NOVEL ONE POT SYNTHESIS OF SUBSTITUTED 1, 2, 4-TRIAZINES

Rishan Lang Nongkhlaw* and Bekington Myrboh
Department of Chemistry, North-Eastern Hill University
Shillong-793022, Meghalaya, India 793022

Abstract: Substituted-1, 2, 4-triazines were conveniently prepared in one pot by the condensation of amides and 1,2-diketones in presence of base, followed by cyclisation with hydrazine hydrate.

Introduction

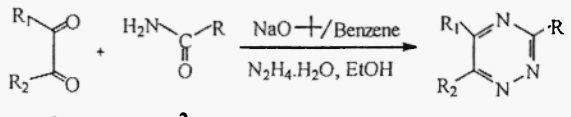
1, 2, 4-triazines and their derivatives have been widely studied in terms of their synthetic methodologies and reactivity since some of these derivatives were reported to have promising biological activities (1a-g). The synthesis of 1, 2, 4-triazines and their derivatives are well documented and their methods of preparations are manifold and varied. A survey of the literature revealed that 1, 2-dicarbonyl compounds (aliphatic, aromatic and aromatic-aliphatic) are the most common reagents used for the synthesis of 1, 2, 4-triazines and their derivatives (2, 3). Laakso and coworkers (4), as well as other groups (5) reported the condensation of acylhydrazides with benzil in acetic acid containing ammonium acetate to give 5, 6-diphenyl-1, 2, 4-triazines with various aromatic and heterocyclic groups attached at position 3. A similar method was also applied by Metze and his group (6) and also Hasselquist (7) using a variety of aliphatic and aromatic 1, 2-diketones and aliphatic, aromatic, and heterocyclic acid hydrazides but with preliminary isolation of the 1, 2-diketones monoacylhydrazones followed by ring closure with alcoholic ammonia under pressure to give substituted 1, 2, 4-triazines.

Results and Discussions

Recently, we have reported the synthesis of trisubstituted pyridazine by the condensation of 1, 2-diketone with acetophenone in the presence of base, followed by cyclisation with hydrazine hydrate (8). We wish to report here the synthesis of 1, 2, 4-triazine starting from amides and 1, 2-dicarbonyl compounds and hydrazine hydrate in the presence of base.

The novelty of the procedure lies in the fact that the whole reaction sequence was carried out by the stepwise addition of the reagents at the completion of each step without isolating the intermediates as they were formed. Thus the one pot synthesis of the title compound was achieved via the monoacyl hydrazone, which was generated in situ by the condensation of amides with 1, 2-dicarbonyl compounds in presence of base. As reported earlier (9), with unsymmetrical diketone a mixture of two possible isomers (10) is obtained. However there is predominance of one over the other (11a, b). With 1-phenyl-1, 2-propanedione a mixture of regioisomeric triazines is obtained.

In general amides like formamide, acetamide and benzamide when condensed with aromatic 1, 2-diketones formed a jelly mass, which is the condensed product. The condensed product can be cylises to stable substituted 1, 2, 4-triazine by treatment with hydrazine hydrate. In all these cases, solid products are obtained.



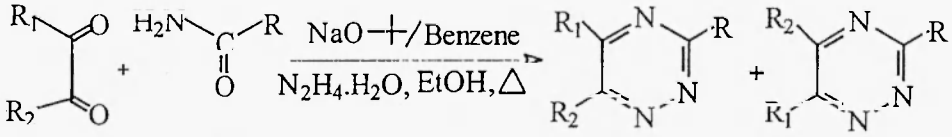
1 2 3

Scheme-1

Table-1: Preparation of 3, 5, 6-trisubstituted 1, 2, 4-triazines.

