Contents lists available at GrowingScience

Current Chemistry Letters

homepage: www.GrowingScience.com

Development of novel spiro benzotriazole-based compounds with 1,3-dicarbonyl scaffolds via one-pot synthesis

Monika R. Kshatriya[a] and Jinal A. Gajjar[a*]

[a]*Jeel Goswami College of Science & Research, Monark University, Vahelal, Ahmedabad, Gujarat, India*

C H R O N I C L E

Article history:
Received October 2, 2024
Received in revised form
November 1, 2024
Accepted January 31, 2025
Available online
January 31, 2025

Keywords:
Benzotriazole
2-Chloro-2-phenyl acetophenone
1,3-Dicarbonyl ,3,2'-indandione
One-pot methodology

A B S T R A C T

In the present study, it was demonstrated that a new series of derivatives of *1,2-diphenyl-3H-spiro[benzo[d]pyrrolo[2,1-b]triazol-3,5'-pyrimidine* (4) and 3,2′-indandione (6) were efficiently designed and synthesized via a novel, and less cumbersome one-pot methodology involving tri-component interactions among benzotriazole, 2-chloro-2-phenylacetophenone, and 1,3-dicarbonyl compounds in CH_2Cl_2 at room temperature 25°C for 3 hours without the use of a catalyst. The resulting compounds' structural configurations were verified with NMR, IR, EI-MS, and elemental analysis exhibiting good yield and high purity.

1. Introduction

Benzotriazole is a versatile, nitrogen-rich heterocyclic compound that has gained prominence in drug discovery, agrochemicals, and materials science.[1] Known for its unique electronic properties, benzotriazole exhibits electron-donating and electron-withdrawing behaviour, enhancing its utility as an electron acceptor and stabilizer in various chemical contexts.[2] This adaptability makes benzotriazole an essential building block in the design of new compounds with targeted biological and physicochemical properties.[3,4] Benzotriazole derivatives demonstrate a wide range of biological activities, such as antimicrobial,[5] antifungal,[6] antitumor,[7] anti-inflammatory,[8,] and antitubercular[9] effects. Beyond pharmaceuticals, these derivatives are essential in developing dyes, corrosion inhibitors, and UV stabilizers, highlighting benzotriazole's importance across multiple industries.[10,11] The bioactivity of the benzotriazole molecular segment is a consequence of the presence of nitrogen atoms in the five-membered heterocyclic ring. This was confirmed regarding many different types of structures.[12-14]

Multicomponent reactions (MCRs) have emerged as a powerful synthetic strategy in modern organic chemistry, largely due to their efficiency, cost-effectiveness, and environmental compatibility.[15,16] Unlike traditional synthesis, which often requires multiple steps with intermediate purification, MCRs enable the simultaneous reaction of three or more starting materials in a single step, minimizing waste and energy consumption.[17,18]

This one-pot approach simplifies reaction workflows and has found broad applications in medicinal chemistry and the synthesis of complex organic molecules.[19,20] Considering benzotriazole's broad applicability, this study explores a catalyst-free, multicomponent reaction approach to synthesize a novel spiro benzotriazole-based compound featuring a 1,3-dicarbonyl skeleton. The spiro framework's unique three-dimensional structure enhances molecular biological activity by improving binding interactions with biological targets.[21,22]

* Corresponding author
E-mail address jinalg112@gmail.com (J. A. Gajjar)

