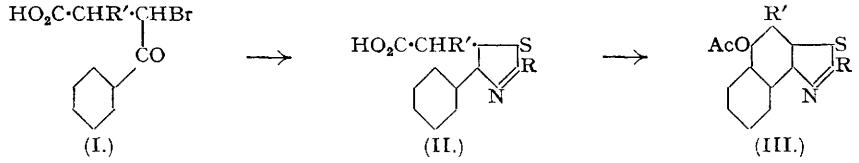
118. *Polycyclic Thiazoles.*

By EDWARD B. KNOTT.

The β-bromo-derivatives of β-benzoylpropionic acid and of β-benzoyl*iso*butyric acid condense with thioamides to give substituted 4-*phenylthiazole*-5-*acetic acids* (II). On cyclisation with acetic anhydride (II) gives derivatives of 4′-*hydroxynaphtha*-1′ : 2′ : 4 : 5-*thiazole* (III). When R = Me, (II) also gives 4′-*hydroxy*-3′-*acetyl*-2-*methylnaphtha*-1′ : 2′ : 4 : 5-*thiazole* (X) as by-product. Similar reactions with β-*bromo*-β-1- and β-*bromo*-β-2-*naphthoylpropionic acids* yield derivatives of 1′-*hydroxyphenanthra*-4′ : 3′ : 4 : 5-*thiazole* (V) and 4′-*hydroxyphenanthra*-1′ : 2′ : 4 : 5-*thiazole* (VII) respectively, and β-*bromo*-β-2-*thienoylpropionic acid* gives substituted 4′-*hydroxythionaphtheno*-7′ : 6′ : 4 : 5-*thiazoles* (IX).

ALL the well-known methods for the preparation of thiazoles containing a condensed carbocyclic or heterocyclic system are based on the final thiazole ring formation from intermediates containing the other desired rings (Jacobson, *Ber.*, 1885, **20**, 1895; Hugershoff, *Ber.*, 1903, **36**, 3121; Hofmann, *Ber.*, 1880, **13**, 1236, etc.). These methods are general for the production of 2-substituted polycyclic thiazoles which are useful as intermediates for photographic sensitising dyes. They suffer, however, from the disadvantage that low yields are obtained when the molecule becomes complex. The following method differs from the above in that the thiazole ring is first formed by a normal Hantzsch condensation, followed by an intramolecular cyclisation to a condensed system, giving, in good yield, a variety of polycyclic thiazoles containing a hydroxyl group in the carbocyclic ring which is fused to the thiazole ring.

The simplest polycyclic thiazole which can be prepared by this method is a β-naphthathiazole. β-Bromo-β-benzoylpropionic acid (1; R′ = H) condensed with various thioamides to give 2-substituted *4-phenylthiazole-5-acetic acid* (II; R′ = H). This acid was also obtained from its *methyl* ester prepared from methyl β-bromo-β-benzoylpropionate. On treatment of compounds of type (11; R′ = H) with acetic anhydride and sodium acetate they readily underwent an intramolecular ring-closure to give 2-substituted *4′-acetoxynaphtha-1′ : 2′ : 4 : 5-thiazoles* (III). In cases where R = Me a by-product, which will be described later, was isolated

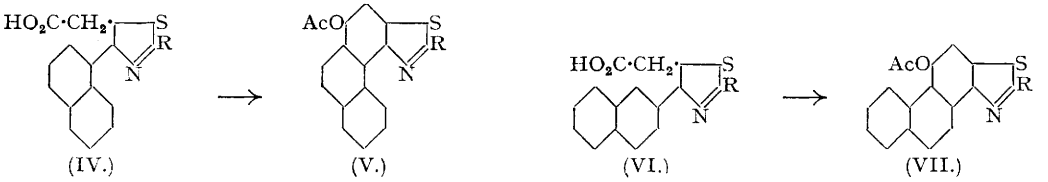


(I.) (II.) (III.)

from the cyclisation reaction mixture. The thioamides used were thiourea and thioacetamide, which yielded thiazoles where R = NH_2 and Me respectively. An extension of the Hantzsch synthesis employing *S*-alkyldithiocarbamates (Buchman, Reims, and Sargent, *J. Org. Chem.*, 1941, **6**, 764) was also applied and gave substances where R = *S*-alkyl.

The generality of this reaction for the preparation of β-naphthathiazoles containing substituents in the benzene ring not forming part of the thiazole ring was shown by commencing with substituted β-benzoylpropionic acids. By commencing with *β-bromo-β-benzoylisobutyric acid* (I; R′ = Me), *3′-methyl-β-naphthathiazoles* were obtained.

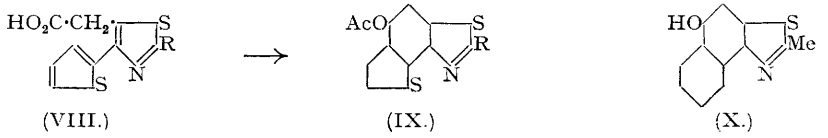
Extending the reaction to *β-bromo-β-1-* and *β-bromo-β-2-naphthoylpropionic acids*, 4-1′- and -2′-*naphthylthiazole-5-acetic acid* derivatives (IV and VI) were prepared, which were cyclised respectively to 2-substituted *1′-acetoxyphenanthra-4′ : 3′ : 4 : 5-thiazoles* (V) and *4′-acetoxyphenanthra-1′ : 2′ : 4 : 5-thiazoles* (VII).



