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A CONVENIENT METHOD FOR THE SYNTHESIS OF α-PHENYLTHIO-α,β-UNSATURATED KETONE BY STANNOUS TRIFLATE PROMOTED REARRANGEMENT OF α-SULFINYL KETONE

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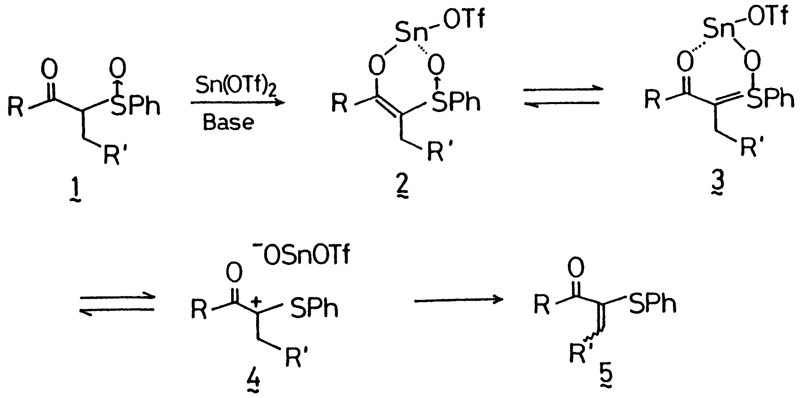
α-Phenylthio-α,β-unsaturated ketones are prepared in fairly good yields on treatment of α-sulfinyl ketone with stannous triflate. α-Phenylthio-α,β-unsaturated cyanides are also prepared from α-sulfinyl cyanides according to the similar procedure.

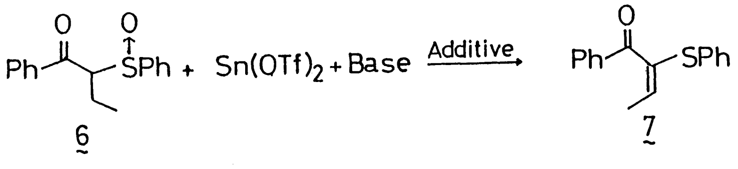
In our continuing work on stannous triflate mediated synthetic reactions,1) it was shown, in the previous paper,2) that generation of an intermediate α-thiocarbocation from α-sulfinyl ketone and stannous triflate is facilitated by way of an interaction between sulfoxide and Sn(II) species.3) The intermediate carbocation in turn reacted with silyl enol ether to form 2-arylthio 1,4-diketone in good yield.

Now we found that α-sulfinyl ketones having α-alkyl substituent with β-hydrogen could be transformed into α-arylthio-α,β-unsaturated ketones in moderate yields by the promotion of Sn(OTf)$_2$ under neutral and aprotic conditions as shown in the following scheme. α-Arylthio-α,β-unsaturated ketones thus prepared are considered to be useful synthetic intermediates e.g., the Michael acceptor and dienophile et al.4)



In the present experiment, the enolate of α-sulfinyl ketone 2 is initially generated on the treatment of α-sulfinyl ketone 1 with stannous triflate in the presence of tertiary amine. The enolate 2 is rearranged into α-thiocarbocation 4 via 3, and α-arylthio-α,β-unsaturated ketone 5 was formed by the subsequent deprotonation of 4.

Table 1. Examination of Reaction Conditions[a)]

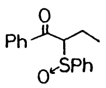
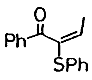
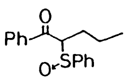
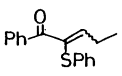
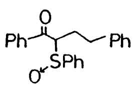
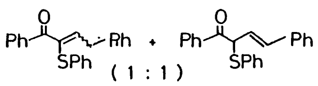
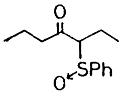
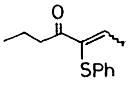


Entry	Base (equiv.)		$Sn(OTf)_2$ (equiv.)	Additive (equiv.)	Yield of 7/%	Recovery of 6/%
1		1.4	1.1	——	31	36
2	"	3.5	3.1	——	58	0
3	LDA	2.0	2.0	——	62	0
4		7.0	2.8	TMSOTf (3.0)	86	5
5	"	4.3	3.2	" (1.1)	64	28
6	"	2.7	0	" (6.2)	29	49

a) Solvent : CH_2Cl_2 0 °C overnight.

