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### A FACILE METHOD FOR THE SYNTHESIS OF NOVEL PYRIDINONE DERIVATIVES VIA KETENE N,S-ACETALS

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## A FACILE METHOD FOR THE SYNTHESIS OF NOVEL PYRIDINONE DERIVATIVES VIA KETENE *N,S*-ACETALS

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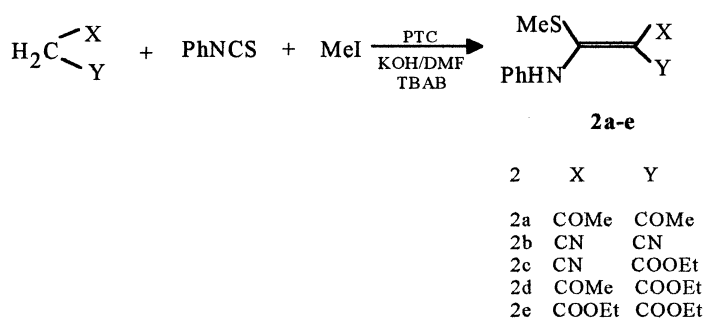
### ABSTRACT

A simple and easy method is provided for the synthesis of the novel pyridinone derivatives (**3a–e**), (**8a–c**) and (**10a–c**) by the reaction of ketene acetals (**2a–e**), (**7a–c**) and (**9a–c**) with ethyl cyanoacetate respectively. Compounds (**3b–d**) reacted with triethyl orthoformate to afford the pyridinone derivatives (**4–6**) respectively. Compound **7a** reacted with ethyl acetoacetate or diethyl malonate to give thiazolopyridinone derivative **11** or **12** respectively.

Heterocyclic ketene *N,S*-acetals<sup>1–7</sup> or amins<sup>8–14</sup> as well as ketoketene or cyanoketene *S,S*-acetals<sup>15–20</sup> are important synthons for the synthesis of a wide variety of new heterocycles and fused heterocycles, therefore, their synthesis and reactions have given rise to much attention.<sup>21,22</sup> As an extension of our recent studies<sup>23,24</sup> in heterocyclic synthesis, we report here the synthesis of some new pyridine derivatives *via* ketene *N,S*-acetals.

Compounds (**2a–e**) were prepared by the reaction of active methylene compounds (**1a–e**) with phenyl isothiocyanate and one equivalent of methyl iodide in a one-pot reaction using phase transfer catalysis (PTC) conditions [KOH/DMF/tetrabutyl ammonium bromide TBAB] in almost 100% yield (Scheme 1).

The formed ketene *N,S*-acetals **2a–e** were then treated with ethyl cyanoacetate in the presence of ammonium acetate and AcOH at 200°C for different periods of times to afford 2-oxo-phenylpyridines (**3a–e**), (Scheme 2). Presumably, the reaction mechanism involves a nucleophilic attack of ketene NH group at the ethyl-cyanoacetate carbonyl carbon atom with subsequent cyclization.



