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Phase-transfer catalysis: A general green tactic in heterocyclic synthesis

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ABSTRACT

The present work describes the use of phase transfer catalyst (PTC) for the synthesis of several heterocycles derived from secondary amine and different dihalides using TBAB (tetrabutylammonium bromide) as PTCs. Reaction of amine with dihalides suffered from the condensation. Utilizing a solid potassium carbonate as base and TBAB as PTC proved to be the best reaction conditions for amines and dihalides, which showed 100% conversion of secondary amine to the corresponding tertiary amine. The constitution of the products has been supported by element analyses, IR, NMR and Mass spectral data. To explore the role of PTC, we carried out modifying the catalyst nature and structure, temperature effect, different solvents and varying the concentration of the reactants and catalysts.

KEYWORDS

PTC;
TBAB;
Dihalides;
Amines;
K_2CO_3.

INTRODUCTION

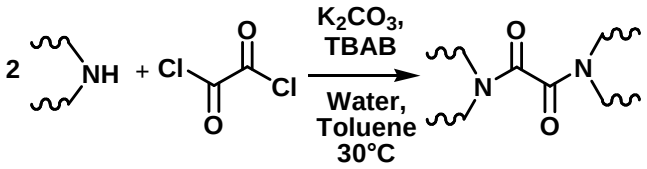
Phase-transfer-catalyzed reactions are some of the most environmentally-friendly processes in synthetic organic chemistry due to their simplicity, mild conditions and high cost performance[1]. Particularly, chiral quaternary ammonium salts have been recognized as powerful asymmetric phase-transfer catalysts (PTCs) since Dolling and O'Donnell independently reported their pioneering studies[2]. Thiazine and its derivatives are important pharmacophore which give protective effect against endotoxin shock in mouse[3], glycine-NMDA receptor antagonists[4], beta-adrenergic blocker[5] and activators of ATP sensitive potassium channels[6]. Its field of application also extends to anticancer[7], anticonvulsant[8], antimycobacterial[9], analgesic, anti-inflammatory[10], antibacterial and antifungal[11] uses. Rhodanine derivatives have proven to be attractive compounds due to their outstanding biological activities and have undergone rapid development as anticonvulsant, antibacterial, antiviral and antidiabetic agents[12]. At the same time, rhodanine derivatives have been reported also as Hepatitis C Virus (HCV) protease inhibitors[13] and used as inhibitors of uridine diphospho-*N*-acetylmuramate/L-alanine ligase[14]. Therefore, the synthesis of these compounds is of considerable interest. 3-methylindole has been shown to be an attractant to gravid mosquitoes in both field and laboratory conditions. Because this compound is present in feces, it is found in combined sewage overflows (CSO) as streams and lakes containing CSO water have untreated human and industrial waste. Knowledge of this attractant makes CSO sites of particular interest when studying mosquito-borne diseases

such as west Nile virus[15].

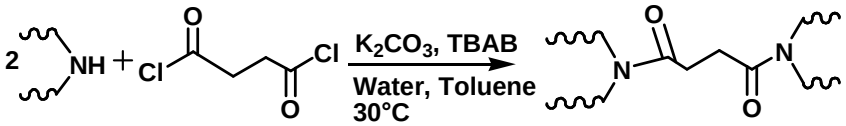
Phase transfer catalysis is one of the unique catalytic phenomena which are well explored and documented by numerous PTC researchers[16-18]. Hence, here we report the use of solid sodium hydroxide and solid potassium carbonate with tetrabutylammonium bromide for condensation of secondary amine with oxalyl chloride (Scheme 1) and condensation of secondary amine with succinyl chloride (Scheme 2) to synthesize alkane dione derivatives with low concentration of base at very short time. Our objective was to develop the process and to explore the role of PTC in these heterocycles syntheses (>90% yield) using simple nonpolar solvent (toluene) which can be effortlessly removed by straight forward vacuum evaporation. We have also examined various effects such as different reactants and catalysts, solvent effect, temperature effect, stirring effect and varying the concentration of reactants and catalysts.

EXPERIMENTAL

The phase transfer catalytic condensation was performed in a four necked round bottom flask. First neck was fitted to stirrer, the second neck was connected to nitrogen gas, the third neck was connected to thermometer pocket and fourth neck was used to load and remove the reaction mixture. The temperature of the reaction vessel was increased by using an water bath. In a typical run, a suspension of substrate (secondary amine) (0.02 mol), TBAB (0.003 mol), K_2CO_3 (0.02 mol) in 25 ml of DM water and 50 ml toluene was stirred at 30°C for 30 minutes and then alkyl chloride (0.01 mol) was added dropwise with constant stirring in the reaction mixture at 30°C. Two different alkyl halide were used for the reaction purpose i.e Oxalyl Chloride (Scheme 1) and Succinyl Chloride (Scheme 2). The progress of the reaction was monitored by TLC



Scheme 1 : Condensation of secondary amine with oxalyl chloride using potassium carbonate, tetrabutylammonium bromide, water and toluene under phase transfer methodology for the synthesis of tertiary amine.



Scheme 2 : Condensation of secondary amine with succinyl chloride using potassium carbonate, tetrabutylammonium bromide, water and toluene under phase transfer methodology for the synthesis of tertiary amine.

(after 3 hrs) and also analyzed by a gas chromatograph (HP 5890) equipped with a flame ionization detector and a capillary column (5% diphenyl, 95% dimethylpolysiloxane gum, 0.25-mm thickness with 30-m long). The product was identified by GC/MS (HP-G1800B) analysis which showed 91-95% conversion of substrate. After completion of reaction, the toluene was distilled out under vacuum at 45°C. Residue was diluted with DM water and extracted with three consecutive portions (3×20 ml) of chloroform. The combined organic layers were washed well with DM water and passed through sodium sulfate. The organic layer was concentrated under reduced pressure to afford the mixture of product and reactants. Pure solid product was obtained by purification on a silica gel (60-120 mesh) column using ethyl acetate and *n*-hexane as the eluents with the ratio of 1:1.

