976. *Acid-catalysed Addition of Thiols to Conjugated Dienes.*

By B. Saville.

In a search for new routes to allylically unsaturated sulphides it has been shown that aliphatic thiols add (1,4) readily under mild conditions to 2-methylpenta-1,3-diene in the presence of a trace of 78% perchloric acid to yield the unknown alkyl 1,3-dimethylbut-2-enyl sulphides with minor amounts of the isomeric alkyl 1,1-dimethylbut-2-enyl sulphides (1,2 addition). Comparable addition of thiols to 2,4-dimethylpenta-1,3-diene gives mainly the cyclic dimer of the diene (probably 3,3,5,5-tetramethyl-*p*-mentha-1,8-diene) with some alkenyl alkyl sulphide, the proportion of the latter being increased by increase in the ratio of thiol to diene undergoing reaction. Propane-2-thiol adds slowly to isoprene under comparable conditions.

In a mechanistically similar process practically pure *S*-(1,3-dimethylbut-2-enyl)thiuronium bromide results from the interaction of 2-methylpenta-1,3-diene, hydrobromic acid, and thiourea at 10°. The syntheses of 4-methylpent-3-ene-2-thiol and 2-methylpentane-2-thiol in high yield and purity are also described.

The literature contains no information on the polar addition of thiols to conjugated diolefins although brief reference[1] has been made to a radical-initiated addition of the form (R = Aryl):

$$2RSH + CH_2{:}CH{\cdot}CH{:}CH_2 \longrightarrow RS{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}SR \quad . \; . \; . \; . \; . \; . \; . \quad (i)$$

When R (eqn. i) is alkyl competing telomerisation is seen to be a further complication. It has also been shown[2] that sulphenyl radicals and t-butoxy-radicals generated from t-butyl hydroperoxide, thiol, and ferrous salt at −10° add competitively to butadiene giving mainly $Bu^t{\cdot}O{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}SR$, the yield being particularly low for $R = Bu^t$. We now present theoretical reasons and experimental evidence leading to the conclusion that acid-catalysed addition (1,4) of thiols to suitably constituted dienes should take place, and confirm the prediction by the synthesis of appropriate alkenyl alkyl sulphides.

It is first necessary to consider classic work on the addition of hydrogen halides to conjugated dienes. Staudinger and his co-workers[3] showed conclusively that the major product of the addition of hydrogen bromide to isoprene (I) in acetic acid is 1-bromo-3-methylbut-2-ene (II):

(I)

(II) . . . . (ii)

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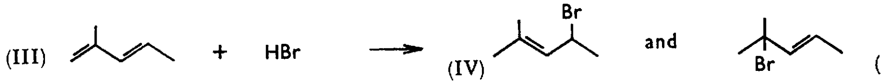
[1] Marvel and Chambers, *J. Amer. Chem. Soc.*, 1948, **70**, 993.

[2] Kharasch, Nudenberg, and Kawahara, *J. Org. Chem.*, 1955, **20**, 1550.

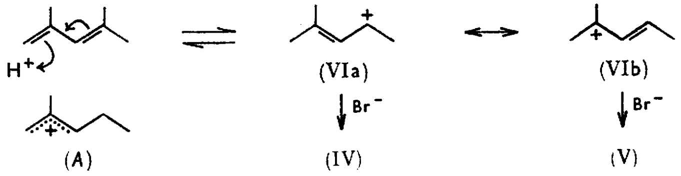
[3] Staudinger, Kreis, and Schilt, *Helv. Chim. Acta*, 1922, **5**, 743.

More recently, Russian workers[4] have concluded that addition of hydrogen bromide to 2-methylpenta-1,3-diene (III) in the presence of a little ether gives a mixture of the alkenyl bromides (IV) and (V):



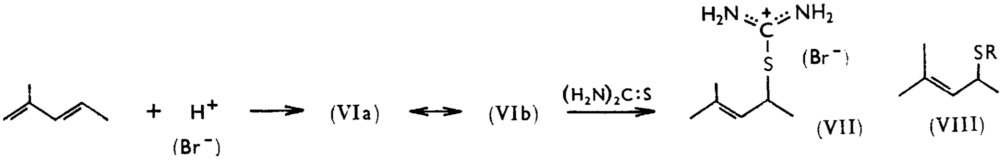
(iii)

