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THERMAL CYCLOADDITIONS OF THIOCARBONYL COMPOUNDS TO CONJUGATED DIENES

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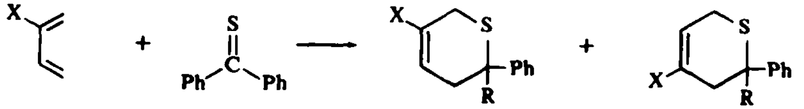
Abstract—Thiobenzophenone and thioacetophenone undergo 1,4-cycloaddition reactions with 1,3-butadiene, isoprene, and chloroprene at room temperature. The reactions with isoprene and chloroprene yield mixtures of two isomers, I and II, the isomer ratios of which have been determined by NMR spectroscopy. The chemical shifts of protons in the NMR spectra of the products and their corresponding sulfones have been assigned.

OF the carbonyl compounds undergoing 1,4-cycloaddition reactions,[1] the most active are the fluorinated ketones.[2] Recent investigations[3] have shown that thiocarbonyl compounds also function as dienophiles in 1,4-cycloaddition reactions, and are several orders of magnitude more reactive than the corresponding carbonyl compounds.[4] Thus, hexafluorothioacetone, trifluorothioacyl fluoride, thiocarbonyl fluoride, and thiophosgene react at $-78°$ with butadiene and/or cyclopentadiene to give one-to-one adducts; ethyl trifluorodithioacetate undergoes the reaction with 2,3-dimethylbutadiene at 0°; and thiofluorenone gives the adduct at room temperature. Thiobenzophenone is also reported to undergo 1,4-cycloaddition reaction with isoprene or with cyclopentadiene at room temperature.[5] However, even when the reaction affords two or more isomeric products, no effort has been made to elucidate the isomer ratios.

We have found that both thiobenzophenone and thioacetophenone are reactive dienophiles and that the 1,4-cycloaddition reactions take place with open-chain dienes at room temperature. The reaction of these thioketones with 2-substituted and unsubstituted 1,3-butadienes results in the formation of derivatives of 4-thiacyclohexene, I and II (Scheme 1). The product ratio was determined by the NMR technique.

SCHEME I



(1)

I(a–f) II(a–f)

a: R = Ph, X = H
b: R = Ph, X = Me
c: R = Ph, X = Cl

d: R = Me, X = H
e: R = Me, X = Me
f: R = Me, X = Cl

RESULTS AND DISCUSSION

1,3-*Butadiene*. When a mixture of thiobenzophenone and excess 1,3-butadiene was kept at room temperature in the dark until the blue colour of thiobenzophenone had completely disappeared (about 10 hr), a quantitative yield of the crystalline adduct,

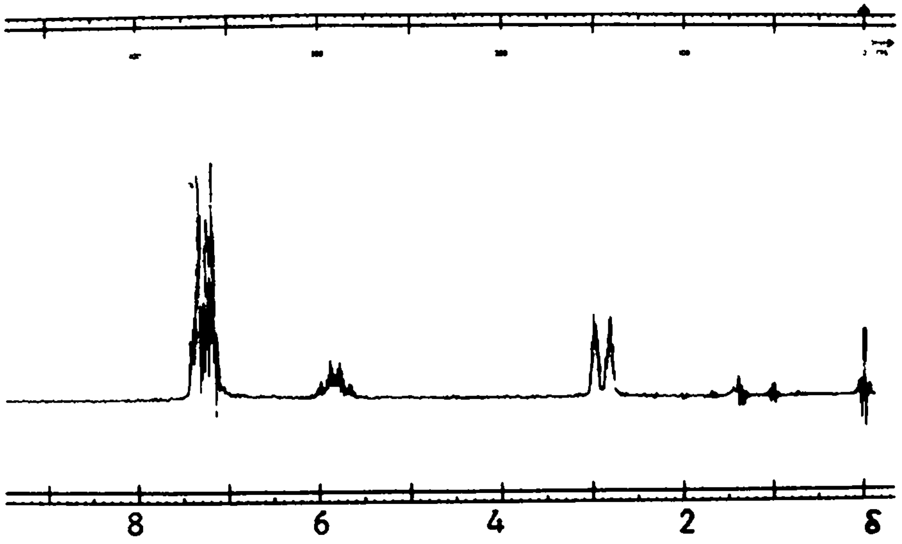


Fig. 1 NMR spectrum of 5,5-Diphenyl-4-thiacyclohexene.

