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(RESEARCH ARTICLE)

Synthesis and Acaricidal Evaluation of Some 2-Arylidene-[1,3]-Thiazolo[3,2 a]Benzimidazol-3(2*H*)-ones Derivatives and Their Impact on Cucumber (*Cucumis sativus L*) Growth Performance

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Abstract

A series of 2-(arylidene)thiazolo[3,2-a]benzimidazol-3(2*H*)-ones derivatives 7a-13a and 7b-13b were synthesized using an efficient and straightforward method. The reaction of 2-mercaptobenzimidazole or its derivatives 3a-c with ethyl 2-bromoacetate 4 under reflux in ethanol afforded thiazolo[3,2-a]benzimidazol-3(2*H*)-one 5a-c through intramolecular cyclization. These intermediates were then condensed with various aryl aldehydes 6a-g to yield the corresponding 2-arylidene derivatives. The structures of all compounds were confirmed by spectral analyses. Preliminary Acaricidal activity of these compounds was evaluate by determined Phytosanitary and agronomic parameters. The results showed that compounds 5b and 7b, exhibited promising dual functionality. These treatments not only significantly reduced pest presence, especially mites and mealybugs, but also enhanced key agronomic traits such as fruit size, weight, and yield.

Keywords: Benzimidazole; Intramolecular cyclization; Thiazolo[3;2-a] benzimidazol-3(2*H*)-one; Acaricidal activity

1. Introduction

The benzimidazole ring is a well-established heterocyclic scaffold widely used in drug design due to its broad spectrum of pharmacological properties. Several clinically approved drugs, such as thiabendazole, albendazole, mebendazole, and flubendazole, are benzimidazole-based anthelmintics. Others, including omeprazole and lansoprazole, serve as proton pump inhibitors, while astemizole functions as an antihistamine [1-3]. Structural modifications of the benzimidazole core have yielded a wide variety of bioactive compounds, with the nature and position of substituents playing a critical role in modulating their biological activities [4-5].

In recent years, the fusion of additional heterocycles to the benzimidazole core have attracted significant attention. Among these, thiazolo[3,2-a]-benzimidazoles have emerged as promising candidates with notable pharmaceutical potential. These fused systems have demonstrated activity against several disease targets, particularly well known as neoplasm inhibitors [6-8]. Additionally, derivatives of thiazolo-benzimidazoles have shown antiviral, antibacterial, anticancer, and antifungal properties [9-16]. Some compounds within this class have also been reported to act as potent non-nucleoside reverse transcriptase inhibitors (NNRTIs) against HIV-1 and to combat resistant fungal strains [8] [17].

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The biological activity of such molecules is strongly influenced by their three-dimensional structure. Many DNA-interacting agents, including transcription inhibitors, feature conjugated heteroaromatic frameworks with an S-shaped conformation. The 2-arylidene-substituted thiazolo[3,2-a] benzimidazole scaffold provides a rigid tricyclic core coupled with a flexible arylidene moiety, enabling multiple hydrogen-bonding interactions. This structural framework may favor binding to DNA or DNA-associated enzymes, enhancing therapeutic potential [18,19].

This study explores the synthesis and biological evaluation of 2-arylidene thiazolo[3,2-a] benzimidazole derivatives, specifically targeting their acaricidal activity and impact on cucumber agronomic performance. These hybrid molecules combine two pharmacologically significant moieties: the 2-mercaptobenzimidazole core, known for its antimicrobial and antiparasitic properties [20-22], and a chalcone-like arylidene group, recognized for disrupting pathogenic enzyme systems [23]. By merging these motifs, the designed compounds aim to achieve enhanced biological efficacy through structural synergy.

2. Materials and methods

2.1. Materials of chemistry

All chemicals were purchased from Aldrich Chemical, Fischer Scientific (France), and were used without further purification unless otherwise stated. The reactions were followed by TLC on pre-coated Merck 60 F254 silica gel plates and revealed using a UV lamp (6 W, 254 nm, and/or 365 nm). The purification of the products was carried out on a Merck G60 silica gel column. Melting points (m.p., °C) were determined using a temperature gradient (40-265°C) Köfler bench. For all compounds, the Nuclear Magnetic Resonance (NMR) spectra of proton ^{1}H and carbon ^{13}C were recorded on a Brucker 300 advance device. Tetramethylsilane (TMS) was used as a reference for chemical displacements expressed in δ (ppm). The NMR spectra description uses the following symbols: s (singlet), d (doublet), dd (double doublet), t (triplet), q (quadruplet), m (multiplet). The mass spectra were recorded on a JEOL JMS DX300 spectrometer in ESI mode (electrospray/quadripolar ionization or ESI mass).

2.2. Materials of Biology

2.2.1. Study site

The experiment was conducted on the campus of Université Félix Houphouët-Boigny in Cocody, Abidjan, located in the southern region of Côte d'Ivoire (5.3453° N, -4.0209° W), at an altitude of approximately 50 meters. The region has a hot and humid subequatorial climate (Eldin, 1971), and the soil is characterized as sandy-clay ferrallitic.

2.2.2. Plant material

The plant material consisted of cucumber plants obtained from seeds of the commercial hybrid variety Tokyo F1, known for its adaptability to both open-field and protected cultivation. This variety produces cylindrical, dark green fruits, 18-20 cm in length, typically maturing 45-50 days after sowing.

2.2.3. Plot Establishment

Sowing was carried out on November 2, 2024. Two (2) to three (3) seeds were placed in each pot, and thinning was performed two weeks later to retain only the most vigorous seedlings for uniform growth.

2.2.4. Experimental design

A completely randomized Fisher block design was implemented with two replicates. Each replicate included seven treatments, corresponding to six synthesized compounds (5a, 5b, 10a, 13a, 7b, and 9b) and one untreated control (T0). Compounds were applied at a concentration of 10 mg/L (10 ppm). Each treatment included 10 cucumber plants arranged in double rows on ridges measuring 2 meters in length and 0.7 meters in width. Plants were spaced 0.5 meters apart within and between rows. The ridges were spaced 1.5 meters apart, yielding a total plot area of 27 m^2.

2.2.5. Crop management

Plants were watered daily and weeded regularly to control competition. Fertilization was performed during the vegetative phase using urea and an NPK compound at a rate of 6-7 g per plant.

2.2.6. Extract application

Each test compound (10 mg) was dissolved in 1L of distilled water, with three drops of Tween 80 added as a surfactant. After thorough mixing, the solution was left to stand for 2 hours before foliar application. Spraying was targeted at the leaves and initiated on November 25th 2024, 23 days after sowing. Applications were repeated every 15 days, for a total of three treatments.