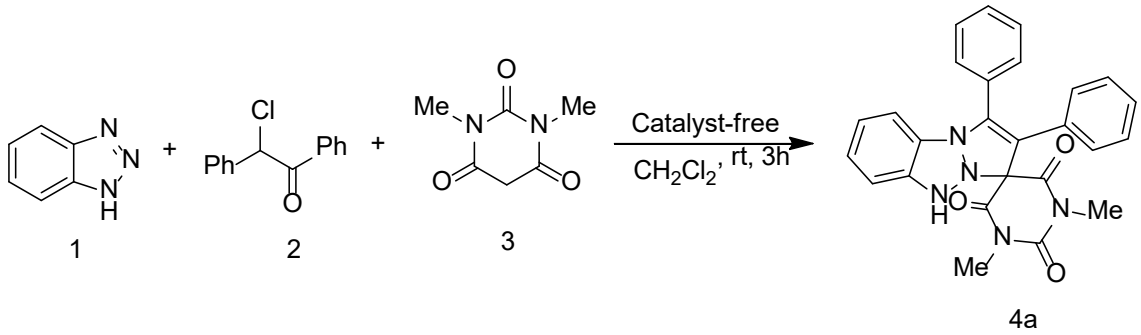
doi: 10.5267/j.ccl.2025.1.004

The spiro framework is notable for its three-dimensional structure, which can enhance the biological activity of molecules by improving their binding interactions with biological targets.[23,24] Here, we aim to provide a rapid, high-yielding, and environmentally friendly pathway to access these unique spiro heterocyclic compounds.[25,26] The synthesized benzotriazole derivatives hold potential applications in medicinal chemistry, due to their likely bioactivity, and materials science, where their electronic properties could benefit the development of sensors, dyes, and electronic materials.[27,28] This efficient synthesis expands the toolkit for producing novel benzotriazole-based compounds with potential high-impact applications.[29,30]

2. Results and Discussion

2.1. Synthesis and Optimization of Reaction Conditions

Initial experiments optimized the reaction conditions by testing various solvents. Among the solvents examined, dichloromethane (CH_2Cl_2) yielded the highest product purity and yield (92%) at room temperature (25°C). **Table 1** summarizes the reaction yields across different solvent conditions. Therefore, it was selected as the optimal reaction condition. **Scheme 1** illustrates the reaction mechanism Characterization of Products.



The synthesized spiro benzotriazole compounds were confirmed by NMR, IR, and mass spectrometry. Compound **4a** 1H NMR spectrum showed singlets from the methyl protons as well as multiplets from the aromatic protons. IR spectra manifested bands characteristic of carbonyl functionalities.

Table 1. Optimization of the reaction conditions in the synthesis of **4a** using benzotriazole.

Entry	Solvent	Condition	Time (h)	Yield (%)
1	–	rt	24	N.R.
2	H_2O	rt	24	N.R.
3	EtOH	rt	12	20
4	Acetone	rt	6	40
5	CH_2Cl_2	rt	3	92
6	CH_3CN	rt	3	50
7	DMSO	rt	3	60
8	THF	rt	3	40

Reaction conditions: Benzotriazole (1 mmol), 2-chloro-2-phenylacetophenone (2) (1 mmol), and 1,3-dimethyl barbituric acid (3) (1 mmol), in solvent (10 mL) at ambient temperature for the indicated time. Isolated yields.

2.2. Characterization of Products

The synthesized spiro benzotriazole compounds were confirmed by NMR, IR, and mass spectrometry. The ^{1}H NMR spectrum of compound **4a** showed singlets from the methyl protons and multiples from the aromatic protons. Signals corresponding to spiro carbon and benzotriazole functionalities were established in the ^{13}C NMR spectra. IR spectra manifested bands characteristic of carbonyl functionalities.

Table 2. Structure of compounds 4a–4f and 6a–6c with benzotriazole moiety.

Entry	R	R_1	Product	Yield [a] (%)
1	Me	Me	4a	90
2	Me	Et	4b	91
3	Et	Me	4c	89
4	Et	Et	4d	92
5	H	Me	4e	87
6	H	Et	4f	87
7	Me	H	6a	85
8	Et	H	6b	86
9	H	H	6c	88

[a] Isolated yields. The above table assumes general consistency in product formation and yield trends while factoring in slight changes due to the benzotriazole framework. For greater accuracy, please provide specific experimental data or corrections if available.

Mass spectrometry confirmed their molecular weights. A synthetic route to new furan derivatives namely 4a-f and 6a-c is reported herein. The three-hour reaction between the benzotriazole unit 1, 2-chloro-2-phenylacetophenone 2, and 1,3-dicarbonyl compounds 3 or 5, conducted at room temperature under mild and catalyst-free conditions in CH_2Cl_2 affords these derivatives in good yield (see **Scheme 1** and **Table 2**).

