Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

# Synthetic Studies on the Reactions of Hydrazine and Aroylhydrazide with 5-Phenyl-1,3,4-Oxadiazol-2-thione

G.A. EL-Saraf [a] & A.M. EL-Sayed [a]
[a] Chemistry Department , Faculty of Science , Sohag, Egypt
Published online: 21 Aug 2006.

To cite this article: G.A. EL-Saraf & A.M. EL-Sayed (1996) Synthetic Studies on the Reactions of Hydrazine and Aroylhydrazide with 5-Phenyl-1,3,4-Oxadiazol-2-thione, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 26:20, 3827-3839, DOI: 10.1080/00397919608003799

To link to this article: http://dx.doi.org/10.1080/00397919608003799

SYNTHETIC COMMUNICATIONS, 26(20), 3827-3839 (1996)

# SYNTHETIC STUDIES ON THE REACTIONS OF HYDRAZINE AND AROYLHYDRAZIDE WITH 5-PHENYL-1,3,4- OXADIAZOL-2-THIONE.

G.A.EL-Saraf and A.M.EL-Sayed.

Chemistry Department, Faculty of Science, Sohag, Egypt.



**Abstract**: The reacton of 5- phenyl - 1,3,4 - oxadiazol-2-thione 1 with hydrazine hydrate in refluxing n-butanol afforded benzoylcarbohydrazide 2 which was cyclized to 4-amino-3-chloro-5-phenyl-1,2,4-triazole 3. Compound 3 was used for the synthesis of some new di-or polyheterocyclic derivatives via its reaction with anilines and treating the products with bidentates .

1,3,4- Oxadiazoles and fused S-triazoles have antiviral [1] , antifungal [2] ,insecticidal [3], and anthelmintic [4] properties. Similarly, S-triazoles, fused S- triazoles, S-triazines and S-diazines have pharmacological activities [5-7]. Our present work deals with the synthesis of some new fused heterocyclic systems containing oxadiazolo-triazole, triazolo-triazole and diazino-triazole moieties.

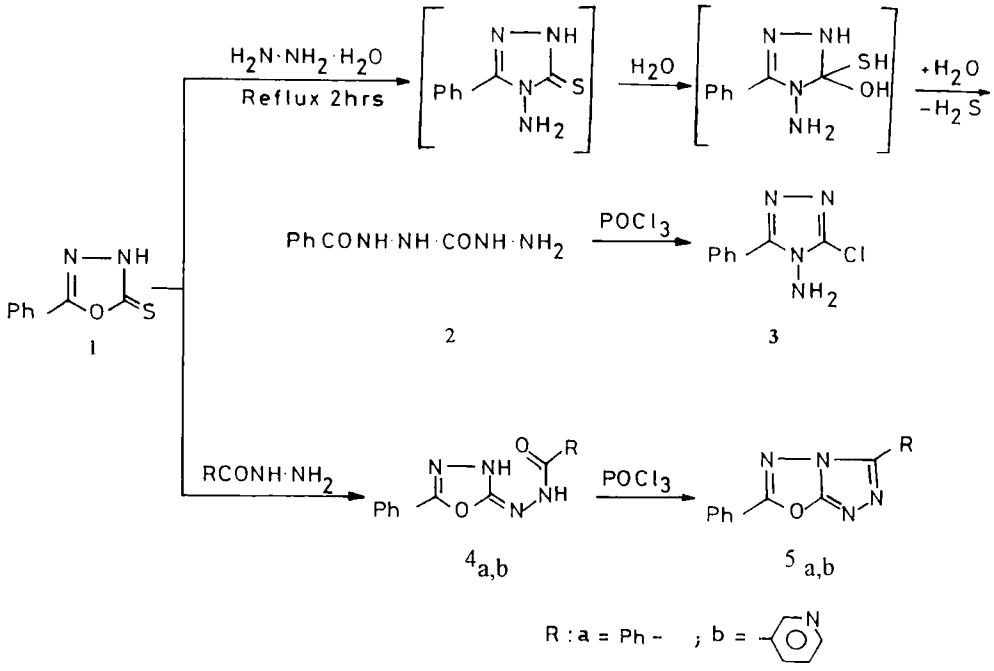
It has been reported [8-13] that -4-amino- 3-mercapto-5-substituted-(4H) -1,2,4 triazoles were synthesized by the reaction of 5-substituted - 1,3,4- oxadiazol-2-thione with hydrazine hydrate in refluxing water [10],

