468. *The Addition of Thiolacetic Acid to Unsaturated Compounds.*

By R. Brown, W. E. Jones, and A. R. Pinder.

The reaction of thiolacetic acid with a variety of unsaturated compounds has been investigated. Addition products have been obtained in high yield, thiolacetic acid being in general a vigorous additive agent.

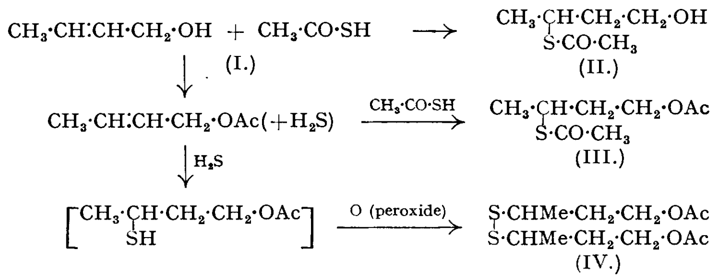
The investigations by Ipatieff and his co-workers (*J. Amer. Chem. Soc.*, 1938, **60**, 2731; 1939, **61**, 71) have shown that the direction of addition to asymmetrical olefinic hydrocarbons of the two fragments produced by scission of the S–H bond in a thiol may be " normal " or " abnormal " with respect to Markownikoff's rule. " Normal " addition occurred in the presence of acids, whereas in the absence of catalysts " abnormal " addition was observed. Jones and Reid (*ibid.*, 1938, **60**, 2452) and Kharasch, Read, and Mayo (*Chem. and Ind.*, 1938, **16**, 752) found that traces of peroxides catalysed " abnormal " addition very strongly.

Thiolacetic acid has been studied as an additive agent by a number of workers. Holmberg (*Arkiv Kemi, Min., Geol.*, 1938, **12**, B, No. 47) obtained 2-phenylethyl thiolacetate by " abnormal " addition of the acid to styrene, and Ipatieff and Friedman (*J. Amer. Chem. Soc.*, 1939, **61**, 71) showed that the addition of thiolacetic acid to a series of aliphatic olefins was " abnormal " in character. More recently, Cunneen (*J.*, 1947, 134) has investigated the addition to cyclic olefins and rubber (cf. U.S.P. 2,419,943, 2,420,194). 3-Chloropropyl thiolacetate was obtained by Sjöberg (*Ber.*, 1941, **74**, 64) by addition of thiolacetic acid to allyl chloride, and addition of the acid to αβ-unsaturated carboxylic acids has been reported by Holmberg and Schjånberg (*Ber.*, 1941, **74**, 1751), Peppel (U.S.P., 2,408,095) and Owen and his co-workers (*J.*, 1947, 1030; 1949, 3105, 3109). Catch, Cook, Graham, and Heilbron (*J.*, 1947, 1609) have found that simple αβ-unsaturated aldehydes react additively with thiolacetic acid. In the majority of cases, addition occurred readily, and the thiolacetates were obtained in high yield. In additions to αβ-unsaturated carbonyl compounds, the thiolacetate group invariably appeared at the β-carbon atom.

The present work, carried out in 1944 and 1945 in connexion with investigations in the penicillin field, describes the addition of thiolacetic acid to some unsaturated hydrocarbons, aldehydes, ketones, alcohols, and esters, in the presence of added peroxide.

The addition of thiolacetic acid to olefinic hydrocarbons occurred exothermically and with great ease (cf. Cunneen, *loc. cit.*). Oct-1-ene and hexadec-1-ene gave high yields of, respectively, *n*-octyl and *n*-hexadecyl thiolacetate, the " abnormal " products. Hydrolysis furnished the corresponding thiols, characterised as the 2 : 4-dinitrophenyl sulphides. With oct-2-ene, a quantitative yield of a product presumed to be a mixture of 2- and 3-acetylthio-*n*-octane was obtained. Thiolacetic acid and α-methylstyrene gave in high yield a product almost certainly resulting from " abnormal " addition, *i.e.*, 2-phenyl-*n*-propyl thiolacetate.