The elucidation of the structure of the newly synthesized compounds was done on the basis of spectral analysis. The isolated yield of product is expressed as the total amount of product obtained after isolation and purification with respect to the substrate used.

RESULTS AND DISCUSSION

A. We studied several different systems for the preparation of certain tertiary amines using TBAB as phase transfer catalysts with two solid bases (NaOH and K_2CO_3) and secondary amines were condensed with different alkyl dihalides at 30°C. Conversion and selectivity results are shown in TABLE 1.

B. We examined the effect of temperature on the reactions. The reaction was performed under solid–liquid phase transfer conditions with toluene as a solvent at

four different temperatures. Results are summarized in TABLE 2. This was indeed the case as shown in Figure 1 where the maximum conversion obtained in reactions is presented as function of temperature. We can conclude that performing reactions at low temperature would decrease the formation of impurity.

TABLE 1 : Base effect of condensation of secondary amine and alkyl dihaildes

Entry	Base	2° amine and oxalyl chloride			2° amine and succinyl chloride		
		Time (min)	Conversion (%)[a]	Selectivity (%)[b]	Time (min)	Conversion (%)[a]	Selectivity (%)[b]
1	K_2CO_3[c]	180	67	86	240	69	83
2	NaOH[d]	30	53	62	30	51	65

[a]Conversion of substrate is based on GC analysis

[b]Selectivity to tertiary amine

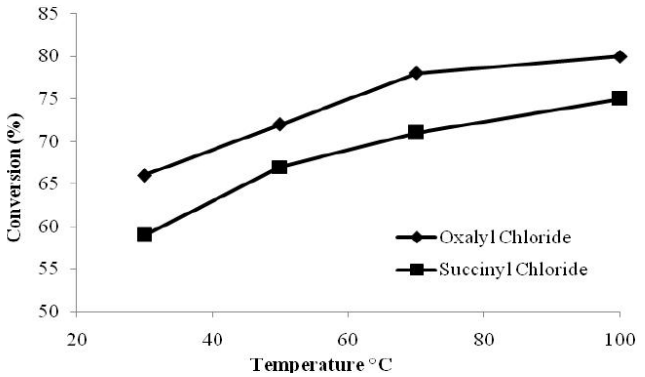
[c]The reaction condition: Secondary amine (10 mmol); dihalide (5 mmol); K_2CO_3 (0.5 mmol); TBAB (0.5 mmol); water (5 ml); toluene (10 ml); temperature (30 °C).

[d]The reaction condition: Secondary amine (10 mmol); dihalide (5 mmol); NaOH (0.5 mmol); TBAB (0.5 mmol); water (5 ml); toluene (10 ml); temperature (30 °C).

TABLE 2 : Study of reaction for alkyl chloride at different temperatures

Entry	Temperature (°C)[b]	2° amine and oxalyl chloride		2° amine and succinyl chloride	
		Time (min)	Conversion (%)[a]	Time (min)	Conversion (%)[a]
1	30	180	67	240	69
2	50	180	65	240	67
3	75	90	75	120	71
4	100	90	78	120	75

[a]Conversion of substrate is based on GC analysis; [b]The reaction condition: Secondary amine (10 mmol); dihalide (5 mmol); K_2CO_3 (0.5 mmol); TBAB (0.5 mmol); water (5 ml); toluene (10 ml).



Reaction conditions: Secondary amine (10 mmol); dihalide (5 mmol); K_2CO_3 (0.5 mmol); TBAB (0.5 mmol); water (5 ml); toluene (10 ml).

Figure 1 : Role of temperature in condensation of Secondary amines and alkyl dichlorides

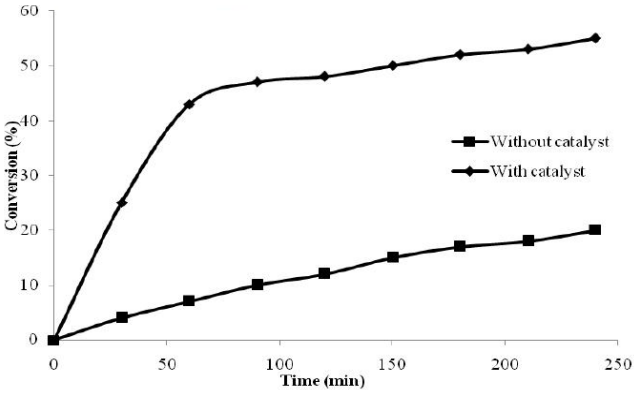
C. Role of solvent in novel heterocycles synthesis

The reaction in scheme 1 and scheme 2 has been studied using two different solvents namely the highly polar dimethylformamide (Figure 2), and non-polar toluene (Figure 3). In all the systems, TBAB was used as catalyst. When the reaction was carried out using DMF as solvent without PTC (Figure 2), the conversion of substrate was found to be 18-20% at 3 h of reaction time. We attribute this low reaction rate to the low solubility of K_2CO_3 in DMF. When TBAB was used as PTC, the reaction proceeded without any interruption and at 4 h of reaction time; we observed a maximum of 51-54% conversion of substrate at high reaction rate due to the transfer of the base into the organic phase. No reaction was observed at all without PTC when toluene was used as a solvent in the reaction of scheme 1 and scheme 2, evidently due to the insolubility of K_2CO_3 in toluene. When TBAB was used as catalyst, we did observe 62-66% conversion of substrate at 3 h of reaction time. In both solvents, the selectivity to tertiary amine was found to be 76-82%. We realized that performing the solid–liquid phase transfer reaction in toluene has the merit of easy separation of product because the latter settles down once the reaction is completed. Hence we have chosen toluene as solvent for the rest of the development and further study.