Although no mechanistic rationale for these polar additions was advanced it is now suggested that they proceed *via* intermediate allylic carbonium ions, *e.g.*:



. . (iv)

The constitution of the postulated carbonium ion (VIa ⟷ VIb) shows it to be a mesomerically well-stabilised entity for whose existence spectral evidence[5] has recently been reported. An alternative carbonium ion (*A*) which might be formed by proton acquisition at the other end of the π-electron system of the diene seems comparatively unimportant on general theoretical grounds. If reaction is consummated by addition of bromide ion to (VIa ⟷ VIb) then the addition to the system of a nucleophil capable of competing for the carbonium ion should lead to alternative products. This concept was tested by use of thiourea as competitor; thus, on shaking the diene (III) with a solution of thiourea (1·1 mole) in 48% aqueous hydrobromic acid (1·1 mole) for 5 minutes at 10° *S*-(1,3-dimethylbut-2-enyl)thiuronium bromide (VII) crystallised suddenly in 70% yield:



. . . . (v)

Proof of the structure assigned to the salt (VII) was adduced as follows. Hydrolysis of (VII) in cold aqueous alkali gave a single thiol (VIII; R = H) as shown by gas–liquid chromatographic analysis. This thiol was devoid of *trans*-dialkylethylenic and terminally unsaturated C=C bonds (infrared spectroscopy), and gave only acetone in the volatile products of its ozonolysis. It is therefore concluded that thiourea attacks the carbonium ion (VIa ⟷ VIb) almost exclusively at the sterically less-hindered secondary carbon atom, conveniently designated by canonical form (VIa), to give (VII). This demonstration that thiourea competes effectively with bromide ion for the allylic carbonium ion strongly suggested the possibility that thiols might likewise engage in a process of the form:

$$\text{(III)} + H^+ \rightleftharpoons \text{(VIa)} \longleftrightarrow \text{(VIb)} \xrightarrow{\text{RSH}} \text{(VIII)} + H^+ \quad (\text{R} = \text{alkyl}) \qquad \text{(vi)}$$

In studying such possible additions of thiols to 2-methylpenta-1,3-diene it was important to choose experimental conditions in which acid-catalysed dimerisation (cf. ref. 6) of the

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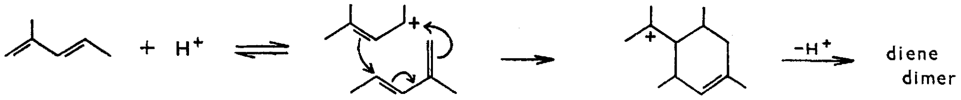
[4] Levina, Fainzil'berg, and Treshchova, *Zhur. obshchei Khim.*, 1952, **22**, 430.

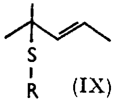
[5] Rosenbaum and Symonds, *J.*, 1961, 1.

[6] Ipatieff and Pines, *J. Amer. Chem. Soc.*, 1945, **67**, 1200.

diene, seen to be the result of the diene acting as a nucleophile reacting with the allylic carbonium ion, *e.g.*:



would be minimised or avoided. This required the diene, after being protonated, to be in an environment where thiol molecules were always in large excess. A generally successful technique yielding 80—95% of the alkyl 1,3-dimethylbut-2-enyl sulphides (VIII; R = alkyl) was to mix the appropriate thiol (1·3 moles) with about 1% (w/w) of 78% aqueous perchloric acid at 5—15° under nitrogen and to add the diene (III) very slowly to this with vigorous stirring. Reaction was quenched by adding a large volume of water. In this way were prepared the sulphides (VIII; R = Et, $\mathrm{Pr^i}$, $\mathrm{Bu^n}$, $\mathrm{Bu^t}$, n-hexyl, 1,1-dimethylbutyl, and 1-ethyl-2-methylpropyl), *i.e.*, the 1,4 polar addition products of thiols with the diene (III). Although the tertiary alkyl derivatives appeared isomerically homogeneous by instrumental analysis, the secondary and primary derivatives contained appreciable proportions of alkyl 1,1-dimethylbut-2-enyl sulphides (IX; R = n- or sec-alkyl). The extent of formation of these isomers by 1,2 addition increased with increasing length of the alkyl chain, as shown by the sequence [percentage of (IX) in (VIII)]: R = Et (2·6%); R = n-Bu (13·8%); R = n-hexyl (23·8%).* The reason for this effect of n-alkyl chain-length on positional selectivity shown by thiols in their addition to 2-methypenta-1,3-diene is at present obscure.


