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Journal of Molecular Catalysis A: Chemical 237 (2005) 191–198
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
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Generation of 4,6-dimethyl-5-[2-(2-methylprop-1-enyl)-1*H*-benzimidazol-1-yl]pyrimidine-2(5*H*)-thiones under kinetically controlled phase transfer catalysis conditions

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Received 13 October 2004; received in revised form 30 April 2005; accepted 4 May 2005
Available online 13 June 2005

Abstract

The insertion of dimethylvinylidene carbene into azo moiety was investigated in order to synthesize 4,6-dimethyl-5-[2-(2-methylprop-1-enyl)-1*H*-benzimidazol-1-yl] pyrimidine-2(5*H*)-thiones [7a–j] under kinetically controlled phase transfer catalysis conditions. In situ generation of dimethylvinylidene carbene was facilitated by the interaction between 3-chloro-3-methyl-1-butyne and alkali at the interface. Interestingly, insertion of this carbene into the ─N═N─ linkage of 2,4-dimethyl-3-arylazo-6-thiopyrimidine afforded newly synthesized desired benzimidazolo pyrimidines. The reaction follows the pseudo-first order rate law. Rational mechanism of the reaction is proposed according to the experimental evidence. The compounds were synthesized in excellent yields (70–80%) and their structures were established on the basis of their IR and ^{1}H NMR spectral data.

Keywords: Phase transfer catalysis; Thiopyrimidine; Dimethylvinylidene carbene; Benzimidazole

1. Introduction

Phase transfer catalysis has an unquestionable industrial advantage and it offers an exceptional area for fundamental research. In fact phase transfer catalysis processes are economically competitive since they allow excellent reaction selectivities and substantially quantitative yields under mild conditions [1–4]. Since Jarrous [5] found that quaternary ammonium salts are an efficient catalyst for enhancing the two-phase reactions, many chemists have investigated phase transfer catalysis in numerous reactions such as substitution, displacement, condensation, epoxidation, ylide-mediated reaction, modification of polymer, etc. As a result, phase transfer catalysis is considered to have a great potential for industrial scale applications [6].

Several benzimidazole derivatives are pharmacologically important compounds as they have been found to possess antimicrobial, antiviral, antifungal, antiparasitic, anthelmintic, pesticidal, herbicidal and plant growth-regulating properties [7–10]. Moreover, benzimidazole nucleus has been found to be associated with various drugs applicable to different disease states as potent antihypertensive, antihistaminic, anticancerous, antiinflammatory, as gastric ulcer inhibitors, and for the treatment of cardiovascular diseases [11–16].

A systematic perusal of literature reveals that a number of methods have been utilized to prepare different benzimidazole derivatives under variable experimental conditions, viz. coupling of arene diazonium chloride with ethyl (1-ethoxycarbonyl)-benzimidazole-2-acetate [17], condensation of substituted benzothiazole with aromatic aldehydes in acetic acid medium [18], chloroacetylation followed by the ring closure of substituted 2-aminobenzothiazoles and 2-hydrazinothiazoles [19], reaction of 3-(2-methylbenzimidazol-1-yl)propanoic acid hydrazide with CS_2/KOH gave oxadiazole which underwent Mannich reaction to give substituted benzimidazole derivatives[20] and treatment of 7,12-dihydro[5,6][1,3]thioazepino[3,3-a] benzimidazole

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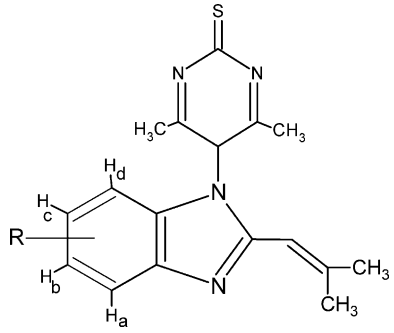
doi:10.1016/j.molcata.2005.05.003

6,6-dioxide with NaH under nitrogen atmosphere followed by addition of propiolate gave benzimidazole derivatives [21]. However, basically in all these methods strategy to design benzimidazole skeleton requires the insertion of C-2 into a precursor with ortho heteroatoms on a benzene ring. Moreover, most of the methods have not been found to be quite accessible from the view points of both yield and economics of the reaction. Thus, in order to satisfy this, herein, we would like to present an hitherto unreported, new approach to the synthesis of benzimidazole derivatives under phase transfer catalysis conditions considering insertion-cyclization of various azo compounds as the substrates.

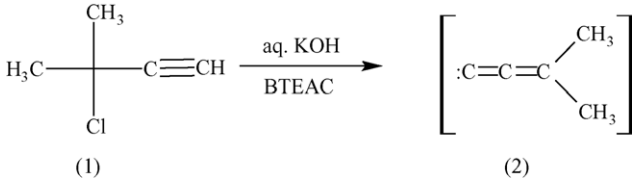
Thus, in continuation of our ongoing research and in quest of development of synthetic strategies for heterocyclic compounds [22–27], some novel benzimidazole derivatives i.e., 4,6-dimethyl-5-[2-(2-methylprop-1-enyl)-1*H*-benzimidazol-1-yl]pyrimidine-2-(5*H*)-thiones [7a–j] have been synthesized. It was achieved by the insertion of a reactive intermediate, viz. dimethylvinylidene carbene into the −N=N− moiety of various 2,4-dimethyl-3-arylazo-6-thiopyrimidines. Dimethylvinylidene carbene is first generated from the reaction of 3-chloro-3-methyl-1-butyne and an alkali compound, which on further reaction with arylazopyrimidine yields appropriately substituted 4,6-dimethyl-5-[2-(2-methylprop-1-enyl)-1*H*-benzimidazol-1-yl]pyrimidine-2(5*H*)-thiones-[7a–j].