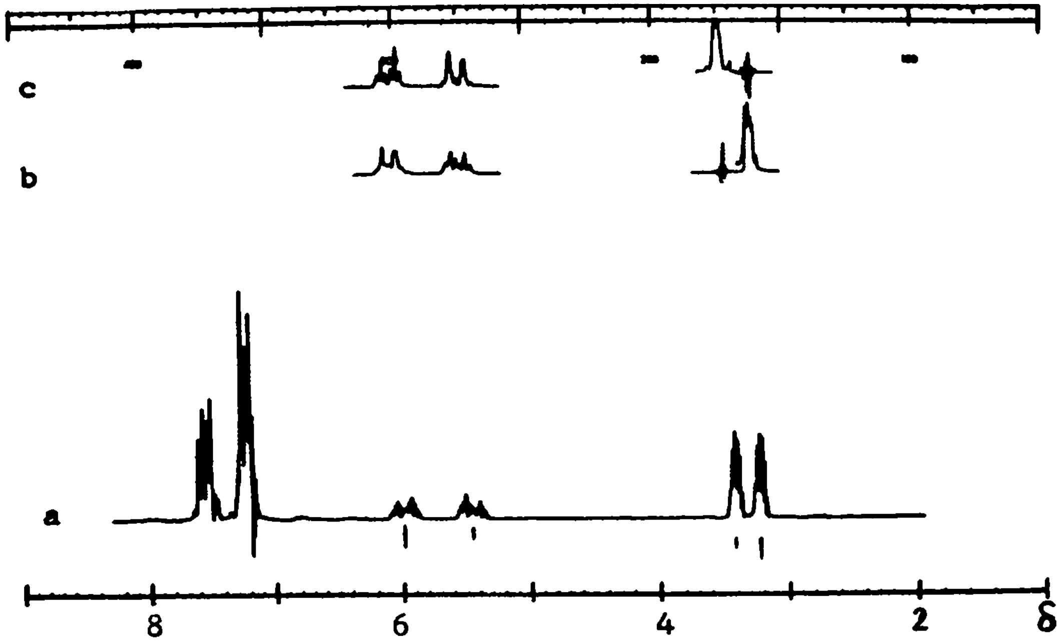
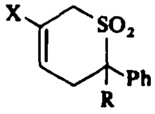


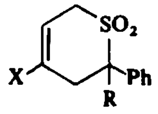
Fig. 2 NMR spectra of (a) 5,5-Diphenyl-4-thiacyclohexene-4,4-dioxide, (b) IIIa; the protons at $\delta = 3{\cdot}28$ being irradiated, and (c) IIIa; the protons at $\delta = 3{\cdot}46$ being irradiated.

5,5-diphenyl-4-thiacyclohexene, Ia, was obtained. The structure of Ia was confirmed by NMR spectroscopy. As shown in Fig. 1, the spectrum of the compound consists of six multiplets centered at (δ from TMS, in $CDCl_3$)[*] 7·30 (4H), 7·18 (6H), 5·82 (1H), 5·78 (1H), 2·99 (2H), and 2·82 (2H). The first two are apparently those for phenyl protons and the last two correspond to methylene protons. In order to make the assignment easy, Ia was oxidized by hydrogen peroxide to the corresponding sulphone, IIIa, whose NMR spectrum is shown in Fig. 2a. A vinyl proton which is deshielded by the oxidation is tentatively assigned as H_c and the other as H_b.[†] When the protons at 3·28 and 3·46 are irradiated, the multiplets at 6·04 and 5·50 respectively appear as an ABX_2 sextet and those at 5·50 and 6·04 respectively become doublet (Figs 2b and 2c). This suggests that the protons which have a signal at 3·28 can be assigned as H_a's and the ones at 3·46 are H_d's consistent with the expectation that H_d's are more deshielded than H_a's by the effect of the sulphone group.



III(a–f)

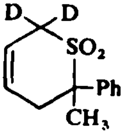
a: R = Ph, X = H
b: R = Ph, X = Me
c: R = Ph, X = Cl



IV(a–f)

d: R = Me, X = H
e: R = Me, X = Me
f: R = Me, X = Cl

Similarly, the reaction of thioacetophenone with 1,3-butadiene gave a quantitative yield of 5-methyl-5-phenyl-4-thiacyclohexene, Id. The assignment of signals in the NMR spectrum of Id was determined, as with Ia, by oxidation with hydrogen peroxide to the corresponding sulphone, IIId, followed by spin-decoupling studies. The assignment was further confirmed by a hydrogen-deuterium exchange reaction; IIId was deuterated by a t-BuOD—t-BuOK system giving IIId-3,3-d_2, whose NMR spectrum lacked a signal at 3·38 (tentatively assigned as H_d's) and a signal at 6·05 (tentatively assigned as H_c) became doublet. This fact unequivocally supports the assignment given.