2.3. Synthesis methods

2.3.1. General procedure for the synthesis of 2-mercaptobenzimidazole derivatives 3a-c [24,25]

To a solution of o-phenylenediamine or its derivatives 1a-c (1.0 eq, 9.25 mmol) in 15 mL of DMF, cooled in an ice bath, carbon disulfide 2 (5eq, 46.23 mmol) was added dropwise. The reaction mixture was then stirred at room temperature for 24 to 48 hours. Upon completion of the reaction, 200 mL of water was added, resulting in the formation of a precipitate. The precipitate formed was filtered, washed several times with water and dried in an oven (80°C). The crude product was purified obtained by recrystallization from an ethanol/water mixture (1/1) to afford compounds 3a-c in 80 to 90% yield.

2-Mercaptobenzimidazole 3a: Beige crystals, yield = 80%, m.p. > 260 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 12.52 (s, 1H, NH), 7.16-7.08 (m, 4H, HAr), 3.40 (s, 1H, SH). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 167.23, 131.40, 125.11, 112.85, 108.60.

HRMS (ESI) Calc. for $C_7H_6N_2S$ ($M + Na^+$) = 173.0252 Found = 173.0354.

2-Mercapto-5-methylbenzimidazole 3b: Brown crystals, yield = 82%, m.p. > 260 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 12.50 (s, 1H, NH), 7.20-7.10 (m, 4H, HAr), 3.20 (s, 1H, SH), 2.35 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 167.23, 131.80, 127.13, 114.85, 112.52, 109.60, 107.61, 20.05.

HRMS (ESI) Calc. for $C_8H_8N_2S$ ($M + Na^+$) = 187.0408 Found = 187.0308

2-Mercapto-5-nitrobenzimidazole 3c: Orange crystals, yield = 90%, m.p. > 260 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 13.50 (s, 1H, NH), 8.30-7.50 (m, 4H, HAr), 2.50 (s, 1H, SH); ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 171.69, 142.48, 141.12, 139.81, 114.15, 112.22, 104.56.

HRMS (ESI) Calc. for $C_7H_5N_3O_2S$ ($M + H^+$) = 196.0102 Found = 196.0208

General procedure for the synthesis of thiazolo[3,2-a]benzimidazol-3(2*H*)-ones 5a-c [24]

To a suspension of 2-mercaptobenzimidazoles 3a-c (1.0 eq, 6.65 mmol) in 20 mL of anhydrous ethanol, ethyl bromoacetate 4 (1.2 eq, 8.0 mmol) was added dropwise. The reaction mixture was then refluxed for 2 to 3 hours. After completion, the reaction mixture was allowed to cool to room temperature, and the solvent was evaporated under reduced pressure. The crude residue was purified either by silica gel chromatography (hexane/ethyl acetate: 70/30) or by recrystallization from a dichloromethane/ethanol mixture to afford thiazolobenzimidazol-3(2*H*)-ones 5a-d in 75 to 90% yield.

Thiazolo[3,2-a]benzimidazol-3(2*H*)-one 5a : white crystals, yield = 85%, m.p. 135-137 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 7.56-7.24 (m, 4H, HAr), 4.32 (s, 2H, CH_2). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 169.28, 149.70, 113.47, 136.34; 34.09.

Mass (m/z) = 190. M+ = 190 (100), m/z (%): 162 (42), 150 (4), 118 (72), 90 (16), 77 (7), 63 (16), 36 (19), 28 (4).

7-Methylthiazolo[3,2-a]benzimidazol-3(2*H*)-one 5b : Beige crystals, yield = 75%, m.p. 169-170 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 7.59-7.27 (m, 3H, HAr), 4.51 (s, 2H, CH_2), 2.46 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 168.65, 149.24, 112.91, 135.01, 52.94, 21.04.

Mass (m/z) = 204. M+ = 204 (100), M+1 = 205 (12), m/z (%) : 175 (16), 163.19 (26), 142.88 (23), 131.97 (45), 130.97 (34), 121 (29), 90 (43), 45 (33), 41 (31).

7-Nitrothiazolo[3,2-a]benzimidazol-3(2*H*)-one 5c et 6-Nitrothiazolo[3,2-a]benzimidazol-3(*2H*)-one 5c': Light green crystals, yield = 90%, m.p. 141-143 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 8.54 (d, *J = 2.1 Hz*, 1H, HAr), 8.31 (d, *J = 2.1 Hz*, 1H, HAr), 8.13-8.19 (m, 2H, HAr), 7.60 (d, *J = 9 Hz*, 1H, HAr), 7.40 (d, *J = 9 Hz*, 1H, HAr), 3.99 (s, 2H, CH_2), 3.97 (s, 2H, CH_2). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 182.8, 155.2, 153.61, 149.6, 140.80, 132.5, 120.6, 112.40, 33.7.

HRMS (ESI) Calc. for $C_9H_5N_3O_3S$ (M + H^+) = 236.0052 Found = 236.0154.

General procedure for the synthesis of 2-(benzylidene)thiazolo[3,2-a]benzimidazol-3(2*H*)-ones 7a-13a et 7b-13b [26,27]

Compounds 5a-b (1 eq, 1.05 mmol) and sodium acetate (1 eq, 1.05 mmol) were dissolved in 20 mL of acetic acid. The mixture was stirred at room temperature for 30 minutes. Subsequently, benzaldehyde or its derivatives 6a-g (1.2 eq, 1.26 mmol) were added, and the reaction mixture was heated under for 4 hours. Upon cooling to room temperature, a precipitate formed, which was filtered, washed with water, and air-dried. The crude product obtained was recrystallized from ethanol to yield 2-benzylidenethiazolo[3,2-a]benzimidazol-3(2H)-ones 7a-13a and 7b-13b with yields ranging from 44 to 54%.

2-benzylidenebenzimidazo[2,1-b]thiazol-3(2*H*)-one 7a: Yellow crystals, yield = 67%, m.p. 212-214 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 8.13 (s, 1H, CH=C), 7.98-7.95 (m, 1H, HAr), 7.78-7.36 (m, 8H, HAr). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 170.28, 145.5, 142.5, 141.5, 135.2, 132.8, 130.7, 128.5, 127.9, 123.05, 119.6, 114.1

HRMS (ESI) Calc. for $C_{16}H_{10}N_2OS$ (M + H^+) = 278.0514 Found = 278.0255.

2-(2-chlorobenzylidene)benzimidazo[2,1-b]thiazol-3(2*H*)-one 8a: Yellow crystals, yield = 45%, m.p. > 260 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 8.40 (s, 1H, CH=C), 8.06-7.52 (m, 4H, HAr), 7.45-7.36 (m, 4H, HAr). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 169.28, 145.6, 142.4, 141.4, 135.1, 132.8, 130.7, 128.5, 127.9, 123.05, 119.3, 114.5

HRMS (ESI) Calc. for $C_{16}H_9ClN_2OS$ (M + H^+) = 312.0124 Found = 312.0146.

2-(4-chlorobenzylidene)benzimidazo[2,1-b]thiazol-3(2*H*)-one 9a: Yellow crystals, yield = 75%, m.p. = 200-201 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 8.12 (s, 1H, CH=C), 8.14-7.60 (m, 4H, HAr), 7.53-7.44 (m, 4H, HAr). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 169.28, 145.6, 142.4, 141.4, 135.1, 132.8, 130.7, 128.5, 127.9, 123.05, 119.3, 114.5

HRMS (ESI) Calc. for $C_{16}H_9ClN_2OS$ (M + H^+) = 312.0124 Found = 312.0156.

