



MICROWAVE ASSISTED SOLVENT FREE SYNTHESIS OF SOME SUBSTITUTED BENZOTHAZOLES OVER ZEOLITE

**MANISH KUMAR RAWAL, KIRTI SHRIMALI, AMIT SAHU,
DIWAKER SITHA, V. K. SHARMA and PINKI B. PUNJABI***

Microwave Chemistry Laboratory, Department of Chemistry, University College of Science,
M. L. Sukhadia University, UDAIPUR – 313 001 (Raj.) INDIA

ABSTRACT

The synthesis of 2-arylidene-hydrazinobenzothiazole, 2-(2-substituted arylidenehydrazino) - benzothiazoles and 2-(2-substituted aryl-1, 3-thiazolidine-4-one)-2-iminobenzothiazoles using 2-mercaptobenzothiazole as a starting material over NaY zeolite under microwave irradiation has been described. This method is clean, fast, efficient, low cost and environmentally benign.

Key words: Microwave, Benzothiazoles, Zeolite, Eco-friendly.

INTRODUCTION

The utility of zeolite as selective adsorbent and as catalyst for petrochemical processes has been known for many years^{1,2}. More recently, the use of these catalysts for preparation of heterocyclic compounds have received increasing attention due to their characteristic properties such as shape selectivity, thermal stability, acidic and basic nature³⁻⁵. Now-a-days, the use of zeolite in many organic reactions has been reported by number of workers, for example alkylation⁶, acetylation⁷, acetalization^{8,9}, etc. are some of the examples, where zeolite plays a significant role.

Substituted benzothiazoles are also found to have antimicrobial^{10,11}, antifungal^{12,13}, anticancer^{14,15} and anti-inflammatory^{16,17} activity. In recent years, the acceleration of a wide range of chemical reactions using microwave dielectric heating has been reported¹⁸. The solvent free conditions under microwave irradiation offers several advantages; solvents are often expensive, toxic and difficult to remove and are polluting agents. Owing to environmental concern, there is an increasing need and interest in developing processes that minimize pollution. In this paper, we have reported the use of NaY zeolite as a reusable

* Author for correspondence; E-mail: pb_punjabi@yahoo.com

catalyst and solid support for the synthesis of some substituted benzothiazoles by microwave irradiation without using solvent.

EXPERIMENTAL

Synthesis of 2-hydrazinobenzothiazole (2)

2-Mercaptobenzothiazole (0.010 mol.) (**1**) and NaY zeolite (4 g) were mixed together in a mortar. Then hydrazine hydrate (0.015 mol.) was added. The reaction mixture was transferred in an Erlenmeyer flask and irradiated under microwave irradiation for 7 min at 960 W with a time interval of 10 seconds. After cooling, the product was separated with ethanol and the catalyst was filtered off. Recrystallization was carried out from ethanol. Catalyst was reused after washing with ethanol, and drying in air overnight.

Synthesis of 2-arylidenehydrazinobenzothiazole (3a-e)

Compound (**2**) (0.010 mol.) and NaY zeolite (6 g) were mixed together in a mortar. Then aldehyde (0.015 mol.) was added. The reaction mixture was transferred in an Erlenmeyer flask and irradiated under microwave irradiation for 1-2 min with a time interval of 10 seconds. After cooling, the product was separated with ethanol and the catalyst was filtered off. Recrystallization was carried out from ethanol. The catalyst was reused after washing with ethanol and drying in air overnight. Compounds (**3b-e**) were also synthesized by a similar method.

Table 1: Physical data of compounds (2) and (3a-e)