IIId-3,3-d_2

Isoprene. The reaction of isoprene and thiobenzophenone gave a quantitative yield of an oily mixture of Ib and IIb. When the oil was dissolved into n-hexane and allowed to stand at about 0° for a week, crystalline material precipitated, whose NMR spectrum was composed of signals at 7·08–7·44 multiplet (10H), 5·63 multiplet (1H), 2·96 multiplet (2H), 2·70 broad singlet (2H), and 1·65 broad singlet (3H). Since it has been established by NMR spectroscopy of Ia that protons at 2 and 3 positions are respectively

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[*] Hereafter chemical shifts will be denoted in terms of δ from TMS in $CDCl_3$ unless otherwise noted.

[†] H_a, H_b, H_c, and H_d are protons attached to carbons at 6, 1, 2, and 3 positions, respectively.

more deshielded than those at 1 and 6 positions by the effect of a S atom, signals of IIb at 2·96 and 2·70 are respectively assigned to H_d's and H_a's. The spin-decoupling study and the NMR spectrum of IVb which has been obtained by the oxidation of IIb support the assignment.*

Consequently, two distinct singlets at (in CCl_4) 1·76 and 1·61 in the NMR spectrum of the mixture of Ib and IIb are, thus, unambiguously determined to be Me protons in Ib and IIb, respectively. The integrations of two signals gave the isomer ratio, IIb/Ib of 1·5. The oily residue, after crystals of IIb had been removed from the mixture, was oxidized by hydrogen peroxide to a sulphone, which proved to be IIIb. This establishes that Ib is preponderant in the oily mixture.

On the other hand, a mixture of products of the reaction of isoprene with thioacetophenone, Ie and IIe, could not be separated into components either as sulphide or as sulphone. However, by analogy with Id, Ib, and IIb, the two signals at 1·78 and 1·66 were assigned to Me protons in Ie and IIe, respectively and their ratio was calculated, from the integrations, to be 1·2:1·0.

Chloroprene. A similar reaction of thiobenzophenone takes place with chloroprene at room temperature. Although each isomer could not be isolated from the product mixture, the oxidation gave a crystalline sulphone, whose NMR spectrum shows signals at 7·57 multiplet (4H), 7·34 multiplet (6H), 5·66 AM_2X_2 nonet (1H), 3·70 quartet (2H), and 3·29 sextet (2H). A comparison of this with the spectrum of a mixture of isomeric sulphones, coupled with a spin-decoupling study, suggests that the isolated sulphone is IIIc. Based on the relationship between NMR spectra of Ia, IIa, Ib, and IIb and their corresponding sulphones, signals in the spectrum of the product mixture were assigned as 5·88 AM_2X_2 nonet (1H), 3·21 quartet (2H), and 2·81 sextet (2H) being H_b, H_d's, and H_a's in Ic, respectively and 5·99 AM_2X_2 nonet (1H), 3·08 sextet (2H), and 2·97 quartet (2H) being H_c; H_d's, and H_a's in IIc, respectively. The ratio of isomers, Ic/IIc, in the product was found to be 1·8 from integrals of signals.

The reaction of chloroprene with thioacetophenone also afforded a quantitative yield of a mixture of If and IIf. The isomer ratio, IIf/If, in the product mixture was found to be 2·0 by the method described above.

Isomer ratios and chemical shifts of protons in I–IV are tabulated in Tables 1 and 2, respectively. As is seen in Table 1, the isomer ratio of the product depends on the structures of the thiocarbonyl compounds and substituents in butadiene.

TABLE 1. RATIOS OF ISOMERIC PRODUCTS OF THE REACTION

R	X = Me I : II	X = Cl I : II
Ph	1·0 : 1·5	1·8 : 1·0
Me	1·2 : 1·0	1·0 : 2·0

Since the present reactions are not affected by the presence of hydroquinone, a

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* If the compound were Ib, signals at 2·99 and 2·73 might be broad singlet and multiplet, respectively, because of the splitting caused by a vinyl proton.

radical scavenger, it is obvious that the reaction does not proceed with the out-of-cage free radical mechanism. However, no evidence is available to distinguish the mechanisms of in-cage free-radical reaction and ionic reactions.

