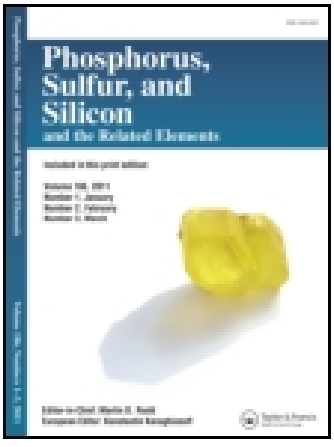

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

MOLECULAR REARRANGEMENT OF SULFUR COMPOUNDS IX: PYROLYSIS OF 2-PHENYLIMINO-3-ARYLAMINO-4-THIAZOLIDINONE DERIVATIVES

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Published online: 24 Sep 2006.

To cite this article: A. M. Gaber , A. A. Atalla & A. M. Kamal El-Dean (1998) MOLECULAR REARRANGEMENT OF SULFUR COMPOUNDS IX: PYROLYSIS OF 2-PHENYLIMINO-3-ARYLAMINO-4-THIAZOLIDINONE DERIVATIVES, Phosphorus, Sulfur, and Silicon and the Related Elements, 133:1, 69-77, DOI: 10.1080/10426509808032454

To link to this article: http://dx.doi.org/10.1080/10426509808032454

Phosphorus, Sulfur and Silicon, 1998, Vol. 133, pp. 69-77
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MOLECULAR REARRANGEMENT OF SULFUR COMPOUNDS IX : PYROLYSIS OF 2-PHENYLIMINO-3-ARYLAMINO-4-THIAZOLIDINONE DERIVATIVES*

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(Received 31 September, 1997; In final form 23 January, 1998)

Pyrolysis of 2-phenylimino-3-arylamino-4-thiazolidinone **I**, **II** (Ar = Ph, *p*-tolyl) by heating at ca. 250 °C in a sealed tube gives rise to H_2S, benzonitrile, acetophenone, arylamines, phenyl isothiocynate, thioglycolic acid, arylhydrazines, *N*-phenyl-*N'*-aryl thiourea, benzimidazole, and 3-phenyl-1,2,4-benzotriazines. Analogous results in addition to toluene, bibenzyl, stilbene, bibenzylamine and acetamide were also obtained on pyrolysis of 2-phenylimino-3-benzylamino-4-thiazolidinone (**III**). In the presence of isoquinoline as a radical trap, (**III**) gave 1-benzylisoquinoline beside the previous products. A free radical mechanism has been postulated to take place through the homolysis of the N-N and C-S bonds to account for the identified products.

Keywords: Molecular rearrangement; pyrolysis; thiazolidin-4-ones; free radicals

INTRODUCTION

The chemistry of thiazolidinone derivatives [1] and their biology continue to attract considerable attention. Thiazolidin-4-one possess hypontic, anesthetic [2], and other biological activity such as streptomyces antibiotic exhibition via in vitro antitubercular activity.[3] Furthermore, 5-arylidene-4-thiazolidinones have been found to possess great bactericidal and fungicidal activity. [4] It was reported [5]that thermal rearrangement of 3-(*N*-phenylbenzamido)-4-phenyl-1,3-thiazole-2-thione derivatives. In

* Previous Part VIII: Phosphorus. Sulfur and Silicon, **117**. 205 (1996).
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order to gain further insight into the mechanism of thermal fragmentation of this class of heterocyclic compounds and in continuation of our work, [6,7,8] the present investigation is devoted to a study of the mechanism of pyrolysis of substituted thiazolidinones.

