

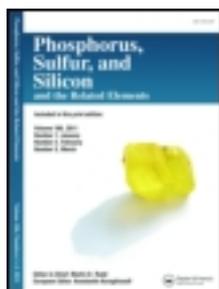
This article was downloaded by: [Purdue University]

On: 28 July 2013, At: 06:11

Publisher: Taylor & Francis

Informa Ltd Registered in England and Wales Registered Number: 1072954

Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/gpss20>

SYNTHESIS OF 3-(1-ARYLAMINOCARBONYL-5-AMINO)-1,2,4-TRIAZOLYL BENZYL SULFIDE, SULFOXIDE AND SULFONE

Rongjian Lu ^a, Huazheng Yang ^a, Guofeng Zhao ^a, Huayin Liu ^a & Zhenfeng Shang ^a

^a National Key Laboratory of Elemento-Organic Chemistry, Institute of Elemento-Organic Chemistry, Nankai University, 94 Weijin Road, Tianjin, 300071, P.R. China

Published online: 24 Sep 2006.

To cite this article: Rongjian Lu, Huazheng Yang, Guofeng Zhao, Huayin Liu & Zhenfeng Shang (1996) SYNTHESIS OF 3-(1-ARYLAMINOCARBONYL-5-AMINO)-1,2,4-TRIAZOLYL BENZYL SULFIDE, SULFOXIDE AND SULFONE, *Phosphorus, Sulfur, and Silicon and the Related Elements*, 108:1-4, 221-230

To link to this article: <http://dx.doi.org/10.1080/10426509608029653>

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden.

Terms & Conditions of access and use can be found at <http://www.tandfonline.com/page/terms-and-conditions>

SYNTHESIS OF 3-(1-ARYLAMINOCARBONYL-5-AMINO)-1,2,4-TRIAZOLYL BENZYL SULFIDE, SULFOXIDE AND SULFONE†

RONGJIAN LU, HUAZHENG YANG,‡ GUOFENG ZHAO, HUAYIN LIU
and ZHENFENG SHANG

*National Key Laboratory of Elemento-Organic Chemistry,
Institute of Elemento-Organic Chemistry, Nankai University,
94 Weijin Road, Tianjin 300071, P.R. China*

(Received August 10, 1995; in final form September 27, 1995)

3-(1-arylamino-carbonyl-5-amino)-1,2,4-triazolyl benzyl sulfides were synthesized by the reaction of 5-amino-3-benzylthio-1,2,4-triazole and its analogue with the aryl isocyanate. It was found that there was great influence by the property and position of substituents X, Y on the chemical shift of H—N₂ in the ¹H NMR spectra. By means of molecular mechanics calculations, the substituent effect on the chemical shift of H—N₂ was rationalized. The chemocontrolled oxidation of 3-(1-arylamino-carbonyl-5-amino)-1,2,4-triazolyl benzyl sulfide to sulfoxide and sulfone respectively was performed after a careful study of the influence of the concentration of H₂O₂ and the reaction temperature on the oxidation reaction. In ¹H NMR spectra of sulfoxides(II), the protons of a methylene group near the SO chiral center coupled to appear as a quartet in the AB pattern. The SO, SO₂ decreased the electronic density around H—N₂, 5-NH₂, and thus moved the proton absorption to a lower field. The experimental showed that the ratio of sulfoxide(II)/sulfone(III) was influenced by the electronic property of substituents X, Y on the aryl moiety.

Key words: Synthesis, triazolylbenzyl sulfide, triazolylbenzyl sulfoxide, triazolylbenzyl sulfone, molecular mechanics, substituent effect, chemocontrolled oxidation, ALS enzyme inhibitor.

INTRODUCTION

ALS enzyme has, over the past twenty years, formed the basis of an enormous amount of herbicides aimed at finding low dose rate, nontoxic, selective herbicides. This stemmed originally from the finding that the sulfonylurea showed activity against ALS enzyme. Recently, Dow and Du Pont have developed the sulfonylurea to triazolo[1,5a]pyrimidine sulfonylamide, using bioisosteric replacement, which shows activity similar to the sulfonylurea. Since then, various herbicides inhibiting ALS enzyme have been synthesized.^{1–4} The chemical structures of typical examples are shown in Figure 1.

It was therefore decided to design novel ALS enzyme inhibitors by means of abstracting the common feature of different ALS enzyme inhibitors. A number of lead compounds have been designed, synthesized and tested for activity against ALS enzyme.^{5–8} Recently we have described the regioselective addition of 5-amino-1,2,4-triazole with the aryl isocyanate.⁹ The encouraging biological activity of 3-(1-arylamino-carbonyl-5-amino)-1,2,4-triazolyl benzyl sulfide **I** prompted us to synthe-

†Study on the Design, Synthesis and Bioactivity of Novel ALS Enzyme Inhibitors (V).

‡To whom correspondence should be addressed.

