Synthesis and Reaction of 2-Imino-1,3-thiazetidines and 2-Imino-1,3-dithietanes

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2-Imino-1,3-thiazetidines and 2-imino-1,3-dithietanes were synthesized and their reactivities were studied. The former readily underwent ring-opening reaction with amines to yield guanidine derivatives. The reaction products were applied to the synthesis of heterocycles such as triazoles and triazines. The latter was converted to isothiocyanate by the reaction of *m*-chloroperbenzoic acid.

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A significant evolution in the use of heterocyclic compounds as synthetic intermediates has been recently observed [2].

Small ring heterocyclic compounds are known to be susceptible to ring-opening due to the ring strain [3]. Previously we reported the synthetic application of 2-methylene-1,3-dithietanes [4]. The utility of these compounds for construction of various heterocycles prompted us to investigate the related four-membered sulfur containing heterocycles: 2-imino-1,3-thiazetidines and 2-imino-1,3-dithietanes.

This paper describes the synthesis of some guanidine derivatives and heterocyclic compounds from 2-imino-1,3-thiazetidines. We also describe some unfamiliar reactions on 2-imino-1,3-dithietanes.

Results and Discussion.

1 The Synthesis of 1,3-Thiazetidines and 1,3-Dithietanes.

1-1 The Synthesis of 2-Acylimino-1,3-thiazetidine.

The synthesis of 2-benzoylimino-3-substituted-1,3-thiazetidines were accomplished according to the method previously reported [5]. The reaction of benzoyl thiourea and diiodomethane in the presence of triethylamine afforded 2-benzoylimino-3-substituted-1,3-thiazetidines **2a-h** in the yield of 72-99% (Scheme 1).

The treatment of *N*-ethoxycarbonyl-*N'*-4-chlorophenylthiourea, prepared from ethoxycarbonylisothiocyanate and 4-chloroaniline [6], in the same manner yielded the corresponding thiazetidine derivative **2i** (Scheme 1). The results were summarized in Tables 1 and 2.

Table 1
Preparation of 1,3-Thiazetidines 2

Compound	R_1	R_2	Method [a]	yield (%)
2a	2,4-Cl_2-C_6H_3-CO-	4-Cl-C_6H_4-	A	quant
2b	4-Me-C_6H_4-CO-	C_6H_5-	A	quant
2c	4-CF_3-C_6H_4-CO-	4-Cl-C_6H_4-	A	88
2d	2,4-Cl_2-C_6H_3-CO-	3-CF_3-C_6H_4-	A	80
2e	4-Me-C_6H_4-CO-	4-Cl-C_6H_4-	A	85
2f	2,4-Cl_2-C_6H_3-CO-	*i*-propyl-	A	73
2g	2,4-Cl_2-C_6H_3-CO-	$EtOCOCH_2$	A	72
2h	2,4-Cl_2-C_6H_3-CO-	6-Cl-C_5H_3N-3-yl	A	48
2i	C_2H_5OCO-	4-Cl-C_6H_4-	A	76
2j	$(C_2H_5O)_2PO$-	4-Cl-C_6H_4-	B	79
2k	H	4-Cl-C_6H_4	C	98
2l	CH_3CO-	4-Cl-C_6H_4-	D	78
2m	CF_3CO-	4-Cl-C_6H_4-	D	67
2n	C_6H_5OCO-	4-Cl-C_6H_4-	D	44
2o	*i*-C_3H_7OCO-	4-Cl-C_6H_4-	D	25
2p	6-Cl-C_5H_3N-3-yl-CO-	4-Cl-C_6H_4-	D	74
2q	$C_6H_5COCH_2$-	4-Cl-C_6H_4-	D	57
2r	$C_6H_5CH_2$-	4-Cl-C_6H_4-	D	24
2s	2-Cl-C_6H_4 SO_2-	4-Cl-C_6H_4-	E	77
2t	2-COOMe-$C_6H_4SO_2$-	4,6-dimethoxy-pyrimidine-2-yl	E	60
2u	2,4-$Cl_2C_6H_3CS$-	4-Cl-C_6H_4-	F	90

[a] A: from *N*-acylthiourea **1**, B: from *N*-phosphorylthiourea **3**. C: from **2j**, D: from **2k**, E: from *N*-sulfonylthiourea **5**, F: from **2a**.