2-(2,4-dichlorobenzylidene)benzimidazo[2,1-b]thiazol-3(2*H*)-one 10a: Yellow crystals, yield = 70%, m.p. > 260 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 8.40 (s, 1H, CH=C), 7.95-7.93 (m, 3H, HAr), 7.82-7.56 (m, 4H, HAr). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 171.30, 146.7, 142.2, 141.8, 136.1, 132.5, 130.9, 128.5, 127.9, 123.05, 119.6, 114.3.

HRMS (ESI) Calc. for $C_{16}H_8Cl_2N_2OS$ (M + H^+) = 345.9734 Found = 345.888.

2-(4-methoxybenzylidene)benzimidazo[2,1-b]thiazol-3(2*H*)-one 11a: Orange crystals, yield = 69%, m.p. = 193-195 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 8.13 (s, 1H, CH=C), 8.08-7.67 (m, 4H, HAr), 7.28-7.22 (m, 2H, HAr), 7.34-6.94 (m, 2H, HAr), 4.17 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 170.45, 146.6, 141.8, 140.7, 136.1, 133.5, 131.8, 128.4, 127.8, 123.15, 119.9, 114.8.

HRMS (ESI) Calc. for $C_{17}H_{12}N_2O_2S$ (M + Na^+) = 331.0619 Found = 331.0517.

2-(4-dimethylaminobenzylidene)benzimidazo[2,1-b]thiazol-3(2*H*)-one 12a: Orange crystals, yield = 59%, m.p.= 243-245 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 8.11 (s, 1H, CH=C), 7.61-7.58 (m, 2H, HAr), 7.45-7.39 (m, 2H, HAr), 7.24-7.19 (m, 2H, HAr), 6.78-6.67 (m, 2H, HAr), 3.40 (s, 6H, $N(CH_3)_2$). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 169.30, 150.3 145.46, 141.8, 140.7, 136.1, 133.5, 131.8, 128.4, 127.8, 123.15, 119.9, 114.8, 41.3HRMS (ESI) Calc. for $C_{18}H_{15}N_3OS$ (M + Na^+) = 344.0936 Found = 344.1006.

2-(thiophen-2-ylmethylene)benzimidazo[2,1-b]thiazol-3(2*H*)-one 13a: Yellow crystals, yield = 61%, m.p. 241-242 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 8.25 (d, 1H, HAr), 7.88 (d, 1H, HAr), 7.75 (s, 1H, CH=C), 7.73-7.65 (m, 3H, HAr), 7.24-7.19 (m, 2H, HAr). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 171.93, 151.95, 142.56, 141.58, 137.92, 132.81, 130.75, 130.58, 129.14, 128.35, 123.05, 119.69, 114.18.

HRMS (ESI) Calc. for $C_{14}H_8N_2OS_2$ (M + Na^+) = 307.0078 Found = 307.0020.

2-benzylidene-7-methylbenzimidazo[2,1-b]thiazol-3(2*H*)-one 7b

Brown crystals, yield = 72%, m.p 182-184 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 8.10 (s, 1H, CH=C), 7.91-7.29 (m, 7H, HAr), 2.43 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 172.34, 145.65, 141.53, 136.81, 132.81, 132, 70, 128.85, 128.55 127.93, 127.78, 125.88, 115.35, 115.18, 21.37.

HRMS (ESI) Calc. for $C_{17}H_{12}N_2OS$ (M + H^+) = 293.0670 Found = 293.0380.

2-(2-chlorobenzylidene)-7-methylbenzo[4,5]imidazo[2,1-b]thiazol-3(2*H*)-one 8b

Yellow crystals, yield = 51%, m.p 235-237 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 8.30 (s, 1H, CH=C), 7.59-7.51 (m, 3H, HAr), 7.43 (s, 1H, HAr), 7.28-7.24 (m, 2H, HAr), 7.08 (m, 1H, HAr), 2.43 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 172.34, 144.62, 141.51, 136.41, 132.51, 132, 77, 127.88, 128.45 127.83, 126.79, 125.94, 115.32, 115.58, 21.32.

HRMS (ESI) Calc. for $C_{17}H_{11}ClN_2OS$ (M + H^+) = 327.0281 Found = 327.0510.

2-(4-chlorobenzylidene)-7-methylbenzo[4,5]imidazo[2,1-b]thiazol-3(2*H*)-one 9b

Yellow crystals, yield = 78%, m.p 258-260 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 8.10 (s, 1H, CH=C), 7.85-7.23 (m, 7H, HAr), 2.43 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 172.34, 144.62, 141.51, 136.41, 132.51, 132, 77, 127.88, 128.45 127.83, 126.79, 125.94, 115.32, 115.58, 21.32.

HRMS (ESI) Calc. for $C_{17}H_{11}ClN_2OS$ (M + H^+) = 327.0281 Found = 327.0510.

2-(2,4-chlorobenzylidene)-7-methylbenzo[4,5]imidazo[2,1-b]thiazol-3(2*H*)-one 10b

Brown crystals, yield = 73%, m.p. > 260 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 8.30 (s, 1H, CH=C), 7.92-7.28 (m, 6H, HAr), 2.43 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 172.14, 144.22, 141.31, 136.21, 132.31, 132, 46, 127.88, 128.45 127.83, 126.79, 125.94, 115.32, 115.58, 21.53.

HRMS (ESI) Calc. for $C_{17}H_{10}Cl_2N_2OS$ (M + Na^+) = 382.9891 Found = 382.9771.

2-(4-methylbenzylidene)-7-methylbenzo[4,5]imidazo[2,1-b]thiazol-3(2*H*)-one 11b Yield crystals, yield = 81%, m.p 235-237 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 8.10 (s, 1H, CH=C), 7.93-6.90 (m, 7H, HAr), 2.50 (s, 3H, CH_3), 2.43 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 170.34, 159.86, 145.91, 141.50, 138.84, 132.71, 130.20, 127.58, 125.69, 125.34, 115.12, 55.80, 21.45.

HRMS (ESI) Calc. for $C_{18}H_{14}N_2O_2S$ (M + H^+) = 323.0776 Found = 323.0872.

2-(4-dimethylaminobenzylidene)-7-methylbenzo[4,5]imidazo[2,1-b]thiazol-3(2*H*)-one 12b Orange crystals, yield = 78%, m.p. > 260 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 8.10 (s, 1H, CH=C), 7.82-6.67 (m, 7H, HAr), 3.30 (s, 6H, $N(CH_3)_2$), 2.43 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 171.43, 150.35, 145.71, 140.51, 138.44, 132.71, 130.25, 127.55, 125.96, 125.43, 115.12, 41.30, 21.45.

