

A NEW SYNTHETIC ROUTE FOR 3,4-DISUBSTITUTED TETRAHYDROTHIOPHENES
AND A NEW FRAGMENTATION OF THEIR RING SYSTEM¹

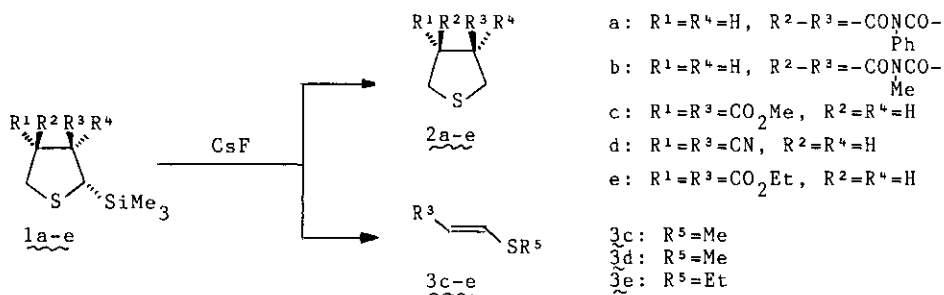
Masahiro Aono, Yoshiyasu Terao, and Kazuo Achiwa*

Shizuoka College of Pharmacy, 2-2-1 Oshika, Shizuoka 422, Japan

Abstract— Desilylation of 2-trimethylsilyl-3,4-disubstituted tetrahydrothiophenes provided a new method for synthesis of title compounds and a new fragmentation reaction of tetrahydrothiophene ring.

Thiocarbonyl ylides stabilized by the trimethylsilyl substituent have been found to afford the 1,3-dipolar cycloadducts in excellent yields with conjugated dipolarophiles¹.

We wish to describe here a further conversion of these cycloadducts (1) into the corresponding tetrahydrothiophene derivatives (2) and a new fragmentation in their desilylation.



As shown in Table 1, treatment of 2-trimethylsilyltetrahydrothiophenes (1) with cesium fluoride in hexamethylphosphoramide (HMPA) containing a little water or in acetonitrile gave the corresponding desilylated tetrahydrothiophene derivatives (2)². A typical experiment is described below.

Cesium fluoride (152 mg, 1 mmol) was added to a solution of 2-trimethylsilyltetrahydrothiophene-3,4-(N-phenyl)dicarboxyimide (1a) (305 mg, 1 mmol) in HMPA (4 ml) containing a drop of water. After stirring for 3 h with heating at 80°C, the mixture was diluted with benzene, washed with water and saturated aqueous sodium chloride, and dried over MgSO₄, and concentrated under reduced pressure.

The residue was subjected to preparative TLC (silica gel, benzene/AcOEt = 9/1 as an eluent) to give pure tetrahydrothiophene-3,4-(N-phenyl)carboxyimide (2a) in 73% yield. 2a: mp 152-153°C (from EtOH), IR(KBr); 1780, 1715 cm^{-1} , $^1\text{H-NMR}(\text{CDCl}_3)$ δ ; 2.88-3.64(6H, m, $-\text{CH}_2\text{CHCHCH}_2-$), 7.15-7.56(5H, m, C_6H_5), $^{13}\text{C-NMR}(\text{CDCl}_3)$ δ ; 36.5 (t, $2\times\text{CH}_2$), 48.5(d, $2\times\text{CH}$), 126.5, 128.7, 129.1, 132.5(d, d, d, s, C_6H_5), 177.1 (s, $2\times\text{CO}$).

Table 1 Desilylation^{a)} of 2-trimethylsilyltetrahydrothiophenes (1)

Substrate	Solvent	Temp.(°C)	Time(h)	Yield(%) of <u>2</u>
<u>1a</u>	HMPA	80	3	73
<u>1b</u>	HMPA	80	4	93
<u>1c</u>	CH_3CN	reflux	20	51
<u>1d</u>	CH_3CN	reflux	5	36
<u>1e</u>	CH_3CN	reflux	20	43

a) Molar ratio : 1 / CsF = 1

Table 2 Fragmentation of 2-trimethylsilyltetrahydrothiophenes (1)