2. Experimental

2.1. Materials

All reagents, including potassium hydroxide, benzyltriethylammonium chloride, 2-methyl-3-butyne-2-ol, benzene, ethanol and other reagents used were of analytical grade chemicals. 3-Chloro-3methyl-1-butyne was prepared by the method of Hennion and Nelson [28] (Scheme 1).



Scheme 1.

2.2. Procedure

^{1}H NMR spectra of 4,6-dimethyl-5-[2-(2-methylprop-1-enyl)-1*H*-benzimidazol-1-yl] pyrimidine-2 (5*H*)-thione [7a–j] were recorded on a Bruker Advance DRX 300 MHz instrument using TMS as internal standard. Infrared spectra were run on a Perkin Elmer model 377spectrophotometer in KBr pellets. The contents of product and reactant were measured by high-performance liquid chromatography. The analysis conditions were: Shimadzu LC 10AS, L7 phenyl packing column, acetonitrile + methanol + water (50:30:20) mobile phase, UV Shimadzu ASVP detector at 254 nm and 1 ml/min flow rate. Melting points were taken in open capillary tubes using an electric melting point apparatus and are uncorrected. Elemental analyses were performed on a Perkin Elmer equipment.

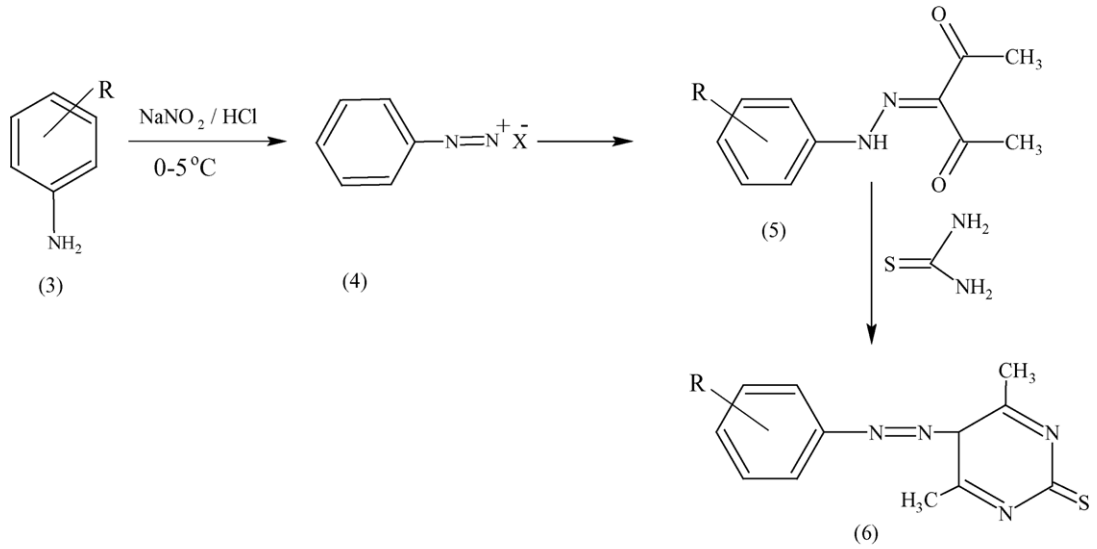
2.2.1. Synthesis of 2,4-dimethyl-3-arylazo-6-thiopyrimidine [6a–j]

In a 250 ml round bottom flask equimolar quantities of 1-ethoxy-2-arylhydra zonobutane-1,3-diones and thiourea were taken together in the presence of freshly prepared sodium ethoxide solution (2.3 g sodium metal in 50 ml absolute ethanol). These were stirred for 3–4 h at room temperature to obtain crystals of required 2,4-dimethyl-3-arylazol-6-thiopyrimidine [6a–j] in good yield (75–80%), filtered at the pump and dried. Systematic methodology of synthetic pathway is depicted in Scheme 2.

2.2.2. Synthesis of 4,6-dimethyl-5-[2-(2-methylprop-1-enyl)-1H-benzimidazol-1-yl] pyrimidine-2(5H)-thione [7a–j] in two-phase solution

In a 100 ml three-necked bolt head flask fitted with a dropping funnel and a mechanical stirrer, a mixture of 50% of aqueous potassium hydroxide (15 ml), benzyltriethylammonium chloride (BTEAC) (1.32 mg, 2.5 mmol), benzene (5 ml) was taken and stirred thoroughly for 30 min. To this, a pertinent 2,4-dimethyl-3-arylazo-6-thiopyrimidine (2.5 mmol) [6a–j] was added slowly and stirred for further 5–7 h under nitrogen atmosphere. While stirring was going on, 3-chloro-3-methyl-1-butyne (25 mmol) in benzene (5 ml) was added slowly to the mixture. The content were diluted with water (120 ml), followed by extraction with ether (120 ml) to afford the crude product. It was purified on an alumina column (benzene as eluent) so as to yield finally 4,6-dimethyl-5-[2-(2-methylprop-1-enyl)-1*H*-benzimidazol-1-yl] pyrimidine-2(5*H*)-thione [7a–j]. An overview of mechanistic steps is depicted in Scheme 3.

