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[2+2] Cycloaddition of Alkenyl Sulfide with α,β-Unsaturated Ketone. A Convenient Route to 1-Cyclobutenyl Ketones

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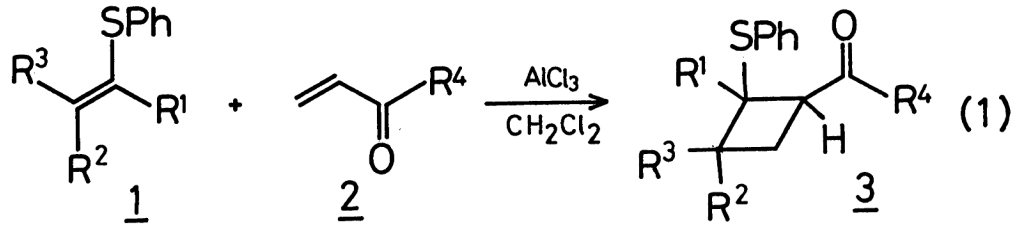
2-Phenylthiocyclobutyl ketones were produced by the reaction of alkenyl sulfides with α,β-unsaturated ketones in the presence of $AlCl_3$. The oxidation with MCPBA and the treatment with LDA or KH of the cycloadducts afford the corresponding 1-cyclobutenyl ketones in good yields.

Polar [2+2] cycloadditions of olefins activated by electron-withdrawing groups with heteroatom-substituted olefins have been extensively studied as simple methods to construct functionalized four-member rings. However, to our knowledge, no successful polar cycloaddition of α,β-unsaturated ketone was reported.[1)]

In this communication, we wish to describe a [2+2] cycloaddition of alkenyl sulfides (1) with α,β-unsaturated ketones (2) and the conversion of the cycloadducts (3) to 1-cyclobutenyl ketones (5).



(1)

The cycloaddition was carried out in the presence of a catalytic amount of $AlCl_3$ in CH_2Cl_2 at -78 °C and the results are summarized in Table 1. When monoalkyl substituted vinyl sulfide or (E)-1,2-dialkyl substituted vinyl sulfide[2)] was employed, the corresponding cyclobutane (3) was obtained in good yield. It was found that $TiCl_4$ was superior to $AlCl_3$ as a catalyst in the reaction utilizing 2-monoalkyl vinyl sulfide (run 1). However, no cycloadduct (3) was produced and the starting material was recovered in the reaction of (Z)-alkenyl sulfide with methyl vinyl ketone under similar reaction conditions (runs 5 and 7). The stereospecificity of the present reaction suggests that the reaction proceeds by a cisoid approach of the two cycloaddends as depicted in Fig. 1. The alkyl group on β carbon (R^3) sterically interferes such an approach of the reactants. As a result, the adducts (3) would be produced stereoselectively. In fact, ^1H NMR signals of methine protons α to carbonyl group of the cyclobutanes (3b, c, d, e, f, g, and h) appear as single triplets (3b; δ= 3.20 (J= 8 Hz), 3c; δ= 2.93 (J= 8 Hz), 3d; δ= 2.83 (J= 8 Hz), 3e; δ= 2.92 (J= 8 Hz), 3f; δ= 2.93 (J= 8 Hz), 3g; δ= 2.92 (J=

Table 1. [2+2] cycloaddition of alkenyl sulfide (1) with α,β-unsaturated ketones (2)[a)]

Run	R^1	R^2	R^3	R^4	Time min	Product[4)] (Yield/%)
1	H	$CH_3(CH_2)_6$	H	CH_3	90	3a (13 (70[b)]))
2	$CH_3(CH_2)_7$	H	H	CH_3	25	3b (51 (0[b)]))
3	$-(CH_2)_4-$		H	CH_3	60	3c (72)
4	$CH_3(CH_2)_7$	$Ph(CH_2)_2$	H	CH_3	60	3d (78)
5	$CH_3(CH_2)_7$	H	$Ph(CH_2)_2$	CH_3	80	(0)
6	$CH_3(CH_2)_3$	$CH_3(CH_2)_2$	H	CH_3	60	3e (66)
7	$CH_3(CH_2)_3$	H	$CH_3(CH_2)_2$	CH_3	60	(0 (82[c)]))
8	$CH_3(CH_2)_7$	$(CH_3)_2CHCH_2$	H	CH_3	90	3f (78)
9	$CH_3(CH_2)_3$	$CH_3(CH_2)_2$	H	$CH_3(CH_2)_3$	180	3g (71[d)])
10	$CH_3(CH_2)_7$	$(CH_3)_2CHCH_2$	H	$CH_3(CH_2)_3$	180	3h (71[d)])