Acraldehyde and crotonaldehyde reacted readily with thiolacetic acid to give β-acetylthiopropaldehyde and -*n*-butaldehyde, respectively. These products were characterised as their 2 : 4-dinitrophenylhydrazones, which were identical with products of proved structure obtained by Catch, Cook, Graham, and Heilbron (*loc. cit.*). With cinnamaldehyde was obtained an addition product to which has been assigned the formula of β-acetylthio-β-phenylpropaldehyde, by analogy. High yields of addition products were also obtained with mesityl oxide and benzylideneacetone; it is almost certain that the thiolacetate group is at $C_{(\beta)}$, in the light of previous experience.



$$\mathrm{CH_3{\cdot}CH{:}CH{\cdot}CH_2{\cdot}OH + CH_3{\cdot}CO{\cdot}SH \longrightarrow \underset{S\cdot CO\cdot CH_3}{CH_3{\cdot}CH}{\cdot}CH_2{\cdot}CH_2{\cdot}OH}\quad \text{(II.)}$$

$$\downarrow\ \text{(I.)}$$

$$\mathrm{CH_3{\cdot}CH{:}CH{\cdot}CH_2{\cdot}OAc(+H_2S) \xrightarrow{CH_3\cdot CO\cdot SH} \underset{S\cdot CO\cdot CH_3}{CH_3{\cdot}CH}{\cdot}CH_2{\cdot}CH_2{\cdot}OAc}\quad \text{(III.)}$$

$$\downarrow\ \mathrm{H_2S}$$

$$\left[\mathrm{\underset{SH}{CH_3{\cdot}CH}{\cdot}CH_2{\cdot}CH_2{\cdot}OAc}\right] \xrightarrow{\text{O (peroxide)}} \begin{matrix}\mathrm{S{\cdot}CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}OAc}\\ \mathrm{S{\cdot}CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}OAc}\end{matrix}\quad \text{(IV.)}$$

The addition of thiolacetic acid to allyl alcohol gave an almost quantitative yield of 3-acetylthio-*n*-propanol which, on hydrolysis, furnished 3-mercapto-*n*-propanol, identified as

Additive reactions of thiolacetic acid.

