·35. Calc. for $C_8H_{16}O$: C, 75·0; H, 12·5%). The semicarbazone, crystallised from alcohol, had m. p. 122·5—123° (Found : C, 58·3; H, 10·4; N, 22·9. Calc. for $C_9H_{19}ON_3$: C, 58·4; H, 10·3; N, 22·7%). The *p*-nitrophenylhydrazone, prepared in cold glacial acetic acid and crystallised from alcohol, had m. p. 92—93°. These two derivatives did not depress the m. p. of specimens prepared from authentic *n*-hexyl methyl ketone (p. 1838) which was synthesised from ethyl acetoacetate and pentyl bromide.

Reductive Fission of 5-Acetylthiopheno(2′ : 3′-2 : 3)thiophen.—The carefully purified ketone (3·8 g.) was refluxed with a suspension of Raney nickel in benzene. The solution became deep yellow and then colourless again (4 hr.). The solid was separated and washed with hot benzene. The united solvents yielded an oil, b. p. 160—162°, with an odour resembling that of octyl alcohol, and gave no precipitate with 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid. The 3 : 5-dinitrobenzoate was an oil which did not solidify. On addition of a small quantity of α-naphthylamine a deep red solid addition product was formed which after five crystallisations from alcohol had m. p. 57—58°, and did not depress the m. p. of a specimen similarly prepared from authentic 5-methylheptan-2-ol.

Oxidation of the alcohol from the Raney nickel reaction to the corresponding ketone. 5 C.c. of a solution containing potassium dichromate (2·5 g.), water (15 c.c.), and sulphuric acid (1·5 c.c.) were heated with the alcohol (0·3 c.c.) for 30 min. and the mixture was distilled in steam. Extraction of the distillate with ether gave an oil having an odour similar to that of 5-methylheptan-2-one. The *semicarbazone*, crystallised twice from aqueous alcohol, had m. p. 131—132° not depressed by the semicarbazone of authentic 5-methylheptan-2-one (Found : C, 58·5; H, 10·2; N, 22·6. $C_9H_{19}ON_3$ requires C, 58·4; H, 10·3; N, 22·7%). The 2 : 4-*dinitrophenylhydrazone* had m. p. 66—67° not depressed by a sample prepared from the authentic ketone (Found : C, 54·5; H, 6·4; N, 18·3. $C_{14}H_{20}O_4N_4$ requires C, 54·6; H, 6·5; N, 18·2%).

Cyclisation of (3-Thienylthio)acetic Acid.—The acid was prepared from thiophen-3-thiol and chloroacetic acid by the method of Challenger, Miller, and Gibson (*loc. cit.*), who give m. p. 50·5—51°, and of Brooks, Howard, and Wehrle (*J. Amer. Chem. Soc.*, 1950, **72**, 1289) who record m. p. 51·5—52·5° (Found : C, 41·4; H, 3·6; S, 36·5. Calc. for $C_6H_6O_2S_2$: C, 41·4; H, 3·5; S, 36·7%). On recrystallisation from water the m. p. was 52—53°. The main specimen of m. p 51—52° (10 g.) was heated on the steam-bath with sulphuric acid (100 c.c.) for 45 min. and poured on ice, and the mixture extracted with chloroform. The extract was twice washed with aqueous sodium hydrogen carbonate and dried, yielding an oil which solidified to a buff-coloured solid, m. p. 97—98 (1·24 g., 13·8%). These conditions were established as the most convenient after numerous small-scale experiments in which the proportions of the ingredients, the time, and the temperature were varied. The use of other condensing agents such as " polyphosphoric acid " (obtained by heating orthophosphoric acid at 150° for 7 days), a mixture of phosphoric oxide and orthophosphoric acid, or active alumina in boiling xylene were ineffective.

The cyclisation product [4 : 5-*dihydro*-4-*oxothiopheno*(3′ : 2′-2 : 3)*thiophen* (or the corresponding 4-hydroxy-form)] from several experiments was crystallised twice from aqueous alcohol and had m. p. 98—98·5°. G. M. Gibson (*loc. cit.*) gives m. p. 98° (Found : C, 46·3; H, 2·9; S, 40·9. $C_6H_4OS_2$ requires C, 46·2; H, 2·6; S, 41·0%). The product was soluble in

sodium hydroxide, from which it was precipitated by carbon dioxide. The *benzylidene* derivative was prepared by Auwers and Arndt's method (*Ber.*, 1909, **42**, 543) for 2-benzylidene-2 : 3-dihydro-3-oxothionaphthen. The cyclisation product (0·05 g.), benzaldehyde (5 drops), and a trace of hydrochloric acid were refluxed in alcohol for 1 hr. On cooling, silver-yellow flakes were deposited, having m. p. 141—142° unchanged on crystallisation from alcohol (Found: C, 63·5; H, 3·5; S, 26·2. $C_{13}H_8OS_2$ requires C, 63·9; H, 3·3; S, 26·2%). No semicarbazone could be obtained in aqueous alcohol.

