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PREPARATION AND ALKYLATION OF SUBSTITUTED β-HYDROXYDITHIOCINNAMIC ACIDS

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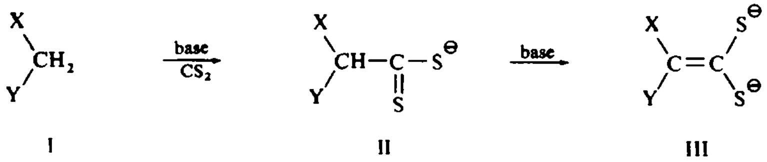
Abstract— A number of substituted β-hydroxydithiocinnamic acids have been prepared. By use of so-called ion-pair extraction technique a general method has been found for the preparation of β-hydroxydithiocinnamic esters in high yields. From these esters both symmetrical and unsymmetrical ketene mercaptals have been synthesized, and in some cases thio-Claisen rearrangement and subsequent ring-closure reactions have been observed.

INTRODUCTION

It is known that active methylene compounds (I) in the presence of a base easily undergo reactions with carbon disulphide giving II, where X and/or Y are electron-withdrawing groups, and II reacts further with the base giving the dianion, III.



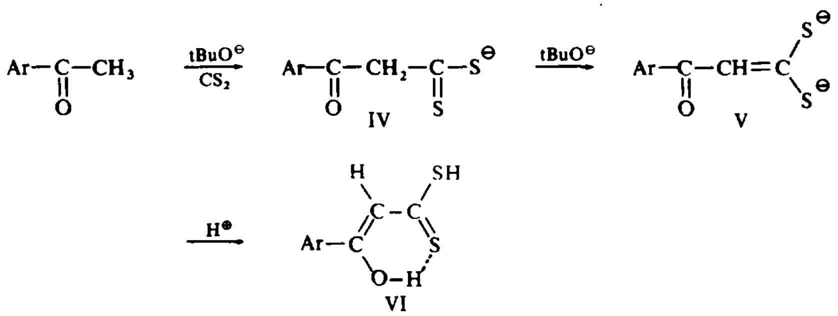
A search in the literature shows that quite a few types of active methylene compounds have been reacted with carbon disulphide: Malodinitril,[1-7] cyano acetates,[1-3,5,6,8,9] cyano acetamide,[1,2,5,6,8,9] nitriles,[1-4,9] nitromethane,[9] ketones,[8-19] aldehydes,[20] lactones,[21] cyclopentadienyl cations,[22] phenols,[23] β-ketoesters,[1] 1,2-dithiol-3-thiones,[24] sulphoxides,[25] sulphones[1,25] and some quaternary pyridines and quinolines.[1]

In all cases, using bases like alkali-hydroxides, -alcoholates, -hydrides, and -amides, the dianion (III) is formed exclusively and subsequent alkylation produces ketene mercaptals. In a few cases the monoanion (II) has been produced from III with one equivalent of acid.[9] It is further observed that very few types of dithioacids, derived from active methylene compounds (I) are stable.[6]

In connection with our work on thio-Claisen rearrangements on thiophenes,[26] enethiols,[27] and ketene mercaptals from malonic esters,[28] cyanoacetates,[29] β-diketones,[29] and β-keto esters,[29] we have also investigated the stable β-hydroxydithiocinnamic acids, the result of which is presented here.

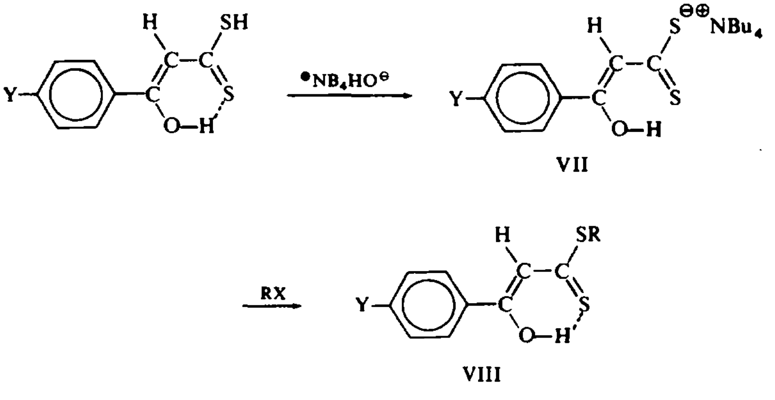
SYNTHETIC STUDIES

The preparation of substituted β-hydroxydithiocinnamic acids has been performed earlier.[10-13, 16, 18, 19] It was now found that by using potassium t-butoxide as a new base, in most cases higher yields of dithioacids are found than by other known methods and also that the choice of solvent was not crucial.



The monoanion IV (or any other tautomeric form) is supposed to be formed first, which then produces the dianion V, as exclusive final salt. Protonation of V gives VI, the structure of which was first deduced by Saquet and Thuillier.[30]

In order to prepare the monoester of VI it was necessary to have the monosalt IV at hand. As Brändström[31, 32] and Starks[33] have pointed out in a series of investigations that only monosalts of active methylene- and other compounds are formed when the ion-pair extraction technique is used, we felt tempted to try to prepare the mono-tetrabutylammonium salt of VI, especially as inspection of Dreiding models showed that the disalt could not exist. Our attempts did meet with success and the monosalt was formed.



The subsequent alkylation of VII gave the ester in quite high yields. When using n-alkyl halides, the yields were high irrespective of what halide was used. With more sterically hindered halides, the iodides gave much higher yields than the corresponding bromides.

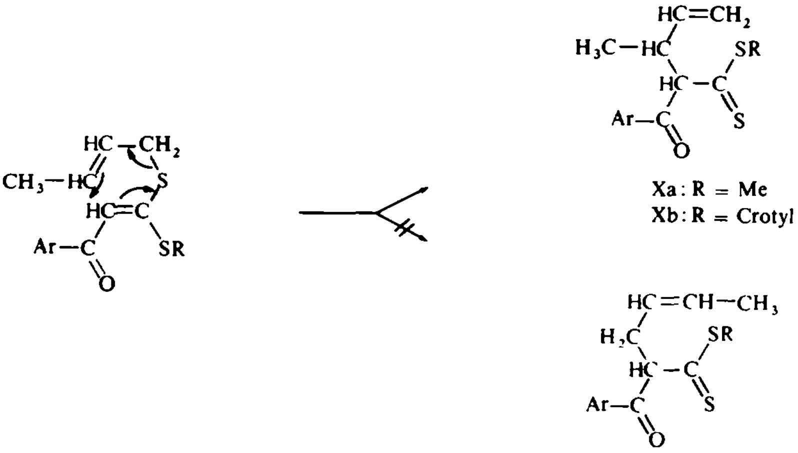
From the prepared dithioesters (VIII) it was possible to synthesize both symmetrical and unsymmetrical ketene mercaptals.

