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STUDIES ON ENETHIOLS VII*

THIO-CLAISEN REARRANGEMENTS OF SOME ENETHIOLDERIVATIVES†

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Abstract—Enethiols, derived from ethyl acetoacetate and ethyl benzoylacetate have been alkylated with allyl-, crotyl- and propargyl bromides to give ethyl 3-alkylthio-crotonates (E- and Z-forms) and ethyl 3-alkylthio-cinnamates (Z-form). The Z-forms of the alkylated crotonates are smoothly converted to the corresponding E-forms by heat or irradiation. The sulphides undergo different rearrangement reactions in solvents like acetic anhydride, pyridine, triethylamine and quinoline leading to a variety of products including derivatives of thiophene and 2*H*-thiopyran.

INTRODUCTION

IN A series of papers we have performed the synthesis of enethiols from so-called active methylene compounds,[1,3,5] H-bonding studies,[1,3,5] mass spectrometric investigations,[2,4] and some reactions of enthiols[6,7]. In connection with the syntheses of vinyl-alkylsulphides from some enethiols[1–6] we observed that a so-called thio-Claisen rearrangement occurred. This prompted us to investigate this reaction more thoroughly and also alkylation studies and thermal and photochemical isomerization reactions were pursued. In the present paper results from enethiols derived from ethyl acetoacetate and ethyl benzoylacetate are presented.

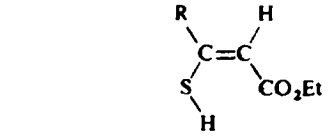
SYNTHESES

The enethiols I and II were prepared from the corresponding oxo-compounds[1,8] and both enethiols exist entirely in the Z-form (for E,Z-nomenclature, see ref.[9]).

In one case of alkylation of enethiols it is claimed that only S-alkylation is exclusive with formation of the Z-isomer.[8] A recent investigation[7] shows that also small amounts of the E-isomer can be formed. In our case alkylation of sodium or tetrabutylammonium salts (for the principles of ion-pair extraction, see Brändström[10–14] and Starks[15]) of I and II, respectively, gave only the S-alkylated products (III–VI). Compound I produced predominantly the Z-isomers III (Z) and IV (Z) and traces of the E-isomers, III (E) and IV (E), whereas II gave only the Z-isomers (V and VI) from the sodium salts (Table1–3). Due to steric hindrance the structures of the tetrabutylammonium- and sodium salts, should differ as to the content of Z- and E-isomers, and the mixture of alkylation products should not be the same. This indeed, was observed. The tetrabutylammonium salt of I gave 69% III (Z) + 31% III (E) on

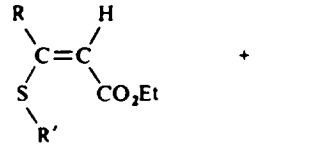
* Part VI. See ref. 6.

† Presented in part at the IVth Symposium on Organic Sulfur Chemistry, Venice, June 1970.



I: R = Me
II: R = Ph

(1) base
(2) R'X



III (Z): R = Me; R' = allyl
IV (Z): R = Me; R' = crotyl
V (Z): R = Ph; R' = allyl
VI (Z): R = Ph; R' = crotyl

III (E): R = Me; R' = allyl
IV (E): R = Me; R' = croty.

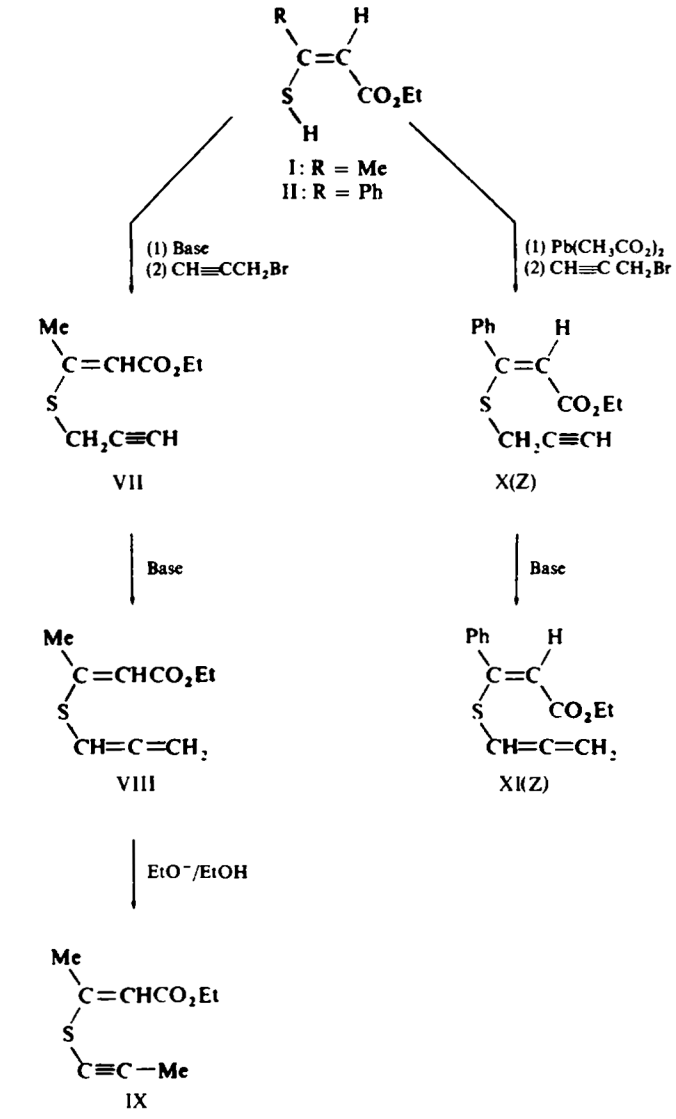
alkylation with allyl bromide

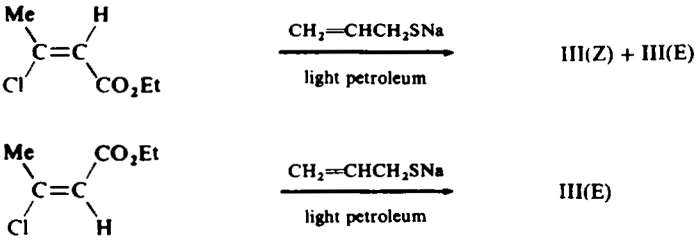
The alkylation of I and II, respectively, with propargyl bromide resulted in mixtures of acetylenic and allenic compounds and in some cases even rearrangement products (thiophenes) could be detected when the alkylations were carried out in the presence of NaH, $LiNH_2$, or n-Bu_4NOH. However, the stable Pb (II) salt[8] of II could be alkylated with propagyl bromide to give the pure acetylenic compound. The propargyl compounds were isomerized to the allenic compounds with catalytic or equimolar amounts of NaH/benzene, $LiNH_2$/liq NH_3, or n-Bu_4NOH/CH_2Cl_2 and isolated in pure form. Further isomerization of VII to the 1-propynyl compounds was carried out with sodium ethoxide in refluxing ethanol.

