Synthesis of Novel 2, 3'-Bipyrrole Derivatives from Chalcone and Amino Acids as Antitumor Agents

Atef Kalmouch, 1 Mohamed A. A. Radwan, 2, 3 Mervat M. Omran, 4 Marwa Sharaky, 4 Gaber O. Moustafa, 1, 5 *

1 Peptide Chemistry Department, Chemical Industries Research Division, National Research Centre, 12622-Dokki, Cairo, Egypt.
2 Department of Applied Organic Chemistry, National Research Centre, Dokki, 12622, Egypt.
3 Department of Chemistry, College of Science, Qassim University, Buraydah, Kingdom of Saudi Arabia.
4 Pharmacology Unit, Cancer Biology Department, National Cancer Institute, Cairo University.
5 Nahda University, New Benisuef City, Postal code (62521), Beni sueif, Egypt.

Abstract

A series of a novel 2, 3'-bipyrrole derivatives was synthesized via the reaction of chalcone, (E)-1-(furan-2-yl)-3-(1H-pyrrol-2-yl) prop-2-en-one, with different amino acids in an alkaline medium. The reaction proceeds throughout the condensation of the amino acids with chalcone to give imine intermediate consequent by decarboxylation, and then intramolecular cyclization to yield 2, 3'-bipyrrole derivatives. Antitumor activities of the newly synthesized bipyrrole were evaluated against different six cancer cell lines, and compounds (3d, 3e, 3c and 3h) derivatives showed the strongest anticancer activity amongst the studied compounds. Compound (3h) showed the broadest spectrum of anticancer activity against all cell lines tested. The results of this work offer a basis for further study of selected 2, 3'-bipyrrole derivatives as antitumor agents.

Keywords: amino acids, pyrrole, bipyrrole, furan, antitumor, chalcone.

1. Introduction

The pyrrole moiety is one of the most vital heterocycles. Pyrrole ring and their derivatives normally exist in various natural products [1, 2] and pharmaceuticals [3]. They are key intermediates for the synthesis of a variety of biologically active molecules [4-7] and act as functional materials [8]. Compounds that bearing a pyrrole ring [9] show several biological and pharmaceutical activities such as antitumor [10], antibacterial [11], antioxidative [12], anti-inflammatory [13], and antifungal properties [14]. Bipyroles are an appreciated pioneer for the synthesis of several marine natural products [15]. Marinopyrroles A (1) and B (2) (Figure 1) with a unique 1,3'-bipyrole structure display anti-bacterial results towards methicillin-resistant Staphylococcus aureus (MRSA) and cytotoxicity contrary to specific human cancer cells [16-18]. Also, bipyroles and their derivatives are the basic components in several natural products and medicines (e.g., prodigiosin) [19-23]. Due to the promising of bipyroles, they have of the interest of several researchers. Some approaches to the bipyrole
and its derivatives have been reported, as well as the Paal-Knorr condensation reaction [24, 25], catalytic dehydrogenation reactions [26], coupling reactions [26-28], and a double Michael addition reaction [29], and the metal-catalyzed 1, 3-dipolar cycloaddition of azomethine ylides [30]. However, the literature covers limited information for the synthesis of bipyrroles, suggesting that methods to their synthesis are limited. Hua and Wu [31] synthesized some of the bis-pyrrole-3, 4-dicarboxylate derivatives by the condensation of diethyl 2, 3-diacetyl succinate with diamines catalyzed by organic acids. Banik et al. [32] presented that 1, 1'-bipyrroles, regularly in small yields, are limiting. Hua and Wu [31] synthesis of 2', 3'-bipyrroles, suggesting that methods to their synthesis are known up to date [33-40]. In this manuscript, we report quick one-step access into novel 2, 3'-bipyrrole derivatives from chalcone. The key point in this technique is the addition of amino acids to (furanpyrrol) prop-2-ene, chalcone. This reaction proceeds in pyridine; firstly, by condensation to give the corresponding imine then, decarboxylation generates carbonyl and followed by cyclization to the 2, 3'-bipyrrole derivatives. Current effort originated as an extension our investigation program directing to the synthesis of a variety of heterocyclic candidates for biological evaluation [41-53].

2. Experimental

Synthesis of Chalcone: 1-(furan-2-yl)-3-(1H-pyrrol-2-yl)prop-2-en-1-one 1, [54].