n-butanol or dioxane [13] for 3-4 h with hydrogen sulfide evolution. It is reported here that treatment of 5- phenyl 1,3,4 - oxadiazole-2-thione 1 with hydrazine hydrate in refluxing n-butanol, until hydrogen sulfide evolution finished (48h), affords a benzoylcarbohydrazide 2 identified by elemental analysis, i.r. and n.m.r. spectra ( Scheme I, Table I). Treatment of compound 2 with phosphorus oxychloride afforded triazole 3 (cf.Scheme I, Table I ).

In extention, when 1 reacted with some aroylhydrazide, namely benzoylhydrazine or isonicotonic acid hydrazine, the corresponding 2-aroylhydrazino derivatives $4_{a,b}$ were obtained. On treatment with phosphorus oxychloride these compounds yielded the corresponding oxadiazolo-triazole derivatives $5_{a,b}$ . The structures of the investigated compounds $4_{a,b}$ and $5_{a,b}$ were established by i.r., and n.m.r. spectral data ( cf. Table I ) .

Compoumd 3 was treated with p- toluidine, p-nitroaniline or o-anisidine, in refluxing ethanol to give triazoles $6_{a-c}$ resepectively.

The nucleophilic character of secondary amino group ( - HN-Ar) in conpounds $6_{a-c}$ was testsd in their reactions with some electrophiles. Thus, reaction of $6_{a-c}$ with carbon disulphide in presence of alcoholic potassium hydroxide afforded the corresponding triazolo-thiotriazole derivatives $7_{a-c}$; whereas with formaldehyde in ethanol, the triazolo-hydrotriazole derivatives $8_{a-c}$ were obtained. Compound 3 when treated with oxalyl chloride or chloroacetylchloride in presence of triethylamine in




Scheme I

dry benzene afforded the corresponding triazolo- triazindione derivatives $9_{a\text{-}c}$ or triazolo-triazinone derivatives $10_{a\text{-}c}$, respectively. The structure of these compounds were confirmed using i.r. and n.m.r spectra and CHN analyses (cf. Table I).

Furthermore, the reaction of compound 3 with malononitrile in ethanol in presence of triethylamine gave the triazolo-pyrazole derivative 11; while the treatment of compound 3 with equimolar ratio of triethylamine in ethanol under refluxing condition, it gave compound 12.

Table I :

| product | m.p[a] | yield[b] % | Mol. Formula (Mol.Wt.) | Analytical data Calc./Found (%) C | H | N |
|---|---|---|---|---|---|---|
| **2** | 214-16 | 83 | $C_8H_{10}N_4O_4$ | 49.48 | 5.19 | 28.85 |
| | | | (194.20) | 49.40 | 5.20 | 28.70 |
| **3** | 212-14 | 63 | $C_8H_7N_4Cl$ | 49.37 | 3.62 | 28.78 |
| | | | (194.63) | 49.50 | 3.50 | 28.80 |
| $\mathbf{4_a}$ | 217-18 | 82 | $C_{15}H_{12}N_4O_2$ | 64.28 | 4.32 | 19.99 |
| | | | (280.29) | 64.20 | 4.10 | 19.80 |
| $\mathbf{4_b}$ | 228-31 | 80 | $C_{14}H_{11}N_5O_2$ | 59.78 | 3.94 | 24.90 |
| | | | (281.28) | 59.70 | 3.80 | 24.80 |
| $\mathbf{5_a}$ | 186-87 | 90 | $C_{15}H_{10}N_4O$ | 68.70 | 3.84 | 21.36 |
| | | | (262.27) | 68.70 | 3.70 | 21.30 |
| $\mathbf{5_b}$ | 170-71 | 83 | $C_{14}H_9N_5O$ | 63.87 | 3.45 | 26.60 |
| | | | (263.26) | 63.60 | 3.30 | 26.40 |
| $\mathbf{6_a}$ | 154-56 | 76 | $C_{15}H_{15}N_5$ | 67.90 | 5.70 | 26.40 |
| | | | (265.32) | 67.90 | 5.60 | 26.20 |
| $\mathbf{6_b}$ | 131-33 | 80 | $C_{14}H_{12}N_6O_2$ | 56.75 | 4.08 | 28.36 |
| | | | (296.29) | 56.60 | 4.00 | 28.20 |
| $\mathbf{6_c}$ | 173-75 | 68 | $C_{15}H_{15}N_5O$ | 64.04 | 5.37 | 24.89 |
| | | | (281.32) | 64.10 | 5.20 | 24.70 |
| $\mathbf{7_a}$ | 190-92 | 52 | $C_{16}H_{13}N_5S$ | 62.52 | 4.26 | 22.78 |
| | | | (307.38) | 62.30 | 4.10 | 22.50 |
| $\mathbf{7_b}$ | 192-4 | 55 | $C_{15}H_{10}N_6O_2S$ | 53.25 | 2.98 | 24.84 |
| | | | (338.35) | 53.00 | 2.70 | 24.80 |
| $\mathbf{7_c}$ | 151-52 | 75 | $C_{16}H_{13}N_5OS$ | 59.43 | 4.05 | 21.66 |
| | | | (323.38) | 59.30 | 4.00 | 21.40 |