2.2.2.1. 4,6-dimethyl-5-[2-(2-methylprop-1-enyl)-1H-benzimidazol-1-yl]pyrimidine-2(5H)-thione [7a]. IR (ν cm^{-1}); 3114 (C–H, sp^2), 2950 (C–H, sp^3), 1689 (C=S), 1628 (C=C/C=N), 1621, 1530, 1447 (C..... C, ring str), 950, 852, 749 (sub. phenyl). ^{1}H NMR (δ ppm): 1.40 (s, 6H, 2× CH_3, isopropenyl), 2.4 (s, 6H, 2× CH_3), 4.6 (s, CH, methine), 7.6 (d, 2H, Ha, Hd), 7.01 (t, 2H, Hb, Hc), 8.35



where R = as shown in scheme 5.

Scheme 2.

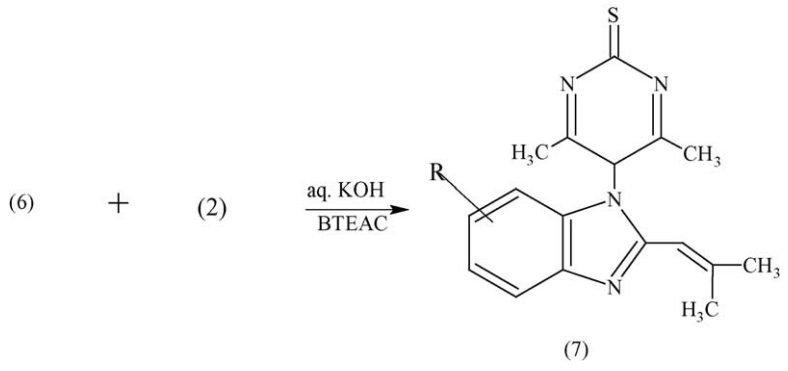
(s, CH, pyrimidine). M.P.: 135–36 °C; Yield: 79 (%); Found (Calcd) (%) C: 65.78 (65.80); H: 5.84 (5.87); N: 18.05 (18.08); S: 10.33 (10.35).

2.2.2.2. 4,6-Dimethyl-5-[2-(2-methylprop-1-enyl)-1H-benzimidazol-1-yl]-6-chloro-pyrimidine-2(5H)-thione [7b]. IR (ν cm^{-1}); 3122 (C–H, sp^2), 2950 (C–H sp^3), 1689 (C=S), 1628 (C=C/C=N), 1618, 1534, 1462 (C..... C, ring str), 952, 852, 749 (sub. phenyl), 605 (C–Cl). ^{1}H NMR (δ ppm): 1.45 (s, 6H, 2× CH_3, isopropenyl), 2.35 (s, 6H, 2× CH_3), 5.1 (s, CH, methine), 7.4 (d, CH, Ha), 7.1 (t, CH, Hb), 7.6 (d, CH, Hc), 8.36 (s, CH, pyrimidine). M.P.: 130–31 °C; Yield: 72 (%); Found (Calcd) (%) C: 59.21 (59.25); H: 4.97 (5.00); N: 16.25 (16.28); S: 9.30 (9.35).

2.2.2.3. 4,6-Dimethyl-5-[2-(2-methylprop-1-enyl)-1H-benzimidazol-1-yl]-6-hydroxy-pyrimidine-2(5H)-thione [7c]. IR (ν cm^{-1}); 3350 (O–H), 3117 (C–H, sp^2), 2951 (C–H. sp^3), 1689 (C=S), 1625 (C=C/C=N), 1621, 1530, 1448 (C..... C, ring str), 950, 849, 744 (sub. phenyl). ^{1}H NMR (δ ppm): 1.42 (s, 6H, 2× CH_3, isopropenyl), 2.40 (s, 6H, 2× CH_3), 5.2 (s, CH, methine), 7.34 (d, CH, Ha), 7.42 (t, CH, Hb), 7.53 (d, CH, Hc), 8.38 (s, CH, pyrimidine). M.P: 126–27 °C; Yield: 75 (%); Found (Calcd) (%) C: 62.55 (62.59); H: 5.56 (5.60); N: 17.16 (17.20); S: 9.82 (9.85).

2.2.2.4. 4,6-Dimethyl-5-[2-(2-methylprop-1-enyl)-1H-benzimidazol-1-yl]-5-ethyl-pyrimidine-2(5H)-thione [7d]. IR (ν cm^{-1}); 3111 (C–H, sp^2), 2951 (C–H, sp^3), 1681 (C=S), 1628 (C=C/C=N), 1624, 1535, 1445 (C..... C, ring str), 951, 854, 740 (sub. phenyl). ^{1}H NMR (δ ppm): 0.9 (t, 3H, CH_3, J = 6.5 Hz), 1.45 (s, 6H, 2× CH_3, isopropenyl), 2.35 (s, 6H, 2× CH_3), 4.5 (q, 2H, CH_2, J = 6.5 Hz), 5.23 (s, CH, methine), 7.36 (d, CH, Ha), 7.41 (d, CH, Hb), 7.47 (s, CH, Hc), 8.32 (s, CH, pyrimidine). M.P.: 110–11 °C; Yield: 80 (%); Found (Calcd) (%) C; 67.42 (67.46); H: 6.55 (6.58); N: 16.55 (16.59); S: 9.47 (9.50).

