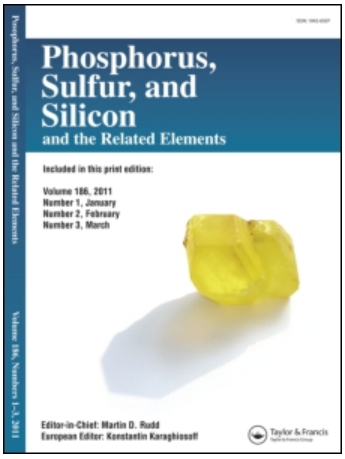


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# Bismuth Chloride Mediated Synthesis, Antimicrobial, and Anti-Inflammatory Activities of New 4-Aryl-2-Amino Thiazoles

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*Synthesis of 4-aryl-2-Amino thiazoles* ***(3a–u)****,* ***(4a–c)****, and* ***(5a–c)*** *was achieved from the reaction of 4-butyl phenacyl chlorides* ***(2a–c)*** *with N-substituted thioureas, in the presence of Bismuth Chloride. The antimicrobial and anti-inflammatory activities of the final products were also studied.*

**Keywords** 4-aryl-2-amino thiazoles; 4-butyl phenacyl chlorides; Bismuth chloride

## INTRODUCTION

Aminothiazole derivatives exhibit anaesthetic,[1] bactericidal and fungicidal activites.[2] It is also reported that the derivatives of fluro-aryl thiazoles are very active, not only as antiarthritic agents, but act as immunomodulators.[3] Aryl amino thiazoles also possess cardio tonic and antiallergic activities.[4]

The wide spectrum of biological activities of amino thiazoles inculcated enthusiasm in us, to synthesize a series of new 4-aryl-2-aminothiazoles and to study their anti-microbial and anti-inflammatory activities. In the present program, the target 4-aryl-2-aminothiazole derivatives were synthesized by the condensation of substituted phenacyl chlorides with different thioureas. The cyclizing agents tried were poly phosphoric acid (PPA), poly phosphoric ester (PPE), but the yields were not satisfactory and the reaction needs prolonged heating for completion. Therefore, there was a need to search for a better cyclizing agent or catalyst with regards to toxicity, handling, easy availability,

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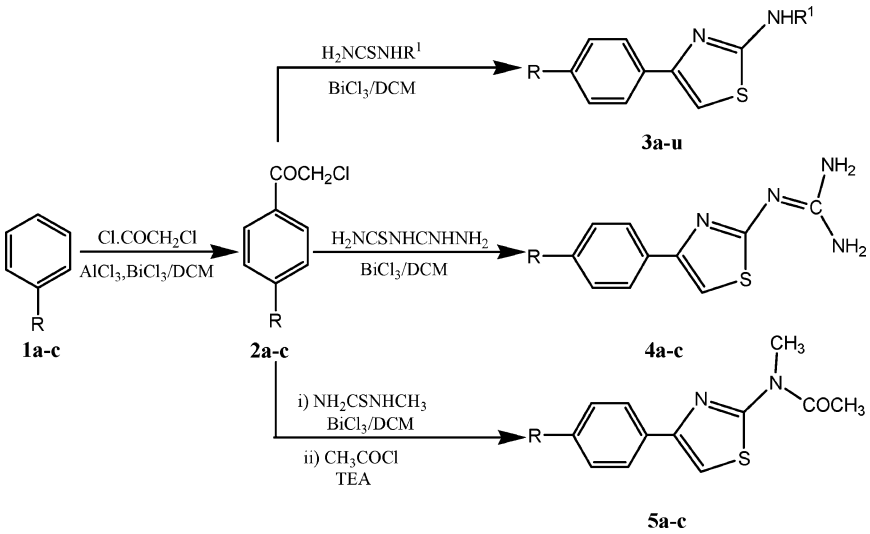



**SCHEME 1** **a** = n-butyl; **b** = isobutyl; and **c** = ter-butyl.

and operational simplicity. Bismuth (III) halides are inexpensive, relatively non-toxic, and insensitive to small amounts of water and environmentally benign reagents, which have been used as mild Lewis catalysts for an array of synthetic organic reactions.[5]

## RESULTS AND DISCUSSION

In continuation of our work on synthesis of new heterocyclics,[6] we are gratified to report the Bismuth chloride mediate synthesis and biological activity of new-4-aryl-2-amino thiazoles herein. It is interesting to note that the yields increased and the reaction times were reduced when $BiCl_3$ in DCM was employed (Scheme I).

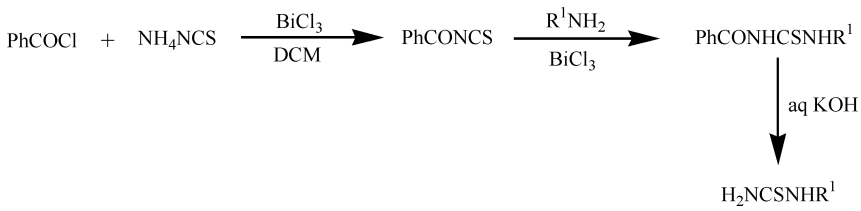
When Guanyl derivative of thiourea reacted with phenacyl chlorides, compounds **4a–c** were obtained. Similarly, compounds **5a–c** were obtained by the acetylation of the products formed when N-methyl urea reacted with compounds **2a–c**. When we attempted to synthesize the unreported p-butyl phenacyl chlorides (**2a–c**), by Friedel-Crafts electrophilic attack of $ClCH_2COCl$ upon butyl benzenes in the presence of $AlCl_3$, mixtures of O- & P- substituted products were obtained. However, the yields of Para products increased up to 90–95% by adding catalytic amounts of $BiCl_3$. N-substituted thioureas[7](Scheme 2) were prepared in the present scheme by an improved method, using $BiCl_3$ catalyst.