(IV.) (V.) (VI.) (VII.)

Cyclisation of (IV) can lead only to (V), but (VI) can, theoretically, give (VII) by closure at the 1′-carbon atom, or an anthrathiazole by closure at the 3′-carbon atom. One product only was obtained which was shown to be (VII) by removing the acetyl group and subjecting the purified phenol to a zinc dust-hydrogen distillation. The distillate consisted chiefly of phenanthrene. This exclusive phenanthrene formation is analogous to the sole formation of ketotetrahydrophenanthrene on cyclisation of β-2-naphthylbutyric acid (Schroeter, Müller, and Huang, *Ber.*, 1929, **62**, 645; Haworth, J., 1932, 1125).

The formation of tricyclic thiazoles containing a second heterocyclic nucleus was also achieved by this method. *β-Bromo-β-2-thienoylpropionic acid* was converted into derivatives of *4-(2′-thienyl)thiazole-5-acetic acid* (VIII), which were cyclicised very smoothly to 2-substituted *4′-hydroxythionaphtheno-7′ : 6′ : 4 : 5-thiazoles* (IX).



(VIII.) (IX.) (X.)

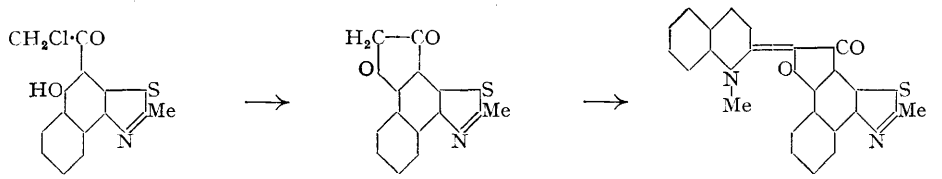
The conditions necessary for good yields of the primary thiazoles vary considerably and the methods described are the best of a great number of experiments. In general the yields fall in the direction R = NH_2 ⟶ CH_3 ⟶ *S*-alkyl. In many cases the addition of sodium carbonate during the condensation increases the yield of base. The period of reflux of the acids necessary for complete cyclisation was much longer for the 4-phenylthiazole-5-acetic acid derivatives than for the corresponding -5-propionic acids or 4-naphthyl or 4-thienyl analogues.

All the acetates were very easily hydrolysed within seconds by cold aqueous-alcoholic sodium hydroxide. Where R = Me or *S*-alkyl the parent *hydroxy-thiazoles* were isolated and characterised as *ethers*. Where R = NHAc the free hydroxy-base is readily oxidised in the atmosphere. All the *hydroxy-thiazoles* reduce silver nitrate and in caustic alkaline solution will function as photographic developing agents. Attempts to remove the hydroxyl group by zinc dust-hydrogen distillation caused destruction of the thiazole ring.

The by-product from the cyclisation of *4-phenyl-2-methylthiazole-5-acetic acid* was isolated from the methyl

alcohol washings and recrystallisation liquors of the primary cyclisation product. It is the *acetate* of *4′-hydroxy-3′-acetyl-2-methylnaphtha-1′ : 2′ : 4 : 5-thiazole* (X). Hydrolysis gave the yellow *hydroxy-ketone* (X), which is distinguished by its intense green fluorescence to ultra-violet light. It can thus be readily detected if contaminating the 3′-unsubstituted product, which does not fluoresce to the same light. It differs considerably from the latter substance by having a much lower melting point, by its solubility in aqueous sodium carbonate or ammonia and by its non-reducing properties. The latter difference is not due to the occupation of the 3′-position *per se*, since the 3′-methyl analogue does reduce silver nitrate; it is attributed rather to the resonance of the *o*-hydroxy-ketonic system, which retains more firmly the electron normally lost on oxidation. This resonance also gives the substance its colour. Its salts give a deep yellow solution which is analogous to the yellow salts of the almost colourless 2-acetyl-1-naphthol (Witt, *Ber.*, 1888, **21**, 821). The formation of (X) and the latter compound appear to depend on the same type of reaction, *i.e.*, heating a phenol and acetic acid in the presence of dehydrating agents.

The identity of (X) was shown by a Fries rearrangement of (III; R = Me, R′ = H) and by the following. 4′-Hydroxy-2-methyl-β-naphthathiazole condensed with acetyl chloride or acetic anhydride in nitrobenzene under the influence of aluminium chloride to give (X). Chloroacetyl chloride also reacted under like conditions, introducing the chloroacetyl group, presumably in the same position as the acetyl group. The *chloroacetyl derivative* (XI), characterised as its *acetate*, lost hydrogen chloride on treatment with aqueous sodium carbonate, giving a solid which, from its properties can only be *3′-keto-2-methylbenzcoumarano-5′ : 4′ : 4 : 5-thiazole* (XII).