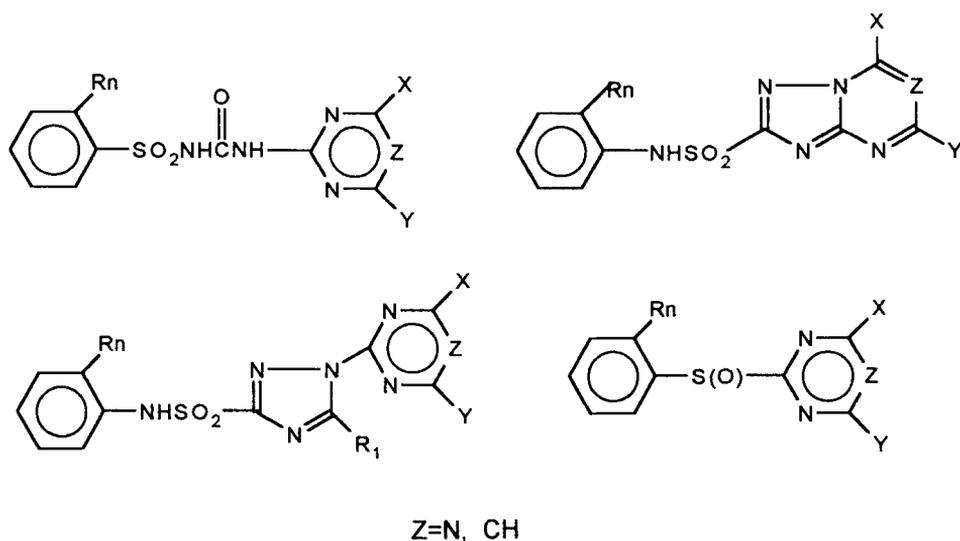
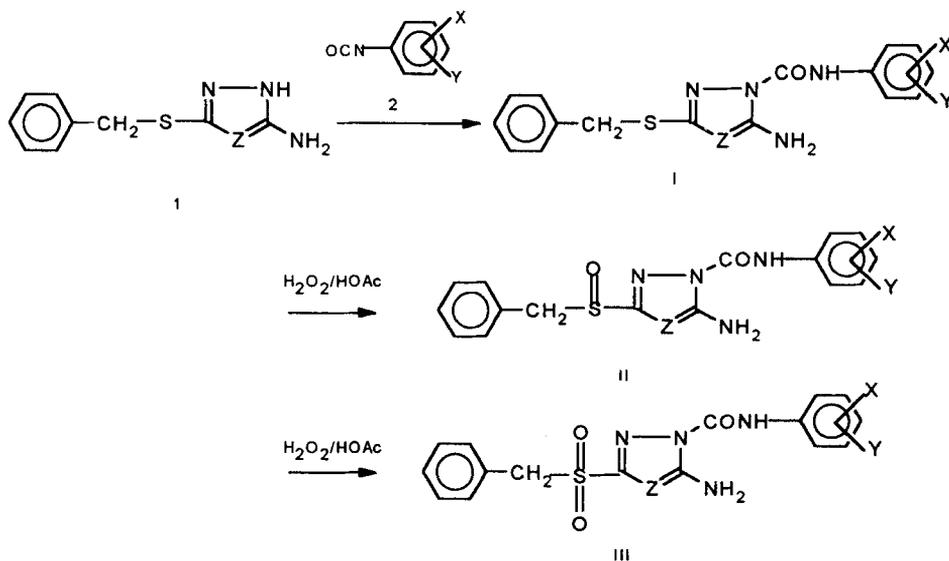


FIGURE 1 Some of typical ALS enzyme inhibitors.

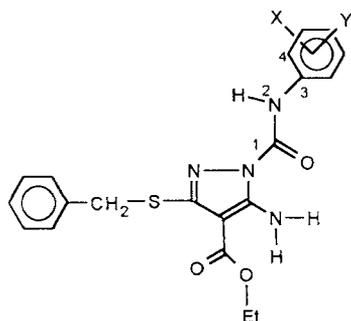
size various 3-(1-arylamino-carbonyl-5-amino)-1,2,4-triazolyl benzyl sulfides **I**, 3-(1-arylamino-carbonyl-5-amino)-1,2,4-triazolyl benzyl sulfoxides **II** and 3-(1-arylamino-carbonyl-5-amino)-1,2,4-triazolyl benzyl sulfones **III**.



RESULTS AND DISCUSSION

Using our reported method,⁹ binucleophilic compounds 5-amino-3-benzylthio-1,2,4-triazole and its analogue **1** were allowed to react with the aryl isocyanate at room temperature in anhydrous THF to afford the 3-(1-arylamino-carbonyl-5-amino)-1,2,4-

TABLE I
 $\delta_{\text{H-N}_2}$, the dihedral angle and MMXE (kJ/mol) of I



No.	I-8	I-9	I-10	I-11	I-12	I-13	I-14	I-15
δ (ppm)	8.496	8.840	8.850	8.718	8.951	9.579	9.520	9.563
X, Y	2,6-Cl ₂	4-Cl	4-OCH ₃	H	3,4-Cl ₂	2,5-Cl ₂	2-OCH ₃	2-Cl
MMXE (kJ/mol)	392	357	348	373	360	371	367	373
θ_{1234}	119	170	169	168	171	159	168	167

triazolyl benzyl sulfide and its analogue, these were identified on the basis of analytical and spectroscopic data. Interestingly, we found that there was great influence by the property and position of substituents X, Y on the chemical shift of H—N₂ in the ¹H NMR spectra. In order to eliminate the disturbance of the sample concentration and test temperature, at the same concentration 12 mg/0.5 ml, ¹H NMR spectra of the following compounds were measured at 25°C. The effect of substituents X, Y on the chemical shift of H—N₂ is summarized in Table I.