2.2.2.5. 4,6-Dimethyl-5-[2-(2-methylprop-1-enyl)-1H-benzimidazol-1-yl]-5-nitro-pyrimidine-2(5H)-thione [7e]. IR (ν cm^{-1}); 3114 (C–H, sp^2), 2940 (C–H, sp^3), 1685 (C=S), 1630 (C=C/C=N), 1621, 1530, 1447 (C..... C, ring



Scheme 3.

str), 1334 (NO_2), 950, 852, 749 (sub. phenyl). ^{1}H NMR (δ ppm): 1.46 (s, 6H, 2× CH_3, isopropenyl), 2.35 (s, 6H, 2× CH_3), 5.1 (s, CH, methine), 7.38 (d, CH, Ha), 7.42 (t, CH, Hb), 7.67 (s, CH, Hc), 8.34 (s, CH, pyrimidine). M.P.: 122–23 °C; Yield: 79 (%); Found (Calcd) (%) C: 57.45 (57.48); H: 4.82 (4.85); N: 19.70 (19.73); S: 9.02 (9.05).

2.2.2.6. 4,6-Dimethyl-5-[2-(2-methylprop-1-enyl)-1H-benzimidazol-1-yl]-4-methyl-pyrimidine-2(5H)-thione [7f]. IR (ν cm^{-1}); 3114 (C–H, sp^2), 2950 (C–H, sp^3), 1689 (C=S), 1628 (C=C/C=N), 1621, 1530, 1447 (C..... C, ring str), 950, 852, 750 (sub. phenyl). ^{1}H NMR (δ ppm): 1.46 (s, 6H, 2× CH_3, isopropenyl), 2.51 (s, 9H$_{13}$, 2× CH_3, aromatic ring), 5.1 (s, CH, methine), 7.31 (d, CH, Ha), 7.25 (t, CH, Hb), 7.18 (d, CH, Hc), 8.31 (s, CH, pyrimidine). M.P.: 131–32 °C, Yield: 73 (%), Found (Calcd) (%) C: 66.63 (66.65); H: 6.21 (6.24); N: 17.27 (17.30); S: 9.08 (9.12).

2.2.2.7. 4,6-Dimethyl-5-[2-(2-methylprop-1-enyl)-1H-benzimidazol-1-yl]-5-methoxy-pyrimidine-2(5H)-thione [7g]. IR (ν cm^{-1}); 3114 (C–H, sp^2), 2950 (C–H, sp^3), 1682 (C=S), 1630 (C=C/C=N), 1625, 1533, 1445 (C..... C, ring str), 955, 848, 759 (sub. phenyl). ^{1}H NMR (δ ppm): 1.38 (s, 6H, 2× CH_3, isopropenyl), 2.42 (s, 6H, 2× CH_3, aromatic ring), 3.43 (s, 3H, OCH_3), 7.15 (d, CH, Ha), 7.00 (d, CH, Hb), 7.78 (s, CH, Hd), 8.37 (s, CH, pyrimidine). M.P.: 130–31 °C, Yield: 78 (%), Found (Calcd) (%) C: 63.50 (63.56); H: 5.92 (5.95); N: 16.46 (16.49), S: 9.05 (9.09).

2.2.2.8. 4,6-Dimethyl-5-[2-(2-methylprop-1-enyl)-1H-benzimidazol-1-yl]-4-carboxy-pyrimidine-2(5H)-thione [7h]. IR (ν cm^{-1}); 3413 (O–H), 3118 (C–H, sp^2), 2955 (C–H sp^3), 1730 (C=O), 1686 (C=S) 1620 (C=C/C=N), 1625, 1535, 1444 (C..... C, ring str), 950, 852, 722 (sub. phenyl). ^{1}H NMR (δ ppm): 1.44 (s, 6H, 2× CH_3, isopropenyl), 2.53 (s, 6H, 2× CH_3, aromatic ring), 7.32 (d, CH, Hb), 7.15 (t, CH, Hc), 7.05 (d, CH, Hd), 8.39 (s, CH, pyrimidine), 10.34 (s, COOH). M.P.: 125–26 °C; Yield: 81 (%); Found (Calcd) (%): C: 61.00 (61.02); H: 5.12 (5.15); N: 15.81 (15.83); S: 9.05 (9.08).