As shown in Table 1, when 1.1 equiv. of stannous triflate was employed, substantial amount of starting material was recovered. On the other hand, starting material was consumed on treatment with 3.1 equiv. of stannous triflate, and the yield of the desired product increased up to 58% (entry 2). Among various tertiary amines screened, N-ethylpiperidine gave the best result. On suspicious of incomplete formation of enolate by tertiary amine as a base, we next tried the same reaction with LDA, but there was little sign of improvement. The results indicate that the formation of the intermediate enolate 2 would be completed by using tertiary amine, and then we speculated that some nucleophilic species such as $^{-}OSnOTf$ would attack the intermediate carbocation 4 to cause complicated side reactions. In order to trap the nucleophilic species, various additives were screened and the satisfactory results were obtained when the

Table 2. Preparation of α-Phenylthio-α,β-unsaturated Ketone[a)]

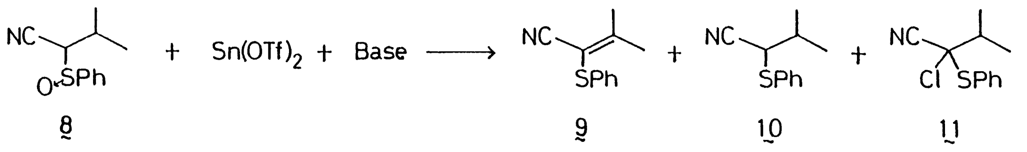
Entry	Sulfoxide	Product	Yield/%
1			86
2			65
3			71
4			31

a) Sulfoxide:$Sn(OTf)_2$:Base:TMSOTf=1:3:7:3, 0 °C, CH_2Cl_2.

reaction was conducted in the presence of TMSOTf at 0 °C in CH_2Cl_2 overnight. It is necessary to note that stannous triflate is essential in this reaction, for instance, when the sulfoxide was treated with TMSOTf alone in the absence of $Sn(OTf)_2$, the corresponding product was obtained in low yield. Thus, it is assumed that nucleophilic species produced during the reaction is silylated by TMSOTf and the counterion of carbocation 4 is substituted for $^-$OTf, by which the formation of 5 by the deprotonation is facilitated.

By the combined use of stannous triflate and TMSOTf, various α-sulfinyl ketones 1 were transformed into the corresponding unsaturated ketones 5 as shown in Table 2.

Table 3. Examination of Reaction Conditions

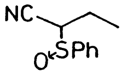
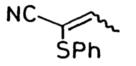
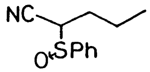
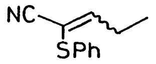
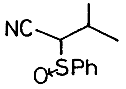
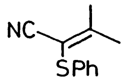
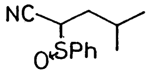
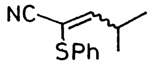
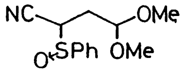
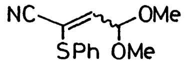


Entry	Base (equiv.)		Sn(OTf)2 (equiv.)	Additive (equiv.)		Yield of 9/%	Yield of 10/%	Yield of 11/%
1		2.3	1.1	——		41	24	—
2	"	3.0	3.0	TMSOTf	3.0	40	—	—
3	"	2.2	1.1	TMSCl	2.2	17	—	63
4	DABCO	5.5	2.2	"	2.3	78	—	8
5		4.4	0	"	2.2	—	—	—