As shown in Table I, the H—N₂ peak with OCH₃, Cl at the ortho-position appeared at lower force than that of unsubstituted and Cl, OCH₃ at the para-position. This might be attributed to an ortho-deshielding effect. However, a H—N₂ peak with 2,6-Cl₂ on the anilino moiety was found upfield at 8.496 ppm compared with that of 2-Cl, 2-OCH₃, 2,5-Cl₂ derivatives. In order to gain insight into the mechanistic details of the above phenomena, we have explored the conformational analysis with MMX program. Table I lists the chemical shift, MMXE (kJ/mol) and dihedral angles of **I-8-I-15**. These calculations suggested that the disappearance of the ortho-deshielding effect of 2,6-Cl₂ derivative might be attributed to the steric hindrance of 2,6-Cl₂ forcing the aryl plane away from the C(O)N₂-H plane.

In view of the stability of —NCONH and the NH₂ group, H₂O₂/HOAc was selected as the oxidizing reagent to transform 3-(1-arylamino-carbonyl-5-amino)-1,2,4-triazolyl benzyl sulfide to the related sulfoxide and sulfone.¹⁰ The chemocontrolled oxidation of 3-(1-arylamino-carbonyl-5-amino)-1,2,4-triazolyl benzyl sulfide to sulfoxide and sulfone respectively was performed after a careful study of the influence of the concentration of H₂O₂ and the reaction temperature on the following oxidation reaction.

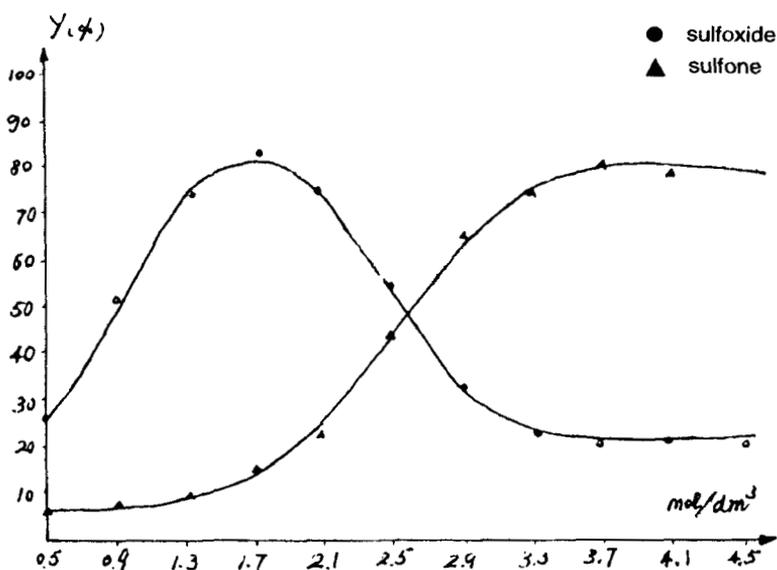
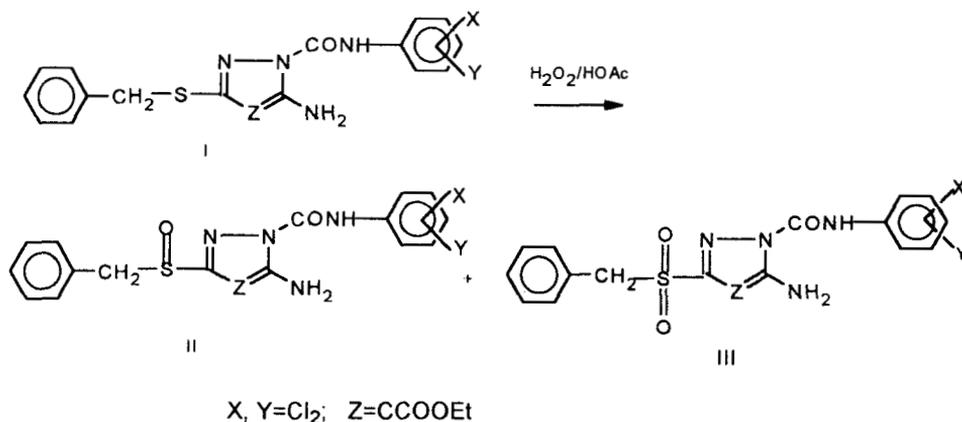


FIGURE 2 The effect of the molar concentration of H_2O_2 on the oxidation reaction.



The result of the influence of the concentration of H_2O_2 on the following reaction is summarized in Figure 2. With the increase of molar concentration of H_2O_2 , the yield of sulfoxide increased. When the molar concentration of H_2O_2 was raised to 1.7 mol dm^{-3} , sulfoxide was obtained in the highest yield (83%). Further addition of H_2O_2 did not improve the yield of sulfoxide, but increased the yield of sulfone. In the case when the molar concentration of H_2O_2 was up to 3.7 mol dm^{-3} , the maximum yield of sulfone reached 79%.