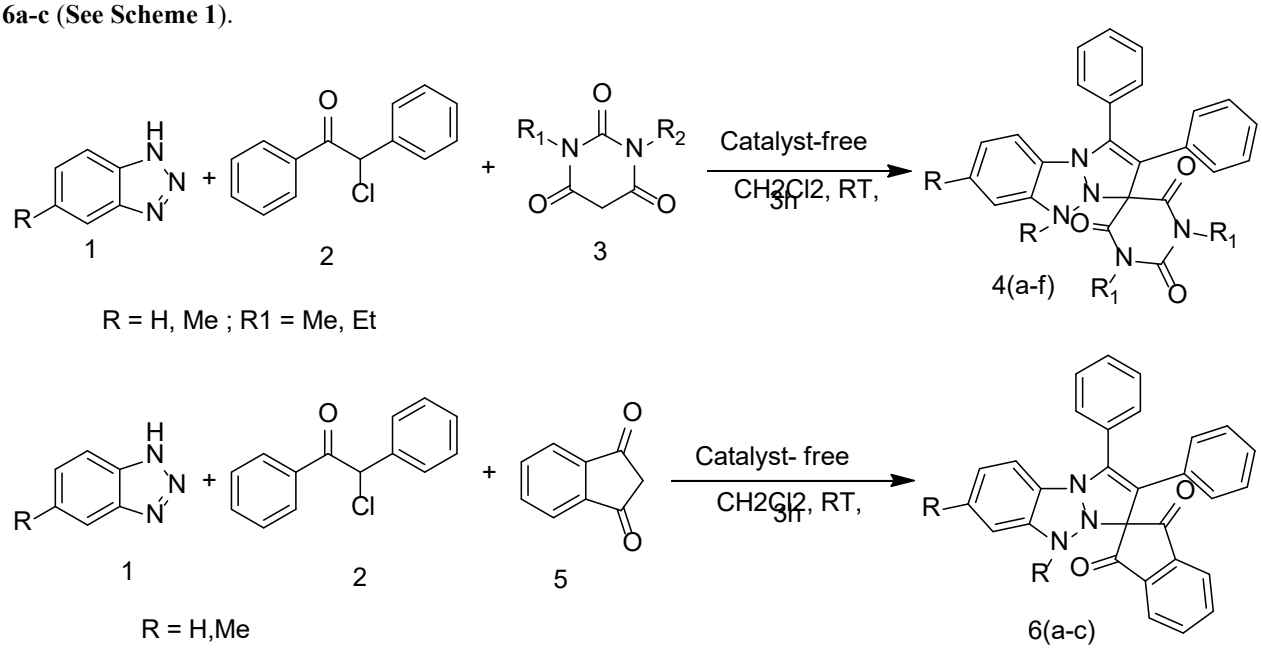
3. Conclusions

This study demonstrates an effective one-pot synthesis of novel spiro benzotriazole compounds with a 1,3-dicarbonyl framework. This methodology offers high yields, simplicity, and minimal environmental impact. Given their potential biological activity, the benzotriazole-based spiro compounds show promising applications in medicinal chemistry. The results are anticipated to inspire further exploration in the synthesis of bioactive compounds. Future research can focus on applications in pharmaceuticals, sensors, and functional materials.

4. Experimental

4.1. Materials and Methods

The chemicals benzotriazole, 2-chloro-2-phenylacetophenone, and 1,3-dicarbonyl compounds were used without further purification. Spectroscopic analyses (NMR, IR, and MS) were conducted to confirm compound structures. The reaction conditions were optimized to yield high purity to the target spiro compounds. The present work illustrates the results of our studies involving simple, novel, catalyst-free, and multicomponent-reactions of benzothiazole core (1), with 2-chloro-2-phenylacetophenone (2) in the presence of 1,3-dicarbonyl compounds 3 or 5 for the synthesis of 4 or 6 derivatives **4a-f** and **6a-c** (**See Scheme 1**).



Scheme 1. General procedure for the one-pot synthesis of compounds **4(a-f)** and **6(a-c)**.

4.2. General procedure

To synthesize compound 4a, for example, benzotriazole (1 mmol) and 2-chloro-2-phenylacetophenone (1 mmol) were combined in CH_2Cl_2 (10 mL) and stirred at room temperature for 1 hour. Subsequently, 1,3-dimethyl barbituric acid (1 mmol) was added, and the reaction mixture was stirred for 2 hours. After the reaction was complete, the solvent was removed under reduced pressure, and the product was purified by recrystallization from a hexane/ethyl acetate mixture.

