ENE REACTION OF N-TOSYLHEXAFLUOROACETONE IMINE[1)]

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As the extension of ene reaction of trifluoromethyl carbonyl compounds, ene reaction of N-tosylhexafluoroacetone imine (**1**) was examined. It reacted with terminal olefins to give α,α-bis(trifluoromethyl)amine derivatives in moderate to good yields. Inner olefins are much less reactive than terminal olefins, probably due to the steric effect of the substituents. Thus, cyclohexene and 2-octene gave the ene reaction products only in poor yields, and 1-phenylpropene did not give the ene reaction product at all but afforded an azetidine compound in a low yield.

KEYWORDS fluorine; hexafluoroacetone; imine; ene reaction; N-tosyl; homoallylamine; azetidine; trifluoromethyl; allyl; enophile

We have developed ene reactions of trifluoromethyl carbonyl compounds[2)] and reported their application[3)] for the synthesis of various kinds of trifluoromethyl compounds including fluorine analogs of mono- and sesquiterpenes. The high reactivity of trifluoromethyl carbonyl compounds as an enophile is due to the high electronegativity of a trifluoromethyl group. Next, we applied this reaction to N-tosylhexafluoroacetone imine (**1**), and found that **1** has two trifluoromethyl groups and a tosylimino group, both of which are highly electronegative, and was expected to react as a good enophile (see Chart 1).

When a solution of **1** and allylbenzene (**2**) in xylene was heated at 150°C for 6 h, N-tosyl-1,1,1-trifluoro-5-phenyl-2-(trifluoromethyl)-4-penten-2-ylamine (**3**) was obtained in 57 % yield. The structure of **3** was determined based on its ^{1}H-NMR, which showed presence of one phenyl, one tosyl, one allylic system and one hydrogen on the nitrogen. Its ^{19}F-NMR showed a singlet, which meant that both trifluoromethyl groups were magnetically symmetrical (see Chart 2).

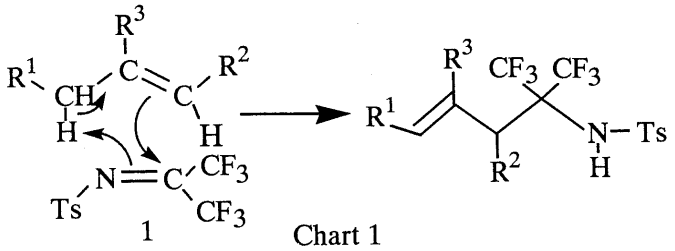

Chart 1

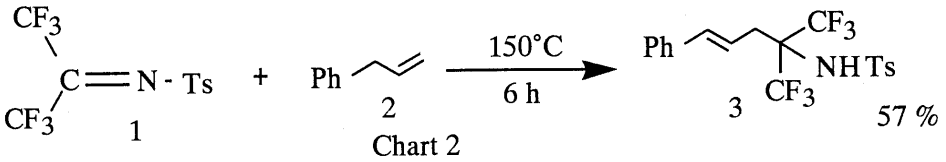

Chart 2

This result showed that **1** reacted with **2** as a good enophile. Its reactions with other olefins were examined, and the results are shown in Table I.[4)]

Terminal olefins, 4-allylanisole (**4**), 2-phenylpropene (**6**), and 1-octene (**10**), reacted with **1** to give ene reaction products in moderate to good yields, while inner olefins were much less reactive. Reaction of **1** with 2-octene (**12**) and cyclohexene (**14**) gave much lower yields of the products, and the reaction of **1** with 1-phenylpropene (**8**) did not give the ene reaction product at all.

These results are explained by the large steric effect of a trifluoromethyl group, which was observed on the ene reaction of hexafluoroacetone.[5)] The ene reaction of hexafluoroacetone with **6** gave a 1:2 adduct in addition to the 1:1 ene adduct, while the ene reaction of **1** with **6** gave only the 1:1 ene adduct (**7**). This shows that the tosylimino group of **1** is so large that further reaction of **7** is inhibited, though its product has a terminal double bond.