HRMS (ESI) Calc. for $C_{19}H_{17}N_3OS$ (M + H^+) = 336.1092 Found = 336.1220.

2-(thiophen-2-ylmethylene)-7-methylbenzo[4,5]imidazo[2,1-b]thiazol-3(2*H*)-one 13b

Beige crystals, yield = 58%, m.p. > 260 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 8.35 (d, 1H, HAr), 7.98 (d, 1H, HAr), 7.85-7.42 (m, 3H, HAr), 7.75 (s, 1H, CH=C), 7.65 (s, 1H, HAr), 7.24-7.19 (m, 2H, HAr). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 171.93, 151.95, 142.56, 141.58, 137.92, 132.81, 130.75, 130.58, 129.14, 128.35, 123.05, 119.69, 114.18, 21.3.

HRMS (ESI) Calc. for $C_{15}H_{10}N_2OS_2$ (M + Na^+) = 321.0235 Found = 321.0113.

2.4. Biological methods

Methods for assessing extract efficacy:

2.4.1. Phytosanitary parameters

Phytosanitary parameters were used to evaluate the biological activity of the synthesized compounds. These included: the presence of mite droppings, whitish flecks on the leaf surface, mite eggs and larvae, total mite count, presence of scale insects, and the number of non-target insects (excluding mites and scale insects). Well-developed cucumber leaves were sampled from three different leaf positions: the upper (Top), middle (Middle), and lower (Bottom) stages, determined from the plant apex toward the base. From each leaf stage, three mature leaves were collected per treatment group, using three plants as biological replicates. The samples were placed in Kraft paper envelopes and transported to the laboratory.

Observations were conducted under a binocular magnifying glass to identify and quantify the presence of mites, mealybugs and other arthropods on the leaf surfaces.

2.4.2. Agronomic parameters

Data collection on agronomic parameters began at fruit harvest. The parameters assessed included fruit size, median diameter, number of healthy and damaged fruits, fruit mass, average fruit weight, and overall yield. At each harvest, ten fruits were randomly selected per treatment group for measurement. Fruit length and median diameter were measured using an electronic caliper. The number of healthy and damaged fruits was recorded for each treatment, and their respective masses were determined using a Roberval balance.

The average fruit weight for each treatment was calculated using the following formula:

The average yield for each plot was calculated per unit area using the expression below:

2.5. Statistical analysis

Phytosanitary parameters such as the presence of mite droppings, whitish flecks, mite eggs and larvae, and scale insects were subjected to the Chi-square test of independence in XLSTAT (Version 2016). Quantitative variables, including the number of mites, the number of other insects, and agronomic parameters, were subjected to an analysis of variance (ANOVA) following a normality test to ensure statistical validity. When significant differences between means were detected, Fisher's Least Significant Difference (LSD) test was applied at the 5% significance level to group treatments with statistically similar effects.

3. Results and discussion

3.1. Chemistry

The synthetic strategy began with the preparation of 2-mercaptobenzimidazole and its derivatives 5-nitro-2-mercaptobenzimidazole and 5-methyl-2-mercaptobenzimidazole 3a-c from ortho-phenylenediamine and its substituted analogues (1a-c). These intermediates were obtained in good yields (80% to 90%) using standard cyclization conditions.

Subsequently, the reaction of these mercaptobenzimidazole derivatives (3a–c) with ethyl 2-bromoacetate (4) under reflux conditions in ethanol resulted in the formation of thiazolo[3,2-a]benzimidazol-3(2*H*)-ones (5a, 5b, and 5c′). The cyclization proceeded smoothly, affording the tricyclic products as the main compounds in this step.

In the final stage, compounds 5a and 5b were subjected to a condensation reaction with various aromatic aldehydes (6), yielding a series of 2-(benzylidene)thiazolo[3,2-a]benzimidazol-3(2*H*)-one derivatives (7a–13a and 7b–13b). These reactions were generally efficient, leading to the targeted arylidene derivatives in moderate to excellent yields. The overall synthetic route is illustrated in Figure 1.

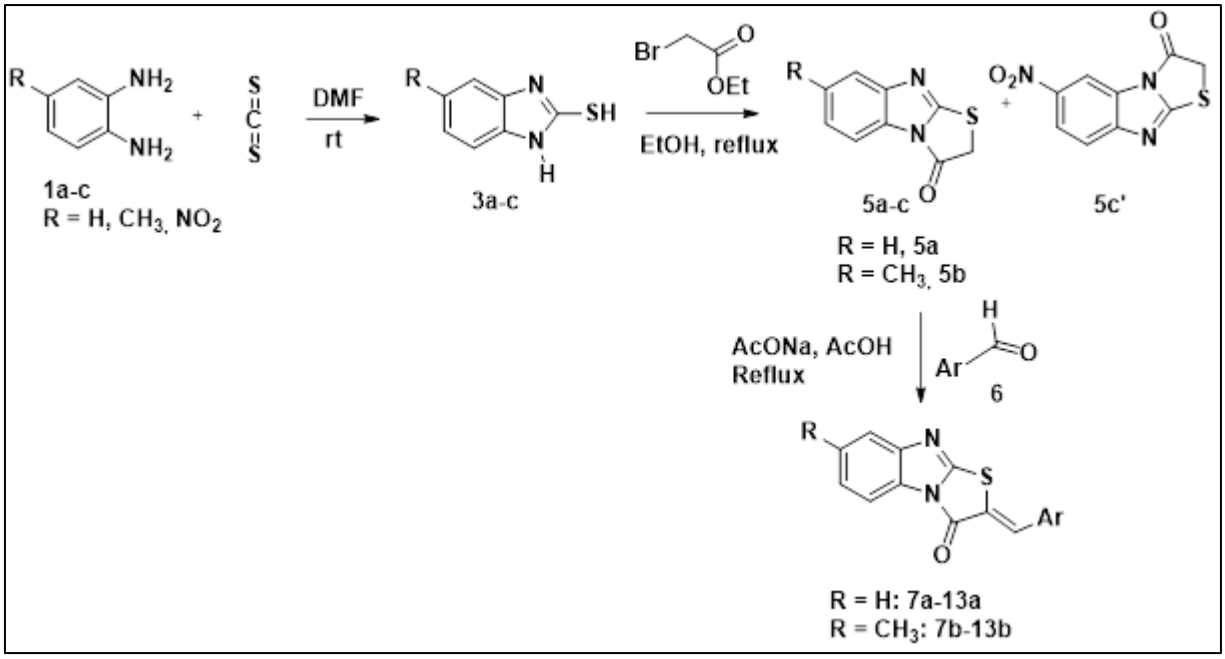

Figure 1 Synthesis of 2-benzylidenebenzo[4,5]imidazo[2,1-b]thiazol-3(2H)-ones 7a-13a and 7b-13b

The synthesis of compounds 3a-c was carried out using the Van Allan method, as modified by Sorba et *al.* [19]. This approach involves the condensation of ortho-phenylenediamine or its derivatives 1a-c with carbon disulfide (CS_2) 2 in *N,N*-dimethylformamide (DMF) at room temperature over 24 hours. The resulting precipitate formed was filtered, washed with water, and recrystallized to yield the corresponding 2 mercaptobenzimidazoles 3a-c. The physico-chemical properties of these thiol compounds were consistent with literature reports.