Scheme 1

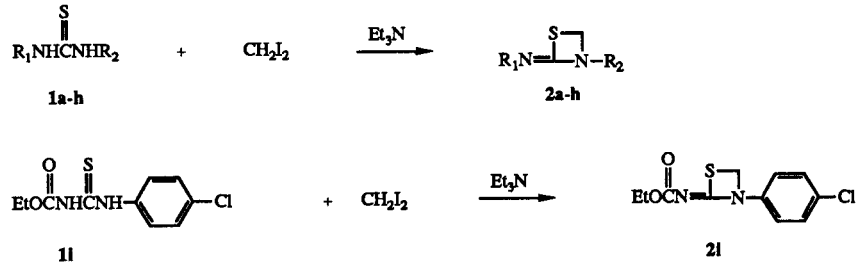


Table 2
Analytical and Spectral Data of 1,3-Thiazetidines 2

Compound	mp (°C)	Formula	Analysis (%) Calcd. (Found) C	H	N	IR ν cm^{-1} (nujol)	^{1}H-NMR [a] δ ppm (TMS)
2a	248-248.5	$C_{15}H_9N_2OSCl_3$ (371.67)	48.47 (48.31	7.54 2.40	7.54 7.51)	1655	5.37 (s, 2H), 7.56 (dd, 4H, J = 9, 12 Hz),7.33-7.56 (m, 2H), 8.03 (d, 1H, J = 9 Hz) [B]
2b	216-217	$C_{16}H_{14}N_2OS$ (282.37)	68.06 (67.76	5.00 4.90	9.92 9.84)	1645	2.40 (s, 3H), 5.10 (s, 2H), 8.13 (d, 2H, J = 9 Hz), 7.17-7.73 (m, 7H) [A]
2c	216-218	$C_{16}H_{10}N_2OSClF_3$ (370.78)	51.83 (51.76	2.72 2.60	7.56 7.56)	1640	5.23 (s, 2H), 7.45 (d, 2H, J = 9 Hz), 7.73 (d, 2H, J = 9 Hz), 7.80 (d, 2H, J = 9 Hz), 8.40 (d, 2H, J = 9 Hz), [C]
2d	182-184	$C_{16}H_9N_2OSCl_2F_3$ (405.22)	47.43 (47.44	2.24 2.26	6.91 6.88)	1650	5.17 (s, 2H), 7.27-7.87 (s, 6H), 7.93-8.13 (m, 2H) [A]
2e	208-209	$C_{16}H_{13}N_2OSCl$ (316.80)	60.66 (60.54	4.14 4.23	8.84 8.80)	1650	2.43 (s, 3H), 5.05 (s, 2H), 7.27 (d, 2H, J = 9 Hz), 7.36 (d, 2H, J = 9 Hz), 8.15 (d, 2H, J = 9 Hz) [A]
2f	123-125	$C_{12}H_{12}N_2OSCl_2$ (303.21)	47.54 (47.56	3.99 3.93	9.24 8.94)	1640	1.23 (s, 3H), 1.33 (s, 3H), 4.23 (m, 1H), 4.72 (s, 2H), 7.26 (dd, 1H, J = 3, 9 Hz), 7.43 (d, 1H, J = 3 Hz), 8.00 (d, 1H, J = 9 Hz) [A]
2g	72-73	$C_{13}H_{12}N_2O_3SCl_2$ (347.22)	44.97 (45.00	3.48 3.46	8.07 8.13)	1735 1650	1.30 (T, 3H, J = 8 Hz), 4.27 (q, 2H, J = 8 Hz), 4.28 (s, 2H), 5.00 (s, 2H), 7.27 (dd, 1H, J = 3, 8 Hz), 7.43 (d, 1H, J = 3 Hz), 8.00 (d, 1H, J = 9 Hz) [A]
2h	259-260	$C_{14}H_8N_3OSCl_3$ (3 72.66)	45.12 (45.11	2.16 2.05	11.28 11.30)	1645	4.72 (s, 2H), 7.26-7.29 (m, 2H), 7.43 (d, 1H, J = 3 Hz), 7.67 (dd, 1H, J = 3, 9 Hz), 8.00 (d, 1H, J = 9 Hz), 8.27 (d, 1H, J = 3 Hz) [A]
2i	135-137	$C_{11}H_{11}N_2O_2SCl$ (270.74)	48.80 (48.90	4.10 4.15	10.35 10.40)	1652	1.27 (t, 3H, J = 7 Hz), 4.18 (q, 2H, J = 7 Hz), 5.07 (s, 2H), 5.60 (s, 1H), 6.93 (d, 2H, J = 9 Hz), 7.33 (d, 2H, J = 9 Hz) [A]
2j	(liquid)	$C_{12}H_{16}N_2O_3SClP$ (334.76)	43.05 (42.87	4.82 5.00	8.37 8.00)	1600	1.40 (t, 6H, J = 8 Hz), 4.23 (s, 2H), 4.24 (q, 4H, J = 8 Hz), 7.33 (d, 2H, J = 9 Hz), 7.57 (d, 2H, J = 9 Hz) [A]
2k	200<	$C_8H_8N_2SCl_2$ (235.11)	40.88 (40.88	3.43 3.41	11.91 11.88)	1635 1716	5.33 (s, 2H), 7.57 (s, 4H) [B]
2l	150-151	$C_{10}H_9N_2OSCl$ (240.70)	49.90 (49.79	3.77 3.65	11.64 11.64)	1580 1665	2.30 (s, 3H), 5.07 (2H, s), 6.93 (d, 2H, J = 9 Hz), 7.33 (d, 2H, J = 9 Hz), [A]
2m	167-168	$C_{10}H_6N_2OSF_3Cl$ (294.68)	40.76 (40.62	2.05 1.96	9.51 9.46)	1585 1670	5.17 (s, 2H), 7.38 (d, 2H, J = 9 Hz), 7.55 (d, 2H, J = 9 Hz) [A]
2n	(liquid)	$C_{15}H_{11}N_2O_2SCl$ (318.78)	56.52 (56.50	3.48 3.29	8.79 8.78)	1645	5.00 (s, 2H), 7.17-7.50 (m, 5H), 7.40 (d, 2H, J = 9 Hz), 7.55 (d, 2H, J = 9 Hz) [A]
2o	123-124	$C_{12}H_{13}N_2O_2SCl$ (284.75)	50.61 (51.05	4.60 4.56	9.84 9.83)	1680	1.28 (d, 6H, J = 8 Hz), 5.16 (hex, 1H, J = 8 Hz), 5.20 (s, 2H), 7.13 (d, 2H, J = 9 Hz), 7.40 (d, 2H, J = 9 Hz) [A]
2p	161-162	$C_{14}H_9N_3OSCl_2$ (338.20)	49.72 (49.50	2.68 2.51	12.42 12.43)	1668	4.72 (s, 2H), 7.33 (d, 2H, J = 9 Hz), 7.40 (d, 1H, J = 9 Hz), 7.57 (d, 2H, J = 9 Hz), 8.23 (dd, 1H, J = 3, 9 Hz), 9.00 (d, 1H, J = 3 Hz) [B]
2q	106-107	$C_{16}H_{13}N_2OSCl$ (316.80)	60.67 (60.61	4.14 4.00	8.84 8.58)	1670	4.10 (s, 2H), 4.87 (s, 2H), 7.15 (d, 2H, J = 9 Hz), 7.37 (d, 2H, J = 9 Hz), 7.50-7.67 (m, 3H), 7.90 (s, 1H), 8.00 (s, 1H) [A]
2r	(liquid)	$C_{15}H_{13}N_2SCl$ (289.80)	62.16 (62.15	4.52 4.51	9.67 9.67)	1600	4.33 (s, 2H), 4.57 (s, 2H), 6.87-7.50 (m, 10H) [B]
2s	199-210	$C_{14}H_{13}N_2O_2S_2Cl_2$ (373.28)	45.04 (44.91	2.70 2.62	7.50 7.44)	1605	5.23 (s, 2H), 7.33-7.60 (m, 7H), 8.13 (m, 1H) [B]
2t	190-190.5	$C_{16}H_{16}N_4O_6S_2$ (424.44)	45.27 (45.12	3.80 3.77	13.20 13.08)	1650	3.92 (s, 9H), 5.16 (s, 2H), 5.78 (s, 1H), 7.73 (m, 3H), 8.47 (m, 1H) [B]
2u	161-163	$C_{15}H_9N_2S_2Cl_3$ (387.73)	46.47 (46.28	2.34 2.23	7.22 6.92)	1565	5.11 (s, 2H), 7.16-7.67 (m, 3H), 7.33 (d, 2H, J = 9 Hz), 7.63 (d, 2H, J = 9 Hz) [A]

[a] Solvent: [A] deuterichloroform, [B] DMSO-d_6, [C] acetonitrile-d_3.

1-2 The Synthesis of 2-Imino-1,3-thiazetidine and Related Compounds.

