

New Synthesis of α -Methylenecyclobutanones and α -Methylenazetidin-2-one Derivatives

By TORU MINAMI,*MASARU ISHIDA, and TOSHIO AGAWA

(Department of Petroleum Chemistry, Faculty of Engineering, Osaka University, Yamadakami, Suita, Osaka 565, Japan)

Summary Methyl(phenylthio)keten reacts with olefins and imines to yield α -(phenylthio)cyclobutanone and α -(phenylthio)azetidin-2-one derivatives which can be converted into α -methylenecyclobutanone and α -methyl-enazetidin-2-one derivatives, respectively.

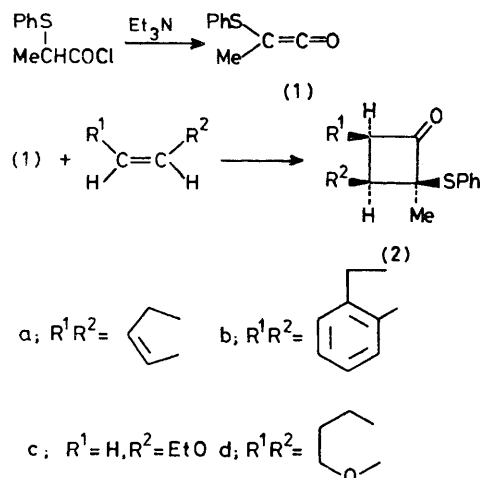
IN connection with synthesis of natural products, many methods for introduction of $\alpha\beta$ -unsaturated carbonyl units have been developed.¹ We report here a versatile synthesis of α -methylenecyclobutanone and α -methylenazetidin-2-one derivatives from methyl(phenylthio)keten, which serves as the precursor of the $\alpha\beta$ -unsaturated carbonyl unit.†

† All compounds described herein provided the expected elemental analysis and spectral data.

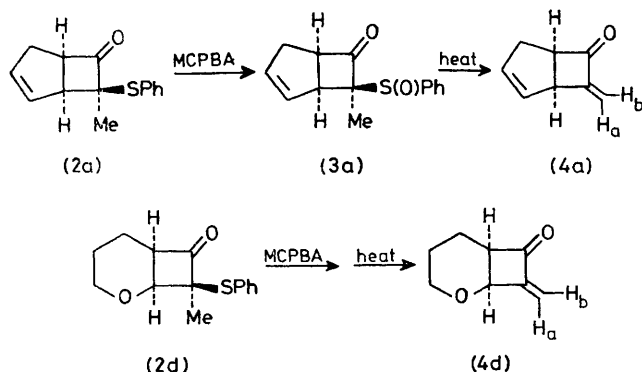
TABLE 1. Synthesis of α -(phenylthio)cyclobutanones (**2**) from (**1**) and olefins

Olefin	Molar ratio olefin : (1)	Product % Yield	M.p. (b.p.)/ $^{\circ}$ C
Cyclopentadiene	5 : 1	(2a) 82	52.5—54
Indene	10 : 1	(2b) 42	100
Ethyl vinyl ether	13 : 1	(2c) 26	(92 at 1 mmHg)
2,3-Dihydropyran	5 : 1	(2d) 65	85—85.5

Methyl(phenylthio)keten (**1**) was generated *in situ* by dehydrochlorination of α -(phenylthio)propanoyl chloride \ddagger with triethylamine. In the presence of excess of olefins, the keten (**1**) gave the α -(phenylthio)cyclobutanones (**2**) in good yields (Table 1). Regardless of the olefin substituents, all the cyclobutanones formed contain the phenylthio-group in the *endo*-configuration. These results suggest a concerted [2 + 2] cycloaddition mechanism.