Entry	Products[a]	R	R^1	R^2	Time/h	Yields[b]/%	Mpt[c](°C)
1	**3a**	H	C_6H_5	C_6H_5	3	56	112
2	**3b**	CH_3	C_6H_5	C_6H_5	4	78	91
3	**3c**	C_6H_5	C_6H_5	C_6H_5	4	61	174
4	**3d**	H	4-$OMeC_6H_4$	C_6H_5	5	64	167
5	**3e**	CH_3	4-$OMeC_6H_4$	C_6H_5	6	57	135
6	**3f**	C_6H_5	4-$OMeC_6H_4$	C_6H_5	5	65	152
7	**3g**	H	4-ClC_6H_4	C_6H_5	3	60	118
8	**3h**	CH_3	4-ClC_6H_4	C_6H_5	4	61	120
9	**3i**	C_6H_5	4-ClC_6H_4	C_6H_5	5	72	108
10	**3j**	H	Furyl	Furyl	5	57	127
11	**3k**	CH_3	Furyl	Furyl	6	61	143
12	**3l**	C_6H_5	Furyl	Furyl	5	58	162
13	**3m**	H	CH_3	CH_3	5	41	46
14	**3n**	CH_3	CH_3	CH_3	6	42	94-96
15	**3o**	C_6H_5	CH_3	CH_3	5	37	79-80
16	**3p**	H	pyridyl	Pyridyl	6	43	87-90
17	**3q**	CH_3	pyridyl	Pyridyl	5	45	115-117
18	**3r**	C_6H_5	Pyridyl	pyridyl	5	51	163-164

a. **Products are characterized by IR, NMR, Mass and elemental analysis.**
b. refer to isolated yields; **c**. M.pts are uncorrected



4 2 5 6

Scheme-2

Table-2: Preparation of regioisomeric di- and tri-substituted 1, 2, 4-triazines

Products[a]	R^1	R^2	R	Yields[b]/%	M.Pt[c](°C)
5s	CH_3	***Ph***	H	25	89-90
6s	Ph	CH_3	H	13	91-93
5t	CH_3	Ph	Ph	27	113-115
6t	Ph	CH_3	Ph	15	110-112

a. Products are characterized by IR, NMR and elemental analysis.
b. refer to isolated yields; **c**. M.pts are uncorrected.

Experimental

Melting points were determined in open capillary tubes with a Thomas-Hoover apparatus and are uncorrected. Infrared spectra were recorded on a BOMEM DA-8 FT-IR instrument and the

frequencies are expressed in cm^{-1}. ^1H NMR (90 MHz) was recorded on Varian EM-390 spectrometer and High-resolution ^1H and ^{13}C NMR (300 MHz) spectra were recorded on a Bruker ACF-300 spectrometer using $CDCl_3$ as the solvent. Chemical shifts are reported in ppm downfield from internal tetramethylsilane and are given on the δ scale. Mass spectral data were obtained with a JEOL D-300 (EI) mass spectrometer. Elemental analyses were carried out on a Heraeus CHN-O Rapid analyzer. All reactions were monitored by TLC using glass plates coated with silica gel (ACME's) containing 13% calcium sulphate as binder and visualization was accomplished by exposure to iodine vapor or by spraying acidic potassium permanganate solution. Column chromatographic separations were carried out on ACME's silica gel (60-120 mesh).

General procedure for the synthesis of di-and tri-substituted-1, 2, 4-triazine:

To a well stirred solution of sodium tertiarybutoxide (0.01 moles) in dry benzene, at room temperature, a solution of 0.01 moles of amide in benzene was added, followed by the addition of 1, 2-diketones (0.01 moles). The solid jelly mass is formed immediately due to the formation of the but-2-ene-1, 4-dicarbonyl systems. 8 ml of ethanol was added to dissolve the solid mass. Hydrazine hydrate (2 ml) was then added and the reaction mixture was further stirred at room temperature. After the reaction was completed (monitored by TLC), the product was extracted with benzene, dried over anhydrous sodium sulphate and the solvent distilled off. After keeping in the fridge for four hours or more, a crystalline solid is formed which was purified by repeated recrystallisation from ethanol or by column chromatography using hexane as the eluent.