D. The effect of concentration of the PTC (TBAB)

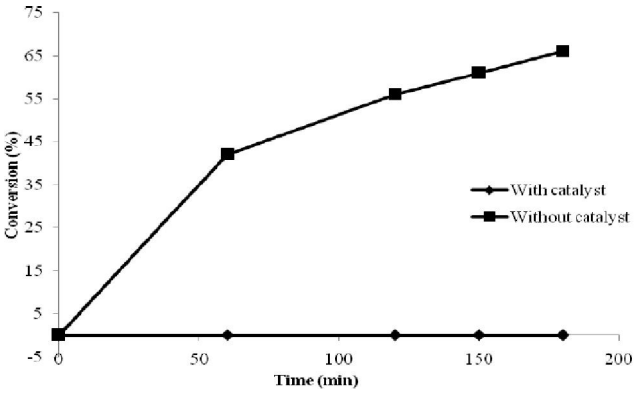
In a series of runs the concentration of the phase transfer catalyst has been varied from 0 to 2.5 mmol (Figure 4). The results clearly suggest that the conversion of the reaction is dependent on the catalyst concentration in a non-linear way reaching saturation at 0.45 mmol. Further increase of the concen-

tration of catalyst did not affect the conversion. This can be rationalized by the limited interfacial area available in the system that can transfer only certain amount of anions per unit time. Above a particular concentration of catalyst, further addition would not increase thesubstrate conversion any further.



Reaction conditions: Secondary amine (10 mmol); dihalide (5 mmol); K_2CO_3 (0.5 mmol); TBAB (0.5 mmol); water (5 ml); DMF (10 ml) and temperature (30°C).

Figure 2 : Role of solvent in condensation of Secondary amines and alkyl dichlorides

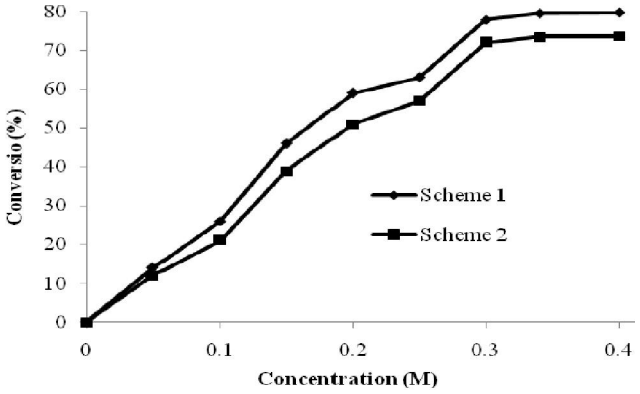


Reaction conditions: Secondary amine (10 mmol); dihalide (5 mmol); K_2CO_3 (0.5 mmol); TBAB (0.5 mmol); water (5 ml); toluene (10 ml) and temperature (30°C).

Figure 3 : Role of solvent in condensation of Secondary amines and alkyl dichlorides

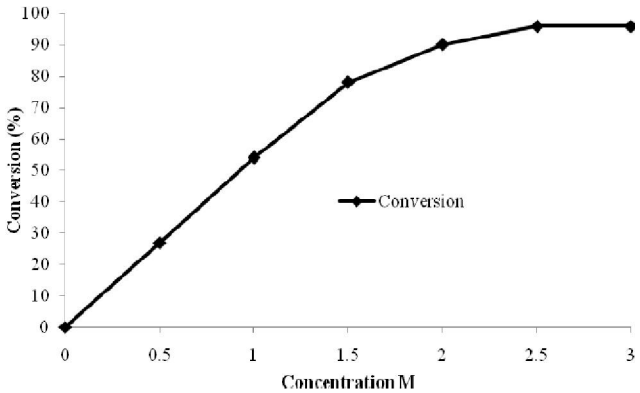
E. Effect of substrate concentration (Secondary amine)

Figure 5 shows the effects of secondary amines concentrations on the rate of formation of tertiary amines under identical condition to the previous experiments. It is evident that the conversion linearly depends on the concentration of secondary amines up to concentration of 22 mmol. When the molar ratio of substrate and alkyl dihalides was 1:1, the reaction was not complete and we found only 45% maximum conversion. When starting with a 2.2:1 molar ratio, rate of the reaction reached a maximum and the conversion was found to be 76% with 88% selectivity to tertiary amines.



Reaction conditions: secondary amine (10 mmol), alkyl chloride (5 mmol), K_2CO_3 (0.5 mmol), water (5 ml); toluene (10 ml),temperature (30°C) and time (3 h).

Figure 4 : Effect of the concentration of PTC in condensation of secondary amines and alkyl dichlorides

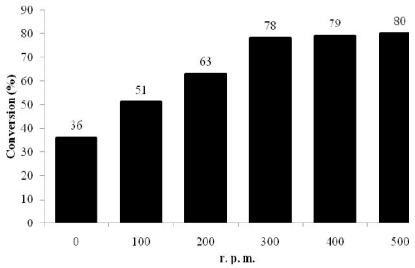


Reaction conditions: alkyl dihalides (5 mmol), K_2CO_3 (0.5 mmol), TBAB (0.5 mmol), water (5 ml); toluene (10 ml), temperature (30°C) and time (3 h).

Figure 5 : Influence on the concentration of secondary amine in condensation of secondary amines and alkyl dichlorides

F. The effect of steering speed on the reaction

At the following stage the effect of steering speed on conversion of the reaction has been studied and the results are shown in Figure 6. In interfacial mechanism, the rate of the reaction is linearly dependent on stirring rate of the reaction mixture from 50 to 2000 rpm whereas, in the extraction mechanism it is linearly dependent up to approximately 500 rpm where it levels off. In our system, above 200 rpm, the initial rate reached a maximum with respect to stirring proving that the ex-



Reaction conditions: secondary amine (10 mmol), alkyl chloride (5 mmol), K_2CO_3 (0.5 mmol), TBAB (0.5 mmol), water (5 ml); toluene (10 ml), temperature (30°C) and time (3 h).

