

Effects of Substituents and Chain Length of Thiobenzophenones on Reactivity in a Thermal Intramolecular Ene Reaction

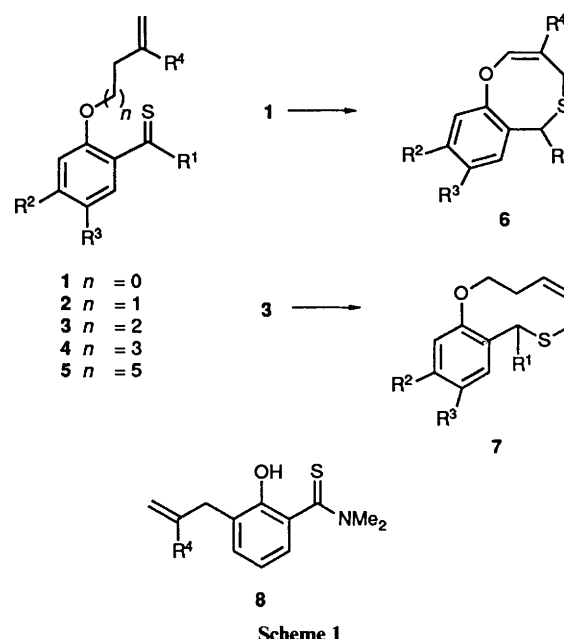
Takao Saito,* Tsumoru Watanabe, Satoshi Kitazawa, Yuko Hayashi and Shinichi Motoki*

Department of Chemistry, Faculty of Science, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162, Japan

Thiobenzophenones **1** and **3** bearing an allylic group attached *via* an *o*-poly(methyleneoxy), $(\text{CH}_2)_n\text{O}$, ($n = 0$ and 2) bridge underwent thermal Type III intramolecular ene reactions giving 8- and 10-membered cyclic sulphides **6** and **7** with newly formed *cis* double bonds. In contrast, with $n = 1, 3$ or 5 or with related *N,N*-dimethylthioarylamides no ene products were observed.

Although the versatility of intramolecular ene reactions makes them important in organic synthesis,^{1,2} there are few examples involving thiocarbonyl compounds.³⁻⁶ Recently we reported that thiobenzophenone **1** bearing an allylic ene unit underwent an intramolecular ene reaction, the first example of a thiocarbonylenophilic Type III reaction,¹ to give a cyclic sulphide **6** with a newly formed *cis* double bond.⁶ The reaction was both regio- and stereo-specific and, where there was a choice, highly site-selective (*e.g.* for $\text{R}^4 = \text{Me}$, Type II *vs.* III).[†] Very recently Kirby *et al.* reported a thiocarbonyl intramolecular ene reaction with ω -vinylalkyl thioacetates to afford Type III-cyclized, 7- to 11-membered ring 3-thiolactones.⁵ We report herein that the efficiency of the intramolecular ene reactions of the thioketones depends largely upon substituents, R^1 - R^4 , and chain lengths, n .