Table I : (Continued ):

| product | m.p[a] | yield [b] % | Mol. Formula (Mol.Wt.) | Analytical data Calc./Found (%) C | H | N |
|---|---|---|---|---|---|---|
| **$8_a$** | 214-16 | 60 | $C_{16}H_{15}N_5$ | 69.30 | 5.45 | 25.25 |
| | | | (277.33) | 69.30 | 5.20 | 25.10 |
| **$8_b$** | 168-70 | 80 | $C_{15}H_{12}N_6O_2$ | 58.44 | 3.92 | 27.26 |
| | | | (308.30) | 58.30 | 3.80 | 27.20 |
| **$8_c$** | 197-99 | 61 | $C_{16}H_{15}N_5O$ | 65.52 | 5.15 | 23.88 |
| | | | (293.33) | 65.40 | 5.10 | 23.80 |
| **$9_a$** | 208-10 | 63 | $C_{17}H_{13}N_5O_2$ | 63.94 | 4.10 | 21.93 |
| | | | (319.33) | 63.80 | 3.90 | 20.80 |
| **$9_b$** | > 300 | 76 | $C_{16}H_{10}N_6O_4$ | 54.84 | 2.88 | 23.99 |
| | | | (350.30) | 54.50 | 2.70 | 24.00 |
| **$9_c$** | 227-28 | 70 | $C_{17}H_{13}N_5O_3$ | 60.89 | 3.91 | 20.88 |
| | | | (332.33) | 60.80 | 3.80 | 20.70 |
| **$10_a$** | 201-3 | 60 | $C_{17}H_{15}N_5O$ | 66.87 | 4.95 | 22.94 |
| | | | (305.34) | 66.60 | 4.80 | 23.00 |
| **$10_b$** | 271-74 | 82 | $C_{16}H_{12}N_6O_3$ | 57.14 | 3.60 | 24.99 |
| | | | (336.31) | 56.90 | 3.50 | 24.80 |
| **$10_c$** | 222-24 | 88 | $C_{17}H_{15}N_5O_2$ | 63.54 | 4.71 | 21.79 |
| | | | (321.34) | 63.40 | 4.60 | 21.80 |
| **11** | 230-32 | 70 | $C_{11}H_8N_6$ | 58.92 | 3.60 | 37.48 |
| | | | (224.23) | 58.80 | 3.70 | 37.40 |
| **12** | 174-76 | 63 | $C_{16}H_{12}N_8$ | 60.75 | 3.82 | 35.42 |
| | | | (316.33) | 60.60 | 3.70 | 35.20 |

(continued)