2.2.2.9. 4,6-Dimethyl-5-[2-(2-methylprop-1-enyl)-1H-benzimidazol-1-yl]-6-ethoxy-pyrimidine-2(5H)-thione [7i]. IR (ν cm^{-1}); 3104 (C–H, sp^2), 2940 (C–H, sp^3), 1681 (C=S), 1625 (C=C/C=N), 1618, 1530, 1447 (C..... C, ring str), 950, 852, 749 (sub. phenyl). ^{1}H NMR (δ ppm): 1.1 (t, 3H, CH_3–CH_2, J = 6.2 Hz), 1.49 (s, 6H, 2× CH_3, isopropenyl), 2.45 (s, 6H, 2× CH_3, aromatic ring), 3.85 (q, 2H, CH_2–CH_3, J = 6.2 Hz), 7.10 (d, CH, Ha), 7.29 (t, CH, Hb), 7.60 (d, CH, Hc), 8.33 (s, CH, pyrimidine). M.P.: 120–21 °C, Yield: 74 (%), Found (Calcd) (%) C: 64.38 (64.41), H: 6.26 (6.30), N: 15.81 (15.84), S: 9.05 (9.09).

2.2.2.10. 4,6-Dimethyl-5-[2-(2-methylprop-1-enyl)-1H-benzimidazol-1-yl]-4-chloro-pyrimidine-2(5H)-thione [7j]. IR (ν cm^{-1}); 3122 (C–H, sp^2), 2950 (C–H, sp^3), 1689 (C=S), 1628 (C=C/C=N), 1618, 1534, 1462 (C..... C, ring str), 952, 852, 749 (sub. phenyl), 605 (C–Cl). ^{1}H NMR (δ ppm): 1.45 (s, 6H, 2× CH_3, isopropenyl), 2.45 (s, 6H, 2× CH_3, aromatic ring), 5.40 (s, CH, methine), 7.41 (d, CH, Hb), 7.11 (t, CH, Hc), 7.01 (d, CH, Hd); M.P.: 111–12 °C, Yield: 73 (%); Found (Calcd) (%); C: 59.21 (59.25); H: 4.97 (5.00); N: 16.25 (16.28); S: 9.30 (9.35).

3. Reaction mechanism and kinetic model

3-Chloro-3-methyl-1-butyne anion ($C_5H_7Cl^-$), which can be converted to dimethylvinylidene carbene (:C=C=C(CH$_3$)$_2$),is generated from 3-chloro-3-methyl-1-butyne in presence of alkaline solution. The organic compound 2,4-dimethyl-3-arylazo-6-thiopyrimidine ($C_{12}H_{12}N_4S$) does not react with dimethylvinylidene carbene to form benzimidazole derivatives because of easy hydrolysis of dimethylvinylidene carbene. Therefore, the addition of phase transfer catalyst to the aqueous solution to generate carbene in organic solution is essential. An intermediate is formed from the reaction of 3-chloro-3-methyl-1-butyne and benzyltriethylammonium chloride (PTC) at the interface of two phases. This intermediate is then treated with 2-ethoxy-3-arylazo-4-methyl-6-thiopyrimidine to produce finally 4,6-dimethyl-5-[2-(2-methylprop-1-enyl)-1*H*-benzimidazol-1-yl]pyrimidine-2-(5*H*)-thiones [7a–j] as depicted in Scheme 4.The reaction mechanism is thus proposed as

$$C_5H_7Cl + KOH_{(aq)} \rightleftharpoons C_5H_7Cl^-K^+_{(interface)} + H_2O_{(aq)}$$

$$C_5H_7Cl^-K^+_{(interface)} + PhCH_2N^+Et_3Cl^-_{(interface)} \rightleftharpoons PhCH_2N^+Et_3C_5H_7Cl^-_{(org)} + KCl_{(aq)}$$

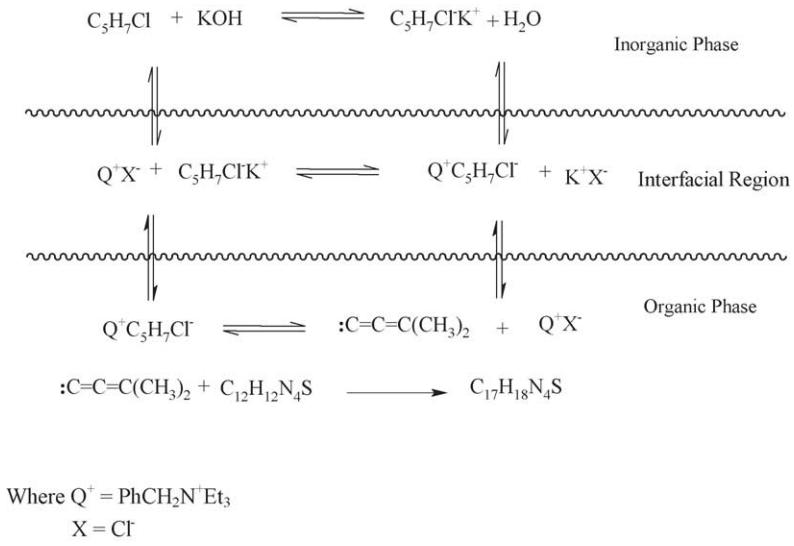
$$PhCH_2N^+Et_3C_5H_7Cl^-_{(org)} \rightleftharpoons : C = C = C(CH_3)_2 + PhCH_2N^+Et_3Cl^-_{(org)}$$

$$C_{12}H_{12}N_4S + : C = C = C(CH_3)_2 \xrightarrow{k} C_{17}H_{18}N_4S_{(org)}$$

where k represents the intrinsic rate constant for the reaction of dimethylvinylidene carbene (:C=C=C(CH$_3$)$_2$) and 2,4-dimethyl-3-arylazo-6-thiopyrimidine ($C_{12}H_{12}N_4S$) to produce the benzimidazole derivatives ($C_{17}H_{18}N_4S$) in the organic solution. Thus the change rate of 2,4-dimethyl-3-arylazo-6-thiopyrimidine due to reaction is expressed as

$$\frac{-d[C_{12}H_{12}N_4S]}{dt} = k[C_{12}H_{12}N_4S]_0[: C=C=(CH_3)_2]_0 \quad (1)$$

