582. *Syntheses in the Thiapyran Series. Part II. Dihydro-derivatives.*

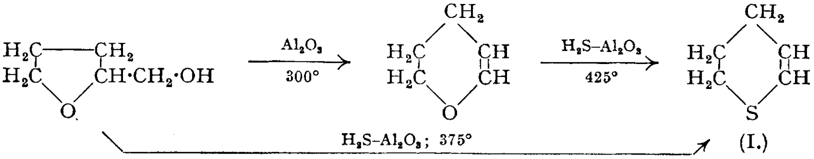
By Ralph F. Naylor.

A number of dihydrothiapyrans of the Δ^2- and Δ^3-series has been prepared. The Δ^2-compounds are obtained by the catalysed reaction of hydrogen sulphide with the corresponding pyran derivatives. For the preparation of the Δ^3-compounds thiapyran-4-ones are converted into thiapyran-4-ols by reduction with aluminium *iso*propoxide or by reaction with methylmagnesium iodide, the thiapyran-4-ols on dehydration giving the Δ^3-dihydrothiapyrans.

These thiapyrans with methyl iodide give mainly tars, but there is evidence of the formation of methiodides at 24° and of ring scission at 100°.

Interest in compounds of the thiapyran series was first aroused in these laboratories by the observation that this ring system was formed in the reactions of $\Delta^{1:5}$-dienes (polyisoprenes) with sulphur or with hydrogen sulphide (Farmer and Shipley, *J.*, 1947, 1519; Naylor, *ibid.*, p. 1532). Syntheses of some of the fully saturated tetrahydro-derivatives have already been reported (Naylor, *J.*, 1947, 1106), but the dihydro-derivatives are largely unknown. The object of the present study has been to prepare a number of representative dihydrothiapyrans, which will show the influence of unsaturation pattern and substitution on the chemical properties and absorption spectra, thereby serving as standards for the examination of the dihydrothiapyrans which are formed in the reaction of sulphur with $\Delta^{1:5}$-dienes.

In the Δ^2-series the parent member, Δ^2-dihydrothiapyran (I) was prepared by the catalysed reaction of hydrogen sulphide with Δ^2-dihydropyran at *ca.* 425°. While the work was in progress an identical mode of synthesis was reported independently by Yur'ev, Dubrovina, and Tregubov (*J. Gen. Chem. U.R.S.S.*, 1946, **16**, 843). The dihydropyran was prepared in the present work by passage of tetrahydrofurfuryl alcohol over alumina at 300°, and it was found possible to combine the two stages by passing the alcohol and hydrogen sulphide over alumina at 375°; the yield by this method was, however, poor.



(I.)

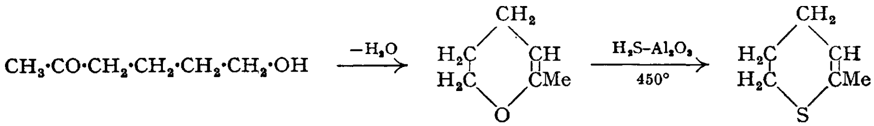
Although it is possible, as reported by the Russian authors, to obtain a product whose analytical figures correspond to Δ^2-dihydrothiapyran it is doubtful whether this compound has, in fact, ever been obtained completely pure. Yur'ev *et al.* do not give analytical data for carbon and hydrogen; in the present work a slightly high value for the hydrogen suggests the presence of tetrahydrothiapyran. When a carefully fractionated sample of the product is treated with mercuric chloride, and the resultant mercurichloride decomposed with alkali or hydrogen sulphide, the Δ^2-dihydrothiapyran is not regenerated but a small quantity of tetrahydrothiapyran is obtained. A number of other metallic salts ($PtCl_4$, $AuCl_3$, $AgNO_3$) appeared to give additive compounds, but the very small amount formed suggested that only the tetrahydrothiapyran impurity was reacting. Similarly the only methiodide which is separable as a pure crystalline compound is that of tetrahydrothiapyran. It would appear therefore that Δ^2-dihydrothiapyran prepared by this method always contains small proportions of tetrahydrothiapyran and possibly also of thiapyran, and that the presence of the double bond in the Δ^2-position militates against the formation of sulphonium compounds.

In the present work a small amount of *mercaptotetrahydrothiapyran* was also isolated from the reaction product. This had evidently been formed by catalytic addition of hydrogen sulphide to Δ^2-dihydrothiapyran, and might be expected to be the 2-mercapto-compound (the 3-position being probably the more electronegative).

The reaction of Δ^2-dihydropyran with phosphorus pentasulphide, effective in replacing oxygen by sulphur in the saturated compounds (Naylor, *J.*, 1947, 1106), failed to give any of the required thiapyran. The conversion of epoxides into episulphides by potassium thiocyanate (Snyder, Stewart, and Ziegler, *J. Amer. Chem. Soc.*, 1947, **69**, 2674) suggested that this reagent might be effective in converting Δ^2-dihydropyran into the corresponding thiapyran, but the method proved unsuccessful.