Oxidation of (**2a**) with *m*-chloroperbenzoic acid (MCPBA) in chloroform at -10°C afforded the sulfoxide (**3a**) (m.p. $94.5\text{--}96^{\circ}\text{C}$, 94%). Thermolysis of (**3a**) at 150°C *in vacuo*



\ddagger α -(Phenylthio)propanoyl chloride was synthesized by treatment with thionyl chloride of α -(phenylthio)propanoic acid, which was obtained by the reaction of sodium benzene thiolate with ethyl α -chloropropionate following by hydrolysis; 85% overall yield; b.p. $87\text{--}93^{\circ}\text{C}$ at 1 mmHg.

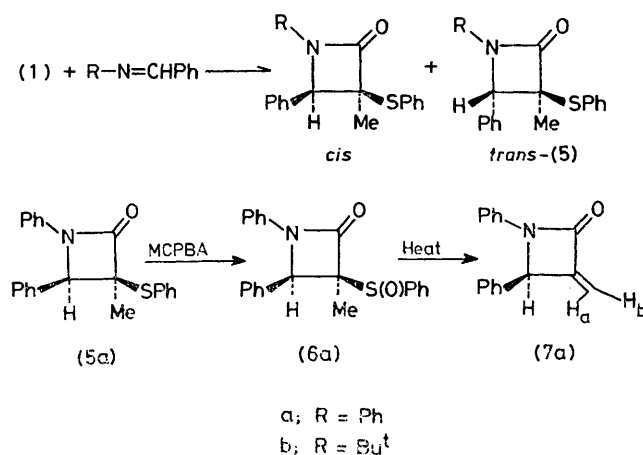
vacuo gave the α -methylenecyclobutanone (**4a**) [b.p. $68\text{--}71^{\circ}\text{C}$ at 15 mmHg, 62%; δ (CDCl_3) 4.92 (1H, s, H_a) and 5.50 (1H, s, H_b)]. Similar treatment of (**2d**) also gave the corresponding product (**4d**) [b.p. 90°C at 15 mmHg; 57%; δ (CDCl_3) 5.40 (1H, s, H_a) and 5.90 (1H, s, H_b)].

TABLE 2. Synthesis of α -(phenylthio)azetidin-2-ones (**5**) from (**1**) and imines

Imine R-N=CHPh	Product % Yield	Product ratio ^a <i>cis</i> : <i>trans</i>	M.p./ $^{\circ}$ C
R = Ph	(5a) 58	100:0	193—194
R = Bu	(5b) 69	40:60	108—110 ^b

^a Determined by n.m.r. spectroscopy. ^b M.p. of mixture; the *trans*-isomer only could be isolated pure, m.p. $118\text{--}120^{\circ}\text{C}$.

In contrast to reactions with olefins, reactions of the keten (**1**) with imines were substituent dependent. The reaction between (**1**) and *N*-benzylidenaniline produced the *cis*- α -(phenylthio)azetidin-2-one (**5a**) as a single isomer, whereas the reaction of *N*-benzylidene-*t*-butylamine led to a mixture of *cis*- and *trans*- α -(phenylthio)azetidin-2-ones (**5b**) (Table 2). Oxidation of (**5a**) afforded the sulfoxide (**6a**) (m.p. $202\text{--}203^{\circ}\text{C}$, 94%). The α -methyleneazetidin-2-one (**7a**) was obtained by thermolysis of (**6a**) at 200°C *in vacuo* [(**7a**), m.p. $146\text{--}147^{\circ}\text{C}$, 77%; δ (CDCl_3) 5.09 (1H, s, H_a) and 5.76 (1H, s, H_b)].



In conclusion, the keten (**1**) can be regarded as a synthon equivalent of methyleneketene.

(Received, 3rd October 1977; Com. 1032.)

¹ See, e.g., P. A. Grieco and J. J. Reap, *Tetrahedron Letters*, 1974, 1097; T. Minami, I. Niki, and T. Agawa, *J. Org. Chem.*, 1974, **39**, 3236; B. M. Trost, T. N. Salzmann, and K. Hiroi, *J. Amer. Chem. Soc.*, 1976, **98**, 4887.