To obtain the required chalcone, 2-acetyl furan (10 mmol), and 2-pyrrrole-carboxyaldehyde (10 mmol) are dissolved in ethanol and stirred under an ice bath for 5 min. The reaction was initiated by dropwise addition of 10 ml of 60 % sodium hydroxide solution in 30 min interval. To ensure the end of the reaction, the mixture was allowed for continuous stirring for another 2-3 h at room temperature. The reaction mixture was kept in a refrigerator for overnight and diluted with ice-cold distilled water (40 mL). The precipitated chalcone was filtered, washed with cold water and air dried. The chalcone was recrystallized from methanol, yield 93% mp = 169-171°C [54].

General procedure for synthesis of the 2-5'-(furan-2-yl)-2', 3'-bipyrrrole derivatives 3a-i.

Chalcone (1.0 mmol) 1 was dissolved in pyridine (4 mL), and the appropriate amino acids 2 (3.0 mmol) were added. The reaction mixture was stirred at room temperature for 5 min. Then, the reaction was heated at 120 °C for 50 min. The reaction was controlled by TLC analysis. Next, the reaction was cooled and concentrated in vacuo, and the resulting product was purified by column chromatography using hexane/ EtOAc (90/10) to obtain the bipyrrrole derivatives 3a-i.

5'-(Furan-2-yl)-2'-isopropyl-3',4'-dihydro-1H,2'H-2,3'-bipyrrrole 3a.

![Structure of 5'-(Furan-2-yl)-2'-isopropyl-3',4'-dihydro-1H,2'H-2,3'-bipyrrrole 3a.](image)

Yield: 85 %; m.p= 94°C oil; Rf x100 (solvent system): 68 (N-hexane: ethyl acetate 7:3). IR in (cm⁻¹, KBr): 3433 (NH-stretching), 2997 (CH-aromatic), 2912 (CH-aliphatic). ¹H-NMR (500 MHz, DMSO-d6) δ : 11.70 (s, 1H, NH), 8.02 (d, 1H, furan, H-5), 7.57-7.60 (d, 1H, furan, H-3), 7.44 (d, 1H, pyrrole, H-5), 7.30-7.32 (d, 1H, furan, H-3). 6.73-6.74 (d, 2H, pyrrole, H-3, H-4), 3.90 (t, 1H, trihydropyrrole, H-2'), 1.90-1.93 (m, 1H, trihydropyrrole, H-3'), 1.85-1.87 (d, 2H, CH₂, trihydropyrrole, H-4'), 1.80 (m, 1H, CH of valine moiety), 0.75-0.55 (d, 6H, 2CH₃). MS (70-eV; EI): m/z (%): 242 (M⁺, 0.28%), 240 (0.79%), 72 (69.45%), 59 (100%), 51(0.51%). Molecular formula (M.wt.), C₁₇H₁₈N₂O (242.1), calculated-analysis; C, 74.35; H, 7.49; N, 11.56; found; C, 74.25; H, 7.40; N, 11.55.

2'-Benzyl-5'-(furan-2-yl)-3',4'-dihydro-1H,2'H-2,3'-bipyrrrole 3b.
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Yield: 8%; m.p. = 96 °C; Rf x100 (solvent system): 78 (N-hexane: ethyl acetate 7:3). IR in (cm⁻¹; KBr): 3432 (NH-stretching), 2998 (CH-aromatic), 2913 (CH-aliphatic). ¹H-NMR (500 MHz, DMSO-d₆) δ : 11.71 (s, 1H, NH), 7.98-8.40 (d, 1H, furan, H-5), 7.56-7.60 (m, 5H, 5CH, Ph), 7.43 (d, 1H, furan, H-3), 7.34, 731 (d, 1H, pyrrole, H-5), 7.13(d, 1H, furan, H-4), 6.22-6.66 (d, 2H, pyrrole, H-3, H-4), 2.5 (t, 2H, CH₂ of benzyl), 3.95 (t, 1H, trihydropyrrole, H-2'), 1.96-1.98 (m, 1H, trihydropyrrole, H-3'), 1.86-1.88 (d, 2H, CH₂, trihydropyrrole, H-4'). MS (70-eV; EI): m/z = 291 (M⁺-1, 0.16%), 290 (M⁺, 0.34%), 114 (2.77%), 72 (64.09%), 59 (100%), 55 (30.57%), 50 (0.50%). Molecular formula (M.wt.), C₁₀H₁₂N₂O₂ (290.4), calculated-analysis; C, 78.39; H, 6.25; N, 9.65; found; C, 78.48; H, 6.21; N, 9.60.