Reduction. 4 : 5-Dihydro-4-oxothiophthen (0·2 g.) in glacial acetic acid (2 c.c.) was refluxed for 1 hr. with zinc dust (0·4 g.), and the mixture made alkaline and distilled in steam. The distillate, which had the odour of a sulphide or thiol, was extracted with ligroin. The extract gave a yellow colour and a green fluorescence with sulphuric acid, suggesting the presence of thiophthen. Evaporation left a trace of oil which solidified in ice and formed a picrate. Only minute amounts of thiophthen could have been present.

Lithium aluminium hydride (0·3 g.) was refluxed with dry ether (40 c.c.) for 10 min. 4 : 5-Dihydro-4-oxothiophthen (0·8 g.) was added, and heating continued overnight. Treatment with wet ether and then with dilute acid, separation, and evaporation of the ether left a pale red oil (0·73 g.) which solidified on cooling and was purified by steam-distillation with aqueous alkali. A white solid (0·45 g.) separated from the distillate, and a further 0·22 g. was obtained on extraction with ligroin. It had m. p. 55·5—56° and did not depress the m. p. of solid thiophthen, m. p. 55·5—56°, obtained from the sulphur–acetylene reaction in 80% yield (Found: C, 51·3; H, 3·5; S, 45·9. Calc. for $C_6H_4S_2$: C, 51·4; H, 2·9; S, 45·7%). Another preparation from 0·5 g. gave a yield of 80% of crude thiophthen, m. p. 53—55°. It was purified through the picrate, m. p. 144—145°, and decomposition with sodium carbonate in steam. The m. p. and mixed m. p. with authentic solid thiophthen was 54·5—55°.

The picrate and the styphnate, recrystallised from methyl alcohol, melted at 145—146° and 111·5—112° respectively alone and in admixture with the corresponding derivatives of solid thiophthen, m. p. 145—146° and 111·5—112° (Found, for the picrate: C, 38·6; H, 2·0; N, 11·4; S, 17·3. Calc. for $C_{12}H_7O_7N_3S_2$: C, 39·0; H, 1·9; N, 11·4; S, 17·3%. Found, for the styphnate: C, 37·5; H, 2·2; N, 10·7; S, 16·5. Calc. for $C_{12}H_7O_8N_3S_2$: C, 37·4; H, 1·9; N, 10·9; S, 16·6%).

α-(3-*Thienylthio*)*propionic Acid.*—Thiophen-3-thiol (5·8 g.) in a solution of sodium hydroxide (2·0 g.) in water (7·5 c.c.) was cooled in ice and stirred while α-bromopropionic acid (7·7 g.) and sodium hydroxide (2·0 g.) in water (8·0 c.c.) were added, the temperature being kept below 40°. Reaction was immediate, and a test portion yielded no thiol with carbon dioxide. Acidification gave an orange oil solidifying in ice to a buff-coloured mass (9·0 g., 90%). Recrystallisation from ligroin (b. p. 60—80°) gave a colourless solid, m. p. 77·5—78·5° (Found: C, 45·2; H, 4·5; S, 33·5. $C_7H_8O_2S_2$ requires C, 44·7; H, 4·2; S, 34·0%). The ester formed from this *acid* (Fischer–Speier) had b. p. 148—150°/23 mm.; it was shaken overnight with excess of concentrated aqueous ammonia, and the clear solution deposited the *amide*, which crystallised from water in colourless needles, m. p. 126—127° (Found: N, 7·5; S, 34·4. $C_7H_9ONS_2$ requires N, 7·5; S, 34·2%)

Cyclisation of α-(3-*Thienylthio*)*propionic Acid.*—The acid (2·0 g.) was cyclised by sulphuric acid (15·0 c.c.) at 100° for 30 min., and worked up as on p. 1839. The alkaline washings of the chloroform extract were acidified and again extracted with ether, finally yielding 4-hydroxy-5-methylthiophthen as a thick red oil (0·614 g., 30%) with a strong phenolic odour.