VIII IX

IXa: R′ = R″ = Me
IXb: R′ = Me; R″ = Et
IXc- R′ = Me; R″ = iso-Pr.

As to the unsymmetrical ones, they were all found to be mixtures of both the Z- and E-forms.[34] Quite recently extensive studies of barriers to rotation around the formal double bonds of 1,1-dimethylthio-2-benzoyl ethenes have been published and coalescence temperatures down to 80° have been recorded,[35] meaning, that at this temperature the reorientation between the two geometric isomers is so fast that they cannot be distinguished by NMR spectroscopy. This might account for the findings that pure Z- or E-forms never are isolated during our working-up procedure. Furthermore, as thallium salts of β-diketones,[36,37] in which there are O—Tl—O— bonds and which by subsequent alkylation and acylation exclusively give C- and O-substitution, respectively, it was thought that Tl-salts of VIII should give stereospecific alkylation. This was not the case for the same reasons as stated above.[35]

When one of the substituents on sulphur was a crotyl or a propargyl group, we did observe a thio-Claisen rearrangement:



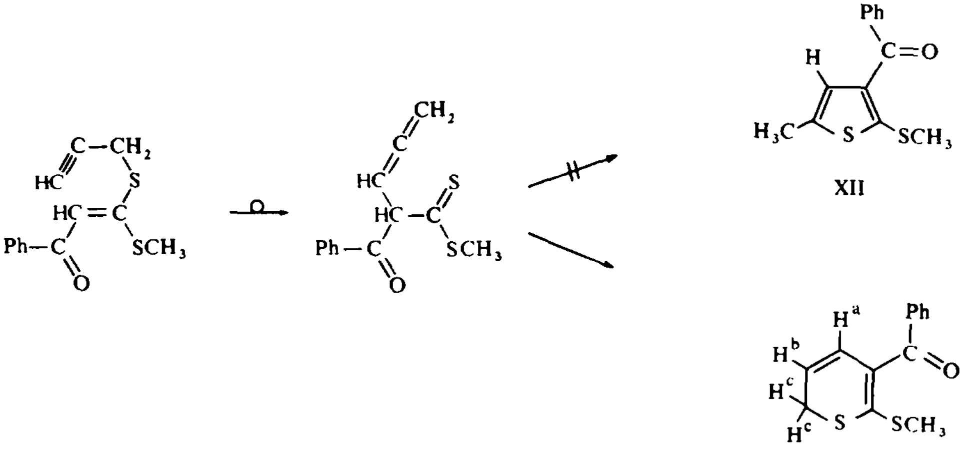
Xa: R = Me
Xb: R = Crotyl

XI

The structures were assigned from spectroscopic evidence: The existence of the dithioester group in Xa was proved by a distinct absorption in the NMR spectrum: δ 2·37 (Me—S), the UV spectrum (λ_{max} 319 nm, log ε 3·80[38,39]), and the carbonyl absorption in IR (1690 cm^{-1}). That it was the normal rearrangement product, X, and not the abnormal one (XI)[27] could be seen from the crucial differences in NMR:

Three olefinic protons (δ 3·2–3·6) and not two, a Me doublet at δ 1·05 with a splitting at 6·5 Hz, a one-proton doublet at δ 2·80 with a splitting of 4 Hz, and a one-proton multiplet at δ 3·2–3·6. The absorption at 1090 cm^{-1} is consistent with that reported for the thiocarbonyl group.[46] The existence of an enol form could not be confirmed by NMR.

Also for Xb the structure was assigned from spectroscopical evidence: The dithioester group was shown by the 1090 cm^{-1} (IR)[40] and 319 nm (UV)[38, 39] absorptions. The S-crotyl group from the δ 1·6 (Me) and 2·78 (—S—CH_2) signals, the 1-methyl allyl from the δ 4·5–5·7 (three olefinic protons), 1·02 (Me), and 3·6 (2H) signals.



XIII

When a propargyl group was introduced, only one product, the thiapyran XIII, was isolated, although the thiophene XII[27, 41-44] could have been formed, too. The structure of XIII was proved by spectroscopical means. The NMR spectrum showed unambiguous coupling patterns. The a-proton (δ 6·12) and the b-proton (δ 5·4) splitting showed a typical cis-coupling (J_{ab} = 9·5 Hz). The b-proton coupled with the c-protons (δ 3·23) with J_{bc} = 5 Hz, and the a- and c-protons had a long-range coupling (J_{ac} = 1 Hz). The chemical shift of the a-proton, δ = 6·12, indicates a conjugated system as does the UV-spectrum, λ_{max} = 362 nm, log ε 3·63. Also, an —S—Me group (δ 2·28) was present, as was an α,α'-unsaturated CO group.[45]

The 2H-thiapyran structure is also indicated by the 1595 cm^{-1} absorption in IR and comparison with NMR spectra of other known 2H-thiapyranes.[41, 42]

SPECTROSCOPIC DATA

In the NMR spectra of the dithioacids (VI), it was observed that the chemical shift of the H-bonded proton was dependent on the concentration. It was thus decided to find the limit value at infinite dilution of this proton and hence dilution experiments were made.

TABLE 1. SPECTROSCOPIC DATA OF THE β-HYDROXYDITHIOCINNAMIC ACIDS, VI, XVII AND XVIII

	Y	NMR-spectra			other	UV		IR cm^{-1}
		δ_A	δ_B	δ_C		λ_{max} nm	log ε	
VIa	4-OMe	15·48	6·96	5·43	Me: 3·87	398	4·36	1173, 1225, 1583, 1604, 2480
b	4-OEt	15·43	6·90	5·33	[a]	412	4·42	1570, 1600, 2480, 1170, 1220
c	4-Me	15·39	6·90	5·39	Me: 2·37	382	4·41	1185, 1240, 1580, 1610, 2480
d	3-Me	15·38	6·91	5·58	Me: 2·38	380	4·23	1248, 1555, 2490
e	H	15·38	6·97	5·48		379	4·23	1070, 1240, 1590, 2490
f	4-Ph	15·37	6·95	[b]		378	4·37	1170, 1220, 1575, 1680, 2480
g	4-F	15·33	6·85	5·42		390	4·26	1168, 1235, 1575, 1605
h	4-Cl	15·32	6·85	5·47		390	4·26	1212, 1235, 1545, 1580, 2480
i	4-Br	15·29	6·87	5·47		373	4·28	1078, 1236, 1590, 2555
j	3-Cl	15·25	6·85	5·40		390	4·17	1070, 1233, 1550, 2440
k	3-Br	15·27	6·87	5·53		343	4·17	1072, 1234, 1555, 1580, 2540
m	4-COMe	15·25	6·93	5·55	Me: 2·62	395	4·22	1260, 1580, 1675, 2430
n	4-CN	15·18	6·90	[c]		390	4·31	
XIV		15·37	6·27	5·38		354	4·41	1065, 1134. 1239, 1550, 2500
XV		15·27	6·82	5·40	[d]	340 414	4·08 4·34	1215, 1240, 1410, 1665, 2500