**TABLE I Yields and Reaction Times of 4-Aryl-2-N-substituted Amino Thiozoles with Different Cyclizing Agents**

| | | | % Yield (Reaction Time in hours) | | |
|---|---|---|---|---|---|
| Compound | R | $R^1$ | By using PPA | By using PPE | By using $BiCl_3$/DCM |
| **3a** | n-butyl | H | 30 (8) | 42 (6) | 68 (1.0) |
| **3b** | iso-butyl | H | 44 (6) | 51 (4) | 90 (1.5) |
| **3c** | tert-butyl | H | 37 (5) | 48 (6) | 97 (1.5) |
| **3d** | n-butyl | $CH_3$ | 23 (7) | 36 (5) | 58 (1.5) |
| **3e** | iso-butyl | $CH_3$ | 35 (8) | 42 (7) | 78 (1.0) |
| **3f** | tert-butyl | $CH_3$ | 27 (6) | 48 (5) | 81 (2.0) |
| **3g** | n-butyl | Ph | 21 (7) | 16 (4) | 52 (2.0) |
| **3h** | iso-butyl | Ph | 23 (8) | 31 (5) | 58 (1.5) |
| **3i** | tert-butyl | Ph | 28 (7) | 35 (5) | 60 (1.5) |
| **3j** | n-butyl | $CH_2Ph$ | 30 (8) | 36 (5) | 68 (2.0) |
| **3k** | iso-butyl | $CH_2Ph$ | 29 (7) | 27 (6) | 57 (1.5) |
| **3l** | tert-butyl | $CH_2Ph$ | 32 (6) | 35 (4) | 65 (1.0) |
| **3m** | n-butyl | $CH_2CH_2Ph$ | 28 (7) | 37 (5) | 70 (2.0) |
| **3n** | iso-butyl | $CH_2CH_2Ph$ | 25 (6) | 32 (4) | 60 (1.0) |
| **3o** | tert-butyl | $CH_2CH_2$ Ph | 42 (7) | 38 (5) | 54 (2.0) |
| **3p** | n-butyl | $CH_2CH_2$-$C_6H_4(OCH_3)P$ | 38 (8) | 42 (6) | 77 (2.0) |
| **3q** | iso-butyl | $CH_2CH_2$-$C_6H_4(OCH_3)P$ | 18 (5) | 27 (5) | 54 (2.5) |
| **3r** | tert-butyl | $CH_2CH_2$-$C_6H_4(OCH_3)P$ | 22 (6) | 29 (4) | 62 (2.0) |
| **3s** | n-butyl | $COCH_3$ | 27 (7) | 32 (4) | 51 (1.5) |
| **3t** | iso-butyl | $COCH_3$ | 23 (8) | 44 (5) | 55 (2.0) |
| **3u** | tert-butyl | $COCH_3$ | 32 (6) | 48 (6) | 64 (1.5) |
| **4a** | n-butyl | — | 11 (5) | 19 (6) | 42 (15) |
| **4b** | iso-butyl | — | 17 (7) | 22 (8) | 35 (1.0) |
| **4c** | tert-butyl | — | 28 (8) | 19 (6) | 35 (1.5) |
| **5a** | n-butyl | — | 22 (8) | 20 (6) | 41 (1.5) |
| **5b** | iso-butyl | — | 16 (7) | 21 (5) | 38 (2.0) |
| **5c** | tert-butyl | — | 26 (6) | 23 (6) | 52 (1.0) |



The IR Spectra of Aryl amino thiazoles exhibit absorption band around 3300–3100 $cm^{-1}$ due to NH bond. The IR spectral band around $1580 \pm 10$ $cm^{-1}$ is due to C= =N and C= =C stretching vibrations. The $^1H$ NMR chemical shifts around $\delta$ 7.3–$\delta$ 7.9 indicate the aromatic protons of 4-aryl systems. The hetero aromatic proton of the thiazole ring is present at $\delta$ 5.5–5.7.[8] The NH proton appears as a broad singlet around $\delta$ 5.2–5.4, which disappears by $D_2O$ exchange. The proton present in the n-butyl side chain of the aromatic ring produces characteristic signals. The benzylic protons appear as triplet near $\delta$ 2.5–2.7. The end methyl of n-butyl is observed as triplet at $\delta$ 0.8–1.0.




**SCHEME 2**

Similarly, characteristic signals are observed in $^1$HNMR for isobutyl side chain. The benzylic protons appear as a doublet around $\delta$ 2.5–2.6. The methyl proton is observed as a multiplet around $\delta$ 1.8–2.0. The gem dimethyls are seen around $\delta$ 0.9–1.0 as a doublet. The ter-butyl protons are observed as a singlet at $\delta$ 2.2–2.5 and the N-$CH_3$ protons appear as a singlet at $\delta$ 3.8. The mass spectra show intense molecular ion peaks along with prominent M + 2 peaks. The general fragmentation includes the loss of alkyl side chains.



## CONCLUSION

In conclusion, $BiCl_3$ acts as an efficient catalyst for the synthesis of 4-aryl-2-amino thiazoles. $BiCl_3$ catalyst is much better than PPA and PPE, in terms of increased yields, decreased reaction timing, ease of operation, and in non-toxic character.

## ANTIMICROBIAL ACTIVITY

The elementary antibacterial[9] and antifungal[10] screening tests were conducted following the standard methods (Table II). The gram-negative bacteria used were *Escherichia coli (E.C)and pseudomonas aeruginosa (P.A),* and *Bacillus subtilis (B.S) and Staphylococcus aureus (S.A)* were the gram-positive bacteria used. Ciprofloxacin (CF) was used as reference standard for antibacterial activity. The fungus used for testing was *Candida albicans (C.A)*. Fluconazole (FZ) was employed as a reference standard for anti-fungal activity.

All the substituted thiozoles exhibit lower antibacterial activity when compared to the standard. But, many of these final compounds exhibit strong anti-fungal activity of comparable range with that of the reference standard namely, the Fluconazole.

## ANTI-INFLAMMATORY ACTIVITY

Screening test of all the substituted thiazoles for anti-inflammatory activity was conducted by carrageenin-induced rat-paw edema model,[11]

**TABLE II Antimicrobial Activity Studies of 4-Aryl-2-N-Substituted Amino Thiozoles**

| Compound | Concentration $\mu$g/ml | Antibacterial activity zone diameter (mm) | | | | Anti-fungal activity zone diameter (mm) |
|---|---|---|---|---|---|---|
| | | BS | SA | EC | PA | CA |
| **3a** | 100 | 8.5 | 8.0 | 11.5 | 12.0 | 9.5 |
| | 500 | 9.0 | 8.5 | 12.0 | 13.0 | 10.0 |
| **3b** | 100 | 8.5 | 8.5 | 13.0 | 12.5 | 10.0 |
| | 500 | 9.0 | 9.0 | 13.5 | 13.5 | 10.5 |
| **3c** | 100 | 8.0 | 8.0 | 12.0 | 13.0 | 11.0 |
| | 500 | 8.5 | 8.5 | 12.5 | 13.5 | 11.5 |
| **3d** | 100 | 8.5 | 8.0 | 11.5 | 12.0 | 12.0 |
| | 500 | 9.0 | 9.0 | 12.5 | 13.0 | 12.5 |
| **3e** | 100 | 8.0 | 9.0 | 11.5 | 12.0 | 11.0 |
| | 500 | 8.5 | 9.5 | 12.0 | 13.0 | 11.5 |
| **3f** | 100 | 8.0 | 9.0 | 11.0 | 12.0 | 11.0 |
| | 500 | 8.5 | 9.5 | 12.5 | 12.5 | 12.0 |
| **3g** | 100 | 9.0 | 8.0 | 12.0 | 12.0 | 8.5 |
| | 500 | 9.5 | 8.5 | 13.0 | 12.5 | 10.0 |
| **3h** | 100 | 8.5 | 8.0 | 11.0 | 12.0 | 9.0 |
| | 500 | 9.0 | 9.0 | 12.0 | 13.0 | 10.0 |
| **3i** | 100 | 8.0 | 9.0 | 11.0 | 12.0 | 11.0 |
| | 500 | 8.5 | 9.5 | 11.5 | 12.5 | 11.5 |
| **3j** | 100 | 7.0 | 7.5 | 10.5 | 11.5 | 10.0 |
| | 500 | 7.5 | 8.0 | 11.0 | 12.5 | 10.5 |
| **3k** | 100 | 8.0 | 7.5 | 11.0 | 12.0 | 9.5 |
| | 500 | 8.5 | 8.5 | 11.5 | 12.5 | 10.0 |
| **3l** | 100 | 8.0 | 8.0 | 11.5 | 12.0 | 9.0 |
| | 500 | 9.0 | 8.5 | 12.0 | 13.0 | 10.0 |
| **3m** | 100 | 8.5 | 8.0 | 11.0 | 12.0 | 10.0 |
| | 500 | 9.5 | 8.5 | 11.5 | 12.5 | 10.5 |
| **3n** | 100 | 8.0 | 8.5 | 11.0 | 12.0 | 9.0 |
| | 500 | 8.5 | 9.5 | 12.0 | 13.0 | 9.5 |
| **3o** | 100 | 9.0 | 9.5 | 11.5 | 11.0 | 11.0 |
| | 500 | 9.5 | 9.5 | 12.0 | 12.0 | 11.5 |
| **3p** | 100 | 8.0 | 8.5 | 11.5 | 11.0 | 8.5 |
| | 500 | 8.5 | 8.5 | 12.5 | 12.5 | 9.0 |
| **3q** | 100 | 7.5 | 8.0 | 10.5 | 11.0 | 10.0 |
| | 500 | 7.5 | 8.5 | 11.0 | 11.5 | 11.0 |
| **3r** | 100 | 8.0 | 7.5 | 9.0 | 11.0 | 8.0 |
| | 500 | 9.0 | 8.5 | 9.5 | 11.5 | 9.0 |
| **3s** | 100 | 8.0 | 8.0 | 9.0 | 11.0 | 9.5 |
| | 500 | 8.5 | 9.0 | 9.5 | 12.0 | 10.0 |
| **3t** | 100 | 7.5 | 8.5 | 11.5 | 12.0 | 12.0 |
| | 500 | 8.0 | 9.5 | 12.0 | 12.5 | 12.5 |
| **3u** | 100 | 8.0 | 9.0 | 11.0 | 11.5 | 11.5 |
| | 500 | 8.5 | 9.5 | 12.0 | 12.5 | 12.0 |