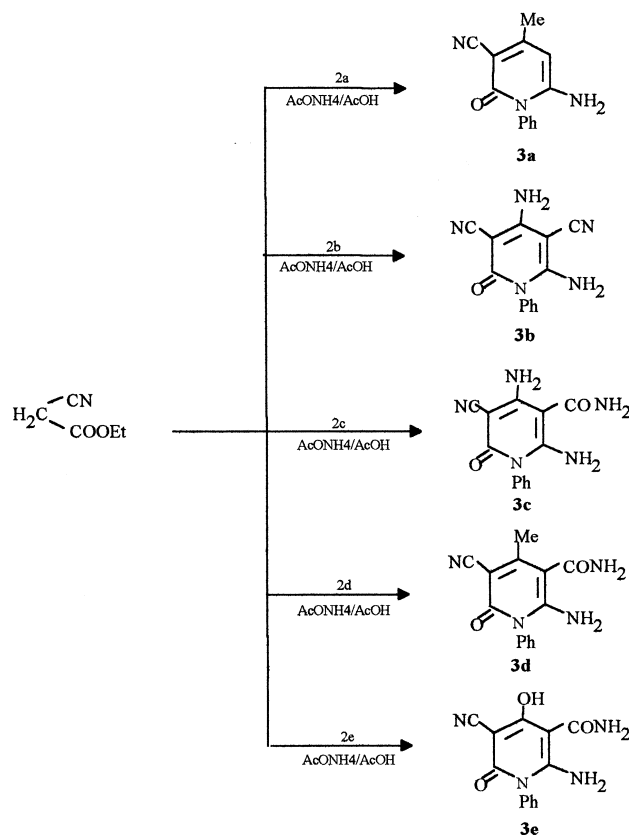
*Scheme 1.*

In case of compounds (**3c–e**), the ester group was converted into the corresponding amide group through the reaction of the evolved  $\text{NH}_3$  from  $\text{AcONH}_4$  during the reaction. Analytical and spectral data (cf. Table) of the obtained products revealed that the carboxamido group was formed.

The structure of these compounds were also confirmed by the reaction of compounds (**3b–d**) with triethyl orthoformate (Scheme 3) to give phenylpyridine-3,5-dicarbo-nitrile **4**, phenylpyrido[4,3-*d*]-pyrimidine **5** and phenylpyrido[2,3-*d*]-pyrimidine **6**.

Moreover, cyclic ketene *N,S*-, *N,O*- or *N,N*-acetals were allowed to react with ethyl cyanoacetate to afford the corresponding fused pyridone derivatives. Namely, the reaction of 2-thiazolidinylidenemalononitrile (**7a**), 2-imidazolidinylidene malono- nitrile (**7b**) or 2-oxazolidinylidenemalononitrile (**7c**) with ethyl cyanoacetate gave dihydrothiazolo(1,2-*a*)pyridin-4-one





Scheme 2.

(8a), dihydroimidazolo(1,2-a)pyridin-4-one (8b) or dihydr-oxazolo(1,2-a)pyridin-4-one (8c), respectively (Scheme 4).

Under these conditions, 2-thiazolidinylideneacetylacetone (9a), 2-imidazolidinylideneacetylacetone (9b) or 2-oxazolidinylideneacetylacetone (9c) reacted with ethyl cyanoacetate to afford thiazolo[3,2-a]-pyridine (10a), midazo[1,2-a]-pyridine (10b) or oxazolo[3,2-a]-pyridine (10c), respectively (Scheme 5).

When ketene acetals with two acyl groups, such as (2a) and (9a-c) react with ethyl cyanoacetate under the above conditions the elimination of one of the acyl groups takes place due to ammonolysis.