Figure 6 : Condensation of secondary amines and alkyl dichlorides

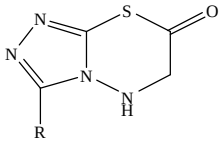
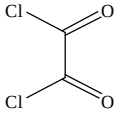
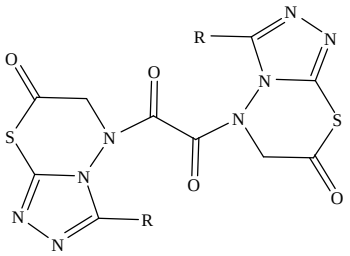
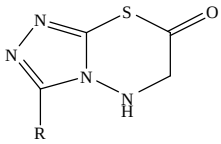
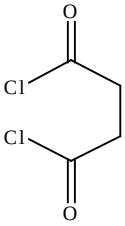
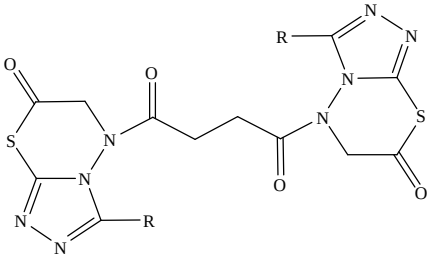
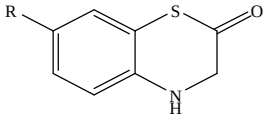
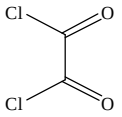
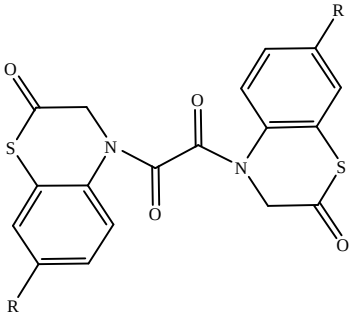
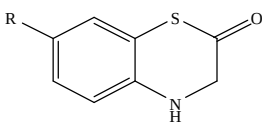
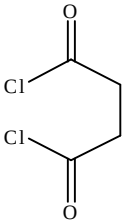
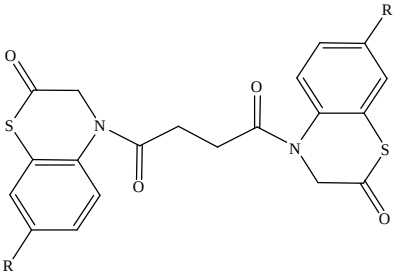
traction mechanism is taking place.

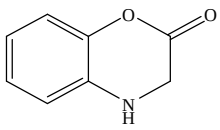
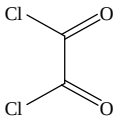
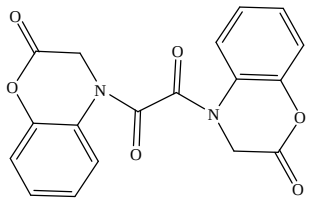
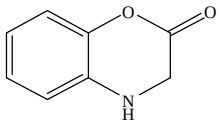
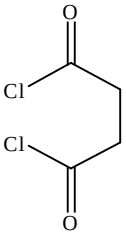
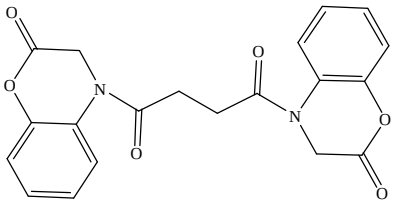
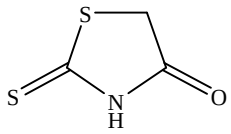
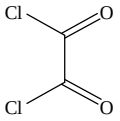
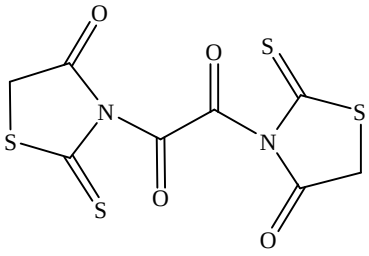
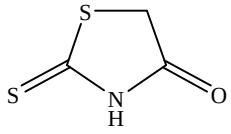
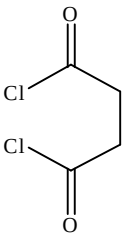
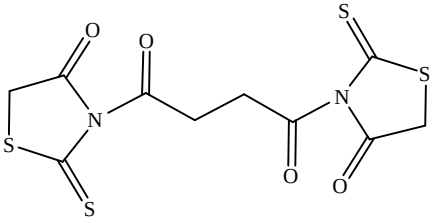
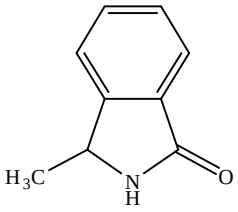
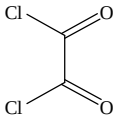
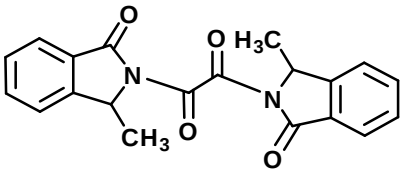
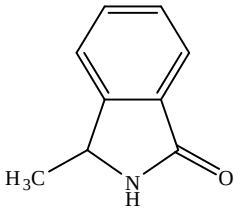
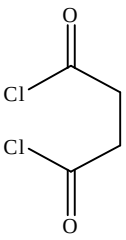
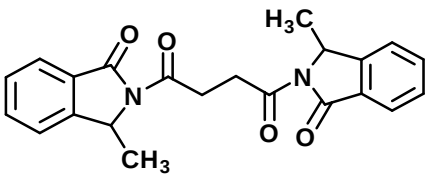
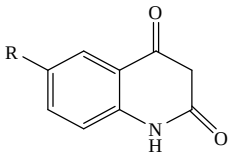
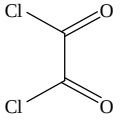
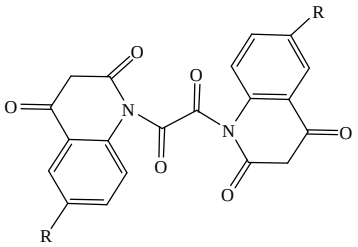
G. Synthesis of tertiary amines with different secondary amines