(*continued on next page*)

**TABLE II Antimicrobial Activity Studies of 4-Aryl-2-N-Substituted Amino Thiozoles (*Continued*)**

| Compound | Concentration $\mu$g/ml | Antibacterial activity zone diameter (mm) | | | | Anti-fungal activity zone diameter (mm) |
|---|---|---|---|---|---|---|
| | | BS | SA | EC | PA | CA |
| **4a** | 100 | 6.5 | 7.0 | 11.0 | 11.5 | 10.0 |
| | 500 | 7.5 | 8.0 | 12.0 | 12.5 | 10.5 |
| **4b** | 100 | 8.0 | 8.0 | 11.5 | 11.0 | 12.0 |
| | 500 | 8.5 | 8.5 | 12.0 | 12.0 | 12.5 |
| **4c** | 100 | 7.5 | 8.0 | 11.5 | 11.0 | 12.0 |
| | 500 | 8.5 | 9.0 | 12.5 | 12.0 | 11.5 |
| **5a** | 100 | 7.0 | 7.5 | 11.0 | 11.5 | 10.5 |
| | 500 | 8.0 | 8.5 | 12.0 | 12.5 | 11.0 |
| **5b** | 100 | 8.0 | 8.5 | 11.5 | 11.0 | 9.0 |
| | 500 | 9.0 | 9.5 | 12.0 | 12.0 | 9.5 |
| **5c** | 100 | 7.5 | 8.0 | 11.0 | 11.5 | 10.0 |
| | 500 | 8.0 | 9.0 | 12.0 | 12.0 | 11.0 |
| CF | 100 | 23.5 | 10.5 | 24.0 | 19.5 | — |
| | 500 | 28.5 | 13.5 | 28.0 | 23.5 | — |
| FZ | 100 | — | — | — | — | 12.0 |
| | 500 | — | — | — | — | 13.5 |



by employing 0.5% carboxymethyl cellulose as vehicle. The percent reduction in inflammation was calculated with respect to vehicle treated control values (Table III). All these new molecules exhibit moderate anti-inflammatory activity.

## EXPERIMENTAL

The melting points were uncorrected. CHNSO analysis was done by Carlo Erba EA 1108 automatic elemental analyzer. I.R Spectra were recorded by Shimadzu FTIR-8108 instrument. $^1$H NMR spectra were recorded on Varian Gemini FT NMR 200 MHz instrument. Mass spectra were recorded on Hewlett Packard MSEM-5989 spectrometer.

### Preparation of New Phenacyl Chlorides (2a–c)—General Procedure

4-Substituted benzene (50.0 mmol) was added to a stirred mixture of anhydrous aluminum chloride (60.0 mmol), Bismuth trichloride 3.153 g (10.0 mmol) and chloroacetyl chloride 11.29 g (100.0 mmol) in Dichloromethane (125 ml) at 0–5°C. The reaction mass was stirred at 0–5°C for 3–4 h. After the reaction was over, it was poured into ice-cold

**TABLE III Anti-inflammatory Activity**

| S. no. | Compound | Dose mg/kg/po | Inhibition (%) |
|---|---|---|---|
| 1. | 3a | 100 | 21 |
| 2. | 3b | 100 | 20 |
| 3. | 3c | 100 | 30 |
| 4. | 3d | 100 | 12 |
| 5. | 3e | 100 | 18 |
| 6. | 3f | 100 | 16 |
| 7. | 3g | 100 | 20 |
| 8. | 3h | 100 | 24 |
| 9. | 3i | 100 | 33 |
| 10. | 3j | 100 | 16 |
| 11. | 3k | 100 | 12 |
| 12. | 3l | 100 | 15 |
| 13. | 3m | 100 | — |
| 14. | 3n | 100 | 31 |
| 15. | 3o | 100 | 15 |
| 16. | 3p | 100 | 26 |
| 17. | 3q | 100 | 19 |
| 18. | 3r | 100 | — |
| 19. | 3s | 100 | 18 |
| 20. | 3t | 100 | 11 |
| 21. | 3u | 100 | — |
| 22. | 4a | 100 | 30 |
| 23. | 4b | 100 | 32 |
| 24. | 4c | 100 | 35 |
| 25. | 5a | 100 | 40 |
| 26. | 5b | 100 | 41 |
| 27. | 5c | 100 | 48 |



water to decompose in aluminum chloride. The organic layer was separated and dichloromethane was completely distilled off under vacuum to get the corresponding phenacyl chloride.

### *4-(N-butyl) Phenacyl Chloride (2a)*

86%. (Found: C, 68.41; H, 7.12; Cl, 16.85%. $C_{12}H_{15}OCl$ requires C, 68.40; H, 7.12; Cl, 16.86%). **IR (KBr, cm$^{-1}$):** 1701–1685(C=O), 1605, (C=C). **PMR (CDCl$_3$, $\delta$ ppm):** 7.85 (d, 2H, Ar-H ortho to C=O), 7.25 (d, 2H, Ar-H meta to C=O), 4.7 (s, 2H, $COCH_2$), 2.6–2.7 (t, 2H, benzylic), 1.5–1.7 (m, 2H, -$CH_2$), 1.2–1.5 (m, 2H, -$CH_2$), 0.85–1.0 (t, 3H, $CH_3$). **Mass (m/z):** 210($M^+$; 3), 161 (M-$CH_2Cl$, 100), 133 (161-CO, 9).