2-Methyl-Δ^2-dihydrothiapyran (II) was synthesised by the following sequence of reactions:

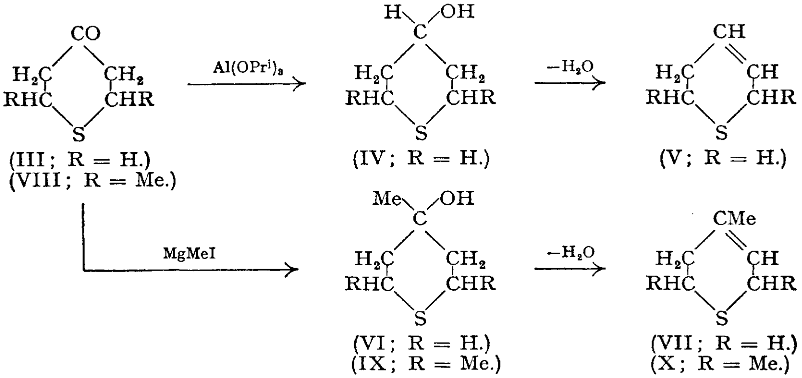
$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CO_2Et + CH_2Br{\cdot}CH_2{\cdot}CH_2Br \xrightarrow{NaOEt} CH_3{\cdot}CO{\cdot}CH(CO_2Et){\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br \xrightarrow{HCl}$$



(II.)

The preparation of the 2-methyl-Δ^2-dihydropyran was essentially that of Lipp (*Annalen*, 1896, **289**, 186). Its reaction with hydrogen sulphide gave a very heterogeneous product and complete purification of the 2-methyl-Δ^2-dihydrothiapyran was not achieved, but again there were indications (high hydrogen : carbon ratio) of the presence of the fully saturated compound.

The first attempts to prepare members of the Δ^3-dihydrothiapyran series were unsuccessful. γ-Pyrone was hydrogenated, with Raney nickel as catalyst, to tetrahydropyran-4-ol, which was then treated with excess of hydrogen bromide. However, although this preparation has been reported by Blanchard and Paul (*Compt. rend.*, 1935, **200**, 1414) the method failed to give appreciable amounts of 1 : 3 : 5-tribromopentane, nor was an attempt to prepare this compound by reduction of acetonedicarboxylic ester to pentane-1 : 3 : 5-triol, etc., more successful. Passage of tetrahydropyran-4-ol in a stream of hydrogen sulphide over heated alumina gave a small quantity of a sulphur compound, probably Δ^3-dihydrothiapyran, but insufficient for purification. The work of Arndt and Schauder (*Ber.*, 1930, **63**, 313) who obtained 2 : 6-diphenyl-4-methyl-Δ^3-dihydrothiapyran by a Grignard reaction on the corresponding thiapyranone, followed by dehydration, suggested the use of tetrahydrothiapyran-4-one (III) as an intermediate in the present syntheses. The method of preparation of this compound from ethyl thiodipropionate reported by Bennett and Scorah (*J.*, 1927, 194) gave unsatisfactory yields, and alternative methods of cyclisation of thiodipropionic esters proved unsuccessful. The author is indebted to Dr. H. M. E. Cardwell (private communication; cf. this vol., p. 717) for details of an improved method of condensation using sodamide. Tetrahydrothiapyran-4-one prepared by this method was the starting material in the following syntheses of Δ^3-*dihydrothiapyran* (V) and 4-*methyl*-Δ^3-*dihydrothiapyran* (VII):



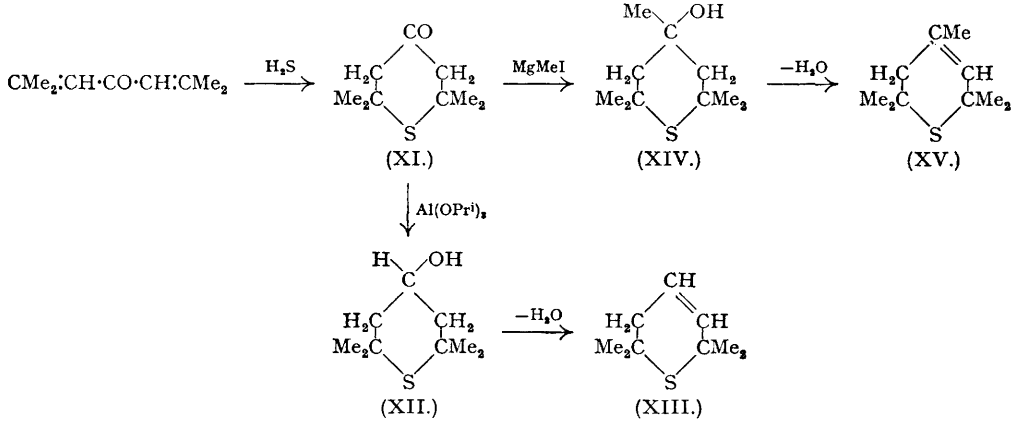
(III; R = H.) (VIII; R = Me.)
(IV; R = H.)
(V; R = H.)
(VI; R = H.) (IX; R = Me.)
(VII; R = H.) (X; R = Me.)