In order to examine the scope of this reaction, various functionalized sulfoxides were screened and it was found that α-sulfinyl cyanide is also transformed into α-phenylthio-α,β-unsaturated cyanide (Table 3). In the case of α-sulfinyl cyanide, the desired product was obtained in low yield along with the reduced product 10 when the reaction was carried out in the absence of additives.$^{5)}$ In analogy to α-sulfinyl ketone, it was found that, when chlorotrimethylsilane was employed as an additive, substantial amount of α-chlorosulfide 11 was obtained and the amount of reduced product 10 was decreased. After examination of the nature of bases, it was found that DABCO was effective when it was employed along with TMSCl. The desired product 9 was not obtained on treatment of 11 with DABCO alone in CH_2Cl_2 at 0 °C. Thus, under the optimized conditions, it is reasonable to consider that 9 is formed directly by deprotonation of α-thiocarbocation intermediate, not from 11. Similarly, several α-phenylthio-α,β-unsaturated cyanides are prepared as summarized in Table 4.

The following example is representative in the case of α-sulfinyl ketone: To a suspension of stannous triflate (187 mg, 0.45 mmol) in 0.5 ml of CH_2Cl_2 were successively added N-ethylpiperidine (119 mg, 1.1 mmol) in 0.5 ml of CH_2Cl_2 at 0 °C, and TMSOTf (100 mg, 0.45 mmol) in 0.5 ml of CH_2Cl_2 at 0 °C. After stirring 5 min at that temperature, 1-phenyl-2-phenylsulfinyl-1-butanone (40.8 mg, 0.15 mmol) in 1.0 ml of CH_2Cl_2 was added at 0 °C. After stirring at 0 °C overnight, saturated $NaHCO_3$ solution was added. After filtration, organic layer was extracted with CH_2Cl_2, and the combined extracts were washed with brine and dried ($MgSO_4$) and concentrated to leave an oil. Purification on silica gel TLC gave 1-phenyl-2-phenylthio-2-buten-1-one.

Table 4. Preparation of α-Phenylthio-α,β-unsaturated Cyanide[a)]

Entry	Sulfoxide	Product	Yield/%
1			66
2			65
3			78
4			57
5			25

a) Sulfoxide:$Sn(OTf)_2$:DABCO:TMSCl=1:2.2:5.6:2.3, 0 °C CH_2Cl_2.

It is noted that α-phenylthio-α,β-unsaturated ketones and cyanides are prepared in fairly good yields on treatment of α-sulfinyl ketones and cyanides, respectively, with stannous triflate. The present method offers new route to the transformation of α-sulfinyl ketones and cyanides into the corresponding α-phenylthio-α,β-unsaturated ketones and cyanides under neutral and aprotic conditions.

References

1) T. Mukaiyama, R. W. Stevens, and N. Iwasawa, Chem. Lett., 1982, 353; R. W. Stevens, N. Iwasawa, and T. Mukaiyama, ibid., 1982, 1459; N. Iwasawa and T. Mukaiyama, ibid., 1982, 1441; T. Mukaiyama, T. Haga, and N. Iwasawa, ibid., 1982, 1601; R. W. Stevens and T. Mukaiyama, ibid., 1983, 595.

2) M. Shimizu, T. Akiyama, and T. Mukaiyama, Chem. Lett., 1984, 1531.

3) I. S. Morrison and H. M. Haendler, J. Inorg. Nucl. Chem., 29, 393 (1967).

4) Similar transformation of α-sulfinylketone to α-arylthio-α,β-unsaturated ketone in the presence of protic acid is known, H. J. Monteiro and A. L. Gemal, Synthesis, 1975, 437.

5) It is assumed that reduced product 10 would be formed by the Sn(II) mediated reduction of sulfoxide. The reducing ability of Sn(II) triflate is influenced by the amount of base such as tertiary amines, and acidic additives such as TMSOTf and TMSCl are thought to interact with tertiary amine to decrease reducing ability.

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