(5'-(Furan-2-yl)-3',4'-dihydro-1H,2'H-[2,3'-bipyrrol]-2'-yl)methanol 3e.

Yield: ∞%; m.p. = 86°C; Rf x100 (solvent system): 58 (N-hexane: ethyl acetate 7:3). IR in (cm⁻¹; KBr): 3431 (NH-stretching), 2998 (CH-aromatic), 2913 (CH-aliphatic). ¹H-NMR (500 MHz, DMSO-d₆) δ : 12.77 (s, 1H, OH), 11.73 (s, 1H, NH), 8.02-8.04 (d, 1H, furan, H-5), 7.61 (d, 1H, furan, H-3), 7.55-7.57 (d, 1H, pyrrole, H-5), 7.44-7.45 (d, 1H, furan, H-4), 7.27-7.34 (d, 2H, pyrrole, H-3, H-4), 4.12-4.2 (d, 2H, CH₂-OH), 3.98 (t, 1H, trihydropyrrole, H-2'), 1.99-2.10 (m, 1H, trihydropyrrole, H-3'), 1.92-1.94 (d, 2H, CH₂, trihydropyrrole, H-4'). MS (70-eV; EI): m/z (%) = 230 (M⁺, 0.44%), 126 (2.29%), 97 (7.19%), 72 (66.29%), 59 (100%), 55 (42.46%), 50 (0.57%). Molecular formula (M.wt.), C₁₉H₁₄N₂O₂ (256.3), calculated-analysis; C, 67.81; H, 6.13; N, 12.17; found; C, 67.77; H, 6.10; N, 0.20.

2'(sec-Butyl)-5'(furany-2-yl)-3',4'-dihydro-1H,2'H-2,3'-bipyrrrole 3d.

Yield: ∞%; m.p. = 81°C; Rf x100 (solvent system): 69 (N-hexane: ethyl acetate 7:3). IR in (cm⁻¹; KBr): 3432 (NH-stretching), 2998 (CH-aromatic), 2913 (CH-aliphatic). ¹H-NMR (500 MHz, DMSO-d₆) δ : 11.72 (s, 1H, NH), 8.01 (d, 1H, furan, H-5), 7.53-7.63 (d, 1H, furan, H-3), 7.45 (d, 1H, pyrrole, H-5), 7.36 (d, 1H, furan, H-3), 6.70-6.76 (d, 2H, pyrrole, H-3, H-4), 3.88 (t, 1H, trihydropyrrole, H-2'), 1.91-1.93 (m, 1H, trihydropyrrole, H-3'), 1.81-1.84 (d, 2H, CH₂, trihydropyrrole, H-4'), 1.70 (m, 1H, CH of isoleucine moiety), 1.60 (m, 2H, CH₂ of isoleucine moiety), 0.94-0.87 (d, 6H, 2CH₃, of isoleucine moiety). MS (70-eV; EI): m/z (%) = 265 (M⁺, 3.08%), 255 (M⁺-1, 4.91%), 115 (6.06%), 82 (46.49%), 69 (69.05%), 59 (76.62%), 57 (99.53%), 55 (100%), 50 (4.16%). Molecular formula (M.wt.), C₂₀H₂₀N₂O₂ (526.3), calculated-analysis; C, 74.97; H, 7.86; N, 10.93; found; C, 74.91; H, 7.75; N, 10.90.

5'(Furan-2-yl)-2'-isobutyl-3',4'-dihydro-1H,2'H-2,3'-bipyrrrole 3e.

