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REACTIONS OF THIOLS WITH UNSATURATED COMPOUNDS

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The addition of thiols to unsaturated compounds has been widely studied, and work up to 1940 has been reviewed by Mayo and Walling (1). With α,β-unsaturated esters and ketones the sulfur atom becomes attached to the electron-deficient β-carbon atom, undoubtedly through an ionic mechanism. While it has been noted that this reaction sometimes takes place without a catalyst (2), many catalysts have been tried, including mercuric salts (3), light (4), and peroxides (5). Most successful, as would be expected, have been the basic catalysts, such as sodium alkoxides (6–8), piperidine (2), benzyltrimethylammonium hydroxide (7, 9), and anhydrous potassium carbonate (9). Addition of mercaptans to water-soluble α,β-unsaturated acids has been carried out on the sodium salts in aqueous solution (7, 10).

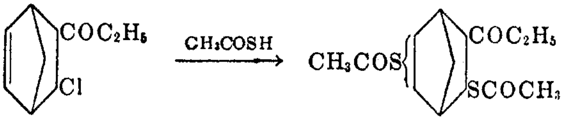
The addition of thiols to isolated double bonds may take two courses: addition in accordance with Markownikoff's rule occurs in the presence of sulfur and sulfuric acid, while in the absence of added catalyst, addition takes place contrary to the rule, apparently by a free radical mechanism. The latter reaction is promoted by oxygen, organic peroxides, and light, and is inhibited by hydroquinone and piperidine.

In connection with a screening program against various pathogens, we were interested in preparing the mercaptan addition products of itaconic esters and the thioacetic acid addition products of certain diene adducts.

The reaction with itaconic esters proceeds readily in the presence of potassium carbonate as catalyst, but no reaction was observed with benzoyl peroxide as catalyst. An attempt to add dodecyl mercaptan to an alkaline, aqueous solution of sodium itaconate was not successful, in contrast to the reaction of benzyl mercaptan with aqueous sodium acrylate, reported by Hurd and Gershbein (7). As might be expected, the potassium carbonate-catalyzed addition of methyl mercaptan to diallyl itaconate inhibited with hydroquinone gave diallyl methylthiomethylsuccinate, no reaction occurring at the isolated double bonds. Tripropyl aconitate was also employed in one experiment with lauryl mercaptan, and addition was achieved in the presence of potassium carbonate.

While the addition product of benzyl mercaptan and diethyl itaconate was readily converted to a crystalline diester sulfone by treatment with hydrogen peroxide in glacial acetic acid, oxidation of most of the other addition products gave syrups.

Thioacetic acid was successfully added in the absence of a catalyst to the ethylenic linkage in the dibutyl ester of the adduct of cyclopentadiene with maleic anhydride, and in the adducts of cyclopentadiene with methyl and ethyl vinyl ketone. In the reaction of thioacetic acid with the adduct of cyclopentadiene and ethyl β-chlorovinyl ketone, not only did addition occur, but the chlorine was displaced by a thioacetyl group:



We were unable to find an analagous reaction in the literature. An attractive mechanism for the introduction of the second thioacetyl residue would involve dehydrohalogenation of the original adduct followed by addition of the thio acid to the conjugated double bond. It is interesting to note, however, that this chlorinated adduct is recovered unchanged after treatment at 90–95° with saturated sodium carbonate solution or with a solution of sodium in the monoethyl ether of diethylene glycol.

EXPERIMENTAL

MERCAPTAN ADDITIONS

In the addition of mercaptans to α,β-unsaturated esters, the mercaptan was added slowly to a stirred mixture of the ester with 10 g. of anhydrous potassium carbonate per mole, the temperature being maintained at 45° or less by cooling the flask as necessary. (The 0.01% hydroquinone present in the itaconates as a polymerization inhibitor was not removed.) When addition was complete and the reaction had subsided the mixture was stirred at room temperature for a period of 3–18 hours, then filtered and distilled at reduced pressure. Equimolar proportions were employed except in the experiments involving methyl mercaptan, where the gas was introduced until heat was no longer evolved. Table I summarizes the data, and several of the experiments are described in greater detail below.

Addition of methyl mercaptan to diethyl itaconate. Methyl mercaptan gas was introduced into a stirred mixture of 93 g. (0.5 mole) of diethyl itaconate and 5 g. of anhydrous potassium carbonate, with cooling to maintain the temperature between 30 and 45°, until heat was no longer evolved. The increase in weight was 23.6 g. (theory 24.0 g.). The gelatinous reaction mixture was taken up in hot benzene and filtered by gravity to remove the catalyst. Although colorless at first, the filtrate began to darken and on cooling formed a gel. The benzene was, therefore, removed and replaced by several hundred ml. of ether, and the solution was filtered from a very small amount of solid. The filtrate was concentrated and the product was distilled under reduced pressure.

