SYNTHESIS AND STUDIES OF CHALCONES AND ITS CYANOPYRIDINE AND ACETYL PYRAZOLINE DERIVATIVES

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ABSTRACT

*Chalcones **6a-e** were achieved upon refluxing of ketone **5** and different substituted aromatic and heterocyclic aldehydes in suitable solvent. Chalcones **6a-e** on cyclisation with malononitrile in presence of ammonium acetate and hydrazine hydrate in presence of acetic acid give cyanopyridines **7a-e** and acetyl pyrazoline **8a-e** respectively. All the synthesised compounds have been characterised by their physical data and spectral data.*

Keywords: *ketone, chalcones, cyanopyridines, acetyl pyrazolines, spectral data*

INTRODUCTION

Chalcones and its derivatives have attracted particular interest during the last few decades due to use of such ring system as the core structure in many drug substances covering wide range of pharmacological application[1]. Chalcone moiety is the backbone of several antiulcer[2], cardiovascular[3] and antispasmodic[4] drugs. Pyridine derivatives have proven to be of great importance in exhibiting and enhancing the biological activities[5]. Substituted pyridine derivatives like cyanopyridines have found to possess different biological activities such as anticancer[6], antihypertensive[7] and arthropodicidal[8]. The literature survey reveals that pyrazolines have been found to possess many biological activities and have variety of industrial application[9]. It has been reported that introduction of acetyl group at 1st position enhance the mollucicidal[10] activity as well as increases the stability of pyrazolines. Pyrazoline derivatives have been found to be effective as diuetic[11], immunosuppressive[12] and tranquillizer[13] agents.

In a continuation of our work[14-18] considering the scope for further studies on chalcones and its derivatives, we herein report some novel chalcones **6a-e**, cyanopyridines **7a-e** and acetyl pyrazolines **8a-e**. The synthesised compounds were ascertained from spectral and physiochemical analysis. Results of IR and ^{1}H NMR analysis confirmed formation of the desired products.

EXPERIMENTAL

All melting points were determined in open capillary and are uncorrected. The IR spectra were recorded on Perkin – Elmer 237 spectrophotometer. ^{1}H NMR spectra on a Bruker Avance DPX 300 MHz spectrometer with $CDCl_3$ used as a solvent and tetramethylsilane (TMS) as internal standard. The chemical shifts are expressed in part per million (ppm) downfield from the internal standard and signals are quoted as *s* (singlet) and *m* (multiplate). The reactions are followed up and the purity of products is carried out on pre-coated TLC plates (Silica gel 60 F254 , Merck) of 0.25mm thickness eluted with visualized with UV (254nm) or iodine.

Preparation of 2-phenylamino- 4, 6-dichloro-*s*-triazine (3):
Aniline (0.01 mol in 10mL acetone) was added slowly to cyanuric chloride (0.01 mol in 30 mL acetone) with constant stirring for 4 hours at 0 to 5 ^{o}C. Periodically, sodium carbonate solution (0.005 mol, 0.53g in 10mL water) was added dropwise to neutralized HCl evolved during the reaction. Finally, the contents were poured into crushed ice. The solid separated out was filtered, washed with water, dried and recrystallized from ethyl alcohol to give **(3)**. Yield 89 %, m.p. 196 ^{o}C.

Preparation of 2-phenylamino-4-(4'-chlorophenylamino)-6-chloro-*s*-triazine (4):
4-Chloroaniline (0.01 mol in 10mL acetone) was added slowly to compound **(3)** (0.01 mol in 35 mL acetone) with constant stirring for 6 hours at room temperature. Periodically, sodium carbonate solution (0.005 mol in10 mL water) was added dropwise to neutralized HCl evolved during the reaction. Finally the contents were poured into crushed ice. The solid separated out was filtered, washed with water, dried and recrystallized from ethyl alcohol to give **(4)**.Yield 84%, m.p. 190^{o}C.

Preparation of 2-phenylamino-4-(4'-chlorophenylamino)-6-(4'-acetylphenyl amino)-*s*-triazine (5):
4-Aminoacetophenone (0.01mol) and compound **(4)** (0.01 mol) were dissolved in DMF (40 mL). The reaction mixture was refluxed for 6 hours, cooled and poured into crushed ice. Periodically, sodium carbonate solution (0.005 in 10 mLwater) was added to neutralize HCl evolved during the reaction. The solid separated out was filtered, washed with water, dried and recrystallized from ethyl alcohol to give **(5)**. Yield 79%, m.p. 208^{o}C; IR (KBr) cm^{-1}: 1660 (-C=O), 806 (C-N, *s*-triazine), 784 (C-Cl). ^{1}H NMR ($CDCl_3$): δ 2.6 (s, 3H, -$COCH_3$), δ 6.9 - 8.8 (m, 16H, Ar-H and NH).