The effect of the reaction temperature on the above oxidation reaction was also examined (Figure 3). With the increase of the reaction temperature, the yield of sulfoxide increased. At 27°C the yield of sulfoxide climbed to the maximum 85%. However, when the reaction temperature was increased continuously, the yield of sulfoxide decreased; and the yield of sulfone increased. At 45°C the sulfone was

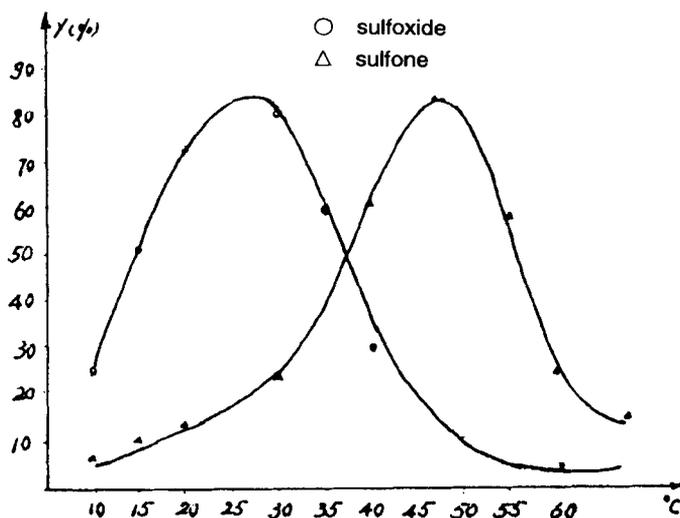


FIGURE 3 The effect of the reaction temperature on the oxidation reaction.

TABLE II

The influence of the substituent X, Y on the ratio of the sulfoxide/sulfone

X, Y	2,6-Cl ₂	3,4-Cl ₂	4-Cl	H	4-CH ₃	4-OCH ₃
Ratio (II/III)	83.0/13.0	84.0/11.7	81.5/15.7	78.2/20.0	77.9/19.5	69.8/28.0

obtained in the highest yield (83%). Above 50°C, the dearylamincarbonyl product was obtained.

In summary, the optimum conditions for the chemocontrolled oxidation of 3-(1-arylamincarbonyl-5-amino)-1,2,4-triazolyl benzyl sulfide to the related sulfoxide and sulfone were 1.7 mol dm⁻³, 27°C; 3.7 mol dm⁻³, 45°C respectively.

When the substituent X, Y was examined (Table II), the ratio of sulfoxide(II)/sulfone(III) was influenced by the property of X, Y. Withdrawing substituents on the aryl moiety caused the decrease of the electronic density on the sulfur atom, resulting in the increase of the ratio of sulfoxide/sulfone; on the contrary, donating substituents

TABLE III
Physical data of I, II, III

No.	Z	n	X,Y	m.p. (°C)	Yield (%)	Elemental Analysis			Eluting Solvent	
						Calcd	(Found)			
						C	H	N		
I-1	N	0	2,6-Cl ₂	152-3	91.5	48.73 (48.59)	3.30 3.27	17.77 17.89)	THF ^C	
I-2	N	0	4-Cl	156-7	92.8	53.41 (53.27)	3.89 3.92	19.47 19.51)	THF ^C	
I-3	N	0	4-CH ₃ O	149-151	92.4	57.46 (57.51)	4.79 4.81	19.72 19.50)	THF ^C	
I-4	N	0	H	173-5	91.8	59.08 (59.17)	4.62 4.79	21.54 21.31)	A:P ^a =1:2	
I-5	N	0	3,4-Cl ₂	171-2	94.1	48.73 (48.91)	3.30 3.41	17.77 17.67)	A:P=1:2	
I-6	N	0	2,5-Cl ₂	192-4	90.5	48.73 (48.67)	3.30 3.41	17.77 17.79)	A:P=1:2	
I-7	N	0	2-CH ₃ O	162-4	89.5	57.46 (57.31)	4.79 4.59	19.72 19.81)	A:P=1:2	
I-8	CCOOEt	0	2,6-Cl ₂	150-1	94.2	51.61 (51.81)	3.87 3.61	12.04 12.21)	A:P=1:3	
I-9	CCOOEt	0	4-Cl	159-160	93.4	55.75 (55.59)	4.41 4.37	13.01 13.21)	A:P=1:3	
I-10	CCOOEt	0	4-CH ₃ O	165-6	90.8	59.15 (59.00)	5.16 5.10	13.15 13.24)	A:P=1:3	
I-11	CCOOEt	0	H	170-2	91.1	60.61 (60.49)	5.05 5.12	14.14 14.07)	A:P=1:3	
I-12	CCOOEt	0	3,4-Cl ₂	161-3	95.1	51.61 (51.81)	3.87 3.77	12.04 12.11)	A:P=1:3	
I-13	CCOOEt	0	2,5-Cl ₂	198-201	91.5	51.61 (51.47)	3.87 3.91	12.04 12.00)	A:P=1:3	
I-14	CCOOEt	0	2-CH ₃ O	172-4	89.8	59.15 (59.00)	5.16 5.27	13.15 13.07)	A:P=1:3	
I-15	CCOOEt	0	2-Cl	178-9	90.6	55.75 (55.49)	4.41 4.21	13.01 13.17)	A:P=1:3	
II-1	N	1	2,6-Cl ₂	131-3	76.1	46.83 (46.95)	3.17 3.20	17.70 17.03)	A:P=1:2	
II-2	N	1	4-Cl	145-7	76.9	51.13 (51.30)	3.73 3.57	18.64 18.57)	EA:P ^b =1:2	
II-3	N	1	4-CH ₃ O	155-7	69.2	54.99 (55.01)	4.58 4.39	18.87 18.76)	EA:P=1:2	
II-4	N	1	3,4-Cl ₂	119-120	80.1	46.83 (46.61)	3.17 3.19	17.07 17.20)	EA:P=1:3	
II-5	N	1	2,5-Cl ₂	151-3	78.1	46.83 (46.81)	3.17 3.27	17.07 17.00)	A:P=1:2	
II-6	CCOOEt	1	2,6-Cl ₂	123-5	81.6	49.90 (49.97)	3.74 3.78	11.64 16.49)	EA:P=1:3	
II-7	CCOOEt	1	4-Cl	129-131	79.8	53.75 (53.60)	4.26 4.28	12.54 12.71)	A:P=1:4	
II-8	CCOOEt	1	4-CH ₃ O	105-7	69.0	57.01 (57.09)	4.98 5.00	12.67 12.45)	EtOAc ^C	
II-9	CCOOEt	1	H	131-3	76.0	58.25 (58.20)	4.85 4.74	13.59 13.71)	EA:P=1:3	
II-10	CCOOEt	1	3,4-Cl ₂	144-6	83.0	49.90 (49.79)	3.74 3.76	11.64 11.80)	EtOAc ^C	
III-1	N	2	2,6-Cl ₂	149-151	70.8	45.07 (45.31)	3.05 3.12	16.43 16.21)	A:P=1:3	
III-2	N	2	4-Cl	150-1	68.8	49.04 (48.99)	3.58 3.54	17.88 17.92)	EA:P=1:3	
III-3	N	2	4-CH ₃ O	163-4	77.9	52.71 (52.59)	4.39 4.50	18.09 18.15)	EA:P=1:4	

