Chinese Chemical Letters Vol. 10, No. 8, pp. 625–628, 1999

A New Rearrangement Reaction of 2-Phenyl Substituted Benzothiazepine with Ethoxycarbonyl Carbene — Mechanism of the Reaction and Structure of the Product

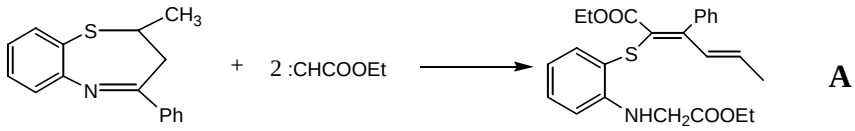
Hong Zhong WANG, Dan YAO, Ruo Xi LAN, Jia Xi XU, Sheng JIN*

College of Chemistry and Molecular Engineering, Peking University, Beijing 100871

Abstract: 2,3-Dihydro-2-phenyl-4-(4-methoxyphenyl)-1,5-benzothiazepine reacts with ethoxy-carbonyl carbene to give an unexpected compound 2,3-disubstituted-4H-1,4-benzothiazine **III**. It was found to be a new rearrangement reaction and the structure of the product was confirmed by IR, NMR, MS .

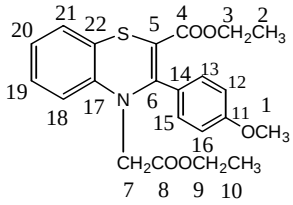
Keywords: Benzothiazepine, ethoxycarbonyl carbene, rearrangement reaction.

In the previous articles[1-2] we have reported that the reaction of benzodiazepine with ethoxycarbonyl carbene may obtain normal [2+1] cycloaddition products regardless the 2-substituent is methyl or phenyl. However under the same conditions the reaction of benzothiazepine with ethoxycarbonyl carbene underwent rearrangement reaction. For example, when the 2-substituent is methyl, the reaction of benzothiazepine with ethoxycarbonyl carbene give a ring-opening product **II** at room or high temperature[3] .



I **II** **A**

When the 2-substituent is phenyl, we unexpectedly found another new rearrangement reaction. For example, 2,3-dihydro-2-phenyl-4-(4-methoxyphenyl)-1,5-benzothiazepine reacts with ethoxycarbonyl carbene to give a white crystal together with the starting material. The new product was in 17.4% yield, m.p. 104℃. The IR, NMR, MS spectrum showed that the new product is neither ring-opening reaction **A**, nor [2+1] cycloadduct. It is a new product with structure **III**.



III

The NMR spectra are as follows:

Table 1 The ^{1}H NMR and ^{13}C NMR spectra for compound **III** [In $CDCl_3$, 400 Hz, δ (ppm)]

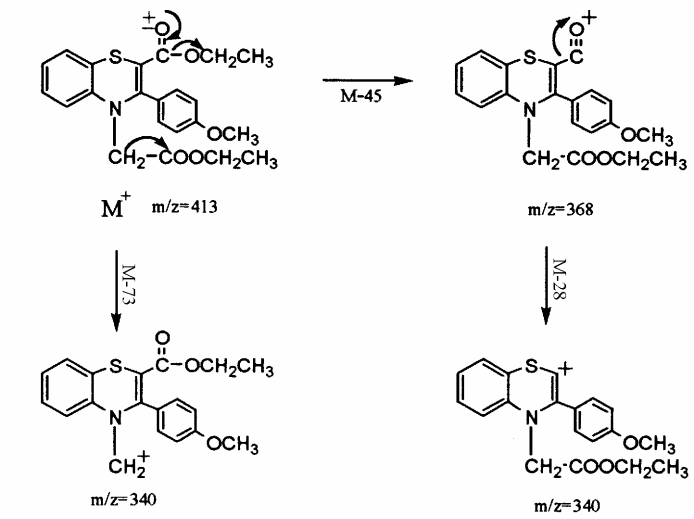
Position	δH			δC[a]	
1	3.38	s	3H	55.316	q
2	1.15	t, J=6.76Hz	3H	14.019	q
3	4.05	q, J=6.76Hz	2H	60.558	t
4				169.126	s[b]
5				160.618	s[b]
6				143,903	s[b]
7	4.14	s	2H	61.400	q
8				163.976	s[b]
9	3.94	q, J=7.12Hz	2H	51.826	q
10	0.95	t, J=7.16Hz	3H	13.875	q
12,13,15, 16,18-21	6.77-7.16	m	8H	113-125	d
11,14, 17,22				113-125	s