(IX)

From 2,4-dimethylpenta-1,3-diene with 2-methylpropane-2-thiol the diene-dimer was the major product. Briefer reaction at 0° still gave mainly dimer, but containing 16·5% of the expected t-butyl 1,1,3-trimethylbut-2-enyl sulphide. The yield of sulphide, also accompanied by dimer, was increased to 75% when 2·5 moles of thiol per mole of diene were employed. Clearly, in this system the diene molecule is an active nucleophilic reagent capable of markedly competing with the thiol for the very stable intermediate tetramethylallylcarbonium ion. The pure sulphide required as a reference compound was made by the remarkably easy acid-catalysed condensation of 2-methylpropane-2-thiol with 2,4-dimethylpent-3-en-2-ol.[7]

In contrast with this behaviour of the very reactive 2,4-dimethylpenta-1,3-diene, isoprene reacts slowly and incompletely with thiols under the standard conditions, presumably because protonation of isoprene to the intermediate 3,3-dimethylallylcarbonium ion does not compare in ease with corresponding formation of carbonium ion from the other dienes.

EXPERIMENTAL

Gas–liquid chromatographic and infrared spectroscopic analyses were carried out by M. B. Evans and G. M. C. Higgins.

Materials and Intermediates.—Hydrobromic acid was of " AnalaR " grade; thiolacetic acid and simple thiols were commercial specimens carefully redistilled immediately before use. Other reagents, except where stated, were used without further purification. 2-Methylpentan-2-ol was made *via* the Grignard reagent from magnesium and n-propyl bromide by reaction with acetone; it had b. p. 48—49°/35 mm., n_D^{20} 1·4111. Dehydrative distillation of this alcohol over 3% anilinium bromide gave a mixture of 2-methylpent-1-ene (23—25%) and 2-methylpent-2-ene (75—77%); the latter was isolated by careful distillation through a 100-plate fractionating column; it had b. p. 67·4° and was >99·9% isomer pure by gas–liquid chromatographic analysis. 2-Methylpenta-1,3-diene was made by slow distillation through a

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* Authentic derivatives of (IX) were available through the work of Moore and Trego, *Tetrahedron*, 1962, **18**, 205.

[7] Cain, Evans, and Lee, *J.*, 1962, 1694.

Vigreux column of a mixture of 2-methylpentane-2,4-diol (500 ml.), aniline (8 ml.), and 48% aq. hydrobromic acid (10 ml.) to give a two-phase distillate of water, diene, and 4-methylpent-4-en-2-ol (cf. Farmer and Warren [8]). The organic phase was washed thrice with water, dried ($MgSO_4$), and fractionated to give diene (142 g.), b. p. mainly 76·4°.

2-Methylpentane-2-thiol. S-(1,1-*Dimethylbutyl*)*thiuronium toluene*-p-*sulphonate* was made by adding 2-methylpentan-2-ol (102 g., 1 mole) to a solution of thiourea (83·6 g., 1·1 moles) in 48% aqueous hydrobromic acid (150 ml.), gently boiling the mixture under reflux for 30 min., removing the resulting organic phase (*ca.* 28—30 ml. of essentially pure 2-methylpentenes), and adding the cooled aqueous phase to a stirred solution of toluene-*p*-sulphonic acid (200 g.) in water (500 ml.). On slight cooling the salt was deposited, washed (10% aq. hydrobromic acid), and dried *in vacuo* to give plates (226 g., 68%), m. p. 122·5—123·0° (Found: C, 50·5; H, 7·3. $C_{14}H_{24}N_2O_3S_2$ requires C, 50·6; H, 7·2%).