In a second experiment 0.5 g. of benzoyl peroxide was substituted for the 5 g. of potassium carbonate. This time no heat was evolved, and the unreacted ester was recovered.

Addition of methyl mercaptan to diallyl itaconate. Methyl mercaptan was introduced into a stirred mixture of 105 g. (0.5 mole) of diallyl itaconate and 5 g. of potassium carbonate, the temperature being maintained at 30–50° by external cooling. After three hours 86 g. of mercaptan had been passed into the flask (theory for three equivalents per mole: 72 g.), and the temperature began to fall. The catalyst was filtered off, and the reaction mixture was concentrated and distilled under reduced pressure. Redistillation was necessary to free the product from 5–10% of unreacted diallyl itaconate.

Attempted addition of n-dodecyl mercaptan to sodium itaconate. One mole (130 g.) of itaconic acid was dissolved in a solution of 82 g. of sodium hydroxide in 500 ml. of water. This solution (*p*H 8) was stirred at 90–95° for four hours with 210 g. (1.04 mole) of *n*-dodecyl mercaptan, and then left at room temperature for two days. The original reactants were recovered unchanged.

Oxidation of the addition product of benzyl mercaptan and diethyl itaconate. The addition product (77.6 g.; 0.25 mole) was dissolved in 85 ml. of glacial acetic acid, and 85 g.

TABLE I

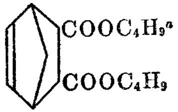
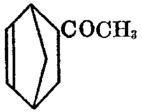
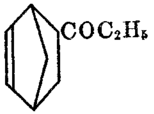
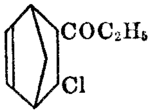
Additional Reactions of Mercaptans with Unsaturated Esters

UNSATURATED ESTER	MERCAPTAN	YIELD, %	B.P., °C.	MM.	d_4^{20}	n_D^{25}	SAP. NO.		FORMULA	ANALYSES					
										Calc'd			Found		
							Calc'd	Found		C	H	S	C	H	S
Diethyl itaconate	Methyl[a, b]	0	—	—	—	—	—	—	—	—	—	—	—	—	—
Diethyl itaconate	Methyl	75	145–147.5	9	1.073	1.4612	479	473	$C_{10}H_{18}O_4S$	51.26	7.74	13.69	51.30	7.70	13.62
Diethyl itaconate	*n*-Butyl	84	134	0.6	1.039	1.4600	406	396	$C_{13}H_{24}O_4S$	56.49	8.75	11.60	56.45	8.77	11.61
Diethyl itaconate	Octyl	82	152–162	.25	0.970	1.4582	337	334	$C_{17}H_{22}O_4S$	61.40	9.70	9.65	61.23	9.83	9.76
Diethyl itaconate	*n*-Dodecyl[b]	33	190–205	.4	0.968	1.4624	289	292	$C_{21}H_{40}O_4S$	64.90	10.38	8.25	64.86	10.31	8.29
Diethyl itaconate	Phenyl	60	143–143.5	.5	1.118	1.5133	379	467[c]	$C_{15}H_{20}O_4S$	60.78	6.80	10.82	60.62	6.77	10.87
Diethyl itaconate	Benzyl	75	165–168	.45	1.115	1.5140	361	376	$C_{16}H_{22}O_4S$	61.91	7.15	10.32	61.88	7.15	10.44
Diallyl itaconate	Methyl	27	110–120	.05	1.091	1.4830	434	444	$C_{12}H_{18}O_4S$	55.79	7.02	12.41	55.73	7.02	12.42
Tripropyl aconitate	*n*-Dodecyl[b]	49	238–245	.9	0.991	1.4620	336	339	$C_{27}H_{50}O_6S$	64.50	10.03	6.38	64.65	10.13	6.21

[a] Benzoyl peroxide catalyst. [b] No noticeable heat evolved. [c] Average of 7 determinations on the products of 2 runs, employing 1, 2, and 3 hr. saponifications in 50–50 ethanol-0.2 *N* aq. caustic. Individual values varied from 445 to 487.

TABLE II

Addition Reactions of Thioacetic Acid with Cyclopentadiene Adducts

ADDUCT	THIOACETIC ADDITION YIELD, %	B.P., °C.	MM.	d_4^{20}	n_D^{25}	FORMULA	ANALYSES					
							Calc'd			Found		
							C	H	S	C	H	S
	77	157–184	0.07	1.128	1.4910	$C_{19}H_{30}O_5S$	61.59	8.16	8.66	61.76	8.26	8.55
	76	94–96	.05	1.107	1.5184	$C_{11}H_{16}O_2S$	62.23	7.60	15.10	62.18	7.62	15.34
	86	107–108	.04	1.120	1.1520	$C_{12}H_{18}O_2S$	63.68	8.02	14.14	63.70	8.15	14.22
	51[b]	155–158	.06	1.194	1.5396	$C_{14}H_{20}O_3S_2$	55.97	6.71	21.35	56.11	6.87	21.27

[a] Prepared by esterifying the anhydride with butanol.