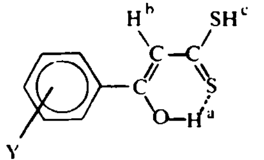
The UV-spectra were recorded in EtOH, except for VIb, g, i, j, k and m, which were run in $CHCl_3$. The IR-spectra were recorded in KBr-tablets.

[a] Shift of —CH_2—O—: δ 4·09; —O—C—Me: δ 1·42.

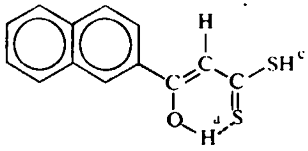
[b] Very broad signal.

[c] Broad signal at *ca* δ 5·5.

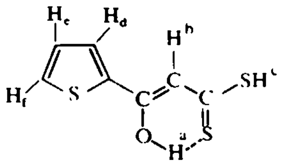
[d] Shifts of aromatic protons: δ_d = 7·75, δ_e = 7·12, and δ_f = 7·60. J_{cd} = 3·8 Hz, J_{ce} = 1·2 Hz and J_{de} = 5·0 Hz.



VI



XIV



XV

TABLE 2. SPECTROSCOPICAL DATA FOR THE DITHIOCINNAMIC ESTERS VIIIa–n

No.	Y	R	NMR-spectra ($CDCl_3$)			other	UV ($CHCl_3$)		IR ($CHCl_3$)* cm^{-1}
			δ_A	δ_B	δ_C		λ_{max} nm	log ε	
VIIIa	H	Me	15·10	6·90	2·63		381	4·34	1230, 1555, 1580
b	OMe	Me	15·12	6·88	2·62	Me: 3·80	400	4·42	1210, 1555, 1580
c	Me	Me	15·07	6·88	2·60	Me: 2·33	386	4·52	1225, 1560
d	Cl	Me	14·97	6·85	2·63		382	4·50	1222, 1580
e	Cl	Et	15·00	6·78	3·23	CMe: 1·35	382	4·44	1227, 1570
f	Cl	n-Pr	15·02	6·80	3·23		382	4·47	1215, 1580
g	Cl	CH_2COOEt	14·78	6·90	4·02		386	4·33	1720, 1205
h	Cl	CH_2CH_2OCOMe	14·92	6·83	3·55	[b]	389	4·45	1740, 1208
i	Cl	CH_2CH_2COOisoPr	14·72	6·80	3·50	[a]	386	4·31	1205, 1575, 1710
j	Cl	$CH_2CH{=}CHMe$	14·45	6·55	3·88	[c]	386	4·31	1243, 1255, 1568, 1595
k	Br	Me	14·95	6·83	2·62		383	4·40	1230, 1365, 1595
m	Br	isoPr	15·03	6·73	4·05		384	4·37	1200, 1580
n	Br	$CH_2CH{=}CH_2$	14·93	6·40	3·92		383	4·45	1210, 1580
p	Br	$CH_2C{\equiv}CH$	14·33	6·57	3·84	CCH: 2·18	387	4·32	1205, 1575, 1700, 2323
q	Br	CH_2Ph	14·93	6·95	4·30		386	4·51	1218, 1580
r	Br	CH_2COOEt	14·77	6·87	4·07	[d]	387	4·45	1205, 1500, 1740
s	Br	CH_2CH_2COOEt	14·97	6·85	3·57	[e]	387	4·35	1205, 1595, 1740
t	Br	$CH_2CH_2CH_2CN$	14·95	6·87	3·58	[f]	388	4·30	1205, 1585, 2240

Supplementary NMR-data (δ-values):

[a] 2·55 (—CH_2—CO), 5·0 (—O—CH_2—), 1·04 (—O—C—Me)

[b] 2·07 (Me), 4·02 (—C—CH_2—O, $J = 6·5$)

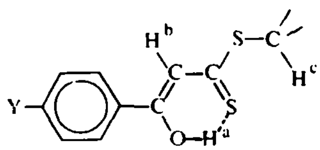
[c] 5·3–5·6 (—CH=CH—), 1·63 (=C—Me)

[d] 1·28 (—C—Me), 4·20 (—O—CH_2—), $J = 7$ c/s

[e] 1·28 (—O—C—Me), 2·82 (C—CH_2—CO—O—), 4·20 (CO—O—CH_2—)

[f] 2·1 (C—CH_2—C—CN), 2·53 (—C—CH_2—CN)

* Except for VIIIa, c, d, e, f, j, q, and r, which were recorded in KBr.