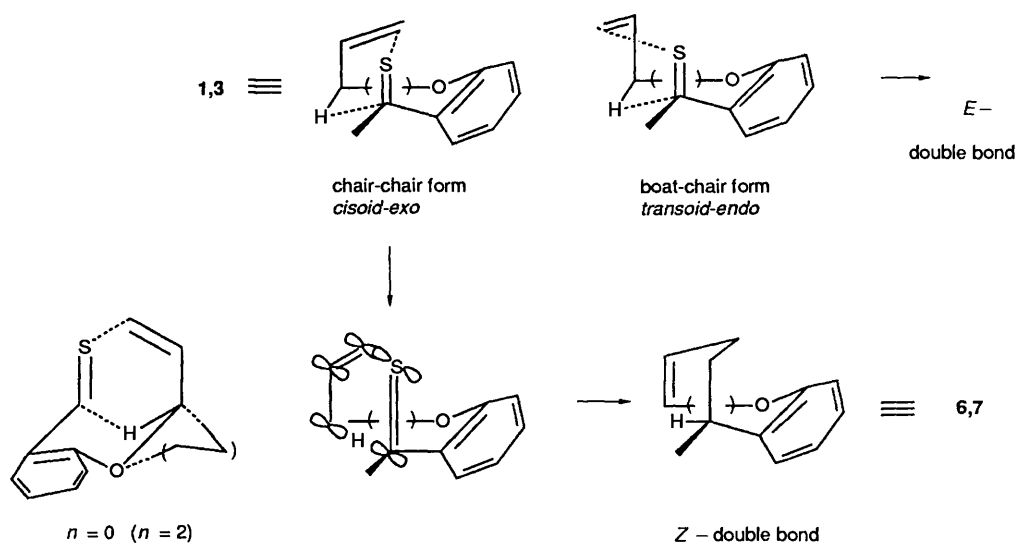
The thioketones **1a-h** ($n = 0$), prepared by thionation of the corresponding ketones with Lawesson's reagent in THF, underwent intramolecular Type III ene reactions smoothly at 140 °C in xylene (Scheme 1, Table 1). The reactions were readily monitored by disappearance of the characteristic colour of **1** and by TLC. Table 1 shows that, as the R^4 -substituent varies $\text{H} \rightarrow \text{Me} \rightarrow \text{Cl}$ (**a-c** and **d-f**), there is an increase in the reaction time required and a small decrease in the yield of **6**. Although substituents MeO in R^2 (**d-f**), Me in R^3 and *p*-Me and *p*-Cl in R^1 (**g** and **h**) have little effect on the efficiency of the ene reaction, strongly thiocarbonyl-stabilizing substitution by



Me_2N greatly retards the reaction (**i-k**), no ene product being obtained. Prolonged heating at higher temperatures resulted in decomposition of **1i** to give ill-defined products or Claisen rearrangement of **1j,k** to give **8** in 86–90% yields.

Thermal reactions of the thioketones **2a,d,g,h** (chain length,

[†] With thioketones **1b,e** ($\text{R}^4 = \text{Me}$), Type II reactions are, in principle, possible. However, such ene products were not detected.



Scheme 2 The terms 'cisoid' and 'transoid' refer to the conformational relationship of the vinyl group relative to the chain around the allyl C–C single bond, which forms the double bond after the ene reaction. The terms 'endo' and 'exo' denote the orientational positions of the chain, as defined by its attachment to the enophile unit, relative to the ene unit. The *E* and *Z* notation denotes the configuration of the double bond formed in the ring of the sulphide.

$n = 1$) were attempted. Reactions conducted in xylene at 140 °C (conditions: A) for 16–64 h or in *o*-dichlorobenzene at 180 °C (conditions: B) for 5–14 h afforded neither ene products nor any identifiable product originating from the thioketones.* Thioketones **4a,d,g,h** ($n = 3$) and **5a,d** ($n = 5$) showed similar results.*

Interestingly, with a chain length of $n = 2$, the corresponding thioketones **3** did undergo an intramolecular ene reaction to produce the 10-membered cyclic sulphides **7**, even though the efficiency was rather reduced compared with $n = 0$ (Scheme 1, Table 2).

Table 1 Intramolecular ene reaction of thioketones **1** ($n = 0$)

	R ¹	R ²	R ³	R ⁴	Reaction condition ^a	Yield of 6 (%)
a ^b	Ph	H	H	H	0.5 h (A)	99
b	Ph	H	H	Me	1 h (A)	91
c	Ph	H	H	Cl	23 h (A)	72
d ^b	Ph	MeO	H	H	1 h (A)	83
e ^b	Ph	MeO	H	Me	1.5 h (A)	83
f ^b	Ph	MeO	H	Cl	24 h (A)	78
g	<i>p</i> -MeC ₆ H ₄	H	Me	H	1 h (A)	79
h	<i>p</i> -ClC ₆ H ₄	H	Me	H	4.5 h (A)	82
i	<i>p</i> -Me ₂ NC ₆ H ₄	H	H	H	50 h (A)	0
					20 h (B)	0
j	NMe ₂	H	H	H	13 h (B)	0
k	NMe ₂	H	H	Me	16 h (B)	0

^a Conditions: A: reflux in xylene (140 °C), B: reflux in *o*-dichlorobenzene (180 °C). ^b Reported in ref. 6.