Preparation of Regioisomeric 1, 2, 4-Triazines from 1-Phenyl-1, 2-Propanedione

To a stirred solution of sodium tertiarybutoxide (0.01 moles) in benzene, formamide is added followed by 1-phenyl-1, 2-propanedione (0.01 moles). Stirring is continued when a jelly liquid is formed. 10 ml of ethanol is added to dissolve the jelly reaction mixture. Then 2 ml of hydrazine hydrate is added and the solution is heated at reflux for 2.5 hours. Evaporation of the solvent under reduced pressure afforded a reddish brown liquid, which was poured into water and extracted with dichloromethane (3x100 ml), washed with sodium bicarbonate solution and dried with sodium sulphate. Evaporation of the solvent under reduced pressure gave reddish brown oil, which contained the regioisomeric 1, 2, 4-triazines. Column chromatography on silica gel and elution with 1:1 dichloromethane/hexanes gave a fraction, which afforded 5s in about 25% yield as a white solid. Further elution with the same solvent gave the second fraction 6s in about 13% yield.

Similarly when benzamide is used in place of formamide and following the same procedure, the two fractions **5t** and **6t** were collected in about 27% and 15% yields respectively.

Spectroscopic and Analytical Data

5, 6-Diphenyl-1, 2, 4-triazine 3a: Yield 56%; Mp: 112°C; *^1H NMR*: δ 7.25-7.94 (m, 10H); 9.60 (s, 1H); *^{13}C NMR*: δ 125.0, 126.4, 127.2, 127.9, 129.4, 130.1, 131.2, 136.1, 155.8, 157.0, 161.2; *Mass*: 233 (M^+); *IR* (cm^{-1}): ν_{max} 3060, 1620, 1585, 1485, 1440, 1405; *Anal. Calcd.* for $C_{15}H_{11}N_3$: C, 77.25; H, 4.72; N, 18.02; *Found*: C, 77.41; H, 4.86; N, 17.87.

5, 6-Diphenyl-3-methyl-1, 2, 4-triazine 3b: Yield 78%; Mp: 91°C; *^1H NMR*: δ 2.42 (s, 3H), 7.24-7.51 (m, 7H), 7.80-8.11 (m, 3H); *^{13}C NMR*: δ 21.4, 124.8, 126.9, 128.7, 128.9, 129.0, 129.2, 129.7, 130.1, 136.9, 156.4, 157.6, 159.9; Mass: 247 (M^+); *IR* (cm^{-1}): ν_{max} 3061, 2921, 1577, 1488, 1445, 1393; *Anal. Calcd.* for $C_{16}H_{13}N_3$: C, 77.73; H, 5.26; N, 17.00, *Found:* C, 77.84; H, 5.15; N, 16.83.

3, 5, 6-Triphenyl-1, 2, 4-triazine 3c: Yield 61%; Mp: 144°C; *^1H NMR*: δ 7.31-7.50 (m, 12H), 7.80 (s, 1H), 8.11-8.13 (m, 2H); *^{13}C NMR*: δ 124.5, 128.1, 128.3, 128.8, 129.0, 129.2, 129.9, 131.2, 134.5, 136.2, 136.5, 136.9, 156.5, 158.4, 162.1; *Mass*: 309(M^+); *IR* (cm^{-1}): ν_{max} 2978, 1672, 1477, 1414; *Anal. Calcd.* for $C_{21}H_{15}N_3$: C, 81.55; H, 4.85; N, 13.59; *Found*: C, 81.43; H 4.63; N, 13.50.