The rate of the reaction also depends on the structure of thiocarbonyl compounds. Thus, thiobenzophenone reacts with dienes at room temperature within a day, while two days are necessary for the reaction of thioacetophenone. O-Ethyl thiobenzoate and thioacetate were recovered unreacted after a week.

TABLE 2. CHEMICAL SHIFTS OF PROTONS IN VARIOUS 4-THIACYCLOHEXENE DERIVATIVES AND THEIR CORRESPONDING SULPHONES (δ FROM TMS)

Compd	Solvent	H_a	H_b	H_c	H_d	Me
Ia	$CDCl_3$	2·82	5·78	5·82	2·99	
	CCl_4	2·74	5·72	5·82	2·93	
Ib	CCl_4	2·69	5·50		2·74	1·76
Ic	$CDCl_3$	2·81	5·88		3·21	
	CCl_4	2·74	5·82		3·15	
Id	$CDCl_3$	—	5·68	5·68	—	1·53
Ie	$CDCl_3$	—	5·50		—	1·60, 1·78
If	$CDCl_3$	2·62	5·83		2·89	1·58
IIb	$CDCl_3$	2·70		5·63	2·96	1·65
	CCl_4	2·60		5·52	2·87	1·61
IIc	$CDCl_3$	2·97		5·99	3·08	
	CCl_4	2·90		5·93	3·01	
IIe	$CDCl_3$	—		5·50	—	1·60, 1·66
IIf	CCl_4	2·80		5·83	2·96	1·58
IIIa	$CDCl_3$	3·28	5·50	6·04	3·46	
IIIb	$CDCl_3$	3·20	5·22		3·35	1·92
IIIc	$CDCl_3$	3·29	5·66		3·70	
IIId	$CDCl_3$	3·20	5·65	6·05	3·38	1·80
IIIf	$CDCl_3$	3·26	5·68		3·35	1·80
IVb	$CDCl_3$	3·17		5·73	3·39	1·70
IVc	$CDCl_3$	3·45		6·17	3·49	
IVf	$CDCl_3$	3·10		6·12	3·52	1·80

EXPERIMENTAL

5,5-Diphenyl-4-thiacyclohexene. Into a 100-ml ampoule of thick glass which contained about 30 ml 1,3-butadiene, 3 g of thiobenzophenone was dissolved under an atmosphere of N_2. The ampoule was cooled, degassed, and sealed, and then was kept at room temp in the dark. The colour of thiobenzophenone disappeared within 10 hr and crystals had formed. Excess butadiene was removed after the completion of the reaction and 4 g (100%) crude Ia was obtained. Recrystallizations from cyclohexane gave a pure material, m.p. 94·5–5·5°. (Found: C, 80·66; H, 6·52. $C_{17}H_{16}S$ requires: C, 80·90; H, 6·39%).

5-Methyl-5-phenyl-4-thiacylohexene. According to this procedure, 10·5 g thioacetophenone was allowed to react with 30 ml 1,3-butadiene. The colour of thioacetophenone disappeared within 3 days. After excess butadiene was evaporated, 16 g (100%) of viscous oil was obtained, which was found, by NMR spectroscopy, to be almost pure Id. No further purification was necessary.

1- and 2-Chloro-5,5-diphenyl-4-thiacyclohexene. Under an atmosphere of CO_2, a mixture of chloroprene (25 g) and thiobenzophenone (5 g) was allowed to stand at room temp in dark for 10 hr. The excess chloroprene was removed under a reduced press and 7·8 g (100%) viscous oil was obtained, which was found, by NMR spectroscopy to be a mixture of Ic and IIc. Without further purification, the oil was subjected to oxidation.

1- *and* 2-*Chloro-5-methyl-5-phenyl-4-thiacyclohexene*. The color of the mixture of thioacetophenone (4 g) and chloroprene (20 g) disappeared within a day at room temp. Removal of excess chloroprene *in vacuo* afforded 7 g (100%) viscous oil, whose NMR spectrum showed that this was a mixture of If and IIf.

1- *and* 2-*Methyl-5,5-diphenyl-4-thiacyclohexene*. The colour of a mixture of 30 g isoprene and 7·2 g thiobenzophenone disappeared within 7 hr at room temp. After evaporation of excess isoprene, 11 g (100%) viscous oil was obtained, which was a mixture of Ib and IIb. When the oily mixture was dissolved in 10 ml n-hexane and allowed to stand at about 0° in a refrigerator for a week, white crystals precipitated, were recrystallized from n-hexane giving IIb, m.p. 56–57°. (Found: C, 81·44; H, 7·06. $C_{18}H_{18}S$ requires: C, 81·20; H, 6·77%).