The reduction with aluminium *iso*propoxide proceeded smoothly without any cleavage of the C–S bonds and gave a good yield of *tetrahydrothiapyran*-4-*ol* (IV). Reaction of (IV) with hydrogen bromide gave very poor yields of the 4-bromo-compound, and direct dehydration to the thiapyran was therefore attempted. Anhydrous copper sulphate and stronger dehydrating reagents caused decomposition but anhydrous magnesium sulphate at 200° was effective in promoting the dehydration with a minimum of side-reaction. 4-*Methyltetrahydro*-

thiapyran-4-*ol* (VI) was readily obtained from tetrahydrothiapyran-4-one by methylmagnesium iodide and was dehydrated to 4-*methyl*-Δ^3-*dihydrothiapyran* (VII) by anhydrous copper sulphate or, better, catalytic amounts of iodine.

In an analogous manner 2 : 6-*dimethyltetrahydrothiapyran*-4-*one* (VIII) * was converted into 2 : 4 : 6-*trimethyltetrahydrothiapyran*-4-*ol* (IX) and the Δ^3-*dihydrothiapyran* (X). Arndt has shown that the ketone (VIII) exists in *cis*- and *trans*-forms, one solid and the other liquid (*Rev. Fac. Sci. Univ. Istanbul, Série A*, 1948, **13**, 62). Thiapyranols (IX) were prepared and were solid and liquid respectively, but the thiapyrans obtained by dehydration of each possessed almost identical physical constants, although the infra-red absorption spectra showed certain differences.

For the synthesis of Δ^3-dihydrothiapyrans containing tertiary carbon atoms in the α-positions phorone was used as a starting material.



Attempts to catalyse the addition of hydrogen sulphide to phorone at room temperature were not very successful and the method of Arndt (*loc. cit.*, p. 60) was adopted. Arndt obtained 2 : 2 : 6 : 6-tetramethyltetrahydrothiapyran-4-ol (XII) as a by-product in the Clemmensen reduction of the thiapyranone (XI), but in the present work it was obtained in excellent yield (99%) by reduction with aluminium *iso*propoxide. Anhydrous magnesium sulphate at 200° then gave 2 : 2 : 6 : 6-*tetramethyl*-Δ^3-*dihydrothiapyran* (XIII). Professor Arndt kindly sent a small sample of the main product of this Clemmensen reduction to check whether it was the presumed saturated compound 2 : 2 : 6 : 6-tetramethyltetrahydrothiapyran. Comparison of its infra-red absorption spectrum with those of the saturated and unsaturated (XIII) thiapyran synthesised in these laboratories shows that it is in fact the compound (XIII). Evidently the Clemmensen reduction had proceeded only as far as the thiapyranol (XII), some of which had become dehydrated under the acid conditions of reaction. This compound (XIII) is of particular interest in that it was suspected to be the principal component of the cyclic sulphide obtained in the reaction of geraniolene with sulphur (Farmer and Shipley, *loc. cit.*). In support of this view examination of the infra-red absorption spectra shows that the principal absorption lines of 2 : 2 : 6 : 6-tetramethyl-Δ^3-dihydrothiapyran are present in the geraniolene–sulphur product, although the latter contains considerable additional absorption attributable to other $C_9H_{18}S$ isomers.

The reaction of methylmagnesium iodide with (XI) and the subsequent dehydration were carried out as in the previous syntheses, the products being 2 : 2 : 4 : 6 : 6-*pentamethyltetrahydrothiapyran*-4-*ol* (XIV) and 2 : 2 : 4 : 6 : 6-*pentamethyl*-Δ^3-*dihydrothiapyran* (XV).

Methyl Iodide Reactions.—The tendency of most of the dihydrothiapyrans to give only oils on reaction with methyl iodide hindered the attempt to correlate the ease of scission of the C–S link with the structure of the sulphide. Admixture of equimolecular proportions of Δ^2-dihydrothiapyran and methyl iodide at room temperature resulted in no reaction, except of the tetrahydrothiapyran impurity; reaction for 24 hours with excess of methyl iodide at 100° gave a tar from which no crystalline compound was isolated. Analysis indicated that this was mainly trimethylsulphonium iodide, resulting from elimination of sulphur from the

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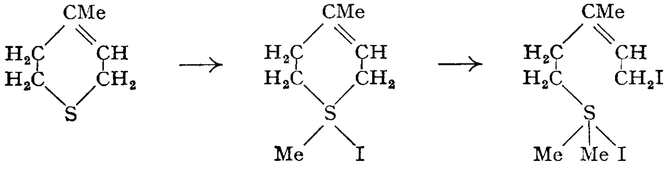
* The author is indebted to Professor F. G. Arndt for the samples of this thiapyranone.

methiodide initially formed. Benzyl chloride and Δ^2-dihydrothiapyran did not react even at 100°.