The reaction of diethylphosphorylisothiocyanate [7] and 4-chloroaniline afforded *N*-phosphorylthiourea **3**. The cyclization reaction of **3** with diiodomethane afforded 2-ethoxyphosphinylimino-1,3-thiazetidine derivatives **2j**. The hydrolysis [8] of **2j** with hydrochloric acid yielded 2-imino-1,3-thiazetidine (**2k**) as hydrochloride (Scheme 2).

Some 2-acylimino- and 2-alkylimino-1,3-thiazetidines **2** were prepared from 2-imino-1,3-thiazetidine **2k** and acyl halide, acid anhydride or alkyl halide in the presence of base (Scheme 2). The reaction of 2-imino-3-(4-chlorophen-

Scheme 2

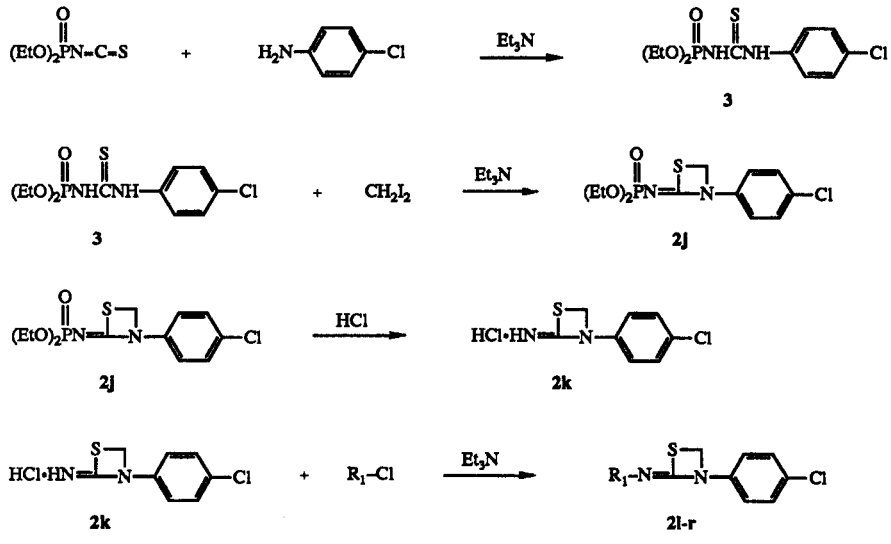
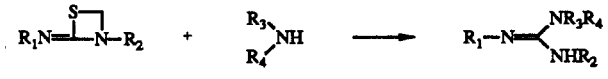


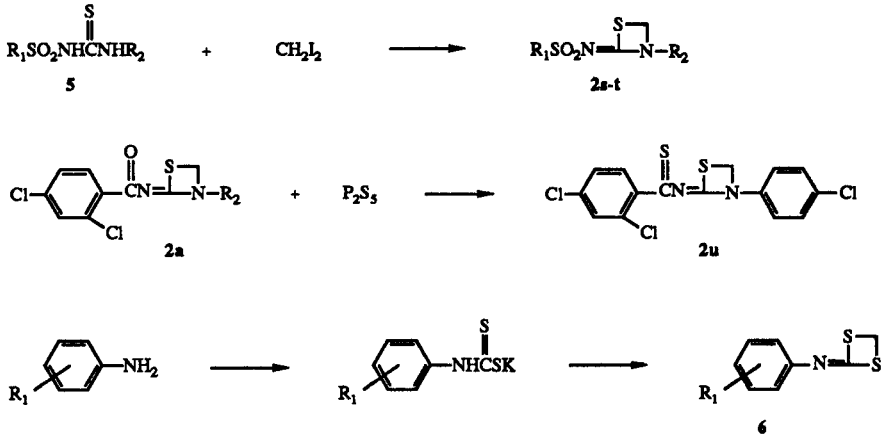
Table 3

Preparation of Acylquanidines 7



Compound	R_1	R_2	R_3	R_4	yield (%)
7a	2,4-Cl_2-C_6H_3-CO-	4-Cl-C_6H_4-	$C_6H_5CH_2$-	H	92
7b	2,4-Cl_2-C_6H_3-CO-	4-Cl-C_6H_4-	CH_3-	H	68
7c	2,4-Cl_2-C_6H_3-CO-	4-Cl-C_6H_4-	n-C_3H_7-	H	90
7d	2,4-Cl_2-C_6H_3-CO-	4-Cl-C_6H_4-	i-C_3H_7-	H	89
7e	2,4-Cl_2-C_6H_3-CO-	4-Cl-C_6H_4-	CH_3-	CH_3-	80
7f	2,4-Cl_2-C_6H_3-CO-	4-Cl-C_6H_4-	$(EtO)_2CHCH_2$-	H	58
7g	4-Me-C_6H_4-CO-	C_6H_5-	CH_3-	CH_3-	99
7h	4-Me-C_6H_4-CO-	C_6H_5-	-$(CH_2)_5$		76
7i	4-Me-C_6H_4-CO-	C_6H_5-	-$(CH_2)_2O(CH_2)_2$-		88

Scheme 3



yl)-1,3-thiazetidine and trifluoroacetic anhydride in the presence of sodium acetate afforded 2-trifluoroacetylimino-3-(4-chlorophenyl)-1,3-thiazetidine (**2m**) in good yield.

The reaction of **2k** and benzyl bromide in the presence of base afforded 2-benzylimino-3-(4-chlorophenyl)-1,3-thiazetidine (**2r**).

The other 2-acylimino, 2-alkylimino-1,3-thiazetidine derivatives were prepared from **2k** by a similar method described above. The results are summarized in Tables 1 and 2.

1-3 The Synthesis of 2-Sulfonylimino- and 2-Thioacylimino-1,3-thiazetidines.

2-Sulfonylimino-1,3-thiazetidine derivatives **2s-t** were prepared by similar methods described above from *N*-arylsulfonylthioures **5** and diiodomethane (Scheme 3).

The reaction of **2a** and phosphorus pentasulfide in pyridine under reflux conditions afforded 2-arylthioacylimino-1,3-thiazetidine **2u** in the yield of 90%.

The results are summarized in Tables 1 and 2.

1-4 The Synthesis of 2-Phenyimino-1,3-dithietanes and Related Compounds.

2-Phenylimino-1,3-dithietanes **6** were prepared by the reaction of the corresponding anilines and carbon disulfide in the presence of potassium carbonate with cooling followed by the cyclization with dibromomethane as reported before [9] (Scheme 3). The results were summarized in Table 9.

2 The Reaction of 2-Imino-1,3-thiazetidines with Amines.

2-1 The Reaction of 2-Acylimino-1,3-thiazetidines and Aliphatic Amines.

