Pergamon

Tetrahedron Letters 40 (1999) 2327–2330

TETRAHEDRON LETTERS

Phosphinecarbothioamide formation in the reaction of tetrazolylsulfinylmethyl(dimethyl)phosphine oxide with amines

Masahiro Takeda, Toshiaki Yoshimura, Takayoshi Fujii, Shin Ono, Choichiro Shimasaki, and Hiroyuki Morita*

Department of System Engineering of Materials and Life Science, Faculty of Engineering, Toyama University, Gofuku Toyama 930-8555, Japan

Received 23 October 1998; revised 11 January 1999; accepted 18 January 1999

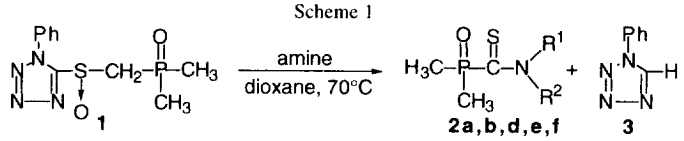
Abstract

In the study of the thermolysis of heteroaryl substituted sulfoxides, we examined the same reaction in the presence of several amines, such as aniline, benzylamine, and morpholine. In the case of 5-(1-phenyl)-1,2,3,4-tetrazolylsulfinylmethyl(dimethyl)phosphine oxide (**1**), the corresponding phosphinecarbothioamide **2** were unexpectedly obtained in moderate yields together with 1-phenyl-1,2,3,4-tetrazole (**3**). These products are considered to be formed by the addition reaction of amines to the sulfine formed initially and then elimination of H_2O.

Keywords: thiocarbonyl oxide (sulfine); sulfoxides; tetrazoles; thioamides

Recently, we reported the cycloaddition reaction of sulfine with 2,3-dimethyl-1,3-butadiene via thermolytic reaction of heteroaryl-substituted β-ketosulfoxide [1,2,3]. The reaction of phenacyl sulfoxide bearing a 2-benzothiazolyl or *N*-oxypyridyl group with butadiene afforded 6-benzoyl-5,6-dihydro-3,4-dimethyl-2*H*-thiapyran, which is considered to be formed by the Diels-Alder reaction of diene with the corresponding thioaldehyde [4,5,6,7,8,9] formed initially. On the other hand, in the case of tetrazolyl phenacyl sulfoxide, the cycloadduct of the corresponding sulfine [11,12] was formed in excellent yield. Since sulfines are known to react with amines to afford sulfinamide derivatives [12], the reaction of tetrazolyl phenacyl sulfoxide in the presence of aniline was studied. However, a complex reaction was observed. Further, we carried out the reaction of tetrazolyl sulfoxide bearing phosphine oxide instead of carbonyl group with several amines in order to obtain the effect of the phosphoryl group.

Scheme 1



0040-4039/99/$ - see front matter
PII: S0040-4039(99)00178-1

Unexpectedly, the reaction of 5-(1-phenyl)-1,2,3,4-tetrazolylsulfinylmethyl(dimethyl)-phosphine oxide (**1**) with 2.2 equiv. of aniline afforded *N*-phenyl(dimethyl)phosphinecarbothioamide (**2a**) and 1-phenyl-1,2,3,4-tetrazole (**3**)in 50 and 83 % yield, respectively.[1] The structure of product **2a** was identified by ^{1}H and ^{13}C NMR, IR, and elemental analysis.

Table 1
Reaction of 5-(1-Phenyl)-1,2,3,4-tetrazolylsulfinyl-methyl(dimethyl)phosphine Oxide with Amine

			yield (%)[a]	
entry	**amine**	**Time (h)**	**2**	**3**
1	$PhNH_2$	1.5	50 (**2a**)	83
2	$PhCH_2NH_2$	2.5	50 (**2b**)	99
3	$(i\text{-}Pr)_2NH$	1.5	0 (**2c**)	81
4	Piperidine	0.75	52 (**2d**)	99
5	Morphorine	1.0	53 (**2e**)	75
6	Pyrrole	0.75	52 (**2f**)	82
7	Imidazole	5.0	0 (**2g**)	99

[a] isolated yield

In this paper we report the formation of several (dimethyl)phosphinecarbothioamides under the same conditions. (Scheme 1) As summarized in Table 1, the reaction of **1** with several amines led to the corresponding phosphinecarbothioamide **2a,b,d,e,f** in moderate yields. However, when diisopropylamine (entry 3) or imidazole (entry 7) was used the expected product **2c** or **2g** was not detected, resulting in the formation of a complex reaction mixture. These results suggest that the nucleophilicity of amine is critical to react with the corresponding sulfine. In order to ascertain this speculation, the reaction of **1** in the presence of both diisopropylamine and 2,3-dimethyl-1,3-butadiene was studied and, as expected, it led to the Diels-Alder cycloadduct of the corresponding sulfine with butadiene (49%) and not to **2**. This result also suggests that sulfine works as an intermediate in this reaction.