5-Anisyl-6-phenyl-1, 2, 4-triazine 3d: Yield 64%; Mp: 167°C; *^{1}H NMR*: δ 3.83 (s, 3H); 7.24-8.03 (m, 9H), 9.55 (s, 1H), *^{13}C NMR*: δ 50.8, 124.3, 126.9, 127.3, 128.7, 129.3, 131.2, 134.3, 135.8 153.4, 156.1, 161.8; *IR* (cm^{-1}): ν_{max} 3023, 2961, 1608, 1568, 1480; Mass: 263(M^+); *Anal. Calcd.* for $C_{16}H_{13}N_3O$: C, 73.00; H, 4.94; N, 15.96; *Found*: C, 72.90; H, 4.85; N, 16.00.

5-Anisyl-3-methyl-6-phenyl-1, 2, 4-triazine 3e: Yield 58%; Mp: 135°C; *^{1}H NMR*: δ 2.60 (s, 3H); 3.85 (s, 3H), 7.3-8.0 (m, 9H); *^{13}C NMR*: δ 28.0, 50.3, 125.3, 127.0, 127.9, 128.7, 129.4, 131.1, 131.3,136.1, 138.1, 154.3, 158.1, 160.2; *IR* (cm^{-1}): ν_{max} 3041, 2930, 1625, 1560, 1482, 1431; *Mass*: 277(M^+); *Anal. Calcd.* for $C_{17}H_{15}N_3O$: C, 73.64; H, 5.41; N, 15.16; *Found*: C, 73.84; H, 5.33; N, 15.00.

6-Anisyl-3, 5-diphenyl-1, 2, 4-triazine 3f: Yield 65%; Mp: 152°C; *^{1}H NMR*: δ 3.84 (s, 3H); 7.31-7.80 (m, 12H), 8.10-8.25 (m, 2H), *^{13}C NMR*: δ 50.5, 125.7, 126.0, 126.4, 127.0, 127.8, 128.6,129.3, 129.7, 130.4, 131.0, 132.4, 135.7, 155.1, 156.4, 160.3; *IR* (cm^{-1}): ν_{max} 3061, 2941, 1618, 1570, 1480; *Mass*: 339 (M^+); *Anal. Calcd.* for $C_{22}H_{17}N_3O$, C, 77.87; H, 5.01; N, 12.38; *Found*: C, 77.70; H, 4.89; N, 12.10.

6-(p-Chlorophenyl)-5-phenyl-1, 2, 4-triazine 3g: Yield 60%; Mp: 118°C; *^{1}H NMR*: δ 7.3-8.0 (m, 9H) 9.72 (s, 1H) ; *^{13}C NMR*: 125.6, 126.0, 127.5, 128.2, 129.7, 132.7, 134.0, 135.6, 154.3, 156.1,162.0; *IR* (cm^{-1}): ν_{max} 3040, 1610, 1568,1460,1405; Mass: 267(M^+); *Anal. Calcd.* for $C_{15}H_{10}N_3Cl$: C 67.28, H 3.73, N 15.70; *Found*: C, 67.12; H, 3.84; N, 15.61.

3-Methyl-6-(p-chlorophenyl)-5-phenyl-1, 2, 4-triazine:3h Yield 61%; Mp: 120°C; *^{1}H NMR*: δ 2.68 (s, 1H), 7.31–8.04(m, 9H); *^{13}C NMR*: 29.8, 125.9, 127.0, 127.9, 128.6, 130.8, 131.8, 133.0, 134.7, 154.0, 155.6, 162.1; *IR* (cm^{-1}): ν_{max} 3050, 2940, 1622, 1591, 1505, 1450; Mass: 281 (M^+); *Anal. Calcd.* for $C_{16}H_{12}N_3Cl$: C, 68.20; H, 4.26; N, 14.92; *Found*: C, 68.45; H, 4.30; N, 14.81.