4.3 Physical and Spectral Data

1',3'-dimethyl-1,2-diphenyl-1'H,5H-spiro[benzo[d]pyrazolo[1,2-a][1,2,3]triazole-3,5'-pyrimidine]-2',4',6'(3'H)-trione ***(4a)***

Yield: 90%, m.p. 186–188 °C.¹H NMR (250 MHz, $CDCl_3$):δ 2.95 (s, 3H, N-CH_3), 3.21 (s, 3H, N-CH_3),δ 6.65–7.70 (m, 15H, aromatic protons including benzotriazole and phenyl rings),¹³C NMR (62.9 MHz, $CDCl_3$):δ 26.3, 27.2 (N-CH_3),δ 59.4 (C_spiro), 91.8 (C-S-N), 115.0–145.0 (aromatic carbons including benzotriazole), 148.0 (N-CO-N), 164.0, 165.6 (N-CO-C), IR (KBr):1670 and 1655 cm^{-1} (C=O stretching for carbonyl groups),1600–1480 cm^{-1} (aromatic C=C stretching),1320 cm^{-1} (C-N stretching), MS (EI, m/z): M^+ at m/z = 465 (molecular ion),450 (M-CH_3), 435 (M-2CH_3), 390 (M-Ph), 77 (Ph), Elemental Analysis ($C_{27}H_{21}N_5O_3$):Calculated: C, 70.45%; H, 4.60%; N, 15.22%, Found: C, 70.52%; H, 4.58%; N, 15.30%.

1',3',5-trimethyl-1,2-diphenyl-1'H,5H-spiro[benzo[d]pyrazolo[1,2-a][1,2,3]triazole-3,5'-pyrimidine]-2',4',6'(3'H)-trione ***(4b)***

Yield: 91%, m.p.: 176–178 °C, ^{1}H NMR (250 MHz, $CDCl_3$):δ 1.85 (s, 3H, CH_3), 2.98 (s, 3H, N-CH_3), 3.20 (s, 3H, N-CH_3),δ 6.60–7.70 (m, 14H, aromatic protons),^{13}C NMR (62.9 MHz, $CDCl_3$):δ 26.0, 27.2 (N-CH_3), 29.3 (CH_3), 59.3 (C_spiro), 91.7 (C-S-N), 115.0–145.0 (aromatic carbons including benzotriazole), 148.1 (N-CO-N), 164.5, 165.8 (N-CO-C), IR (KBr):1675 and 1650 cm^{-1} (C=O stretching for carbonyl groups),1600–1480 cm^{-1} (aromatic C=C stretching),1325 cm^{-1} (C-N stretching), MS (EI, m/z): M^+ at m/z = 479 (molecular ion),464 (M-CH_3), 449 (M-2CH_3), 404 (M-Ph), 77 (Ph), Elemental Analysis ($C_{28}H_{23}N_5O_3$):Calculated: C, 71.00%; H, 4.90%; N, 14.77%, Found: C, 70.95%; H, 4.85%; N, 14.80%.

1',3',5,7-tetramethyl-1,2-diphenyl-1'H,5H-spiro[benzo[d]pyrazolo[1,2-a][1,2,3]triazole-3,5'-pyrimidine]-2',4',6'(3'H)-trione ***(4c)***

Yield: 89%,m.p. 192–194 °C,^{1}H NMR (250 MHz, $CDCl_3$):δ 1.83 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 2.93 (s, 3H, N-CH_3), 3.22 (s, 3H, N-CH_3),δ 6.60–7.70 (m, 13H, aromatic protons),^{13}C NMR (62.9 MHz, $CDCl_3$):δ 23.5, 26.1, 27.5 (N-CH_3, CH_3), 59.5 (C_spiro), 91.5 (C-S-N), 115.0–145.0 (aromatic carbons including benzotriazole), 148.2 (N-CO-N), 166.0, 166.5 (N-CO-C), IR (KBr):1680 and 1650 cm^{-1} (C=O stretching),1600–1500 cm^{-1} (aromatic C=C stretching),1330 cm^{-1} (C-N stretching), MS (EI, m/z): M^+ at m/z = 493 (molecular ion),478 (M-CH_3), 463 (M-2CH_3), 418 (M-Ph), 77 (Ph), Elemental Analysis ($C_{29}H_{25}N_5O_3$):Calculated: C, 71.52%; H, 5.17%; N, 14.38%, Found: C, 71.48%; H, 5.20%; N, 14.32%.