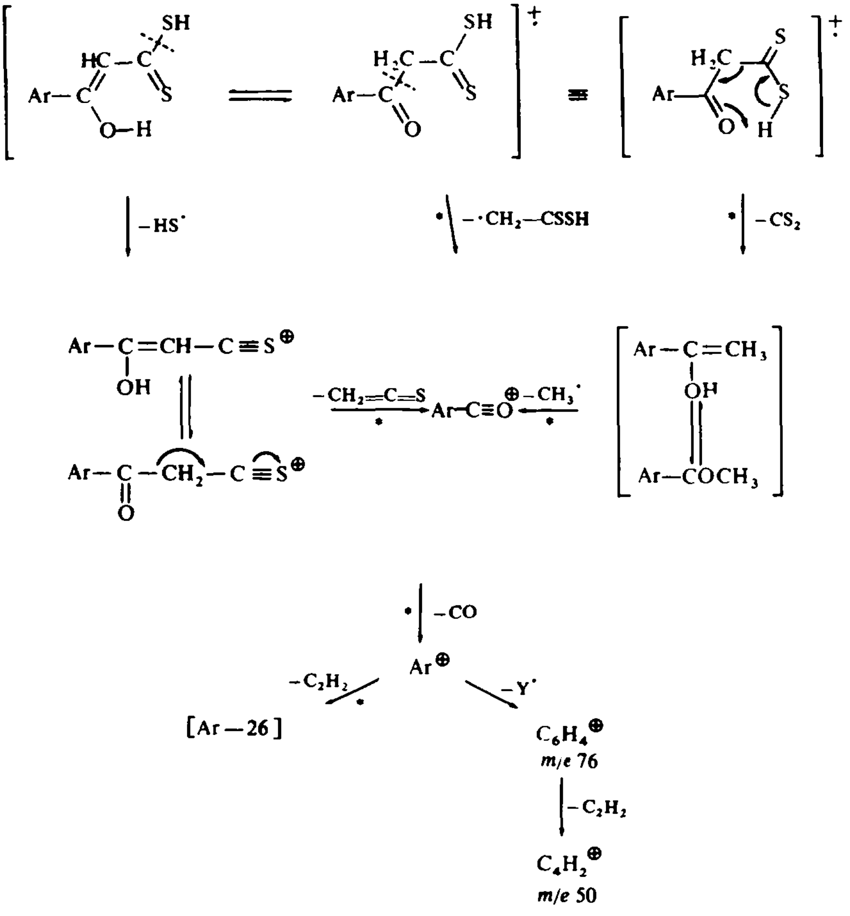
In Table 1 all spectral data for the dithiocinnamic acids are listed. The IR absorptions of the SH group (2430–2555 cm^{-1}) and of the aryl group (1545–1680 cm^{-1}) are in accordance with the literature.[46] Also the very strong UV absorptions (λ_{max} 343–412 nm, $\log \varepsilon = 4{\cdot}1–4{\cdot}4$) as well as the IR thiocarbonyl absorption at 1225–1260 cm^{-1} are in accordance with absorptions of other thiocarbonyl compounds.[38–40, 47]

Also in the dithiocinnamic esters we find characteristic absorptions of the thiocarbonyl group in UV (382–400 nm, $\log \varepsilon$ 4·3–4·5) and in IR (1200–1230 cm^{-1}).[38–40, 47]

MASS SPECTROSCOPIC STUDIES

Until now mass spectroscopic studies on dithio acids have not been reported. For the dithio acids investigated we found a characteristic fragmentation pattern:

SCHEME 1



Another fragmentation way does exist, giving the characteristic fragment at *m/e* 85:

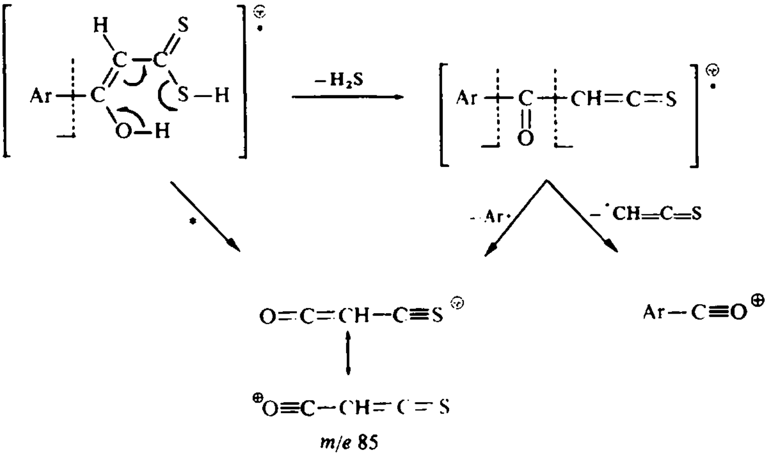


TABLE 3. MASS SPECTRA OF THE DITHIOCINNAMIC ACIDS VI AND XVIII

VIa	*m/e*	69	77	85	92	95	107	135	150	192	193	226 (M⁺)				
	I(%)	15	29	13	26	5	8	100	6	6	16	4				
VIb	*m/e*	49	51	53	63	64	65	69	76	77	85	92	93	94	95	107
	I(%)	32	13	23	18	14	41	13	18	13	37	10	31	8	5	6
	m/e	121	122	135	138	148	149	163	178	205	206	207	240 (M⁺)			
	I(%)	100	11	13	7	74	8	21	12	6	34	5	13			
VIc	*m/e*	41	45	50	51	57	62	63	64	65	74	75	76	77	85	86
	I(%)	6	5	6	13	5	6	21	4	44	6	4	14	7	18	4
	m/e	87	88	89	90	91	92	104	115	119	120	134	135	139	147	176
	I(%)	4	8	16	10	97	12	6	11	100	21	22	4	4	15	4
	m/e	177	178	179	195	210 (M⁺)	211	212								
	I(%)	97	12	6	5	65	7	6								
VIe	*m/e*	51	76	77	78	95	105	106	120	162	163	164	195	196 (M⁺)	197	
	I(%)	39	13	18	11	38	98	9	13	38	100	14	9	76	11	
	m/e	198														
	I(%)	9														
VIg	*m/e*	34	45	50	51	57	69	74	75	76	85	94	95	96	109	123
	I(%)	25	7	9	6	7	8	5	30	7	39	6	80	7	6	100
	m/e	124	138	181	182	214 (M⁺)										
	I(%)	9	20	23	7	30										
VIh	*m/e*	43	45	50	51	57	58	59	63	71	74	75	76	77	85	111
	I(%)	7	6	26	14	8	5	7	5	7	18	59	16	6	51	90
	m/e	112	113	135	139	140	141	154	156	158	196	197	198	199	230 (M⁺)	
	I(%)	8	27	4	100	14	49	12	20	5	8	68	9	21	22	
	m/e	232 (M⁺)														
		9														

TABLE 3—*continued*

VIi	*m/e*	50	51	53	57	58	63	67	74	75	76	77	85	90	103	104
	I(%)	52	20	9	17	10	9	9	32	72	74	20	77	9	5	7
	m/e	105	135	155	157	158	162	163	183	184	185	186	198	200	241	242
	I(%)	14	9	59	7	5	58	12	100	9	82	8	15	13	42	8
	m/e	243	274 (M^+)		276 (M^+)											
	I(%)	41	19		19											
VIj	*m/e*	50	56	57	58	63	74	75	76	77	85	89	111	112	113	139
	I(%)	15	13	8	5	5	11	49	13	6	72	6	68	8	22	100
	m/e	140	141	154	156	197	198	199	230 (M^+)		231	232 M($^+$)				
	I(%)	7	30	15	6	82	10	31	33		5	15				
VIk	*m/e*	74	75	76	77	85	87	105	121	123	128	134	135	139	149	155
	I(%)	31	71	68	28	22	40	10	20	12	9	13	7	9	24	71
	m/e	156	157	158	160	162	163	164	165	183	184	185	186	192	198	200
	I(%)	9	69	7	8	2	68	10	5	100	8	100	9	11	12	16
	m/e	202	241	242	243	244	274 (M^+)		276 (M^+)							
	I(%)	6	29	23	35	21	2·1		1·8							
VIm	*m/e*	43	45	55	57	69	73	76	91	119	128	147	148	149	162	198
	I(%)	34	15	13	15	12	12	16	15	15	17	100	12	17	42	5
	m/e	238 (M^+)														
	I(%)	1·5														
VIn	*m/e*	90	91	102	103	117	118	121	127	130	131	145	146	164	165	166
	I(%)	6	6	54	14	9	5	8	8	100	14	22	5	7	18	5
	m/e	179	180	194	221 (M^+)											
	I(%)	9	5	10	2											
VIm	*m/e*	45	57	79	86	91	92	93	94	95	111	112	113	126	168	169
	I(%)	44	44	10	5	5	5	14	5	19	100	7	6	7	5	9
	m/e	202 (M^+)														
	I(%)	3														