(XI.) (XII.) (XIII.)

In alcoholic sodium hydroxide or ethoxide, solutions of (XII) rapidly develop an intense red colour characteristic of simpler coumaranones (Fries and Finck, *Ber.*, 1908, **41**, 2271; Fries and Pfaffendorf, *Ber.*, 1910, **43**, 213). The reactive methylene group of the coumaranone ring coupled readily with 2-methylthioquinoline methiodide to give the dye (XIII). An alcoholic solution of (XII) shows an intense blue fluorescence to ultra-violet light. At pH 1·1 this changes to white and below pH 1·0 to an intense yellow. It may therefore be of use as a fluorescent indicator. Standard solutions at these low pH values lose their fluorescing properties after a time.

Experimental.

(Microanalyses are by Drs. Weiler and Strauss, Oxford: m. p.'s are not corrected.)

β-1- and β-2-Naphthoylpropionic Acids.—The procedure of Haworth (J., 1932, 1124) was used, but by increasing the amount of solvent nitrobenzene by 25% a complete separation of the isomers was obtained on decomposing the Friedel–Crafts reaction mixture. The β-2-isomer was precipitated as a solid, and the β-1-isomer remained in the nitrobenzene layer, from which it was extracted by aqueous sodium carbonate. The isomers were thus obtained in equal yield.

β-Bromo-acids.—The acid (250 g.; 1 mol.) was dissolved in hot chloroform (2 l.), and bromine (5 c.c.) added. Heating was continued until the bromine was absorbed. The remainder of the bromine (1 mol. in all) was then readily absorbed without further heating. The chloroform solution was washed four times with water, dried, and the solvent removed. The acid was usually left as an oil which crystallised on addition of carbon disulphide.

β-Bromo-β-1-naphthoylpropionic acid crystallised almost completely during the washing process. Unless otherwise stated, all the acids were recrystallised from carbon disulphide. For other such bromo-acids see Bougault (*Ann. Chim.*, 1908, **15**, 464).

β-Bromopropionic acid.	Crystal form.	M. p.	Formula.	% Br. Found.	% Br. Required.
β-4-*Methylbenzoyl*	Flat needles	122—124°	$C_{11}H_{11}O_3Br$	29·35	29·5
β-4-*Ethylbenzoyl*	Pale yellow oil [a]	—	$C_{12}H_{13}O_3Br$	27·8	28·0
β-4-iso*Propylbenzoyl*	Irregular [a]	73—75	$C_{13}H_{15}O_3Br$	27·4	26·7
β-2 : 4-*Dimethylbenzoyl*	Needles	98·5	$C_{12}H_{13}O_3Br$	28·15	28·0
β-4-*Chlorobenzoyl*	Needles	115—116	$C_{10}H_8O_3ClBr$	39·4 (Hal)	39·6
β-4-*Ethoxybenzoyl*	Needles	130	$C_{12}H_{13}O_4Br$	26·5	26·55
β-1-*Naphthoyl*	Silky needles [b]	172—173	$C_{14}H_{11}O_3Br$	26·35	26·0
β-2-*Naphthoyl*	Needles [b]	133—135	$C_{14}H_{11}O_3Br$	26·2	26·0
β-2-*Thienoyl*	Prisms	127—128	$C_8H_7O_3BrS$	30·25	30·4

a, from ligroin; *b*, from benzene.

β-Bromo-β-benzoylisobutyric Acid.—β-Benzoyl*iso*butyric acid (Oppenheim, *Ber.*, 1901, **34**, 4228) was brominated as for the propionic acids, giving the required *acid* as tiny needles, m. p. 163°, from chloroform–ligroin (Found: Br, 29·25. $C_{11}H_{11}O_3Br$ requires Br, 29·5%).

Methyl β-bromo-β-benzoylpropionate was obtained similarly as an oil which decomposed on attempted vacuum distillation.

Condensations with Thiourea.—The acid (1 g.-mol.), thiourea (1 g.-mol.), and *iso*propyl alcohol (500 c.c.) were boiled for 15 minutes, anhydrous sodium carbonate (0·5 g.-mol.) added, and heating continued until the evolution of carbon

dioxide had ceased. The precipitation of the *base* was completed by addition of water. Crystallisations were from alcohol or aqueous alcohol. The yield was 90—98%.

2-*Aminothiazole-5-acetic acid.*	Crystal form.	M. p.	Formula.	Found, %.	Required, %.
4-*Phenyl*	Needle rosettes	230—231°	$C_{11}H_{10}O_2N_2S$	C, 56·45	56·4
				H, 4·4	4·3
				N, 11·8	11·95
4-(4′-*Methylphenyl*)	Threads	224	$C_{12}H_{12}O_2N_2S$	N, 10·75	10·65
4-(1′-*Naphthyl*)	Yellow grains	258—259	$C_{15}H_{12}O_2N_2S$	S, 11·1	11·3
4-(2′-*Naphthyl*)	Colourless grains	255—256	$C_{15}H_{12}O_2N_2S$	N, 10·05	9·85
				S, 11·6	11·3
4-(2′-*Thienyl*)	Irregular	202—203	$C_9H_8O_2N_2S_2$	S, 24·9	24·8

α-5-(2-*Amino*-4-*phenylthiazole*)*propionic acid* (II; R = NH_2, R′ = Me) formed a white powder, m. p. 240° from *iso*propyl alcohol in 83% yield (Found: S, 12·65. $C_{12}H_{12}O_2N_2S$ requires S, 12·9%).