Dimethylvinylidene carbene was not detectable during the reaction; however the concentration of dimethylvinylidene



Scheme 4.

carbene was kept at a constant throughout the reaction Thus, Eq. (1) can be written as

$$\frac{-d[C_{12}H_{12}N_4S]}{dt} = k_{app}[C_{12}H_{12}N_4S]_0 \quad (2)$$

where

$$k_{app} = k[:=C=C(CH_3)_2]_0 \quad (3)$$

Therefore, the reaction of 2,4-dimethyl-3-arylazo-6-thiopyrimidine and dimethylvinylidene carbene is irreversible and is expressed as

$$C_{12}H_{12}N_4S \xrightarrow{k_{app}} C_{17}H_{18}N_4S \quad (4)$$

As shown in Eq. (4), the change rates of these components is

$$\frac{-d[C_{12}H_{12}N_4S]}{dt} = -k_{app}[C_{12}H_{12}N_4S]_0 \quad (5)$$

$$\frac{-d[C_{17}H_{18}N_4S]}{dt} = k_{app}[C_{12}H_{12}N_4S]_0 \quad (6)$$

Eq. (5) is integrated as

$$[C_{12}H_{12}N_4S]_0 = [C_{12}H_{12}N_4S]_{0,i} \exp(-k_{app}, t) \quad (7)$$

where $[C_{12}H_{12}N_4S]_{0,i}$ is the initial concentration of 2,4-dimethyl-3-arylazo-6-thiopyrimidine.The conversion of 2,4-dimethyl-3-arylazol-6-thiopyrimidine, '*X*' can be defined as

$$X = 1 - \frac{[C_{12}H_{12}N_4S]_0}{[C_{12}H_{12}N_4S]_{0,i}} \quad (8)$$

Thus Eq. (7) is expressed as

$$-\ln(1 - X) = k_{app}t \quad (9)$$

The value of k_{app} can be obtained by plotting the experimental data of $-\ln(1 - X)$ versus time.