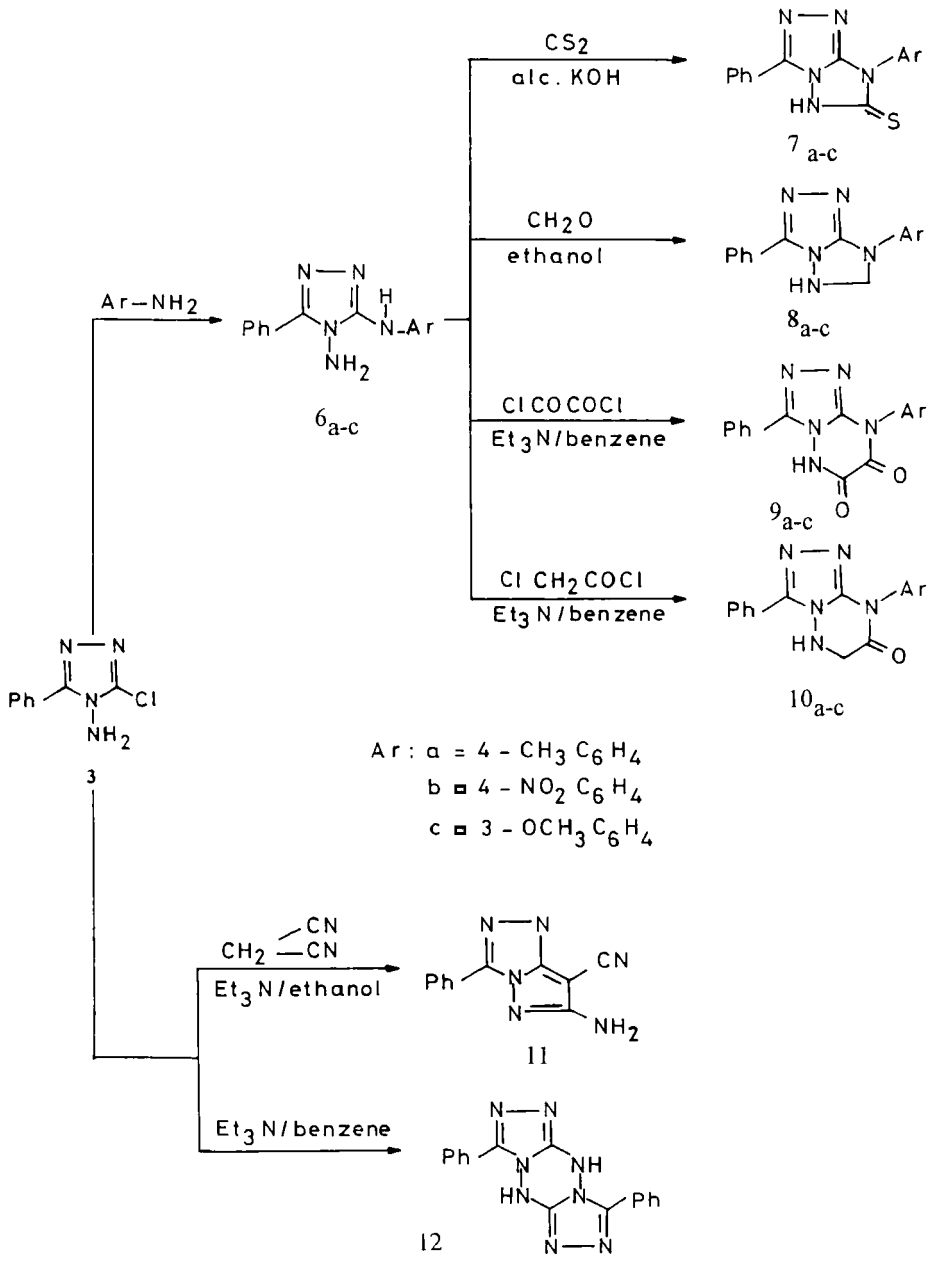
Table I : (Continued ):