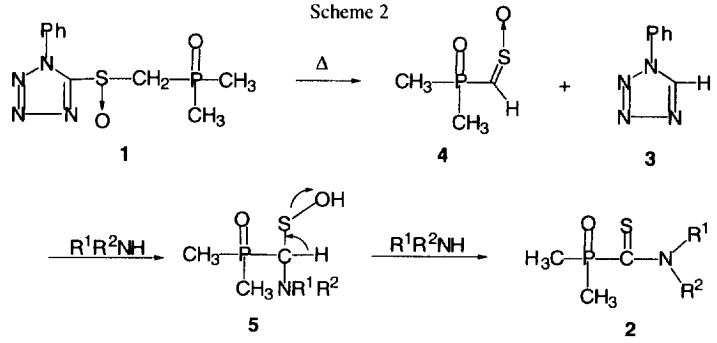
*FAX: +81-764-45-6851; E-mail: morita@eng.toyama-u.ac.jp

[1] Typical run is as follows; to a stirred solution of 56 mg of **1** in 1.5 mL of dioxane was added 0.042 mL of aniline at 70°C. This reaction mixture was stirred at 70°C for 1.5h. After cooling, this mixture was evaporated and the residual yellow oil was separated by preparative layer chromatography on silicagel using AcOEt-hexane (1/1) as eluent. Products **2a** and **3** were obtained in 50 and 83% yield, respectively. Spectral data of **2a.** yellow crystals. mp. 139.1-147.1 (dec.). ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.81 (d, J = 28.4 Hz, 6H), 7.32 (t, J = 7.6 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 8.05 (d, J = 7.6 Hz, 2H), 10.75 (br, 1H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 15.7 ($^{1}J_{C\text{-}P}$ = 74.0 Hz), 121.5, 127.5, 129.1, 138.2 ($^{3}J_{C\text{-}P}$ = 11.5 Hz), 197.0 ($^{1}J_{C\text{-}P}$ = 85.5 Hz). IR (neat): 3700-2800, 1180 cm^{-1}. Anal. Calcd for $C_9H_{12}NOPS$: C, 50.70; H, 5.67; N, 6.57 %. Found: C, 50.71; H, 5.73; N, 6.57 %.

The reaction of **1** in the presence of sodium 4-methylthiophenolate instead of amine was also studied. However, no formation of the corresponding expected product **2** and **3** was detected, but 5-(1-phenyl)-1,2,3,4-tetrazolyl tolyl sulfide (30%) accompanied with complex reaction mixtures was obtained. This product was probably formed by the *ipso*-substitution on the 5-position of the tetrazole ring with thiolate anion.

The probable mechanism of the formation of phosphinecarbothioamide **2** is shown in Scheme 2. First, the thermolytic reaction of starting sulfoxide **1** afforded the corresponding sulfine **4**. To the carbon atom of the thiocarbonyl oxide group of **4** the nucleophilic addition of amine occurs to afford a substituted sulfenic acid intermediate **5**. Finally, the elimination of H_2O from this intermediate led to the product **2**.

Scheme 2



In contrast to our results, it is reported that in the reactions of common sulfines with nucleophiles, the attack of nucleophiles takes place on the partially positive-charged sulfur (thiophilic attack) predominantly and, in the case of primary and secondary amines, the products were the corresponding sufinyl amides [13,14,15,16]. Only in the case of chlorosulfine, attack on the carbon (carbophilic attack) occurred [17,18,19,20] . In order to clarify the limitations of the reaction and the detailed mechanism, we are now continuing further studies, such as the reaction with other nucleophiles, the solvent effect and so on.

References

[1] Morita H, Takeda M, Kamiyama H, Hashimoto T, Yoshimura T, Shimasaki C, Tsukurimichi E. Tetrahedron Lett. 1996;37:3739.

[2] Takeda M, Yoshimura T, Shimasaki, C, Morita H. Phosphorus, Sulfur, and Silicon 1997;120 & 121:409.

[3] Morita H, Takeda M, Fujii T, Yoshimura T, Shimasaki, C. J. Org. Chem. 1997;62:9018.

[4] Okazaki R: Chemistry of Thioaldehyde. In: Page P, editor. Organosulfur Chemistry. London: Academic Press, 995:225-258.

[5] Vedejs E, Eberlein TH, Varie DL. J. Am. Chem. Soc. 1982;104:1445.

[6] Vedejs E, Eberlein TH, Mazur DJ, McClure CK, Perry DA, Ruggeri R, Schwartz E, Stults JS, Varie DL, Wilde RG, Wittenberger S. J. Org. Chem. 1986; 51:1556.
[7] Vedejs E, Perry DA, Houk KN, Rondan NG. J. Am. Chem. Soc. 1983;105: 6999.
[8] Vedejs E, Stults JS, Wilde R G. J. Am. Chem. Soc. 1988;110:5452. Vedejs E, Eberlein TH, Wilde RG. J. Org. Chem. 1988;53:2220.
[9] Vedejs E, Stults JS. J. Org Chem. 1988;53:2226.
[10] Boger DL, Weinreb SM. Hetero Diels-Alder Methodology in Organic Synthesis. London: Academic Press Inc.,1987:120-145.
[11] Zwanenburg B. Recl. Trav. Chim. Pays-Bas 1982;101:1.
[12] Schwab M, Sundermeyer W. Chem. Ber. 1986;119:2458.
[13] Schultz AG, Schlessinger RH. Chem. Commun. 1970:747.
[14] Rewinkel JBM, Porskamp PATW, Zwanenburg B. Recl. Trav. Chim. Pays-Bas 1988;107:563.
[15] Zwanenburg B, Kielbasinski P. Tetrahedron 1979;35:169.
[16] Porskamp PATW, Lammerink BHM, Zwanenburg B. J. Org. Chem. 1984, 49, 263.
[17] Zwanenburg B, Thijs L, Strating J. Recl. Trav. Chim. Pays-Bas 1970;89:687.
[18] Loontjes JA, van der Leij M, Zwanenburg B. Recl. Trav. Chim. Pays-Bas 1980;99:39.
[19] Holm A, Carlsen L. Tetrahedron Lett. 1973:3203.
[20] Carlsen L, Holm A, Snyder JP, Koch E, Stilkerieg B. Tetrahedron 1977;33:2231.