The treatment of 2-(2,4-dichlorobenzoylimino)-3-(4-chlorophenyl)-1,3-thiazetidine (**2a**) with two equivalents of benzylamine in acetonitrile at room temperature for 2 hours afforded 1-(2,4-dichlorobenzoyl)-2-benzyl-3-(4-chlorophenyl)guanidine (**7a**) in the yield of 92% (Scheme 4). The reaction was not complete even after a prolonged reaction time when one equivalent of the amine was applied, thus it was shown that the presence of excess amine is necessary in this reaction.

The reaction of **2a** with excess dimethylamine afforded 1-(2,4-dichlorobenzoyl)-2,2-dimethyl-3-(4-chlorophenyl)quanidine (**7e**) in the yield of 80%.

Similarly the reaction of 2-acylimino-1,3-thiazetidines **2** with excess aliphatic amines afforded corresponding guanidines **7** as summarized in Tables 3 and 4.

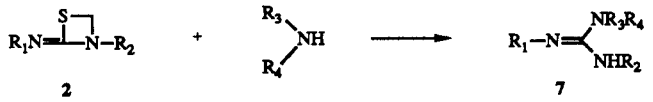
The reaction of **2a** with excess *n*-propylamine in acetonitrile at room temperature gave a mixture of guanidine derivative **7c** and 5-*n*-propyldihydro-1,3,5-dithiazine (**8**) (Scheme 4). The formation of **7c** is explicable by a three step process: Michael addition of *n*-propylamine to the sp^2-

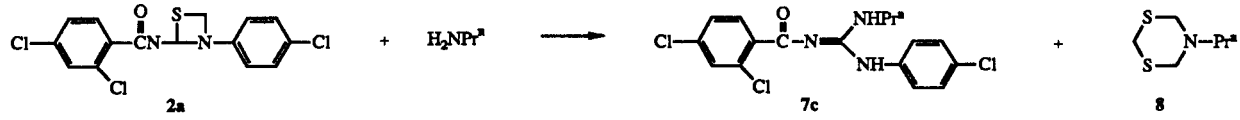
Table 4

Analytical and Spectral Data of Acylguanidines 7

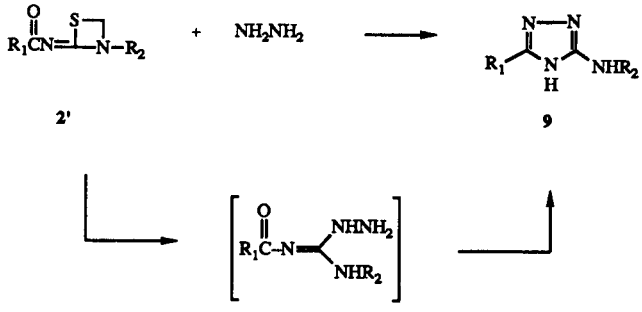
Compound	mp (°C)	Formula	Analysis (%) Calcd. (Found) C	H	N	IR ν cm^{-1} (nujol)	^{1}H-NMR [a] δ ppm (TMS)
7a	176-178	$C_{21}H_{16}N_3OCl_3$ (432.74)	58.29 (58.30	3.73 3.71	9.71 9.89)	1580 3300	4.65 (s, 2H, J = 6 Hz), 7.17-7.47 (m, 13H), 7.73 (d, 1H, J = 9 Hz) [B]
7b	136-137.5	$C_{15}H_{12}N_3OCl_3$ (356.60)	50.52 (50.45	3.39 3.38	11.78 11.76)	1620 3200 3280	3.00 (d, 3H, J = 5 Hz), 7.13-7.43 (m, 6H), 7.90 (d, 1H, J = 9 Hz) [A]
7c	129-130	$C_{17}H_{16}N_3OCl$ (384.73)	53.07 (52.83	4.19 4.27	10.92 10.84)	1600 3300	0.93 (t, 3H, J = 8 Hz), 1.37 (q, 2H, J = Hz), 3.30-3.53 (m, 2H), 7.10-7.50 (m, 6H), 7.88 (d, 1H, J = 9 Hz), 11.50 (s, 1H, br) [A]
7d	117-118	$C_{17}H_{16}N_3OCl_3$ (384.69)	53.08 (52.81	4.19 4.18	10.92 10.80)	1620 3300	1.20 (d, 6H, J = 6 Hz), 4.33 (hex, 1H, J = 6 Hz), 7.10-7.46 (m, 6H), 7.88 (d, 1H, J = 9 Hz), 11.50 (s, 1H, br) [A]
7e	150-152	$C_{16}H_{14}N_3OCl_3$ (370.67)	51.85 (51.60	3.81 3.77	11.34 11.46)	1600 3050 3130	3.00 (s, 6H), 7.00 (d, 2H, J = 9 Hz), 7.31 (d, 2H, J = 9 Hz), 7.20-7.46 (m, 2H), 7.90 (d, 2H, J = 9 Hz) [A]
7f	123-124	$C_{20}H_{22}N_3O_3Cl_3$ (458.77)	52.36 (52.35	4.83 4.82	9.16 9.02)	1580 3300	1.20 (t, 6H, J = 9 Hz), 3.60 (q, 4H, J = 9 Hz), 3.43-3.93 (m, 2H), 4.61 (t, 1H, J = 9 Hz), 7.20 (d, 1H, J = 3 Hz), 7.29 (d, 2H, J = 9 Hz), 7.38 (d, 1H, J = 3, 9 Hz), 7.40 (d, 2H, J = 9 Hz), 7.88 (d, 1H, J = 9 Hz), 11.80 (1H, br) [A]
7g	139-140	$C_{17}H_{19}N_3O$ (281.36)	72.57 (72.58	6.81 6.81	14.93 14.78)	1600 3180 3250	2.37 (s, 3H), 3.00 (s, 6H), 6.97-7.40 (m, 7H), 8.12 (s, 1H), 8.20 (s, 1H), 11.80 (s, 1H, br) [A]
7h	142-144	$C_{20}H_{23}N_3O$ (321.41)	74.74 (74.77	7.21 7.22	13.07 13.00)	1600 3150	1.59 (s, br, 6H), 2.40 (s, 3H), 3.50 (s, br, 4H), 7.00-7.47 (m, 7H) [A]
7i	157-159	$C_{19}H_{21}N_3O_2$ (323.40)	70.56 (70.19	6.55 6.55	12.99 13.00)	1605 3150	2.37 (s, 3H), 3.43-3.80 (m, 8H), 7.00-7.47 (s, 7H), 8.01 (s, 1H), (m, 7H), 8.01 (s, 1H), 8.15 (s, 1H), 11.87 (s, 1H, br) [A]

Scheme 4





Scheme 5



carbon of 1,3-thiazetidine, the ring-opening of the adduct to afford a guanidine derivative **7c** with concomitant liberation of thioformaldehyde and condensation of the latter with *n*-propylamine to yield dihydro-1,3,5-dithiazine **8**.