| product | IR ($cm^{-1}$) [c] | $^1$H-NMR[d] (s.ppm) |
|---|---|---|
| **2** | 3478 (OH ); 3408, 3302 ($NH_2$);3200 (NH) ; 1640 (-CO-amidic); 1625 (N=C) | 8.23-7.36 (m,5H,aromatic ); 6.64-6.54 (br,3H, 3NH); 5.64 (s,2H,$NH_2$). |
| **3** | 3464 - 3380 ($NH_2$); 1618 (N=C ); 745 (C-Cl) | 8.53-7.45 (m,5H,aromatic ); 6.63 (s, 2H,$NH_2$). |
| **$4_a$** | 3153 (NH); 1660 (NH - CO); 1608 (N=C) | 9.80 (s,1H,NH.CO); 8.84 (s,1H, NH); 8.24- 7.34 (m,10H,aromatic ); |
| **$4_b$** | 3415 (OH), 3196 (NH); 1668 (NHO); 1632 (N=C) | 10.80 (s,1H,NHCO); 10.54 (s,1H, NH); 9.32-7-46 (m,9H,aromatic ); |
| **$5_a$** | 1636 (N=C) | 8.18-7.40 (m,10H,aromatic ). |
| **$5_b$** | 1622 (N=C) | 9.30-7.40 (m,9H,aromatic ). |
| **6a** | 3471,3390($NH_2$) ; 3224(NH); 1628 (N=C). | 7.82-5.84 (m,12H,aromatic +NH+$NH_2$);2.24 (s,3H,$CH_3$). |
| **$6_b$** | 3478,3360 ($NH_2$);3230 (NH); 1634 (N=C); 1476, 1302 (NO2). | 8.94(s, IH,NH); 8.32-7.35 (m,9H,aromatic ); 6.70 (s,2H,$NH_2$) |
| **$6_c$** | 3416,3310 ($NH_2$); 3100 (NH);1623 (N=C). | 7.32-6.36 (m,12H,aromatic +NH+$NH_2$); 3.92 ( s,3H,$OCH_3$) |
| **$7_a$** | 3150 (NH); 1616 (N=C). | 8.68 (s,IH , NH) 8.38-7.44 (m,9H, aromatic ); 2.43 (s,3H,$CH_3$). |
| **$7_b$** | 3216 (NH); 1622 (N-C); 1492, 1317 ($NO_2$ ). | 8.10 (s,IH , NH) ; 7.89-7.36 (m,9H, aromatic ). |
| **$7_c$** | 3143 (NH); 1612 (N=C) | 8.84 (s,IH , NH) 8.18-7.32 (m,9H,aromatic ); 4.14 (s,3H,$OCH_3$). |
| **$8_a$** | 3280 (NH); 1624 (N=C) | 8.30 -7.48 (m,10H,aromatic + NH ); 2.54(s,2H,N-$CH_2$-N) |

Table I : (Continued ):

| product | IR ($cm^{-1}$) [c] | $^1$H-NMR[d] (s.ppm) |
|---|---|---|
| **$8_b$** | 3366(NH ); 1597 (N=C), 1500, 1319 ($NO_2$) | 9.10 (s, IH,NH); 8.20-7.38 (m,9H,aromatic); 2.60 (s, 2H,N-$CH_2$-N). |
| **$8_c$** | 3319 (NH), 1610 (N=C) | 8.60-7.58 (m,10H,aromatic +NH ); 4.00 (s,3H,$OCH_3$);2.64 (s, 2H,N-$CH_2$-N); |
| **$9_a$** | 3408 (OH) ; 3163 (NH) ; 1686 (CO) , 1670 (NH.CO); 1626 (N=C) | 8.63-7.42 (m,10H,aromatic + NH); 2.60 (s,3H ,$CH_3$) |
| **$9_b$** | 3477 (OH); 3322 (NH); 1700 (CO); 1665 (NHCO); 1603 (N=C). | 8.60 (s,1H,NH);8.18-7.46 (m,9H,aromatic). |
| **$9_c$** | 3415 (OH); 3196 (NH); 1698 (CO); 1668 (NHCO); 1632 (N=C). | 8.90 (s,1H,NH);8.33-7.48 (m,9H,aromatic); 4.24 (s,3H,$OCH_3$) |
| **$10_a$** | 3404 (OH); 3183 (NH); 1675 (NHCO); 1624 (N=C). | 8.78-7.40 (m,9H,aromatic +NH); 4.12 (s,2H,N-$CH_2$ -CO);2.64 (s,3H,-$CH_3$). |
| **$10_b$** | 3476(OH) ; 3222(NH); 1687 (NHCO)1622 (N=C). | 10.93 ( s,IH,NH); 8.50-7.80 (m,9H,aromatic);4.30 (s,2H,N-$CH_2$ CO). |
| **$10_c$** | 3423(OH); 3145 (NH); 1660 (NHCO) ; 1611 (N=C) . | 8.48 (s,IH,NH) ; 8.16-7.40 (m,9H aromatic); 4.32 (s,3H,$OCH_3$). |
| **11** | 3315,3197 ($NH_2$);3095 (NH), 2199 (CN); 1622 (N=C). | 13.73 (s,IH,NH);8.30-7.40 (m,5H,aromatic); 5.37 (s,2H,$NH_2$) |
| **12** | 3158 (NH); 1625 (N=C). | 8.90 ( s,2H,2NH) ; 8.48-7.34 (m,10H,aromatic ). |