Yield: 8%; m.p. = 87°C; Rf x100 (solvent system): 55 (N-hexane: ethyl acetate 7:3). IR in (cm⁻¹; KBr): 3426 (NH-stretching), 3001 (CH-aromatic), 2915 (CH-aliphatic). ¹H-NMR (500 MHz, DMSO-d₆) δ : 11.70 (s, 1H, NH), 8.02 (d, 1H, furan, H-5), 7.54-7.57 (d, 1H, furan, H-3), 7.41 (d, 1H, pyrrole, H-5), 7.24-7.26 (d, 1H, furan, H-3), 6.72-6.73 (d, 2H, pyrrole, H-3, H-4), 3.92 (t, 1H, trihydropyrrole, H-2'),
1.90-1.92 (m, 1H, trihydropyrrole, H-3'), 1.87-1.89 (d, 2H, CH₂, trihydropyrrole, H-4'), 1.75 (m, 1H, CH of leucine moiety), 1.60 (m, 2H, CH₂ of leucine moiety), 0.93-0.86 (d, 6H, 2CH₃, of leucine moiety). MS (70-eV; EI): m/z (%): 257 (M⁺+1, 0.41%), 256 (M⁺, 1.38%), 255 (M⁺-1, 0.76%), 114 (4.25%), 72 (66.02%), 59 (100%), 50 (0.32%). Molecular formula (M.wt.), C₁₆H₂₀N₂O (256.3), calculated-analysis: C, 74.97; H, 7.86; N, 10.93; found: C, 74.92; H, 7.76; N, 10.82.

4-((Furan-2-yl)-3′,4′-dihydro-1H,2′H-[2,3′-bipyrrrol]-2′-yl)methyl]phenol 3f.

Yield: 75%; m.p. = 90°C; Rf x100 (solvent system): 73 (N-hexane: ethyl acetate 7:3). IR in (cm⁻¹; KBr): 3431 (NH-stretching), 2998 (CH-aromatic), 2912 (CH-aliphatic). ¹H-NMR (500 MHz, DMSO-d₆) δ: 12.75 (s, 1H, NH), 11.70 (s, 1H, NH), 8.02-8.04 (d, 1H, furan, H-5), 7.75 (s, 1H, indole-H-2), 7.56 (d, 1H, indole-H-4), 7.52 (d, 1H, furan, H-3), 7.44-7.46 (m, 2H, indole-H-5,H-6), 7.40 (d, 1H, indole-H-7), 7.34-7.35 (d, 1H, pyrrole, H-5), 7.31-7.32 (d, 1H, furan, H-4), 7.22-7.24 (d, 2H, pyrrole, H-3, H-4), 3.98 (t, 1H, trihydropyrrole, H-2'), 2.5 (2H, CH₂), 1.99-2.10 (m, 1H, trihydropyrrole, H-3'), 1.92-1.94 (d, 2H, CH₂, trihydropyrrole, H-4'). MS (70-eV; EI): m/z (%): 329 (M⁺, 0.12%), 238 (1.94%), 126 (3.56%), 72 (72.86%), 59 (100%), 55 (39.06%), 50 (0.27%). Molecular formula (M.wt.), C₁₇H₁₈N₂O (329.4), calculated-analysis: C, 76.57; H, 5.81; N, 12.76; found: C, 76.52; H, 5.70; N, 12.72.

5′-(Furan-2-yl)-2′-methyl-3′,4′-dihydro-1H,2′H-2,3′-bipyrrrole 3h.

Yield: 79%; m.p. = 91°C; Rf x100 (solvent system): 60 (N-hexane: ethyl acetate 7:3). IR in (cm⁻¹; KBr): 3435 (NH-stretching), 2996 (CH-aliphatic, 2912 (CH-aliphatic). ¹H-NMR (500 MHz, DMSO-d₆) δ: 11.70 (s, 1H, NH), 8.03 (d, 1H, furan, H-5), 7.61 (d, 1H, furan, H-3), 7.74 (d, 1H, pyrrole, H-5), 7.34-7.35 (d, 1H, pyrrole, H-3), 3.90 (t, 1H, trihydropyrrole, H-2'), 1.90-1.93 (m, 1H, trihydropyrrole, H-3'), 1.85-1.87 (d, 2H, CH₂, trihydropyrrole, H-4'). 0.98 (3H, CH₃). MS (70-eV-
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EI)-m/z(%) =214 (M+, 0.45%), 149 (2.07%), 72 (61.76%), 59 (100%), 55 (30.30%), 50 (0.25%).

Molecular formula (M.wt.), C_{13}H_{14}N_{2}O (214.3), calculated-analysis; C, 72.87; H, 6.59; N, 13.07; found; C, 72.77; H, 6.48; N, 13.01.

5'-(Furan-2-yl)-3',4'-dihydro-1H,2'H-2,3'-bipyrrrole 3i.