The alkylated enethiols, III, easily undergo thermal Z → E isomerization, *e.g.* during fractional distillation. This isomerization of similar compounds bearing an electron-donating substituent in the β-position and an electron-attracting substituent in the α-position is known.[18] Also on prolonged standing in the dark at 0–5° or by the action of UV-light the Z-forms of III and IV isomerize to the corresponding E-forms. On the contrary, the Z-forms of V and VI cannot be isomerized and are very stable.

Determination of the configuration of geometrical isomers of the type MeCX=$CHCO_2Et$ by the use of NMR chemical shift is well-known. Jones *et al.*[16] state that the chemical shifts for the vinylic Me groups occur at higher field in the Z-isomer than in the E-isomer, whereas the reverse is true for the vinylic proton. In Table 1 it is seen that our assignment of configuration of the crotonates is in agreement with this statement (except in the case of IX), and is supported by the independent synthesis of III by the stereoselective nucleophilic displacement of the chlorine in ethyl 3-chlorocrotonate by the allylthio-ion.

The assignment of IX (Z and E) by chemical shifts does not agree with the outlined statement. The chemical shift for the vinylic Me group in the Z-isomer is identical with that of the E-isomer, when the NMR is run with CCl_4 as solvent. Furthermore, the chemical shift of the vinyl proton occurs at higher field in the Z-isomer than in the E-isomer, which is contrary to what is observed for the other crotonates. The


I: R = Me
II: R = Ph
(1) Base
(2) CH≡CCH2Br
(1) Pb(CH3CO2)2
(2) CH≡C CH2Br
VII
X(Z)
Base
Base
VIII
XI(Z)
EtO⁻/EtOH
IX


CH2=CHCH2SNa
light petroleum
III(Z) + III(E)
CH2=CHCH2SNa
light petroleum
III(E)

difficulties in making an assignment based on these data are overcome by the use of C_6D_6 as solvent. It is now observed that the Me group has a different chemical shift in the two isomers and we assume that the isomer in which the Me group occurs at highest field is the Z-isomer in spite of the fact that the chemical shift of the vinyl proton in this isomer occurs at higher field than in the E-isomer. An explanation could be that when the distance between the vinyl proton and the acetylenic bond is as small as possible, *i.e.* when the acetylene group is in a S-*cis* configuration to the vinyl group in the E-isomer, the vinyl proton is placed in the deshielding field of the triple bond. In other possible configurations the field strength from the triple bond is weaker and the overall effect is that the vinyl proton is found at lower field in the E-isomer than in the Z-isomer.

TABLE 1. CHEMICAL SHIFTS (δ-VALUES, PPM) AND COUPLING CONSTANTS (C/S) OF ETHYL-3-ALKYLTHIO-CROTONATES AND CINNAMATES) $R^dC(SR') = CH^cCO_2CH_2{}^bCH_3{}^a$. THE SOLVENT IS CCl_4

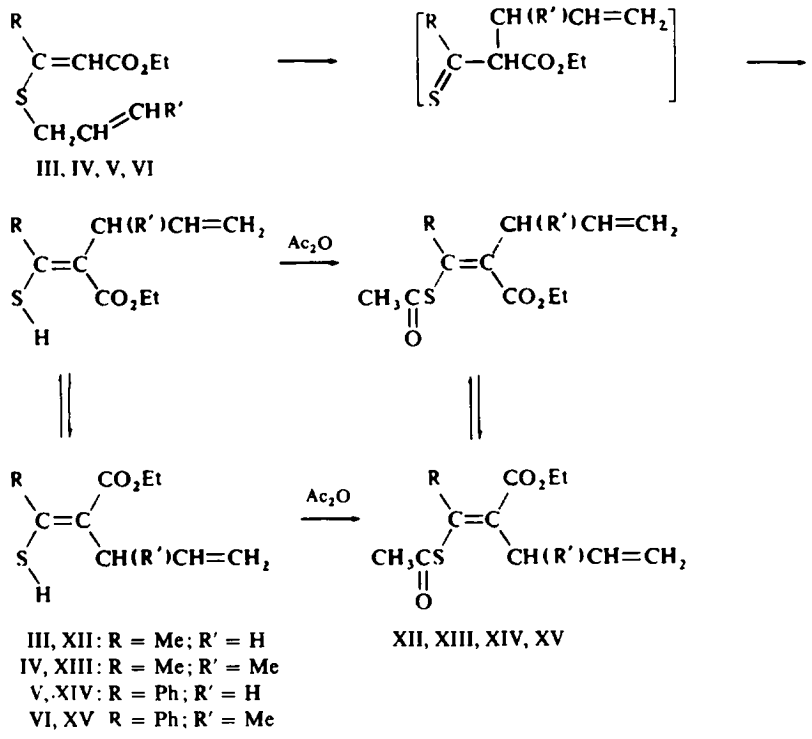
	R′	δ_c	δ_d	$J_{c,d}$	δ_f	$\delta_{g,h}$	$J_{f,g}$	Remarks
III (Z)		5·67	2·18	1	3·46	5·0–6·3	6	
III (E)		5·43	2·32	1	3·42	5·0–6·3	6	
IV (Z)	$CH_2{}^fCH^g{=}CH^hR''$	5·65	2·19	1	3·40	5·2–5·9	6	R″ = CH_3; δ = 1·69 ppm; J = 5 c/s (broad d)
IV (E)		5·43	2·33	1	3·35	5·3–6·0	6	R″ = CH_3; δ = 1·69 ppm; J = 5 c/s (broad d)
V (Z)		5·84	7·22–7·27		3·00	4·5–5·7	6	
VI (Z)		5·77	7·24		2·90	5·0–5·7	6	R″ = CH_3; δ = 1·50 ppm; J = 5 c/s (broad d)
VII (Z)		5·70	2·30	1·1	3·45	2·22	2·7	
VII (E)	$CH_2{}^fC{\equiv}CH^g$	5·54	2·34	1·1	3·46	2·22	2·7	
X (Z)		5·87	7·31		3·05	2·05	2·5	
VIII (Z)		5·72	2·19	1·2	5·93	4·90	6·3	AX_2 system
VIII (E)	$CH^f{=}C{=}CH_2$	5·64	2·35	1·2	5·82	5·0	6·0	AX_2 system
XI (Z)		5·87	7·30		5·25	4·79	6·3	AB_2 system
IX (Z)		5·82	2·32	1·2	2·13			
IX (E)	$C{\equiv}C{-}CH_3{}^f$	6·02	2·32	1·1	2·02			
IX (Z)		5·82	2·12	1·2	1·60			Solvent: C_6D_6
IX (E)		6·40	2 26	1·1	1 55			Solvent: C_6D_6