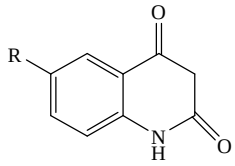
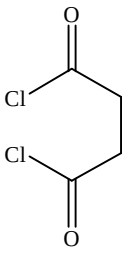
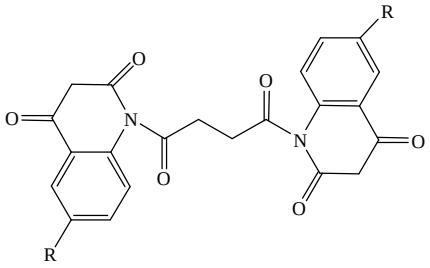
After the successful studies of the above condensation reactions we have developed procedures for the synthesis of tertiary amines based on the reactions studied in this work. The preparation of tertiary amines with various secondary amines and the isolated yield in all the examples are given in TABLE 3. The detailed procedures are reported in the experimental section.

TABLE 3 : Physical data of newly synthesized compounds

Condensation of secondary amines and alkyl dihalides to tertiary amines under PTC[a]

Entry	Substrate[b]	Dihalide	Product[c]	R	Yield (%)[d]	m. p. (°C)
1				1a= CH_3	52	37-40
				1b= C_2H_5	49	42-44
				1c= H	51	39-41
2				2a= CH_3	52	Semisolid
				2b= C_2H_5	56	Semisolid
				2c= H	58	Semisolid
3				3a= CH_3	54	49-52
				3b= H	52	55-58
				3c= Cl	49	72-75
				3d= Br	56	64-67
				3e= OCH_3	60	62-64
4				4a= CH_3	52	56-59
				4b= H	53	53-56
				4c= Cl	46	49-51
				4d= Br	50	48-51
				4e= OCH_3	55	53-55

Entry	Substrate[b]	Dihalide	Product[c]	R	Yield (%)[d]	m. p. °C)
5				--	49	72-75
6				--	56	46-48
7				--	56.	64-67
8				--	60	39-41
9				--	60	62-64
10				--	61	49-52
11				11a= CH_3 11b= H 11c= Cl 11d= Br 11e= OCH_3	48 51 52 50 49	78-80 85-87 88-91 67-70 72-75

Entry	Substrate[b]	Dihalide	Product[c]	R	Yield (%)[d]	m. p. (°C)
12				12a= CH_3	62	48-52
				12b= H	60	46-49
				12c= Cl	69	41-43
				12d= Br	67	42-44
				12e= OCH_3	65	46-49

[a]**The reaction condition:- substrate (20 mmol); dihalide (10 mmol); TBAB (1 mmol); K_2CO_3 (1 mmol); temperature (30°C); water (10 ml); toluene (20 ml); time (3 h);** [b]**Conversion of substrate was between 65 to 76 % (GC analysis);** [c]**Selectivity of product was between 75 to 84 % (GC analysis);** [d]**Isolated yield.**

Spectral and elemental analysis of compounds (1-12)

bis{3-methyl-1, 2, 4-triazolo[4, 5-b]-6-oxo-1, 3, 4-thiadiazin-4-yl}-1, 2-dioxo ethane (1a)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O), 1642, 1610 (C=N);

^{1}H NMR (TMS) δPPM: 2.49 (s, 6H, 2×CH_3), 4.54 (s, 4H, 2×CH_2);

^{13}C NMR: 10.15 (2×CH_3), 62.35 (2×CH_2), 149.74 (2×C=N), 165.49 (2×N=C-S), 169.19 (2×C=O), 174.23 (2×C=O);

m/z: 362 [M]$^-$, 181, 153, 64.

Elem. Anal Calcd for $C_{12}H_{10}N_8O_4S_2$: C 36.54; H 2.53; N 28.42; Found 36.51, 2.49, 28.37.

bis{3-ethyl-1, 2, 4-triazolo[4, 5-b]-6-oxo-1, 3, 4-thiadiazin-4-yl}-1, 2-dioxo ethane (1b)

IR (KBR) νcm^{-1}: 1660, 1705 (C=O), 1620, 1561(C=N);

^{1}H NMR (TMS) δPPM: 2.13 (t, 6H, 2×CH_3), 2.94 (q, 4H, 2×CH_2), 4.19 (s, 4H, 2×CH_2);

^{13}C NMR: 14.12 (2×CH_3), 19.84 (2×CH_2), 63.48 (2×CH_2), 148.92 (2×C=N), 161.14 (2×N=C-S), 171.48 (2×C=O), 176.23 (2×C=O);

m/z: 422 [M]$^-$, 211, 183, 155, 112, 64.

Elem. Anal Calcd for $C_{14}H_{14}N_8O_4S_2$: C 39.81; H 3.31; N 26.54; Found 39.77, 3.28, 26.49.

bis{3-methyl-1, 2, 4-triazolo[4, 5-b]5H 6-oxo-1, 3, 5-thiadiazin-4-yl}-1, 4-dioxo butane (2a)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O), 1642, 1610 (C=N);

^{1}H NMR (TMS) δPPM: 2.18 (s, 6H, 2×CH_3), 4.48 (s, 4H, 2×CH_2), 3.85 (t, 4H, 2×CH_2);

^{13}C NMR: 11.31 (2×CH_3), 32.19 (2×CH_2), 62.43 (2×CH_2), 159.13 (2×C=N), 166.08 (2×N=C-S), 170.28 (2×C=O), 174.78 (2×C=O);

m/z: 422 [M]$^-$, 211, 169, 81.