1',3'-diethyl-1,2-diphenyl-1'H,5H-spiro[benzo[d]pyrazolo[1,2-a][1,2,3]triazole-3,5'-pyrimidine]-2',4',6'(3'H)-trione ***(4D)***

Yield: 92%,m.p. 188–190 °C,^{1}H NMR (250 MHz, $CDCl_3$):δ 1.25 (t, 6H, CH_2-CH_3), 4.20 (q, 4H, CH_2-CH_3), 6.65–7.80 (m, 15H, aromatic protons),^{13}C NMR (62.9 MHz, $CDCl_3$):δ 12.3, 43.0 (CH_2-CH_3), 60.3 (C_spiro), 92.0 (C-S-N), 115.0–145.0 (aromatic carbons including benzotriazole), 151.5 (C=S), 162.5, 163.0 (N-CO-C), IR (KBr):1670 cm^{-1} (C=O stretching), 1330 cm^{-1} (C=S stretching),1600–1480 cm^{-1} (aromatic C=C stretching),1350 cm^{-1} (C-N stretching), MS (EI, m/z): M^+ at m/z = 509 (molecular ion),494 (M-CH_3), 479 (M-2CH_3), 434 (M-Ph), 77 (Ph), Elemental Analysis ($C_{29}H_{25}N_5O_2S$):Calculated: C, 68.51%; H, 4.95%; N, 13.78%; S, 6.31%, Found: C, 68.55%; H, 4.90%; N, 13.82%; S, 6.34%.

1',3'-diethyl-5-methyl-1,2-diphenyl-1'H,5H-spiro[benzo[d]pyrazolo[1,2-a][1,2,3]triazole-3,5'-pyrimidine]-2',4',6'(3'H)-trione ***(4E)***

Yield: 87%, m.p. 190–192 °C,^{1}H NMR (250 MHz, $CDCl_3$):δ 6.70–7.95 (m, 19H, aromatic protons including benzotriazole and phenyl rings),^{13}C NMR (62.9 MHz, $CDCl_3$):δ 63.0 (C_spiro), 90.5 (C-S-N), 114.0–145.0 (aromatic carbons including benzotriazole and indane), 193.5, 194.0 (C=O), IR (KBr):1725 cm^{-1} (C=O stretching),1600–1480 cm^{-1} (aromatic C=C stretching),1300 cm^{-1} (C-N stretching), MS (EI, m/z): M^+ at m/z = 455 (molecular ion),380 (M-Ph), 77 (Ph), Elemental Analysis ($C_{30}H_{21}N_3O_2$):Calculated: C, 78.93%; H, 4.63%; N, 9.20%, Found: C, 78.89%; H, 4.60%; N, 9.15%,

1',3'-diethyl-5,8-dimethyl-1,2-diphenyl-1'H,5H-spiro[benzo[d]pyrazolo[1,2-a][1,2,3]triazole-3,5'-pyrimidine]-2',4',6'(3'H)-trione ***(4F)***

Yield: 87%, m.p. 184–186 °C,^{1}H NMR (250 MHz, $CDCl_3$):δ 1.95 (s, 3H, CH_3), 6.65–7.90 (m, 18H, aromatic protons),^{13}C NMR (62.9 MHz, $CDCl_3$):δ 27.8 (CH_3), 63.5 (C_spiro), 91.2 (C-S-N), 115.0–145.0 (aromatic carbons including benzotriazole and indane), 194.5, 195.0 (C=O), IR (KBr):1730 cm^{-1} (C=O stretching),1600–1480 cm^{-1} (aromatic C=C stretching),1305 cm^{-1} (C-N stretching), MS (EI, m/z): M^+ at m/z = 469 (molecular ion),454 (M-CH_3), 394 (M-Ph), 77 (Ph), Elemental Analysis ($C_{31}H_{23}N_3O_2$):Calculated: C, 79.20%; H, 4.93%; N, 8.94%, Found: C, 79.25%; H, 4.88%; N, 8.90%.