TABLE III (Continued)

No.	Z	n	X,Y	m.p. (°C)	Yield (%)	Elemental Analysis			Eluting Solvent	
						Calcd	(Found)			
						C	H	N		
III-4	N	2	3,4-Cl ₂	134-5	71.3	45.07 (45.31)	3.05 3.09	16.43 16.18)	EA:P=1:4	
III-5	N	2	2,5-Cl ₂	174-6	72.1	45.07 (45.21)	3.05 3.06	16.43 16.50)	A:P=1:2	
III-6	CCOOEt	2	2,6-Cl ₂	148-150	81.5	48.29 (48.41)	3.62 3.27	11.27 11.27)	EA:P=1:4	
III-7	CCOOEt	2	4-Cl	147-8	81.0	51.89 (51.79)	4.11 4.12	12.11 12.00)	EA:P=1:4	
III-8	CCOOEt	2	4-CH ₃ O	129-130	87.1	55.02 (55.20)	4.80 4.78	12.23 12.09)	EtOAc ^c	
III-9	CCOOEt	2	H	153-4.5	85.0	56.07 (56.18)	4.67 4.74	13.08 13.11)	EA:P=1:3	
III-10	CCOOEt	2	3,4-Cl ₂	160-3	81.8	48.29 (48.41)	3.62 3.71	11.27 11.09)	CHCl ₃ ^c	
IV	N	1		158-160	68.5	48.65 (48.41)	4.50 4.41	25.23 25.41)	EtOAc ^c	

a: A-acetone; P-petroleum(60-90°C); b: EA-ethyl acetate, P-petroleum(60-90°C);
c: recrystallization solvent

caused the increase of the electronic density on the sulfur atom, resulting in the decrease of the ratio of sulfoxide(II)/sulfone(III).

Taking compounds **I-8**, **II-6**, **III-6** as an example. The ¹H NMR spectrum of **I-8** in CDCl₃ showed signals at 8.50 ppm (1H NHCO), 6.96 ppm (b 2H NH₂), 4.25–4.38 (m 4H OCH₂ PhCH₂), 7.25–7.48 ppm (m 8H C₆H₅ ArH), 1.32–1.39 (t 3H OCCH₃). The Mass spectrum showed no molecular ion peak as the N—C—{(O)NHAr} was easy to cleave to produce ion peak m/e 277 through the r-H rearrangement. The behavior of 5-NH₂, NHCO protons of compound **II-6** **III-6** resembled that of compound **I-8**. The SO, SO₂ shifted the protons of 5-NH₂, NHCO downfield to 7.02, 8.61; (**II-6**), 7.13, 8.71 (**III-6**). In the ¹H NMR spectrum of **II-6**, the protons of the methylene group near the SO group showed coupling with each other appearing as a quartet 4.26, 4.48 ppm $J_{AB} = 13.0$ Hz in the AB pattern, which might be attributed to the SO chiral center. The IR spectrum of **II-6** **III-6** showed the presence of strong absorption bands at 1073 cm⁻¹ (SO); 1327, 1149 cm⁻¹ (SO₂) respectively. The ¹H NMR spectrum of compound **IV** was quite consistent with the assigned structure. Compared with **I-8**, signal of NHCO in the ¹H NMR spectrum of **IV** and the stretching band for C=O in the IR spectrum of **IV** disappeared.

EXPERIMENTAL

General: 10-40 silica gel GF₂₅₄ was used for the TLC and detection was carried out on a UV-detector. The reaction mixture was analyzed by HPLC on a HP1090 instrument equipped with a Hypersil 5 μm 200 × 4.6 mm (79916 SI-574) column at 210 nm, Solvents: petroleum (60–90°C), methanol, isopropanol. The melting points were uncorrected. ¹H NMR spectra were obtained using a Bruker AC-P200 spectrometer and were referenced to internal TMS. IR spectra were recorded with a Shimadzu-IR 435 infrared-spectrometer using KBr pellets. MS were measured on a VG ZAB-HS instrument. Elemental analyses were obtained using a CHN Recorder MT-3 Elemental Analyzer.