| Compd. | Ar | Mol. Formula | Mol. weight | M.P. (°C) | Yield ^a (%) [Time] (hr.) | Yield ^b (%) [Time] (min.) | Yield ^c (%) [Time] (min.) |
|-----------|--|---|-------------|-----------|-------------------------------------|--------------------------------------|--------------------------------------|
| 2 | - | C ₇ H ₇ N ₃ S | 165 | 198 | 86 [10] | 86 [10] | 90 [7] |
| 3a | 2-ClC ₆ H ₄ | C ₁₄ H ₁₀ N ₃ SCl | 287 | 130 | 78 [1] | 82 [2] | 88 [1.5] |
| 3b | 4-ClC ₆ H ₄ | C ₁₄ H ₁₀ N ₃ SCl | 287 | 139 | 74 [1] | 75 [2] | 85 [1.5] |
| 3c | 4-BrC ₆ H ₄ | C ₁₄ H ₁₀ N ₃ SBr | 332 | 125 | 80 [1] | 85 [2] | 92 [1.5] |
| 3d | 4-OCH ₃ C ₆ H ₄ | C ₁₅ H ₁₃ N ₃ OS | 283 | 168 | 66 [1] | 70 [2] | 85 [1.5] |
| 3e | 4-NO ₂ C ₆ H ₄ | C ₁₄ H ₁₀ N ₄ O ₂ S | 298 | 115 | 78 [1] | 80 [2] | 92 [1.5] |

a = Conventional, b = Microwave + Solvent, c = On zeolite (solvent free) under micro-wave irradiation

Synthesis of 2-(2-phenyl-1, 3-thiazolidine-4-one)-2-iminobenzothiazole (4a-e)

HY zeolite (5 g) and compound (**3a**) (0.1 mol.) were mixed in a mortar. Then thioglycolic acid (0.01 mol.) was added to it and mixture was irradiated under microwave irradiation for 7 minutes at 1200 W. After cooling the mixture, product was extracted with ethanol and the catalyst was filtered off. Product was recrystallized from ethanol. Catalyst was reused after washing with ethanol and drying on air overnight. Similarly, other compounds (**4b-e**) were also synthesized.

Table 2: Analytical data of compounds (2) and (3a-e)

| Compd. | Calculated /Found (%) | | | |
|-----------|-----------------------|-------------|---------------|---------------|
| | C | H | N | S |
| 2 | 50.89 / 50.85 | 4.27 / 4.25 | 25.43 / 25.39 | 19.41 / 19.40 |
| 3a | 58.43 / 58.40 | 3.50 / 3.48 | 14.60 / 14.54 | 11.14 / 11.12 |
| 3b | 58.43 / 58.41 | 3.50 / 3.45 | 14.60 / 14.59 | 11.14 / 11.11 |
| 3c | 50.61 / 50.55 | 3.03 / 3.02 | 12.65 / 12.66 | 9.95 / 9.93 |
| 3d | 63.58 / 63.52 | 4.62 / 4.60 | 14.83 / 14.79 | 11.32 / 11.30 |
| 3e | 56.37 / 56.31 | 3.38 / 3.36 | 18.78 / 18.77 | 10.75 / 10.71 |

Table 3: Spectral data of compounds (2) and (3a-e)

| Compd. | IR (cm ⁻¹) | ¹ H NMR(δ) |
|-----------|---|---|
| 2 | 3380, 3270 (-NH ₂), 3335 (N-H str.), 1636 (C=N str.), 736 (C-Cl str.), 3030 (C-H str., Ar-H), 1560, 1155, 1050, 640 (benzothiazole nucleus) | 4.66 (s, 2H, NH ₂), 7.77 (s, 1H, NH), 6.80 – 7.75 (m, 4H, Ar -H). |
| 3a | 3340 (N-H str.), 1640 (C=N str., cyclic), 1610 (C=N str., open), 736 (C-Cl str.), 3038 (C-H str., Ar-H), 1550, 1160, 1066, 652 (benzothiazole nucleus) | 4.88 (s, 1H, -N=CH), 7.87 (s, 1H, NH), 6.85 – 7.66 (m, 4H, Ar -H). |
| 3b | 3341 (N-H str.), 1636 (C=N str., cyclic), 1613 (C=N str., open), 3030 (C-H str., Ar-H), 1554, 1167, 1060, 647 (benzothiazole nucleus) | 4.84 (s, 1H, -N=CH), 7.88 (s, 1H, NH), 6.87 – 7.68 (m, 4H, Ar -H). |

Cont...