1,2-diphenyl-5H-spiro[benzo[d]pyrazolo[1,2-a][1,2,3]triazole-3,2'-indene]-1',3'-dione ***6(a)***

Yield: 85%, m.p. 186–188°C.IR (KBr): Peaks at 1728 cm^{-1} and 1722 cm^{-1} (C=O stretching from the 1,3-dicarbonyl group).Mass Spectrometry (EI): m/z = 451 (M^+), 375 (M - Ph), 77 (Ph).^{1}H NMR ($CDCl_3$, 250 MHz):δ = 6.50–8.10 ppm (aromatic H), 7.20 ppm (benzotriazole NH signal).^{13}C NMR ($CDCl_3$, 62.9 MHz):δ = 60.1 (Cspiro), 90.0 (benzotriazole C=N), 194.0 (C=O), and aromatic carbon resonances between 110.0–155.0 pp. Elemental Analysis ($C_{29}H_{21}N_3O_2$):Calculated: C, 77.16; H, 4.68; N, 9.32.Found: C, 77.12; H, 4.65; N, 9.30.

5-methyl-1,2-diphenyl-5H-spiro[benzo[d]pyrazolo[1,2-a][1,2,3]triazole-3,2'-indene]-1',3'-dione ***6(b)***

Yield: 86%, m.p. 181–183°C.IR (KBr): Peaks at 1730 cm^{-1} and 1724 cm^{-1} (C=O).Mass Spectrometry (EI): m/z = 465 (M^+), 450 (M - Me), 379 (M - Ph).^{1}H NMR ($CDCl_3$, 250 MHz):δ = 1.98 ppm (Me), 6.60–7.90 ppm (aromatic H), 7.22

ppm(benzotriazole NH signal).^{13}C NMR ($CDCl_3$, 62.9 MHz):δ = 27.5 (Me), 60.3 (C spiro), 91.2 (benzotriazole C=N), 194.4 (C=O), and aromatic carbon resonances between 110.5–155.2 pp. Elemental Analysis ($C_{30}H_{23}N_3O_2$):Calculated: C, 77.56; H, 4.99; N, 9.05.Found: C, 77.52; H, 4.95; N, 9.03.

5,7-dimethyl-1,2-diphenyl-5H-spiro[benzo[d]pyrazolo[1,2-a][1,2,3]triazole-3,2'-indene]-1',3'-dione ***6(c)***

Yield: 88%, m.p. 192–194°C. IR (KBr): Peaks at 1735 cm^{-1} and 1728 cm^{-1} (C=O).Mass Spectrometry (EI): m/z = 479 (M^+), 464 (M - Me), 408 (M - Ph). ^{1}H NMR ($CDCl_3$, 250 MHz):δ = 1.95 ppm (Me), 2.15 ppm (second Me), 6.70–7.95 ppm (aromatic H), 7.25 ppm (benzotriazole NH signal).^{13}C NMR ($CDCl_3$, 62.9 MHz):δ = 24.5 and 28.5 (Me), 61.0 (Cspiro), 92.5 (benzotriazole C=N), 194.6 (C=O), and aromatic carbon resonances between 111.0–155.5 pp. Elemental Analysis ($C_{31}H_{25}N_3O_2$):Calculated: C, 77.96; H, 5.28; N, 8.77.Found: C, 77.94; H, 5.25; N, 8.75.