**Table.** Analytical and Spectral Data of the Reported New Compounds

Product	Yield (%)	M.p. (°C) <sup>a</sup>	Mol. form. <sup>b</sup> Mol. wt.	Analysis (%) Calcd./Found			IR (KBr) <sup>c</sup>	<sup>1</sup> H-NMR <sup>d</sup> DMSO-d <sub>6</sub>
				C	H	N		
<b>3a</b>	94	281	C <sub>13</sub> H <sub>11</sub> N <sub>3</sub> O 225.24	69.32 68.99	4.88 4.89	18.65 18.51	3220, 3111 (NH <sub>2</sub> ), 2220 (CN), 1644(C=O).	7.80–7.30 (m, 5H, arom.), 6.50 (s, 1H, =CH), 6.30–6.10 (br, 2H, NH <sub>2</sub> ), 2.50 (s, 3H, CH <sub>3</sub> ).
<b>3b</b>	89	208	C <sub>13</sub> H <sub>9</sub> N <sub>3</sub> O 251.24	62.14 62.11	3.58 3.60	27.86 27.89	3310, 3240, 3150 (NH <sub>2</sub> ), 2191 (CN), 1650 (C=O).	6.80–6.40 (m, 5H, arom.), 6.35–6.10 (br, 4H, 2NH <sub>2</sub> ).
<b>3c</b>	91	131	C <sub>13</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> 269.26	57.98 58.11	4.09 3.97	25.99 26.01	3316, 3202, 3110 (NH <sub>2</sub> ), 2195 (CN), 1630 (C=O).	6.80–6.40 (m, 5H, arom.), 4.90–4.60 (br, 4H, 2NH <sub>2</sub> ), 3.80–3.60 (br, 2H, CONH <sub>2</sub> ).
<b>3d</b>	63	169	C <sub>14</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> 268.27	62.67 62.54	4.57 4.43	20.13 20.22	3320, 3210, 3140 (NH <sub>2</sub> ), 2208 (CN), 1645 (C=O).	6.90–6.50 (m, 5H, arom.), 5.80–5.40 (br, 2H, NH <sub>2</sub> ), 3.50–3.20 (br, 2H, CONH <sub>2</sub> ), 2.70 (s, 3H, CH <sub>3</sub> ).
<b>3e</b>	66	161	C <sub>13</sub> H <sub>10</sub> N <sub>4</sub> O <sub>3</sub> 270.24	57.77 57.81	3.70 3.69	19.98 20.10	3460 (OH), 3330, 3240, 3131 (NH <sub>2</sub> ), 2220 (CN), 1650 (C=O).	6.90–6.40 (m, 5H, arom.), 6.30 (br, 2H, NH <sub>2</sub> ), 3.40 (s, 1H, OH), 3.30–3.10 (br, 2H, CONH <sub>2</sub> ).
<b>4</b>	87	> 320	C <sub>19</sub> H <sub>17</sub> N <sub>5</sub> O <sub>3</sub> 363.37	62.79 62.66	4.68 4.71	19.26 19.32	2195 (CN), 1610 (C=O).	8.20–7.70 (m, 5H, arom.), 5.20 (s, 2H, =CH), 3.80–3.60 (q, 4H, 2CH <sub>2</sub> ), 1.30–1.00 (t, 6H, 2CH <sub>3</sub> ).
<b>5</b>	45	319	C <sub>18</sub> H <sub>15</sub> N <sub>5</sub> O <sub>3</sub> 349.34	61.88 61.90	4.29 4.32	20.04 19.98	3250 (NH), 2210 (CN), 1630 (C=O).	8.90 (s, 1H, NH), 7.90–7.50 (m, 5H, arom.), 5.10 (s, 1H, =CH), 3.70–3.50 (q, 2H, CH <sub>2</sub> ), 1.10–0.90 (t, 3H, CH <sub>3</sub> ).
<b>6</b>	43	156	C <sub>13</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> 278.27	64.74 64.75	3.59 3.61	20.12 20.13	3304 (NH), 2197 (CN), 1653 (C=O).	9.70 (br, 1H, NH), 8.20–7.70 (m, 5H, arom.), 6.00 (s, 1H, =CH), 2.30 (s, 3H, CH <sub>3</sub> ).
<b>8a</b>	86	216	C <sub>9</sub> H <sub>6</sub> N <sub>4</sub> O <sub>5</sub> 218.23	49.53 49.54	2.75 2.74	25.66 25.67	3223, 3120 (NH <sub>2</sub> ), 2210 (CN), 1632 (C=O).	6.70–6.40 (br, 2H, NH <sub>2</sub> ), 3.80–3.40 (d, 2H, CH <sub>2</sub> ), 3.35–3.00 (d, 2H, CH <sub>2</sub> ).