Preparation of 2-phenylamino-4-(4'-chlorophenylamino)-6-[4'-{3''-(2'''-methoxyphenyl)-2''-propenon-1''-yl } phenyl amino]-*s*-triazine 6a:
Compound **5** (0.01mol) was dissolved in DMF (30 mL) and 2-methoxybenzaldehyde (0.01 mol) was added to it. Then solution of KOH (5 mL of 40%) was added to the reaction mixture with constant stirring at room temperature. After 24 h the reaction mixture was poured into crushed ice and neutralized with HCl. The product separated out was filtered, washed with water, dried and recrystallized from ethyl alcohol to give **6a**.
IR (KBr) cm^{-1}: -C=O (1655), C-O-C (1259), C-N, *s*-triazine (805), C-Cl (770). ^{1}H NMR ($CDCl_3$) δ ppm : 3.78 (s, 3H, OCH_3), 6.88 (d, lH, -CO-CH=), 7.0 – 7.9 (m, 19H, Ar-H and NH), 8.2 (d, 1H, Ar-CH=).
Similarly the remaining compounds **6b-e** were prepared by this method. Their physical data are given in **Table-1**

Preparation of 2-phenylamino-4-(4'-fluorophenylamino)-6-[4'-{2"-amino-3"- cyano- 4"-(2'''-methoxyphenyl)-pyridine-6"-yl} phenylamino]-*s*-triazine 7a:
Compound **6a** (0.01mol) in alcohol (40 mL) malononitrile (0.01mol) and ammonium acetate was refluxed for 8 h. The reaction mixture was then cooled, poured into crushed ice and product separated out was filtered, washed with water, dried and recrystallized from ethyl alcohol to give **7a**.

IR (KBr) cm^{-1}: $-NH_2$ (3468), C≡N (2207), C-O-C (1227). C-N, *s*-triazine (803), C-Cl (776), ^{1}H NMR ($CDCl_3$) δ ppm : 3.80 (s, 3H, OCH_3), 5.73 (s, 2H, $-NH_2$), 6.9 to 7.7 (m, 20H, Ar-H and NH).
Similarly the remaining compounds **7b-e** were prepared by this method. Their physical data are given in **Table-1**

Preparation of 2-phenylamino-4-(4'-chlorophenylamino)-6-[4'-{1''-acetyl-5''- (2'''-methoxyphenyl)- 2''-pyrazolin- 3''-yl} phenylamino]-*s*-triazine 8a:
Compound **(6a)** (0.01mol) was dissolved in glacial acetic acid (30 mL) and hydrazine hydrate (0.01mol) was added to it. Then the reaction mixture was refluxed for 6 h. The reaction mixture was then cooled, poured into crushed ice and product separated out was filtered, washed with water, dried and recrystallized from ethyl alcohol to give **8a**.
IR (KBr) cm^{-1}: -C=N (1575), C-O-C (1249), C-N, *s*-triazine (808), 750 (C-Cl); ^{1}H NMR (DMSO) δ ppm : 2.46 (s, 3H, $-COCH_3$), 3.24 (dd, 1H, $-CH_A$), 3.40 (dd, 1H, $-CH_B$), 3.90 (s, 3H, OCH_3), 5.7 (dd, 1H, -CH), 6.8 - 7.7 (m, 20H, Ar-H and NH).
Similarly the remaining compounds **8b-e** were prepared by this method. Their physical data are given in **Table-1.**

RESULTS AND DISCUSSION

The IR spectrum of compounds **6a** in KBr shows the characteristic band in the region of 1700-1647 cm^{-1} which indicate the presence of -C=O group. The IR spectrum of compounds **7a** shows characteristic band in region the of 2200-2000 cm^{-1} due to –C≡N group. It also shows band in region the of 3500-3300 cm^{-1} due to $-NH_2$ group. The IR spectrum of compounds **8a** shows the characteristic band in the region of 1650-1580 cm^{-1} due to (-C=N). The IR spectrum of compounds **7a** and compounds **8a** does not show any absorption band in the region of 1700-1647 cm^{-1} which indicate the absence of -C=O group. ^{1}H NMR spectrum of compounds **6a** shows doublet of -CO-CH= at δ 6.88 confirmed the presence of chalcone moiety. The ^{1}H NMR spectrum of compounds **7a** shows sharp singlet of $-NH_2$ at δ 3.8 confirmed the present of amino group in cyanopyridine derivatives. The ^{1}H NMR spectrum of compounds **8a** shows double doublet of CH_A at δ 3.24 and double doublet of CH_B at δ 3.40 confirmed the cyclisation in pyrazoline moiety. Result of IR and ^{1}H NMR analysis confirmed formation of desired products.