Chemical shifts of a and b protons were similar for all the compounds: δ_a = 1·21–1·29 (t) ppm; δ_b = 4·05–4·18 (q) ppm: $J_{a,b}$ = 7 c/s.

Determination of Z- and E-configurations of the ethyl 3-alkylthio-cinnamates is more ambiguous because only one isomer is isolated, but similarities in the IR and UV spectral data between the crotonates and the cinnamates support the assignment of Z-configuration to the cinnamates.

Rearrangement reactions of the sulphides in acetic anhydride

By heating the sulphides without solvent or dissolved in solvents like diglyme or decaline, only mixtures of high-boiling products were obtained, which have not been identified. However, in refluxing acetic anhydride at 140° the sulphides III, IV, V, and VI gave thiocarbonyl compounds, which tautomerized to the corresponding

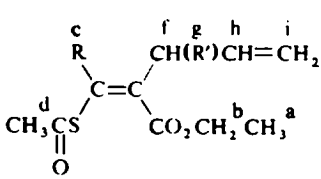


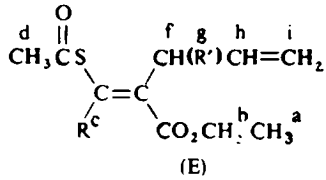
enethiols. The enethiols were then acylated by the solvent to give the isolated products in good yields, (XII, XIII, XIV, and XV).

The allylic moiety of the molecule is inverted by the rearrangement and it was observed that the crotyl derivatives rearrange slower than the allyl sulphides, which is evidence for a concerted mechanism. A radical or ionic mechanism would probably give mixtures with both inverted and non-inverted allylic groups, as found in other cases.[19, 20] The relative yield of Z- and E-form of the isolated product varied from equal amounts of Z- and E-forms for allylic derivatives to predominantly Z-form for crotyl derivatives, probably because of thermal isomerization of the product under prolonged reaction time.

The NMR data (Table 2) of the rearranged products (XII, XIII, XIV, XV) are in agreement with the postulated structures. The assignment of the Z- and E-configurations is based on the chemical shift differences of the c- and f-protons in the isomers of XII and XIII. These differences are small when the spectra are run with CCl_4 as solvent: $\delta_c(E) - \delta_c(Z) = 0{\cdot}14$ ppm, and $\delta_f(E) - \delta_f(Z) = 0{\cdot}07$ ppm, but more pronounced with C_6D_6 as solvent: $\delta_c(E) - \delta_c(Z) = 0{\cdot}38$ ppm and $\delta_f(Z) - \delta_f(E) = 0{\cdot}30$ ppm. As is seen from these values the c-protons are shifted to lower field when interaction with the ethoxycarbonyl group can occur, *i.e.* in the E-isomer. The f-protons are shifted in the same direction when interaction with the acetylthio group can occur, as in the E-isomer. This elucidation is based on the assumption that the ethoxycarbonyl group is more bulky than the allyl group, and that the acetylthio group is more bulky than the methyl group. The Z- and E-isomers of the rearrangement

TABLE 2. CHEMICAL SHIFTS (δ-VALUES, PPM) AND COUPLING CONSTANTS (C/S) OF ETHYL 3-ACETYLTHIO-2-ALKENYL-CROTONATES AND CINNAMATES. THE SOLVENT IS CCl_4



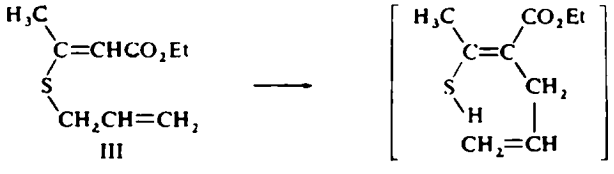


(E)

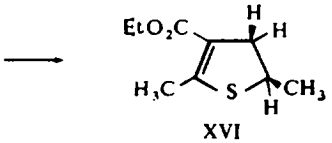
	δ_a	δ_b	δ_c	δ_d	$\delta_{f,g}$	δ_g	$\delta_{h,i}$	Remarks
XII (Z)	1·23	4·11	2·10	2·24	3·11		4·8–6·0	
XII (E)	1·25	4·17	2·24	2·30	3·18		4·7–6·0	
XIII (Z)	1·25	4·12	2·08	2·23	2·8–3·7	1·19	4·8–6·2	
XIV (Z)	1·26	4·17	7·26	2·18	3·02		4·8–6·0	
XIV (E)	0·78	3·78	7·20	2·20	3·31		4·8–6·0	
XV (Z)	1·25	4·18	7·26	2·15	2·9–3·6	1·14	4·7–6·2	
XV (E)	0·75	3·75	7·18	2·16	3·7*	1·25	4·8–6·2	
XII (Z)	1·02	4·03	2·02	1·88	2·98		4·8–6·0	Solvent: C_6D_6
XII (E)	0·98	3·98	2·40	1·88	3·28		4·8–6·0	Solvent: C_6D_6
XIII (Z)	1·04	4·05	2·02	1·88	3·0–3·5	1·20	4·8–6·0	Solvent: C_6D_6
J C/S	7 (t)	7 (q)	(s)†	(s)	5 (d)‡ (broad)	7 (d)	(m)	

* Estimated from decoupling experiment
† Homoallylcoupling for XII (Z and E). $J \sim 1$ c/s
‡ For XIII and XV: (m)

products XIV and XV (R = phenyl) showed pronounced differences due to the anisotropy effect of the phenyl group. In the E-isomer the a- and b-protons in the ethoxycarbonyl group lies in the shielding field of the phenyl group, and are shifted to higher field ($\delta_a = 0{\cdot}78$ ppm). In the NMR spectrum of XV(E) the f-proton resonance is hidden under the quartet for the b-protons of the ethoxycarbonyl group as shown by double resonance experiments (spindecoupling); irradiation at $\delta = 3{\cdot}70$ ppm causes collapse of the g-protons doublet to a singlet. The UV spectra shows only weak absorption above 200 nm, which is unexpected as compared to the UV spectra of ethyl 3-acetylthio-crotonate λ_{max} (log ε) = 272 nm (3·79). It is believed



III



XVI

that this is due to distortion of the unsaturated ester chromophore and in fact models show considerable steric crowding, which forces the ethoxycarbonyl group out of the plane made by the vinylic moiety of the molecules.