At 24° 4-methyl-Δ^3-dihydrothiapyran gave a crystalline *methiodide* (XVI), but at 100° cleavage of the C–S link occurred to give a mixture which appeared (from analyses) to be mainly *dimethyl*-5-*iodo*-3-*methylpent*-3-*enylsulphonium iodide* (XVII) :



(XVI.) (XVII.)

2 : 4 : 6-Trimethyl-Δ^3-dihydrothiapyran united very slowly with methyl iodide at 24° to give the ordinary *methiodide.*

The dihydrothiapyrans containing methyl or *gem*-dimethyl groups in the 2- and 6-positions also reacted with methyl iodide extremely slowly at 0° or 24°, and only moderately rapidly at 50—100°, to give tarry products containing both the methiodide and the scission products of the types obtained from 4-methyl-Δ^3-dihydrothiapyran.

EXPERIMENTAL.

(Microanalyses were carried out by Dr. W. T. Chambers, Miss E. Farquhar, and Mr. A. van der Schee.)

Δ^2-Dihydropyran, prepared from tetrahydrofurfuryl alcohol (*Org. Synth.*, **23**, 25), was purified by fractional distillation over sodium to give a liquid, b. p. 88—90°, n_D^{20} 1·4378.

Δ^2-*Dihydrothiapyran* (I).—(a) *From* Δ^2-*dihydropyran.* A 24-mm. glass tube packed with a 48-cm. length of coarse activated alumina was inclined at 10° to the horizontal and maintained at 425° by an electric furnace. Δ^2-Dihydropyran (45 g.) in a steady stream of hydrogen sulphide was passed over the alumina during 4 hours. The product, which was in two layers, was salted out by anhydrous magnesium sulphate, the separated upper layer being extracted 3 times with 10% aqueous sodium hydroxide. After being washed with water and dried (K_2CO_3), the neutral portion was twice fractionally distilled, to give Δ^2-dihydrothiapyran (20 g.), b. p. 138—144°/750 mm. The products from several runs were combined and repeatedly fractionated over sodium until Δ^2-dihydrothiapyran was obtained as a liquid, b. p. 142·5°, 81°/100 mm., n_D^{20} 1·5330 (Found : C, 59·8; H, 8·2, 8·3; S, 31·8. Calc. for C_5H_8S : C, 60·0; H, 8·0; S, 32·0%). The alkaline extract was acidified with hydrochloric acid and extracted with ether. After being dried ($MgSO_4$) the product distilled at 83°/10 mm. to give impure 2-(or 3-)*mercaptotetrahydrothiapyran* as a liquid, n_D^{20} 1·5583, with a typical mercaptan odour (Found : C, 46·0; H, 7·6; S, 45·5. $C_5H_{10}S_2$ requires C, 44·7; H, 7·5; S, 47·7%).

(b) *Direct from tetrahydrofurfuryl alcohol.* Tetrahydrofurfuryl alcohol was dripped into the furnace tube and passed in a stream of hydrogen sulphide over the heated alumina at 375° (113 g. in 5 hours), the product being collected over anhydrous potassium carbonate (20 g.). The upper layer of product was separated, extracted with 10% aqueous sodium hydroxide, and combined with an ethereal extract of the combined lower layer and alkaline extract. Distillation of the dried ethereal extract gave a variety of products including crude dihydropyran (*ca.* 19 g.) and dihydrothiapyran (*ca.* 26 g.). Fractionation of the latter gave a somewhat impure product, b. p. 28—30°/8 mm., n_D^{20} 1·5315 (Found : C, 61·6; H, 8·8; S, 29·6%).

Δ^2-*Dihydrothiapyran and Metallic Salts.*—Δ^2-Dihydrothiapyran (12 g.) was added to a hot solution of mercuric chloride (32·4 g.) in 95% alcohol (100 ml.). The white *mercurichloride* was immediately precipitated and was purified by recrystallisation from alcohol, in which it was only very slightly soluble, to give a white powder, decomp. 122·5° (Found : Hg, 54·25. $C_5H_8SCl_2Hg$ requires Hg, 54·0. $C_5H_{10}SCl_2Hg$ requires Hg, 53·7%). The product became brown on storage and showed great variation of decomposition point after recrystallisation (122—140°). The finely powdered mercurichloride (24 g.) was shaken with excess of 6% aqueous sodium hydroxide (150 ml.), and the liberated sulphide extracted with ether. After drying, distillation gave tetrahydrothiapyran (1 g.) as a colourless liquid, b. p. 74—75°/100 mm., n_D^{20} 1·5044 (Found : C, 58·7; H, 9·75; S, 30·8. Calc. for $C_5H_{10}S$: C, 58·8; H, 9·8; S, 31·4%). The identity of the compound was confirmed by infra-red absorption spectra by comparison with an authentic sample.