a) All reactions were performed with the same procedure as described in the text, unless otherwise noted.
b) The yield of the cycloadduct when the reaction was carried out at -30 °C for 30 min in the presence of an equimolar amount of $TiCl_4$ as a catalyst.
c) Recovered alkenyl sulfide.
d) 1.5 equiv. of α,β-unsaturated ketone and 0.3 equiv. of $AlCl_3$ were used.

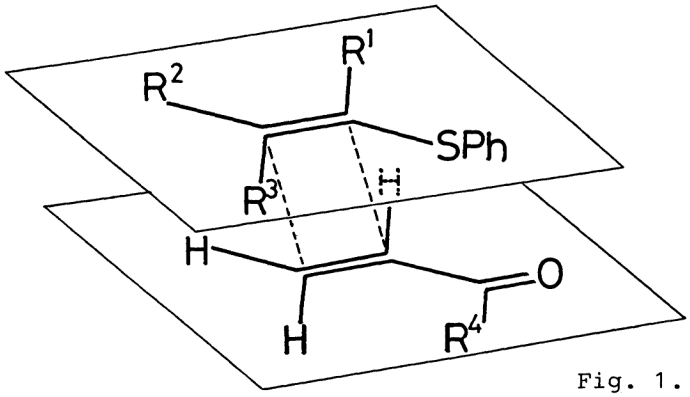


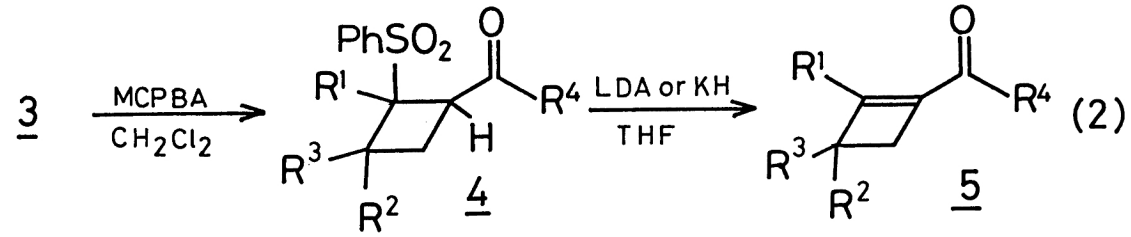
Fig. 1.

8 Hz), 3h; δ= 2.90 (J= 8 Hz)).[3)] This fact suggests that these products are single stereoisomers, although their stereochemistry is not determined.

The typical experimental procedure for the cycloaddition is as follows; to a CH_2Cl_2 (2 ml) suspension of $AlCl_3$ (46 mg, 0.34 mmol) was added a CH_2Cl_2 (4 ml) solution of (E)-2-methyl-5-(phenylthio)-4-tridecene (1) (521 mg, 1.71 mmol) and

methyl vinyl ketone (144 mg, 2.06 mmol) at -78 °C and the reaction mixture was stirred for 1.5 h. After addition of ether (2 ml) at -78 °C, the reaction was quenched with a saturated $NaHCO_3$ aqueous solution and the organic material was extracted with CH_2Cl_2. The extract was dried (Na_2SO_4) and condensed under reduced pressure. The residue was chromatographed on silica gel (AcOEt-hexane) and 1-acetyl-3-isobutyl-2-octyl-2-(phenylthio)cyclobutane (3) (500 mg) was isolated in 78% yield.

Next, the transformation of the adducts to 1-cyclobutenyl ketones was examined. The cycloadducts (3) were oxidized with 2.5 equiv. of MCPBA in CH_2Cl_2 to give the corresponding sulfones (4). Then 4 were treated with LDA or KH in THF and 1-cyclobutenyl ketones (5) were obtained in good yields.