Building on the methodology reported by Siomenan *et al.* [17], the 2-mercaptobenzimidazoles (3a–c) were then reacted with ethyl 2-bromoacetate (4) under reflux in ethanol to afford the desired thiazolo[3,2-a]benzimidazol-3(2H)-ones (5a, 5b, 5c, and 5c′). Compounds 5a and 5b were purified by silica gel chromatography, yielding 85% and 75%, respectively. Compounds 5c and 5c′, formed as a mixture of isomers, were isolated by recrystallization with a combined yield of 90 %.

The structures of compounds 5a and 5b were confirmed by ^1H and ^{13}C NMR spectroscopy. In the ^1H NMR spectra, the disappearance of signals corresponding to the the pyrrolic (NH) and the thiol group (SH) protons present in the precursors 3a and 3b indicated successful cyclization. Instead, singlets at 4.32 ppm (5a) and 4.51 ppm (5b) were observed, corresponding to the two methylene (CH_2) protons. These findings were supported by corresponding signals in the ^{13}C NMR spectra. In the case of compounds 5c and 5c', the ^1H NMR spectra reveals the presence of two isomers. Ten protons signals were observed, including two singlets on their ^1H NMR spectrum. One at 3.99 ppm and another 3.97 ppm, each integrating for two protons, consistent with methylene protons (CH_2). Additionally, six aromatic protons appeared between 8.54 and 7.40 ppm, three from each isomer. The absence of NH and SH signals further confirmed the formation of cyclized products 5c and 5c′. The proposed reaction mechanism involves nucleophilic substitution (SN_2) of the halogen-bearing carbon by the sulfur atom's lone pair, followed by elimination of hydrobromic acid (HBr). Protonation of the carbonyl oxygen, due to the acidic nature of the medium facilitates nucleophilic attack by the nitrogen atom on the ester's electrophilic carbon. This leads to intramolecular cyclization and subsequent elimination of ethanol (Figure 2).

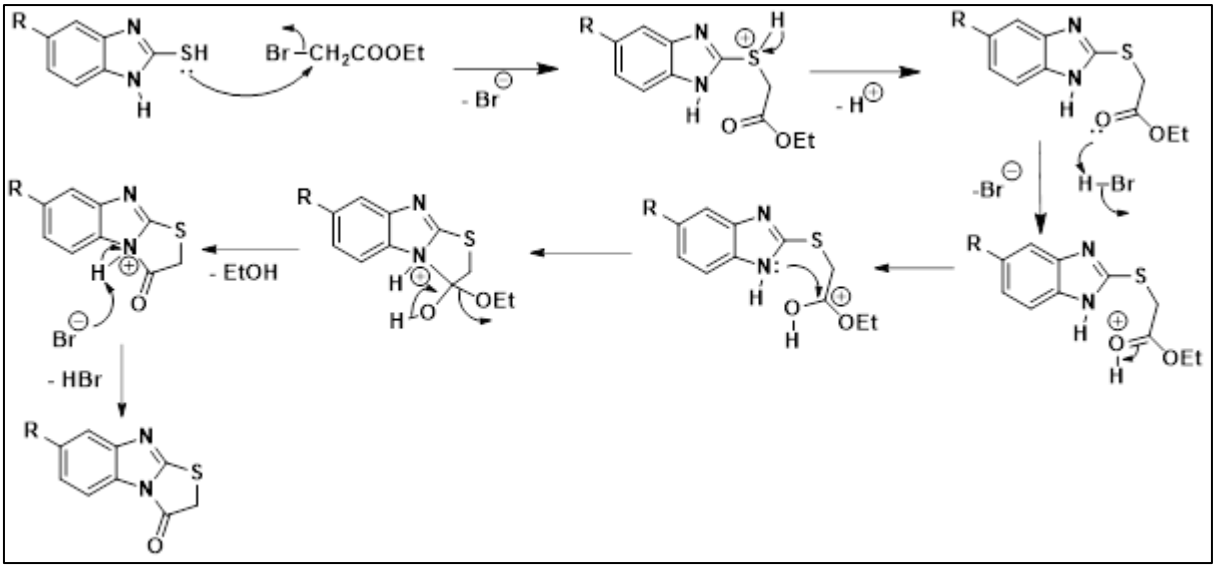

Figure 2 Mechanism for obtaining compounds 5

In contrast, compound 5b exhibits an electron-donating effect. The formation of compound 5c' can be attributed to the electron-withdrawing nature of the nitro group (NO_2), which promotes tautomerization. This effect facilitates the migration of the proton from the pyrrolic nitrogen (N-H) to the imine nitrogen (C=N), by a tautomeric effect, resulting in an equilibrium between two tautomeric forms (Figure 3).

In contrast the methyl group in compound 5b, exhibits an electron-donating which reduces the acidity of the pyrrolic proton and inhibits its migration. As a result, tautomerization is suppressed, and only a single cyclized product is formed.

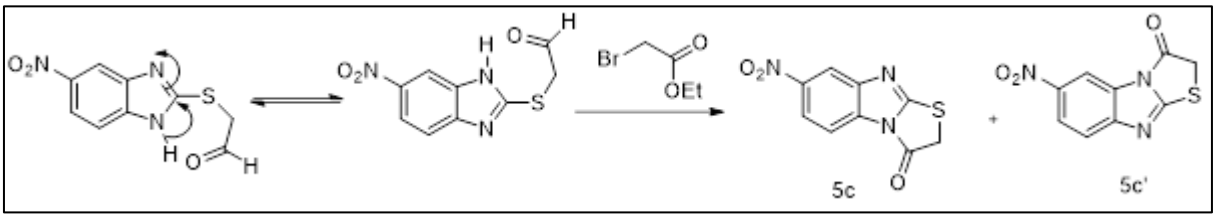

Figure 3 Migration of the proton from the pyrrolic nitrogen to the second nitrogen atom

These two isomeric forms of compound 5c/5c′ could not be separated using standard techniques. Efforts are ongoing to achieve separation through selective crystallization or high-performance liquid chromatography (HPLC).

Following this, compounds 5a and 5b were then condensed with various aromatic aldehydes, following the procedure reported by Om Prakash et *al.* [20]. The reactions between compounds 5 and aldehydes 6 yielded a series of 2-(benzylidene)thiazolo[3,2-a]benzimidazol-3(2*H*)-ones (7a-13a and 7b-13b) which were isolated in yields ranging from 45% to 81% after purification by recrystallization or silica gel chromatography.