Table 2 Intramolecular ene reaction of thioketones **3** ($n = 2$)^a

	R ¹	R ²	R ³	R ⁴	3 ($n = 2$)		1 ($n = 0$)	
					Reaction time	Yield of 7 (%)	Reaction time	Yield of 6 (%)
a ^b	Ph	H	H	H	15 h	63	0.5 h	99
d	Ph	MeO	H	H	64 h	54	1 h	83
g	<i>p</i> -MeC ₆ H ₄	H	Me	H	6 d	36	1 h	79
h	<i>p</i> -ClC ₆ H ₄	H	Me	H	7 d	55	4.5 h	82

^a Conditions: reflux in xylene (140 °C). ^b Reported in ref. 6.

Inspection of molecular models (see Scheme 2) shows that access to the reaction centres at a Type III transition state are conformationally feasible only in the thioketones **1** and **3** with chain lengths of $n = 0$ and 2.

Experimental

6-Phenyl-4H,6H-1,5-benzoxathiocin 6a.—2-Allyloxythiobenzophenone **1a** (240 mg, 0.944 mmol) was heated in dry xylene (15 ml) for 30 min under a nitrogen atmosphere. The solvent was evaporated and the residue was column-chromatographed on silica gel using dichloromethane–hexane (1:1) as eluent to give the title compound **6a** (238 mg, 99%) as an oil (Found: M^+ , 254.0760. C₁₆H₁₄OS requires M , 254.0766); $\nu_{\max}(\text{neat})/\text{cm}^{-1}$ 1648 (*cis*-olefin) and 705 (=CH); $\delta_{\text{H}}(100 \text{ MHz}, \text{CDCl}_3)$ 2.75 (1 H, dd, J 14.6 and 9.3), † 2.96 (1 H, ddd, J 9.3, 9.3 and 1.4), 4.69 [1 H, ddd, J 9.3, 9.3 and 7.7 (*cis*)], 5.79 (1 H, s), 6.48 [1 H, dd, J 7.7 (*cis*) and 1.4] and 6.72–7.68 (9 H, m); $\delta_{\text{C}}(25.5 \text{ MHz}, \text{CDCl}_3)$ 24.92 (t), 45.11 (d), 101.21 (d) (olefin), 119.93 (d), 126.19 (d), 127.42 (d), 131.92 (s), 139.06 (s), 145.09 (d) (olefin) and 153.69 (s); m/z 254 (M^+ , 10%), 221 ($M^+ - \text{SH}$, 24) and 181 (100).

* The reactions of thioketones **2a,d,g,h**, **4a,d,g,h** and **5a,d** ($R^4 = \text{H}$) were tested several times in each case: for **2a**, 16–20 h (A), 5–14 h (B); **2d**, 24–29 h (A), 5–14 h (B); **2g**, 28 h (A); **2h**, 64 h (A); **4a**, 80 h (A), **4d**, 79–85 h (A), 5–14 h (B); **4g,h**, 5–14 h (B); **5a**, 50 h (A), 5–14 h (B); and for **5d**, 50 h (A), 5–14 h (B).
† J values in Hz.

References

- 1 W. Oppolzer and V. Snieckus, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 476.
- 2 For inter- and intra-molecular ene reactions, H. M. R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, 1969, **8**, 556; J. M. Conia and P. Le Perchec, *Synthesis*, 1975, 1; B. B. Snider, *Acc. Chem. Res.*, 1980, **13**, 426; D. F. Taber, *Intramolecular Diels-Alder and Alder Ene Reactions*, Springer Verlag, Berlin, 1984.
- 3 Type II: E. Vedejs, T. H. Eberlein and R. G. Wilde, *J. Org. Chem.*, 1988, **53**, 2220.
- 4 Type I: S. S.-M. Choi and G. W. Kirby, *J. Chem. Soc., Chem. Commun.*, 1988, 177.
- 5 Type III: S. S.-M. Choi, G. W. Kirby and M. P. Mahajan, *J. Chem. Soc., Chem. Commun.*, 1990, 138.
- 6 Type III: S. Motoki, T. Watanabe and T. Saito, *Tetrahedron Lett.*, 1989, **30**, 189.

Paper 0/05536K

Received 10th December 1990

Accepted 11th December 1990