3,5-Diphenyl-(6-p-chlorophenyl)-1, 2, 4-triazine. 3i Yield 72%; Mp: 108°C; *^{1}H NMR*: δ 7.29-7.96 (m, 12H), 8.07-8.22 (m, 2H); *^{13}C NMR*: δ 125.3, 126.5, 127.2, 127.6, 128.0, 128.6, 129.0, 129.7, 131.8, 132.1, 133.2, 134.1, 155.4, 157.0, 161.9; *IR* (cm^{-1}): ν_{max} 3045, 1630, 1592, 1500, 1470; Mass: 343(M^+) *Anal. Calcd.* for $C_{21}H_{14}N_3Cl$: C, 73.36; H, 4.07; N, 12.22; *Found*: C, 73.44; H, 4.20; N, 12.12.

5,6-Difuryl-1, 2, 4-triazine 3j: Yield 57%; Mp: 95°C; *^{1}H NMR*: δ 6.24-6.61 (m, 6H), 9.71 (s, 1H); ^{13}C NMR: δ 112.1, 113.3, 116.1, 120.0, 123.1, 124.3, 154.1, 158.0, 160.3; *IR* (cm^{-1}): ν_{max} 2978, 1624, 1477, 1415, 1074; *Mass*: 213(M^+), *Anal. Calcd.* for $C_{11}H_7N_3O_2$: C, 61.97; H, 3.28; N, 19.72; *Found*: C, 62.08; H, 3.20; N, 19.50.

5,6-Difuryl-3-methyl-1, 2, 4-triazine 3k: Yield 61%; Mp: 143°C; *^{1}H NMR*: δ 2.61 (s, 3H) 6.26-8 (m, 6H), *^{13}C NMR*: δ 27.9, 112.1, 112.6, 113.0, 114.3, 116.7, 120.6, 124.0, 125.3, 154.1, 158.9, 160.0; *IR* (cm^{-1}): ν_{max} 3002, 2924, 1620, 1495, 1415, 1033, *Mass*: 227(M^+), *Anal. Calcd.* for $C_{12}H_9N_3O_2$: C, 63.43, H, 3.96, N, 18.50, *Found*: C, 63.57; H, 3.84; N, 18.38.

5,6-Difuryl-3-phenyl-1, 2, 4-triazine 3l Yield 58%; Mp: 162°C; *^{1}HNMR*: δ 6.25-6.75 (m, 6H), 7.71-8.01 (m, 5H); *^{13}C NMR*: 112.0, 112.8, 113.6, 114.3, 115.0, 115.7, 117.1, 120.6, 129.0, 130.1, 132.6, 134.3, 153.6, 154.1, 161.2; *IR* (cm^{-1}): ν_{max} 3010, 1631, 1505, 1430, 1035; *Mass*: 289 (M^+); *Anal. Calcd.* for $C_{17}H_{11}N_3O_2$: C, 70.58, H, 3.80, N, 14.53; *Found*: C, 70.74; H, 3.71; N, 14.62.

5,6-Dimethyl-1, 2, 4-triazine 3m[12]: Yield: 45%; Mp: 46°C; *^{1}H NMR*: δ 2.37 (s, 3H), 2.41 (s, 3H), 9.75 (s, 1H); *^{13}C NMR*: δ 19.9, 21.3, 156.9, 159.9, 160.2. *IR* (cm^{-1}): ν_{max} 2931, 2919, 1511, 1483, *Anal. Calcd.* for $C_5H_7N_3$, C, 55.04; H, 6.42; N, 38.53; *Found*: C, 55.10; H, 6.45; N, 38.42.

3,5,6-Trimethyl-1, 2, 4-triazine 3n[12]: Yield: 52%; Mp 95°C; *^{1}H NMR*: δ 2.35-2.40 (m, 6H), 2.42 (s, 3H), *^{13}C NMR*: δ 20.1, 20.6, , 21.4, 157.1, 158.9, 161.3. *IR* (cm^{-1}): ν_{max} 2925, 2911, 1520, 1495, *Anal. Calcd.* for $C_6H_9N_3$, C, 58.53; H, 7.31; N, 34.14; *Found*: C, 58.55; H, 7.34; N, 34.00.