The salt (166 g., 0·5 mole) was added in portions to a cold * solution of sodium hydroxide (30 g., 0·75 mole) and sodium cyanide (1 g.) in water (350 ml.), stirred by a slow nitrogen stream. After 2 hours' stirring the crude thiol was removed by distillation directly to b. p. 95—96°. The thiol was separated *per se* from water in the distillate, washed with water, dried ($MgSO_4$), and distilled to afford a nearly quantitative yield of 2-methylpentane-2-thiol, b. p. 122·5—123°/764 mm., n_D^{20} 1·4389 (Found: C, 60·95; H, 11·95; S, 27·1. Calc. for $C_6H_{14}S$: C, 61·0; H, 11·9; S, 27·1%), of >99·5% purity by (gas–liquid chromatography and titrimetric [9] methods). It gave a mercuric derivative (with warm aqueous mercuric cyanide), m. p. (from ethanol) 77·7° (lit.[10] gives 75—76° for a derivative made from an impure preparation of this thiol).

2-Methylpentane-3-thiol. This was prepared essentially as previously described,[11] from 2-methylpent-2-ene (50·4 g., 1 mol.) and thiolacetic acid (68·4 g., 1·5 mol.), to give 3-acetylthio-2-methylpentane, except that excess of acid was removed by saturated aqueous sodium hydrogen carbonate solution rather than by distillation. The thiolester, after being distilled, was hydrolysed in alkaline aqueous methanol to give the thiol which was isolated by steam-distillation and fractional distillation. The physical properties of these compounds differ slightly from those previously recorded: [11] 3-acetylthio-2-methylpentane, b. p. 77°/18 mm., n_D^{20} 1·4642 (Found: C, 59·9; H, 10·0; S, 20·1. Calc. for $C_8H_{16}OS$: C, 60·0; H, 10·0; S, 20·0%) (lit. b. p. 70°/13 mm., n_D^{25} 1·4603); 2-methylpentane-3-thiol, b. p. 132·5—133·5°, n_D^{20} 1·4498 (Found: C, 61·05; H, 11·9; S, 27·1. Calc. for $C_6H_{14}S$: C, 61·0; H, 11·9; S, 27·1%) (lit. b. p. 135°, n_D^{20} 1·4467). The thiol now described contained 99·7% of 2-methylpentane-3-thiol and only 0·3% of the isomeric 2-methylpentane-2-thiol, a result of interest with regard to the orientation of free-radical addition of thiolacids to a trialkylethylene.

Experiments with 2-Methylpenta-1,3-diene.—(i) *Interaction with hydrobromic acid–thiourea solution.* The diene (82 g., 1·0 mole) was added to a solution of thiourea (83·6 g., 1·1 moles) in 48% aqueous hydrobromic acid (150 ml.) at 10° and the mixture shaken vigorously, with cooling. After 5—6 min. the mixture solidified, exothermically, and the cake, after another 30 min., was shaken into a slurry with cold 20% aqueous hydrobromic acid (100 ml.), filtered off, sucked fairly dry (2 hr.), resuspended in acetone (200 ml.), filtered off, and dried *in vacuo*. The crystalline S-(1,3-*dimethylbut-2-enyl*)*thiuronium bromide* (165 g., 69%) had m. p. 133·5—134·3° (Found: C, 35·2; H, 6·3. $C_7H_{15}N_2SBr$ requires C, 35·2; H, 6·3%).† When an aqueous solution of the thiuronium bromide was heated for 5 min. at 70° there was an odour characteristic of methylpentenols. The resulting solution did not yield a picrate with aqueous picric acid (a sensitive reagent for all *S*-alkenyl- and *S*-alkyl-thiuronium cations) and did not give a

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* This point is most important. At higher temperatures a competing S_N1 hydrolysis (alkyl–S fission) becomes significant, leading to 2-methylpentan-2-ol (b. p. 122°) which cannot easily be removed from the desired thiol.

† [*Added in proof.*] The author is grateful to a Referee for pointing out that the filtrate from this preparation should have been examined for the presence of the isomeric *S*-(1,1-dimethylbut-2-enyl)-thiuronium bromide. This has now been checked by repeating the preparation and adding an excess of alkali to the filtrate. The thiol thus produced was still 99% 4-methylpent-3-ene-2-thiol and contained less than 1% of 1,1-dimethylbut-2-ene-thiol corresponding to the alternative isomeric thiuronium salt. This result served to strengthen the views expressed on p. 5041.

[8] Farmer and Warren, *J.*, 1931, 3221.