The reaction of **2a** with aniline or aqueous ammonia under the same reaction condition as above did not proceed.

2-2 The Reaction of 2-Thioacylimino- and 2-Sulfonylimino-1,3-thiazetidines and Aliphatic Amines.

The reaction of 2-arylsulfonyliminothiazetidine **2s-t**, 2-arylthioacyliminothiazetidine (**2u**) and 2-ethoxyphosphinylimino-1,3-thiazetidine (**2j**) with dimethylamine in acetonitrile at room temperature afforded the corresponding guanidine derivatives (Scheme 4).

The 2-imino-1,3-thiazetidine derivatives **2**, thus, easily reacted with amines to afford guanidine derivatives with good yields. This new ring-opening reaction provides an attractive synthetic route to guanidines bearing electron-withdrawing groups on imino nitrogen atom.

3 The Synthetic Application of 2-Imino-1,3-thiazetidines for Heterocycles.

3-1 The Synthesis of 5-Amino-1,2,4-triazoles.

The reaction of **2a** and hydrazine monohydrate in acetonitrile under reflux condition afforded 3-(2,4-dichlorophenyl)-5-(4-chloroanilino)-1,2,4-triazole (**9**) in good yield (Scheme 5). This reaction is considered to proceed through the formation of **10** as intermediates and subsequent intramolecular cyclization to triazole.

In a similar manner, the other thiazetidines **2** were converted to triazoles as summarized in Tables 5 and 6.

3-2 The synthesis of 1,3,5-Triazines.

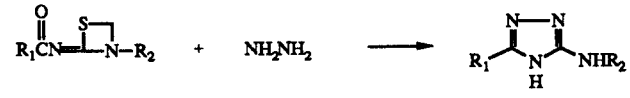
The treatment of 2-imino-1,3-thiazetidine **2** with isothioureas in acetonitrile yielded 1,3,5-triazine derivatives **11a-e** in good yields (Scheme 6). Similarly some 2-alkylthio-1,3,5-triazines were prepared.

The reaction of 2-imino-1,3-thiazetidine derivatives **2** and guanidine in acetonitrile afforded 2-amino-1,3,5-triazine derivatives **11f-g** (Scheme 6).

The results were summarized in Tables 7 and 8.

Table 5

Preparation of 1,2,4-Triazoles **9**



Compound	R_1	R_2	yield (%)
9a	2,4-Cl_2-C_6H_3-	4-Cl-C_6H_4-	87
9b	4-CF_3-C_6H_4-	4-Cl-C_6H_4-	56
9c	2,4-Cl_2-C_6H_3-	*i*-C_3H_7-	25
9d	4-Me-C_6H_4-	4-Cl-C_6H_4-	85
9e	CF_3-	4-Cl-C_6H_4-	77
9f	CH_3-	4-Cl-C_6H_4-	84

Scheme 6

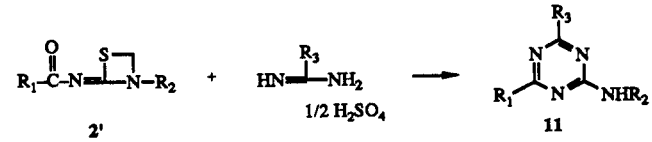
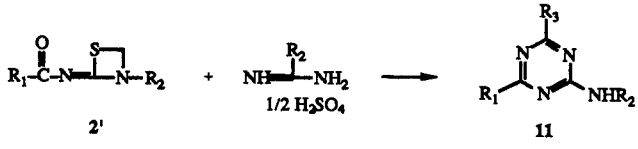


Table 6
Analytical and Spectral Data of 1,2,4-Triazoles 9

Compound	mp (°C)	Formula	Analysis (%) Calcd. (Found) C	H	N	IR ν cm^{-1} (nujol)	^{1}H-NMR [a] δ ppm (TMS)
9a	263-263.5	$C_{14}H_9N_4Cl_3$ (339 .61)	49.51 (49.33	2.67 2.74	16.50 16.20)	3275 1610	7.27 (d, 2H, J = 9 Hz), 7.50 (dd, J = 3, 9 Hz), 7.55 (d, 1H, J = 3 Hz), 7.70 (d, 2H, J = 9 Hz), 7.97 (d, 1H, J = 9 Hz), 9.47 (s, 1H) 13.17 (s, 1H, br) [B]
9b	173-174	$C_{15}H_{10}N_4ClF_3$ (338.71)	53.19 (53.00	2.98 2.90	16.54 16.43)	3280 1600	7.25 (d, 2H, J = 9 Hz), 7.66 (s, 1H, br), 7.67 (d, 2H, J = 9 Hz), 7.75 (d, 2H, J = 9 Hz), 8.27 (d, 2H, J = 9 Hz), 9.10 (s, 1H, br) [B]
9c	216-217	$C_{11}H_{12}N_4Cl_2$ (271.15)	48.73 (48.65	4.46 4.30	20.66 20.53)	3280 1605	1.20 (d, 6H, J = 6 Hz), 3.77 (hex, 1H, J = 6 Hz), 6.00 (d, 1H, J = 6 Hz), 7.33 (dd, 1H, J = 3, 9 Hz), 7.47 (d, 1H, J = 3 Hz), 7.90 (d, 1H, J = 9 Hz), 12.10 (s, 1H, br) [B]
9d	168-170	$C_{15}H_{13}N_4Cl$ (284.75)	63.27 (63.30	4.60 4.17	19.68 19.88)	3300 1610	2.40 (s, 3H), 7.18 (d, 2H, J = 9 Hz), 7.27 (d, 2H, J = 9 Hz), 7.63 (d, 2H, J = 9 Hz), 7.90 (d, 2H, J = 9 Hz), 9.13 (s, 1H) [B]
9e	142-143	$C_9H_6N_4ClF_3$ (262.62)	41.16 (41.11	2.30 2.12	21.33 21.22)	3285 1610	7.33 (d, 2H, J = 9 Hz), 7.50 (d, 2H, J = 9 Hz), 9.77 (s, 1H, br), 9.90 (s, 1H, br), [B]
9f	263-265 [b]	$C_9H_9N_4Cl$ (208.65)	51.55 (51.54	4.80 4.88	26.73 26.59)	3285 1610	2.20 (s, 3H), 7.35 (d, 2H, J = 9 Hz), 7.52 (d, 2H, J = 9 Hz), 9.77 (s, 1H, br), 9.90 (s, 1H, br) [B]

[a] Solvent: [A] deuteriochloroform, [B] DMSO-d_6. [b] lit. [10] mp 265°.