Unsaturated compound.	Product.	B. p., etc.	Yield, %.	Formula.	S, %. Found.	S, %. Reqd.	Derivative.	Formula.	Found, %.	Reqd., %.
α-Methylstyrene	2-Phenyl-*n*-propyl thiolacetate	105°/4 mm. n_D^{20} 1·5429	90	$C_{11}H_{14}OS$	16·6	16·5	2-Phenyl-*n*-propanethiol; b. p. 74°/1 mm.; n_D^{20} 1·5510	$C_9H_{12}S$	S, 21·3	S, 21·05
Oct-1-ene	*n*-Octyl thiolacetate	132—133°/23 mm. n_D^{20} 1·4648	100	$C_{10}H_{20}OS$	17·4	17·0	2 : 4-Dinitrophenylthio-*n*-octane; plates, m. p. 78° [1]	$C_{14}H_{20}O_4N_2S$	N, 8·9	N, 9·0
Oct-2-ene	2- and 3-Acetylthio-*n*-octane	123—126°/28 mm.	100	$C_{10}H_{20}OS$	17·4	17·0	*n*-Octane-2- and -3-thiol; b. p. 92°/36 mm.	$C_8H_{18}S$	S, 21·9	S, 21·5
Hexadec-1-ene	*n*-Hexadecyl thiolacetate	168°/1·5 mm. m.p. 30·5°	75	$C_{18}H_{36}OS$	10·0	10·7	2 : 4-Dinitrophenylthio-*n*-hexadecane; plates, m. p. 91° [2]	$C_{22}H_{36}O_4N_2S$	N, 6·4	N, 6·6
Acraldehyde	β-(Acetylthio)propaldehyde [3]	66—70°/1 mm. n_D^{20} 1·5079	65	$C_5H_8O_2S$	24·1	24·2	2 : 4-Dinitrophenylhydrazone; yellow needles, m.p. 128° [4]	$C_{11}H_{12}O_5N_4S$	C, 42·4 H, 3·9 N, 17·9	C, 42·3 H, 3·85 N, 17·9
Crotonaldehyde	β-Acetylthio-*n*-butaldehyde [5]	59—60°/2 mm. n_D^{20} 1·5025	100	$C_6H_{10}O_2S$	22·8	21·9	2 : 4-Dinitrophenylhydrazone; golden prisms, m. p. 95° [6]	$C_{12}H_{14}O_5N_4S$	C, 44·9 H, 4·4 N, 17·5	C, 44·2 H, 4·3 N, 17·2
Cinnamaldehyde	β-Acetylthio-β-phenylpropaldehyde	115—117°/1 mm. m. p. 44°	90	$C_{11}H_{12}O_2S$	15·3	15·4	2 : 4-Dinitrophenylhydrazone; yellow needles, m. p. 145°	$C_{17}H_{16}O_5N_4S$	C, 53·1 H, 4·2 N, 14·5	C, 52·6 H, 4·1 N, 14·4
Mesityl oxide	4-Acetylthio-4-methyl-*n*-pentan-2-one	84—86°/6 mm.	92	$C_8H_{14}O_2S$	18·4	18·4	2 : 4-Dinitrophenylhydrazone; orange-red prisms, m. p. 83—84°	$C_{14}H_{18}O_5N_4S$	C, 47·7 H, 5·0 N, 15·6	C, 47·5 H, 5·1 N, 15·8
Benzylideneacetone	4-Acetylthio-4-phenyl-*n*-butan-2-one	m. p. 67—68°	90	$C_{12}H_{14}O_2S$	13·8	14·4	2 : 4-Dinitrophenylhydrazone; orange-red prisms, m. p. 128—129°	$C_{18}H_{18}O_5N_4S$	C, 54·4 H, 4·4 N, 14·0	C, 53·7 H, 4·5 N, 13·9
Allyl alcohol	3-Acetylthio-*n*-propan-1-ol	72—75°/1·5 mm. n_D^{20} 1·4827	97	$C_5H_{10}O_2S$	23·9	23·9	*p*-Nitrobenzoate; plates, m. p. 76°	$C_{12}H_{13}O_5NS$	C, 51·3 H, 4·7 N, 5·1	C, 50·9 H, 4·6 N, 5·0
							3-Mercapto-*n*-propanol bis-α-naphthylurethane, needles, m. p. 174—175° [7]	$C_{25}H_{23}O_3N_2S$	N, 6·8	N, 6·5
Crotyl alcohol	3-Acetylthio-*n*-butan-1-ol	85°/15 mm. n_D^{20} 1·4605	55	$C_6H_{12}O_2S$	21·5	21·6	—	—	—	—
2-Methylallyl alcohol	3-Acetylthio-2-methyl-*n*-propan-1-ol	121—122°/23 mm. n_D^{20} 1·4856	77	$C_6H_{12}O_2S$	21·7	21·6	—	—	—	—
Eugenol	3′-Acetylthio-4-hydroxy-3-methoxy-*n*-propylbenzene	180°/1·5 mm.	78	$C_{12}H_{16}O_3S$	13·1	13·3	Benzoate; prisms, m. p. 80—81°	$C_{19}H_{20}O_4S$	C, 66·0 H, 6·0 S, 9·4	C, 66·3 H, 5·8 S, 9·3
Allyl acetate	3-Acetylthio-*n*-propyl acetate	125°/24 mm. 90°/4 mm. n_D^{20} 1·4720	100	$C_7H_{12}O_3S$	18·3	18·2	3-Mercapto-*n*-propanol bis-α-naphthylurethane, needles, m. p. 174—175° [7]	$C_{25}H_{22}O_3N_2S$	N, 6·8	N, 6·5
Crotyl acetate	3-Acetylthio-*n*-butyl acetate	110°/11 mm. n_D^{20} 1·4674	74	$C_8H_{14}O_3S$	16·5	16·8	—	—	—	—
2-Methylallyl acetate	3-Acetylthio-2-methyl-*n*-propyl acetate	133—134°/24 mm. n_D^{20} 1·4693	80	$C_8H_{14}O_3S$	16·8	16·8	—	—	—	—
Cinnamyl acetate	3-Acetylthio-3-phenyl-*n*-propyl acetate	124—130°/1 mm. n_D^{20} 1·5292	38	$C_{13}H_{16}O_3S$	13·2	12·7	—	—	—	—
Maleic anhydride	(Acetylthio)succinic anhydride	m. p. 76—77°	83	$C_6H_6O_4S$ *	18·6	18·4	—	—	—	—

