XXXI.—*Studies in the Penthian* Series. Part I. The Action of Sodium Ethoxide on Ethyl β-Thiodipropionate.*

By GEORGE MACDONALD BENNETT and LESLIE VIVIAN DONALD SCORAH.

THE researches of V. Meyer and his students led to the isolation of 3-methylpenthiophen (3-methyl-$\Delta^{2:5}$-penthiadiene) in very poor yield from the products of distillation of α-methylglutaric acid with phosphorus trisulphide (Krekeler, *Ber.*, 1886, **19**, 3266), but very

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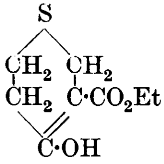
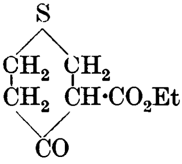
* In order to simplify the nomenclature of this group, we propose, after consultation with the Editor, to name the parent substance (tetrahydropenthiophen or pentamethylene sulphide) *penthian*.

little has since been added to our knowledge of the chemistry of compounds containing this ring system. Penthian itself (v. Braun and Trümpler, *Ber.*, 1910, **43**, 547; Clarke, J., 1912, **101**, 1805) and its 2-methyl derivative (Grischkevitsch-Trochimovski, *J. Russ. Phys. Chem. Soc.*, 1916, **48**, 928) have been prepared by the closure of the ring by the action of sodium sulphide on the αε-dihalogenated paraffin, whilst Apitzsch (*Ber.*, 1904, **37**, 1599; 1905, **38**, 2888; 1908, **41**, 4028; 1909, **42**, 2940) has shown that the products of condensation of carbon disulphide and ketones are derived from penthiadien-4-one.

Simple substituted derivatives of penthian have not hitherto been prepared by smooth ring-closure from open-chain compounds. V. Meyer suggested (*Ber.*, 1886, **19**, 3260) the application of the malonic ester method to ββ′-dichlorodiethyl sulphide for this purpose, but this reaction has recently been shown by Davies (J., 1920, **117**, 297) to yield under various conditions, not the desired penthiandicarboxylic ester, but solely the open-chain tetracarboxylic ester, $S[CH_2{\cdot}CH_2{\cdot}CH(CO_2Et)_2]_2$. We have now subjected ethyl β-thiodipropionate, $S(CH_2{\cdot}CH_2{\cdot}CO_2Et)_2$, to the Dieckmann reaction: the reaction proceeds readily in presence of sodium ethoxide or sodamide to yield the oily enolic ester (I), *ethyl* Δ^3-*penthien-4-ol-3-carboxylate,* which gives an intense purple coloration with ferric chloride. This ester, on keeping, ultimately deposits long needles of the ketonic ester (II), *ethyl penthian-4-one-3-carboxylate,* which gives a delayed reaction with ferric chloride and dissolves only slowly in aqueous solutions of sodium hydroxide.


(I.)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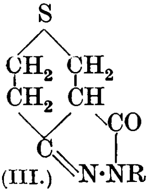
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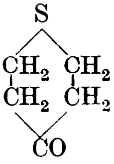
(IV.)

That this ester has a β-ketonic structure is confirmed by its condensation with hydrazines to yield pyrazolones of the general formula (III), and by its hydrolysis by cold dilute alkali or hot dilute acid to give a crystalline ketone, *penthian-4-one* (IV), readily volatile in steam. Penthianone furnishes, not only the usual derivatives of a cyclic ketone, such as the *oxime*, the *semicarbazone*, the *dinitrophenylhydrazone* and the *dibenzylidene* derivative, but also others due to the reactivity of the sulphur atom, namely, a crystalline *sulphonium methiodide* and a *platinic chloride* compound of the composition $2C_5H_8OS,PtCl_4$.

The yield of cyclic ester (43%) obtained in this investigation was consistently lower than that (60%) in the analogous reaction with ethyl pimelate carried out by Dieckmann (*Annalen*, 1901, **317**, 93). This raises the question whether the substitution of a sulphur atom for a methylene group in a chain diminishes the tendency to ring closure.

As far as we are aware, these experiments constitute the first instance of the closure of a simple heterocyclic ring by means of the Dieckmann reaction. The method should be applicable in a similar manner to analogous substances where sulphur is replaced by oxygen, nitrogen, or other element.