3-Phenyl-5, 6-dimethyl-1, 2, 4-triazine 3o: Yield: 48%; Mp: 80°C; *^{1}H NMR*: δ 2.34-2.39 (m, 6H), 7.76-7.81 (m, 5H), *^{13}C NMR*: δ 20.3, 21.1 , 126.1, 128.0, 128.8, 129.4, 130.1, 158.0, 159.4, 162.1. *IR* (cm^{-1}): ν_{max} 3020, 2918, 1610, 1508, 1494,. *Anal. Calcd.* for $C_{11}H_{11}N_3$, C, 71.35; H, 5.94; N, 22.70; *Found*: C, 71.48; H, 5.90; N, 22.62.

5,6-Dipyridyl-1, 2, 4-triazine 3p[12]: Yield: 44%; Mp: 121-123°C; *^{1}H NMR* δ 8.9-9.38 (m, 4H), 9.51-9.63 (m, 4H), 9.73 (s, 1H); *^{13}C NMR*: δ 158.0, 158.7, 159.8, 160.0, 161.0, 161.5, 162.8, 163.0, 163.8, 164.0, 164.9, 165.4, 166.3, *IR* (cm^{-1}): ν_{max} 1605, 1508, 1495, 1410.... *Anal. Calcd.* for $C_{13}H_9N_5$, C, 66.38; H, 3.82; N, 29.78; *Found*: C, 66.45; H, 3.89; N, 29.69.

3-Methyl-5, 6-dipyridyl-1, 2, 4-triazine 3q[12]: Yield: 49%; Mp: 127°C; *^{1}H NMR*: δ 2.32 (s, 3H), 9.01-9.45 (m, 4H), 9.49-9.60 (m, 4H), 9.73 (s, 1H); *^{13}C NMR*: δ 160.3, 160.9, 161.1, 161.5, 162.2, 162.9, 164.0, 164.7, 165.1, *IR* (cm^{-1}): ν_{max} 1612, 1501, 1485, 1413 *Anal. Calcd.* for $C_{14}H_{11}N_5$, C, 67.46; H, 4.41; N, 28.11; *Found*: C, 67.37; H, 4.50; N, 28.20.

3-phenyl-5, 6-dipyridyl-1, 2, 4-triazine 3r[12]: Yield: 55%; Mp: 163°C; *^{1}H NMR*: δ 8.31-8.68 (m, 5H), 8.95-9.37 (m, 4H), 9.41-9.56 (m, 4H), *^{13}C NMR*: δ 131.6, 134.1, 137.0, 141.1, 157.4, 158.0, 158.5, 159.2, 159.8, 160.0, 161.0, 161.9, 164.0, 164.7, 165.7, 166.0, 166.4; *IR* (cm^{-1}): ν_{max} 3040, 1620, 1504, 1490; *Anal. Calcd.* for $C_{19}H_{13}N_5$, C, 73.31; H, 4.18; N, 22.50; *Found*: C, 73.24; H, 4.11; N, 22.41.

5-Methyl-6-phenyl-1, 2, 4-triazine 5s: Yield 25 %; Mp: 89-90°C; *^{1}H NMR*: δ 2.64 (s, 3H); 7.64-8.16 (m, 5H); 9.80 (s, 1H); *^{13}C NMR*: δ 27.6, 124.6, 125.2, 129.0, 131.4, 133.6, 135.4, 158.0, 159.2, 161.5; *IR* (cm^{-1}): ν_{max} 3046, 1610, 1590, 1515, 1480, 1455, 1405; *Anal. Calcd.* for $C_{10}H_9N_3$: C, 70.17; H, 5.26; N, 24.56; *Found*: C, 70.22; H, 5.29; N, 24.67.