Methyl 2-*amino*-4-*phenylthiazole*-5-*acetate* formed pale yellow prisms, m. p. 167—168°, from ethyl alcohol in 87% yield (Found: S, 12·6. $C_{12}H_{12}O_3N_2S$ requires S, 12·9%).

Condensations with Thioacetamide.—(*a*) 4-(2′-*Thienyl*)-2-*methylthiazole*-5-*acetic acid.* β-Bromo-β-2-thienoylpropionic acid (13·15 g.; 0·05 mol.), thioacetamide (3·75 g.; 0·05 mol.), and cold *iso*propyl alcohol (50 c.c.) were shaken until the solid had dissolved and left for 24 hours. A mass of crystals of the hydrobromide separated. The *base* (10 g.) formed colourless needle clusters, m. p. 158—159°, from benzene (Found: S, 26·8. $C_{10}H_9O_2NS_2$ requires S, 26·8%).

(*b*) β-Bromo-β-aroylpropionic acid (1 g.-mol.), thioacetamide (1 g.-mol.), and *iso*propyl alcohol (500 c.c.) were heated to 50°. Heat was evolved but the temperature was kept below 65° by cooling. After the reaction mixture had cooled to 40° (1—2 hours), anhydrous sodium carbonate (0·5 g.-mol.) was added with good shaking, and the mixture left for 1—2 days. In most cases the base crystallised. It was then diluted with water, a little dilute hydrochloric acid added, and the solid collected after 2 hours. It was shaken with ether to remove any oil and recrystallised from methyl or ethyl alcohol.

2-*Methylthiazole*-5-*acetic acid.*	Crystal form.	M. p.	Yield, %.	Formula.	Found, %.	Required, %.
4-*Phenyl*	Thick needles	202—203°	93·5	$C_{12}H_{11}O_2NS$	C, 61·7	61·75
					H, 4·8	4·75
					S, 13·7	13·75
4-(4′-*Methylphenyl*)	Cubes or needles	200—202	90	$C_{13}H_{13}O_2NS$	S, 13·3	13·0
4-(4′-*Ethylphenyl*)	Flat cream needles	155	60	$C_{14}H_{15}O_2NS$	S, 12·5	12·3
4-(4′-iso*Propylphenyl*)	Flat cream needles	173—174	74	$C_{15}H_{17}O_2NS$	S, 11·5	11·65
4-(2′ : 4′-*Dimethylphenyl*)	Needles	189—190	86	$C_{14}H_{15}O_2NS$	S, 12·1	12·3
4-(4′-*Chlorophenyl*)	Short needles	200—204	91	$C_{12}H_{10}O_2NClS$	S, 12·2	12·0
4-(1′-*Naphthyl*)	Needles	212—213	43	$C_{16}H_{13}O_2NS$	C, 67·5	67·8
					H, 4·6	4·65
					S, 11·35	11·35
4-(2′(-*Naphthyl*)	Irregular	226—229	68	$C_{16}H_{13}O_2NS$	S, 11·2	11·35

4-(4′-*Methoxyphenyl*)-2-*methylthiazole*-5-*acetic Acid.*—On recrystallisation the first crop (45% yield), m. p. 189—190°, showed a weak white fluorescence in ultra-violet light (Found: S, 12·2. $C_{13}H_{13}O_3NS$ requires S, 12·2%). The second crop (43% yield), m. p. 171—179°, fluoresced intensely blue-green in ultra-violet light and reverted to the higher melting form on recrystallisation (Found: S, 12·2%).

4-(4′-*Ethoxyphenyl*)-2-*methylthiazole*-5-*acetic Acid.*—The first crop on recrystallisation formed needles, m. p. 188—190° (12% yield) (Found: S, 11·4. $C_{14}H_{15}O_3NS$ requires S, 11·6%). The second crop (73% yield) formed large glassy crystals, m. p. 169—190°, with a bright green fluorescence in ultra-violet light, reverting to needles, m. p. 188—190°, on recrystallisation (Found: S, 11·45%).

α-5-(4-*Phenyl*-2-*methylthiazole*)*propionic Acid.*—It formed hard, glinting needle rosettes, m. p. 172—173°, in 10% yield (Found: S, 12·95. $C_{13}H_{13}O_2NS$ requires S, 12·95%).

Condensations with S-*Alkyldithiocarbamates.*—(*a*) The bromo-acid (1 g.-mol.) and alkyldithiocarbamate (1 g.-mol.) were dissolved by shaking at room temperature in *iso*propyl alcohol (1 l.), left for 48 hours, and water then added to precipitate the base as an oil, which usually solidified on standing. It was crystallised from benzene–light petroleum or aqueous alcohol.