### *4-(Isobutyl) Phenacyl Chloride (2b)*

87%. (Found: C, 68.42; H, 7.11; Cl, 16.87%. $C_{12}H_{15}OCl$ requires C, 68.40; H, 7.12; Cl, 16.86%). **IR (KBr, cm$^{-1}$):** 1701–1685(C=O), 1605, (C=C). **PMR (CDCl$_3$, $\delta$ ppm):** 7.9 (d, 2H, Ar-H ortho to C=O), 7.3

(d, 2H, Ar-H meta to C═O), 4.7 (S, 2H, $COCH_2$), 2.5–2.6 (d, 2H, benzylic), 1.8–2.0 (m, 1H, -$CH(CH_3)_2$, 0.9–1.0 (d, 6H, -$CH_3$). **Mass (m/z):** 210($M^+$; 3), 167 (M- $C_3H_7$, 3) 161 (M-$CH_2Cl$, 100), 133 (161-CO, 10).

### *4-(Ter-butyl) Phenacyl Chloride (2c)*

92%. (Found: C, 68.39; H, 7.13; Cl, 16.87% $C_{12}H_{15}OCl$ requires C, 68.40; H, 7.12; Cl, 16.86%). **IR (KBr, cm$^{-1}$):** 1701–1685(C═O), 1605, (C═C). **PMR ($CDCl_3$, $\delta$ ppm):** 7.9 (d, 2H, Ar-H ortho to C═O), 7.5 (d, 2H, Ar-H meta to C═O), 4.7 (s, 2H, $COCH_2$), 1.35 (s, 9H, $CH_3$). **Mass (m/z):** 210($M^+$; 2), 195 (M- $CH_3$, 15), 161 (M-$CH_2Cl$, 100), 146(161- $CH_3$, 15), 133(161-CO, 5).

## Preparation of 2-Amino-4-Aryl Thiazole Derivatives (3a-u): General Procedure



Thiourea 3.80 6g (50.0 mmol), phenacyl chloride (50.0 mmol) along with $BiCl_3$ 3.153 g (10.0 mmol) and 60 ml of Dichloromethane was charged and the reaction mixture was stirred for an additional 30 min at the same temperature. The temperature was raised to reflux, and the reaction mixture was maintained at reflux for 1 to 2 h. Then, it was cooled to ambient temperature and poured into ice-cold water. The product was then separated by ether extraction and evaporation. The product was washed with 10% sodium hydroxide solution followed by water until washing were neutral to $P^H$ and then dried. The product were recrystallized from aqueous methanol.

### *2-Amino-4-/(4-N-butyl) Phenyl/Thiazole (3a)*

(68%), m.p. 234–238°C. (Found C, 67.27; H, 6.90; N, 12.07; S, 13.77%. $C_{13}H_{16}N_2S$ requires C, 67.24; H, 6.89; N, 12.06; S, 13.79%). (**IR cm$^{-1}$):** 3363–3069 (NH), 1640–1620 (C═C, C═N), 1575, 1560. **PMR ($CDCl_3$, $\delta$ ppm):** 8.5–9.3 (br, s, 2H, $NH_2$), 7.7 (d, 2H, Ar-H, ortho to thiazole), 7.30 (d, 2H, ortho to butyl), 7.2 (s, 1H, thiazole-H), 2.6–2.8 (t, 2H, benzylic), 1.5–1.7 (m, 2H, $CH_2$), 1.25–1.45 (m, 2H, $CH_2$), 0.8–1.0 (t, 3H, $CH_3$). **Mass (m/z):** 232 ($M^+$; 68), 203 (M-$C_2H_5$, 4), 189 (M-$C_3H_7$, 100).

### *2-Amino-4-/(4-Iso-butyl) Phenyl/Thiazole (3b)*

(90%), m.p. 112%116°C. (Found C, 67.25; H, 6.90; N, 12.03; S, 13.76%. $C_{13}H_{16}N_2S$ requires C, 67.24; H, 6.89; N, 12.06; S, 13.79%). (**IR cm$^{-1}$):** 3313–3107, 1630, 1598, and 1536. **PMR ($CDCl_3$, $\delta$ ppm):** 5.2–5.4 (br, s, 2H, $NH_2$), 7.7 (d, 2H, Ar-H, ortho to thiazole), 7.20 (d, 2H, ortho to iso butyl), 6.7 (s, 1H, thiazole-H), 2.5 (d, 2H, benzylic), 1.8 (m, 1H, $CH(CH_3)_2$), 0.9 (d, 6H, $CH_3$). **Mass (m/z):** 232 ($M^+$; 47), 217 (M-$CH_3$, 40), 203 (M-$C_2H_5$, 4), 189 (M-$C_3H_7$, 100), 147 (189-NCN $H_2$, 13).

### *2-Amino-4-/(4-Ter-butyl) Phenyl/Thiazole (3c)*

(97%), m.p. 228–230°C. (Found C, 67.26; H, 6.89; N, 12.0; S, 13.77%. $C_{13}H_{16}N_2S$ requires C, 67.24; H, 6.89; N, 12.06; S, 13.79%). **(IR $cm^{-1}$):** 3450–3100, 1628, 1606, 1570, 1530. **PMR (DMSO-$d_6$, $\delta$ ppm): 8**.2–8.6 (br, s, 2H, $NH_2$ disappeared with $D_2O$), 7.7 (d, 2H, Ar-H, ortho to thiazole), 7.45 (d, 2H, ortho to ter-butyl), 7.1 (s, 1H, thiazole-H), 1.3 (s, 9H, $CH_3$). **Mass (m/z):** 232 ($M^+$; 60), 217 (M-$CH_3$, 100), 175 (M-$C_4H_9$, 5), 142 (217-$HNCSNH_2$, 15).

### *4-/(4-N-butyl) Phenyl/-2-(N-methyl Amino) Thiazole (3d)*

(58%), m.p. 93–95°C. (Found C, 68.31; H, 7.30; N, 11.39; S, 12.98%. $C_{14}H_{18}N_2S$ requires C, 68.29; H, 7.31; N, 11.38; S, 13.00%). **IR ($cm^{-1}$):** 3210–3190, 1589, 1570, and 1491. **PMR ($CDCl_3$, $\delta$ ppm):** 7.7 (d, 2H, Ar-H ortho to thiazole), 7.2 (d, 2H, Ar-H ortho to butyl), 6.65(s, 1H, thiazole-H), 6.15 (br, s, 1H, NH), 2.95(s, 3H, N-$CH_3$), 2.65(t, 2H, benzylic), 1.5–1.7(m, 2H, $CH_2$), 1.3–1.5(m, 2H, $CH_2$), 0.9–1.0(t, 3H, $CH_3$), **Mass (m/z):** 246($M^+$; 72), 218 (M-$C_2H_4$, 8), 203(M-$C_3H_7$, 100), 147 (203-$NCNHCH_3$, 8).