Substrate	Method ^{a)}	Temp.(°C)	Time(h)	Yield(%) of <u>3</u> ^{b)}
<u>1c</u>	A	80	5	30
<u>1d</u>	B	110	2	50
<u>1e</u>	A	110	1.5	20

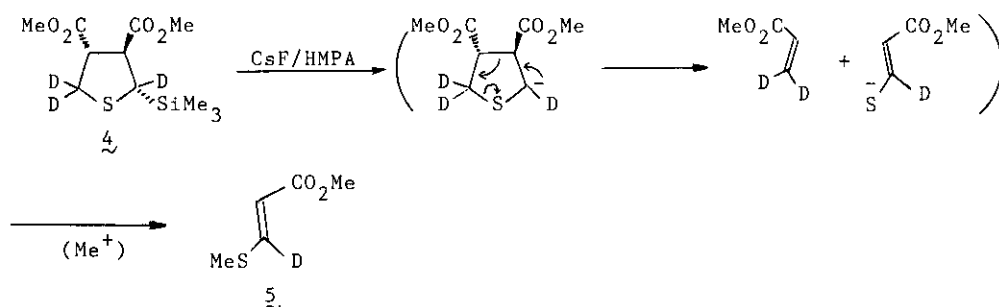
a) A; Molar ratio: 1 / CsF = 1, B; Molar ratio: 1 / CsF / MeI = 1 / 1 / 2.

b) The corresponding 2,3-disubstituted tetrahydrothiophene was detected as a minor product.

Although HMPA was suited for the desilylation of 1a and 1b, treatment of dimethyl 2-trimethylsilyltetrahydrothiophene-3,4-dicarboxylate (1c) with CsF in HMPA, instead of acetonitrile, afforded methyl methylthioacrylate (3c)³ as a main product. In order to clarify this new fragmentation, 2,5-deuterated dimethyl 2-trimethylsilyltetrahydrothiophene-3,4-dicarboxylate (4) was allowed to react under the similar conditions and was found to give the only product (5)⁴ bearing a deute-

rated vinyl group and the non-deuterated S-methyl group. This fact clearly indicated that the S-methyl group was transferred from methoxycarbonyl group of 4. This conclusion was also supported by the facts that the same desilylation of 2-trimethylsilyltetrahydrothiophene-3,4-dicarbonitrile (1d) only in the presence of excess methyl iodide afforded expected methylthioacrylonitrile (3d) in a 50% yield, and the compound (1e) gave ethyl ethylthioacrylate (3e) in a 20% yield under the similar treatment, as indicated in Table 2.

From these experiments this new fragmentation may proceed via the double retro-Michael addition reaction as illustrated below⁵.



It should be also noted that successful desilylation of 1,3-dipolar cycloadducts (1) provided a new efficient method for synthesis of tetrahydrothiophene derivatives. Further investigation in this area is under way.

REFERENCES

1. Thiocarbonyl ylides. II., part I; Y. Terao, M. Tanaka, N. Imai, and K. Achiwa, *Tetrahedron Lett.*, 1985, 26, 3011.
2. Satisfactory analytical and spectral data were obtained for these compounds.
3. 3c: ¹H-NMR(CDCl₃) δ ; 2.34(3H, s, SCH₃), 3.73(3H, s, OCH₃), 5.67(1H, d, J=14.9 Hz, =CHCO), 7.75(1H, d, J=14.9 Hz, =CHSMe), ¹³C-NMR(CDCl₃) δ ; 14.4(q), 51.4(q), 113.1(d), 147.3(d), 165.6(s).
4. 5: ¹H-NMR(CDCl₃) δ ; 2.34(3H, s, SCH₃), 3.73(3H, s, OCH₃), 5.66(1H, s, =CHCO).
5. Some recent reports deal with release of thiolate anion via retro-Michael reaction by strong base; I. Yamamoto, K. Okuda, S. Nagai, J. Motoyoshiya, H. Gotoh, and K. Matsuzaki, *J. Chem. Soc., Perkin Trans. I*, 1984, 435; P. G. Baraldi, A. Barco, S. Benetti, F. Moroder, G. P. Pollini, D. Simoni, and V. Zanirato, *J. Chem. Soc., Chem. Comm.*, 1982, 1265.

Received, 14th October, 1985