(2)

The following experimental procedure is representative; to a CH_2Cl_2 (6.5 ml) solution of MCPBA (564 mg, 3.27 mmol) was added a CH_2Cl_2 (3.9 ml) solution of 1-isobutyl-2-octyl-2-(phenylthio)-3-valerylcyclobutane (3) (545 mg, 1.31 mmol) at 0 °C. After being warmed up to r.t., the reaction mixture was stirred overnight. The reaction was quenched by addition of a 1 M NaOH aqueous solution and the usual work-up and purification by silica gel TLC (AcOEt-hexane) gave the sulfone (4) (545 mg) in 93% yield. A THF (3.6 ml) solution of the sulfone (4) (539 mg, 1.20 mmol) was added to a THF (3.6 ml) suspension of KH (1.44 mmol) at 0 °C and reaction mixture was stirred overnight at r.t. The reaction was quenched with a phosphate buffer solution (pH 7) and the organic material was extracted with ether. The usual

Table 2. Synthesis of 1-cyclobutenyl ketones (5)

R^1	R^2 (R^3= H)	R^4	Oxidation Product[4] (Yield/%)	Elimination Base(equiv.)	Product[4] (Yield/%)
H	$CH_3(CH_2)_6$	CH_3	4a (99)	KH (1.0)	5a (81)
$CH_3(CH_2)_7$	H	CH_3	4b (86)	LDA (1.2)	5b (86)
$-(CH_2)_4-$		CH_3	4c (93)	LDA (2.5)	5c (49)
$CH_3(CH_2)_7$	$Ph(CH_2)_2$	CH_3	4d (97)	LDA (1.2)	5d (87)
$CH_3(CH_2)_7$	$(CH_3)_2CHCH_2$	CH_3	4f (85)	LDA (1.2)	5f (74)
$CH_3(CH_2)_3$	$CH_3(CH_2)_2$	$CH_3(CH_2)_3$	4g (98)	KH (1.2)	5g (66)
$CH_3(CH_2)_7$	$(CH_3)_2CHCH_2$	$CH_3(CH_2)_3$	4h (93)	KH (1.2)	5h (68)

work-up and purification by silica gel TLC (AcOEt-hexane) gave 3-isobutyl-2-octyl-1-valeryl-1-cyclobutene (5) (250 mg, 68%).

In a similar manner, several 1-cyclobutenyl ketones (5) were synthesized as shown in the Table 2.

Concerning the preparation of 1-cyclobutenyl ketones (5), Snider et al. reported that the $ZnCl_2$ catalyzed cycloaddition of olefins with 1-butyn-3-one gave 1-acetyl-1-cyclobutenes.[5] The yields, however, were low in general owing to the preferential formation of the ene adducts. Although preparation of 1-benzoyl-1-cyclobutene by selenenylation and selenoxide elimination of the corresponding cyclobutyl ketone was also reported,[6] it is apparent that the method has the inability to synthesize the aliphatic ketones. Therefore, it should be noted that the present reactions constitute the first practical way to prepare 1-cyclobutenyl ketones (5).

References

1) It was reported by Fleming and Karger that only the dihydropyran derivative was produced and the cyclobutane was not obtained by the reaction of methyl vinyl ketone with enamine; I. Fleming and M. H. Karger, J. Chem. Soc., C, 1967, 226.
2) (E)-1,2-Dialkyl vinyl sulfides can be stereoselectively prepared using 2-methoxyalkyl phenyl sulfides by the simple reaction procedure; T. Takeda, H. Furukawa, M. Fujimori, K. Suzuki, and T. Fujiwara, Bull. Chem. Soc. Jpn., 57, 1863 (1984).
3) The corresponding sulfones (4b, c, d, e, f, g, and h) also showed their ^1H NMR signals of the methine protons at δ= 3.87 (t, J= 9 Hz), 3.46 (t, J= 10 Hz), 3.82 (t, J= 9 Hz), 3.72 (t, J= 9 Hz), 3.75 (t, J= 9 Hz), 3.72 (t, J= 9 Hz), and 3.82 (t, J= 9 Hz), respectively.
4) All products were identified by IR and NMR spectra.
5) B. B. Snider, L. A. Brown, R. S. Eichen, and T. A. Killnger, Tetrahedron Lett., 1977, 2831.
6) H. J. Reich, J. M. Renga, and I. L. Reich, J. Am. Chem. Soc., 97, 5434 (1975).

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