Table 7
Preparation of 1,3,5-Triazines 11



2' 11

Compound	R_1	R_2	R_3	yield (%)
11a	2,4-Cl_2-C_6H_3-CO-	4-Cl-C_6H_4-	MeS-	85
11b	4-CF_3-C_6H_4-CO-	4-Cl-C_6H_4-	MeS-	83
11c	4-Me-C_6H_4-CO-	4-Cl-C_6H_4-	MeS-	43
11d	2,4-Cl_2-C_6H_3-CO-	*i*-C_3H_7-	MeS-	40
11e	CF_3-	4-Cl-C_6H_4-	MeS-	69
11f	2,4-Cl_2-C_6H_3-CO-	4-Cl-C_6H_4-	NH_2-	42
11g	4-CF_3-C_6H_4-CO-	4-Cl-C_6H_4-	NH_2-	49

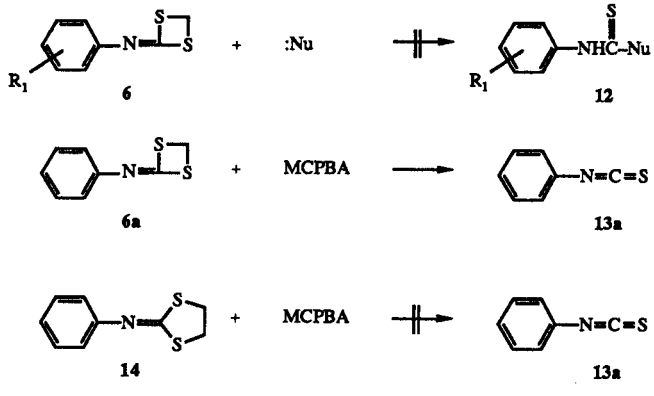
4 The Reaction of 2-Imino-1,3-dithietanes with Oxidizing Agent.

Little attention has been devoted to the oxidation reaction of 2-imino-1,3-dithietanes [11]. The studies [12] on increased reactivity of oxidized ketendithioacetale to the nucleophile encouraged us to attempt the reaction of 2-phenylimino-1,3-dithietane and oxidizing agent.

As previously reported 2-methylene-1,3-dithietanes [4] and 2-imino-1,3-thiazetidines bearing electron withdrawing groups were subject to nucleophilic attack to cause ring-opening reactions. However the reaction of 2-phenylimino-1,3-dithietanes and nucleophiles such as amines, alcohols and mercaptans under the same reaction conditions before did not proceed.

The reaction of 2-phenylimino-1,3-dithietane and *m*-chloroperbenzoic acid in chloroform with ice-cooling afforded a relatively nonpolar compound. The isolated reaction product was identified as phenyl isothiocyanate by its infrared spectrum (Scheme 7). The yield after isolation was 70%. The other 2-(substituted phenylimino)-1,3-dithietanes were similarly converted to the corresponding isothiocyanate derivatives by the reaction of *m*-chloroperbenzoic acid as summarized in Table 9. The reaction of 2-phenylimino-1,3-dithietane and hydrogen peroxide was unsuccessful.

Scheme 7



The arylisothiocyanates can be prepared from ammonium aryldithiocarbamates by the thermal decomposition or by the treatment of metallic salt [13]. The present method is superior to the previous methods in terms of the reaction conditions in which high temperature and metallic salt are needless.

To clarify whether the ease of formation of isothiocyanate derivatives attribute to the ring strain of dithietanes, 2-phenylimino-1,3-dithiolane [14] was treated with *m*-chlo-

Table 8

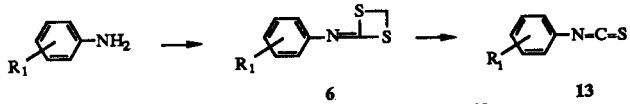
Analytical and Spectral Data of 1,3,5-Triazoles **11**

Compound	mp (°C)	Formula	Analysis (%) Calcd. (Found) C	H	N	IR ν cm^{-1} (nujol)	^{1}H-NMR [a] δ ppm (TMS)
11a	165-166	$C_{16}H_{11}N_4SCl_3$ (397.71)	48.32 (48.33	2.79 2.81	14.09 14.33)	1605 3400	2.57 (s, 3H), 7.29 (d, 2H, J = 9 Hz), 7.26-7.57 (m, 3H), 7.66 (d, 2H, J = 9 Hz), 7.83 (d, 1H, J = 9 Hz) [B]
11b	187-188	$C_{17}H_{12}N_4SClF_3$ (396.82)	51.45 (51.39	3.05 3.11	14.12 14.02)	1600 3385	2.60 (s, 3H), 7.33 (d, 2H, J = 9 Hz), 7.80 (d, 2H, J = 9 Hz), 7.83 (d, 2H, J = 9 Hz), 8.51 (d, 2H, J = 9 Hz), 10.27 (s, 1H) [B]
11c	145-146	$C_{17}H_{15}N_4SCl$ (342.85)	59.56 (59.55	4.41 4.44	16.34 16.33)	1605 3405	2.40 (s, 3H), 2.57 (s, 3H), 7.26 (d, 4H, J = 9 Hz), 7.80 (d, 2H, J = 9 Hz), 8.30 (d, 2H, J = 9 Hz), 9.60 (s, 1H, br) [B]
11d	128-130	$C_{13}H_{14}N_4SCl_2$ (329.24)	47.42 (47.44	4.29 4.30	17.01 17.00)	1610 3400	1.33 (d, 6H, J = 8 Hz), 2.50 (s, 3H), 4.50 (hex, 1H, J = 8 Hz), 7.10-7.60 (m, 3H), 10.43 (d, 1H, J = 8 Hz) [B]
11e	110-111	$C_{11}H_8N_4SClF_3$ (320.72)	41.19 (41.00	2.51 2.55	17.47 17.55)	1600 3405	2.57 (s, 3H), 7.29 (d, 2H, J = 9 Hz), 7.66 (d, 2H, J = 9 Hz), 9.60 (s, 1H, br) [B]
11f	171-173	$C_{15}H_{10}N_5Cl_3$ (365.75)	49.14 (49.11	2.75 2.77	19.10 19.01)	1595 3400	7.29 (d, 2H, J = 9 Hz), 7.26-7.57 (m, 3H), 7.66 (d, 2H, J = 9 Hz), 7.83 (d, 1H, J = 9 Hz) [B]
11g	161-163	$C_{16}H_{11}N_5ClF_3$ (365. 76)	54.52 (52.38	3.03 3.09	19.15 18.84)	1605 3400	7.27 (s, 2H, br), 7.37 (d, 2H, J = 9 Hz), 7.88 (d, 2H, J = 9 Hz), 7.97 (d, 2H, J = 9 Hz), 8.57 (d, 2H, J = 9 Hz), 9.80 (s, 1H) [B]

[a] Solvent: [A] deuteriochloroform, [B] DMSO-d_6.