[b] Based on thioacetic acid.

of 30% hydrogen peroxide was added with cooling. When the reaction had subsided the mixture was allowed to stand at room temperature for two days. It was then concentrated and cooled. The crystalline product was recrystallized from ethanol; m.p. 68–69°; yield 67 g. (78%).

Anal. Calc'd for $C_{16}H_{22}O_6S$: C, 56.12; H, 6.48; S, 9.37; Sapon. no. (3 groups), 492.
Found: C, 55.96; H, 6.51; S. 9.39; Sapon. no., 494.

Infrared absorption. The absence of vinyl absorption bands at 6.1 and 10.5 microns showed the itaconic ester addition products to be free from starting material. Spectra were taken in chloroform.

THIOACETIC ACID ADDITIONS

Thioacetic acid was added to the ethylenic linkages in several Diels-Alder adducts of cyclopentadiene. The purified adduct was mixed with 1.3 moles of thioacetic acid without a catalyst. The reaction was strongly exothermic, and it was necessary to add the thioacetic acid dropwise with cooling. Distillation under reduced pressure gave the products described in Table II. They were colorless liquids except where otherwise noted.

Addition of thioacetic acid to the ethyl β-chlorovinyl ketone adduct of cyclopentadiene. The adduct (37 g.; 0.2 mole) was added dropwise to thioacetic acid (20 g.; 0.26 mole) with cooling. The temperature rose briefly to 80°, then dropped. After all the adduct had been added the mixture was allowed to stand at room temperature for an hour and then was distilled in a vacuum. Redistillation of the crude product gave 20 g. of a pale-yellow, viscous product, collected at 155–158° at 0.06 mm. The elemental analysis is given in Table II. These data, together with a value of 0.02% chlorine, demonstrate that two thioacetyl groups have entered the molecule.

Infrared absorption. Addition of thioacetic acid to these diene adducts introduces a new peak into the infrared spectrum at 5.95–6.0 microns, corresponding to the carbonyl of the thioacetyl group and distinguishable from the ketone or ester carbonyl band which is at slightly lower wavelength. As can be seen from Figure 1, the addition product of the ethyl chlorovinyl ketone adduct has a stronger band at 5.95 than at 5.85, consistent with the fact that two thioacetyl groups are present. In the other ketone products these bands are of equal intensity, and in the dibutyl ester, the ester carbonyl is the stronger.

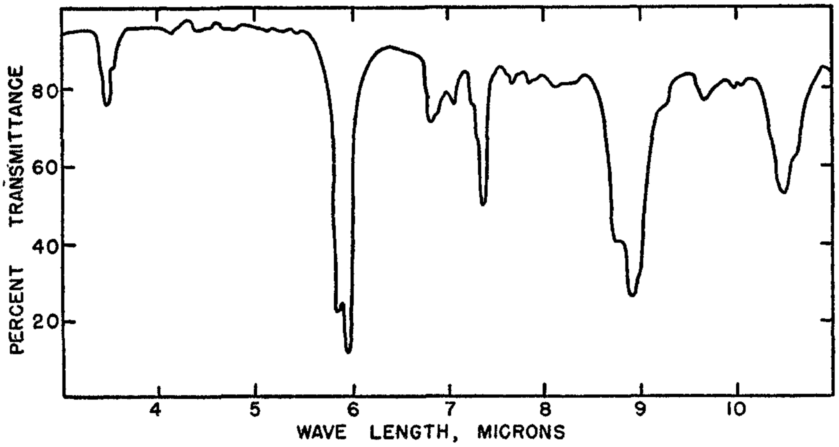
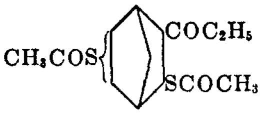


FIGURE 1. INFRARED ABSORPTION SPECTRUM OF



New absorption not present in the spectra of the original adducts is also found at 8.9 and 10.5 microns. These two peaks are also present in the spectrum of acetylthioitamalic acid (I) and are absent in thioitamalic acid (II).

(I) $CH_3COSCH_2CH(COOH)CH_2COOH$ (II) $HSCH_2CH(COOH)CH_2COOH$

These peaks are also given by ethyl and *n*-butyl thiolacetates, as reported by Noda, *et al.* (11), who tentatively assign the 8.9 peak to stretching vibration of the C—S linkage.

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SUMMARY

Addition products of mercaptans with itaconic, and in one case aconitic, esters have been prepared with potassium carbonate as catalyst.

The addition of thioacetic acid to the residual unsaturation of certain diene adducts proceeds readily with evolution of heat, no catalyst being added.

Addition of thioacetic acid to the double bond of the ethyl β-chlorovinyl ketone adduct of cyclopentadiene is accompanied by displacement of the chlorine by a second thioacetyl group.

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