For all compounds except VIb the base peak is the substituted benzoyl ion at M-91. For VIb the base peak (*m/e* 121) can be regarded as derived from the analogous benzoyl ion:[48]

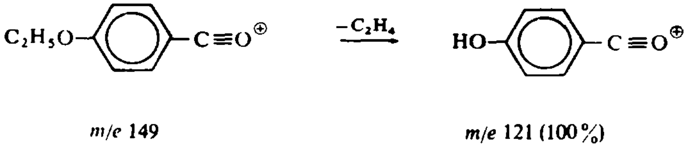
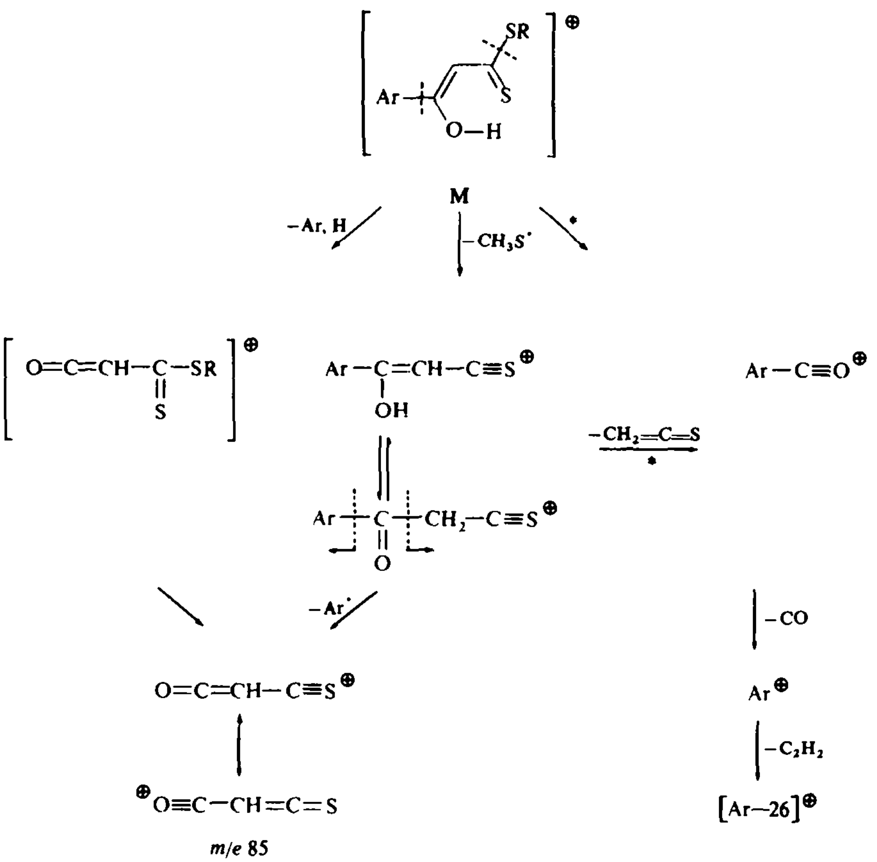


TABLE 4. MASS SPECTRA OF THE DITHIOCINNAMIC ESTERS VIII

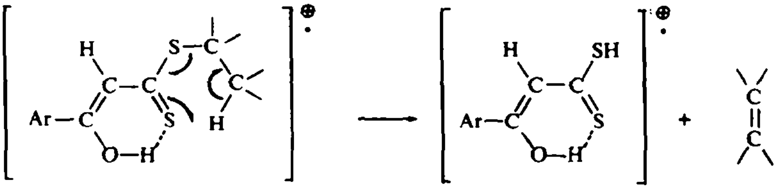
VIIIa	*m/e*	50	51	57	58	61	74	75	76	77	78	85	91	103	105	106
	I(%)	15	47	8	8	5	5	5	6	96	10	69	8	5	99	14
	m/e	163	164	165	210 (M^+)		211	212								
	I(%)	100	13	7	30		7	5								
VIIc	*m/e*	51	63	65	77	85	89	91	105	119	120	177	178	209	244 (M^+)	
		10	10	34	6	61	7	59	6	100	11	73	8	5	22	
VIIIf	*m/e*	50	51	58	71	75	76	85	111	113	139	140	141	154	156	197
	I(%)	9	9	11	7	26	9	48	55	18	100	9	40	10	5	84
	m/e	198	199	230	232	272 (M^+)		274 (M^+)								
	I(%)	8	33	25	11	11		4								
VIIIg	*m/e*	45	47	57	74	75	76	85	93	111	113	120	122	139	140	141
	I(%)	9	10	7	5	13	5	6	5	35	14	7	6	100	8	33
	m/e	142	156	197	199	315 (M^+)		317 (M^+)								
	I(%)	16	5	11	5	20		9								
VIIIh	*m/e*	74	75	76	85	87	89	111	113	139	140	141	144	145	146	154
	I(%)	6	37	9	67	5	9	79	20	100	9	36	19	19	9	9
	m/e	197	199	228	230	232	256	258	316 (M^+)		318 (M^+)					
	I(%)	56	22	26	31	8	23	8	2		1					
VIIIi	*m/e*	61	73	75	85	106	111	113	115	139	140	141	154	156	198	199
	I(%)	11	23	19	20	11	37	37	6	100	10	37	5	6	10	34
	m/e	219	230	232	285	287	344 (M^+)		346 (M^+)							
	I(%)	10	17	6	6	3	5		2·5							
VIIIk	*m/e*	46	47	48	50	57	58	59	61	62	63	67	69	73	74	75
	I(%)	8	18	12	63	21	29	10	27	7	15	6	10	9	43	96
	m/e	76	77	85	86	87	89	91	93	101	102	104	105	131	132	155
	I(%)	100	28	97	9	8	21	17	7	9	12	15	20	6	24	97
	m/e	156	157	158	162	164	183	184	185	186	241	242	243	244	245	
	I(%)	10	95	10	95	8	99	17	98	17	96	16	95	15	7	
	m/e	288 (M^+)		289	290 (M^+)		291	292								
	I(%)	53		10	54		8	6								
VIIIs	*m/e*	76	77	85	101	104	105	134	139	155	157	162	183	184	185	186
	I(%)	30	32	40	16	8	10	12	14	32	36	34	100	9	89	8
	m/e	218	241	242	243	244	274	329	331	374 (M^+)		376 (M^+)				
	I(%)	9	65	8	66	13	14	2	2	3		3				
VIIIt	*m/e*	41	50	54	68	75	76	77	85	101	134	155	157	162	183	184
	I(%)	56	21	42	28	29	30	11	35	32	5	42	43	38	100	8
	m/e	185	186	193	200	221	241	242	243	244	274	276	341 (M^+)		343 (M^+)	
	I(%)	100	8	6	7	7	65	8	63	5	8	8	8		9	