Elem. Anal Calcd for $C_{14}H_{14}N_8O_4S_2$: C 39.81; H 3.31; N 26.54; Found 39.78, 3.27, 26.51.

bis{3-ethyl-1, 2, 4-triazolo[4, 5-b]5H6-oxo-1, 3, 5-thiadiazin-4-yl}-1, 4-dioxo butane (2b)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O), 1642, 1610 (C=N);

^{1}H NMR (TMS) δPPM: 2.13 (t, 6H, 2×CH_3), 2.68 (q, 4H, 2×CH_2), 4.25(s, 4H, 2×CH_2), 4.61(t, 4H, 2×CH_2);

^{13}C NMR: 12.31 (2×CH_3), 18.51 (2×CH_2), 32.19 (2×CH_2), 63.47 (2×CH_2), 148.98 (2×C=N), 163.41 (2×N=C-S), 172.72 (2×C=O), 178.16 (2×C=O);

m/z: 450 [M]$^-$, 225, 183, 95.

Elem. Anal Calcd for $C_{16}H_{18}N_8O_4S_2$: C 42.66; H 4.00; N 24.88; Found 42.61, 3.96, 24.81.

bis[3H-2-oxo-7-methyl-1,4-benzothiazin-4-yl]1, 2-dioxo ethane (3a)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 2.23 (s, 6H, 2×CH_3), 3.78 (s, 4H, 2×CH_2), 7.08-7.98 (m, 6H, Ar-H);

^{13}C NMR: 22.48 (2×CH_3), 59.43 (2×CH_2), 122.48—138.41 (Aromatic C), 172.41 (2×C=O), 176.32 (2×C=O);

m/z: 412 [M]$^-$, 206, 178, 91, 90, 77.

Elem. Anal Calcd for $C_{20}H_{16}N_2O_4S_2$: C 58.25; H 3.88; N 6.79; Found 58.19, 3.81, 6.72.

bis[3H-2-oxo-1,4-benzothiazin-4-yl]1, 2-dioxo ethane (3b)

IR (KBR) νcm^{-1}: 1681, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 3.80 (s, 4H, 2×CH_2), 7.11-7.92 (m, 8H, Ar-H);

^{13}C NMR: 59.68 (2×CH_2), 121.72-138.24 (Aromatic C), 172.04 (2×C=O), 177.52 (2×C=O);

m/z: 398 [M]$^+$, 199, 182, 94, 77.

Elem. Anal Calcd for $C_{18}H_{12}N_2O_4S_2$: C 56.24; H 3.15; N 7.29; Found 56.12, 3.03, 7.13.

bis[3H-2-oxo-7-chloro-1,4-benzothiazin-4-yl]1, 2-dioxo ethane (3c)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 3.78 (s, 4H, 2×CH_2), 7.08-7.98 (m, 6H, Ar-H);

^{13}C NMR: 59.40 (2×CH_2), 122.14-137.67 (Aromatic C), 172.24 (2×C=O), 177.04 (2×C=O);

m/z: 432 [M]$^+$, 216, 188, 100.

Elem. Anal Calcd for $C_{18}H_{10}Cl_2N_2O_4S_2$: C 47.69; H 2.22; N 6.18; Found 47.51, 2.10, 6.12.

bis[3H-2-oxo-7-methoxy-1,4-benzothiazin-4-yl]1, 2-dioxo ethane (3e)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 3.88 (s, 6H, 2×OCH_3), 4.28 (s, 4H, 2×CH_2), 7.28-7.86 (m, 6H, Ar-H);

^{13}C NMR: 55.42 (2×OCH_3), 62.61 (2×CH_2), 121.42-136.21 (Aromatic C), 172.43 (2×C=O), 176.28 (2×C=O);

m/z: 444 [M]$^+$, 222, 194, 106.

Elem. Anal Calcd for $C_{20}H_{16}N_2O_4S_2$: C 54.05; H 3.60; N 6.30; Found 54.01, 3.52, 6.26.

bis[3H-2-oxo-7-methyl-1,4-benzothiazin-4-yl]1, 4-dioxo butane (4a)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 2.31 (s, 6H, 2×CH_3), 3.63 (s, 4H, 2×CH_2), 4.32 (d, 4H, 2×CH_2), 7.53-8.19 (m, 6H, Ar-H);

^{13}C NMR: 22.48 (2×CH_3), 33.15 (CH_2), 59.43 (2×CH_2), 122.48-138.41 (Aromatic C), 172.41 (2×C=O), 176.32 (2×C=O);

m/z: 420 [M]$^+$, 210, 196, 168, 91, 88.

Elem. Anal Calcd for $C_{22}H_{20}N_2O_4S_2$: C 60.00; H 4.54; N 6.36; Found 59.93, 4.48, 6.31.

bis[3H-2-oxol-1,4-benzothiazin-4-yl]1, 4-dioxo butane (4b)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 3.64 (s, 4H, 2×CH_2), 4.33 (d, 4H, 2×CH_2), 7.55-8.13 (m, 8H, Ar-H);

^{13}C NMR: 33.17 (CH_2), 59.49 (2×CH_2), 125.09-138.64 (Aromatic C), 173.01 (2×C=O), 176.79 (2×C=O);

m/z: 406 [M]$^+$, 203, 189, 161, 88, 77.

Elem. Anal Calcd for $C_{20}H_{16}N_2O_4S_2$: C 58.24; H 3.91; N 6.79; Found 58.18, 3.84, 6.71.

bis[3H-2-oxo-7-chloro-1,4-benzothiazin-4-yl]1, 4-dioxo butane (4c)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 3.63 (s, 4H, 2×CH_2), 4.31 (d, 4H, 2×CH_2), 7.52-8.13 (m, 6H, Ar-H);

^{13}C NMR: 33.16 (CH_2), 59.46 (2×CH_2), 123.47-139.38 (Aromatic C), 172.84 (2×C=O), 176.05 (2×C=O);

m/z: 440 [M]$^+$, 220, 206, 178, 90, 88.