The reaction mechanism of compounds 7a-13a and 7b-13b proceeds *via* a base-catalyzed aldol condensation mechanism followed by crotonization. Initially, the acetate ion abstracts an α-proton adjacent to the carbonyl group, generating a carbanion. This reactive intermediate subsequently attacks the carbonyl carbon of the aromatic aldehyde to form a β-hydroxy intermediate. The final step involves dehydration of this intermediate, leading to the formation of the conjugated arylidene product (Figure 4).

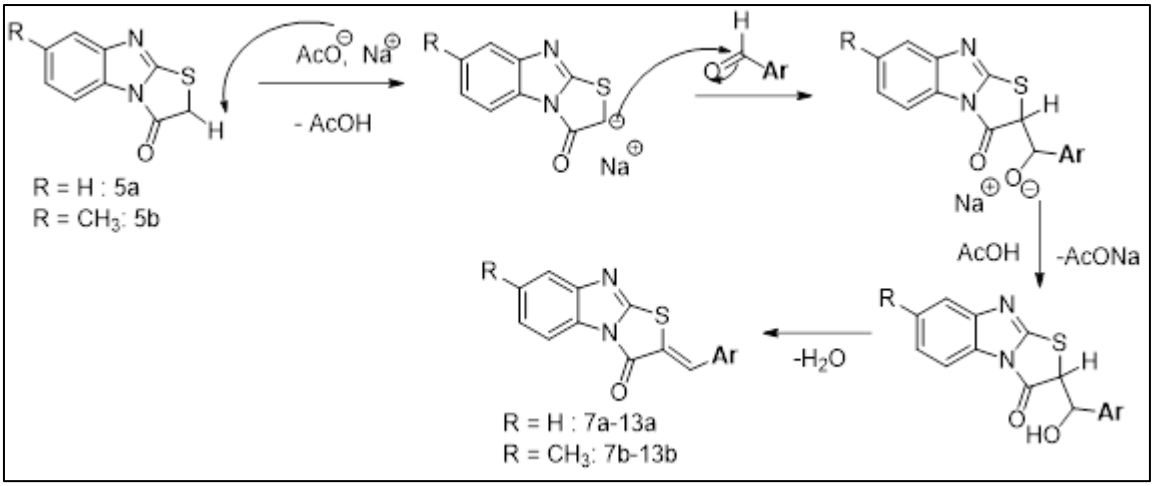

Figure 4 Mechanism for obtaining compounds 7a-13a and 7b-13b

All synthesized compounds 7a-13a and 7b-13b were fully characterized by ^{1}H NMR, ^{13}C NMR and HRMS. The ^{1}H NMR spectra confirmed the successful formation of the target structures. Specifically, the disappearance of the singlets signals at 4.32 ppm and 4.51 ppm, corresponding to the two methylene protons (CH_2) present in precursors 5a and 5b, indicates successful condensation. In their place, a new singlet appears around 8.4 ppm, attributed to the vinylic protons (-CH=) of the newly formed arylidene moiety.

This downfield shift is consistent with the deshielding effect caused by conjugation with the adjacent carbonyl group, a result of extended π-electron delocalization. Additionally, the ^{1}H NMR spectra of compounds 7a–13a and 7b–13b show an increased number of aromatic proton signals, reflecting the introduction of substituted aryl rings through the condensation with aromatic aldehydes.

3.2. Biology

3.2.1. Phytosanitary parameters

Presence of mite droppings on leaves

The Chi-square (χ^2) test of independence shows that the treatments had no statistically significant effect on the presence of mite droppings on cucumber leaves (p = 0.074 > 0.05), suggesting no association between treatment and this parameter (Table 1). However, notable differences were observed among individual treatments. Specifically, compound 5b resulted in 0% mite droppings, distinguishing it from all other treatments. In contrast, the highest incidence of droppings (41.67%) was recorded in treatment 7b.

Table 2 Percentages of mite droppings on leaves

Percentages / Line (Trts / Presence of droppings)				**Test of independence between rows and columns (χ^2):**	
compounds	No	Yes	Total	χ^2 (Observed value)	11.507
5a	91.667	8.333	100.000	χ^2(Critical value)	12.592
5b	100.000	0.000	100.000	DDL	6
10a	91.667	8.333	100.000	*p*-value	0.074
13a	91.667	8.333	100.000	α	0.05
7b	58.333	41.667	100.000		
9b	91.667	8.333	100.000		
To	83.333	16.667	100.000		
Total	86.9047619	13.0952381	100		

3.2.2. Presence of whitish flecking on leaves

The χ^2 test of independence revealed no significant association between treatments and the presence of whitish flecking on cucumber leaves (Table 2). This indicates that the occurrence of leaf flecking was not statistically linked to any specific treatment. Nevertheless, the treatment with compound 5b showed no signs of whitish flecking, while the highest incidence (33.33%) was observed in both the compound 10a treatment and the untreated control (T0).

Table 3 Percentages of whitish speckles on the leaves

Percentages / Line (Trts / Presence of whitish speckling)				**Test of independence between rows and columns (χ^2) :**	
compounds	No	Yes	Total	χ^2 (Observed value)	8.400
5a	83.333	16.667	100.000	χ^2 (Critical value)	12.592
5b	100.000	0.000	100.000	DDL	6
10a	66.667	33.333	100.000	*p*-value	0.210
13a	91.667	8.333	100.000	α	0.05
7b	83.333	16.667	100.000		
9b	91.667	8.333	100.000		
To	66.667	33.333	100.000		
Total	83.3333333	16.6666667	100		

3.2.3. Scale insects on leaves

The χ^2 test of independence showed that treatments had a significant effect on the presence of mealybugs on cucumber leaves (*p*-value = 0.001 < α = 0.05), indicating a strong association between treatment and mealybug infestation (Table 3). The most effective treatments were compounds 5b, 10a, and 7b, all of which resulted in the complete absence of mealybugs on the leaves.

Table 3 Percentages of scale insects on the leaves

Percentages / Line (Trts / Presence of scale insects)				**Test of independence between rows and columns (χ^2)**	
compounds	No	Yes	Total	χ^2 (Observed value)	22.022
5a	83.333	16.667	100.000	χ^2 (Critical value)	12.592
5b	100.000	0.000	100.000	DDL	6
10a	100.000	0.000	100.000	*p*-value	0.001
13a	91.667	8.333	100.000	α	0.05
7b	100.000	0.000	100.000		
9b	50.000	50.000	100.000		
To	91.667	8.333	100.000		
Total	88.0952381	11.9047619	100		

3.2.4. Number of mites and other insects on leaves

Significant differences were observed in the number of mites and other insects present on cucumber leaves across treatments. Compounds 5b, 10a, and 13a were the most effective in reducing mite infestation, showing the lowest mite counts. In contrast, treatment with compound 9b resulted in the highest level of infestation and was statistically distinct

from all other treatments. Treatments T0 (control), 5a, and 7b occupied an intermediate position, with no significant separation from the extremes.