TABLE IV
¹H NMR, IR, MS data of I, II, III

No.	¹ H NMR(ppm)	IR(cm ⁻¹)	MS(m/e)
I-1 ^a	4.34(s 2H PhCH ₂), 6.47(b 2H NH ₂), 7.26-7.45(m 8H ArH C ₆ H ₅), 8.29(b 1H CONH)	3410, 3258(NH) 1723(CONH)	
I-2 ^b	4.38(s 2H PhCH ₂), 7.24-7.71(m 11H NH ₂ ArH C ₆ H ₅), 10.05 (b 1H CONH)	3406, 3266(NH) 1728(CONH)	
I-3 ^b	3.73(s 3H OCH ₃), 4.38(s 2H PhCH ₂), 6.89(b 2H NH ₂), 7.31-7.53 (m 9H C ₆ H ₅ ArH), 9.83(s 1H CONH)	3410, 3261(NH) 1720(CONH)	
I-4 ^b	4.40(s 2H PhCH ₂), 7.13-7.67(m 12H NH ₂ C ₆ H ₅), 9.92(s 1H CONH)	3401, 3274(NH) 1723(CONH)	
I-5 ^a	4.33(s 2H PhCH ₂), 6.32(b 2H NH ₂), 7.24-7.75(m 8H C ₆ H ₅ ArH), 8.54(s 1H CONH)	3437, 3323(NH)	393, 206, 187 173,161,124,91
I-6 ^a	4.36(s 2H PhCH ₂), 6.80(b 2H NH ₂), 7.12-8.34(m 8H ArH C ₆ H ₅), 9.25(s 1H CONH)	3409, 3276(NH) 1744(CONH)	
I-7 ^a	3.94(s 3H OCH ₃), 43.5(s 2H PhCH ₂), 6.47(b 2H NH ₂), 6.96-8.20(m 9H ArH C ₆ H ₅)		355, 206, 149 134, 124, 91
I-8 ^a	1.32-1.39(t 3H OCCH ₃), 4.25-4.38(m 4H OCH ₂), 6.96(s 2H NH ₂), 7.25-7.48(m 8H ArH C ₆ H ₅), 8.50(s 1H CONH)		277, 231, 187 161, 126, 91
I-9 ^a	1.33-1.40(t 3H OCCH ₃), 4.25-4.37(m 4H CH ₂ OCH ₂), 7.40-7.69(q 4H ArH J _{AB} =8.8Hz), 8.84(s 1H CONH)		
I-10 ^a	1.33-1.39(t 3H OCCH ₃), 3.71(s 3H OCH ₃), 4.24-4.37(m 4H CH ₂ OCH ₂), 6.90, 7.43(q 4H ArH J _{AB} =8.6Hz), 7.03(s 2H NH ₂), 7.26-7.34(m 5H C ₆ H ₅), 8.85(s 1H CONH)	3447,3358(NH) 1726(CONH), 1668(COO)	
I-11 ^a	1.33-1.40(t 3H OCCH ₃), 4.29-4.35(m 4H CH ₂ OCH ₂), 6.93(s 2H NH ₂), 7.30-7.53(m 10H C ₆ H ₅), 8.72(s 1H CONH)	3444, 3335, 3326 (NH),1728(CONH), 1665(COO)	277, 231, 119 100, 91
I-12 ^a	1.33-1.40(t 3H OCCH ₃), 4.24-4.34(m 4H CH ₂ OCH ₂), 6.98(b 2H NH ₂), 7.25-7.79(m 8H C ₆ H ₅ ArH), 8.95(s 1H CONH)	3445, 3332, 3328 (NH), 1729(CONH), 1665(COO)	
I-13 ^a	1.32-1.39(t 3H OCCH ₃), 4.25-4.34(m 4H CH ₂ OCH ₂), 7.05-8.39(m 10H ArH C ₆ H ₅ NH ₂), 9.58(s 1H CONH)		
I-14 ^a	1.32-1.39(t 3H OCCH ₃), 3.61(s 3H OCH ₃), 3.90(s 2H CH ₂), 4.24-4.35(q 2H OCH ₂), 6.95-8.21(m 11H NH ₂ ArH C ₆ H ₅), 9.52(s 1H CONH)		
I-15 ^a	1.33-1.39(t 3H OCCH ₃), 4.25-4.36(m 4H CH ₂ OCH ₂), 7.05-8.31(m 11H NH ₂ C ₆ H ₅ ArH), 9.56(s 1H CONH)		
II-1 ^a	4.43, 4.46(q 2H J _{AB} =5.4Hz CH ₂), 6.73(b 2H NH ₂), 7.25-7.44 (m 8H ArH C ₆ H ₅), 8.35(s 1H CONH)	3419, 3289(NH),1730 (CONH), 1067(S=O)	222, 187, 91
II-2 ^b	4.46, 4.54(q 2H J _{AB} =13.6Hz CH ₂), 7.42, 7.69(q 4H J _{AB} =8.7Hz ArH), 7.24-7.50(m 5H C ₆ H ₅), 7.79(b 2H NH ₂), 10.44(s 1H CONH)	3405, 3266(NH), 1730 (CONH), 1024(S=O)	
II-3 ^b	3.73(s 3H OCH ₃), 4.48, 4.55(q 2H J _{AB} =12.5Hz CH ₂), 6.92, 7.52 (q 4H J _{AB} =8.8Hz ArH), 7.32-7.74(m 7H C ₆ H ₅ NH ₂), 10.18(s 1H CONH)		222, 149, 91
II-4 ^a	4.45, 4.53(q 2H J _{AB} =6.0Hz CH ₂), 6.72(b 2H NH ₂), 7.25-7.76(m (m 8H C ₆ H ₅ ArH), 8.56(s 1H CONH)	3441,3221(NH), 1728 (CONH), 1024(S=O)	
II-5 ^a	4.42, 4.45(q 2H J _{AB} =5.7Hz CH ₂), 7.18-8.34(m 10H NH ₂ ArH C ₆ H ₅), 9.81(s 1H CONH)		
II-6 ^a	1.39-1.46(t 3H OCCH ₃), 4.34-4.41(q 2H OCH ₂), 4.26, 4.48(q 2H J _{AB} =13.0Hz CH ₂), 7.02(b 2H NH ₂), 7.22-7.44(m 8H C ₆ H ₅ ArH), 8.61(s 1H CONH)	3431 3301(NH), 1729(CONH), 1073 (S=O),1677(COO)	293, 247, 91
II-7 ^b	1.25-1.32(t 3H OCCH ₃), 4.25-4.33(q 2H OCH ₂), 4.22, 4.75 (q 2H J _{AB} =10.8Hz CH ₂), 7.35-7.43(m 7H NH ₂ C ₆ H ₅), 7.45, 7.69(q 4H J _{AB} =8.8Hz ArH), 10.31(s 1H CONH)	3437, 3336(NH), 1729 (CONH), 1662(COO) 1023(S=O)	