Elem. Anal Calcd for $C_{20}H_{14}Cl_2N_2O_4S_2$: C 49.90; H 2.93; N 5.82; Found 49.83, 2.88, 5.71.

bis[3H-2-oxo-3-dihydro-7-methoxybenzothiazin-4-yl]1, 4-dioxo butane (4e)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 3.88 (t, 6H, 2×OCH_3), 3.97 (d, 4H, 2×CH_2), 4.28 (s, 4H, 2×CH_2), 7.28-7.86 (m, 6H, Ar-H);

^{13}C NMR: 31.93 (2×CH_2), 55.42 (2×OCH_3), 62.61 (2×CH_2), 121.42-136.21 (Aromatic C), 172.43 (2×C=O), 176.28 (2×C=O);

m/z: 436 [M]$^+$, 218, 204, 176, 108, 88.

Elem. Anal Calcd for $C_{22}H_{20}N_2O_6S_2$: C 55.93; H 4.23; N 5.93; Found 55.90, 4.20, 5.83.

bis[3H,4H-2oxo-1,4-benzoxazin-4-yl]1, 2-dioxo ethane (5)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 3.91 (s, 4H, 2x CH_2), 7.08-7.93 (m, 8H, Ar-H);

^{13}C NMR: 55.28 (2×CH_2), 123.48-139.19 (Aromatic C), 169.82 (2×C=O), 176.47 (2×C=O);

m/z: 352 [M]$^+$, 176, 148, 77, 74.

Elem. Anal Calcd for $C_{18}H_{12}N_2O_6$: C 61.36; H 3.40; N 7.95; Found 61.31, 3.34, 7.91.

bis[3H-2-oxo-1,4-benzoxazin-4-yl]1, 4-dioxo butane (6)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 2.89 (s, 4H, 2×CH_2), 4.13 (t, 4H, 2×CH_2), 7.13-7.89 (m, 6H, Ar-H);

^{13}C NMR: 32.21 (2×CH_2), 55.18 (2×CH_2), 131.21-138.29 (Aromatic C), 172.21 (2×C=O), 177.87 (2×C=O);

m/z: 404 [M]$^-$, 202, 188, 160, 86, 77.

Elem. Anal Calcd for $C_{22}H_{16}N_2O_6$: C 63.15; H 4.21; N 7.36; Found 63.11, 4.16, 7.31.

bis[2-thioxo-4-oxo-5-dihydro-thiazol-3-yl]1, 2-dioxo ethane (7)

IR (KBR) νcm^{-1}: 1245 (C=S), 1732 (C=O);

^{1}H NMR (TMS) δPPM: 3.53 (s, 4H, 2×CH_2);

^{13}C NMR: 40.13 (2×CH_2), 170.28 (2×C=O), 178.23 (2×C=O), 187.73 (C=S);

m/z: 320 [M]$^-$, 160, 133.

Elem. Anal Calcd for $C_8H_4N_2O_4S_4$: C 30.00; H 1.25; N 8.75; Found 29.96, 1.21, 8.72.

bis[5H 2-thioxo-4-oxo-5 -thiazol-3-yl]1, 4-dioxobutane (8)

IR (KBR) νcm^{-1}: 1245 (C=S), 1732 (C=O);

^{1}H NMR (TMS) δPPM: 2.63 (s, 4H, 2×CH_2), 4.28 (t, 4H, 2×CH_2);

^{13}C NMR: 33.41 (2×CH_2), 36.63 (2×CH_2), 176.19 (2×C=O), 178.23 (2×C=O), 188.69 (C=S);

m/z: 348 [M]$^-$, 174, 162, 134.

Elem. Anal Calcd for $C_{10}H_8N_2O_4S_4$: C 34.48; H 2.29; N 8.04; Found 34.41, 2.26, 8.00.

bis[3-methyl oxindol-2-yl]-1, 2-dioxo ethane (9)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 1.98 (d, 6H, 2×CH_3), 5.13 (q, 2H, 2×CH), 7.24-7.92 (m, 8H, Ar-H);

^{13}C NMR: 19.32 (2×CH_3), 42.35 (2×CH), 127.38-145.21 (Aromatic C), 169.72 (2×C=O), 174.13 (2×C=O);

m/z: 348 [M]$^-$, 174, 145, 107, 77.

Elem. Anal Calcd for $C_{20}H_{16}N_2O_4$: C 68.96; H 4.59; N 8.04; Found 68.91, 4.52, 8.00.

bis[3methyl oxindole-2-yl]-1, 4-dioxobutane (10)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 2.08(d, 6H, 2×CH_3), 4.13 (t, 4H, CH_2), 4.97 (q, 2H, 2×CH), 7.01-7.84 (m, 8H, Ar-H);

^{13}C NMR: 19.32 (2×CH_3), 33.14 (CH_2), 42.35 (2×CH), 127.38-145.21 (Aromatic C), 169.72 (2×C=O), 174.13 (2×C=O);

m/z: 376 [M]$^-$, 188, 174, 146, 107, 77.

Elem. Anal Calcd for $C_{22}H_{20}N_2O_4$: C 70.21; H 5.31; N 7.44; Found 70.18, 5.28, 7.39.

bis[2, 4-dioxo-3H -6-methylquinolin-1-yl]1, 2-dioxo ethane (11a)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 2.18 (s, 6H, 2×CH_3), 3.28 (s, 2H, 2×CH_2), 7.02-8.23 (m, 6H, Ar-H);

^{13}C NMR: 21.51 (2×CH_3), 62.63 (2×CH_2), 121.56-134.74 (Aromatic C), 167.52 (2×C=O), 171.25 (2×C=O), 173.80 (2×C=O);

m/z: 404 [M]$^-$, 202, 174, 91, 84.