1,5- *and* 2,5-*Dimethyl-5-phenyl-4-thiacyclohexene*. The colour of a mixture of thioacetophenone (4 g) and isoprene (18 g) disappeared within 2 days· Removal of excess isoprene gave 5·5 g (100%) oily material, whose NMR spectrum showed that this was a mixture of Ie and IIe. Without further purification, the mixture was subjected to the oxidation.

5,5-*Diphenyl- and* 5-*Methyl-5-phenyl-4-thiacyclohexene-4,4-dioxide*. To an AcOH soln containing 0·5 g 30% H_2O_2, 0·3 g of Ia was added and the soln kept below 50° for 3 hr. Crystals formed were filtered off and 0·4 g (~100%) of crude IIIa was obtained. Recrystallizations from EtOH gave pure IIIa, m.p. 145–146°. (Found: C, 71·80; H, 5·44. $C_{17}H_{16}O_2S$ requires: C, 71·80; H, 5·67%).

Similarly, 6·7 g of Id gave 5·6 g (90%) crude IIId, which was recrystallized from EtOH to give the pure material, m.p. 101–102°. (Found: C, 65·05; H, 6·26. $C_{12}H_{14}O_2S$ requires: C, 64·83; H, 6·35%).

1- *and* 2-*Chloro-5,5-diphenyl-4-thiacyclohexene-4,4-dioxide and* 1- *and* 2-*Chloro-5-methyl-5-phenyl-4-thiacyclohexene-4,4-dioxide*. The oily mixture of Ic and IIc (2·1 g) was oxidized with H_2O_2 in AcOH to a crystalline mixture of IIIc and IVc, from which IIIc, m.p. 115–156°. (Found: C, 63·74; H, 4·70. $C_{17}H_{15}ClO_2S$ requires: C, 64·04; H, 4·74), was obtained by fractional recrystallizations from n-hexane–benzene.

Although IVc could not be isolated, repeated fractional recrystallization gave a one to one mixture* of IIIc and IVc, m.p. 141–144°.

Oxidation of a mixture of If and IIf with H_2O_2 followed by fractional recrystallization from n-hexane–benzene afforded IVf, m.p. 120–125°. (Found: C, 56·32; H, 5·42. $C_{12}H_{13}ClO_2S$ requires: C, 56·13; H, 5·10), which contained about 5% of IIIf.

1- *and* 2-*Methyl-5,5-diphenyl-4-thiacyclohexene-4,4-dioxide and* 1,5- *and* 2,5-*Dimethyl-5-phenyl-4-thiacyclohexene-4,4-dioxide*. Similarly, 0·4 g of IIb was oxidized to IVb. Recrystallization from EtOH gave 0·4 g pure material, m.p. 111–113°. (Found: C, 72·12; H, 6·17. $C_{18}H_{18}O_2S$ requires: C, 72·45; H, 6·08%).

An oily mixture of Ib and IIb, obtained by the reaction of thiobenzophenone with isoprene, from which most of IIb had been removed as described above, was oxidized in the usual manner. Recrystallization from EtOH gave IIIb, m.p. 132–133°. (Found: C, 72·63; H, 5·86. $C_{18}H_{18}O_2S$ requires: C, 72·45; H, 6·08%).

On the other hand, neither IIIe nor IVe could be isolated by oxidation of a mixture of Ie and IIe. Recrystallization from EtOH gave only a mixture of IIIe and IVe, m.p. 111–113°.

5-*Methyl-5-phenyl-4-thiacyclohexene-4,4-dioxide*-3,3-d_2. In an evacuated sealed tube, 20 ml t-butanol-O-d, 150 mg K, and 500 mg of the material were placed and allowed to stand for 2 days at room temp. The reaction mixture was slightly acidified with HCl aq and the resulting ppt filtered off. Recrystallization from EtOH gave IIId-3,3-d_2. The NMR spectrum of the deuterated compounds showed that protons on the C atom adjacent to the sulphone group had been exchanged by deuterium.

NMR *spectroscopy*. NMR spectra were obtained on a Varian HA-100 instrument. Although most of the compounds dissolved into $CDCl_3$, some appeared as colloids. In such cases CCl_4 was used as a solvent.

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* The proportion was determined by NMR spectroscopy.