Other rearrangement reactions

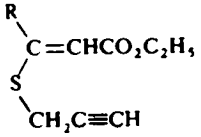
Other reactions have been performed with different solvents and substrates.

Compound III was heated under reflux in quinoline under nitrogen for 6 hr and the only isolated product was XVI.

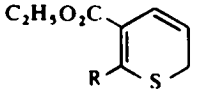
The enethiol as the assumed intermediate underwent a normal addition reaction. As spectroscopic proof of the structure of XVI the NMR (CCl_4) shows a homoallylic coupling, J = 1·7 c/s, between the vinylic Me group (δ = 2·26 ppm) and the vinylic methylene group (δ = 2·45–3·3 ppm). The Me group (δ = 1·36 ppm) on saturated carbon in the α-position to the sulphur couples to the methine proton (δ = 3·3–3·9 ppm) with J = 7 c/s. The ester protons are at δ = 1·26 ppm and δ = 4·10 ppm (J = 7 c/s).

Rearrangement of VII, VIII, X, and XI

The rearrangements of ethyl 3-propargylthio-crotonate, VII, in pyridine at 160° gave mainly XVII together with smaller amounts of XIX. Similarly ethyl 3-propargyl-

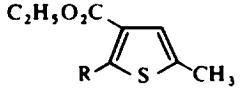


VII: R = CH_3
X: R = ϕ

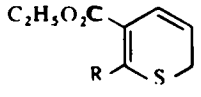


XVII: R = CH_3
XVIII: R = ϕ

+

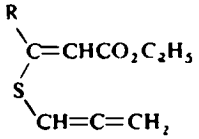


XIX: R = CH_3
XX: R = ϕ

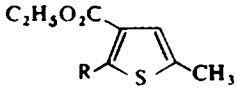


XVII: R = CH_3

+

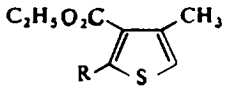


VIII: R = CH_3
XI: R = ϕ



XIX: R = CH_3
XX: R = ϕ

+



XXI: R = CH_3
XXII: R = ϕ

+

IX (Z) + IX (E)

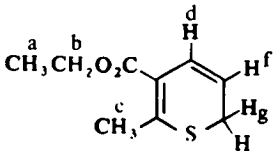
thio-cinnamate, X, was rearranged in quinoline and gave mainly XVIII and smaller amounts of XX. However, rearrangements of X in triethyl amine gave the thiophene, XX, as the only product. Also with VII the yield of the thiophene, XIX, was increased, but in this case the main product was the thiopyran, XVII. By using still stronger bases like NaH/benzene or n-Bu_4NOH/CH_2Cl_2 isomerization was the main reaction, but also thiophenes were formed. Rearrangements of VIII in quinoline gave the same products as VII together with smaller amounts of XXI, while XI gave XX and traces of XXII.

Rearrangement of the allenyl-vinyl sulphides, VIII and XI, gave the same products as the propargyl compounds, (VII and X) together with traces of XXI and XXII, respectively, which are anomalous products in the rearrangements of allenyl-vinyl sulphides. Attempts to rearrange XI in triethylamine were fruitless and the starting material was recovered. It was also attempted to trap an intermediate with acetic anhydride as solvent, but only a thiophene and isomerization products were obtained (see Table 3).

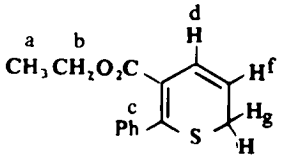
TABLE 3. REARRANGEMENT OF VII, VIII, X AND XI (rel. % YIELD)

	XVII	XVIII	XIX	XX	XXI	XXII	IX (Z)	IX (E)	Solvent	Temp. (°C)	Time (h)
VII	92		8						pyridine	160	4
VII	66·5		33·5						NEt_3	89½	4½
VIII	22		53		8		5	12	quinoline	180	5
	34		36						quinoline	180	1½
VIII			44		56				Ac_2O	140	20
X		64		36					quinoline	180	1½
X				100					NEt_3	89½	3¼
X				100					Ac_2O	160	3
XI				85		15			pyridine	160	½

TABLE 4. CHEMICAL SHIFTS (δ-VALUES. PPM) AND COUPLING CONSTANTS (C/S) OF 6-METHYL-5-ETHOXYCARBONYL 2H-THIOPYRANE AND 6-PHENYL-5-ETHOXYCARBONYL-2H-THIOPYRANE AND 6-PHENYL-5-ETHOXYCARBONYL-2H-THIOPYRANE. THE SOLVENT IS CCl_4



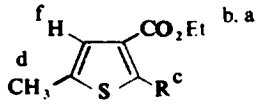
XVII



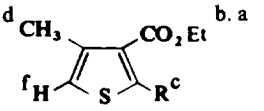
XVIII

		a	b	c	d	f	g
XVIII	δ	1·28	4·15	2·33	6·5	5·4	3·2
	J	7 (t)	7 (q)	0·70 (d)	10 (d)	10 (d)	5 (d)
				0·50 (d)	0·70 (q)	5 (t)	1·35 (d)
				0·20 (t)	1·35 (t)	0·5 (q)	0·2 (q)
XVIII	δ	0·80	3·82	7·26	6·66	5·50	3·28
	J	7 (t)	7 (q)	(s)	10 (d)	10 (d)	5 (d)
					1·2 (t)	5 (t)	1·2 (d)