5-Phenyl-6-methyl-1, 2, 4-triazine 6s: Yield 13%; Mp: 91-93°C; *^{1}H NMR*: δ 2.70 (s, 3H); 7.71-8.20 (m, 5H); 9.81 (s, 1H); *^{13}C NMR*: δ 29.8, 124.2, 125.0, 128.8, 130.9, 133.4, 135.0, 158.7, 159.8, 162.0; *IR* (cm^{-1}): ν_{max} 3041, 1605, 1595, 1500, 1495, 1405, *Anal. Calcd.* for $C_{10}H_9N_3$: C, 70.17; H, 5.26; N, 24.56; *Found*: C, 70.27; H, 5.34; N, 24.62.

3,6-Diphenyl-5-methyl-1, 2, 4-triazine 5t: Yield 27%; Mp: 113-115°C; *^{1}H NMR*: δ 6.80-7.70 and 8.40-8.50 (m, 10H); 2.65 (s, 3H); *^{13}C NMR*: δ 27.0, 124.8, 128.2, 128.6, 130.1, 131.1, 134.0, 135.7, 137.0, 157.6, 158.4, 162.4; *IR* (cm^{-1}): ν_{max} 3050, 1605, 1590, 1510, 1450, 1380, *Anal. Calcd.* for $C_{16}H_{13}N_3$: C, 77.73; H, 5.26; N, 17.00; *Found*: C, 77.85; H, 5.40; N, 17.09.

3,5-Diphenyl-6-methyl-1, 2, 4-triazine 6t: Yield 15%; Mp: 110-112°C; *^{1}H NMR*: δ 6.85-7.80 and 8.43-8.55 (m, 10H); 2.78 (s, 3H); *^{13}C NMR*: δ 29.2, 124.5, 127.9, 128.3, 129.6, 130.8, 133.8, 135.6, 136.3, 156.8, 158.0, 162.2; *IR* (cm^{-1}): ν_{max} 3054, 1602, 1595, 1505, 1480, 1425, *Anal. Calcd.* for $C_{16}H_{13}N_3$: C, 77.73; H, 5.26; N, 17.00; *Found*: C, 77.80; H, 5.46; N, 17.15.

References

1. (a) K. Wasti and M. M. Joullie, *Heterocycles* **4**, 1341 (1976). (b) K. Wasti and M. M. Joullie, *J. Chem. Soc., Perkin Trans.* **1**, 2521 (1976). (c) C. H. Hitchings, P. B. Russel andf Whittakar, *ibid*, 1019 (1956). (d) R. W. A. Rees, P. B. Russel, T. J. Foell and R. E. Bright, *J. Med. Chem.* **15**, 859 (1972). (e). L. C. March, G. S. Bajwa., J. Lee, K. Wasti and M. M. Joullie, ibid, **19**, 845 (1976). (f) A. K. Mansour, S. B. Awad and S. Antoun, *Z. Naturforsch.* **29B**, 792 (1974). (g) S. Watanabe, and T. Ueda, *Chem. Pharm. Bull.* **11**, 1551 (1963).