The reaction of **8** gave a small amount of an azetidine compound, 3-methyl-4-phenyl-1-tosyl-2,2-bis(trifluoromethyl)azetidine (**9**). ^{1}H-NMR of **9** showed a doublet-quartet of the methyl protons, which suggested that the methyl group was fixed near one of the trifluoromethyl groups. One sharp quartet and one broad quartet were observed on ^{19}F-NMR. The broad quartet is due to the small coupling with the methyl protons. Formation of **9** could be explained as shown in Chart 3.

Compound **8** is sterically hindered, and the electrophilic center of **1** attacks the double bond to form a benzyl cation, which cyclizes to the azetidine (**9**).

Table I. Ene Reaction of Hexafluoroacetone Imine

Run	Starting materials $R^1CH_2CH(R^3)=CHR^2$			Condition		Ene products[a]
	R^1	R^2	R^3	Temp. °C	Time h	Yield %
1	Ph	H	H (**2**)	150	6	(**3**) 57
2	Anis	H	H (**4**)	150	6	(**5**) 64
3	H	H	Ph (**6**)	150	11	(**7**) 82
4	H	Ph	H (**8**)	160	42	– [b]
5	Pent	H	H (**10**)	140	36	(**11**) 69
6	Bu	Me	H (**12**)	150	36	(**13**) 21
7	$-(CH_2)_3-$		H (**14**)	160	30	(**15**) 5
8	PhS	H	H (**16**)	150	30	(**18**) 21[c]

a) R^1, R^2 and R^3 are same as shown in Chart 1.
b) 3-Methyl-4-phenyl-1-tosyl-2,2-bis(trifluoromethyl)azetidine (**9**) was obtained in 1 % yield.
c) Besides the ene reaction product (**18**), 3-methyl-4-phenylthiomethyl-1-tosyl-2,2-bis(trifluoromethyl)azetidine (**17**) was obtained in 32 % yield.

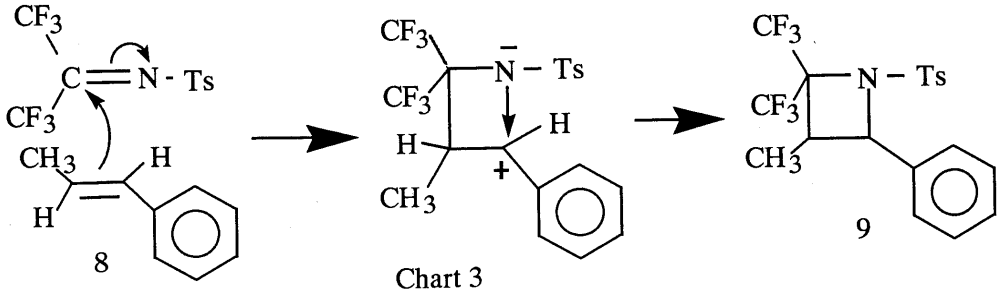

Chart 3

While hexafluoroacetone reacts with allyl phenyl thioether (**16**) to give the ene reaction product in a good yield,[6] reaction of **1** with **16** gave a poor yield of the ene reaction product (**18**). An azetidine derivative (**17**) was obtained in a moderate yield. The ene reaction of hexafluoroacetone with allyl phenyl ether gave a poor yield of the ene adduct. This was explained by the electron withdrawing effect of the oxygen.[6] If **1** is less reactive than hexafluoroacetone, even the less electronegative sulfur of **16** than the oxygen of hexafluoroacetone may repress the reaction of **16** with **1**.

In conclusion, compound **1** was found to react with terminal olefins as a good enophile to give α,α-bis(trifluoromethyl)homoallylamine derivatives in moderate to good yields, while it was much less reactive with inner olefins, probably because of the large steric effects of the trifluoromethyl groups and the tosyl group. Now, studies on the reaction of various trifluoromethylated imines are going on.

REFERENCES AND NOTES

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