### *4-/(4-Iso-butyl) Phenyl/-2-(N-methyl Amino) Thiazole (3e)*

(78%), m.p. 118–119°C. (Found C, 68.27; H, 7.33; N, 11.36; S, 13.02%. $C_{14}H_{18}N_2S$ requires C, 68.29; H, 7.31; N, 11.38; S, 13.00%). **IR ($cm^{-1}$):** 3268, 1581, 1570, 1492, 1465. **PMR ($CDCl_3$, $\delta$ ppm):** 7.7 (d, 2H, Ar-H ortho to thiazole), 7.15 (d, 2H, Ar-H ortho to isobutyl), 6.65(s, 1H, thiazole-H), 6.0 (br, s, 1H, NH), 2.95(s, 3H, N-$CH_3$), 2.5(d, 2H, benzylic), 1.8–2.0(m, 1H, -CH $(CH_3)_2$), 0.95(d, 6H, $CH_3$), **Mass (m/z):** 246($M^+$; 74), 203 (M-$C_3H_7$, 100), 174(203-HCN,$H_2$, 3), 149(203-$NCNCH_2$, 5).

### *4-/(4-Ter-butyl) Phenyl/-2-(N-methyl Amino) Thiazole (3f)*

(81%), m.p. 124–128°C. (Found C, 68.27; H, 7.33; N, 11.37; S, 13.01%. $C_{14}H_{18}N_2S$ requires C, 68.29; H, 7.31; N, 11.38; S, 13.00%). **IR ($cm^{-1}$):** 3214–3130, 1587, 1566, 1507, 1491. PMR ($CDCl_3$, $\delta$ **ppm):** 7.75 (d, 2H, Ar-H ortho to thiazole), 7.4 (d, 2H, Ar-H ortho to ter-butyl), 6.65(s, 1H, thiazole-H), 5.75 (br, s, 1H, NH), 3.0(s, 3H, N-$CH_3$), 1.35(s, 9H, $CH_3$), **Mass (m/z):** 246($M^+$; 72), 231(M-$CH_3$, 100), 216 (M-$C_2H_6$, 8), 203(M-$C_3H_7$, 16), 190(M-$C_4H_8$, 9).

### *4-/(4-N-butyl) Phenyl/-2-(N-phenyl Amino) Thiazole (3g)*

(52%), m.p. 162–166°C. (Found C, 74.01; H, 6.48; N, 9.08; S, 10.39%. $C_{19}H_{20}N_2S$ requires C, 74.02; H, 6.49; N, 9.09; S, 10.38%). **IR ($cm^{-1}$):** 3242–3188, 1620, 1604, 1578, 1498. **PMR ($CDCl_3$, $\delta$ ppm):** 7.75 (d, 2H, H-7, H-11), 7.45 (m, 5H, N-$C_6H_5$), 7.1–7.3(d, 2H, H-8, H-10, 1H,

thiazole-H), 6.7 (s, 1H, NH disappeared with $D_2O$), 2.65(t, 2H, $CH_2$), 1.65(m, 2H,$CH_2$), 1.35(m, 2H, $CH_2$), 0.95(t, 3H, $CH_3$), **Mass (m/z):** 308 ($M^+$; 100), 265 (M-$C_3H_7$, 71), 187(265-$C_6H_6$, 3).

### *4-/(4-Iso-butyl) Phenyl/-2-(N-phenyl Amino) Thiazole (3h)*

(58%), m.p. 169–173°C. (Found C, 74.00; H, 6.47; N, 9.10; S, 10.36%. $C_{19}H_{20}N_2S$ requires C, 74.02; H, 6.49; N, 9.09; S, 10.38%). **IR ($cm^{-1}$):** 3244–3042, 1623, 1592, 1567, 1499. **PMR ($CDCl_3$, $\delta$ ppm):** 7.75 (d, 2H, H-7, H-11), 7.45 (m, 5H, N-$C_6H_5$), 7.25 (d, 2H, H-8, H-10, 1H, thiazole-H), 6.65 (s, 1H, NH disappeared with $D_2O$), 2.55(d, 2H, $CH_2$), 1.9(m, 1H, -$CH(CH_3)_2$), 0.95(d, 6H, $CH_3$), **Mass (m/z):** 308 ($M^+$; 89), 265 (M-$C_3H_7$, 100).



### *4-/(4-Ter-butyl) Phenyl/-2-(N-phenyl Amino) Thiazole (3i)*

(60%), m.p. 136–140°C. (Found C, 74.01; H, 6.48; N, 9.09; S, 10.39%. $C_{19}H_{20}N_2S$ requires C, 74.02; H, 6.49; N, 9.09; S, 10.38%). **IR ($cm^{-1}$):** 3208–3111, 1589, 1561, 1496. **PMR ($CDCl_3$, $\delta$ ppm):** 7.8 (d, 2H, H-7, H-11), 7.4 (m, 5H, N-$C_6H_5$, and 2H, H-8, H-10, 1H, thiazole-H), 6.8 (s, 1H, thiazole-H), 1.35(s, 9H, $CH_3$), **Mass (m/z):** 308 ($M^+$; 98), 293 (M-$CH_3$, 100), 265 (293-$C_2H_4$, 12), 251 (M-$C_4H_9$, 5).

### *4-/(4-N-butyl) Phenyl/-2-(N-benzyl Amino) Thiazole (3j)*

(68%), m.p. 120–122°C. (Found C, 74.55; H, 6.81; N, 8.67; S, 9.91%. $C_{20}H_{22}N_2S$ requires C, 74.53; H, 6.83; N, 8.69; S, 9.93%). **IR ($cm^{-1}$):** 3242–3188, 1620, 1604, 1579, 1443. **PMR ($CDCl_3$, $\delta$ ppm):** 7.65 (d, 2H, H-7, H-11), 7.4 (s, 5H, N-$C_6H_5$), 7.25 (d, 2H, H-8, H-10), 6.5 (s, 1H, thiazole-H), 10.35 (s, 1H, NH disappeared with $D_2O$), 4.55 (d, 2H, $NHCH_2$, coalesced to singlet with $D_2O$ exchange) 2.65(t, 2H, $CH_2$, benzylic), 1.6 (m, 2H,$CH_2$), 1.35(m, 2H, $CH_2$), 0.95(t, 3H, $CH_3$), **Mass (m/z):** 322 ($M^+$; 74), 279 (M-$C_3H_7$, 10), 218(M-$C_6H_5CN$,H, 16), 91($C_7H_7$, 100).

### *4-/(4-Iso-butyl) Phenyl/-2-(N-benzyl Amino) Thiazole (3k)*

(57%), m.p. 113–116°C. (Found C, 74.51; H, 6.83; N, 8.68; S, 9.95%. $C_{20}H_{22}N_2S$ requires C, 74.53; H, 6.83; N, 8.69; S, 9.93%). **IR ($cm^{-1}$):** 3244–3042, 1623, 1592, 1567, 1499. **PMR ($CDCl_3$, $\delta$ ppm):** 7.7 (d, 2H, H-7, H-11), 7.35 (s, 5H, N-$C_6H_5$), 7.1 (d, 2H, H-8, H-10), 6.65 (s, 1H, thiazole-H), 5.8 (br, 1H, NH disappeared with $D_2O$), 4.5 (d, 2H, $NHCH_2$, coalesced to singlet with $D_2O$ exchange) 2.5(d, 2H, $CH_2$, benzylic), 1.9 (m, 1H,$CH(CH_3)_2$), 0.95 (d, 6H, $CH_3$), **Mass (m/z):** 322 ($M^+$; 74), 279 (M-$C_3H_7$, 10), 218(M-$C_6H_5CN$, H, 16), 91($C_7H_7$, 100).