[a]) Uncorrected, [b]) Crystallizion solvents are : butanol for **2,4 $_{a\cdot b}$**; ethanol for **6 $_a$, $7_a$, $8_{b,c}$ ,$9_{a,c}$ ,11,12;** elhanol/ water for **3,5$_{a\cdot b}$, 6 $_{a\cdot b}$ ,$7_{a\cdot b}$ ,$8_{a\cdot}$ , $9_b$, $10_{a-c}$**[c]) Measured on Nicolet 710 FT-IR spectrophotomer [d]) Measured with a varian EM 360L using TMS as internal standard.




Scheme II

***Experimental procedure.***

***Benzoyl carbohydrazide 2***

Hydrazine hydrate (5 mL, 0.1 mol) was added to a solution of oxadiazole 1 (17.8 g. 0.1 mol) in n-butanol (100 mL) and the reaction mixture was refluxed for 48 h until the evolution of $H_2S$ stopped. The solution was cooled, and the preciptate was filtered and recrystallized from an appropriate solvent.cf . Table I.

***4-Amino-3-chloro-5-phenyl-1,2,4-triazole 3***

A solution of compound **2** (9.7 g, 0.05 mol) in phosphorus oxychloride (20 mL) was refluxed with stirring for 4 h. The reaction mixture cooled, poured on crushed ice and the precipitate was filtered and recrestallized from suitable solvent, cf. Table I. MS: m/z (relative intensity) 196 ( 0.84), 194 (5.98), 192 (100), 162 (8.08).

***Action of acid hydrazide on compound 1: $4_{a,b}$***

***(General procedure)***

A mixture of compound **1** (1.78g ,0.01 mol) and an appropriate acid hydrazide (0.01 mol) in n-butanol (30 mL) was refluxed for 10 h. The solution was concentrated, cooled, filtered, and the product was recrystallized from an appropriate solvent, cf. Table I.

***Cyclization of compounds $4_{a,b}$: $5_{a,b}$***

***(General procedure)***

Phosphorus oxychloride (20 mL) was added to dry compounds $\mathbf{5_{a,b}}$ (3g), and the reaction mixture was refluxed for 2 h, poured on ice water

(500 mL), and filtered. The product was washed with water and recrystallized from an appropriate solvent, cf. Table I.

***Reaction of compound 3 with aromatic amine : 6 $_{a-c}$ .***

***(General procedure)***

A solution of an equimolar ratio (0.05 mol) of compound **3**, an appropriate primary aromatic amine and triethylamine in ethanol (50 mL) was refluxed for 6 h. The mixture was evaporated in vacuo and the residue was washed with water and recrystallized from suitable solvent,cf. Table I. MS of compound **( $6_b$):** m/z (relative intensity) 296 (0.64), 268 (0.82), 192 (5.10), 108 (100).