Synthesis of the 5-Methyl Derivative of Solid Thiophthen.—Lithium aluminium hydride (2 g.) was boiled for a short time with dry tetrahydrofuran (50 c.c.). The oily 4-hydroxy-5-methylthiophthen (0·614 g.) in the same solvent (50 c.c.) was slowly added. Reaction was vigorous. Next day, wet ether, dilute acid, and more ether were added as usual, and the mixed solvents separated and evaporated, leaving a red oil with a slightly phenolic odour. Distillation in steam from sodium hydroxide gave an orange oil (1·72 g., 32%) which solidified in a freezing mixture but melted again below room temperature. The whole of the oil was converted into its 1 : 3 : 5-*trinitrobenzene* derivative, which separated from methyl alcohol as yellow needles (3·3 g.), m. p. 107—108°, and 110° after two further crystallisations from the same solvent (Found: C, 42·6; H, 2·3; N, 11·6; S, 17·7. $C_{13}H_9O_6N_3S_2$ requires C, 42·5; H, 2·4; N, 11·5; S, 17·5%). This was decomposed in steam by 2N-aqueous sodium hydroxide (Challenger and Fishwick, *f*). Extraction of the distillate with ligroin gave 5-methylthiopheno(3′ : 2′-2 : 3)-thiophen as a pale yellow oil (1·4 g.) with an odour resembling that of solid thiophthen. It gave a yellow solution and a green fluorescence with sulphuric acid. The *picrate* separated from methyl alcohol in orange needles, m. p. 108—109° (Found: C, 40·8; H, 2·4; N, 11·0; S,

17·0. $C_{13}H_9O_7N_3S_2$ requires C, 40·7; H, 2·4; N, 11·0; S, 16·7%). The *styphnate* formed yellow needles, m. p. 101—102°, from methyl alcohol, in which they are very soluble (Found: C, 39·3; H, 2·3; N, 10·7; S, 16·0. $C_{13}H_9O_8N_3S_2$ requires C, 39·1; H, 2·3; N, 10·5; S, 16·1%).

α-(3-*Thienylthio*)-n-*butyric Acid*.—Thiophen-3-thiol (58 g.) was condensed with α-bromo-*n*-butyric acid (84 g.) as for the lower homologue. When the mixture had cooled to room temperature, acidification and extraction with ether yielded an orange oil which did not solidify in a freezing mixture. Any thiol was then removed with ether in presence of sodium hydrogen carbonate; acidification again gave a halogen-free oil (89 g.) which could not be solidified. It was heated to 140—150°/15 mm. to remove any α-hydroxybutyric acid and was then distilled, forming a thick, pale yellow oil, b. p. 148—150°/0·2 mm. It did not solidify during a month in a refrigerator. The ethyl ester (Fischer–Speier method) had b. p. 159—160°/19 mm. It was converted into the *amide* by concentrated aqueous ammonia. This slowly crystallised at 0°, and had m. p. 92—93° when pressed on tile and washed with ligroin. After two crystallisations from water it melted at 103—103·5° (Found: N, 7·2. $C_8H_{11}ONS_2$ requires N, 7·0%). On hydrolysis of the amide with 2N-sodium hydroxide and acidification, the acid was re-formed, but again could not be solidified. It must be assumed that α-(3-thienylthio)-*n*-butyric acid is an oil.

Cyclisation of α-(3-*Thienylthio*)-n-*butyric Acid*.—The acid (25 g.) was cyclised by sulphuric acid (150 c.c.) by 30 min.' heating on the steam-bath; the mixture was poured on ice and extracted with ether. The usual treatment yielded the cyclisation product, 5-ethyl-4-hydroxythiopheno(3′ : 2′-2 : 3)thiophen (IV; R = Et) as a red oil (6·12 g., 27%) which did not solidify. The ethereal layer containing the neutral products of the reaction gave a red oil (2·7 g.) which was not studied further.