### *4-/(4-Ter-butyl) Phenyl/-2-(N-benzyl Amino) Thiazole (3l)*

(65%), m.p. 173–176°C. (Found C, 74.52; H, 6.84; N, 8.68; S, 9.94%. $C_{20}H_{22}N_2S$ requires C, 74.53; H, 6.83; N, 8.69; S, 9.93%). **IR ($cm^{-1}$):** 3208–3111, 1589, 1561, 1496. **PMR ($CDCl_3$, $\delta$ ppm):** 7.8 (d, 2H, H-7, H-11), 7.1 (s, 5H, -$C_6H_5$), 7.3 (d, 2H, H-8, H-10), 6.7 (s, 1H, thiazole-H), 5.6 (br, 1H, NH disappeared with $D_2O$), 2.3 (d, 2H, coalesced to singlet with $D_2O$ exchange) 1.4 (s, 9H, $CH_3$). **Mass (m/z):** 322 ($M^+$; 28), 265 (M-$C_4H_9$, 10), 91($C_7H_7$, 100).

### *4-/(4-N-butyl) Phenyl/-2-/N- (2-Phenyl) Ethyl Amino/ Thiazole (3m)*

(70%), m.p. 126–129°C. (Found C, 74.97; H, 7.15; N, 8.31; S, 9.5%. $C_{21}H_{24}N_2S$ requires C, 74.99; H, 7.14; N, 8.33; S, 9.52%). **IR ($cm^{-1}$):** 3204–3125, 1591, 1493. **PMR ($CDCl_3$, $\delta$ ppm):** 7.7 (d, 2H, H-7, H-11), 7.1–7.4 (m, 5H, N-$C_6H_5$, and 2H, H-8, H-10), 6.65 (s, 1H, thiazole-H), 5.4 (br, s, 1H, NH disappeared with $D_2O$), 3.55 (q, 2H, $NHCH_2$, coalesced to triplet with $D_2O$ exchange), 3.0 (t, 2H, $NCH_2\underline{CH_2}$), 2.65 (t, 2H, $CH_2$,benzylic), 1.65 (m, 2H,$CH_2$), 1.35(m, 2H, $CH_2$), 0.95(t, 3H, $CH_3$), **Mass (m/z):** 336 ($M^+$; 54), 245 (M-$C_7H_7$, 100), 232(M-$C_8H_8$, 94), 189(245-$C_4H_8$, 40).

### *4-/(4-Iso-butyl) Phenyl/-2-/N- (2-Phenyl) Ethyl Amino/ Thiazole (3n)*

(60%), m.p. 107–109°C. (Found C, 75.01; H, 7.13; N, 8.35; S, 9.54%. $C_{21}H_{24}N_2S$ requires C, 74.99; H, 7.14; N, 8.33; S, 9.52%). **IR ($cm^{-1}$):** 3208, 1583, 1570, 1508, 1495. **PMR ($CDCl_3$, $\delta$ ppm):** 7.7 (d, 2H, H-7, H-11), 7.1–7.4 (m, 5H, $C_6H_5$, and 2H, H-8, H-10), 6.65 (s, 1H, thiazole-H), 5.9 (br, s, 1H, NH disappeared with $D_2O$), 3.6 (t, 2H, $NHCH_2$), 3.0 (t, 2H, $NCH_2\underline{CH_2}$), 2.5 (d, 2H, $CH_2$, benzylic), 1.9 (m, 1H,$CH(CH_3)_2$), 0.95(d, 6H, $CH_3$). **Mass (m/z):** 336 ($M^+$; 62), 293 (M-$C_3H_7$, 12), 245(M-$C_7H_7$, 96), 232(M-$C_8H_8$, 100), 189(245-$C_4H_8$, 45).

### *4-/(4-Ter-butyl) Phenyl/-2-/N- (2-Phenyl) Ethyl Amino/ Thiazole (3o)*

(54%), m.p. 147–149°C. (Found C, 74.96; H, 7.12; N, 8.35; S, 9.55%. $C_{21}H_{24}N_2S$ requires C, 74.99; H, 7.14; N, 8.33; S, 9.52%). **IR ($cm^{-1}$):** 3211, 1587, 1495, and 1473. **PMR ($CDCl_3$, $\delta$ ppm):** 7.8 (d, 2H, H-7, H-11), 7.4 (d, 2H, H-8, H-10), 7.2–7.3 (m, 5H, $C_6H_5$), 6.7 (s, 1H, thiazole-H), 5.5 (br, s, 1H, NH disappeared with $D_2O$), 3.6 (q, 2H, $NHCH_2$, coalesced to triplet with $D_2O$ exchange), 3.0 (t, 2H, $NCH_2\underline{CH_2}$), 1.4(s, 9H, $CH_3$). **Mass (m/z):** 336 ($M^+$; 64), 321(M-$CH_3$, 10), 245 (M-$C_7H_7$, 73), 232(M-$C_8H_8$, 100), 189(245-$C_4H_8$, 43).

### *4-/(4-N-butyl) Phenyl/-2-/N- (2-(4-Methoxyphenyl) Ethyl) Amino/Thiazole (3p)*

(77%), m.p. 108–110°C. (Found C, 72.15; H, 7.11; N, 7.62; S, 8.76%. $C_{22}H_{26}N_2OS$ requires C, 72.13; H, 7.10; N, 7.65; S, 8.74%). **IR ($cm^{-1}$):** 3208, 1610, 1591, 1512, and 1491. **PMR ($CDCl_3$, $\delta$ ppm):** 7.8 (d, 2H, H-7, H-11), 6.9 (d, 2H, H-8, H-10), 7.1–7.3(m, 4H,H-18, H-19, H-21 and H-22), 6.65 (s, 1H, thiazole-H), 5.6 (br, s, 1H, NH disappeared with $D_2O$), 3.8 (s, 3H, $OCH_3$), 3.55 (q, 2H, $NHCH_2$, coalesced to triplet with $D_2O$ exchange), 2.95 (t, 2H, $NCH_2\underline{CH_2}$), 2.65 (t, 2H, benzylic), 1.65 (m, 2H,$CH_2$), 1.4(m, 2H, $CH_2$), 1.0(t, 3H, $CH_3$), **Mass (m/z):** 336 ($M^+$; 10), 245 (M-$C_8H_9O$, 100), 232(M-$C_9H_{10}O$, 100), 189(245-$C_4H_8$, 28).

### *4-/(4-Iso-butyl) Phenyl/-2-/N- (2-(4-Methoxyphenyl) Ethyl) Amino/Thiazole (3q)*

(54%), m.p. 95–98°C. (Found C, 72.11; H, 7.09; N, 7.66; S, 8.72%. $C_{22}H_{26}N_2OS$ requires C, 72.13; H, 7.10; N, 7.65; S, 8.74%). **IR ($cm^{-1}$):** 3383, 3208, 1612, 1585, 1556, 1512, 1491. **PMR ($CDCl_3$, $\delta$ ppm):** 7.7 (d, 2H, H-7, H-11), 6.85 (d, 2H, H-8, H-10), 7.1–7.2(m, 4H,H-18, H-19, H-21 and H-22), 6.65 (s, 1H, thiazole-H), 5.45 (br, s, 1H, NH disappeared with $D_2O$), 3.8 (s, 3H, $OCH_3$), 3.5 (q, 2H, $NHCH_2$, coalesced to triplet with $D_2O$ exchange), 2.95 (t, 2H, $NCH_2\underline{CH_2}$), 2.6 (t, 2H, benzylic),1.9 (m,1H, $CH(CH_3)_2$), 0.95 (d, 6H, $CH_3$), **Mass (m/z):** 336 ($M^+$; 10), 245 (M-$C_8H_9O$, 17), 232 (M-$C_9H_{10}O$, 100), 189(245-$C_4H_8$, 35).