For the dithiocinnamic esters the very similar fragmentation scheme was found:

SCHEME 2

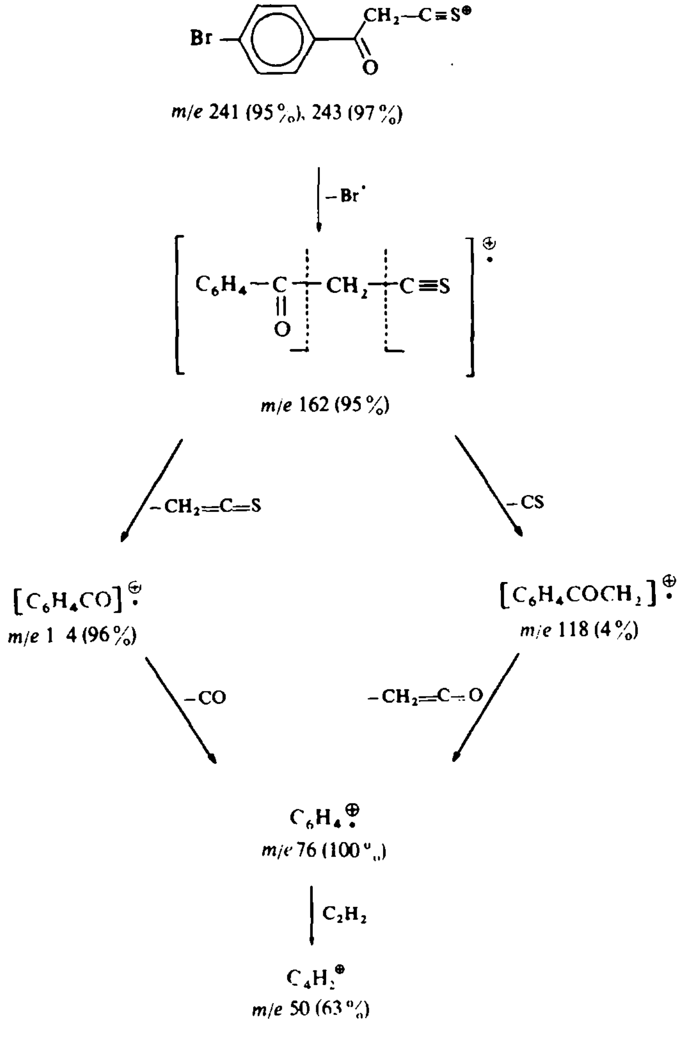


When a β-hydrogen was present in the ester group, a McLafferty rearrangement[49] was dominant, giving an ion identical with the molecular ion of the dithioacid:



For VIIIk also some other fragmentations are found:

SCHEME 3



It can be concluded that the mass spectra of the β-hydroxy dithiocinnamic acids and esters show a characteristic fragmentation pattern, from which it should be possible to identify these compounds.

HAMMETT CORRELATION

In the NMR spectra of the substituted β-hydroxydithiocinnamic acids (VI) a correlation was found between the Hammett-σ-constants of the substituents on the aromatic nucleus ("Y") and the limit value of the chemical shift of the hydrogen-bonded proton at infinite dilution.

TABLE 5. HAMMETT-σ-CONSTANTS AND CHEMICAL SHIFTS OF THE HYDROGEN-BONDED PROTONS AT INFINITE DILUTION

	Y	σ_Y^{50}	δ_{Ha}
VIa	4-OMe	−0·268	15·48
b	4-OEt	−0·24	15·43
c	4-Me	−0·170	15·39
d	3-Me	−0·060	15·38
e	H	0·000	15·38
f	4-Ph	0·009	15·37
g	4-F	0·062	15·33
h	4-Cl	0·226	15·32
i	4-Br	0·232	15·29
j	3-Cl	0·373	15·25
k	3-Br	0·391	15·27
m	4-COMe	0·502	15·25
n	4-CN	0·660	15·18
XIV		0·177	15·37

The chemical shifts are plotted against the α values in Fig 2, from which is found that

$$\delta^{i}_{\mathrm{OH}_Y} = -0{\cdot}315\cdot\sigma_Y + 15{\cdot}38$$

where $\delta^{i}_{\mathrm{OH}_Y}$ is the chemical shift of the hydrogen-bonded proton at infinite dilution in $CDCl_3$ of the Y-substituted β-hydroxy dithio- and σ_Y is the Hammett-σ-constant of the Y-substituent.[51]

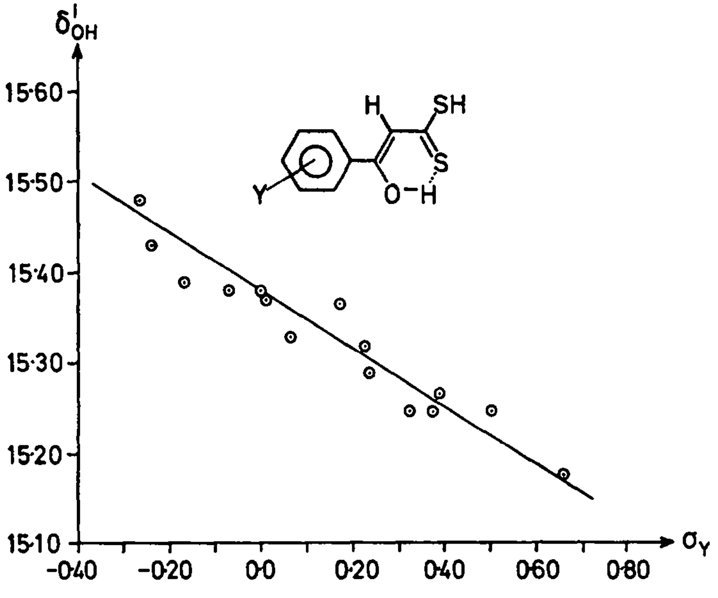


FIG 1

EXPERIMENTAL

NMR spectra were recorded in $CDCl_3$ at 60 Mc/s on a Varian A-60 spectrometer. The chemical shifts are expressed in ppm from TMS taken as 0·00 (δ-units).