When kept with Δ^2-dihydrothiapyran in alcoholic solution platinic chloride gave yellowish-brown crystals, auric chloride yellow crystals, and silver nitrate white crystals which slowly blackened; yields were in each case too small to permit purification and identification.

Δ^2-*Dihydrothiapyran and Methyl Iodide.*—A mixture of the Δ^2-dihydrothiapyran (2·0 g.) and methyl iodide (3·12 g.) was set aside at room temperature for 24 hours. The precipitated methiodide (0·2 g.) was recrystallised from 95% alcohol to give tetrahydrothiapyran methiodide, m. p. *ca.* 145° (decomp.) (Found : C, 29·65; H, 5·2; S, 13·45; I, 52·0. Calc. for $C_6H_{13}SI$: C, 29·5; H, 5·3; S, 13·1; I, 52·1. Calc. for $C_6H_{11}SI$: C, 29·8; H, 4·5; S, 13·2; I, 52·5%). Reaction of Δ^2-dihydrothiapyran (5·0 g.) with methyl iodide (28·8 g.) for 24 hours at 100° gave a tarry solid containing mainly trimethylsulphonium iodide (Found : C, 19·9; H, 4·6; I, 61·4. Calc. for C_3H_9SI : C, 17·7; H, 4·4; I, 62·2%).

Δ^2-*Dihydropyran and Phosphorus Pentasulphide.*—On mixing, the reactants underwent a vigorous exothermic reaction with the formation of a yellowish-brown tarry material from which no volatile products could be obtained by direct distillation or by heating it with aqueous sodium hydroxide and extracting the product with ether.

Δ^2-*Dihydropyran and Potassium Thiocyanate.*—To a solution of potassium thiocyanate (33 g.) in water (25 ml.) were added ethanol (18 ml.) and dihydropyran (12 g.). After vigorous stirring for 4 hours at 15° no reaction was apparent, and a further 10 g. of dihydropyran were added, the stirring being continued for 8 hours at 55—60°. The product was salted out with sodium chloride, dried, and distilled, whereafter it was found to contain only unchanged dihydropyran.

2-*Methyl*-Δ^2-*dihydropyran.*—To a cold solution of sodium (96 g.) in dry ethanol (1040 g.) was slowly added, with cooling, ethyl acetoacetate (520 g.). Trimethylene dibromide (800 g.) was then added and the mixture warmed slowly to the b. p. and finally heated under reflux for 1 hour, by which time the solution was neutral. After removal of ethanol by distillation, sufficient water was added to dissolve the sodium bromide, and the upper layer was separated and shaken twice with 2N-potassium hydroxide. The product was decarboxylated and hydrolysed by being boiled under reflux with hydrochloric acid (160 g.) and water (1040 g.) for 4 hours. The lower oil, containing trimethylene dibromide and diacetopimelic ester, was removed, and 20 ml. were distilled from the aqueous layer (to remove residual bromide). After salting out with potassium carbonate (2 kg.) the mixture of ethanol and product was distilled to give a mixture (131 g.) of hexan-1-ol-5-one and 2-methyl-Δ^2-dihydropyran, which was dried (K_2CO_3) and redistilled at 75—140°. This distillate was dried over sodium, redistilled quickly, and then fractionally distilled through a Widmer column to give 2-methyl-Δ^2-dihydropyran (38 g.), b. p. 105—107°, n_D^{20} 1·4457 (Found: C, 73·3; H, 10·2. Calc. for $C_6H_{10}O$: C, 73·5; H, 10·2%). It is almost impossible to remove the last traces of water.

2-*Methyl*-Δ^2-*dihydrothiapyran* (II).—2-Methyl-Δ^2-dihydropyran (80 g.) was passed in a stream of hydrogen sulphide over activated alumina at 450° at the rate of 15 g. per hour. The product was worked up in the same manner as dihydrothiapyran and after repeated fractional distillation, finally over sodium, was obtained as rather impure 2-*methyl*-Δ^2-*dihydrothiapyran*, b. p. 50—53°/16 mm., 40°/9 mm., n_D^{20} 1·5000 (Found: C, 65·6; H, 9·8; S, 24·7; C : H ratio, 6·70. $C_6H_{10}S$ requires C, 63·2; H, 8·8; S, 28·0%; C : H ratio, 7·18).

Attempted Syntheses of Δ^3-*Dihydrothiapyran* (V) *via Tetrahydropyran*-4-*ol.*—Chelidonic acid (5 g.) (*Org. Synth.*, Coll. Vol. II., p. 126), powdered pumice (5 g.), and copper powder (10 g.) were intimately mixed and heated over a naked flame. The distillate (0·5—1·0 ml.) containing water and γ-pyrone was redistilled to give γ-pyrone, b. p. 90—100°/11 mm., m. p. 32° (average yield, *ca.* 30%). When copper was replaced by copper-bronze the method failed to give appreciable yields.