### *4-/(4-Ter-butyl) Phenyl/-2-/N- (2-(4-Methoxyphenyl) Ethyl) Amino/Thiazole (3r)*

(62%), m.p. 124–127°C. (Found C, 72.10; H, 7.13; N, 7.67; S, 8.75%. $C_{22}H_{26}N_2OS$ requires C, 72.13; H, 7.10; N, 7.65; S, 8.74%). **IR ($cm^{-1}$):** 3285, 1612, 1564, 1512, and 1489. **PMR ($CDCl_3$, $\delta$ ppm):** 7.8 (d, 2H, H-7, H-11), 7.4 (d, 2H, H-8, H-10), 7.1(d, 2H, H-19, H-21), 6.9 (d, 2H, H-18, H-22), 6.7 (s, 1H, thiazole-H), 5.7 (br, s, 1H, NH disappeared with $D_2O$), 3.8 (s, 3H, $OCH_3$), 3.5 (q, 2H, $NHCH_2$, coalesced to triplet with $D_2O$ exchange), 2.9 (t, 2H, $NCH_2\underline{CH_2}$), 1.4 (s, 9H, $CH_3$), **Mass (m/z):** 336 ($M^+$; 10), 245 (M-$C_8H_9O$, 10), 232 (M-$C_9H_{10}O$, 100), 189(245-$C_4H_8$, 15).

### *4-/(4-n-Butyl) Phenyl/-2- (N-Acetyl Amino) Thiazole (3s)*

(51%), m.p. 191–193°C. (Found C, 65.65; H, 6.55; N, 10.22; S, 11.7%. $C_{15}H_{18}N_2OS$ requires C, 65.69; H, 6.56; N, 10.21; S, 11.67%). **IR ($cm^{-1}$):** 3237 (NH), 1654 (C=O), 1575, 1557, and 1490. **PMR ($CDCl_3$, $\delta$ ppm):** 7.7 (d, 2H, Ar-H ortho to thiazole), 7.3 (d, 2H, Ar-H ortho to n-butyl), 6.8 (s, 1H, thiazole-H), 6.4 (br, s, 1H, NH, disappeared with $D_2O$ exchange),

2.65 (t, 2H, n-butyl), 1.65 (m, 2H, n-butyl), 2.1(s, 3H, $COCH_3$), 1.4 (m, 2H, n-butyl) 1.1 (s, 3H, n-butyl). **Mass (m/z):** 274($M^+$; 43), 217 (M-$C_4H_9$, 18), 202 (217-$CH_3$, 48).

### *4-/(4-Iso-butyl) Phenyl/-2- (N-acetyl Amino) Thiazole (3t)*

(55%), m.p. 189–192°C. (Found C, 65.71; H, 6.58; N, 10.20; S, 11.65%. $C_{15}H_{18}N_2OS$ requires C, 65.69; H, 6.56; N, 10.21; S, 11.67%). **IR ($cm^{-1}$):** 3237 (NH), 1654 (C═O), 1575, 1557, 1490. **PMR ($CDCl_3$, $\delta$ ppm):** 7.8 (d, 2H, Ar-H ortho to thiazole), 7.2 (d, 2H, Ar-H ortho to isobutyl), 7.1(s, 1H, thiazole-H), 11.8 (br, s, 1H, NH), 2.5(d, 2H, benzylic), 1.9(m, 1H, CH), 1.75 (s, 3H, $COCH_3$), 0.9(d, 6H, $CH_3$), **Mass (m/z):** 274($M^+$; 52), 232 (M-$CH_2CO$, 78), 189(232-$C_3H_7$, 100), 147(189-$NCNCH_2$, 17).

### *4-/(4-Ter-butyl) Phenyl/-2-(N-acetyl Amino) Thiazole (3u)*

(64%), m.p. 232–235°C. (Found C, 65.67; H, 6.54; N, 10.19; S, 11.68%. $C_{15}H_{18}N_2OS$ requires C, 65.69; H, 6.56; N, 10.21; S, 11.67%). **IR ($cm^{-1}$):** 3230 (NH), 1660 (C═O), 1571, 1556, and 1491. **PMR (DMSO-$d_6$, $\delta$ ppm):** 7.8 (d, 2H, Ar-H ortho to thiazole), 7.4 (d, 2H, Ar-H ortho to ter-butyl), 7.1(s, 1H, thiazole-H), 11.2–11.6 (br, s, 1H, NH disappeared with $D_2O$), 1.8 (d, 3H, $COCH_3$ coalesced to a singlet with $D_2O$ exchange), 1.4 (s, 9H, $CH_3$), **Mass (m/z):** 274($M^+$; 62), 259(M-$CH_3$, 22), 232 (M-$CH_2CO$, 69), 217(232-$CH_3$ or M-$C_4H_9$, 100), 189(217-CO, 12).

### *4-/(4-N-butyl)/Phenyl/- 2-(Diamino Methyleneimino) Thiazole (4a)*

(42%), m.p. 256–258°C. (Found C, 61.33; H, 6.57; N, 20.41; S, 11.65%. $C_{14}H_{18}N_4S$ requires C, 61.31; H, 6.56; N, 20.43; S, 11.67%). (**IR $cm^{-1}$):** 3425–3116, 1657, 1649, 1599, 1549, and 1484. **PMR ($CDCl_3$+DMSO-$d_6$, $\delta$ ppm):** 7.7 (d, 2H, Ar-H, ortho to thiazole), 7.2 (d, 2H,Ar-H, ortho to n-butyl), 6.75 (s, 1H, thiazole-H), 6.0–7.0 (br, s, 4H, $NH_2$, disappeared with $D_2O$), 2.65 (t, 2H, benzylic), 1.6(m, 2H, H-13), 1.35 (m, 2H, H-14), 0.95 (t, 3H, $CH_3$). **Mass (m/z):** 274 ($M^+$; 100), 257 (M-$NH_3$, 61), 232 (M-$C_3H_6$ or M-$NCNH_2$, 27), 214 (257-$C_3H_7$, 80), 189 (232-$C_3H_7$, 60) 147 (189-$NCNH_2$, 29).

### *4-/(4-Iso-butyl) Phenyl/-2-(Diamino Methyleneimino) Thiazole (4b)*

(35%), m.p. 238–240°C. (Found C, 61.29; H, 6.56; N, 20.41; S, 11.68%. $C_{14}H_{18}N_4S$ requires C, 61.31; H, 6.56; N, 20.43; S, 11.67%). (**IR $cm^{-1}$):** 3440–3172, 1601, 1649, 1536, 1500, and 1460. **PMR (DMSO-$d_6$, $\delta$ ppm):** 7.75 (d, 2H, Ar-H, ortho to thiazole), 7.2 (d, 2H, Ar-H, ortho to Isobutyl), 7.05 (s, 1H, thiazole_H), 6.8–7.0 (br, s, 4H, $NH_2$, disappeared with $D_2O$), 2.45 (d, 2H, benzylic), 1.82–2.0(m, 1H, $CH(CH_3)_2$),

0.9 (d, 6H, $CH_3$). **Mass (m/z):** 274 ($M^+$; 43), 257 (M-$NH_3$, 17), 232 (M-$C_3H_6$ or M-$NCNH_2$, 44), 189 (232-$C_3H_7$, 100), 147 (189-$NCNH_2$, 19).