The IR spectra were measured on either a Perkin–Elmer 137 or a Beckman IR-18 spectrophotometer and the ultra-violet spectra on a Bausch and Lomb 505 spectrophotometer.

The mass spectra were recorded on a CEC 21–104 GC operating at 70 eV, except for the mass spectrum of VIn, recorded on a MS-9 double focusing mass spectrometer. Inlet temperature 130°, ion source temp 170°.

PLC was carried out on Kiselgel $PF_{254+366}$ (Merck) support (20 × 40 cm and 3 mm thick). M.ps. are uncorrected. Analyses were made by Løvens Kemiske Fabrik, Copenhagen, and by Novo A/S, Copenhagen.

3-Chloro acetophenone, 4-cyano acetophenone, and 4-ethoxy acetophenone were synthesized in known ways.[52-54] Other substituted acetophenones were commercially available.

Synthesis of substituted β-hydroxydithiocinnamic acids (VI)

General procedure. 0·040 mole of the acetophenone and 0·040 mole (3·80 g) of CS_2 in 20 ml anhyd ether were added dropwise to 0·080 mole (9·30 g) of KOtBu in 50 ml anhyd diethyl ether (N_2). Stirring was then continued for 40 min. Then the mixture was poured into water, the ether phase removed, the aqueous layer acidified (dil H_2SO_4) and extracted with ether. The ether extracts were collected and dried (Na_2SO_4). The ether was stripped off and the residue recrystallized from EtOAc–light petroleum (b.p. 60–80°) giving 60–90% yield of the acid.

TABLE 6. PHYSICAL DATA FOR THE DITHIOACIDS VI

No.	m.p. °C	Yield (%)	Analyses Calculated (%) C	H	S	Hal	Found (%) C	H	S	Hal
VIa	98[c]	93								
b	111–113	52	55·00	5·04	26·65		55·59	5·16	26·55	
c	85[d]	79								
d	66	72	57·12	4·79	29·55		57·14	4·73	29·55	
e	63[e]	90								
f	119[f]	65[a]								
g	74	55	50·45	3·30	29·93	8·86	50·32	3·27	29·55	
h	99·5[g]	83								
i	105[h]	79								
j	65	65	46·85	3·06	27·78	15·36	47·10	2·95	26·80	15·53
k		58	39·29	2·57	23·30	20·03	39·41	2·53	19·28	20·12
m	109	6	[b]							
n	110	2	[b]							
XIV	93	63	63·37	4·09	26·03		62·67	4·02	26·22	
XV	88	93	41·56	2·99	47·55		41·90	3·06	46·85	

[a] From THF–diethyl ether (1:1).

[b] Composition checked by high resolution mass spectrometry.

[c] Lit.[13]: m.p. 98°.

[d] Lit.[11, 13]: m.p. 84–85°.

[e] Lit.[10, 13]: m.p. 63°.

[f] Lit.[13]: m.p. 118–119°.

[g] Lit.[13]: m.p. 99–101°.

[h] Lit.[13]: m.p. 105°.

TABLE 7. PHYSICAL DATA FOR THE DITHIOESTERS VII

No.	Y	RX	m.p. (°C)	Yield (%)	Analyses									
					Calculated (%)					Found (%)				
					C	H	S	Hal	N	C	H	S	Hal	N
VIIIa	H	MeI	57*	46										
b	OMe	MeI	75	55	55·00	5·04	26·64			54·81	5·11	26·69		
c	Me	MeI	54–55	39	58·90	5·40	28·51			59·30	5·37	28·16		
d	Cl	MeI	70–71	72	49·09	3·71	26·21	14·49		48·88	3·59	25·76	14·95	
e	Cl	EtBr	54–57	66	51·07	4·29	24·79	13·70		50·79	4·60	25·00	13·67	
e	Cl	EtI	54–57	72										
f	Cl	nPrI	43–44	59	52·78	4·80	23·51	12·99		52·95	4·92	23·16	12·89	
g	Cl	$ClCH_2COOEt$	86–87	61	49·27	4·14	20·25	10·94		49·28	4·58	19·45	10·65	
h	Cl	$MeCOOCH_2CH_2Br$	85–86	59	49·27	4·14	20·25	10·94		49·35	4·34	20·27	11·08	
i	Cl	$ClCH_2CH_2COO$isoPr	65–67	28	52·25	4·18	18·60	10·28		51·59	5·20	16·44	10·51	
j	Cl	CrotylBr	70–72	55	54·82	4·61	22·51	12·45		54·45	4·68	22·60	12·44	
k	Br	MeI	71–74	48	41·53	3·14	22·10	27·63		42·00	3·21	21·52	27·25	
m	Br	isoPrBr	81–83	7	45·44	4·14	20·21	25·18		45·51	4·20	19·94	25·40	
m	Br	isoPrI	81–83	66										
n	Br	allylBr	40	33	45·44	4·14	20·20	25·18		45·80	3·57	20·20	25·15	
p	Br	propargylBr	70–72	90	46·02	2·90	20·47	25·57		46·20	2·99	19·65	25·40	
q	Br	$PhCH_2Br$	80–81	35	52·61	3·59	17·56	21·88		52·63	3·79	18·39	21·94	
r	Br	$BrCH_2COOEt$	93–94	52	43·19	3·62	17·75	22·12		43·28	3·71	17·72	22·26	
s	Br	$BrCH_2CH_2COOEt$	61–63	50	44·80	4·04	17·08	21·29		44·47	4·01	16·23	21·70	
t	Br	$ClCH_2CH_2CH_2CN$	79–80	96	45·63	3·54	18·74	23·35	4·09	45·54	4·06	16·56	25·79	4·73

* lit.[9] m.p. 56–57°

Synthesis of alkyl β-hydroxydithiocinnamates (VIII).