Regarding the presence of other insects (excluding mites), treatment with compound 5a significantly favored their occurrence. The control (T0) showed a moderate presence of other insects, without a statistically significant difference from the majority of treatments. In contrast, treatments 5b, 10a, 13a, 7b, and 9b were the least favorable to insect presence, with no insects observed under these conditions (Table 4).

Table 4 Number of mites and other insects on leaves

Modality	Estimated averages (Number of mites)	Groups	
9b	0.837	A	
T0	0.415	A	B
7b	0.360	A	B
5a	0.334	A	B
13a	-0.002		B
5b	-0.002		B
10a	-0.002		B

Modality	Estimated averages (Number of other insects)	Groups	
5a	0.583	A	
T0	0.250	A	B
9b	0.000		B
13a	0.000		B
5b	0.000		B
10a	0.000		B
7b	0.000		B

3.3. Agronomic parameters

3.3.1. Fruit size

Treatments 5b, 7b, 9b, and 5a showed the most significant improvements in fruit length, with values ranging from 19.74 to 17.60 cm (Table 5, Figure 5). These results were statistically higher than those of the control treatment (16.36 cm). In terms of fruit diameter, treatments 5b and 7b recorded the highest values 61.726 mm and 60.467 mm, respectively, and were grouped exclusively in statistical group A (Table 6, Figure 6). In contrast, treatment 13a exhibited the lowest average fruit diameter (50.323 mm) and was classified solely in group C, indicating the poorest performance for this parameter

Table 5 Fruit length depending on treatment

Modality	Estimated Averages (cm)	Standard Error	Lower Terminal (95%)	Upper Terminal (95%)	Groups		
5b	19.740	0.556	18.633	20.848	A		
7b	19.705	0.556	18.598	20.812	A		

9b	19.446	0.556	18.338	20.553	A		
5a	19.359	0.556	18.252	20.467	A		
10a	18.201	0.556	17.094	19.308	A	B	
13a	17.606	0.556	16.499	18.713		B	C
T0	16.364	0.556	15.257	17.472			C

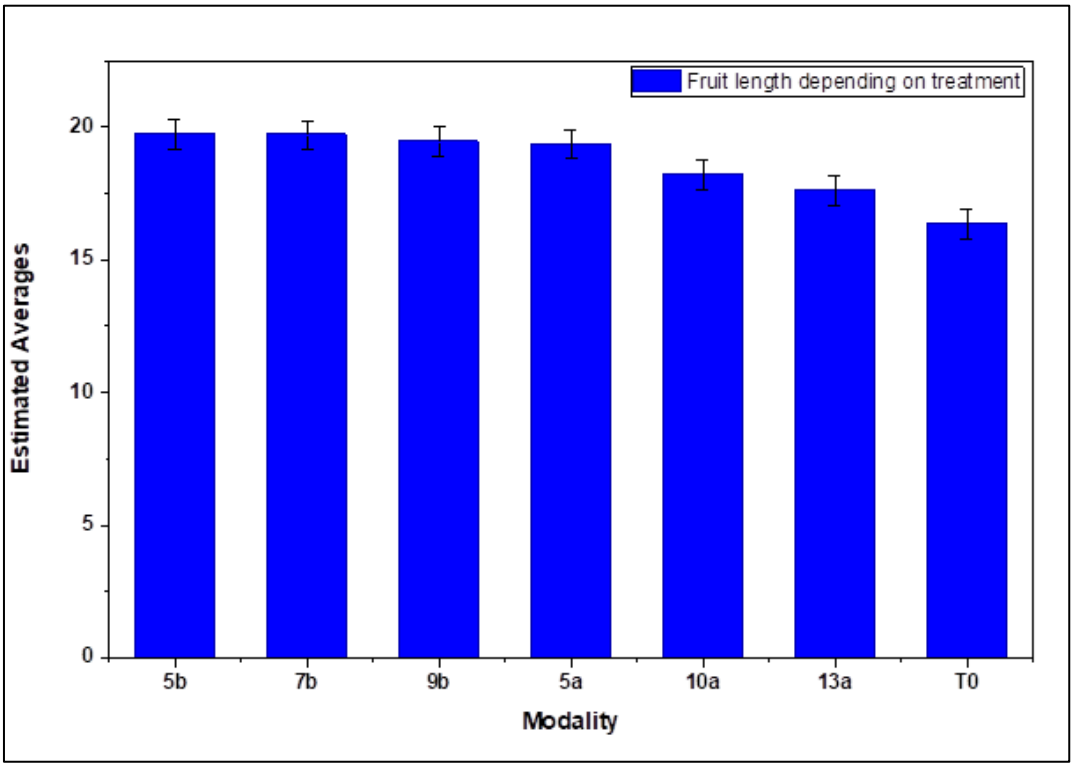

Figure 5 Fruit length (cm) depending of treatments

Table 6 Fruit widths depending to treatments

Modality	**Estimated Averages (mm)**	**Standard Error**	**Lower Terminal (95%)**	**Upper Terminal (95%)**	**Groups**		
5b	61.726	2.381	56.979	66.472	A		
7b	60.467	2.381	55.721	65.214	A		
10a	57.934	2.381	53.188	62.681	A	B	
5a	57.888	2.381	53.141	62.634	A	B	
9b	55.524	2.381	50.777	60.271	A	B	C
T0	52.678	2.381	47.931	57.424		B	C
13a	50.323	2.381	45.576	55.069			C