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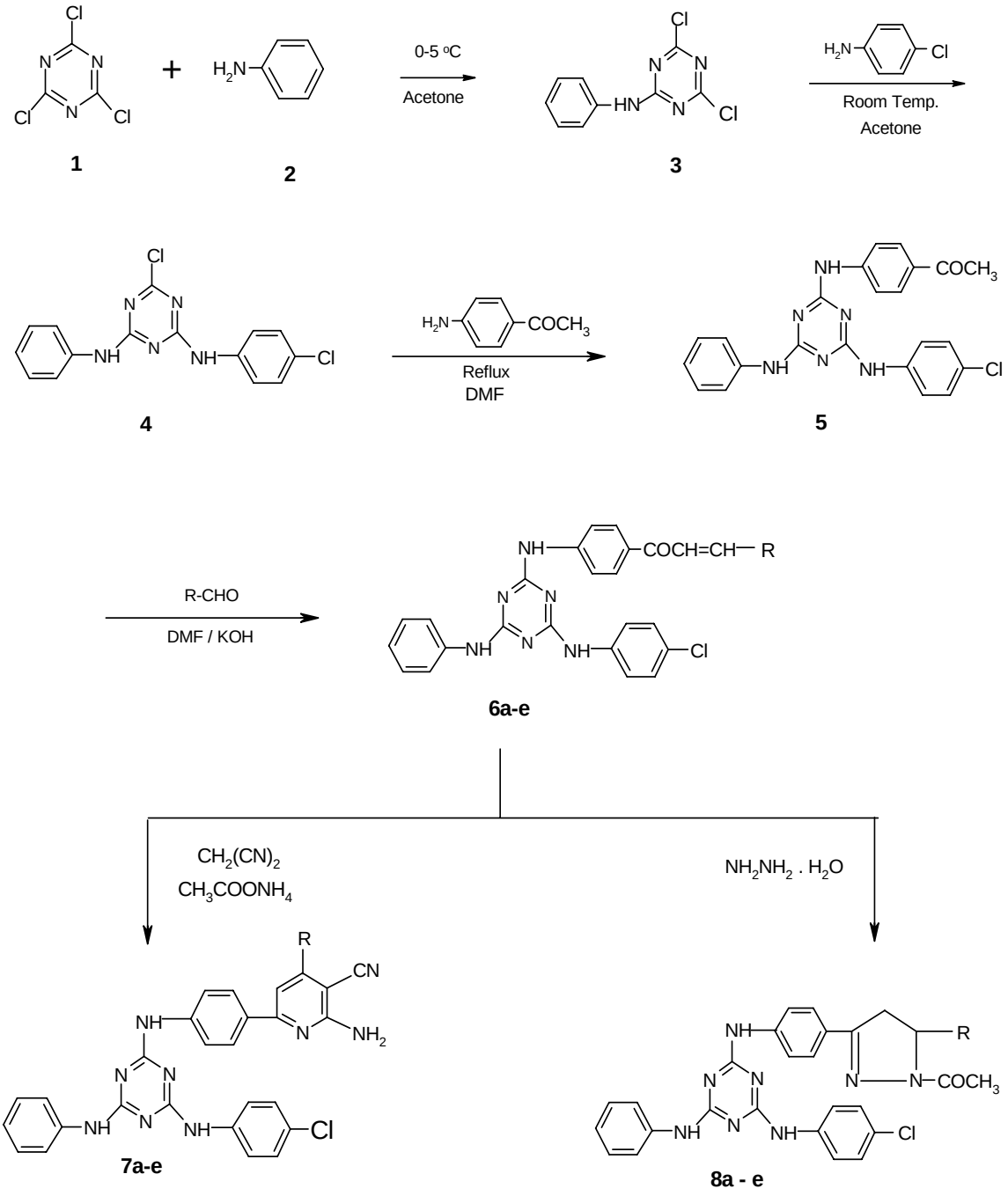
REFERENCES

1. M. Lochi, *J. Heterocycl.*, **24**, 1697 (1989).
2. K. Kyogoku, K. Hatayama, S. Yokomori, R. Saziki, S. Nakane, M. Sasajima, J. Sawada, M.Ohzeki and I. Tanaka, *Chem. Pharm. Bull.*, **27(12)**, 2943 (1979); *Chem. Abstr.*, **93**, 26047_r (1980).
3. E. Marmo, A. P. Caputi and S. Cataldi, *Farmaco, Ed. Prat.*, **28(3)**, 132 (1973); *Chem. Abstr.*, **79**, 13501_v (1973).
4. S. Shoji, H. Masatoshi and B. Widago, *Yakugaku Zasshi*, **80**, 620 (1960); *Chem. Abstr.*, **54**, 21488_e (1960).