EXPERIMENTAL.

Preparation of β-Thiodipropionic Acid and its Derivatives.—The preparation described by Loven (*Ber.*, 1896, **29**, 1136) was modified as follows: To a solution of potassium hydroxide (23·5 g.) and sodium sulphide (72 g. of $Na_2S,9H_2O$) in water (190 c.c.), β-iodopropionic acid (100 g.) was added and the mixture was boiled for 15 minutes, cooled to — 10°, and acidified with concentrated hydrochloric acid (50 c.c.). The acid, filtered off after a few hours and washed with a little water, was practically pure (yield 70%). It may be recrystallised from hot water or xylene. It was more economically obtained and in slightly better yield by substituting β-bromopropionic acid (77 g.) for the iodo-acid in the above preparation, and boiling the mixture for 1 hour. A further addition to the yield is obtained by extracting the mother-liquor with ether.

Thiodipropiondiamide, prepared by the action of concentrated aqueous ammonia on the ester (see below) or on the acid chloride obtained from thiodipropionic acid by the action of thionyl chloride, crystallised from ethyl alcohol in colourless plates, m. p. 177—178·5° (Found: N, 15·6; S, 18·2. $C_6H_{12}O_2N_2S$ requires N, 15·9; S, 18·2%).* *Thiodipropiondianilide*, prepared from the acid and boiling aniline in the usual manner, separated from toluene in colourless scales, m. p. 163·5° (Found: N, 8·5; S, 9·8. $C_{18}H_{20}O_2N_2S$ requires N, 8·5; S, 9·8%).

Ethyl thiodipropionate was obtained as a pale straw-coloured oil, b. p. 174°/15 mm. (yield 70% by the Fischer and Speier method; 90% by the continuous process as in " Organic Syntheses," **1**, 68). It has a strong, unpleasant odour, and does not solidify at — 20° (Found: S, 13·8, 13·6; equiv. by saponification, 117·4. $C_{10}H_{18}O_4S$ requires S, 13·7%; equiv., 117·1). The following constants were determined: $d_{4^\circ}^{20^\circ}$ (vac.) 1·1034, $n_\alpha^{20^\circ}$ 1·46938, $n_\beta^{20^\circ}$ 1·47911, whence $[R_L]_\alpha$ 59·17 (calc., 59·30) and $[R_L]_\beta$ 60·20 (calc., 60·29).

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* Determinations of sulphur were made by the method of Leonard (*J. Amer. Chem. Soc.*, 1923, **45**, 255).

Ethyl Penthian-4-one-3-carboxylate.—Preliminary experiments showed that ethyl thiodipropionate, subjected to the action of sodium metal in boiling toluene (Bouveault, *Bull. Soc. chim.*, 1899, **21**, 1019), suffered profound decomposition with production of much sodium sulphide. It was found best to use sodium ethoxide at a low temperature in the following manner: To sodium ethoxide, made from Brühl sodium (8 g.) in a flask fitted with a stirrer and a reflux condenser, a solution of ethyl thiodipropionate (40 g.) in dry ether (150 c.c.) was carefully added. The mixture, cooled in a freezing mixture, was stirred for 6 hours, allowed to rise to the ordinary temperature over-night, and then poured into a mixture of ice and acetic acid (22 g.). The lower aqueous layer was removed and extracted twice with ether and the extracts were added to the original ethereal layer. The ethereal solution was then shaken seven times with diminishing amounts of 5% potassium hydroxide solution (530 c.c. in all), the alkaline solution in each case being immediately run into a mixture of ice and acetic acid. The oil thus precipitated was collected in carbon tetrachloride and the extract was shaken twice with $N/2$-sodium carbonate (100 c.c.) to remove the acid ester which was present, and distilled. *Ethyl Δ^3-penthien-4-ol-3-carboxylate* (I) (14 g.; 43% yield) was thus obtained as an almost colourless oil of characteristic odour, b. p. 150—151°/16 mm. (Found: C, 50·7; H, 6·5; S, 17·3. $C_8H_{12}O_3S$ requires C, 51·0; H, 6·4; S, 17·0%). This ester gives an immediate purple coloration with alcoholic ferric chloride and dissolves at once in aqueous sodium hydroxide. The residual ethereal solution in the above preparation yielded ethyl thiodipropionate (4 g.) on distillation. A slightly higher yield of the cyclic ester was obtained when sodamide (2 mols.) was used in place of sodium ethoxide. The following constants were determined with a freshly-prepared specimen of the ester which had been twice redistilled, the initial and the final fractions being rejected: $d_{4^\circ}^{20^\circ}$ (vac.) 1·2011, $n_{\alpha}^{20^\circ}$ 1·51574, $n_{\beta}^{20^\circ}$ 1·52938, whence $[R_L]_\alpha$ 47·29 (calc., 47·35) and $[R_L]_\beta$ 48·34 (calc., 48·33).*