### *4-/(4-Ter-butyl) Phenyl/-2-(Diamino Methyleneimino) Thiazole (4c)*

(35%), m.p. 242–243°C. (Found C, 61.30; H, 6.57; N, 20.41; S, 11.68%. $C_{14}H_{18}N_4S$ requires C, 61.31; H, 6.56; N, 20.43; S, 11.67%). (**IR $cm^{-1}$):** 3445–3435, 1599, 1649, 1558, and 1497. **PMR ($CDCl_3$, $\delta$ ppm):** 7.80 (d, 2H, Ar-H, ortho to thiazole), 7.45 (d, 2H, Ar-H, ortho to terbutyl), 7.15 (s, 1H, thiazole-H), 6.95–7.15 (br, s, 4H, $NH_2$, disappeared with $D_2O$), 1.35 (s, 9H, $CH_3$). **Mass (m/z):** 274 ($M^+$; 65), 257 (M-$NH_3$, 20), 242 (257-$CH_3$), 232 (M-$C_3H_6$ or M-$NCNH_2$, 59), 217 (M-$C_4H_9$, 100), 189 (232-$NCNH_2$, H, 18) 175 (232-$C_4H_9$, 15).

### *4-/(4-N-butyl) Phenyl/-2–(N-methyl-N-acetyl Amino) Thiazole (5a)*

(41%), m.p. 119–121°C. (Found C, 66.70; H, 6.95; N, 9.70; S, 11.09%. $C_{16}H_{20}N_2OS$ requires C, 66.66; H, 6.94; N, 9.72; S, 11.11%). (**IR $cm^{-1}$):** 3115 (CH), 1663 (C=O), 1542, and 1491. **PMR ($CDCl_3$, $\delta$ ppm):** 7.80 (d, 2H, Ar-H, ortho to thiazole), 7.20 (d, 2H, ortho to ter butyl), 7.1 (s, 1H, thiazole-H), 3.8 (s, 3H, $NCH_3$), 2.65 (t, 2H, benzylic), 2.4 (s, 3H, $COCH_3$), 1.6 (m, 2H, $CH_2$), 1.4(m, 2H, -$CH_2$-), 0.9 (t, 3H, $CH_3$). **Mass (m/z):** 288 ($M^+$; 39), 246 (M-$CH_2CO$, 100), 203 (246-$C_3H_7$, 77).

### *4-/(4-Iso-butyl) Phenyl/-2–(N-methyl-N-acetyl Amino) Thiazole (5b)*

(38%), m.p. 130–132°C. (Found C, 66.63; H, 6.92; N, 9.75; S, 11.14%. $C_{16}H_{20}N_2OS$ requires C, 66.66; H, 6.94; N, 9.72; S, 11.11%). (**IR $cm^{-1}$):** 3108 (CH), 1670 (C=O), 1536, and 1493. **PMR ($CDCl_3$, $\delta$ ppm):** 7.80 (d, 2H, Ar-H, ortho to thiazole), 7.20 (d, 2H, ortho to ter butyl), 7.1 (s, 1H, thiazole-H), 3.8 (s, 3H, $NCH_3$), 2.5 (d, 2H, benzylic), 2.4 (s, 3H, $COCH_3$), 1.9 (m, 1H, $CH(CH_3)_2$), 0.9 (d, 6H, $CH_3$). **Mass (m/z):** 289 ($MH^+$, 42), 288 ($M^+$; 47), 246 (M-$CH_2CO$, 97), 203 (246-$C_3H_7$, 100).

### *4-/(4-Ter-butyl) Phenyl/-2–(N-methyl-N-acetyl Amino) Thiazole (5c)*

(52%), m.p. 120–122°C. (Found C, 66.68; H, 6.97; N, 9.71; S, 11.13%. $C_{16}H_{20}N_2OS$ requires C, 66.66; H, 6.94; N, 9.72; S, 11.11%). (**IR $cm^{-1}$):** 3112 (CH), 1668 (C=O), 1536, and 1493. **PMR ($CDCl_3$, $\delta$ ppm):** 7.80 (d, 2H, Ar-H, ortho to thiazole), 7.50 (d, 2H, ortho to ter butyl), 7.1 (s, 1H, thiazole-H), 3.8 (s, 3H, $NCH_3$), 2.4 (s, 3H, $COCH_3$), 1.4 (s, 9H, $CH_3$). **Mass (m/z):** 288 ($M^+$; 37), 246 (M-$CH_2CO$, 89), 231 (M-$C_4H_9$, 100).

## REFERENCES

[1] A. Bizhev, N. Boyadhziev, and V. Natova, *Farmatziya*, **37** (5), 14, (1987); *Chem. Abstr.*, **108,** 180074g (1988).
[2] G. J. Mean Rejon and R. O. Mocelo Castell, *Afinidad*, **50**, 447 (1993); 319–322. *Chem. Abstr.*, **120,** 244806e (1994).
[3] Y. Ozato, N. Tamura, H. Masumori, A. Kojima, F. Nishikaku, and Y. Kimura, JP, **88,** 152368 and 93247014, Drugs of the future., **19**(4), 347, (1994).
[4] J. Yoshinaga, T. Shogaki, J. Katika, H. Ozeki, and Y. Kato, *Eur. Pat. EP.,* 321 115; *Chem. Abstr.*, **112,** p7490z (1990).
[5] (a) Y. Matano and T. Ikegami, In *Organobismuth Chemistry*, H. Suzuki, Y. Matano, Eds. (Elsevier, New York, 2001), 329–469. Vol. 21; (b) N. M. Leonard, L. C. Wieland, and R. S. Mohan, *Tetrahedron.,* **58,** 8373 (2002).
[6] (a) B. Prasanna and G. V. P. Chandra Mouli, *Phosphorous, Sulfur, and Silicon, and the Related Elements*., **179**(10), 2059, (2004); (b) P. Vijay Kumar Reddy, P. Naveen Kumar, and G. V. P. Chandra Mouli, *J. Heterocyclic. Chem.,* **41,**1 (2004).
[7] (a) Y. M. Zhang, T. B. Wei, and L. L Wang, *Synth. Commun*., **27,** 751, (1997); (b) Y. M. Zhang, T. B. Wei, and L. M. Gao, *Synth. Commun*., **31,** 3099 (2001).
[8] A. Geronikaki and G. Theophilidis, *Eur. J. Med. Chem.,* **27**(7), 709 (1992).
[9] J. G. Vincent and H. W. Vincent, *Proc. Soc. Boil. Medica.*, **55,** 162 (1944).
[10] Anonymous, *Phytopathology*, **37,** 992 (1947).
[11] C. A. Winter, E. A. Risley, and G. W. Nuss, *Proc. Soc. Exp. Biol. Med.,* **111,** 544 (1962).