| Compd. | IR (cm ⁻¹) | ¹ H NMR(δ) |
|-----------|---|---|
| 3c | 3329 (N-H str.), 1648 (C=N str., cyclic), 1617 (C=N str., open), 3044 (C-H str., Ar-H), 1541, 1172, 1056, 642 (benzothiazole nucleus) | 4.90(s, 1H, -N=CH), 7.91 (s, 1H, NH), 6.90 – 7.83 (m, 4H, Ar –H). |
| 3d | 3333 (N-H str.), 1630 (C=N str., cyclic), 1604 (C=N str., open), 3041 (C-H str., Ar-H), 1170 (C-O-CH ₃ str.) 1540, 1144, 1047, 655 (benzothiazole nucleus) | 3.68 (s,3H, OCH ₃), 4.91(s, 1H, -N=CH), 7.90 (s, 1H, NH), 6.89 – 7.80 (m, 4H, Ar –H). |
| 3e | 3336 (N-H str.), 1643 (C=N str., cyclic), 1619 (C=N str., open), 1540, 1400 (NO ₂ str.) 3041 (C-H str., Ar-H), 1545, 1161, 1070, 650 (benzothiazole nucleus) | 4.77(s, 1H, -N=CH), 7.81 (s, 1H, NH), 6.70 – 7.59 (m, 4H, Ar –H). |

Table 4: Physical data of compounds (4a-e)

| Compd. | Ar | Mol. formula | Mol. weight | M.P. (°C) | Yield ^a (%) | Yield ^b (%) | Yield ^c (%) |
|-----------|--|--|-------------|-----------|------------------------|------------------------|------------------------|
| | | | | | [Time] (hr.) | [Time] (min.) | [Time] (min.) |
| 4a | 2-ClC ₆ H ₄ | C ₁₆ H ₁₂ N ₃ OS ₂ Cl | 361 | 120 | 74 [10-12] | 85 [9] | 90 [7] |
| 4b | 4-ClC ₆ H ₄ | C ₁₆ H ₁₂ N ₃ OS ₂ Cl | 361 | 125 | 72 [10-12] | 77 [9] | 89 [7] |
| 4c | 4-BrC ₆ H ₄ | C ₁₆ H ₁₂ N ₃ OS ₂ Br | 406 | 140 | 83 [10-12] | 89 [9] | 95 [7] |
| 4d | 4-OCH ₃ C ₆ H ₄ | C ₁₇ H ₁₅ N ₃ O ₂ S ₂ | 357 | 121 | 70 [10-12] | 82 [9] | 90 [7] |
| 4e | 4-NO ₂ C ₆ H ₄ | C ₁₆ H ₁₂ N ₄ O ₃ S ₂ | 372 | 110 | 73 [10-12] | 81 [9] | 92 [7] |

a = Conventional, b = Microwave + Solvent, c = On zeolite (solvent free) under microwave irradiation

Table 5: Analytical data of compounds (4a-e)

| Compd. | Calculated /Found (%) | | | |
|-----------|-----------------------|-------------|---------------|---------------|
| | C | H | N | S |
| 4a | 53.11 / 53.07 | 3.31 / 3.28 | 11.61 / 11.60 | 17.72 / 17.70 |

Cont...

| Compd. | Calculated /Found (%) | | | |
|--------|-----------------------|-------------|---------------|---------------|
| | C | H | N | S |
| 4b | 53.11 / 53.08 | 3.31 / 3.29 | 11.61 / 11.59 | 17.72 / 17.69 |
| 4c | 47.29 / 47.21 | 2.95 / 2.90 | 10.34 / 10.32 | 15.78 / 15.70 |
| 4d | 57.12 / 57.06 | 4.22 / 4.19 | 11.75 / 11.71 | 17.96 / 17.85 |
| 4e | 51.57 / 51.51 | 3.22 / 3.18 | 15.06 / 15.00 | 17.22 / 17.21 |