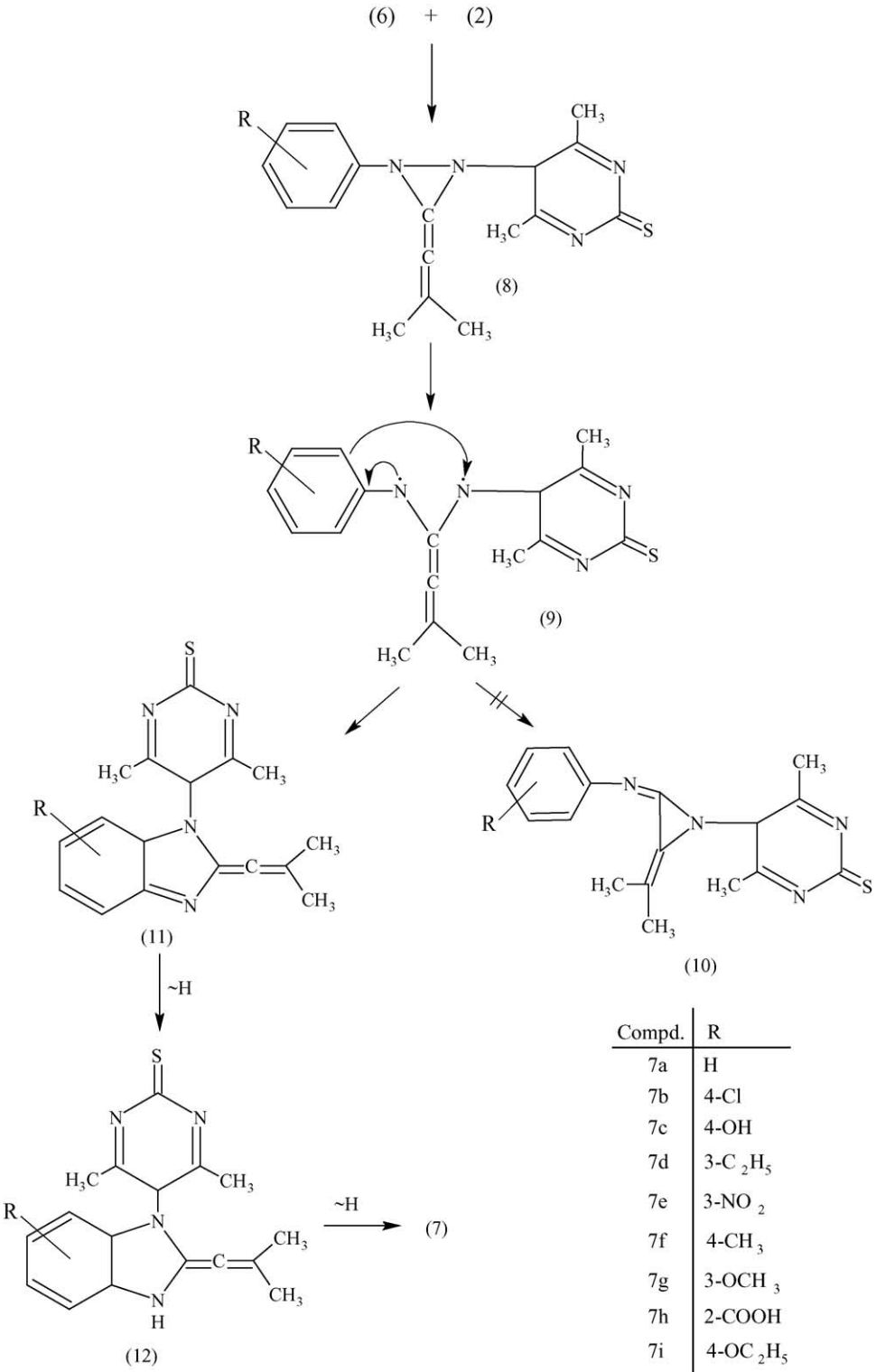
4. Results and discussion

The experimental results show a material balance between the reactant and the product, i.e. the consumption of the amount of reactant (2,4-dimethyl-3-arylazo-6-thiopyrimidine) parallels the generation of the amount of 4,6-dimethyl-5-[2-(2-methylprop-1-enyl)-1*H*-benzimidazol-[1-yl]pyrimidine-2(5*H*)-thione [7a–j]. No by products were formed during or after the reaction. In the absence of phase transfer catalyst no final product was found from the reaction of 3-chloro-3-methyl-1-butyne and potassium hydroxide solution for 2 h. The main reason is that dimethylvinylidene carbene can be easily hydrolyzed in aqueous solution. Under this situation, no dimethylvinylidene carbene can react with 2,4-dimethyl-3-arylazol-6-thiopyrimidine to produce the desired product. However the reaction is dramatically enhanced by adding a small amount of catalyst (BTEAC). The formation of 7a–j was established by the chemical conversion on catalytic hydrogenation (10% Pd–C) to hexahydro derivatives (8).

The formation of 4,6-dimethyl-5-[2-(2-methylprop-1-enyl)-1*H*-benzimidazol-[1-yl] pyrimidine-2(5*H*)-thione [7a–j] in the above reaction could be rationalized by an initial trap of dimethylvinylidene carbene (2) by 2,4-dimethyl-3-arylazol-6-thiopyrimidine [6a–j] to give corresponding adduct (9), which should be thermally labile compared with the carboxylic analogue because of much smaller bond dissociation energy of N–N than C–C [29], and hence rearranged to [7a–j] probably via (11) and (12) as delineated in Scheme 5.

4.1. Effect of stirring speed

The effect of stirring speed on the rate of dimethylvinylidene carbene addition to 2,4-dimethyl-3-arylazol-6-thiopyrimidine was studied in the rate of 100–1000 rpm in



Compd.	R
7a	H
7b	4-Cl
7c	4-OH
7d	3-C_2H_5
7e	3-NO_2
7f	4-CH_3
7g	3-OCH_3
7h	2-COOH
7i	4-OC_2H_5
7j	2-Cl

Scheme 5.

the presence of 2.5 mmol of catalyst and 15 ml of 50% aqueous potassium hydroxide. It is observed that at 200 rpm the reaction rate is comparatively slower than at higher stirring speeds. The increased rates are attributed to the increase in the interfacial area. Similar observation was reported by Chiellius et al. [30] for the heterogeneous ethylation of phenyl acetonitrile in aqueous–organic medium in the presence of tetrabutylammoniumbromide [31].

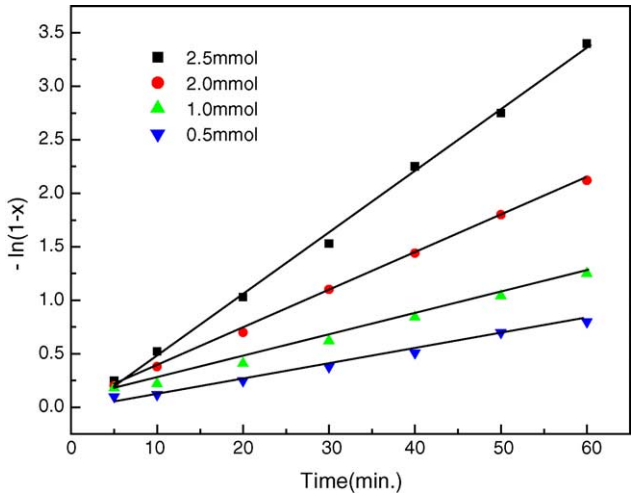


Fig. 1. A plot of $-\ln(1-x)$ vs. time of different amounts of catalyst BTEAC; 25 mmol of 2,4 dimethyl-3-arylazol-6-thiopyrimidine; 15 ml of 50% KOH; 800 rpm; 25 °C.