Table 9

Preparation of 2-Phenylimino-1,3-dithietanes **8** and Phenylisothiocyanates **13**



	6			**13**
R_1	mp (°C)	yield (%)	ν N=C	yield (%)
H	liquid	71	2050	60
4-Cl	87-88	76	2058	72
4-I	139-140	71	2055	83
4-Me	168-169	69	2050	60
2-Cl	42-43	50	2050	62
2-Me	liquid	50	2045	42

roperbenzoic acid under the same reaction condition as described above. However, 2-phenylimino-1,3-dithiolane was not converted to isothiocyanate derivative. In view of the experimental results 2-phenylimino-1,3-dithietanes were easily converted to isothiocyanantes due to its ring strain. From the analogy to the formation of sulfene from 3-hydroxythietane 1,1-dioxide [15], the formation of isothiocyanates are considered to the ease of the release of sulfene, however, we shall not indulge in detailed speculation until we have investigated further studies on the reaction mechanism.

In summary, this study reported some examples of the synthesis and reaction of the 2-imino-1,3-thiazetidines and 2-imino-1,3-dithietanes. It could be stated that the imino-1,3-thiazetidines and 1,3-dithietanes act as masked thioureas or 2-methylthio-pseudoureas under certain conditions.

EXPERIMENTAL

All melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. The ir spectra were recorded with a Shimadzu IR-420 spectrophotometer. The ^{1}H-nmr spectra were recorded on a Varian EM-390 (90 MHz) spectrometer using tetramethylsilane as an internal standard.

Preparation of 1,3-Thiazetidine Derivative **2a**. General Procedure for the Preparation of **2a-i**.

A solution of *N*-2,4-dichlorobenzoyl-*N'*-4-chlorophenylthiourea (**1a**, 14.8 mmoles), diiodomethane (47 mmoles) and triethylamine (47 mmoles) in absolute acetone (60 ml) was refluxed for 7 hours. After cooling the resulting precipitate was collected by filtration, recrystallized from ethanol to afford **2a** as white crystals.

2-Diethylphosphorylimino-3-(4-chlorophenyl)-1,3-thiazetidine (**2j**).

To a solution containing diethyl phosphorylisothiocyanate [5] (10.0 g, 52 mmoles) in acetonitrile (30 ml) was added 4-chloroaniline (8.0 g, 63 mmoles). The reaction mixture was stirred for 5 hours at room temperature. The resulting precipitate was collected by filtration afforded *N*-diethoxyphosphinyl-*N'*-4-chloroanilinothiourea (**3**, 15.0 g, 76%) as crystals, mp 115-117°; ^{1}H nmr (deuteriochloroform): δ 1.40 (t, 6H, J = 6 Hz), 4.27 (q, 4H, J = 6 Hz), 7.30-7.63 (m, 4H), 7.90 (m, 1H), 10.77 (s, 1H).

Anal. Calcd. for $C_{11}H_{16}N_2O_3PSCl$: C, 40.94; H, 5.00; N, 8.68. Found: C, 40.84; H, 5.12; N, 8.70.

To the mixture of **3** (4.0 g, 12.4 mmoles) and potassium carbonate (4.7 g, 35 mmoles) in dry acetone (30 ml) was added diiodomethane (25.0 g, 95 mmoles). The reaction mixture was stirred at room temperature. The contents were concentrated under reduced pressure, the residue was poured onto water and extracted with dichloromethane. The organic layer was washed with water and dried over magnesium sulfate. The solvent was removed under reduced pressure and obtained residue was chromatographed on a silica-gel column using hexane-ethyl acetate (1:5 by volume) as eluent to yield **2j** (3.2 g, 79%) as a resinous material.

2-Imino-3-(4-chlorophenyl)-1,3-thiazetidine (**2k**).

A mixture of **2j** (5.0 g, 15 mmoles) and hydrochloric acid (12 ml) was stirred at room temperature for 72 hours. After adding a mixture of acetone (30 ml) and diethyl ether (15 ml) and cooling, the resulting precipitate was collected by filtration to afford **2k** (3.5 g, 98%) as crystals.

Preparation of 1,3-Thiazetidine Derivative **2m**. General Procedure for the Preparation of **2l-p**.

To a mixture of **2k** (1.2 g, 5.1 mmoles), ether (30 ml) and trifluoroacetic anhydride (20 ml) was added anhydrous sodium acetate (4.5 g, 50 mmoles) below 10°. The reaction mixture was stirred for 8 hours at room temperature. After insoluble material was removed by filtration and concentrated under reduced pressure. The residue was extracted with ether and concentrated under reduced pressure. The obtained residue was recrystallized from ethanol to afford 2-trifluoromethylimino-3-(4-chlorophenyl)-1,3-thiazetidine (**2m**) as yellow crystals.

Preparation of 1,3-Thiazetidine Derivative **2r**. General Procedure for the Preparation of **2g-r**.

To a mixture of **2k** (1.5 g, 6.3 mmoles), ether (30 ml) and benzylbromide (1.2 g, 7.0 mmoles) was added anhydrous sodium acetate (0.6 g, 7.3 mmoles) below 10°. The reaction mixture was stirred for 8 hours at room temperature. The reaction mixture was poured onto ice-water (100 ml), extracted with ethyl acetate and the organic layer was dried over magnesium sulfate. The organic layer was concentrated under reduced pressure and the residue was chromatographed on a silica-gel column using hexane-ethyl acetate (3:1 by volume) as eluent to yield 2-benzylimino-3-(4-chlorophenyl)-1,3-thiazetidine (**2r**) as a colorless liquid.

2-(2-Chlorobenzenesulfonylimino)-3-(4-chlorophenyl)-1,3-thiazetidine (**2s**).

To a solution of *N*-(2-chlorobenzenesulfonyl)-*N'*-(4-chlorophenyl)thiourea (5.0 g, 15 mmoles) in acetone (30 ml) was added diiodomethane (12.2 g, 45 mmoles) and triethylamine (4.5 g, 45 mmoles). The reaction mixture was refluxed for 8 hours. The resulting precipitate was collected by filtration, washed with water and recrystallized from acetonitrile to afford **2s** as crystals.

2-(2,4-Dichlorothiobenzoylimino)-3-(4-chlorophenyl)-1,3-thiazetidine (**2u**).

The mixture of **2a** (1.0 g, 2.7 mmoles) and phosphorus pentasulfide (2.0 g, 9.0 mmoles) in pyridine (25 ml) was heated at 80° for 4 hours. After cooling, the reaction mixture was poured onto ice-water and resulting precipitate was collected by filtration to afford **2u** as crystals.