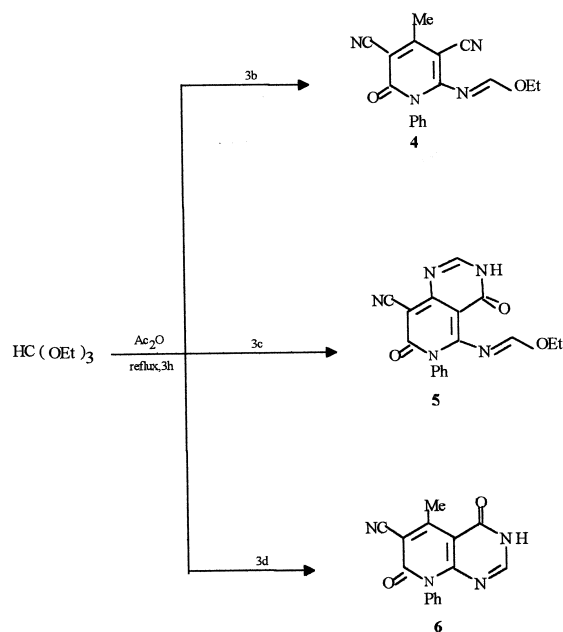
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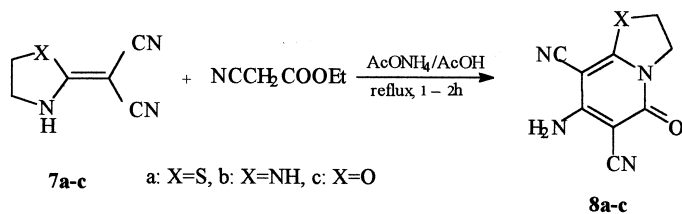
<b>8b</b>	91	277	$C_9H_7N_5O$ 201.18	53.73 53.75	3.48 3.50	34.79 34.77	3350, 3273, 3100 (NH, NH <sub>2</sub> ), 2220 (CN), 1610 (C=O).	6.50–6.20 (br, 2H, NH <sub>2</sub> ), 3.80–3.40 (d, 4H, 2CH <sub>2</sub> ).
<b>8c</b>	78	> 320	$C_9H_6N_4O_2$ 202.17	53.46 53.48	2.97 2.97	26.71 26.69	3230, 3121 (NH <sub>2</sub> ), 2214 (CN), 1647 (C=O).	6.30–6.00 (br, 2H, NH <sub>2</sub> ), 3.90–3.50 (d, 2H, CH <sub>2</sub> ), 3.40–3.00 (d, 2H, CH <sub>2</sub> ).
<b>10a</b>	88	242	$C_9H_8N_2OS$ 192.23	56.23 56.20	4.16 4.21	14.56 14.53	3086 (arom.), 2210 (CN), 1637 (C=O).	5.10 (s, 1H, =CH), 3.80–3.40 (d, 2H, CH <sub>2</sub> ), 3.35–3.10 (d, 2H, CH <sub>2</sub> ), 2.30 (s, 3H, CH <sub>3</sub> ).
<b>10b</b>	67	306	$C_9H_9N_5O$ 175.18	61.70 61.83	5.14 5.17	23.98 23.98	2220 (CN), 1620 (C=O).	5.30 (s, 1H, =CH), 3.80–3.40 (d, 4H, 2CH <sub>2</sub> ), 2.30 (s, 3H, CH <sub>3</sub> ).
<b>10c</b>	45	311	$C_9H_8N_2O_2$ 176.17	61.36 61.30	4.54 4.56	15.89 15.92	2218 (CN), 1640 (C=O).	5.20 (s, 1H, =CH), 3.90–3.50 (d, 2H, CH <sub>2</sub> ), 3.40–3.00 (d, 2H, CH <sub>2</sub> ), 2.30 (s, 3H, CH <sub>3</sub> ).
<b>11</b>	77	> 300	$C_{10}H_6N_3O_2S$ 235.26	51.10 50.99	3.83 3.87	17.85 17.94	3223, 3120 (NH <sub>2</sub> ), 2210 (CN), 1660, 1635 (C=O).	6.70–6.40 (br, 2H, NH <sub>2</sub> ), 3.80–3.40 (d, 2H, CH <sub>2</sub> ), 3.35–3.00 (d, 2H, CH <sub>2</sub> ), 2.80 (s, 3H, CH <sub>3</sub> ).
<b>12</b>	56	> 300	$C_{11}H_{11}N_3O_3S$ 265.28	49.80 50.00	4.15 4.01	15.83 15.81	3254, 3140 (NH <sub>2</sub> ), 2220 (CN), 1710, 1620 (C=O).	6.50–6.20 (br, 2H, NH <sub>2</sub> ), 4.30–4.00 (q, 2H, CH <sub>2</sub> ester), 3.80–3.40 (d, 2H, CH <sub>2</sub> ), 3.35–3.00 (d, CH <sub>2</sub> ), 1.30–1.00 (t, 3H, CH <sub>3</sub> ).