TABLE 5. CHEMICAL SHIFTS (δ-VALUES, PPM) AND COUPLING CONSTANTS (C/S) OF ETHYL 2.5- AND 2,4-DIALKYL-3-THIENYLCARBOXYLATE. THE SOLVENTS ARE GIVEN IN THE TABLE



XIX, XX
(ref. 22)



XXI, XXII
(ref. 21)

	δ_a	δ_b	δ_c	δ_d	δ_f	Solvent
XIX	1·35	4·24	2·62	2·32	6·95	CCl_4
XIX	1·08	4·10	2·59	2·04	7·10	C_6D_6
XXI	1·35	4·25	2·62	2·32	6·51	CCl_4
XXI	1·05	4·10	2·52	2·35	6·30	C_6D_6
XX	1·11	4·05	7·25	2·43	7·08	CCl_4
XXII	1·11	4·05	7·25	2·35	6·75	CCl_4

$J_{a,b} = 7$ c/s; $J_{c,d} = 1{\cdot}1$ c/s

As spectroscopic proof for the structure of the 2*H*-thiopyranes the NMR (Table 4) shows unambiguous coupling patterns. The c protons show decreasing long range couplings in going from the d proton ($J_{cd} = 0{\cdot}7$ c/s) to the f proton ($J_{cf} = 0{\cdot}5$ c/s), and the g protons ($J_{cg} = 0{\cdot}2$ c/s). The chemical shift of the d proton, $\delta = 6{\cdot}5$ ppm, indicates a conjugated system as the UV spectrum: $\lambda_{max} = 330$ nm (XVII) and 350 nm (XVIII).

The thiophenes are all known compounds,[21,22] and the spectral data (Table 5) are in agreement with the literature. The thiophenes XIX and XX were separated in pure form from reaarrangement of VII and X, but VIII and XI gave unseparable mixtures of XIX and XX or XX and XXII. Unfortunately the c and d protons of XIX and XXI have identical chemical shifts in CCl_4, but the NMR could be resolved when C_6D_6 was used as solvent.

EXPERIMENTAL

NMR spectra were recorded at 60 Mc/s on a Varian A-60 spectrometer. The temps of the 15–20% solns (w/w) were 33 ± 1°. TMS was used as internal reference standard and the chemical shifts are expressed in δ-values downfield from TMS and are believed to be correct within ± 0·02 ppm. The coupling constants, expressed numerically in c/s, were measured with an accuracy of ± 0·1 c/s on the 50 c/s scale. The IR spectra were recorded as 5% solns on a Perkin–Elmer infracord 137 and the UV spectra on a Bausch & Lomb Spectronic 505 spectrophotometer with EtOH as solvent. B.ps are uncorrected. Analyses were made by Løvens kemiske Fabrik, Copenhagen. UMC or PLC was carried out of silica gel $PF_{254+366}$ (Merck) support (200 × 400 × 3 mm) and eluated twice with light petroleum ether—diethyl ether in the ratio 10:1 (by volume). R_f-values were obtained using the same support with light petroleum ether—diethylether in the ratio 5:1 as eluent (eluation once).

Alkylation of the enethiols I *and* II—*ethyl* 3-*allylthio-crotonate*, III (*Z and E*)

Procedure 1. To a stirred suspension of excess NaH, [from 10 g (0·2 mole) 50% NaH in oil, washed with benzene] in 100 ml benzene, 14·6 g (0·1 mole) of I was added dropwise at 5°. After about 1 hr, 12·1 g (0·1 mole) allyl bromide was added dropwise. The stirring was continued for about 3 hr and then the mixture was filtered. The soln was washed with water and dried ($CaSO_4$). The benzene was removed at room temp

with a rotation evaporator to give 18·6 g (100%) crude III, n_D^{25} = 1·5286, R_f = 0·42 (and a trace with R_f = 0·58). The product was identified as III (Z) and traces of III (E) (not visible in the NMR spectrum). A fraction with b.p. 96–98°/0·2 mm Hg was analysed. (Found: C, 58·17; H, 7·60. $C_9H_{14}O_2S$ requires: C, 58·05; H, 7·58%); IR ν_{max}^{Film} (cm^{-1}) 1690 (C═O), 1570 (C═C); UV (EtOH) λ_{max} (log ε_{max}) 286 nm (4·18). On prolonged standing the Z isomer was completely converted to the E isomer, n_D^{25} = 1·5150, R_f = 0·58, IR ν_{max}^{Film} (cm^{-1}) 1705 (C═O), 1590 (C═C); UV (EtOH) λ_{max}(log ε_{max}) 276 nm (4·18).

Procedure 2. 3·39 g (0·01 mole) tetrabutylammonium hydrogen sulphate (commercially available from Astra Meditec, Mölndal, Sweden) was dissolved in 15 ml (0·0030 mole) 2 M NaOH and mixed with a soln of 2·5 (0·017 mole) I and 4·5 g (0·037 mole) allyl bromide in $CHCl_3$. After 1½ hr stirring the lower phase was separated and the $CHCl_3$ removed. The residue was poured into ether and the crystallized $(n\text{-}Bu)_4NBr$ filtered off. The ether phase was dried ($CaSO_4$) and the ether evaporated to give 2·05 g (65%) crude product, which consisted of III (Z) (69%) and III (E) (31%) (measured by NMR).

Procedure 3. 10 g (0·14 mole) allyl mercaptan was added dropwise to a suspension of 10 g (0·2 mole) 50% NaH in loq-boiling hydrocarbons. 14 g (0·094 mole) and ethyl 3-chloro-crotonate (Z-isomer) was then added and the mixture stirred for 2½ hr at room temp. The mixture was filtered and the solvent removed to give 11 g (yield: 63%) crude product. The NMR showed that the product is a mixture of 43% III (Z) and 57% III (E).

As above, 14 g (0·09 mole) ethyl 3-chloro-crotonate (E isomer) was reacted with sodium allyl mercaptide, giving crude product (12 g; 69%); NMR showed 100% of III (E).

Photochemical Z → E isomerization of III

After photolysis of 250 ml $3 \cdot 10^{-2}$ mole/ether solution of III (Z) with 3·000 Å light for 4 hr, complete isomerization occurred to give the E form.