A solution of γ-pyrone (24 g.) in methanol (200 ml.) containing Raney nickel (5 g.) was hydrogenated at 110° and 50 atmospheres for 3 hours (most of the absorption occurred during the first 20 minutes). After removal of catalyst and solvent the product was twice distilled at 85—88°/12 mm., to give tetrahydropyran-4-ol, $n_D^{19·5}$ 1·4612 (Found: C, 58·5; H, 9·9. Calc. for $C_5H_{10}O_2$: C, 58·8; H, 9·8%).

In an attempt to convert the pyranol into 1 : 3 : 5-tribromopentane, dry hydrogen bromide was passed through its ethereal solution for 4 hours. The product separated into two layers; the lower aqueous layer was extracted with ether, and the combined ethereal extracts distilled, but none of the required product was obtained.

Tetrahydropyran-4-ol (12 g.) was passed in a stream of hydrogen sulphide over activated alumina at 400° during 1·5 hours. The *product* was shaken simultaneously with ether and 10% aqueous sodium hydroxide. After separation, the ethereal layer was extracted with alkali, the alkaline extracts were shaken with ether, and the combined ethereal layers washed with water and dried. Distillation gave a few drops, b. p. 46—47°/11 mm., too small a quantity for purification (Found: S, 19·4. C_5H_8S requires 32·0%).

In another attempt tetrahydropyran-4-ol (5 g.) and phosphorus pentasulphide (14 g.), sealed under nitrogen in a Carius tube, were heated for 4 hours at 100—110°. Excess of pentasulphide was destroyed with water, and the whole was extracted 4 times with ether. The ethereal extract was shaken with 5% aqueous sodium hydroxide, dried ($MgSO_4$), and distilled to give *ca.* 0·1 g. of product (Found: S, 22·8%).

Tetrahydrothiapyran-4-*one* (III).—(a) *Attempted synthesis from* β-*chloropropionic acid.* β-Chloropropionic acid was heated with catalytic and with equimolecular proportions of barium hydroxide until distillation occurred. In each case the main reaction was elimination of hydrogen chloride, and no condensation to the thiapyranone took place. $\beta\beta'$-Thiodipropionic acid (8 g.), prepared from β-chloropropionic acid by the method of Bennett and Scorah (*J.*, 1927, 194), and powdered baryta (1 g.) heated together at 300° also failed to give the required thiapyranone.

(b) *From ethyl acrylate.* Diethyl $\beta\beta'$-thiodipropionate was prepared from ethyl acrylate by the method of Gershbein and Hurd (*J. Amer. Chem. Soc.*, 1947, **69**, 241). The ester (300 g.) in ether (500 ml.) was slowly run on sodamide (100 g.) in ether at −15° with good stirring (1¾ hours). Stirring was continued for a further 7 hours at −15° before the mixture was allowed to warm to room temperature overnight. After addition of ice and water the supernatant liquid was poured into 2N-sulphuric acid at 0°; the upper layer was separated and to it were added ethereal extracts of the aqueous layer. After drying ($MgSO_4$), distillation gave ethyl tetrahydrothiapyran-4-one-3-carboxylate (70 g.) as a liquid, b. p. 97—99°/0·1 mm., n_D^{20} 1·5223. Hydrolysis was effected by boiling the ester under reflux with 2N-sulphuric acid (500 ml.) for 4 hours. Some tetrahydrothiapyran-4-one crystallised and the remainder was extracted with ether; recrystallisation gave plates (36 g.), m. p. 65—67°.

Tetrahydrothiapyran-4-*ol* (IV).—Tetrahydrothiapyran-4-one (5 g.), aluminium *iso*propoxide (26·4 g.), and *iso*propyl alcohol (125 ml.) were heated to boiling in the type of apparatus described in "Organic Reactions," Vol. 2, p. 203, using a modified Hahn partial condenser. The distillate was collected at the rate of 5—6 drops per minute until all acetone had distilled (*ca.* 3 hours). After hydrolysis with ice-cold hydrochloric acid (46 ml. of concentrated acid in 250 ml. of water), the product was extracted with ether, washed with aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and distilled. The *tetrahydrothiapyran*-4-*ol* (3·8 g., 76%) distilled at 70°/0·05 mm. and condensed to a white solid, m. p. 53° (Found: C, 50·8; H, 8·7; S, 26·9. $C_5H_{10}OS$ requires C, 50·8; H, 8·5; S, 27·1%).

Δ^3-*Dihydrothiapyran* (V).—Dehydration of (IV) by copper sulphate and pumice at 190° gave poor yields and impure products. An intimate mixture of tetrahydrothiapyran-4-ol (2 g.) and anhydrous magnesium sulphate (20 g.) was heated in a slow stream of nitrogen for 4 hours at 200°. The product was distilled at atmospheric temperature and 10^{-5} mm., dissolved in ether, dried ($MgSO_4$), and distilled, to give Δ^3-*dihydrothiapyran* (0·5 g.), b. p. 35—36°/12 mm., n_{D}^{20} 1·5328 (Found: C, 60·2; H, 8·2; S, 31·7. C_5H_8S requires C, 60·0; H, 8·0; S, 32·0%).