Thiazole-5-acetic acid.	Crystal form.	M. p.	Yield, %.	Formula.	S, %. Found.	S, %. Required.
2-*Methylthio*-4-*phenyl*	Needle rosettes	145°	39	$C_{12}H_{11}O_2NS_2$	24·25	24·2
2-*Ethylthio*-4-*phenyl*	Fine needles	116	23	$C_{13}H_{13}O_2NS_2,H_2O$	21·55	21·5
2-*Methylthio*-4-(4′-*methylphenyl*)	Needles	176	38	$C_{13}H_{13}O_2NS_2$	22·55	22·95
2-*Methylthio*-4-(2′-*naphthyl*)	Needles or prisms	154	42	$C_{16}H_{13}O_2NS_2$	20·4	20·35

(*b*) 2-*Methylthio*-4-(1′-*naphthyl*)*thiazole*-5-*acetic Acid.*—The reactants were heated to 60°, and anhydrous sodium carbonate (0·5 g.-mol.) added to the solution, which was then left for 48 hours. When the carbonate addition was omitted the bromo-acid crystallised on cooling. The *base* was precipitated with water and crystallised from benzene. It formed light needle clusters, m. p. 125° (Found: S, 20·55. $C_{16}H_{13}O_2NS_2$ requires S, 20·35%).

Cyclisation.—The acid (10 g.), anhydrous sodium acetate (2·5 g.), and acetic anhydride (40 c.c.) were refluxed. The 4-phenylthiazole-acetic acids required 3 hours, the 4-naphthyl analogues 5—30 minutes depending on R, the 4-thienyl analogue 30 minutes and where R′ = Me, 10—30 minutes. Where R = NH_2 in all cases the cyclisation product crystallised during the refluxing. The reaction mixture was diluted with acetic acid (10 c.c.) and poured into water (250 c.c.). The resultant solid was washed with methyl alcohol and recrystallised from the same solvent. The washings and crystallisation liquors contained the by-product. Where R = NH_2 the yields were about 90%, where R = Me, 50—70% and when R = *S*-alkyl, 30—40%.

The *acetates* were hydrolysed by dissolving them in hot or cold alcohol and adding an excess of cold, aqueous 2N-sodium hydroxide. After a few seconds the whole was diluted with water, and the clear solution acidified. The hydroxythiazoles were crystallised from methyl or ethyl alcohol. The ethers were obtained by treatment of the phenols at 60° with alkaline alkyl sulphates and crystallised from methyl alcohol.