Ethyl 3-crotylthio-crotonate (Z and E)

Prepared as above (procedure 1) from 13·5 g (0·1 mole) crotyl bromide gave 17·6 g (88%) of the title compound, n_D^{25} = 1·5270, R_f = 0·33 (and a trace with R_f = 0·58), b.p. 90–105°/0·1 mm Hg, n_D^{25} = 1·5142. (Found: C, 59·92; H, 7·97. $C_{10}H_{16}O_2S$ ·equires: C, 59·98; H, 8·05%), IR ν_{max}^{Film} (cm^{-1}) 1690 (C═O), 1570 (C═C); UV (EtOH) λ_{max} (log ε_{max}) 286 nm (4·18).

On prolonged standing the Z isomers were completely converted to the E isomers, n_D^{25} = 1·5122, R_f = 0·58, IR ν_{max}^{Film} (cm^{-1}) 1705 (C═O), 1590 (C═C): UV (EtOH) λ_{max} (log ε_{max}) 276 nm (4·18).

Ethyl 3-allylthio-cinnamate (Z)

Prepared as above (procedure 1) from 21·8 g (0·105 mole) II, 10 g (0·2 mole) 50% NaH and 14·5 g (0·12 mole) allyl bromide, yield 22·7 g (92%), n_D^{25} = 1·5657, R_f = 0·33 crude product, b.p. 100–106°/0·1 mm Hg (Found: C, 67·70; H, 6·60. $C_{14}H_{16}O_2S$ requires: C, 67·76; H, 6·50%); IR ν_{max}^{Film} (cm^{-1}) 1695 (C═O), 1570 (C═C); UV (EtOH) λ_{max} (log ε_{max}) 240 nm (3·85) and 296 nm (3·90).

Procedure 2. 22 g (0·11 mole) II, 30 g (0·2 mole) allyl bromide, 34 g (0·1 mole) $(n\text{-}Bu)_4NHSO_4$; 100 ml 2 M NaOH and 100 ml CH_2Cl_2 gave 24·1 g (92%) of V (Z).

Ethyl 3-crotonylthio-cinnamate VI (*Z*)

Procedure 2. 20 g (0·1 mole) II. 14 g (0·1 mole) crotylbromide: 34 g (0·1 mole) $(n\text{-}Bu)_4NHSO_4$; 100 ml 2 M NaOH (0·2 mole) and 100 ml CH_2Cl_2 gave 22·5 g (86%). n_D^{25} = 1·5650. R_f = 0·33 of V (Z). b.p.–134°/0·1 mm Hg. (Found. C. 68·60; H. 6·95. $C_{15}H_{18}O_2S$ requires: C. 68·68; H. 6·92%); IR ν_{max}^{Film} (cm^{-1}) 1695 (C═O). 1570 (C═C); UV (EtOH) λ_{max}) (log ε_{max}) 240 nm (3·85) and 296 nm (3·90).

Ethyl 3-propargylthio-crotonate VII (*Z and E*)

Compound I (14·6 g, 0·1 mole), 4 8 g (0·1 mole) 50% NaH; 20 g (0·17 mole) propargylbromide gave 16 g (yield 87%), n_D^{25} = 1·5320, R_f = 0·28 and 0·48 (E) NMR showed a mixture of 85% Z and 5% E isomers of VII and 10% of VIII. Distillation of 2·6 g of crude product with small amounts of hydroquinone as stabilizer gave 1·7 g (58%), b.p. 80–86°/0·05 mm Hg. n_D^{25} = 1·5306. (Found: C, 58·69; H, 6·57. $C_9H_{12}O_2S$ requires: C. 58·91; H. 6·60%); NMR of the distilled product showed 45% Z and 45% E isomers. and 10% VIII. On prolonged standing pure Z isomers crystallized (m.p. 36°) from the crude mixture; IR $\nu_{max}^{CCl_4}$ cm^{-1}) 3300 (s) (acetylene C—H), 1720 (s) (α,β-unsaturated ester C═O), 1600 (s) (C═C); UV (EtOH) λ_{max} (log ε_{max}) 282 nm (4·18).

Ethyl 3-allenylthio-crotonate VIII (*Z and E*)

Procedure 2. 14·6 g (0·1 mole) I: 11·9 g (0·1 mole) propargylbromide in 100 ml CH_2Cl_2 were mixed with

40 g (0·118 mole) $(n\text{-Bu})_4NHSO_4$ and 120 ml (0·24 mole) 2 M NaOH, stirring for 5½ hr yielding as crude product 18·4 g (100%) of VIII (21% Z and 79% E isomers). Distillation of 3·6 g at 70–80°/0·2 mm Hg gave 1·26 g (40%): 20% Z and 80% E isomers, n_D^{25} = 1·5422, R_f = 0·27 (Z isomer). (Found: C, 58·39; H, 6·62. $C_9H_{12}O_2S$ requires: C, 58·69; H, 6·57%); IR ν_{max}^{Film} (cm^{-1}) 1940 (w) (C=C=C), 1690 (s) (α,β-unsaturated ester C=O), 1580 (s) (C=C); UV (EtOH) λ_{max} (log ε_{max}) 290 nm (4·08) (Z isomer) and 280 nm (4·08) (E isomer).

Procedure 4. 14·6 g (0·1 mole) I was added to 100 ml liq. NH_3 at −33° and 2·5 g (0·11 mole) $LiNH_2$. Then 12 g (0·1 mole) propargylbromide was added, and the mixture stirred for 3½ hr. After the ammonia had evaporated, the residue was extracted with low-boiling hydrocarbons, crude product 11·51 g (63%), n_D^{25} = 1·5528. 93% Z and 7% E isomer.

Procedure 1. 14·6 g (0·1 mole) I; 5 g (0·104 mole) (small excess!) 50% NaH in 50 ml low-boiling hydrocarbons; 12 g (0·1 mole) propargylbromide. Stirring for 2 hr at 25–30°, crude product 14 g (76%), n_D^{25} = 1 5548, R_f = 0·27 and 0·40, 76% Z and 24% E isomers (by NMR).

In another experiment 2·696 g (0·01465 mole) VII was dissolved in 25 ml dry benzene and 60 mg (0·0015 mole) 60% NaH and stirred for 17 hr at room temp. The solvent was stripped off. NMR showed a mixture of 44% VIII and 56% VII. Distillation of 2·596 g at 80–86°/0·1 mm Hg gave 1·092 g, n_D^{25} = 1·5370, 0·992 g of this mixture was partly separated by PLC to give the following fractions: 0·271 g (80% VIII + 20% XIX), 0·521 g (68% VII + 32% VIII) and 0·172 g (100% VII). The composition was thus 9% XIX, 35% VIII, and 56% VII.