RESULTS AND DISCUSSION

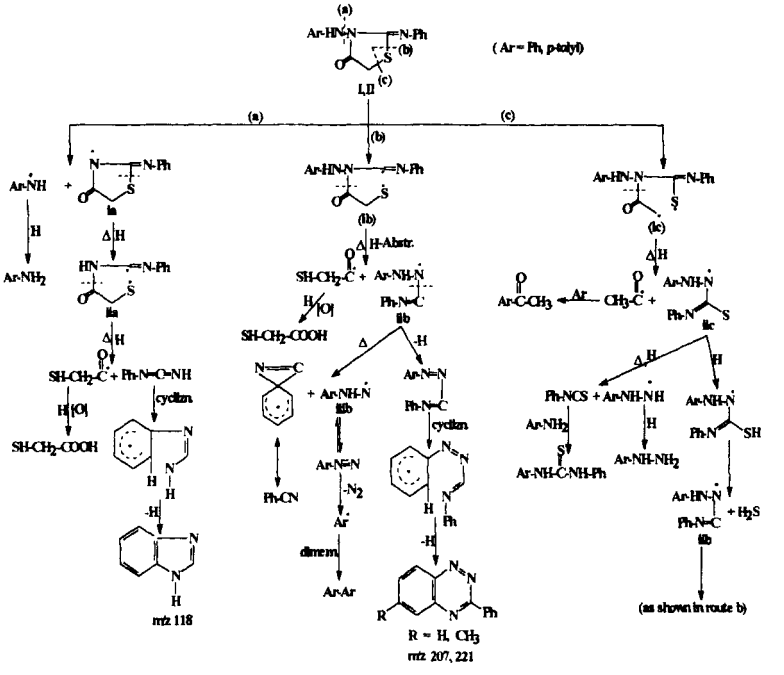
This work is a continuation of our recent studies on the pyrolysis of organic compounds containing heteroatoms. Pyrolysis of 2-phenylimino-3-anilino-4-thiazolidinone (**I**) by heating in a sealed tube at 250 °C gave rise to H_2S, benzonitrile, biphenyl, acetophenone, thiocarbanilide, thioglycolic acid, phenyl isothiocyanate, phenylhydrazine, benzimidazole and 3-phenyl-1,2,4-benzotriazine as shown in Scheme 1. Although some of the products are present in small amounts due to the variable rate of decay of the free radical intermediates, their presence is of great importance for mechanistic interpretation.

The formation of these products can be assumed to follow the series of reactions shown in Scheme 1, which implies the preliminary homolysis of N-N (route a) and C-S (route b) bonds according to bond dissociation energy values.[9] However, homolysis of an N-N bond by route *a* gives anilino and 2-phenylimino-4-thiazolidinone (ia) radical pairs. The anilino radical may abstract hydrogen from a suitable source to form aniline whereas the latter undergoes decomposition into the biradical (iia) and with continous heating gives the thioloacetyl radical and phenyl cyanamide. The thioloacetyl radicals may abstract hydrogen from a suitable source followed by oxidation with trace oxgyen during the working-up process to form thioglycolic acid [10] (Scheme 1). The formation of benzimidazole may be rationalized through heating of phenylcyanimde, possibly with an initial hydrogen shift occuring, with a subsequent intramolecular cyclization as suggested previously [11] (Scheme 1).

Another competing pathway in the pyrolysis of 2-phenylimino-3-anilino-4-thiazolidinone (**I**) is the homolysis of C-S bond (route b) leading to the formation of biradical (ib) which ultimately undergoes fragmentation into thioloacetyl radical and radical species (iib). The thioloacetyl radical gave thioglycolic acid as mentioned above.

A possible pathway for the formation of 3-phenyl-1,2,4-benzotriazine through H-absraction and subsequent intramolecular cyclization of radical

species (iib).[12] Furthermore, the radical species (iib) undergoes fragmentation into phenylhydrazinyl and phenyisocynide radical pairs. The phenylhydrazinyl radical undergoes tautomerization to form phenylazo[13] which ultimately expels nitrogen to give a phenyl radical. Dimerization of the phenyl radical produced biphenyl. The phenylisocyanide radical undergoes rearrangement to benzonitrile[14] (Scheme 1).



SCHEME 1

Scheme 1 also includes the C-S bond homolysis route (c) to give the biradical (ic) which may extract hydrogen from a suitable source and subsequently decompose into acetyl radical and biradical (iic). The acetyl radical may couple with a phenyl radical to form acetophenone whereas the biradical (iic) may extract hydrogen followed by fragmentation under the present conditions to produce phenyl isothiocyanate and phenylhydrazinyl radicals. The phenyl isothiocyanate may couple with aniline, which is readily available in the reaction medium, to give thiocarbanilide.[15] Also, the phenylhydrazinyl radicals undergo H-abstraction to form phenylhydrazine which is thermally stable under the same conditions[16] as shown in Scheme 1.