Synthesis of the 5-*Ethyl Derivative of Solid Thiophthen* [5-*Ethylthiopheno*(3′ : 2′-2 : 3)*thiophen*].—Lithium aluminium hydride (3 g.) was refluxed with tetrahydrofuran (50 c.c.) for 10 min. and a solution of the 5-ethyl-4-hydroxy-derivative of solid thiophthen (IV; R = Et) (6·12 g.) in tetrahydrofuran (50 c.c.) was added dropwise. A very vigorous reaction occurred. The mixture was refluxed overnight and treated as in the two similar experiments. The final steam-distillate gave a yellow oil (2·9 g., 52%). A very dilute solution in ligroin gave a yellow colour and a green fluorescence with sulphuric acid. 1 : 3 : 5-Trinitrobenzene (0·22 g.) was added to the oil (0·17 g.) and the complex recrystallised twice from methyl alcohol. The yellow crystals, m. p. 85·5—86° (Found: C, 44·2; H, 3·0; N, 11·0; S, 16·7. Calc. for $C_{14}H_{11}O_6N_3S_2$: C, 44·1; H, 2·9; N, 11·0; S, 16·8%), did not depress the m. p. of the 1 : 3 : 5-trinitrobenzene derivative, m. p. 85·5—86°, of the ethylthiophthen obtained by Wolff–Kishner reduction of the methyl ketone from solid thiophthen. This was shown to be the 5-derivative (Challenger and Fishwick, *f*). The picrate, crystallised twice from methyl alcohol, had m. p. 73—73·5° (Found: N, 11·1; S, 16·5. Calc. for $C_{14}H_{11}O_7N_3S_2$: N, 10·6; S, 16·1%), not depressing the m. p. of the picrate of 5-ethylthiophthen obtained by Challenger and Fishwick as stated above.

Preparation of Reference Compounds.—5-*Methylheptan*-2-*ol*. A solution of *sec*.-butylmagnesium chloride was prepared from magnesium (27 g.), ether (400 c.c.), and the alkyl halide (117 c.c.). The reaction became violent in the early stages and some loss occurred but the experiment was continued. Gaseous formaldehyde, produced by passing nitrogen over paraformaldehyde (65 g.) at 180—200°, was then introduced through a wide delivery tube terminating about 1 cm. above the Grignard reagent. The almost solid reaction mixture was treated with ice-water (300 g.) and excess of 30% sulphuric acid, the insoluble paraformaldehyde filtered off, and the ethereal layer mixed with three ether-extracts of the aqueous liquor. Removal of solvent and fractionation of the residue yielded in addition to water two main fractions: (*a*) b. p. 125—127°, was the required 2-methylbutanol (46 g., 50%); (*b*) b. p. 80—80·5°/11 mm., the *formal*, gave no reaction with sodium and no ester odour with glacial acetic acid (Found: C, 70·0; H, 12·4. $C_{11}H_{24}O_2$ requires C, 70·0; H, 12·75. Calc. for di-2-methylbutyl ether, $C_{10}H_{22}O$: C, 76·0; H, 14·0%).

When refluxed with aqueous hydrobromic acid (*d* 1·47; 50 c.c.) the oil (*b*) (15 g.) yielded a product (12 g.; b. p. 114—115°) which was presumably 2-methylbutyl bromide. A sample prepared from 2-methylbutanol (45 g.), sulphuric acid (32 g.), and hydrobromic acid (*d* 1·47; 105 g.) had b. p. 114—116°. It was submitted to the ketone synthesis with ethyl acetoacetate. The resulting 5-methylheptan-2-one did not form a sodium hydrogen sulphite compound; it was therefore purified through the semicarbazone, m. p. 131—132° (Found: C, 58·1; H, 10·3; N, 23·2. Calc. for $C_{19}H_{19}ON_3$: C, 58·3; H, 10·3; N, 22·7%). The 2 : 4-dinitrophenylhydrazone, prepared in 2N-hydrochloric acid, formed orange crystals, m. p. 66—67° (Found: C, 54·5; H, 6·6; N, 17·5. Calc. for $C_{14}H_{20}O_4N_4$: C, 54·6; H, 6·5; N, 18·2%).

5-*Methylheptan*-2-*ol*.—The synthetic ketone (0·7 g.) in ether was added dropwise to lithium aluminium hydride (0·1 g.) in dry ether (15 c.c.) and refluxed for 30 min. Wet ether and then dilute sulphuric acid were added. The ether yielded a colourless oil, micro-b. p. 170°/757 mm. Welt (*loc. cit.*) gives b. p. 167—169°/750 mm. The hydrogen 3-nitrophthalate and the 3 : 5-dinitrobenzoate were oils and could not be crystallised but the latter readily formed an addition product with α-naphthylamine which had m. p. 57—58° after five crystallisations from alcohol (Found : C, 64·4; H, 6·3; N, 9·0. Calc. for $C_{25}H_{29}O_6N_3$: C, 64·2; H, 6·2; N, 9·0%).

We are much indebted to the Vacuum Oil Company Limited, of England, and the Socony Vacuum Oil Company Inc., of Paulsboro, New Jersey, U.S.A., for gifts of thiophen and its 3-thiol derivative and to the Ministry of Education for an F.E.T.S. grant to J. L. H.

THE UNIVERSITY, LEEDS. [*Received, January 30th*, 1953.]