Ethyl 3-(1-propynylthio)-crotonate IX (*Z and E*)

Compound VII (5·46 g, 0·03 mole) was dissolved in 25 ml abs EtOH with catalytic amounts of EtONa. The mixture was refluxed for 1½ hr, filtered, and the EtOH evaporated. The residue was dissolved in ether, filtered again, and the ether stripped off giving 3 g crude product. Distillation gave (1) 0·98 g, b.p. 129–132°/10 mm Hg; n_D^{25} = 1·5314 (68% Z + 32% E); (2) 0·55 g, b.p. 132–136°/10 mm Hg; n_D^{25} = 1·5379 (50% Z and 50% E). (Found: C, 58·64; H, 6·78. $C_9H_{12}O_2S$ requires: C, 58·69; 6·59%); IR ν_{max}^{Film} (cm^{-1}) 1700 (s) (α,β-unsaturated ester C=O), 1610 (s) (C=C); UV (EtOH) λ_{max} (log ε_{max}) = 288 nm (4·08).

Ethyl 3-propargylthio-cinnamate X (*Z*)

The lead salt of II[8] (31 g, 0·1 mole) was dissolved in 100 ml DMF and 20 g (0·17 mole) propargyl bromide and stirred overnight at room temp. Excess water and ether was added and the ether phase separated, dried ($CaSO_4$), and the solvent stripped off, crude product 24·38 g (99%), n_D^{25} = 1·5865, R_f = 0·38. Distillation (with oil diffusion pump) at 45–60°/10^{-5} mm Hg gave analytical pure material. (Found: C, 67·44; H, 5·72. $C_{14}H_{14}O_2S$ requires: C, 68·24; H, 5·72%); IR ν_{max}^{Film} (cm^{-1}) 3290 (w) (acetylenic C—H), 1700 (s) (α,β-unsaturated ester C=O), 1570 (m) (C=C); UV (EtOH) λ_{max} (log ε_{max}) = 290 nm (3·88).

Procedure 1. 20 g (0·1 mole) of II; 10 g (0·2 mole) 50% NaH; 17 g (0·14 mole) propargyl bromide; stirring for 3 hr; crude product 24 g (97%).

Ethyl 3-allenylthio-cinnamate XI (*Z*)

(a) 2·93 g (0·012 mole) of X was dissolved in 50 ml liq. NH_3 and stirred for 20 hr with 50 mg $LiNH_2$. The ammonia was evaporated and the mixture separated with PLC, which gave 1·1 g (38%) of XI, n_D^{25} = 1·6077, R_f = 0·53. Distillation at 60°/10^{-5} mm Hg gave analytic pure material. (Found: C, 68·08; H, 5·67. $C_{14}H_{14}O_2S$ requires: C, 68·24; H, 5·73%); IR ν_{max}^{Film} (cm^{-1}) 1947 (m) (C=C=C), 1705 (s) (α,β-unsaturated ester C=O), 1580 (s) (C=C). UV (EtOH) λ_{max} (log ε_{max}) 246 nm (3·90) and 303 nm (3·91).

(b) 2·60 g (0·0011 mole) of X was dissolved in 25 ml dry benzene and stirred for 16 hr with 1·00 g (0·025 mole) 60% NaH. The solvent was evaporated and the mixture separated with PLC to give 0·676 g (26%) of XI.

(c) 1·22 g (5 mmole) of X was dissolved in 10 ml CH_2Cl_2 and mixed with 2 ml (4 mmole) 2 M NaOH, 10 ml H_2O, and 250 mg (0·7 mmole) $(n\text{-Bu})_4NHSO_4$, stirred for 20 min, work-up as in procedure 2; NMR showed a mixture of 62% XI + 37% X + 1% XX.

(d) 1·10 g (4·5 mmole) of X in 10 ml CH_2Cl_2, 0·2 ml (0·4 mmole) 2 M NaOH in 2 ml H_2O and 20 mg (0·059 mmole) $(n\text{-Bu})_4NOH$ 97% X + 2% XI + 1% XX.

Ethyl 3-acetylthio-2-allyl-crotonate XII (*Z and E*)

Compound III (Z + E) (2·24 g, 0·012 mole) was dropped into 10 ml refluxing (140°) Ac_2O. After 3 hr the Ac_2O was distilled off at 40°/10 mm Hg and the residue dissolved in ether, washed with water and dried

($CaSO_4$). The NMR of the crude product showed 50% XII (Z) and 50% XII (E). Distillation gave 1·68 g (75%), b.p. 80–100°/0·2 mm Hg. (Found: C, 58·02; H, 7·09. $C_{11}H_{16}O_3S$ requires: C, 57·88; H, 7·07%). 0·975 g separated by UMC gave 0·540 g, R_f = 0·40 (E) and 0·450 g, R_f = 0·28 (Z); IR ν_{max}^{Film} (cm^{-1}) 1700–1710 (s) (C=O); UV (EtOH) no maximum above 220 nm. (Z and E isomers showed no significant differences in IR and UV).

Ethyl 3-acetylthio-2-(1-methylallyl)-crotonate XIII (*Z*)

Compound IV (2 + E) (5·02 g, 0·025 mole) was added dropwise to 50 ml refluxing Ac_2O. After 24 hr the mixture was worked up as described for XII. Distillation gave 3·03 g, b.p. 77–80°/0·1 mm Hg. n_D^{25} = 1·4910, and 0·805 g, b.p. 80–87°/0·1 mm Hg, n_D^{25} = 1·4978 (76%). Further purification of 0·5615 g with UMC gave 0·222 g (30%), b.p. 100°/0·2 mm Hg, n_D^{25} = 1·4942, R_f = 0·28 of XIII (Z). (Found: C, 59·46; H, 7·63. $C_{12}H_{18}O_3S$ requires: C, 59·49; H, 7·49%); UV (EtOH) no maximum above 220 nm.