4-*Methyltetrahydrothiapyran*-4-*ol* (VI).—To an ethereal solution of methylmagnesium iodide, prepared from magnesium (7 g.) and methyl iodide (36 g.), was added rapidly at 0° tetrahydrothiapyran-4-one (20 g.) in ether (200 ml.), with stirring which was continued for 1 hour. The product was hydrolysed with 2N-sulphuric acid (300 ml.) and ice, extracted with ether, washed with aqueous sodium hydrogen carbonate, and dried ($MgSO_4$). Distillation gave 4-*methyltetrahydrothiapyran*-4-*ol* (22 g., 97% theory), b. p. 54—55°/1·0 mm., 46°/0·1 mm., which condensed to a white solid, m. p. 45·5° (Found: C, 54·4; H, 9·2; S, 24·2. $C_6H_{12}OS$ requires C, 54·5; H, 9·1; S, 24·2%).

4-*Methyl*-Δ^3-*dihydrothiapyran* (VII).—The thiapyranol (VI) (7 g.) was dripped on a mixture of anhydrous copper sulphate (15 g.) and pumice (5 g.) at 180—210°, the products being distilled at reduced pressure. The 4-*methyl*-Δ^3-*dihydrothiapyran* was extracted with ether, dried, and twice distilled, to give a colourless liquid, b. p. 54°/11 mm., n_{D}^{20} 1·5239 (Found: C, 62·8; H, 8·9; S, 27·9. $C_6H_{10}S$ requires C, 63·2; H, 8·8; S, 28·0%). In another experiment the thiapyranol (10 g.) was heated with iodine (0·1 g.) for 3 hours at 150°, the product being separated as before, washed with aqueous sodium thiosulphate, and distilled. After redistillation over sodium 4-methyl-Δ^3-dihydrothiapyran was obtained, having b. p. 57°/12 mm., n_{D}^{20} 1·5241 (Found: C, 63·2; H, 8·8; S, 28·1%).

4-*Methyl*-Δ^3-*dihydrothiapyran and Methyl Iodide.*—A mixture of the thiapyran (1·14 g.) and methyl iodide (5·75 g.) was maintained at 24° for 24 hours. The white crystals of methiodide (XVI) (2·5 g.) were washed with light petroleum and twice recrystallised from 95% alcohol, to be obtained as colourless plates, m. p. 142·5° (decomp.) (Found: C, 32·7; H, 5·1; I, 49·1. $C_7H_{13}SI$ requires C, 32·8; H, 5·1; I, 49·6%).

Interaction for 24 hours at 100° gave a dark reddish-brown semi-solid oil, from which were separated by repeated recrystallisation red-brown needles, decomp. *ca.* 200°, which appeared to be slightly impure *dimethyl*-5-*iodo*-3-*methylpent*-3-*enylsulphonium iodide* (XVII) (Found: C, 22·9; H, 3·8; I, 64·9. $C_8H_{16}SI_2$ requires C, 24·1; H, 4·0; I, 63·8%).

2 : 4 : 6-*Trimethyltetrahydrothiapyran*-4-*ol* (IX).—The solid form of 2 : 6-dimethyltetrahydrothiapyran-4-one (VIII) (4 g.) (Arndt, *loc. cit.*) was treated with methylmagnesium iodide as in the previous preparation and 2 : 4 : 6-*trimethyltetrahydrothiapyran*-4-*ol* (2·9 g., 87%) was obtained as a white crystalline solid, m. p. 35—36°, b. p. 60—62°/0·3 mm. (Found: C, 59·5; H, 10·2; S, 20·3. $C_8H_{16}OS$ requires C, 60·0; H, 10·0; S, 20·0%).

Similarly the liquid form of (VIII) (6·5 g.) was converted into a liquid form of (IX) (6·2 g., 86% theory) having b. p. 62—64°/0·01 mm., n_{D}^{20} 1·5018 (Found: C, 59·1; H, 10·1; S, 19·9%).

2 : 4 : 6-*Trimethyl*-Δ^3-*dihydrothiapyran* (X).—The solid thiapyranol (1·9 g.) was dehydrated by heating with iodine (0·008 g.) (as previously described) to give 2 : 4 : 6-*trimethyl*-Δ^3-*dihydrothiapyran* (1·5 g., 89% theory) as a colourless liquid, which after redistillation over sodium had b. p. 60°/11 mm., n_{D}^{20} 1·4981 (Found: C, 67·5; H, 10·1; S, 22·7. $C_8H_{14}S$ requires C, 67·6; H, 9·9; S, 22·5%). The thiapyran (X) from the liquid form of (IX) had b. p. 62—63°/11 mm., n_{D}^{20} 1·4983 (Found: C, 67·2; H, 9·8; S, 22·7%).