General procedure. 0·025 mole (8·45 g) of tetra-n-butylammonium hydrogen sulphate* and 0·050 mole (2·00 g) of NaOH were dissolved in 50 ml water. Then 0·025 mole of VI in 50 ml $CHCl_3$ were added and after stirring for 30 min the aqueous phase was removed and 5 ml alkyl halide added. After stirring for another hr, the chloroform was distilled off and the residue extracted with diethyl ether. The ether was dried (Na_2SO_4) and stripped off, the residue recrystallized from EtOH, giving 50–95 % yield of dithioester.

Synthesis of ketone mercaptals (IX)

General procedure. 0·005 Mole of VIII and 0·005 mole (1·115 g) of thallous ethoxide were dissolved in 100 ml benzene and stirred for 30 min. Then 15 ml alkyl halide were added and the mixture refluxed for 2 hr TlI was then filtered off and the solvent stripped off, giving 70–88 % yield of ketene mercaptal.

3,3-*Dimethylthio*-1-(4-*bromophenyl*)-2-*propenon* (IXa), Yield 88 %, m.p. 107° (lit.:[13] 106–107°).

3-*Ethylthio*-3-*methylthio*-1-(4-*chlorophenyl*)-2-*propenon* (IXb), yield 78 % from VIIIe with MeI, 58 % from VIIId with EtI. (Found: C, 53·09; H, 4·90; S, 23·20; Cl, 13·08; $C_{12}H_{13}ClOS_2$ requires: C, 52·86; H, 4·78; S, 23·50; Cl, 13·02 %); NMR: 1·32 (S—C—Me), 2·92 (—S—CH_2, J = 7 Hz), 2·42 (—S—Me), 6·45 (═CH—); IR (CCl_4): 1090, 1220, 1475, 1590 cm^{-1}. UV ($CHCl_3$): λ_{max} (log ε): 350 (4·07).

3-*Isopropylthio*-3-*methylthio*-1-(4′-*bromophenyl*)-2-*propenon* (IXc), yield 70 % from VIIIm with MeI. (Found: C, 47·03; H, 4·63; S, 19·22; Br, 23·98; $C_{13}H_{15}BrOS_2$ requires: C, 47·10; H, 4·56; 19·38; Br, 24·12 %); NMR: 1·33, 1·38 (—S—C—Me, J = 6·5 Hz), *ca* 3·6 (S—CH), 2·38, 2·45 (—S—Me), 6·42, 6·58 (═CH—) (shifts for E- and Z-forms). IR ($CHCl_3$): 950, 1005, 1070, 1235, 1470, 1590, 1620, 1670, 2970, 2985 cm^{-1}; UV ($CHCl_3$): λ_{max} (log ε): 272 (4·02), 352 (4·21).

Methyl 2-(1-*methylallyl*)-4′-*chlorobenzoyl dithioacetate* (Xa). 2·552 g (0·0105 mole) of VIIId and 1·188 g (0·0105 mole) KOtBu were dissolved in 50 ml DMF and stirred for 20 min. Then 1·485 g (0·011 mole) of crotyl bromide were added and stirring was continued for 2 hr. The mixture was poured into 100 ml water, extracted with 3 × 100 ml ether, the collected ether phases washed with water and dried (Na_2SO_4). The ether was stripped off, giving a mixture from which after PLC (10 % $CHCl_3$ in light petroleum) 1·774 g (56 %) of XIIIa could be isolated. Distillation at high vacuum (10^{-4} torr) was then performed. (Found: C, 56·17; H, 5·16; S, 21·19; Cl, 12·31; $C_{14}H_{15}ClOS_2$ requires: C, 56·02; H, 5·02; S, 21·47; Cl, 11·88 %); NMR (CCl_4): 1·05 (C—Me, d, J = 6·5 Hz), 2·37 (S—Me), 2·80 (1H, d, J = 4 Hz), 4·8–5·9 (3H, allyl), 3·2–3·6 (1H, multiplet), 7·3–8·1 (Ar—H); IR ($CHCl_3$): 1090, 1255, 1595, 1690 cm^{-1}; UV ($CHCl_3$): λ_{max} (log ε): 268 (4·10), 319 (3·80).

Similarly, alkylation of 0·3211 g VIIIj with MeI and the subsequent separation (PLC) produced 0·2294 g (70 %) XIII.

Crotyl 2-(1-*methylallyl*)-4′-*bromobenzoyl dithioacetate* (Xb). 4·98 g *p*-bromoacetophenone and 4 ml CS_2 in 50 ml ether were added dropwise to 5·6 g KOtBu in 100 ml ether (N_2). Stirring was then continued for 40 min. Then 9 ml crotyl bromide were added and stirred for 40 min. The mixture was poured into water, separated, the aqueous phase extracted with ether, and the collected ether phases dried (Na_2SO_4). The ether was stripped off and after PLC (10 % acetone in light petroleum) 4·615 g (48 %) yield of XIIIb was isolated. (Found: C, 52·46; H, 4·84; S, 16·06; Br, 22·53; $C_{17}H_{19}BrOS_2$ requires: C, 53·25; H, 5·00; S, 16·73; Br, 20·84 %); NMR: 1·02 (—CH—$\underline{\text{Me}}$), 1·6 (—CH═CH—$\underline{\text{Me}}$), 2·78 (—S—CH_2—), 4·7–5·9 (3H, allyl), 3·6 (2H); IR (film): 1595, 1700 cm^{-1}; UV ($CHCl_3$): λ_{max} (log ε): 251 (4·18), 321 (3·90).

5-*Benzoyl*-6-*methylthio*-2*H*-*thiapyran* (XIII). 1·1394 g (0·0054 mole) of VIIIa and 0·622 g (0·0055 mole) KOtBu were dissolved in 110 ml DMF and stirred for 1 hr. Then 5 ml propargyl bromide were added and stirring continued for 30 min. Work-up as for XIIIa (PLC: eluated twice with 10 % acetone in petroleum ether), yield 1·0353 g (77 %) of XVI. (Found: C, 61·77; H, 4·89; S, 24·05; $C_{13}H_{12}OS_2$ requires: C, 62·84; H, 4·87; S, 25·81 %); NMR: 2·28 (—S—Me), 7·1–7·7 (ArH), —CH_2 (a) —CH (b) ═CH (c)—: $\delta_a = 3·23$, $\delta_b = 5·2–5·6$, $\delta_c = 6·12$, $J_{ab} = 5$ Hz, $J_{ac} = 1$ Hz, $J_{bc} = 9·5$ Hz; IR ($CHCl_3$): 1270, 1595, 1660, 1685 cm^{-1}; UV ($CHCl_3$): λ_{max} (log ε): 255 (4·04); 362 (3·63).

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