[9] Saville, *Analyst*, 1961, **86**, 29.

[10] Moore and R. W. Saville, *J.*, 1954, 2093.

[11] Bordwell and Hewett, *J. Org. Chem.*, 1957, **22**, 980.

thiol on addition of alkali. These results demonstrate the sensitivity of the alkenyl–sulphur bond to S_N1 solvolysis and emphasise the importance of using low temperatures for the alkaline hydrolysis of the thiuronium salt to thiol. Pure 4-*methylpent*-3-*ene*-2-*thiol* was thus obtained as follows: Finely powdered *S*-(1,3-dimethylbut-2-enyl)thiuronium bromide (160 g., 0·67 mole) was added in portions to a cold, stirred solution of sodium hydroxide (40 g., 1·0 mole) and sodium cyanide (0·5 g.) in water (200 ml.) under nitrogen. After 2 hr. the thiol was isolated as described in the preparation of 2-methylpentane-2-thiol. Final distillation over a trace of quinol gave the unsaturated thiol (*ca.* 85—92% yields), b. p. 133·7°/747 mm., n_D^{20} 1·4741 (Found: C, 62·0; H, 10·4; S, 27·6. $C_6H_{12}S$ requires C, 62·05; H, 10·35; S, 27·6%). It was shown to be 99·7% pure by gas–liquid chromatography and titrimetric [9] methods. Infrared spectra showed the absence of *trans*-dialkylethylenic and terminal ethylenic groups, while a band at 838 cm.$^{-1}$ was consistent with the presence of trialkylethylenic groups.

When ozonised oxygen was passed through the thiol (0·864 g.) in ethanol (60 ml.) until free ozone was detected in the effluent gas the ozone consumption was 1·225 moles of ozone/mole of thiol. Bulb-to-bulb high-vacuum distillation was then used to trap volatile products which when added to 2,4-dinitrophenylhydrazine (2·0 g.) in 2N-aqueous hydrochloric acid (500 ml.) gave a crude hydrazone (1·357 g.), 69·5% assuming it to be the acetone derivative, m. p. 110—113°, raised by one crystallisation from ethanol to m. p. 124—125·5° and mixed m. p. with pure acetone 2,4-dinitrophenylhydrazone, 124—125·5° (Found: C, 45·7; H, 4·2. Calc. for $C_9H_{10}N_4O_4$: C, 45·4; H, 4·2%).

(ii) *Acid-catalysed addition of thiols to 2-methylpenta*-1,3-*diene*. In preliminary experiments, made with ethanethiol and 2-methylpropane-2-thiol, little condensation could be effected by shaking the thiol–diene mixture with 48% aqueous hydrobromic acid, and the main product (after shaking for 12 hr. at room temperature) was crude alkenyl bromide which decomposed on attempted distillation. Some addition occurred when the thiol–diene mixtures were added to 3 volumes of glacial acetic acid containing up to 2% perchloric acid (w/w) but the sulphidic products were always contaminated with hydrocarbon material, probably the diene dimers (dimethyl-*p*-menthadienes [6]) formed immediately in at least 90% yield on adding 78% aqueous perchloric acid (1 ml.) to 2-methylpenta-1,3-diene (8·2 g.) in glacial acetic acid (50 ml.). This product could not be distilled because of excessive foaming (Found: C, 86·7; H, 12·3%; *M*, 179—182. Calc. for $C_{12}H_{20}$: C, 87·8; H, 12·2%; *M*, 164).

Conditions suitable for obtaining pure sulphides in 80—95% yield are as follows: to the thiol (0·13 mole) was added with stirring under nitrogen at 5—15° 78% perchloric acid (0·06—0·14 ml., according to the molecular weight of the thiol). The diene (8·2 g., 0·10 mole) was then added from a microburette during 45—60 min. (or up to 2 hr. in larger-scale preparations). The cooling source was removed and stirring continued for 1 hr. before adding water (30 ml.). extracting with ether (2 × 25 ml.), and washing the extracts with aqueous sodium hydrogen carbonate solution. The ethereal extracts were then dried ($MgSO_4$), the solvent removed, and the residue distilled to give the sulphides detailed in Table 1.

TABLE 1.

Products ($Me_2C{:}CH{\cdot}CHMe{\cdot}SR$) of acid-catalysed 1,4-addition of thiols to 2-methylpenta-1,3-diene.