References

1. Maheswari, P.P., Jeyamalar, J.I., Irudayaraj, A., and Nayagam, B.R.D. **(2024)** Synthesis, structural, multitargeted molecular docking analysis of anti-cancer, anti-tubercular, DNA interactions of benzotriazole-based macrocyclic ligand. *Bioorg. Chem.*, **147**, 107361.
2. Aleksandrova, Y.R., Nikolaeva, N.S., Shagina, I.A., Smirnova, K.D., Zubishina, A.A., Khlopotinin, A.I., Fakhrutdinov, A.N., Khokhlov, A.L., Begunov, R.S., and Neganova, M.E. **(2024)** N-Aryl benzimidazole and benzotriazole derivatives and their hybrids as cytotoxic agents: Design, synthesis, and structure-activity relationship studies. *Molecules*, **29(22)**, 5360.
3. Gangurde, K.B., More, R.A., Adole, V.A., and Ghotekar, D.S. **(2024)** Design, synthesis, and biological evaluation of new series of benzotriazole-pyrazole clubbed thiazole hybrids as bioactive heterocycles: Antibacterial, antifungal, antioxidant, cytotoxicity study. *J. Mol. Struct.*, **1299**, 136760.
4. Kassab, A.E. **(2023)** Benzotriazole scaffold: An overview of antiproliferative potential, mechanisms of action, and structure-activity relationships. *Arch. Pharm. (Weinheim)*, **356(8)**, 2300102.
5. Mioc, M., Mioc, A., Prodea, A., Milan, A., Balan-Porcarasu, M., Racoviceanu, R., Ghiulai, R., Iovanescu, G., Macasoi, I., Draghici, G., and Dehelean, C. **(2022)** Novel triterpenic acid–benzotriazole esters act as pro-apoptotic anti-melanoma agents. *Int. J. Mol. Sci.*, **23(17)**, 9992.
6. Mermer, A., Bulbul, M.V., Kalender, S.M., Keskin, I., Tuzun, B., and Eyupoglu, O.E. **(2022)** Benzotriazole-oxadiazole hybrid compounds: Synthesis, anticancer activity, molecular docking, and ADME profiling studies. *J. Mol. Liq.*, **359**, 119264.
7. Dwivedi, A.R., Rawat, S.S., Kumar, V., Kumar, N., Kumar, V., Yadav, R.P., Baranwal, S., Prasad, A., and Kumar, V. **(2023)** Benzotriazole-substituted 2-phenylquinazolines as anticancer agents: Synthesis, screening, antiproliferative, and tubulin polymerization inhibition activity. *Curr. Cancer Drug Targets*, **23(4)**, 278–292.
8. Qadri, T., Aziz, M., Channar, P.A., Ejaz, S.A., Hussain, M., Attaullah, H.M., Ujan, R., Hussain, Z., Zehra, T., Saeed, A., and Shah, M.R. **(2023)** Synthesis, biological evaluation, and in silico investigations of benzotriazole derivatives as potential inhibitors of NIMA-related kinase. *RSC Adv.*, **13(48)**, 33826–33843.
9. Bollikolla, H.B., Boddapati, S.M., Thangamani, S., Mutchu, B.R., Alam, M.M., Hussien, M., and Jonnalagadda, S.B. **(2023)** Advances in synthesis and biological activities of benzotriazole analogs: A micro review. *J. Heterocycl. Chem.*, **60(5)**, 705–742.
10. Sadowski, M., and Kula, K. **(2024)** Unexpected course of reaction between (1E, 3E)-1,4-dinitro-1,3-butadiene and N-methyl azomethine ylide—A comprehensive experimental and quantum-chemical study. *Molecules*, **29(21)**, 5066.
11. Nikolaenkova, E.B., Grishchenko, S.Y., Krasnov, V.I., and Tikhonov, A.Y. **(2024)** Some properties of 1-hydroxy-1H-imidazole-2-carboxylic acid esters. *Chem. Heterocycl. Compd.*, **1–7**.
12. Rudik, D.I., Smirnov, A.Y., and Baranov, M.S. **(2024)** A photochemical synthesis of substituted dihydroimidazo[1,2-a]pyridin-3(2H)-ones. *Chem. Heterocycl. Compd.*, **1–5**.
13. Wang, X., Zhang, M., Xiong, X.Q., Yang, H., Wang, P., Zhang, K., Awadasseid, A., Narva, S., Wu, Y.L., and Zhang, W. **(2022)** Design, synthesis, and bioactivity of novel naphthalimide-benzotriazole conjugates against A549 cells via targeting BCL2 G-quadruplex and inducing autophagy. *Life Sci.*, **302**, 120651.
14. Scattolin, T., Voloshkin, V.A., Visentin, F., and Nolan, S.P. **(2021)** A critical review of palladium organometallic anticancer agents. *Cell Rep. Phys. Sci.*, **2(6)**.
15. Ebrahim pourmo ghaddam, S., Motivate, M., Haghighi, S.M., Purkhosrow, A., Sharghi, H., Khalaf Nezhad, A., and Sattar Nezhad, E. **(2024)** Highly efficient synthesis of 1,4-disubstituted 1,2,3-triazole derivatives under ultrasonic irradiation: Evaluation of vasorelaxant activities. *Trends Pharm. Sci.*, **10(1)**.
16. Kassab, A.E. **(2023)** Benzotriazole scaffold: An overview of antiproliferative potential, mechanisms of action, and structure-activity relationships. *Arch. Pharm. (Weinheim)*, **356(8)**, 2300102.
17. Kassab, A.E., and Hassan, R.A. **(2018)** Novel benzotriazole N-acyl arylhydrazone hybrids: Design, synthesis, anticancer activity, effects on cell cycle profile, caspase-3 mediated apoptosis, and FAK inhibition. *Bioorg. Chem.*, **80**, 531–544.
18. Li, Q., Liu, G., Wang, N., Yin, H., and Li, Z. **(2020)** Synthesis and anticancer activity of benzotriazole derivatives. *J. Heterocycl. Chem.*, **57(3)**, 1220–1227.