2 : 4 : 6-*Trimethyl*-Δ^3-*dihydrothiapyran and Methyl Iodide.*—Interaction of 2 : 4 : 6-trimethyl-Δ^3-dihydrothiapyran (0·7 g.) with methyl iodide (2·15 g.) for 3 days at 24° gave pale yellow crystals of the methiodide (0·2 g.), m. p. 124° (decomp.) (Found: C, 38·2; H, 6·2; I, 44·2. $C_9H_{17}SI$ requires C, 38·0; H, 6·0; I, 44·6%).

2 : 2 : 6 : 6-*Tetramethyltetrahydrothiapyran*-4-*one* (XI) (cf. Arndt, *loc. cit.*).—Hydrogen sulphide was passed through a solution of phorone (*Annalen*, 1866, **140**, 297, 301) (20 g.) and potassium hydroxide (0·4 g.) in ethanol (40 ml.) under reflux for 7 hours. After dilution with water the product was extracted with ether, washed, dried, and twice distilled, 2 : 2 : 6 : 6-tetramethyltetrahydrothiapyranone (9·5 g.) being obtained as a liquid, b. p. 90—100°/13 mm., n_{D}^{20} 1·4861. Purification by conversion into the semicarbazone, which recrystallised from 95% alcohol (m. p. 212°), and regeneration by hot hydrochloric acid, gave a product, b. p. 92°/14 mm., n_{D}^{20} 1·4895 (Found: C, 63·1; H, 9·4; S, 18·9. Calc. for $C_9H_{16}OS$: C, 62·7; H, 9·4; S, 18·6%).

The hydrogen sulphide addition could not be effected at room temperature with such alkaline catalysts as sodium methoxide and phenyldimethylbenzylammonium hydroxide.

2 : 2 : 6 : 6-*Tetramethyltetrahydrothiapyran*-4-*ol* (XII).—The thiapyranone (XI) (5 g.) was reduced as in previous experiments with aluminium *iso*propoxide (17·8 g.), and 2 : 2 : 6 : 6-tetramethyltetrahydrothiapyran-4-ol (5 g., 99%) was obtained as a white crystalline solid, b. p. 95°/0·1 mm., m. p. 67° (Found: C, 62·1; H, 10·6; S, 18·2. Calc. for $C_9H_{18}OS$: C, 62·1; H, 10·4; S, 18·4%).

2 : 2 : 6 : 6-*Tetramethyl*-Δ^3-*dihydrothiapyran* (XIII).—The thiapyranol (XII) (4 g.) was dehydrated by anhydrous magnesium sulphate (40 g.) at 200°, as in the preparation of Δ^3-dihydrothiapyran. The product was redistilled over sodium to give 2 : 2 : 6 : 6-*tetramethyl*-Δ^3-*dihydrothiapyran* (1·3 g., 36% theory), b. p. 66°/11 mm., n_{D}^{20} 1·4883 (Found: C, 69·2; H, 10·4; S, 20·5. $C_9H_{16}S$ requires C, 69·2; H, 10·3; S, 20·5%).

2 : 2 : 4 : 6 : 6-*Pentamethyltetrahydrothiapyran*-4-*ol* (XIV).—The thiapyranone (XI) (12 g.) was treated with methylmagnesium iodide [from magnesium (2·2 g.) and methyl iodide (10·9 g.)] as in previous preparations and the product (8 g.) twice distilled. 2 : 2 : 4 : 6 : 6-*Pentamethyltetrahydrothiapyran*-4-*ol* was thus obtained as a colourless viscous liquid, b. p. 105—106°/12 mm., n_{D}^{20} 1·4990 (Found: C, 63·6; H, 10·6; S, 16·9. $C_{10}H_{20}OS$ requires C, 63·8; H, 10·6; S, 17·0%).

2 : 2 : 4 : 6 : 6-*Pentamethyl*-Δ^3-*dihydrothiapyran* (XV).—The thiapyranol (XIV) (5·7 g.) was dehydrated by heating it with a trace of iodine (0·01 g.) at 160°. The resultant 2 : 2 : 4 : 6 : 6-*pentamethyl*-Δ^3-*dihydrothiapyran* (3·3 g., 64% theory), after redistillation over sodium, was a colourless liquid, b. p. 69°/11 mm., 106—110°/40 mm., n_{D}^{20} 1·4849 (Found: C, 71·0; H, 10·9; S, 18·6. $C_{10}H_{18}S$ requires C, 70·6; H, 10·6; S, 18·8%).

2 : 2 : 4 : 6 : 6-*Pentamethyl-Δ³-dihydrothiapyran and Methyl Iodide.*—Interaction of 2 : 2 : 4 : 6 : 6-pentamethyl-Δ³-dihydrothiapyran (0·85 g.) with methyl iodide (2·15 g.) gave no product after 3 days at 0°; after 20 minutes at 100° and then 5 hours at 50° a tar was separated which appeared to contain the methiodide and its scission product (Found: C, 25·5; H, 4·5; I, 48·8. Calc. for $C_{11}H_{21}SI$: C, 42·1; H, 6·8; I, 40·8. Calc. for C_3H_9SI: C, 17·7; H, 4·4; I, 62·2%).

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