When this enolic ester had been kept for about a week, it began to deposit crystals of its ketonic tautomeric form, *ethyl penthian-*

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* The values in brackets have been calculated using the constants for sulphides found by Price and Twiss (J., 1912, **101**, 1259). No allowance was made for ring-closure, this being justified by the value for penthian itself found by Clarke (*ibid.*, 1800): $[R_L]_\alpha$ 30·61 (calc., 30·84). The values calculated for the ketonic form of the ester would have been 46·21 and 47·20, respectively. It must be admitted that the agreement obtained above may be in part fortuitous, since an exaltation due to conjugation is to be expected in an enolic form: moreover, it is probable that the enolic ester examined already contained some of the ketonic form.

4-*one*-3-*carboxylate* (II), which was dried on porous earthenware and obtained as colourless needles having a high double refraction and an oblique extinction, being probably monoclinic; m. p. 59° (Found : C, 51·05; H, 6·0. $C_8H_{12}O_3S$ requires C, 51·0; H, 6·4%).

This substance differs from the enolic ester in that it dissolves only slowly in aqueous sodium hydroxide and gives no immediate coloration with ferric chloride, the purple colour appearing and increasing in intensity for several minutes. The coloration is not destroyed by the addition of dilute acetic acid. Concentrated aqueous barium hydroxide acts on either of the esters to produce a sparingly soluble, pale yellow *barium* salt. No crystalline copper salt could be obtained.

Pyrazolone Derivatives (III).—The freshly-distilled enolic ester (2 g.) condensed with phenylhydrazine (1·19 g.) on being heated with it and two drops of acetic acid at 100° for 2 hours. The *phenylpyrazolone* crystallised from methyl alcohol in cream-coloured needles, m. p. 219° (Found: N, 12·1. $C_{12}H_{12}ON_2S$ requires N, 12·1%). The reactions between the ester and *p*-bromo- and *p*-nitrophenylhydrazine were carried out in ethyl-alcoholic solution, equimolecular quantities being heated at its boiling point in presence of a few drops of acetic acid for 4 hours. The p-*bromophenylpyrazolone* crystallises from glacial acetic acid in almost colourless plates, m. p. 221·5° (Found: N, 8·7; Br, 25·8. $C_{12}H_{11}ON_2BrS$ requires N, 9·0; Br, 25·7%). The p-*nitrophenylpyrazolone* forms buff-coloured plates from alcohol; m. p. 210·5° (Found : N, 15·1. $C_{12}H_{11}O_3N_3S$ requires N, 15·2%).

Hydrolysis of the Cyclic Ester to yield Penthian-4-*one*.—The cyclic ester (5 g.) was kept for 3 days at the ordinary temperature with 5% potassium hydroxide solution (60 c.c.), the mixture was then extracted with ether, and the ether evaporated. The residue (1·5 g.), which crystallised at once, was *penthian*-4-*one* (IV). This substance separates from petroleum (b. p. 40—60°) in tufts of colourless plates, m. p. 65—66° (Found : C, 51·7; H, 6·9. C_5H_8OS requires C, 51·7; H, 6·9%). The crystals are biaxial with a straight extinction, being probably monoclinic; an optic axis is visible in convergent polarised light and the double refraction is exceptionally high. The substance is appreciably volatile at the ordinary temperature and readily so in steam. It has a strong, characteristic odour and is readily soluble in all the usual organic solvents, slightly less soluble in light petroleum, and moderately easily soluble in cold water.