Preparation of 2-Acylguanidine Derivative **7a**. General Procedure for the Preparation of **7a-i**.

1-(4-Chlorophenyl)-2-(2,4-dichlorobenzoyl)-3-benzylguanidine (**7a**).

To the mixture of **2a** (3.0 g, 8.1 mmoles) and acetonitrile (30 ml) was added benzylamine (1.7 g, 16.2 mmoles). The reaction mixture was refluxed for 2 hours. After cooling, the resulting precipitate was collected by filtration and washed with ether to afford **7a** as crystals.

1-(4-Chlorophenyl)-2-(2,4-dichlorobenzoyl)-3-*n*-propylguanidine (**7c**) and 5-*n*-Propyl-1,3,5-dihydrodithiazine (**8**).

To a solution of **2a** (2.0 g, 5.4 mmoles) and acetonitrile (30 ml) was added *n*-propylamine (1.0 g, 17.0 mmoles) at room temperature. The reaction mixture was refluxed for 3 hours. The contents were concentrated under reduced pressure, the obtained residue was chromatographed on a silica-gel column using hexane-ethyl acetate (2:1 by volume) to afford **7c** (1.8 g) and **8** (0.4 g). 5-*n*-Propyl-1,3,5-dihydrodithiazine (**8**) was a yellow liquid; ^{1}H nmr (deuteriochloroform): δ 0.93 (t, 3H, J = 6 Hz), 1.47 (hex, 2H, J = 6 Hz), 3.00 (t, 2H, J = 6 Hz), 4.10 (s, 2H), 4.43 (s, 4H).

Anal. Calcd. for $C_6H_{13}NS_2$: C, 44.13; H, 8.02; N, 8.57. Found: C, 44.10; H, 8.12; N, 8.60.

1-(4-Chlorophenyl)-2-(2-chlorobenzenesulfonyl)-3-dimethylaminoguanidine (**7j**).

To a solution of **2s** (0.8 g, 2.1 mmoles) in acetonitrile (30 ml) was added dimethylamine (0.3 g, 6.4 mmoles). The reaction mixture was refluxed for 2 hours. The contents were concentrated under reduced pressure and obtained residue was chromatographed on a silica-gel column using hexane-ethyl acetate (1:1 by volume) as eluent to afford **7j** (0.8 g, 80%) as crystals, mp 175-176°; ^{1}H nmr (deuteriochloroform): δ 2.80 (s, 6H), 6.70 (d, 2H, J = 9 Hz), 7.20 (d, 2H, J = 9 Hz), 7.26-7.50 (m, 3H), 8.01 (m, 1H), 8.50 (1H, br).

Anal. Calcd. for $C_{15}H_{15}N_3O_2SCl_2$: C, 48.40; H, 4.06; N, 11.29. Found: C, 48.45; H, 4.07; N, 11.19.

1-(4-Chlorophenyl)-2-(2,4-dichlorothiobenzoyl)-3-dimethylaminoguanidine (**7k**).

To a solution of **2u** (0.8 g, 2.1 mmoles) in acetonitrile (30 ml) was added dimethylamine (0.3 g, 6.4 mmoles). The reaction mixture was refluxed for 2 hours. The contents were concentrated under reduced pressure and obtained residue was chromatographed on a silica-gel column using hexane-ethyl acetate (1:5 by volume) as eluent to afford **7k** (0.6 g, 75%) as crystals, mp 155-158°; ^{1}H nmr (deuteriochloroform): δ 3.00 (s, 6H), 7.05 (d, 2H, J = 9 Hz), 7.33 (d, 2H, J = 9 Hz), 7.18-7.50 (m, 2H), 7.80 (d, 2H, J = 8 Hz).

Anal. Calcd. for $C_{16}H_{14}N_3SCl_3$: C, 49.70; H, 3.65; N, 10.87. Found: C, 49.50; H, 3.66; N, 10.88.

1-(4-Chlorophenyl)-2-(diethoxyphosphinyl)-3-dimethylaminoguanidine (**7l**).

To a solution of **2j** (2.0 g, 5.9 mmoles) in acetonitrile (30 ml was added dimethylamine (0.8 g, 20 mmoles). The reaction mixture was refluxed for 48 hours. The contents were concentrated under reduced pressure and obtained residue was chromatographed on a silica-gel column using hexane-ethyl acetate (1:5 by volume) as eluent to afford **7l** (0.8 g, 42%) as crystals, mp 90-91°; ^{1}H nmr (deuteriochloroform): δ 1.30 (t, 6H, J = 9 Hz), 2.87 (s, 6H), 4.00 (q, 2H, J = 9 Hz), 6.90 (d, 2H, J = 8 Hz), 7.28 (d, 2H, J = 8 Hz), 8.67 (1H, br).

Anal. Calcd. for $C_{13}H_{21}N_3O_3PCl$: C, 46.78; H, 6.34; N, 12.59. Found: C, 46.68; H, 6.28; N, 12.31.

Preparation of 5-Substituted-1,2,4-triazole **9a**. General Procedure for the Preparation of **9a-f**.

To a solution containing **2a** (4.0 g, 10.7 mmoles) in acetonitrile (30 ml) was added hydrazine hydrate (1.6 g, 35 mmoles) at room temperature. The reaction mixture was refluxed for 3 hours. The resulting precipitate was collected to afford **9a** as crystals.

Preparation of 5-Substituted-1,3,5-triazine **11a**. General Procedure for the Preparation of **11a-g**.

To a solution containing **2a** (0.9 g, 2.4 mmoles) in acetonitrile (30 ml) was added *S*-methylisothiourea sulfate (1.4 g, 5.0 mmoles) at room temperature. The reaction mixture was refluxed for 5 hours. After cooling the reaction mixture was concentrated under reduced pressure, the obtained residue was chromatographed on a silica-gel column using hexane-ethyl acetate (5:1 by volume) as eluent to afford **11a** as crystals.

Preparation of Phenylisothiocyanate **13a**. General Procedure for the Preparation of **13a-e**.

To a solution containing **6a** [9] (4.0 g, 22.0 mmoles) in chloroform (30 ml) was added *m*-chloroperbenzoic acid (10.9 g, 44.0 mmoles) at 10°. The reaction mixture was stirred for 1 hour at 10° and 2 hours at room temperature. After removing insoluble material by filtration and washed with chilled water, chill 5%-aqueous sodium carbonate and chilled water, successively. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure. The obtained liquid was distilled under reduced pressure to yield **13a** as colorless liquid, bp 90° (28 mm Hg) (lit [16] bp 221°).

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