Naphtha-1′ : 2′ : 4 : 5-*thiazoles.*	Crystal form.	M. p.	Formula.	Found, %.	Required.
2-*Acetamido*-4′-*acetoxy*-	Pale yellow needles	286°	$C_{15}H_{12}O_3N_2S$	C, 60·15	59·95
				H, 4·3	4·05
				N, 9·35	9·35
2-*Acetamido*-4′-*acetoxy*-6′-*methyl*	Cream plates	286	$C_{16}H_{14}O_3N_2S$	N, 8·8	8·9
4′-*Acetoxy*-2-*methyl*-	Long cream needles	140—141	$C_{14}H_{11}O_2NS$	C, 65·55	65·35
				H, 4·4	4·3
				S, 12·35	12·45
4′-*Hydroxy*-2-*methyl*-	Yellow needles	252 (subl.)	$C_{12}H_9ONS$	C, 66·55	66·95
				H, 4·15	4·2
4′-*Methoxy*-2-*methyl*-	Yellow prisms	100	$C_{13}H_{11}ONS$	C, 68·2	68·1
4′-*Ethoxy*-2-*methyl*-	Yellow prisms	147—148	$C_{14}H_{13}ONS$	S, 12·95	13·2
4′-*Benzoyloxy*-2-*methyl*-	Long silky needles	169	$C_{19}H_{13}O_2NS$	S, 10·1	10·05
4′-*Acetoxy*-2 : 6′-*dimethyl*-	Long silky needles	162	$C_{15}H_{13}O_2NS$	S, 12·0	11·8
4′-*Hydroxy*-2 : 6′-*dimethyl*-	Pale yellow needles	260 (decomp.)	$C_{13}H_{11}ONS$	S, 14·15	14·0
4′-*Methoxy*-2 : 6′-*dimethyl*-	Greenish plates	103—104	$C_{14}H_{13}ONS$	S, 13·0	13·2
4′-*Ethoxy*-2 : 6′-*dimethyl*-	Pale yellow needles	121—122	$C_{15}H_{15}ONS$	S, 13·05	12·45
4′-*Benzoyloxy*-2 : 6′-*dimethyl*-	Silky needles	162—163	$C_{20}H_{15}O_2NS$	S, 9·6	9·6
4′-*Acetoxy*-2-*methyl*-6′-*ethyl*-	Silky needles	122·5	$C_{16}H_{15}O_2NS$	S, 11·25	11·25
4′-*Hydroxy*-2-*methyl*-6′-*ethyl*-	Flat needles	248 (decomp.)	$C_{14}H_{13}ONS$	S, 13·45	13·2
4′-*Methoxy*-2-*methyl*-6′-*ethyl*-	Needle rosettes [a]	65	$C_{15}H_{15}ONS$	S, 12·4	12·45
4′-*Ethoxy*-2-*methyl*-6′-*ethyl*-	Yellow needles	87—88	$C_{16}H_{17}ONS$	S, 11·5	11·8
4′-*Acetoxy*-2-*methyl*-6′-iso*propyl*-	Silky needles	101—101·5	$C_{17}H_{17}O_2NS$	S, 10·65	10·7
4′-*Hydroxy*-2-*methyl*-6′-iso*propyl*-	Flat yellow needles	231 (solid)	$C_{15}H_{15}ONS$	S, 12·35	12·45
4′-*Methoxy*-2-*methyl*-6′-iso*propyl*-	Pale yellow plates	63—64	$C_{16}H_{17}ONS$	S, 11·95	11·8
4′-*Ethoxy*-2-*methyl*-6′-iso*propyl*-	Thick yellow needles	91	$C_{17}H_{19}ONS$	S, 11·5	11·25
4′-*Acetoxy*-2 : 6′ : 8′-*trimethyl*-	Matted needles	181	$C_{16}H_{15}O_2NS$	S, 11·15	11·25
4′-*Hydroxy*-2 : 6′ : 8′-*trimethyl*-	Yellow needles	198	$C_{14}H_{13}ONS$	S, 13·0	13·2
4′-*Methoxy*-2 : 6′ : 8′-*trimethyl*-	Colourless needles	91—92	$C_{15}H_{15}ONS$	S, 12·35	12·45
4′-*Ethoxy*-2 : 6′ : 8′-*trimethyl*-	Pale yellow plates	131	$C_{16}H_{17}ONS$	S, 12·05	11·8
4′-*Acetoxy*-6′-*methoxy*-2-*methyl*-	Needles, threads	161—162	$C_{15}H_{13}O_3NS$	S, 11·25	11·15
4′-*Hydroxy*-6′-*methoxy*-2-*methyl*-	Flat needles	257 (decomp.)	$C_{13}H_{11}O_2NS$	S, 13·15	13·1
4′ : 6′-*Dimethoxy*-2-*methyl*-	Thick needles	74	$C_{14}H_{13}O_2NS$	S, 12·3	12·4
6′-*Methoxy*-4′-*ethoxy*-2-*methyl*-	Flat, pale yellow needles	115—116	$C_{15}H_{15}O_2NS$	S, 11·9	11·75
4′-*Acetoxy*-6′-*ethoxy*-2-*methyl*-	Flat, yellow needles	160—162	$C_{16}H_{15}O_3NS$	S, 10·5	10·65
4′-*Hydroxy*-6′-*ethoxy*-2-*methyl*-	Tiny cream needles	243 (decomp.)	$C_{14}H_{13}O_2NS$	S, 12·0	12·3
4′-*Methoxy*-6′-*ethoxy*-2-*methyl*-	Pale yellow needles	120—121	$C_{15}H_{15}O_2NS$	S, 11·55	11·75
4′ : 6′-*Diethoxy*-2-*methyl*-	Flat yellow needles	145—146	$C_{16}H_{17}O_2NS$	S, 11·25	11·15
6′-*Chloro*-4′-*acetoxy*-2-*methyl*-	Colourless threads	209—210	$C_{14}H_{10}O_2NClS$	S, 11·15	11·0
6′-*Chloro*-4′-*hydroxy*-2-*methyl*-	Flat needles	280 (decomp.)	$C_{12}H_8ONClS$	S, 12·55	12·85
6′-*Chloro*-4′-*methoxy*-2-*methyl*-	Flat, pale yellow spikes	134·5	$C_{13}H_{10}ONClS$	S, 12·25	12·2
6′-*Chloro*-4′-*ethoxy*-2-*methyl*-	Yellow needles	183·5	$C_{14}H_{12}ONClS$	S, 11·65	11·55
4′-*Acetoxy*-2-*methylthio*-	Pale yellow plates	143	$C_{14}H_{11}O_2NS_2$	S, 22·0	22·2
4′-*Hydroxy*-2-*methylthio*-	Pale yellow needles	255	$C_{12}H_9ONS_2$	S, 25·8	25·95
4′-*Methoxy*-2-*methylthio*-	Slender needles	110—111	$C_{13}H_{11}ONS_2$	S, 24·35	24·55
4′-*Acetoxy*-2-*ethylthio*-	Colourless flakes	101—103	$C_{15}H_{13}O_2NS_2$	S, 21·45	21·15
4′-*Hydroxy*-2-*ethylthio*-	Needles	206	$C_{13}H_{11}ONS_2$	S, 24·55	24·55
4′-*Acetoxy*-2-*methylthio*-6′-*methyl*-	Yellow needles	155—156	$C_{15}H_{13}O_2NS_2$	S, 21·2	21·15
4′-*Hydroxy*-2-*methylthio*-6′-*methyl*-	Yellow needles	213 (subl.)	$C_{13}H_{11}ONS_2$	S, 24·45	24·55
4′-*Methoxy*-2-*methylthio*-6′-*methyl*-	Needles	109—110	$C_{14}H_{13}ONS_2$	S, 23·6	23·3
4′-*Acetoxy*-2 : 3′-*dimethyl*-	Needle rosettes	171—172	$C_{15}H_{13}O_2NS$	S, 11·6	11·8
4′-*Hydroxy*-2 : 3′-*dimethyl*-	Needles	300	$C_{13}H_{11}ONS$	S, 14·15	14·
4′-*Methoxy*-2 : 3′-*dimethyl*-	Pale yellow needles	91—92	$S_{14}H_{13}ONS$	S, 12·95	13·2
4′-*Ethoxy*-2 : 3′-*dimethyl*-	Pale yellow needles	100—101	$C_{15}H_{15}ONS$	S, 12·35	12·45
2-*Acetamido*-6′-*acetoxy*-3′-*methyl*-	Asbestos-like needles	300	$C_{16}H_{14}O_3N_2S$	S, 10·25	10·25
Phenanthra-4′ : 3′ : 4 : 5-*thiazoles* (*Type V*).					
2-*Acetamido*-1′-*acetoxy*-	Needles	279°	$C_{19}H_{14}O_3N_2S$	S, 9·4	9·15
1′-*Acetoxy*-2-*methyl*-	Flat needles	167—169	$C_{18}H_{13}O_2NS$	C, 70·2	70·3
				H, 4·1	4·25
				S, 10·6	10·45
1′-*Hydroxy*-2-*methyl*-	Pale yellow plates	250 (subl.)	$C_{16}H_{11}ONS$	S, 12·35	12·1
1′-*Methoxy*-2-*methyl*-	Pale yellow needles	136—137	$C_{17}H_{13}ONS$	S, 11·7	11·5
1′-*Ethoxy*-2-*methyl*-	Pale yellow flat needles	144—145	$C_{18}H_{15}ONS$	S, 11·05	10·95
1′-*Acetoxy*-2-*methylthio*-	Pale yellow flat needles	128—129	$C_{18}H_{13}O_2NS_2$	S, 19·1	18·9
1′-*Hydroxy*-2-*methylthio*-	Yellow needles	162—164	$C_{16}H_{11}ONS_2$	S, 21·6	21·6
Phenanthra-1′ : 2′ : 4 : 5-*thiazoles* (*Type VII*).					
2-*Acetamido*-4′-*acetoxy*-	Irregular [b]	290	$C_{19}H_{14}O_3N_2S$	S, 9·0	9·15
4′-*Acetoxy*-2-*methyl*-	Silky needles	159·5	$C_{18}H_{13}O_2NS$	C, 70·1	70·3
				H, 4·1	4·25
				S, 10·5	10·45
4′-*Hydroxy*-2-*methyl*-	Yellow needles	278—280 (subl.)	$C_{16}H_{11}ONS$	S, 11·8	12·1
4′-*Methoxy*-2-*methyl*-	Yellow needles	173	$C_{17}H_{13}ONS$	S, 11·45	11·5
4′-*Ethoxy*-2-*methyl*-	Yellow needles	177·5	$C_{18}H_{15}ONS$	S, 10·85	10·95
4′-*Acetoxy*-2-*methylthio*-	Threads	152	$C_{18}H_{13}O_2NS_2$	S, 18·9	18·9
4′-*Hydroxy*-2-*methylthio*-	Yellow needles	240 (subl.)	$C_{16}H_{11}ONS_2$	S, 21·4	21·6