5. N. V. Makarova, M. N. Zemtsova and I. J. Moiseev, *Chem. Heterocycl. Comps.*, **37(7)**, 840 (2001)*;Chem. Abstr.*, **136**, 355209$_n$ (1960).
6. F. E. Reinhart, J. H. Gray and W. G. Batt, *J. Franklin Inst.*, **261**, 669 (1956); *Chem. Abstr.*, **50**, 10930$_c$ (1956).



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7. J. J. Baldwin, A. Scriabine, C. T. Ludden and G. Morgan, *Experientia*, **35(3)**, 653 (1979); *Chem. Abstr.*, **91**, 83212$_y$ (1979).

8. D. A. Frasier, Jr. W. C. Holyoke, Jr. M. H. Howard, G. E. Lapone, J. E. Powell and R. J. Pasteris, *(E. I. Du Pont De Nemours and Company) PCT Int. Appl. WO* 97 11,057 (Cl. C07D211/90), 27 Mar (1997); *US Appl.* 7,277, 06 Nov (1995); 107 pp; *Chem. Abstr.*, **126**, 305586_f (1997).
9. K. S. Rao, G. V. Subbaraju, *Indian J. Heterocycl. Chem.,* **4**, 19 (1994).
10. N. Mishriky, F. M. Asaad, Y. A. Ibrahim and A. S. Girgis, *Indian J. Chem.*, **35B**, 935 (1996).
11. Z. Brzozowski, Z. Kaminski and S. Angielski, *Acta Pol. Pharm.*, **36(6)**, 645 (1979); *Chem. Abstr.*, **93**, 204525_e (1980).
12. J. G. Lombardino and I. G. Otterrness, *J. Med. Chem.*, **24**, 830 (1981).
13. H. Bruderer, R. Richle and R. Ruegg, *(Hoffmann-La Roche, Inc.) U.S.* 3,822,283 (C1. 260-310R; C07d), 02 Jul (1974), *Appl.* 296-691, 11 Oct (1972); 9 pp; *Chem. Abstr.*, **81**, 105495_r (1974).
14. A. Solankee, K. Kapadia, I. Thakor, J. Patel and S. Lad, *Asian J. Chem.*, **16(2)**, 921 (2004); *Chem. Abstr.*, **142**, 219248_w (2005).
15. A. Solankee and I. Thakor, *Indian J. Chem.*, **45B**, 517 (2006); *Chem. Abstr.*, **145**, 489200_x (2006).
16. A. Solankee, K. Kapadia, H. Patel, Y. Prajapati, P. Solankee and S. Solankee, *Indian J. Heterocycl. Chem.*, **16**, 287 (2007).
17. A. Solankee, K. Kapadia, P. Solankee, H. Patel, Y. Prajapati and S. Solankee, *Indian J. Chem.*, **46B**, 1707 (2007).
18. A. Solankee, S. Solankee and G. Patel, *Orient. J. Chem.*, **24(1)**, 277 (2008).

Table-1 Characterization data of compounds (6a-e), (7a-e) and (8a-e)

Compd	R	Molecular Formula	M.P °C	% Yield
6a	2-Methoxyphenyl	$C_{31}H_{25}ClN_6O_2$	144	71
6b	3-Nitrophenyl	$C_{30}H_{22}ClN_7O_3$	129	68
6c	4-Nitrophenyl	$C_{30}H_{22}ClN_7O_3$	190	69
6d	2-Furanyl	$C_{28}H_{21}ClN_6O_2$	215	69
6e	2-Thienyl	$C_{28}H_{21}ClN_6OS$	212	72
7a	2-Methoxyphenyl	$C_{34}H_{26}ClN_9O$	135	66
7b	3-Nitrophenyl	$C_{33}H_{23}ClN_{10}O_2$	170	64
7c	4-Nitrophenyl	$C_{33}H_{23}ClN_{10}O_2$	120	62
7d	2-Furanyl	$C_{31}H_{22}ClN_9O$	143	64
7e	2-Thienyl	$C_{31}H_{22}ClN_9S$	150	67
8a	2-Methoxyphenyl	$C_{33}H_{29}ClN_8O_2$	139	65
8b	3-Nitrophenyl	$C_{32}H_{26}ClN_9O_3$	138	63
8c	4-Nitrophenyl	$C_{32}H_{26}ClN_9O_3$	126	61
8d	2-Furanyl	$C_{30}H_{25}ClN_8O_2$	179	63
8e	2-Thienyl	$C_{30}H_{25}ClN_8OS$	160	65

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