a: s=C, d=CH, t=CH_2, q=CH_3

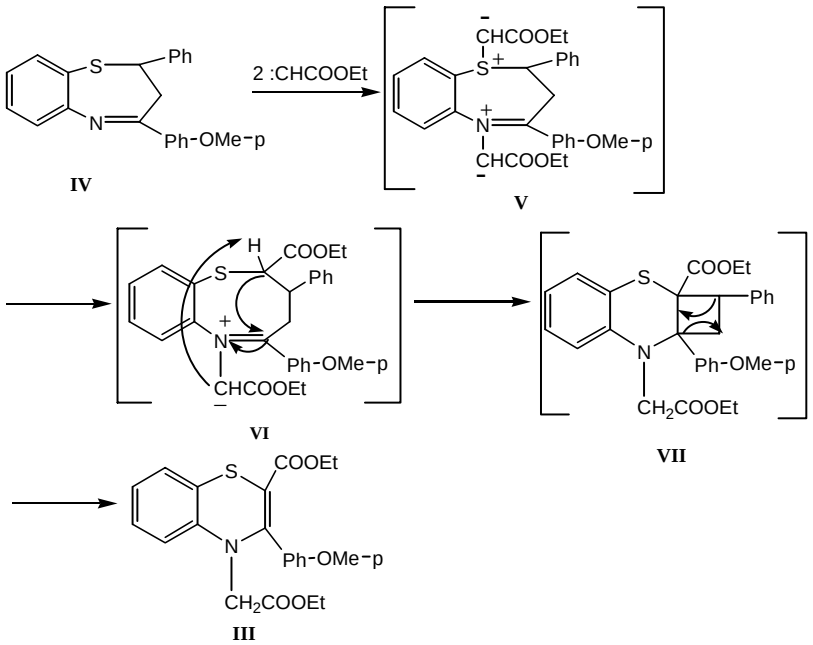
b: Type of carbon by DEPT method

The ^{1}H NMR spectrum gave 23 hydrogen signals, consistent with the structure of compound **III**. The ^{13}C NMR spectrum gave 18 carbon signals. C4, C5, C6 and C8, the four quaternary carbons, were determined by DEPT method.

The structure of compound **III** was also supported by MS analysis. The FAB-MS gave the peak of molecular ion of compound III at m/z 413 ($M^{\pm}$), indicating molecular formula $C_{22}H_{23}NO_5S$. Its fragments are as follows:



Since the reaction gives a new rearrangement product, it is obvious that the reaction follows a different mechanism from that reported earlier[3]. We think that the presence of phenyl group at the 2-position leads to change of the reaction. We propose a possible mechanism as follows:

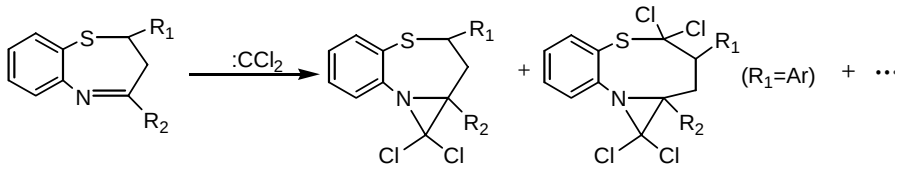


2,3-Dihydro-2-phenyl-4-(4-methoxyphenyl)-1,5-benzothiazepine reacts with etho-xycarbonyl carbene to form nitrogen ylide and sulfur ylide **V**. Stevens rearrangement[4] of the sulfur ylide gives an eight-numbered cyclic intermediate **VI**.

However for the compound 2.3-dihydro-2-methyl-4-(4-methoxyphenyl)-1.5-benzothiazepine in which the 2-substitution is methyl, the Stevens Rearrangement can not take place, and thus the eight-numbered cyclic intermediate can not be generated .

Then the carbanion of the nitrogen ylide **VI** reacts with the H atom at the 2-position and the C atom of the 2-position attacks the C atom of the 5-position which forms intermediate **VII**. The intermediate **VII** has a four-numbered cycle ring with high strain which is unstable and undergoes decomposition to form compound **III** and one molecule of styrene.

This result is very similar with our research on the reaction of 2-substitued phenyl benzothiazepine with dichlorocarbene[5]:



VIII

Compound **VIII** was observed only when R1 is phenyl while there was no **VIII** when R1 is a methyl group[6]. Because there is no H atom at the 2-position of compound **VIII**, the compound **VIII** can not form the cyclic intermediate like **VII**, so the reaction can not go further from **VIII** to the product like **III**.

References

1. B.Y. Mi and S. Jin; *Chinese Chem. Lett.*, **1991**, *2*, 925.
2. J. Chun, *Master Degree Thesis*, Department of Chemistry, Peking University, **1995.**
3. D.Yao, B.Y. Mi, S. Jin et al; *Synthetic Chemistry*, **1998**, *3*, 272.
4. W.R.Bamford and T.S.Stevens, *J.Chem.Soc.* , **1952**, 4735.
5. R.X. Lan, *Doctor Degree Thesis*, Department of Chemistry, Peking University, **1990**.
6. J.X. Xu, R.X. Lan and S. Jin; *Chem. J. Chin. Univ.* , 1998,*19*(11), 1774.

Received 3 February 1999