Yield: \% m.p. 93 °C; Rf x100 (solvent system): 63 (N-hexane: ethyl acetate 7:3). IR in (cm⁻¹; KBr): 3427 (NH-stretching), 3000 (CH-aromatic), 2915 (CH-aliphatic), 1H-NMR (500 MHz, DMSO-d6) δ : 11.70 (s, 1H, NH of pyrrole ring), 8.23 (d, 1H, furan, H-5), 7.55 (d, 1H, furan, H-3), 7.44 (d, 1H, pyrrole, H-5), 7.31-7.33 (d, 1H, furan, H-3), 6.76-6.80 (d, 2H, pyrrole, H-3, H-4), 4.12 (d, 2H, CH₂, trihydropyrrole, H-2'), 1.90-1.93 (m, 1H, trihydropyrrole, H-3'), 1.85-1.87 (d, 2H, CH₂, trihydropyrrole, H-4'). MS (70-eV; EI)-m/z(%) =200 (M+, 0.49%), 187 (92.44%), 158 (55.49%), 130 (51.83%), 92 (51.53%), 72 (57.72%), 58 (100%), 55 (39.87%), 50 (16.21%). Molecular formula (M.wt.), C_{12}H_{12}N_{2}O (200.2), calculated-analysis; C, 71.98; H, 6.04; N, 13.99; found; C, 71.90; H, 6.96; N, 13.97.

2.1. Human cancer cell line

In this study, a panel of human cancer cell lines was tested for their chemosensitivity to 2',3'-bipyrrrole derivatives: Human Breast carcinoma cell line (MCF7), Human Colon carcinoma cell line (HCT116), Human Lung carcinoma cell line (A549), Human Pharyngeal carcinoma cell line (FADU), Human Liver carcinoma cell line (HEPG2), were obtained frozen in liquid nitrogen (-180°C) from American Type Culture Collection (ATCC; Washington, DC, USA). Human Tamoxifen Resistant MCF7 Breast carcinoma cell line (TMR10), prepared in pharmacology Unit Lab, National Cancer Institute to be resistant to 10µM Tamoxifen, and were maintained at National Cancer Institute as monolayer cultures in RPMI-1640 supplemented with 10% FBS and 1% penicillin-streptomycin.

2.1.1. Cytotoxicity assay

Cytotoxicity was determined using sulforhodamine-B (SRB) method [55]. Cells were seeded in 96-well microtiter plates at a concentration of 3 x 10^3 cells/well. They were left to attach for 24 h before incubation with drugs. The cells were treated for 48 h with single dose (100 µg/ml) of compound and for IC₅₀ the cells were treated by different concentrations (0, 5, 12.5, 25 and 50 µg/ml) of compounds. The optical density (O.D) of each well was measured spectrophotometrically at 570 nm using ELISA microplate reader (TECAN Sunrise TM, Germany). The mean values were estimated as percentage of cell viability as follows: O.D (treated cells) / O.D (control cells) x 100. The IC₅₀ value (the concentration that produces 50% inhibition of cell growth) of each drug was calculated using dose response curve-fitting models (Graph-Pad Prism software, version 5).

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Figure (1): % inhibition in Surviving fractions in different cancer cell lines after treatment with single dose (100ug/ml) of 2, 3′-bipyrrrole derivatives. MCF7 Human breast carcinoma cell line (A), HCT116 Human colon carcinoma cell line (B), A549 Human lung carcinoma cell line (C), FADU Human Pharyngeal carcinoma cell line (D), HEPG2 Human Liver carcinoma cell line (E), TMR10 Human Tamoxifen Resistant Breast carcinoma cell line (F). Values are the means ± SD of three independent experiments performed in triplicates.
FIGURE (2): Cytotoxicity of 2, 3'-bipyrrole derivatives on cancer cell lines after 48h. Surviving fraction of: (A) MCF7 treated with (3d). (B) HCT116 treated with (3b, 3d, 3e and 3h). (C) A549 treated with (3c and 3h). (D) FADU treated with (3b, 3c, 3e, 3f, 3g, 3h and 3i).
3. Results and Discussion