TABLE IV (Continued)

No.	¹ H NMR(ppm)	IR(cm ⁻¹)	MS(m/e)
II-8 ^a	1.37-1.44(t 3H OCCH ₃), 3.80(s 3H OCH ₃), 4.30-4.39(q 2H OCH ₂), 4.17, 4.44(q 2H J _{AB} =13.6Hz CH ₂), 6.90, 7.43(q 4H J _{AB} =8.8 Hz ArH), 7.09(b 2H NH ₂), 7.26-7.35(m 5H C ₆ H ₅), 8.97(s 1H CONH)	3422, 3306(NH) 1720(CONH), 1043 (S=O)	
II-9 ^b	1.26-1.33(t 3H OCCH ₃), 4.23-4.31(q 2H OCH ₂), 4.35, 4.63(q 2H J _{AB} =13.0Hz CH ₂), 7.21-7.86(m 12H NH ₂ C ₆ H ₅), 10.13(s 1H CONH)		
II-10 ^a	1.26-1.33(t 3H OCCH ₃), 4.23-4.31(q 2H OCH ₂), 4.36, 4.63(q 2H J _{AB} =16.4Hz CH ₂), 7.03(b 2H NH ₂), 7.26-7.85(m 8H ArH C ₆ H ₅), 9.17(s 1H CONH)	3449, 3322(NH) 1727(CONH), 1698 (COO), 1020(S=O)	
III-1 ^a	4.80(s 2H CH ₂), 7.02(b 2H NH ₂), 7.26-7.51(m 8H ArH C ₆ H ₅), 8.40 (s 1H CONH)	3438, 3300(NH), 1727(CONH), 1301, 1117(SO ₂)	238, 187, 91
III-2 ^b	4.79(s 2H CH ₂), 7.25-7.80(m 7H C ₆ H ₅ NH ₂), 7.41, 7.68(q 4H J _{AB} =8.5Hz ArH), 10.28(s 1H CONH)	3420, 3275(NH), 1731 (CO), 1319, 1124(SO ₂)	
III-3 ^b	3.73(s 3H OCH ₃), 4.85(s 2H CH ₂), 6.92-7.53(m 11H NH ₂ C ₆ H ₅ ArH), 10.21(s 1H CONH)		
III-4 ^a	4.81(s 2H CH ₂), 7.00(b 2H NH ₂), 7.24-7.75(m 8H ArH C ₆ H ₅), 8.53(s 1H CONH)	3451, 3319, 3278(NH), 1729(CONH), 1310, 1121(SO ₂)	
III-5 ^a	4.79(s 2H CH ₂), 7.19-8.40(m 10H NH ₂ ArH), 9.78(s 1H CONH)		
III-6 ^a	1.41-1.49(t 3H OCCH ₃), 4.39-4.49(q 2H OCH ₂), 4.79(s 2H CH ₂), 7.13(b 2H NH ₂), 7.24-7.43(m 8H ArH C ₆ H ₅), 8.70(s 1H CONH)	3449, 3348, 3306 (NH), 1729(CONH), 1697(COO), 1327, 1149(SO ₂)	309, 173, 110 91
III-7 ^b	1.30-1.37(t 3H OCCH ₃), 4.25-4.34(q 2H OCH ₂), 4.68(s 2H CH ₂), 7.45-7.71(q 4H J _{AB} =8.9Hz ArH), 7.36-7.43(m 7H C ₆ H ₅ NH ₂), 10.32(s 1H CONH)	3442, 3339, 3301(NH) 1729(CONH), 1690 (COO), 1309, 1129 (SO ₂)	
III-8 ^a	1.40-1.49(t 3H OCCH ₃), 3.81(s 3H OCH ₃), 4.30-4.39(q 2H OCH ₂), 4.78(s 2H CH ₂), 6.89, 7.44(q 4H J _{AB} =8.9Hz ArH), 7.11(b 2H NH ₂), 7.25-7.35(m 5H C ₆ H ₅), 8.61(s 1H CONH)	3427, 3310(NH), 1722 (CONH), 1686(COO), 1319, 1139(SO ₂)	
III-9 ^a	1.43-1.49(t 3H OCCH ₃), 4.40-4.50(q 2H OCH ₂), 4.81(s 2H CH ₂), 7.21-7.50(m 12H C ₆ H ₅ NH ₂), 8.83(s 1H CONH)		
III-10 ^a	1.29-1.37(t 3H OCCH ₃), 4.40-4.50(q 2H OCH ₂), 4.80(s 2H CH ₂), 7.12(b 2H NH ₂), 7.25-7.78(m 8H ArH C ₆ H ₅), 9.20(s 1H CONH)	3451, 3320(NH), 1728 (CONH), 1696(COO), 1324, 1139(SO ₂)	
IV	4.42, 4.46(q 2H J _{AB} =8.1Hz CH ₂), 6.74(b 2H NH ₂), 7.25-7.37(m 5H C ₆ H ₅), 12.51(s 1H NH)	3465, 3366, 3289 (NH), 1068(S=O)	222, 91