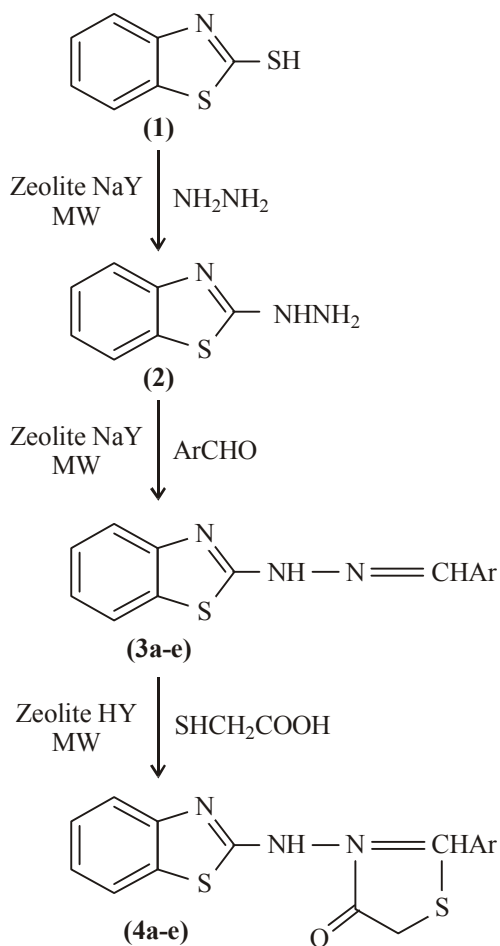
Table 6: Spectral data of compounds (4a-e)

| Compd. | IR (cm ⁻¹) | ¹ H NMR(δ) |
|--------|---|---|
| 4a | 3370 (N-H str.), 3030 (C-H str., Ar-H), 3000 (-N-CH-S), 2950 (CH ₂ S), 1725 (C=O str.), 1629 (C=N str., cyclic), 722 (C-Cl str.), | 7.80 (s, 1H, NH), 6.80 – 7.70 (m, 4H, Ar – H), 4.77 (s, 1H, -N-CH), 3.60 (s, 2H, -CH ₂ S) |
| 4b | 3372 (N-H str.), 3034 (C-H str., Ar-H), 2998 (-N-CH-S), 2953 (CH ₂ S), 1722 (C=O str.), 1631 (C=N str., cyclic), 725(C-Cl str.). | 7.81 (s, 1H, NH), 6.82 – 7.73 (m, 4H, Ar – H), 4.80 (s, 1H, -N-CH), 3.64 (s, 2H, -CH ₂ S) |
| 4c | 3380 (N-H str.), 3040 (C-H str., Ar-H), 3012 (-N-CH-S), 2961(CH ₂ S), 1736 (C=O str.), 1634 (C=N str.,cyclic), | 7.77 (s, 1H, NH), 6.76 – 7.65 (m, 4H, Ar – H), 4.71 (s, 1H, -N-CH), 3.62 (s, 2H, -CH ₂ S) |
| 4d | 3376 (N-H str.), 3023 (C-H str., Ar-H), 3010 (-N-CH-S), 2959 (CH ₂ S), 1731 (C=O str.), 1640 (C=N str., cyclic), 1167 (C-O-CH ₃) | 7.84 (s, 1H, NH), 6.86 – 7.50 (m, 4H, Ar – H), 4.81 (s, 1H, -N-CH), 3.70 (s, 2H, -CH ₂ S), 3.50 (s,3H, OCH ₃). |
| 4e | 3360 (N-H str.), 3015 (C-H str., Ar-H), 2990 (-N-CH-S), 2937 (CH ₂ S) 1700 (C=O str.), 1620 (C=N str., cyclic), 1545, 1412 (C=C str.), 1510, 1350 (NO ₂ str.) | 7.70 (s, 1H, NH), 6.69 – 7.60 (m, 4H, Ar – H), 4.64 (s, 1H, -N-CH), 3.54 (s, 2H, -CH ₂ S) |

RESULTS AND DISCUSSION

Hydrazinolysis of 2-mercaptobenzothiazole afforded 2-hydrazinobenzothiazole (**2**). Formation of this compound was confirmed by appearance of stretching vibration at 3380 and 3335 cm⁻¹ in IR spectrum corresponding to –NH₂ and –NH group, respectively.