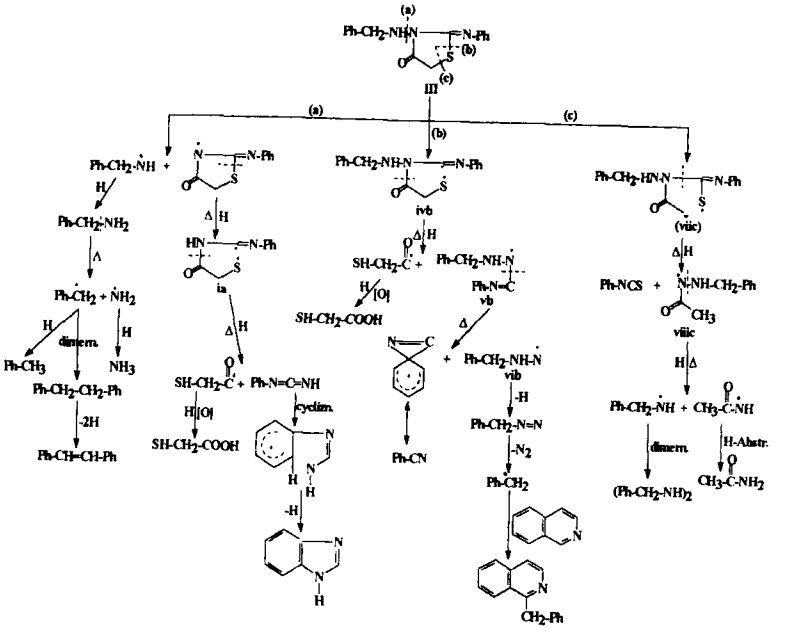
Analogous results were also obtained in the pyrolysis of 2-phenylimino-3-*p*-tolyl-4-thiazolidinone (**II**) under the same conditions which lead to the formation of H_2S, benzonitrile, thioglycolic acid, phenyl isothiocyanate, *p*-toylhydrazine, *p*-toluidene, *p,p*-ditolyl, *N*-phenyl-*N'*-p-tolylthiourea, benzimidazole, and 6-methyl-3-phenyl-1,2,4-benzotriazine as shown in Scheme 1. Such products can be interpreted with the same mechanism suggested previously.

Pyrolysis of 2-phenylimino-3-benzylamino-4-thiazolidinone (**III**) under the same conditions gave rise to H_2S, ammonia, benzonitrile, acetamide, toluene, bibenzyl, stilbene, thioglycolic acid, phenyl isothiocyanate, benzimidazole and bibenzylamine as shown in Scheme 2. The formation of toluene, bibenzyl, stilbene, thioglycolic acid, and benzimidazole can be assumed to proceed through the homolysis of the N-N bond (route a, Scheme 2) to form benzylaminyl radical and radical species (ia). The normal fate of radical species (ia) was described previously (Scheme 1, route a) whereas the benzylaminyl radical may abstract hydrogen to produce benzyl amine which ultimately decomposes [17] to give benzyl radical and ammonia. The benzyl radical can be considered as the precursor of toluene and bibenzyl through processes of H-abstraction and dimerization, respectively. Formation of stilbene may be attributed to hydrogen abstraction from bibenzyl by free radicals present in the reaction medium as shown in previous work.[18]

Route b gives rise to biradical (ivb) which leads to thioglycolic acid and benzonitrile via the same mechanism as mentioned before in Scheme 1, route b. Scheme 2 also includes the homolysis of the C-S bond (route c) to give biradical (viic) which undergoes fragmentation into phenyl isothiocyanate and radical species (viiic) which then decomposes through the homolysis of N-N bond to give benzylaminyl and acetamidyl radical pairs. The benzylaminyl undergoes dimerization to give bibenzylamine.[19] whereas, the acetamidyl may abstract hydrogen to form acetamide as shown in Scheme 2.

The similarity of the products obtained from these pyrolyses in the case of **I**, **II** and **III** confirms the trends of their pyrolytic behaviour. The presence of toluene, bibenzyl, and ammonia among the products suggests a free radical mechanism. This suggestion was further supported through a study of the thermolysis of 2-phenylimino-3-benzylamino-4-thiazolidinone (**III**) in isoquinoline as free radical scavenger which produces, in

addition to the previous products, 1-benzylisoquinoline(11%, yield) as in Scheme 2.