***Reaction of compound 6 $_{a-c}$ with carbon disulfide : $7_{a-c}$***

***(General procedure)***

To a mixture of compound **$6_{a-c}$** (0.01 mol), carbon disulfide (1.14 g, 0.015 mol) and absolute ethanol (50 mL), a solution of potassium hydroxide (0.34 g, 0.015 mol) in 2 mL water was added. The reaction mixture was refluxed until the evolution of $H_2S$ finished (12 h). The reaction mixture was concentrated, cooled, poured on water (100 mL), filtered and the filterate was acidified with dil. HCl. The precipitant was collected and recrystallized from an appropriate solvent, cf. Table I.

***Mannich reaction of compound 6 $_{a-c}$ : 8 $_{a-c}$***

***(General procedure )***

A mixture of compound **6 $_{a-c}$** ( 0.005 mol) and formaldehyde (1.5 mL, 40 %) in ethanol (60 mL) was refluxed for 2 h. The solvent was

evaporated and the residue was recrystallized from an appropriate solvent, cf. Table I.

***Reaction of compounds $6_{a-c}$ with oxalyl chloride or chloroacetylchloride : 9 $_{a-c}$ , 10 $_{a-c}$***

***(General procedure)***

To a solution of an equimolar ratio ( 0.005 mol ) of compound $6_{a-c}$ and oxalyl chloride or chloroacetylchloride in benzene (50mL) , (0.01mol) of triethylamine was added. The mixture was refluxed for 4h, filtered while hot and the filterate was concentrated and cooled . The solid precipitated was filtered off, washed with water and recrystallized from a suitable solvent, cf. Table I.

***Reaction of compound 3 with malononitrile : 11***

To a solution of compound **3** (0.778 g, 0.004 mol) and triethylamine (0.041 g, 0.0004 mol) in ethanol (50 mL), malononitrile (0.264 g., 0.004 mol) was added, the mixture refluxed for 4 h, and the solvent was evaporated. The residue washed with water and recrystallized from an appropriate solvent, cf. Table I.

***Action of triethylamine on compound 3 : 12***

A mixture of an equimolar ratio (0.004 mol) of compound **3** and triethylamine in ethanol was refluxed for 4 h. The solvent was evaporated and the residue washed with water and recrystallized from a suitable solvent, cf. Table I.

*Note:*

Mass Spectra (ms) measured on a Micromaso 7070E Spectrometer operating at 70ev using direct inlet.

## *References*

1- Bell, S.C. and Wei, P.H.L., J. Med. Chem., 19, 524 (1976) .

2- Bala, S; Gupta, R.P; Sachedeva, M.L.; Singh, A. and Pujari, H.K., Indian J. chem., 16 B, 481 (1978) . C.A, 90:38884q (1979)

3- Laurenz, G and willy, M., Ger. Offen, 12, 739 (1977).

4- Howes (Jr) H.L. and Lynch, J.E., J. Parasit., 53, 1085 (1967) . C.A , 11541g (1968)

5- Postevskii, I.Y. and Vereshchagina, N.N., Zh. Obshch. Khim., 26, 2583 (1956). C.A., 51, 5055 (1957) .

6- Shah, M.H.; Mhasalkar, M.Y.; Varaya, N.A.; Bellare, R.A. and Deliuala, C.V., Indian J. Chem., 5, 391 (1967). C.A ., 68,105106w (1968)

7- Kumar, A. and Asthana, B.P., J. Indian Chem.Soc. ,60, 682 (1983) . C.A.100,120974a (1984 ).

8- Kanaok, M.: J. Pharm. Soc. Jap., 76, 1133 (1956) .

9 - Hoggarth E.: J. Chem. Soc., 4811 (1952).

10- Reid, J.R. and Heindel, N.D., J. Heterocyclic. Chem., 13, 925 (1976).

11- Anwar, M.; Abdel-Megeed,M.F.; Islam, I. and Sorour, N. , Egypt J. Chem. 24 (1) , 117 (1982) .C.A.99, 88118x (1983)

12- Ghattas, A.B.A.G; El-wassimy, MM.T. : Abdel. Rahman, M. and El-Saraf, G.A., Sulfur Lett., 6 (1) , 7 (1987) .C.A.108, 9447b (1988)

13- Artemovo, V.N. and Shavaika, O.P., Khim Geterotsikl Soedin , 905 (1971) .C.A. 76. 140741m (1972).

(Received in the USA 18 May 1996)