a, from aqueous alcohol; *b*, from acetic anhydride; *c*, from ligroin.

Naphtha-1′ : 2′ : 4 : 5-*thiazoles*.	Crystal form.	M. p.	Formula.	Found, %.	Required.
Thionaphtheno-7′ : 6′ : 4 : 5-*thiazoles* (*Type IX*).					
2-*Acetamido*-4′-*acetoxy*	Flat cream needles	285—289	$C_{13}H_{10}O_3N_2S_2$	S, 21·25	20·95
4′-*Acetoxy*-2-*methyl*-	Pink needles[c]	130—130·5	$C_{12}H_9O_2NS_2$	C, 54·7	54·7
				H, 3·35	3·55
				S, 24·35	24·35
4′-*Hydroxy*-2-*methyl*-	Needles	268 (subl.)	$C_{10}H_7ONS_2$	S, 28·85	29·0
4′-*Methoxy*-2-*methyl*-	Plates	127·5—128	$C_{11}H_9ONS_2$	S, 27·5	27·25

4′-*Acetoxy*-3′-*acetyl*-2-*methylnaphtha*-1′ : 2′ : 4 : 5-*thiazole*.—The methyl-alcoholic washings and crystallisation liquors from the primary cyclisation product of 4-phenyl-2-methylthiazole-5-acetic acid were concentrated and left for several days. The *ketone* separated and was recrystallised from methanol. It formed colourless needles, m. p. 205°, in 20% yield (Found: S, 10·55. $C_{16}H_{13}O_3NS$ requires S, 10·7%).