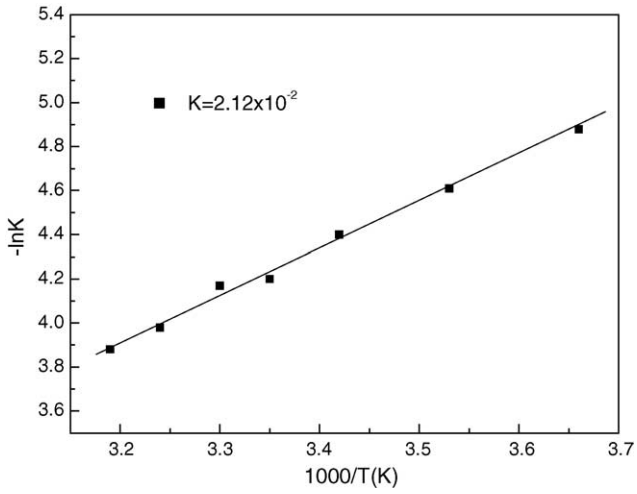


Fig. 3. A plot of apparent rate constants vs. various reaction temperatures of catalyst BTEAC; 25 mmol of 2,4-dimethyl-3-arylazol-6-thiopyrimidine; 15 ml of 50% KOH; 800 rpm; k: 2.12×10^{-2}; E: 9.70 kcal/mol.

4.2. Effect of catalyst amount

The effect of variation in the amount of phase transfer catalyst on the rate of dimethylvinylidene carbene addition to 2,4-dimethyl-3-arylazol-6-thiopyrimidine was studied by varying the amount of catalyst from 0.5 to 2.5 mmol. The rate of reaction is directly proportional to the amount of catalyst added. A plot of observed rate constant against time of the reaction gives the straight line over a wide range of concentration and its slope is found to be 0.057 (Fig. 1). The increased rate is due to the increase in the number of active sites.

4.3. Effect of temperature

The effect of temperature on the rate of reaction was studied by employing 2.5 mmol of the catalyst at 800 rpm taking 15 ml of 50% KOH. The kinetic profile was studied under various reaction temperatures, viz. 20, 25, 30 and 35 °C. As expected, the rate increases with the increase in temperature as shown in Fig. 2. Moreover, the reaction follows a pseudo-first order rate law .As depicted in Fig. 3, the activation energy data deduced from the plot of $-\ln k$ versus $1/T$ is found to be 9.70 kcal/mol.

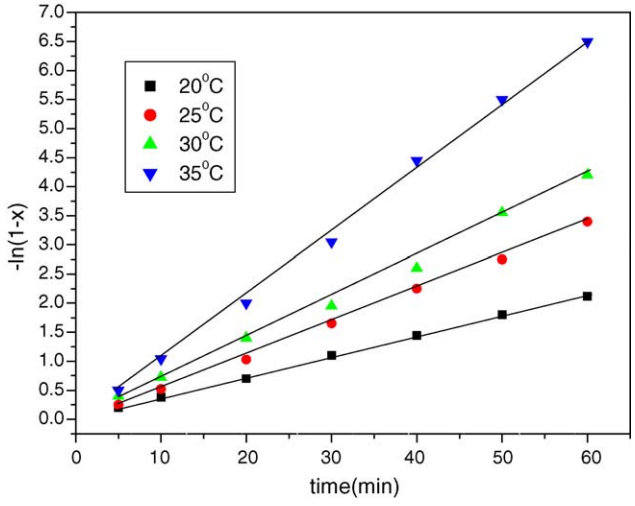


Fig. 2. A plot of $-\ln(1-x)$ vs. time of catalyst BTEAC at different temperatures; 25 mmol of 2,4-dimethyl-3-arylazol-6-thiopyrimidine; 15 ml of 50% KOH; 800 rpm.

5. Conclusion

In this work, a new route to the design of the benzimidazole skeleton has been devised following the phase transfer methodology. A high yield of product and a high reaction rate from the insertion followed by cyclization of 2,4-dimethyl-3-arylazo-6-thiopyrimidine was obtained as a result of interaction between 3-chloro-3-methyl-1-butyne and 2,4-dimethyl-3-arylazol-6-thiopyrimidine in an alkaline solution catalyzed by benzyltriethylammonium chloride. According to the experimental evidence, the reaction follows an interfacial reaction mechanism, in which the reaction rate is highly dependent on the stirring speed up to 800 rpm. An optimum reaction rate is obtained using 2.5 mmol of catalyst. The conversion of 4,6-dimethyl-5-[2-(2-methyl prop-1-enyl)-1*H*-benzimidazol-[1-yl]pyrimidine-2(5*H*)-thione [7a–j] decreases with the increase in the amount of 2,4-dimethyl-3-arylazol-6-thiopyrimidine and 3-chloro-3-methyl-1-butyne. The reason is that both the molar ratio of catalyst to 2,4-dimethyl-3-arylazol-6-thiopyrimidine and the concentration of dimethylvinylidene carbene decreases with the increase in the amount of 2,4-dimethyl-3-arylazol-6-thiopyrimidine and 3-chloro-3-methyl-1-butyne. However, the reaction rate increases with the increase in the amount of catalyst and alkaline concentration.

Acknowledgement

Authors are thankful to CentralDurg Research Institute, Lucknow for providing analytical facilities.

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