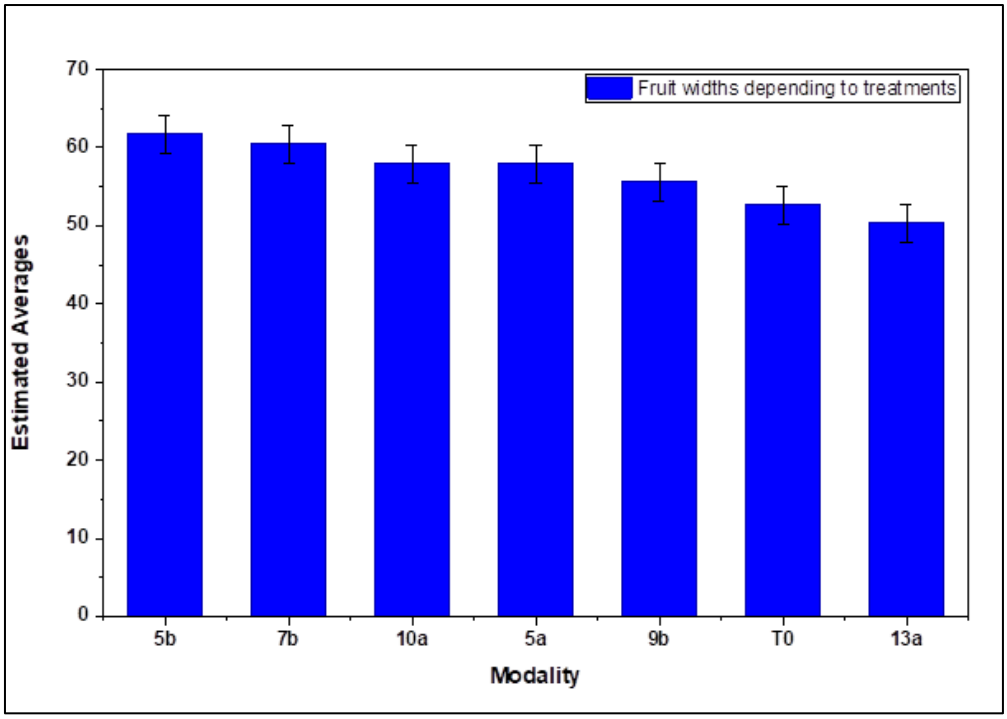

Figure 6 Fruit widths (mm) depending of treatments

3.3.2. Number of healthy and damaged fruits at harvest

Table 7 Number of healthy fruits by treatment at harvest

Modality	Estimated averages (No. of healthy fruits)	Groups		
5a	12.250	A		
9b	11.750	A	B	
7b	11.250	A	B	
5b	8.750	A	B	C
T0	6.500		B	C
13a	6.250		B	C
10a	5.000			C

Table 8 Number of damaged fruits according to harvest treatments

Modality	Estimated averages (No. of spoiled Fruits)	Groups
T0	1.000	A
5a	0.500	A
9b	0.500	A
7b	0.000	A
5b	0.000	A
10a	0.000	A
13a	0.000	A

Table 9 Fruit mass according to harvest treatments

Modality	Estimated averages (Mass Healthy fruits (kg))	Groups		
5a	3.323	A		
7b	3.300	A		
9b	3.275	A	B	
5b	2.625	A	B	C
T0	1.600	A	B	C
10a	1.525		B	C
13a	1.250			C

3.4. Average fruit weight and yield

Treatments showed significant differences in average fruit weight at harvest (Tables 10 and 11. The highest values were recorded for treatments 5b (293 g), 7b (291 g), and 9b (284 g), all of which were classified in statistical group A, indicating superior performance. In contrast, treatment 13a, with an average fruit weight of 182 g, was the lowest performer and was placed in group B. Regarding average yield, treatments 5a and 7b achieved the best results, with 2.373 kg/m^2 and 2.357 kg/m^2 of fruit, respectively. Conversely, treatment 13a produced the lowest yield at 0.893 kg/m^2.

Table 10 Average fruit weight according to harvest treatments

Modality	Estimated averages (Average weight (kg)	Groups	
5b	0.293	A	
7b	0.291	A	
9b	0.284	A	
5a	0.270	A	B
10a	0.258	A	B
T0	0.233	A	B
13a	0.182		B

Table 11 Average fruit yield according to harvest treatments

Modality	Estimated averages (Average Yield)	Groups		
5a	2.373	A		
7b	2.357	A		
9b	2.339	A	B	
5b	1.875	A	B	C
T0	1.143	A	B	C
10a	1.089		B	C
13a	0.893			C

The synthesized compounds demonstrated varying degrees of effectiveness in controlling pests and enhancing cucumber agronomic performance (Table 12). Compound 5b consistently stood out across multiple parameters, showing complete suppression of mite droppings, whitish flecking, and mealybug presence, as well as the lowest number of mites and other insects. It also yielded the longest fruits, the highest fruit diameter and weight, and one of the best yields. Treatments 7b and 9b also performed well, particularly in fruit size and pest control. In contrast, treatment 13a was the least effective, with the lowest fruit diameter, average fruit weight, and yield, and limited impact on pest suppression. These findings suggest that compounds 5b and 7b have strong potential as dual-purpose agents for crop protection and yield enhancement

Table 12 Summary of agronomic parameters

Modality	Mites	Other insects	Yield 1	Yield 2	Healthy fruits (no)	Tainted fruit	Healthy fruit mass	Average weight (kg)	Average yield (kg)	Final assessment
5b	✅ 0.000	✅ 0.000	🟢 A	🟢 A	🟠 Medium	✅ 0.000	🟠 Medium	🟢 A	🟠 Medium (A–B–C)	🥇 Ideal & clean
7b	⚠️ 0.360	✅ 0.000	🟢 A	🟢 A	🟢 Very good	✅ 0.000	🟢 Very good	🟢 A	🟢 High (A)	🥈 Highly efficient
5a	⚠️ 0.334	❌ 0.583	🟢 A	🟡 A–B	🟢 Excellent	⚠️ 0.500	🟢 Very good	🟡 A–B	🟢 High (A)	⚠️ Very good but at risk
9b	❌ 0.837	✅ 0.000	🟢 A	🟡 A–B–C	🟢 Very good	⚠️ 0.500	🟢 Very good	🟢 A	🟡 good (A–B)	⚠️ Productive, but very infected
10a	✅ 0.000	✅ 0.000	🟡 A–B	🟡 A–B	🔴 Low	✅ 0.000	🔴 Low	🟡 A–B	🔴 Low (B–C)	🔸 Clean, but not profitable
13a	✅ 0.000	✅ 0.000	🔴 B–C	🔴 C	🔴 Low	✅ 0.000	🔴 Low	🔴 B	🔴 Low (C)	❌ Discard
T0	⚠️ 0.415	⚠️ 0.250	🔴 C	🔴 B–C	🔴 Low	🔴 1.000	🔴 Low	🟡 A–B	🔴 Low (A–C)	❌ Control — very low

4. Conclusion

In this study, we successfully synthesized a series of novel 2-(arylidene)thiazolo[3,2-a]benzimidazol-3(2H)-one derivatives and six of them were evaluated for their acaricidal effects alongside with their impact on the agronomic performance of cucumber (*Cucumis sativus L.*). The compounds were obtained through an efficient three-step synthetic route, and their structures were confirmed by spectral analysis (^{1}H NMR, ^{13}C NMR, and HRMS. Notably, the formation of isomeric products in the case of nitro-substituted intermediates (5c/5c′) underscores the influence of electronic effects on tautomeric equilibrium and product distribution. These findings can highlight the synthetic versatility of the thiazolo[3,2-a]benzimidazole scaffold.

Biological evaluations revealed that several of the synthesized molecules, particularly compounds 5b and 7b, exhibited promising dual functionality. These treatments not only significantly reduced pest presence, especially mites and mealybugs, but also enhanced key agronomic traits such as fruit size, weight, and yield. Compound 5b, in particular, stood out as the most effective treatment across nearly all parameters, highlighting its potential as an integrated pest management agent with plant growth-promoting effects. In contrast, compound 13a consistently performed poorly in both phytosanitary and agronomic assessments, emphasizing the importance of structural variations in determining biological efficacy. The control treatment (T0) performed poorly across most parameters. Overall, the study demonstrates the potential of hybrid benzimidazole-based scaffolds as environmentally safer alternatives to conventional pesticides, with added agronomic benefits. Further studies, including field trials and environmental toxicity assessments, are recommended to confirm the broader applicability and safety of these compounds in sustainable agriculture.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

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