3.1. Chemistry

Throughout our investigation program, we found that the chemistry of amino acids is promising in the synthesis of biologically active compounds [56-76]. Herein, we describe a convenient strategy for the synthesis of a series of novel 2', 3'-bipyrrole derivatives via the reaction of chalcone 1, with different amino acids in an alkaline medium. The reaction proceeds in pyridine, which initiates a successive immunization, decarboxylation, and subsequently cyclization, leading to an efficient synthesis of novel 2', 3'-bipyrrole derivatives 3a-i, Scheme 1. Decarboxylation would give carbanion and followed by the electrocyclization to give 2', 3'-bipyrrole derivatives in one step, Scheme 2. To test this anticipated method, the study starting using chalcone 1 and glycine 2a in pyridine at 120 °C for 50 minutes yields 2', 3'-bipyrrole 3a. Structure elucidation of the final product was established on the basis of its spectral data and elemental analysis. The IR (KBr, cm⁻¹) spectra of this compound released a distinct NH group between 3121-3355 cm⁻¹ and the absence of a carbonyl group. Also, ¹H-NMR data of compound 3a displayed aliphatic signal at δ: 8.57 ppm for NH proton and aromatic signals at δ: 2.3-3.73 ppm in addition to aromatic signals at δ: 7.32-8.02 ppm (see experimental section).

![Scheme 1](image)

Scheme 1. Synthetic route for 5'-((furan-2-yl)-2', 3', 4'-trihydro-2', 3'-bipyrrole derivatives 3a-i.

3.2. Anticancer activity

After performing single dose (100µg/ml) testing for all 2', 3'-bipyrrole derivatives on different 6 cancer cell lines. Figure 1 showing the inhibition % of the 2', 3'-bipyrrole derivatives on the used 6 cancer cell lines. All the compounds exert mild effect (~ 85% inhibition) on both HEPG-2 and TMR10. On the other hand, 2', 3'-bipyrrole derivatives exert moderate to severe effect on MCF7, HCT116, A549, and FADU. (3d) showing ≥85% inhibition on MCF7 cell line with IC50=17, 14 µg/ml, respectively (Figure 2A). (3d) exert the better effect on MCF7 cell line. (3h, 3d, 3e, and 3b) showing ≥85% inhibition on HCT116 cell line with IC50=17, 13, 18, 18.2µg/ml, respectively (Figure 2B). (3h, and 3e) showing ≥85% inhibition on A549 cell line with IC50=16, 14µg/ml, respectively (Figure 2C). Compound (3e) exert the better effect on A549 cell line. (3d) derivative exert the better effect on HCT116 cell line. (3h, 3c, 3e, 3f, 3j, 3g, and 3b) showing ≥85% inhibition on FADU cell line with IC50=12, 17, 10, 28, 18.8, 22, and 14 µg/ml, respectively (Figure 2D). L- Leu (3e) derivative exert the better effect on FADU cell line.

Structure-Activity Relationship

Generally, bipyrrole derivatives represent promising building blocks as candidates for biological activity. Antitumor activities of the newly synthesized bipyrrole derivatives were evaluated in different six cancer cell lines, and (3d, 3e, 3c and 3h) derivatives showed the strongest anticancer activity amongst the studied compounds. Compound 3d with 2'-sec-butyl-bipyrrole derivative showed the

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strongest anticancer activity against both HCT_{116} & MCF7 cell lines. While compound 3e with 2'-isobutyl-bipyrrole derivative showed the strongest anticancer activity against FADU cell line. Compound 3c with 2'-hydroxy methyl-bipyrrole derivative showed the strongest anticancer activity against A549 cell line. On the other hand, Compound 3h with 2'-methyl-bipyrrole derivative showed the broadest spectrum anticancer activity all over most of the tested cell lines. Further investigations are required for studying the mechanism of action and toxicity of bipyrrole derivatives especially bipyrrole substituted with aliphatic groups at 2'-position.

4. Conclusion

In this article, we report fast one-step access into novel 2, 3'-bipyrrrole derivatives from chalcone and amino acids. The key point in this technique is the addition of amino acids to chalcone. This reaction proceeds in pyridine; firstly, by condensation to give the corresponding imine then, decarboxylation generates carbon and followed by cyclization to the 2, 3'-bipyrrrole derivatives. Antitumor activities of the newly synthesized bipyrrole were evaluated against different six cancer cell lines, and compounds (3d, 3e, 3c and 3h) derivatives showed the strongest anticancer activity amongst the studied compounds. Compound (3h) showed the broadest spectrum of anticancer activity against all cell lines tested. Further investigations are required for studying the mechanism of action and toxicity of these compounds.

5. References


36. Silvestri G., Gambino S., Filardo G., Petruso S.,...