<sup>a</sup>Not Corrected. <sup>b</sup>Satisfactory microanalysis obtained: C  $\pm$  0.4, H  $\pm$  0.4, N  $\pm$  0.3%. <sup>c</sup>Measured on a Nicolet 710 FT-IR Spectrometer. <sup>d</sup>Measured on Varian EM 360 A Spectrometer using TMS as internal standard.

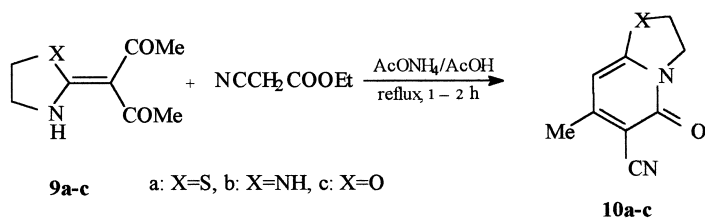




Scheme 3.



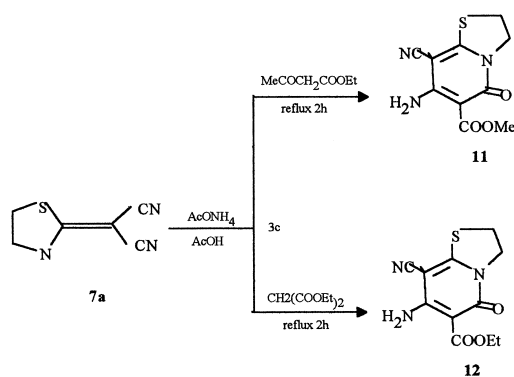
Scheme 4.



Scheme 5.



Compound (**7a**) was also allowed to react with different esters, such as ethyl acetoacetate or diethyl malonate to give thiazolo[3,2-*a*]-pyridine (**11**) or **12**, respectively (Scheme 6).



Scheme 6.

## EXPERIMENTAL

All melting points were determined on a Kofler melting points apparatus and were determined. IR spectra were obtained on a Nicolet 710 FT-IR spectrometer.  $^1\text{H}$ -NMR spectra were recorded on a Varian EM 360 A at 60 MHz using TMS as an internal standard. The elemental analyses were carried out on an elemental analyzer model 240C. Analytical and spectral data for compounds (**3–6**), (**8**) and (**10–12**) were tabulated in the above table.

### Synthesis of 1,2-Dihydro-2-oxo-1-phenylpyridine Derivatives (**3a–e**)

#### General Procedure

A stirred mixture of ketene *N,S*-acetals (**2a–e**) (0.01 mol), ethyl cyanoacetate (0.01 mol), ammonium acetate (3.0 g) and acetic acid (0.6 ml) were heated at  $200^\circ\text{C}$  for different period of times, then left to cool and recrystallized with ethanol.





**6-Amino-1,2-dihydro-4-methyl-2-oxo-1-phenylpyridine-3-carbonitrile (3a).** The general procedure using heating for 2 h was used to give (3e) as yellow crystals.

**Diamino-1,2-dihydro-2-oxo-1-phenylpyridine-3,5-dicarbonitrile (3b).** The general procedure using heating for 3 h was used to give (3e) as pale yellow crystals.

**4,6-Diamino-1,2-dihydro-2-oxo-3-cyano-1-phenylpyridine-5-carboxamide. (3c).** The general procedure using heating for 3 h was used to give (3e) as white crystals.

**6-Amino-1,2-dihydro-3-cyano-4-methyl-2-oxo-1-phenylpyridine-5-carboxamide (3d).** The general procedure using heating for 3 h was used to give (3e) as white crystals.