			Found (%)			Required (%)		
R	B. p./mm.	n_D^{20}	C	H	S	C	H	S
Ethyl	60·5—61·5°/13	1·4753	66·5	11·1	22·3	66·7	11·1	22·2
Isopropyl	66—68°/15	1·4706	68·2	11·4	20·2	68·4	11·4	20·2
n-Butyl	38°/0·08	1·4737	69·4	11·7	19·3	69·8	11·6	18·6
t-Butyl	80·0°/10	1·4690	69·6	11·7	18·7	69·8	11·6	18·6
n-Hexyl	66·0°/0·08	1·4738	71·8	12·1	16·1	72·0	12·0	16·0
1,1-Dimethylbutyl	40—41°/0·03	1·4730	72·1	12·0	15·9	72·0	12·0	16·0
1-Ethyl-2-methylpropyl	97—98·5°/6	1·4728	71·8	12·1	16·0	72·0	12·0	16·0

Some of the primary alkyl derivatives contained substantial proportions of isomeric alkyl 1,1-dimethylbut-2-enyl sulphides (via 1,2-addition) as determined by infrared spectra and gas–liquid chromatography by reference to authentic derivatives.

Experiments with 2,4-Dimethylpenta-1,3-*diene*.—The diene [12] (0·4 mole) was added to

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[12] Kelso, Greenlee, Derfer, and Boord, *J. Amer. Chem. Soc.*, 1955, **77**, 1751.

2-methylpropane-2-thiol (1 mole) in acetic acid (200 ml.) containing 78% perchloric acid (2 ml.) under nitrogen during 10 hr. The product, isolated as usual, had b. p. 91—98°/15 mm., n_D^{20} 1·4803 (Found: S, 2·2%), and was mainly 3,3,5,5-tetramethyl-*p*-mentha-1,8-diene (cf. lit.[13-15]) whose structure was confirmed by infrared spectral analysis. Similar results were obtained when the diene addition was performed explicitly according to the technique successful for 2-methylpenta-1,3-diene reactions.

When the diene (0·1 mole) was added during 15 min. to the thiol (0·13 mole) and 78% perchloric acid (0·1 ml.) at 0°, and the mixture worked up after a further 30 min. at room temperature, a fraction, b. p. 94—96°/15 mm., n_D^{20} 1·4792, was obtained which contained 16·5% of t-butyl 1,1,3-trimethylbut-2-enyl sulphide. By adding the diene (0·1 mole) to 2-methylpropane-2-thiol (0·25 mole) and 78% perchloric acid (0·1 ml.) during 3·5 hr. at 10°, the product had b. p. 86—87·5°/15 mm., n_D^{20} 1·4797 (Found: C, 71·7; H, 11·8; S, 14·2. Calc. for $C_{11}H_{22}S$: C, 70·9; H, 11·9; S, 17·2%), and was 75% sulphide still contaminated by the cyclic diene dimer. Authentic t-butyl 1,1,3-trimethylbut-2-enyl sulphide required to establish the quantitative aspects of this work, was prepared by Mr. M. E. Cain [7] (see p. 5042) by a method already published.

Attempted Addition of Propane-2-thiol to Isoprene.—To the thiol (19·8 g., 0·26 mole) containing 78% perchloric acid (0·2 ml.) at 10°, under nitrogen, isoprene (13·6 g., 0·20 mole) was added during 1 hr. The mixture was stirred for a further hour at 10° and was then added to water (100 ml.), extracted with ether (2 × 50 ml.), and the extracts dried and distilled. Much unchanged thiol and isoprene were recovered and the residue (1·39 g.) (Found: C, 63·8; H, 11·3; S, 23·8. Calc. for $C_8H_{16}S$: C, 66·7; H, 11·1; S, 22·2%) was a mixture of isopropyl 3-methylbut-2-enyl sulphide and unidentified material.

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[13] Mereshkowski, *J. Russ. Phys. Chem. Soc.*, 1913, **45**, 1967.

[14] Whitby and Gallay, *Canad. J. Res.*, 1932, **6**, 282, 287.

[15] Levina and Jegorova, *Zhur. obshchei Khim.*, 1946, **16**, 824.