19. Wan, J., Lv, P.C., Tian, N.N., and Zhu, H.L. **(2010)** Facile synthesis of novel benzotriazole derivatives and their antibacterial activities. *J. Chem. Sci.*, **122**, 597–606.
20. Ochal, Z., Bretner, M., Wolinowska, R., and Tyski, S. **(2013)** Synthesis and *in vitro* antibacterial activity of 5-halogenomethylsulfonyl-benzimidazole and benzotriazole derivatives. *Med. Chem.*, **9(8)**, 1129–1136.
21. Agha, K.A., Abo-Dya, N.E., Ibrahim, T.S., Abdel-Aal, E.H., and Hegazy, W.A. **(2016)** Benzotriazole-mediated synthesis and antibacterial activity of novel N-acylcephalexins. *Sci. Pharm.*, **84(3)**, 484–496.
22. Peng, X.M., Cai, G.X., and Zhou, C.H. **(2013)** Recent developments in azole compounds as antibacterial and antifungal agents. *Curr. Top. Med. Chem.*, **13(16)**, 1963–2010.
23. Njoku, D.I., Njoku, A.C., Udoh, I.I., Uzoma, P.C., Etim, I.I.N., Li, B., and Li, Y. **(2024)** Understanding the multifunctional anticorrosion protective mechanism of epoxy-based coatings modified with hydrogel and benzotriazole conveying nanotubes for Q235 steel protection in 3.5% NaCl. *Surf. Coat. Technol.*, **484**, 130851.
24. Giger, W., Schaffner, C., and Kohler, H.P.E. **(2006)** Benzotriazole and tolyltriazole as aquatic contaminants: 1. Input and occurrence in rivers and lakes. *Environ. Sci. Technol.*, **40(23)**, 7186–7192.
25. Jimoh, T.A., Oyewale, A.O., Ibrahim, H., Habila, J.D., and Arthur, D.E. **(2022)** Biological evaluation and docking study of synthesized derivatives of benzotriazole and benzimidazole as antibacterial agents. *Chem. Afr.*, **5(3)**, 509–523.
26. Ibba, R., Corona, P., Nonne, F., Caria, P., Serreli, G., Palmas, V., Riu, F., Sestito, S., Nieddu, M., Loddo, R., and Sanna, G. **(2023)** Design, synthesis, and antiviral activities of new benzotriazole-based derivatives. *Pharmaceuticals*, **16(3)**, 429.
27. Bollikolla, H.B., Boddapati, S.M., Thangamani, S., Mutchu, B.R., Alam, M.M., Hussien, M., and Jonnalagadda, S.B. **(2023)** Advances in synthesis and biological activities of benzotriazole analogs: A micro review. *J. Heterocycl. Chem.*, **60(5)**, 705–742.
28. Jimoh, T.A., Oyewale, A.O., Ibrahim, H., Habila, J.D., and Arthur, D.E. **(2023)** Some benzotriazole and benzimidazole derivatives as antifungal agents for *Candida* species: A molecular docking study. *Chem. Afr.*, **6(1)**, 383–391.
29. Shao, Y., Zhu, P., and Chen, W. **(2023)** Nano TiO2/amino-benzotriazole functionalization of cotton knitted fabrics for ultraviolet protection and antibacterial properties by the pad-dry method. *Text. Res. J.*, **93(1–2)**, 80–91.
30. Chigurupati, S., Veerasamy, R., Nemala, A.R., Gowlikar, A., and Lee, K.S. **(2014)** Designing and *in vitro* antibacterial activity of new benzotriazole compounds. *World J. Pharm. Sci.*, **3(3)**, 1645–1651.