a: CDCl₃, b: DMSO-d₆

General Procedure for the Synthesis of the 3-(5-amino-1-arylamino-carbonyl)-1,2,4-triazolyl Benzyl Sulfide and its Analogue (I)

2.5 mmol aryl isocyanate in 5 ml anhydrous THF was added dropwise to a solution of 2.5 mmol 5-amino-3-benzylthio-1,2,4-triazole (or its analogue) **I** in 10 ml anhydrous THF, the mixture was stirred at room temperature until **I** disappeared detected by TLC (acetone: petroleum 60–90°C 1:2). Then THF was removed under reduced pressure and the residue was purified by flash column chromatography or recrystallization. The experimental data were listed in Tables III and IV.

General Procedure for the Synthesis of the 3-(5-amino-1-arylamino-carbonyl)-1,2,4-triazolyl Benzyl Sulf-oxide and its Analogue (II)

To a solution of 3-(5-amino-1-arylamino-carbonyl)-1,2,4-triazolyl benzyl sulfide and its analogue **I** 1 mmol in 16.2 ml glacial acid was added dropwise hydrogen peroxide (3.8 ml H₂O₂ 30%). The mixture was

stirred at 25–27°C. After the consumption of I, the reaction solution was diluted with 20 ml ice water and extracted with ethyl acetate. After the combined extracts were washed with water and dried over anhydrous MgSO₄. The solvent was removed and the resulting residue was purified by recrystallization or chromatography.

General Procedure for the Synthesis of 3-(5-amino-1-arylamino-carbonyl)-1,2,4-triazolyl Benzyl Sulfone and its Analogue (III)

To a solution of 3-(5-amino-1-arylamino-carbonyl)-1,2,4-triazolyl benzyl sulfide and its analogue I 1 mmol in 11.6 ml glacial acid was added dropwise hydrogen peroxide (8.4 ml H₂O₂ 30%). The mixture was stirred at 47°C detected by TLC. After the completion of the oxidation reaction, the reaction solution was diluted with 20 ml ice water and extracted with ethyl acetate. Removal of the solvent gave crude product, which was purified by recrystallization or chromatography.

Synthesis of 3-(5-amino)-1,2,4-triazolyl Benzyl Sulfoxide

To a solution of 0.394 g I-1 in 10 ml glacial acid was added dropwise 10 ml hydrogen peroxide (30%). The mixture was stirred at 60°C for 5 h. The reaction mixture was diluted with 20 ml ice water and extracted with ethyl acetate. The organic solution was concentrated to give the crude IV, which was recrystallized from ethyl acetate. m.p. 158–160°C, yield 0.15 g (68.05%).

The Effect of the Molar Concentration of H₂O₂ on the Oxidation Reaction (I-8)

3-(5-amino-1-2',6'-dichlorophenylaminocarbonyl)-1,2,4-triazolyl benzyl sulfide 1 mmol was added to 20 ml hydrogen peroxide solution (relevant molar concentration) in glacial acid. The mixture was stirred at 25°C for 24 h, and then detected by HPLC. The result was shown in Figure 2.

The Effect of the Reaction Temperature on the Oxidation Reaction (I-8)

3-(5-amino-1-2'-6'-dichlorophenylaminocarbonyl)-1,2,4-triazolyl benzyl sulfide 1 mmol was added to 20 ml hydrogen peroxide solution (1.7 mol dm³) in glacial acid. The mixture was stirred at relevant temperature for 24 h and then detected by HPLC. The result was shown in Figure 3.

REFERENCES

1. J. V. Hay, *Pestic. Sci.*, **29**, 269 (1990).
2. W. A. Kleschick, M. J. Costales and J. E. Dunbar, *Pestic. Sci.*, **29**, 341 (1990).
3. A. Percival, *Pestic. Sci.*, **31**, 569 (1991).
4. J. A. Dixon, US Patent, 5 149 357 (1992).
5. R. Lu, H. Yang and Z. Shang, *Scientia Sinica, Series B*, in press.
6. R. Lu, H. Yang and Z. Shang, submitted to *Scientia Sinica, Series B*.
7. R. Lu and H. Yang, *Synthetic Communication*, **24**, 59 (1994).
8. R. Lu and H. Yang, *Chem. J. Chinese Univ.*, in press.
9. R. Lu, H. Yang, B. Qian and H. Deng, *J. Heterocyclic Chem.*, in press.
10. X. Huang and Z. Cheng, "Organic Synthetic Chemistry," Chemical Industry Publishing House, China, 1983, Chap. 26, pp. 671–675.