[1] Bost, Turner, and Norton, *J. Amer. Chem. Soc.*, 1932, **54**, 1985, give m. p. 78°. [2] *Idem, ibid.*, give m. p. 91°. [3] Catch, Cook, Graham, and Heilbron, *J.*, 1947, 1610, give b. p. 92—93°/14 mm., yield 68%. [4] *Idem, ibid.*, give m. p. 127·5°. [5] *Idem, ibid.*, give b. p. 91—92°/11 mm. and yield 65%. [6] *Idem, ibid.*, give m. p. 96°. [7] Undepressed on admixture with an authentic specimen, m. p. 174—175°. * Found : C 41·8; H, 3·6. Calc. : C, 41·4; H, 3·45%.

its bis-α-naphthylurethane. Allyl acetate behaved in a similar manner. Crotyl alcohol (I) gave a product presumed by analogy to be 3-acetylthio-*n*-butan-1-ol (II), together with (probably) the acetate of this product (III) and the disulphide (IV). The formation of these substances is envisaged on page 2123.

Addition products, probably of analogous structure, have also been obtained in good yield with 2-methylallyl alcohol, eugenol, crotyl acetate, and 2-methylallyl acetate, but with cinnamyl acetate a poor yield was afforded. No addition was observed to occur with cinnamyl alcohol and stilbene (cf. Posner, *Ber.*, 1905, **38**, 646).

The results are summarised in the Table.

EXPERIMENTAL.

Preparation of Thiolacetates.—The following are typical reaction conditions. Thiolacetic acid (1—2 mols.) was added dropwise, with shaking and cooling, to a mixture of the unsaturated compound (1 mol.) and ascaridole (few drops) or benzoyl peroxide (few mg.). In some cases reaction was immediate; in others the reaction was completed by heating the solution under reflux on the water-bath for several hours. The mixture was worked up by fractional distillation *in vacuo*. In a few cases the reaction product crystallised, and was collected and recrystallised from a suitable solvent.

Characterisation of Thiolacetates.—Hydrolysis of the thiolacetates was effected by boiling with aqueous potassium hydroxide. The thiols so obtained were characterised as their phenyl- or α-naphthylurethanes, or as their condensation products with chloro-2 : 4-dinitrobenzene. Aldehydic and ketonic thiolacetates were characterised as their 2 : 4-dinitrophenylhydrazones. Alcoholic products were converted into the benzoate or *p*-nitrobenzoate.

Addition of Thiolacetic Acid to Crotyl Alcohol.—Crotyl alcohol (50 g.), thiolacetic acid (53 g.), and ascaridole (5 drops) were mixed and kept overnight, and then heated under reflux on the water-bath for 2 hours. Fractionation gave three products: (i) 57 g. of 3-*acetylthio*-n-*butan*-1-*ol*, b. p. 85°/15 mm., n_D^{20} 1·4605 (Found: S, 21·5. $C_6H_{12}O_2S$ requires S, 21·6%); (ii) 20 g. of 3-*acetylthio*-n-*butyl acetate*, b. p. 90°/4 mm. (Found: S, 16·7; Ac, 45·2. $C_8H_{14}O_3S$ requires S, 16·8; Ac, 45·3%); (iii) 10 g. of *bis*-3-*acetoxy*-1-*methyl*-n-*propyl disulphide*, b. p. 158°/3 mm. (Found: S, 22·2; Ac, 31·9. $C_{12}H_{22}O_4S_2$ requires S, 21·8; Ac, 29·3%).

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