4′-*Hydroxy*-3′-*acetyl*-2-*methylnaphtha*-1′ : 2′ : 4 : 5-*thiazole* (X).—(*a*) The above acetate was dissolved in hot spirit, and an excess of 2N-sodium hydroxide added. The deep yellow solution was immediately diluted with water, and the yellow *ketone* precipitated by acidifying with acetic acid. From methyl alcohol it formed yellow needles, m. p. 126—127° (Found: C, 65·25; H, 4·4; N, 5·6; S, 12·55. $C_{14}H_{11}O_2NS$ requires C, 65·35; H, 4·3; N, 5·45; S, 12·45%).

(*b*) 4′-Hydroxy-2-methyl-β-naphthathiazole (0·5 g.), nitrobenzene (5 c.c.), acetyl chloride (0·2 g.) or acetic anhydride (0·3 g.), and aluminium chloride (1·0 g.) were mixed and heated on the steam-bath for 4 hours. Decomposition with dilute hydrochloric acid gave yellow flocks of (X). A further yield was obtained by extracting the nitrobenzene layer, diluted with ether, with aqueous sodium carbonate. The total yield was 0·35 g. From methyl alcohol it formed yellow needles, m. p. 126°, not depressed on admixture with (X) from (*a*).

(*c*) (III; R = Me, R′ = H) (0·5 g.), aluminium chloride (2·0 g.), and nitrobenzene (5 c.c.) were heated together on the steam-bath for 4 hours, and the product (0·2 g.) isolated as for (*b*). It gave no depression in m. p. on admixture with the product from (*a*).

The 2 : 4-*dinitrophenylhydrazone* formed scarlet needles from alcohol, m. p. 300° (Found: N, 15·7. $C_{20}H_{15}O_5N_5S$ requires N, 16·0%), the *hydrazone* orange prisms, m. p. 173° (solid, and turned scarlet), from alcohol (Found: N, 15·2. $C_{14}H_{13}ON_3S$ requires N, 15·5%), and the *methyl ether* pale yellow prisms, m. p. 113—114°, from methyl alcohol (Found: S, 12·05. $C_{15}H_{13}O_2NS$ requires S, 11·8%).

4′-*Acetoxy*-3′-*acetyl*-2 : 6′-*dimethylnaphtha*-1′ : 2′ : 4 : 5-*thiazole*.—Cyclisation of 4-(4′-methylphenyl)-2-methylthiazole-5-acetic acid gave a 15% yield of the *ketone*. It formed cream needles, m. p. 216°, from alcohol (Found: S, 9·9. $C_{17}H_{15}O_3NS$ requires S, 10·25%). The 2 : 4-*dinitrophenylhydrazone* formed orange needles, m. p. 306°, from alcohol (Found: N, 14·35. $C_{23}H_{19}O_6N_5S$ requires N, 14·2%).

4′-*Hydroxy*-3′-*acetyl*-2 : 6′-*dimethylnaphtha*-1′ : 2′ : 4 : 5-*thiazole*.—Obtained by hydrolysing the above acetate, it formed yellow needles, m. p. 165—166°, from methyl alcohol (Found: S, 11·6. $C_{15}H_{13}O_2NS$ requires S, 11·85%).

4′-*Hydroxy*-3′-*chloroacetyl*-2-*methylnaphtha*-1′ : 2′ : 4 : 5-*thiazole* (XI).—Proceeding as for the preparation of (X) (*b*) but using chloroacetyl chloride, a solid was obtained on decomposing the reaction mixture. It could not be crystallised. A portion was heated with acetic anhydride and anhydrous sodium acetate until the yellow colour had disappeared. The *acetate* was precipitated with water and formed silky needles, m. p. 170—171°, from alcohol (Found: S, 10·2. $C_{16}H_{12}O_3NClS$ requires S, 10·4%).

3′-*Keto*-2-*methylbenzcoumarano*-5′ : 4′ : 4 : 5-*thiazole* (XII).—(XI), dissolved in hot 2N-sodium carbonate, gave a yellow solution, from which the *coumaranone* separated almost immediately. From benzene with charcoal treatment it formed pale yellow needles, m. p. 233° (Found: C, 66·0; H, 3·7; S, 12·25. $C_{14}H_9O_2NS$ requires C, 65·85; H, 3·55; S, 12·55%).

2-(1-*Methyl*-1 : 2-*dihydroquinolylidene*)-2′-(3′-*keto*-2-*methylbenzcoumarano*-5′ : 4′ : 4 : 5-*thiazole*) (XIII).—The coumaranone (258 mg.) and 2-methylthioquinoline methiodide (317 mg.) were dissolved by refluxing in ethyl alcohol (300 c.c.). Triethylamine (2 drops) was then added, whereupon the dye separated. Boiling was continued until the evolution of mercaptan had ceased (15 minutes), and the dye collected when cold and recrystallised from alcohol. It formed silky, red needles, m. p. 300° (Found: S, 8·15. $C_{24}H_{16}O_2N_2S$ requires S, 8·1%). It sensitised a silver chloride photographic emulsion with maxima at 4850 and 5200 A.

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