2. (a) W. B. Lacefield, E. Lilly and Co, *US Pat* **3**, 979, 516, 07, September **1976**, Appl. 438, 158, 31, Jan (1974); *Chem. Abstr.* **86**, 624 (1977). (b) M. Semonsky and M. Beran, Czech 150, 007, 15, August. (1973), Appl, 4411-70, 24, June, (1974), *Chem. Abstr.* **80**, (1974), 37180m. (c) A. K. Mansour, S. B. Awad and S. Antoun, *Chem. Abstr.* **82**, (1975), 10084z. (d) L. D. Trepanier, *Ger Offen* **1**, 937, 961 (11, Mar 1971, Appl. 25, Jul 1969); *Chem. Abstr.* **75**, (1971), 36149t. (e) A. M. Abdul Halium, R. M. Abdul Rahman and E. A. Mohammed, *Acta. Pharm. Jugosl.* **89** 103, (1985).
3. (a) H. R. Sullivan, W. M. Miller, D. G. Stark, and P. G. Wood, *Xenobiotica* **9**, 548 (1981). (b) R. Carboni and R. V. Lindsay, *J. Am. Chem. Soc.* **81**, 4342 (1959). (c) R. M. A. Rahman and M. Ghareib, *Ind. J. Chem.* **26B**, 496 (1987). (d) A. K. Mansour, M. M. Eid, R. A. Hassan, *J. Heterocycl. Chem.* **25**, 279 (1988). (e) R. M. A. Rahman, *Ind. J. Chem.* **27B**, 548 (1988).
4. P. V. Laakso, R. Robinson, "Festchrift Karrer," 1948, Birkhauaer, Zurich, 38. (b) P. V. Laakso, R. Robinson and H. P. Vandrewala, *Tetrahedron* **1**, 103 (1957).
5. (a) CIBA Ltd., *Belg. Pat.* 615, 619 (Sept. 27, 1962); *Chem. Abstr.* **58**, 12583a (1963). (b) A. G. Kalle, *Ger. Pat.* 1, 009, 846 (Feb, 16, 1961); *Chem. Abstr.* **58**, 11382h (1963).
6. (a) R. Metze, *Chem. Ber.* **91**, 1861 (1958). (b) R. Metze, G. Rolle, *Chem. Ber.* **91**, 422 (1958). (c) R. Metze, S. Meyer, *Chem. Ber.* **90**, 481 (1957). (d) R. Metze, *Chem. Ber.* 89, 2056 (1956). (e) *Ibid.* **88**, 772 (1955). (f) R. Metze, *East Ger. Pat.* 13, 175, (May, 3, 1957); *Chem. Abstr.* **53**, 7216i (1959). (g) R. Metze, and W. Kort, *Chem. Ber.* **91**, 417 (1957).
7. H. Hasselquist, *Ark. Kem.* **15**, 387 (1960).
8. R. L. Nongkhlaw, R. Nongrum, B. Myrboh, *Heterocycl. Communn* **9**(5), 465-472 (2003).
9. C. M. Atkinson and H. D. Cossey; *J. Am. Chem. Soc.* 1805 (1962).
10. (a) H. Neunhoeffer and H. W. Fruhauf, *Ann. Chem.* **102**, 760 (1972). (b) H. Neunhoeffer and F. Weischedel, *Ann. Chem.* **101**, 749 (1971). (c) H. G. O. Becker, G. pauli, H-J. Timpe and H. D. Steinleitner, *Z. Chem.* **8**, 105 (1968). (d) M. M. Bursey, T. A. Elwood, *J. Org. Chem.* **35**, 793 (1970). (e) F. H. Case, *J. Heterocycl. Chem.* **10**, 353 (1973). (g) *Ibid.* **8**, 1043, 173 (1971). (h) *Ibid.* **7**, 1001 (1970). (i) *Ibid.* **5**, 413, 223 (1968). (j) F. H. Case, *J. Org. Chem.* **31**, 2398 **1966**. (k) *Ibid.* **30**, 931 (1965). (l) F. H. Case and L. Kennon, *J. Heterocycl. Chem.* **4**, 483 (1967). (m) B. M. Culbertson, and G. R. Parr, *J. Heterocycl. Chem.* **4**, 422 (1967). (n) J. F. Geldord, *Inorg. Chem.* **4**, 417 (1965). (o) E. Kiss, *Anal. Chim. Acta.* **72**, 127 (1974). (p) H. Neunhoeffer, L. Motitschke, H. Hennig, and K. Ostheimer, *Ann. Chem.* **88**, 760 (1972).
11. (a) H. Neunhoeffer and H. Hennig, *Chem. Ber.* **101**, 3952 (1968). (b) H. Paul, S. Chatterjee and G. Hilgetag, *Chem. Ber.* **101**, 3696 (1968).
12. H. Neunhoeffer, H. Hennig, *Tet. Lett.* 3147-3150 (1969).

Received on May 05, 2005.