SCHEME 2

EXPERIMENTAL

All melting points were measured with a Gallenkamp apparatus and are uncorrected. The IR spectroscopic analyses were carried out on a Pye-Unicam IR spectrophotometer, Model SP 3–100, Analytical tlc was performed using 10 × 3 cm glass plates coated with silica gel (60–80 mesh) and eluting with acetone-pet.ether (60–80 °C) (1:4 v/v). Column chromatographic separations were carried out using 100 × 2.5 cm glass columns packed with neutral alumina obtained and using the following solvents via elution successively with pet.ether (40–60 °C) and pet.ether (60–80 °C) (1:2 v/v), followed by pet.ether (60–80 °C)-benzene (1:1 v/v), (1:2 v/v), and (2:3 v/v), benzene, benzene-ether mixtures (1:1 v/v). Finally, 1% and 2% ether-pentane mixtures were used. Gas-liquid chromatographic analysis was carried out using a Perkin-Elmer model Sigma 3B apparatus, 8 ×

1/8 cm column, packed with 30% SE 30 on Chromosorb W (35–80 mesh), and equiped with a thermal conductivity detector, using nitrogen as a carrier gas. GC/MS analyses were carried out using a Finnigan MAT SSQ 7000 instrument with (5% phenyl) methylpolysiloxane using a 30 m DB.1 capillary column. Products were identified either by co-injection with authentic materials and/or by comparison with known gc/ms library fragmentation patterns. ^{1}H-NMR spectra for some reaction products were recorded using an EM.390.90 MHz NMR spectrophotometer.

Starting Materials

2-phenylimino-3-anilino--4-thiazolidinone (**I**), m,p. 205–210 °C (lit.[20], m.p. 210°C).
2-phenylimino-3-p-tolyl-4-thiazolidinone (**II**), m.p. 135–140 °C (lit,[20], m.p. 142 °C).
2-phenylimino-3-benzylamino-4-thiazolidinone (**III**), m.p. 135–137 °C (lit.[20], m.p. 135 °C).

Thermal Decomposition of Thiaizolidin-4-one Derivatives I-III

General Procedure. Thiazolidin-4-one derivatives **I-III** (10 g) were placed in a sealed tube under nitrogen either alone or in 5 ml of isoquinoline as a radical scavenger. The gases evolved were detected by chemical means (H_2S by lead acetate and NH_3 by Nessler's reagent). The pyrolysate was separated into its constituents by fractional distillation under reduced pressure and gave the following compounds: Toluene was collected at b.p. 105–110 °C and exhibited a single peak at 1.0 min at 90 °C, comparable with an authentic sample. Acetophenone was collected at b.p. 65–70 °C/10 Torr; Dn_D^{20} : 1.5325; 2,4-dinitro derivative m.p. and mm.p. 250 °C. Thioglycolic acid was collected at b.p. 94–7 °C/ 10 Torr; Dn_D^{20} : 1.5030, Benzonitrile was collected at b.p. 140–5 °C/10 Torr; Dn_D^{20} : 1.5271. The nitrile on hydrolysis, gave benzoic acid. Phenylhydrazine was collected at b.p. 188–190 °C/13 Torr; its hydrochloride, m.p. and mm.p. 250–2 °C. Aniline was collected at b.p. 75–80 °C/3 Torr; acetyl derivative, mp. and mm.p. 113 °C. Phenyl isothiocyanat was collected at b.p. 110–5 °C/10 Torr; Dn_D^{20} : 1.6265. *p*-Toluidene was collected at b.p. 65–70 °C/3 Torr; m.p. and mm.p. 45–46 °C; benzoyl derivative, m.p. and mm.p. 144–145°C. Bibenzylamine was collected at b.p. 145–150 °C/6 Torr as a pale yellow