Characteristic signal of -NH and -NH_2 protons at δ 7.77 and δ 4.66 in ^1H NMR also confirms the presence of both these groups. Reaction of compound **(2)** with different aldehydes on zeolite led to the formation of corresponding Schiff bases **(3a-e)**. Disappearance of -NH_2 band at 3380 cm^{-1} and appearance of C=N band at 1610 cm^{-1} in IR spectrum indicates the formation of Schiff bases. Signal at δ 4.88 in ^1H NMR due to -N=CH proton also favored the formation of Schiff bases.



When compounds **(3a-e)** react with thioglycolic acid, they underwent cyclisation giving compounds **(4a-e)**. Disappearance of -CH=N band at 1610 cm^{-1} in IR spectrum and signals at δ 4.88 in ^1H NMR due to -N=CH proton indicates that the cyclisation occur. Further, presence of a band at 2950 cm^{-1} due to $\text{-CH}_2\text{S}$ group and signals of $\text{-CH}_2\text{S}$ protons at δ 3.60 also supported the formation of compounds **(4a-e)**.

A comparison of time required for synthesis, and yield of products in conventional method and microwave method (with and without using NaY zeolite) has been reported, which indicates the utility of zeolite as a solid support as well as an ecofriendly catalyst.

ACKNOWLEDGEMENTS

Authors are thankful to Prof. Suresh C. Ameta for critical and valuable suggestions from time to time. The authors are also thankful to Head, Department of Chemistry, M.L. Sukhadia University, Udaipur (Raj.) for providing laboratory facilities and to the Director, RSIC, CDRI, Lucknow for spectral and analytical studies.

REFERENCES

1. J. A. Martens., W. Soucerijns, R. Parton, G. F. Forment and P. A. Jacobs, *Angew Chem. Int. Ed. Engl.*, **34**, 2528 (1995).
2. C. D. Chang, *Cat. Rev. Sci. Eng.*, **25**, 1(1983).
3. W. Holderich, H. Hesse and F. Naumann, *Angew. Chem. Int. Ed. Engl.*, **27**, 226 (1988).
4. M. E. Davis., *Acc. Chem. Res.*, **26**, 111 (1993).
5. S. L. Srib, *Chem. Rev.*, **93**, 803 (1993).
6. S. E. Sen, Y. Z. Zhang and S. L. Roach, *J. Org. Chem.*, **61**, 9534 (1996).
7. R. Bllini, M. Bordono, G. Bosica, R. Maggi and G. Sartori, *Tetrahedron Lett.*, **39**, 6049 (1998).
8. R. Ballini, G. Bosica, B. Frullanti, R. Maggi, G. Sartori and F. Schroce, *Tetrahedron Lett.*, **39**, 1615 (1998).
9. A. Corma, M. I. Climent, H. Carcia and J. Primo, *Appl. Catal.*, **59**, 333 (1990).
10. D. P. Mingas and D. R. Baghurst, *Chem. Soc. Rev.*, **20**, 1 (1991).
11. R. A. Abrakmvoich, *Org. Prep Proceed. Int.*, **23**, 685 (1991).
12. H. Kucukbav, E. Cetinkava and R. Durmaz, *Arzneim Forsch*, **45**, 1331 (1995).
13. S. R. Pattan, B. S. N. Narendra and J. S. Angadi, *Indian Drugs*, **39**, 515 (2002).
14. C. Ameya and R. P. Nandini, *Molecules*, **12**, 2467 (2007).
15. Caleta, M. Grdisa, D. S. Mrvos, M. Cetina, K. V. Tralic, K. Pavelic and G. I. L. Karminski, *Farmaco*, **59**, 297 (2004).

16. W. Geoffrey, D. B. Tracey, D. Patrizia, S. Angela, F. S. Dong, D. W. Andrew and F. G. S. Malcolm, *Bioorg Med. Chem. Lett.*, **10**, 513 (2000).
17. P. R. Naik, S. N. Pandeya and A. Pandey, *Indian J. Physiol. Pharmacol.*, **40**, 189 (1996).
18. S. B. Sushilkumar and B. S. Devanand, *J. Korean Chem. Soc.*, **47**, 237 (2003).

Revised : 15.11.2009

Accepted :19.11.2009