**6-Amino-3-cyano-1,2-dihydro-4-hydroxy-1-phenylpyridine-5-carboxamide (3e).** The general procedure using heating for 3 h was used to give (3e) as white crystals.

#### **Synthesis of 4,6-Bisethoxymethyleneamino-1,2-dihydro-2-oxo-1-phenyl-pyridine-3,5-dicarbonitrile (4)**

A mixture of (3b) (2.51 g, 0.01 mol) and triethyl orthoformate (2.96 g, 0.02 mol), was refluxed in (20 mL) acetic anhydride for 3 h, then concentrated to half of its volume and left to cool. The solid product was filtered off and recrystallized from  $\text{CHCl}_3$  to give compound (4) as white crystals.

#### **Synthesis of 5-Ethoxymethyleneamino-3,4,6,7-tetrahydr-4,7-dioxo-6-phenyl-pyrido[4,3-*d*]pyrimidine-8-carbonitrile (5)**

A mixture of (3c) (2.69 g, 0.01 mol) and triethyl orthoformate (2.96 g, 0.02 mol), was refluxed in (20 mL) acetic anhydride for 3 h, then concentrated to half of its volume and left to cool. The solid product was filtered off and recrystallized from dioxan to give compound (5) as white crystals.

#### **Synthesis of 3,4,7,8-Tetrahydro-5-methyl-4,7-dioxo-8-phenylpyrido[2,3-*d*]pyrimidine-6-carbonitrile (6)**

A mixture of (3d) (2.68 g, 0.01 mol) and triethyl orthoformate (1.48 g, 0.01 mol), was refluxed in (20 mL) acetic anhydride for 3 h, then



concentrated to half of its volume and left to cool. The solid product was filtered off and recrystallized from dioxan to give (6) as white crystals.

### Synthesis of (8a–c)

#### General Procedure

A mixture of cyanoketene *N,S*, *N,N* or *N,O*-acetal (7a–c) (0.01 mol), ethyl cyanoacetate (1.13 g, 0.01 mol), ammonium acetate (3.0 g) and acetic acid (0.6 mL) was heated with stirring at 200°C for different period of times, then left to cool and recrystallized from ethanol.

**7-Amino-2,3-dihydro-5-oxo-5H-thiazolo[3,2-*a*]pyridine-6,8-dicarbonitrile (8a).** The general procedure using heating for 3 h was used to give (8a) as white crystals.

**7-Amino-1,2,3,5-tetrahydro-5-oxo-imidazo[1,2-*a*]pyridine-6,8-dicarbonitrile (8b).** The general procedure using heating for 2 h was used to give (8b) as colorless crystals.

**7-Amino-2,3-dihydro-5-oxo-5H-oxazolo[3,2-*a*]pyridine-6,8-dicarbonitrile (8c).** The general procedure using heating for 2.5 h was used to give (8c) as deep yellow crystals.

### Synthesis of (10a–c)

#### General Procedure

A mixture of ketoketene *N,S*, *N,N* or *N,O*-acetal (9a–c) (0.01 mol), ethyl cyanoacetate (0.01 mol), ammonium acetate (3.0 g) and acetic acid (0.6 mL) was heated with stirring at 200°C for different period of times, then left to cool and recrystallized from ethanol.

**2,3-Dihydro-7-methyl-5-oxo-5H-thiazolo[3,2-*a*]pyridine-6-carbonitrile (10a).** The general procedure using heating under reflux for 2 h was used to give (10a) as orange crystals.

**1,2,3,5-Tetrahydro-7-methyl-5-oxo-5H-imidazolo[1,2-*a*]pyridine-6-carbonitrile (10b).** The general procedure using heating under reflux for 2 h was used to give (10b) as pale brown crystals.

**2,3-Dihydro-7-methyl-5-oxo-5H-oxazolo[3,2-*a*]pyridine-6-carbonitrile (10c).** The general procedure using heating under reflux for 2 h was used to give (10c) as white crystals.