Ethyl 3-acetylthio-2-allyl-cinnamate XIV (*Z and E*)

Compound V (2) (8·73 g, 0·035 mole) was reacted as above for 5½ hr giving 1) 5·35 g, b.p. 119°/0·05 mm Hg, n_D^{25} = 1·5516, and 2) 0·79 g, b.p. 119–124°/0·05 mm Hg, n_D^{25} = 1·5526 (70%). 0·900 g of fraction 1 gave 0·239 g, R_f = 0·25 (Z) and 0·249 g, R_f = 0·33 (E), total yield: 55%. (Found: C, 66·68; H, 6·28. $C_{16}H_{18}O_3S$ requires: C, 66·19; H, 6·25%); IR ν_{max}^{Film} (cm^{-1}) 1720 (s) (C=O). UV (EtOH) $\lambda_{shoulder}$ (log ε) 250 nm (3·85), (Z and E isomers had similar IR and UV).

Ethyl 3-acetylthio-2-(1-methylallyl)-cinnamate XV (*Z and E*)

Compound VI (2) (5·21 g, 0·02 mole) was added dropwise to 100 ml refluxing Ac_2O during 3 hr and refluxed for another 4 days. Work-up was usual gave 5·09 g crude product. Separation of 2·2985 g with UMC gave 0·4415 g of the E isomer, b.p. 130–140°/0·1 mm Hg, R_f = 0·38, and 0·9167 g of the Z isomer, b.p. 140–145°/0·2 mm Hg, R_f = 0·28, yield: 59%. (Found: C, 66·88; H, 6·56. $C_{17}H_{20}O_3S$ requires: C, 67·09; H, 6·62%); IR ν_{max}^{Film} (cm^{-1}) 1720 (s) (C=O); UV (EtOH) $\lambda_{shoulder}$ (log ε) 250 nm (3·85).

Ethyl 2,5-dimethyl-2,3-dihydrothienyl-4-carboxylate XVI

Compound III (Z and E) (6·25 g, 0·034 mole) of III (Z and E) was added dropwise to 25 ml quinoline at 155° under N_2. After 6½ hr the mixture was diluted with ether, extracted with 2 M HCl and dried ($CaSO_4$). Work-up with PLC gave 1·627 g (29%) of XVI, b.p. 46°/0·05 mm Hg, n_D^{25} = 1·5164. (Found: C, 58·14; H, 7·64. $C_9H_{14}O_2S$ requires: C, 58·05; H, 7·58%); IR ν_{max}^{Film} (cm^{-1}) 1690 (s) (α,β-unsaturated C=O), 1595 (m) (C=C); UV (EtOH) λ_{max} (log ε_{max}) 294 nm (4·08).

Rearrangement of VIII (*Z and E*) *in quinoline*

(a) 5·50 g (0·03 mole) of VIII was added dropwise to quinoline at 180° under N_2, reaction time 1½ hr. Work-up as under XVI gave 3·66 g crude product. 1·05 g were separated with UMC to give 220 mg (21%), R_f = 0·50 of XIX and 130 mg (12%), R_f = 0·56 of XVII, 2-methyl-3-ethoxy-carbonyl-6*H*-thiopyrane, n_D^{25} = 1·5446. (Found: C, 58·34; H, 6·70. $C_9H_{12}O_2S$ requires: C, 58·69; H, 6·57%); IR ν_{max}^{Film} (cm^{-1}) 1700 (s) (C=O); UV (EtOH) λ_{max} (log ε_{max}) 330 nm (3·56) and 238 nm (3·94).

(b) 3·38 g (0·018 mole) of VIII was reacted as above for 5 hr to give a mixture, b.p. 70–80°/0·2 mm Hg, consisting of (22% XVII + 53% XIX + 8% XXI + 12% IX (E) + 5% IX (Z).

Rearrangement of VIII (*Z and E*) *in acetic anhydride*

Compound VIII (Z and E) (2·732 g, 0·0148 mole) was added dropwise to 25 ml refluxing Ac_2O, reaction time 20 hr. The Ac_2O was distilled off and the residue partly separated with UMC. (1) 90 mg (44% XIX + 56% XXI), (2) 110 mg (55% XIX + 45% XXI), (3) 120 mg (95% IX (E) + 5% IX (Z)), (12% yield).

Rearrangement of VII (*Z and E*) *in pyridine*

Compound VII (Z and E) (7·08 g, 0·039 mole) was dissolved in 1·3 ml pyridine and heated to 160° for 4 hr in a degassed ampule. The mixture was then distilled to give 2·9 g (24½%), b.p. 120°/10 mm Hg (92% XVII + 8% XIX).

Rearrangement of VII (*Z and E*) *in triethyl amine*

Compound VII (Z and E) (1·495 g, 1 mole), dissolved in 15 ml Et_3N was refluxed at 89½° for 4½ hr. Distillation gave 1·019 g (68%), b.p. 139°/14 mm Hg, n_D^{25} = 1·5308. (66⅔% XVII + 33⅓% XIX).

Rearrangement of X (Z) *in quinoline*

Compound X (Z) (6·13 g, 0·025 mole) was added dropwise to 25 ml quinoline at 180° under N_2, reaction time 1½ hr. Work-up as usual gave 6·76 g; 4·62 g of this was distilled to give 1·41 g, b.p. 146–156°/0·3 mm Hg. Further purification of 1 g with UMC gave 500 mg (9%). R_f = 0·50 of XX and 700 mg (15%). R_f = 043 of XVIII, 2 phenyl-3-ethoxycarbonyl-6H-thiopyrane, n_D^{25} = 1·6046. (Found: C, 68·21; H, 5·64. $C_{14}H_{14}O_2S$ requires: C, 68·28; H, 5·73%); IR ν_{max}^{Film} (cm^{-1}) 1700 (C=O); UV (EtOH) λ_{max} (log ε_{max}) 350 nm (3·65).

Rearrangement of X (Z) *in acetic anhydride*

Compound X (Z) (1·815 g, 0·0074 mole) was dissolved in 10 ml Ac_2O and heated at 160° for 3 hr in a degassed ampule. Distillation of 0·98 g crude product gave 114 mg (11%) of XX.

Rearrangement of X *in triethyl amine*

Compound X (3·18 g, 0·013 mole) was dissolved in 25 ml Et_3N and refluxed (89½°) for 3¼ hr. Distillation gave 1·635 g (52%) of crystalline XX, m.p. 36°, b.p. 140–143°/0·3 mm Hg, n_D^{25} = 1·5842.

Rearrangement of XI (Z) *in pyridine*

Compound XI (Z) (0·270 g, 1·1 m mole) was dissolved in 0·8 ml pyridine and heated at 160° for ½ hr in a degassed ampule. Distillation at 110–130°/0·5 mm Hg gave a mixture of 85% XX and 15% XXII.

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