Preliminary experiments had shown the hydrolysis of the cyclic ester by means of barium hydroxide solution to be very slow and incomplete, probably owing to the sparing solubility of the barium salt which was at once precipitated. On the other hand, acid hydrolysis was very effective; the ester (1·2 g.) was boiled with 10% sulphuric acid (10 c.c.) for 4 hours; the solution then deposited some of the ketone in a crystalline condition on cooling. Extraction with ether and crystallisation of the residue from light petroleum gave the pure ketone (0·64 g.; 85% yield).

Direct Preparation of Penthianone from Ethyl Thiodipropionate.—The ketone is most conveniently prepared by allowing ethyl thiodipropionate (40 g.) to react with sodium ethoxide (from 8 g. of sodium) as previously described, pouring the reaction mixture into water, removing the upper ethereal layer and extracting it three times with potassium hydroxide solution (5%: 300 c.c.), and keeping the combined alkaline aqueous solutions for 3 days; extraction with ether then yields the ketone (6·7 g.; 33% yield).

Derivatives of Penthianone.—The *oxime*, prepared in aqueous solution and isolated by extraction with ether, is readily soluble in most solvents. It crystallises from warm water, in which it is easily soluble, in colourless, flat needles, m. p. 84—85° (Found: N, 10·7. C_5H_9ONS requires N, 10·7%). The *semicarbazone*, prepared by means of semicarbazide acetate, was crystallised once from toluene, in which it is sparingly soluble, and once from ethyl acetate, in which it is readily soluble, as silvery plates, m. p. 151° (Found: N, 24·2. $C_6H_{11}ON_3S$ requires N, 24·3%). The 2 : 4-*dinitrophenylhydrazone* was precipitated at once on mixing the ketone and the hydrazine (1 mol.) in glacial acetic acid solution; it crystallised from this solvent, in which it is very sparingly soluble, in orange plates, m. p. 186° (Found: N, 18·9. $C_{11}H_{12}O_4N_4S$ requires N, 18·9%).

To a solution of the ketone (0·15 g.) and benzaldehyde (0·35 g.) in ethyl alcohol (2 c.c.), 25% potassium hydroxide solution (10 drops) was added. After a short time, the mixture became a paste of crystals of *dibenzylidenepenthianone*. The substance was crystallised once from ethyl alcohol and once from petroleum (b. p. 90—120°), from which it separated in yellow, compact tufts of crystals, m. p. 149—151° (Found: C, 77·8; H, 5·6. $C_{19}H_{16}OS$ requires C, 78·0; H, 5·5%).

The *dipiperonylidene* derivative, prepared in a precisely similar manner, crystallised from ethyl acetate in yellow tufts of pointed needles, m. p. 181°. It is more soluble in the common solvents than is the benzylidene derivative.

A *compound* with platinic chloride was obtained as a microcrystalline powder by mixing the components in dilute methylalcoholic solution, the precipitate appearing after the mixture had remained for a short time at the ordinary temperature. It was collected, washed with a little water, and dried in a desiccator. It is easily soluble in epichlorohydrin, from which it crystallises in small, yellow polyhedra which decompose on heating without melting (Found : Pt, 35·2. $C_{10}H_{16}O_2Cl_4S_2Pt$ requires Pt, 34·3%).

The ketone combined slowly with methyl iodide in cold benzene solution, but much more rapidly in the absence of a solvent, a solution of the ketone in an excess of methyl iodide depositing a mass of crystals in the course of a few days. The *penthianone-methylsulphonium iodide* thus obtained was insoluble in benzene, acetone or absolute ethyl alcohol, very soluble in water, and separated from 96% alcohol in pale yellow crystals, m. p. 112—113° (with effervescence due to dissociation) (Found : I, 48·9. $C_6H_{11}OIS$ requires I, 49·2%). An aqueous solution of this salt was digested with an excess of freshly-precipitated silver chloride and the resulting solution of the corresponding chloride was mixed with an excess of platinic chloride, but no chloroplatinate separated from solution even after long keeping. This chloroplatinate must therefore be unusually soluble in water.

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