### Synthesis of (11) and (12)

#### General Procedure

A mixture of cyanoketene *N,S*-acetal (**7a**) (0.01 mol), ethyl acetoacetate or diethyl malonate (0.01 mol), ammonium acetate (3.0 g) and acetic acid (0.6 mL) was heated with stirring at 200°C for different period of times, then left to cool and recrystallized from ethanol.

**7-Amino-6-acetyl-2,3-dihydro-5-oxo-5H-thiazolo[3,2-*a*]-pyridine-8-carbonitrile (11).** The general procedure using heating under reflux for 3 h was used to give (**11**) as red crystals.

**Ethyl-7-amino-8-cyano-2,3-dihydro-5-oxo-5H-thiazolo[3,2-*a*]pyridine-6-carbonitrile (12).** The general procedure using heating under reflux for 2 h was used to give (**12**) as brown crystals.

#### REFERENCES

1. Augustin, M.; Doelling, N. J. Prakt. Chem. **1982**, 324, 3.
2. Gompper, R.; Topfel, N. Chem. Ber. **1962**, 95, 2891.
3. Hirai, K.; Matsuda, H.; Kishida, Y. Chem. Pharm. Bull. (Tokyo) **1971**, 20, 97.
4. Mansour, N.B.; Rudolf, N.-D.; Augustin, M.Z. Z. fur. Chem. **1981**, 21, 97.
5. Rajappa, S.; Advani, B.G. Proc. Indian Acad. Sci. (Chem. Sci.) **1982**, 91, 463.
6. Huang, Z.-T.; Shi, X. Synthesis **1990**, 162.
7. El-Sayed, A.M.; El-Saghier, A.M.M.; Ali, M.A.; El-Shafei, A.K. Gazzetta Chem. Italiana **1997**, 127, 605.
8. Gompper, R.; Schafer, H. Chem. Ber. **1967**, 100, 591.
9. Rajappa, S.; Sreenivasan, R.; Advani, B.G.; Summerville, R.H.; Hoffmann, R. Indian J. Chem. Sect. B **1977**, 15, 297.
10. Rajappa, S.; Nair, M.D.; Sreenivasan, R.; Advani, B.G. Tetrahedron **1982**, 36, 1673.
11. Huang, Z.-T.; Liu, Z.-R. Synthesis **1987**, 357.
12. Nang, L.-B.; Huang, Z.-T. Synthetic Commun. **1996**, 26(3), 459.
13. Zhang, J.-H.; Nang, M.-X.; Huang, Z.-T. J. Chem. Soc. Perkin Trans 1 **1999**, 2087.
14. Zhang, J.H.; Nang, M.-X.; Huang, Z.-T. J. Chem. Soc. Perkin Trans. 1 **1999**, 321.
15. Thuller, A.; Vialle, J. Bull. Soc. Chem. Fr. **1959**, 1398.



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3567

16. Kobayashi, G.; Matsuda, Y.; Natsuk, R. Chem. Pharm. Bull. (Tokyo) **1973**, *21*, 921.
17. Wang, X.; Chen, X.; Lian, H.; Pan, Y.; Shi, Y. Synthetic Commun. **1999**, *29*(9), 1553.
18. Mashraqui, S.H.; Harinarasubrahmanian, H. J. Chem. Research (S) **1999**, 492.
19. Lee, G.H.; Pak, C.S. Synthetic Commun. **1999**, *29*(14), 2539.
20. Zhang, Q.H.; Su, J. Synthetic Commun. **1999**, *29*(20), 3467.
21. Smith, K.; Anderson, D.; Mathew, I. J. Org. Chem. **1996**, *61*, 662.
22. Attaby, F.A.; Eldin, S.M.; Abu-Abdou, Phosphorous, Sulphur and Silicon **1977**, *129*, 121.
23. Al-Afaleq, E.I.; Synthetic Commun. **2000**, *30*(11).
24. El-Saghier, A.M.M.; Al-Afaleq, E.I. Phosphorous, Sulphur and Silicon **1998**, *139*, 63.

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