oil; Dn^{20}: 1.5743 (lit.[21], b.p. 300 °C); its hydrochloride, m.p. end mm.p 256 °C. The remaining residue was separated by column chromatography over silica gel using gradient elution technique as follow: Bibenzyl was eluted using pet.ether (40–60 °C)-pet. ether (60–80 °C) (1:2 v/v) and showed a glc peak at 3.3 min at 1.40 °C; m.p. and mm.p. 52 °C (lit. 22, m.p. 52 °C). Biphenyl was Eluted using pet.ether (60–80 °C), and showed a glc peak at 3.0 min at 140 °C, m.p. and mm.p. 70 °C.*p,p*-Bitolyl was eluted using pet.ether (60–80 °C)-benzene (1:1 v/v), m.p. and mm.p. 120–122 °C (lit.[23], m.p. 122°C). Stilbene was eluted using per.ether (60–80°C)-benzene (1:2 v/v), m.p. and mm.p. 124 °C (lit.[24], m.p. 124 °C). Thiocarbanilide was eluted using pet.ether (60–80 °C)-benzene (2:3 v/v), m.p. and mm.p.150–155 °C (lit.[25], m.p. 154 °C). *N*-Phenyl-*N'*p-tolylthiourea was eluted using pet.ether (60–80 °C)-benzene (1:2 v/v), m.p. and mm.p. 140–142 °C (lit.[26], m.p. 142 °C). *p*-Tolylhydrazine was eluted using benzene, m.p. and mm.p. 62–65 °C (lit.[27], m.p. 65–66 °C). Acetamide was eluted using ether-benzene (1:1 v/v), m.p. and mm.p. 80 °C; picrate derivative m.p. and mm.p. 117 °C; *N*-acetyl derivatives, m.p. and mm.p. 79 °C. Benzimidazole was eluted using 1 % ether-pentane, m.p. 172–174 °C; *N*-acetyl derivatives, m.p. and mm.p. 113–114 °C; picrate derivative m.p. and mm.p. 226–228 °C; *m/z* 118; analysis, found: N; 23.3, calcd. N, 23.7 %. 3-Phenyl-1,2,4-benzotriazine was eluted using 2 % ether-pentane, m.p. 113–114 °C; (lit.[28], 113 °C); *m/z* 207; analysis (corresponding to $C_{13}H_9N_3$) found : C, 75.22; H, 4.42; N, 20.36 %. Calcd. C,75.36; H, 4.35; N, 20.29 %; ^{1}H-NMR (DMSO, d_6) δ 7.5–7.6 (4 H, m, Ar), 7.7–7.8 (5 H, m, Ar). 6-Methyl-3-phenyl-1.2,4-benzotriazine was eluted using 2% ether-pentane, m.p. 93–95 °C; (lit.[29], 95–96 °C); *m/z* 221; analysis (corresponding to $C_{14}H_{11}N_3$): foundd C, 75.95; H, 5.02; N, 19.03 %. Calcd: C, 76.02; H, 4.98; N, 19.00 %; ^{1}H.NMR (DMSO, d_6) δ 2.81 (3H, s, CH_3), 7.3- 7.5 (3 H, m, Ar), 7.5–7.7 (5 H, m, Ar). 1-Benzylisoquinoline was eluted using pet.ether (60–80°C)-benzene (1:1 v/v), m.p. and mm.p. 55 °C (lit.[30], m.p. 56 °C); picrate (ethanol), m.p. and mm.p. 182 °C.

TABLE I Pyrolysis Products of Thiazolidin-4-one Derivatives I-III in % Yield

*Products**	*I*	*II*	*III*[a]
Toluene	–	–	8
Benzonitrile	9	6	7
Thioglycolic acid	12	10	14
Bibenzyl	–	–	7
Biaryl	5	4	–
Acetophenone	8	6	–
Phenyl isothiocyanate	7	9	10
Stilbene	–	–	6
Arylamines	10	9	–
N-Phenyl-N'-arylthiourea	7	6	–
Arylhydrazine	8	10	–
Bibenzylamine	–	–	8
Acetamide	–	–	6
Benzimidazole	6	8	10
3-Phenyl-1,2,4-benzotriazines	9	10	–
1-Benzylisoquinoline	–	–	11[a]
Residue (g)	(0.5)	(0.6)	(0.8)

* H_2S and NH3 was detected by chemical means.
a Heating of 2-phenylimino-3-benzylamino-4-thiazolidinone (III) in the presence of isoquinoline.

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