Elem. Anal Calcd for $C_{22}H_{16}N_2O_6$: C 65.34; H 3.96; N 6.93; Found 65.29, 3.92, 6.90.

bis[2, 4-dioxo-3H-quinolin-1-yl]1, 2-dioxo ethane (11b)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 3.29 (s, 2H, 2×CH_2), 7.10-8.20 (m, 8H, Ar-H);

^{13}C NMR: 62.68 (2×CH_2), 121.72-135.54 (Aromatic C), 167.26 (2×C=O), 171.87 (2×C=O), 173.48 (2×C=O);

m/z: 390 [M]$^-$, 195, 167, 85, 77.

Elem. Anal Calcd for $C_{20}H_{12}N_2O_6$: C 63.83; H 3.21; N 7.44; Found 63.76, 3.15, 7.38.

bis[2, 4-dioxo-3H -6-chloroquinolin-1-yl]1, 2-dioxo ethane (11c)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 3.28 (s, 2H, 2×CH_2), 7.08-8.19 (m, 6H, Ar-H);

^{13}C NMR: 62.18 (2×CH_2), 122.11-135.83 (Aromatic C), 166.84 (2×C=O), 171.09 (2×C=O), 173.93 (2×C=O);

m/z: 424 [M]$^-$, 212, 184, 99, 85.

Elem. Anal Calcd for $C_{20}H_{10}Cl_2N_2O_6$: C 53.96; H 2.26; N 6.29; Found 53.89, 2.18, 6.22.

bis[3H 2, 4-dioxo-3-dihydro-6-methoxyquinolin-1-yl]1, 2-dioxoethane (11e)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 3.89 (d, 6H, 2×OCH_3), 3.68 (q, 2H, 2×CH_2), 7.02-7.48 (m, 6H, Ar-H);

^{13}C NMR: 61.34 (2×CH_2), 55.92 (2×OCH_3), 124.51-128.63 (Aromatic C), 163.78 (2×C=O),

169.78 (2×C=O), 172.70 (2×C=O);

m/z: 420 [M]$^{-}$, 210, 182, 99, 85.

Elem. Anal Calcd for $C_{22}H_{16}N_2O_8$: C 60.55; H 3.66; N 6.42; Found 60.49, 3.62, 6.38.

bis[3H 2, 4-dioxo-3-dihydro-6-methylquinolin-1-yl]1, 4-dioxobutane (12a)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 2.23 (s, 6H, 2×CH_3), 3.28 (s, 2H, 2×CH_2), 3.98 (t, 4H, 2×CH_2), 7.14-8.04 (m, 6H, Ar-H);

^{13}C NMR: 22.35 (2×CH_3), 31.85 (2×CH_2), 62.63 (2×CH_2), 121.56-134.74 (Aromatic C), 167.52 (2×C=O), 171.25 (2×C=O), 173.80 (2×C=O);

m/z: 432 [M]$^{-}$, 216, 202, 174, 91, 85, 77.

Elem. Anal Calcd for $C_{24}H_{20}N_2O_6$: C 66.66; H 4.62; N 6.48; Found 66.61, 4.58, 6.42.

bis[3H 2, 4-dioxo-3-dihydroquinolin-1-yl]1, 4-dioxobutane (12b)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 3.27 (s, 2H, 2×CH_2), 3.99 (t, 4H, 2×CH_2), 7.12-8.05 (m, 8H, Ar-H);

^{13}C NMR: 31.76 (2×CH_2), 62.60 (2×CH_2), 122.09-135.15 (Aromatic C), 167.47 (2×C=O), 171.85 (2×C=O), 173.73 (2×C=O);

m/z: 418 [M]$^{-}$, 209, 195, 167, 85, 82.

Elem. Anal Calcd for $C_{22}H_{16}N_2O_6$: C 65.34; H 3.99; N 6.93; Found 65.28, 3.93, 6.85.

bis[3H 2, 4-dioxo-3-dihydro-6-chloroquinolin-1-yl]1, 4-dioxobutane (12c)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 3.28 (s, 2H, 2×CH_2), 3.97 (t, 4H, 2×CH_2), 7.13-8.01 (m, 6H, Ar-H);

^{13}C NMR: 31.64 (2×CH_2), 62.56 (2×CH_2), 1212.07-134.43 (Aromatic C), 167.82 (2×C=O), 171.46 (2×C=O), 173.74 (2×C=O);

m/z: 452 [M]$^{-}$, 228, 212, 184, 99, 85.

Elem. Anal Calcd for $C_{22}H_{14}Cl_2N_2O_6$: C 55.83; H 2.98; N 5.92; Found 55.76, 2.91, 5.86.

bis[2, 4-dioxo-3-dihydro-6-methoxyquinolin-1-yl]1, 4-dioxobutane (12e)

IR (KBR) νcm^{-1}: 1680, 1732 (C=O);

^{1}H NMR (TMS) δPPM: 3.89 (s, 6H, 2×OCH_3), 3.68 (s, 2H, 2×CH_2), 4.13 (t, 4H, 2×CH_2), 7.02-7.48 (m, 6H, Ar-H);

^{13}C NMR: 33.15 (2×CH_2), 55.92 (2×OCH_3), 61.34 (2×CH_2), 124.51-128.63 (Aromatic C), 163.78 (2×C=O), 169.78 (2×C=O), 172.70 (2×C=O);

m/z: 448 [M]$^{-}$, 224, 210, 182, 97.

Elem. Anal Calcd for $C_{24}H_{20}N_2O_8$: C 62.06; H 4.31; N 6.03; Found 62.01, 4.28, 6.00.

CONCLUSIONS

Preparation of bis heterocycles has been studied by phase transfer catalytic route using TBAB and NaOH/ K_2CO_3 as PTC and base, respectively. In the first system (TBAB and NaOH) we found that the desired reaction to stall at a certain conversion, less yield and formation of impurities. In the second system (TBAB and K_2CO_3) where mild base potassium carbonate was used, we obtained maximum conversion of secondary amines with very high selectivity to the desired product. The different studies also suggest that the phase transfer catalysis is proceeding via an extraction mechanism. Using these novel platforms different tertiary amines have been successfully prepared and obtained with >90% isolated yields.

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