TÜBİTAK

Turkish Journal of Chemistry

http://journals.tubitak.gov.tr/chem/

Research Article

Turk J Chem
(2013) 37: 239 – 251

doi:10.3906/kim-1206-47

Ionic liquid mediated synthesis, reactions, and insecticidal activity of 1-[(1*H*-benzoimidazol-2-yl)amino]spiro[azetidine-4,4′-[4′*H*]chroman]-2-ones

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Received: 22.06.2012 • **Accepted:** 23.01.2013 • **Published Online:** 17.04.2013 • **Printed:** 13.05.2013

Abstract: Ionic liquid mediated synthesis of novel heterocyclic compounds 1-[(1*H*-benzoimidazol-2-yl)amino]-2′-phenylspiro[azetidine-4,4′-[4′*H*]chroman]-2-ones (**3**) and 1-[(1*H*-benzoimidazol-2-yl)amino]-3-chloro-2′-phenylspiro[azetidine-4,4′-[4′*H*] chroman]-2-ones (**4**) was accomplished by condensing substituted 2-hydrazino benzimidazole (**1**), flavanone (**2**), and acetyl chloride/chloroacetyl chloride in ionic liquid, [bmim]PF_6 with or without using catalyst in excellent yield (90%–95%). Further, compounds **3** and **4** were acylated with trifluoroacetic anhydride to give *N*-acylated products (**5** and **10**); **3** when treated with HCHO and $(C_2H_5)_2NH$ gave Mannich bases (**6**) and with aldehydes afforded 3-arylidene-2-azetidinone (**7**). Compounds **4** underwent nucleophilic substitution with (i) KI (Finkelstein reaction) and (ii) phenols to give the corresponding iodo and phenoxy derivatives (**8** and **9**). The synthesized compounds were characterized by analytical and spectral (IR, ^{1}H NMR, ^{13}C NMR, and HRMS) data and evaluated for insecticidal activity against *Periplaneta americana* using cypermethrin as standard and found to exhibit excellent results.

Key words: Benzoimidazolyl spiro [azetidine-chroman], ionic liquid mediated synthesis, insecticidal activity

1. Introduction

It is well known that heterocyclic compounds are found as a major contributing entity to the structure of many biological active compounds. Benzimidazoles are important nitrogen-containing heterocycles known for their diverse biological activities[1,2] such as antifungal,[3] CNS depressant,[4] antitubercular,[5] antihistaminic,[6] anticancer,[7] anti-HIV,[8] and antimicrobial[9] activities. Flavanones are polyphenolic compounds that act as pigments giving color to plants. Most plant species are a good source of flavanones, the best being citrus fruits. These show antioxidative,[10,11] antimicrobial,[12] antibacterial,[13] etc. activities. Detailed synthesis and biological activities of natural flavonoids have been reported by Harborne and Baxter.[14]

Azetidinones, commonly known as β-lactams, are well-known heterocyclic compounds present in synthetic and naturally occurring compounds. Antibiotics like penicillin, carbapenams, and cephalosporins contain a 2-azetidinone nucleus. Synthesis of azetidine and azetidinone has been reviewed by Brandi et al.,[15] while the pharmacological activities have been reviewed by Mehta et al.[16] These derivatives show antifungal,[17] antimicrobial,[18] antitubercular,[19] and anti-inflammatory[20] activities.

In view of sustainable chemistry, there is a need for new protocols that are not only truly efficient, high yielding, responsive to mild reaction conditions, and by-product–free but also environmentally benign. From the environmental and economic point of view, the use of nonvolatile solvents and green catalysts is very promising

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and interesting. In this regard, task specific ionic liquids (ILs) have frequently been used in recent years as alternative reaction media for a broad range of chemical transformations over volatile organic solvents owing to their tunable properties and green credentials,[21,22] while ionic liquid could be recycled and reused, in contrast to the traditional solvent catalyst system. In continuation of our work on the synthesis of novel bioactive heterocycles,[23–26] some novel benzoimidazolyl-spiro[azetidine-chroman] derivatives were synthesized in ionic liquid medium for the first time incorporating benzimidazole, flavanone, and azetidinone moieties.

Although there are references[27–29] regarding the synthesis of azetidinone derivatives in ionic liquid, the synthesis of benzoimidazolyl-spiro[azetidine-chroman] has not been reported in this medium. Further, *N*-methylation of benzimidazoles was carried out using the environmentally safe and less toxic methylating reagent dimethyl carbonate in the presence of DMF.[30]

With a view to developing an efficient and fast procedure using the green chemistry concept, a 1-pot, 3-component (hydrazino benzimidazoles, flavanone, and acetyl chloride/chloroacetyl chloride) synthesis of 1-[(1*H*-benzoimidazol-2-yl)amino]-2′-phenyl spiro[azetidine-4,4′-[4′*H*]chroman]-2-ones (**3**) and 1-[(1*H*-benzoimidazol-2-yl)amino]-3-chloro-2'-phenyl-spiro [azetidine-4,4′-[4′*H*] chroman]-2-ones (**4**) was developed for the first time by us using an ionic liquid, 1-butyl-3-methyl-1-imidazolium hexafluorophosphate [bmim]PF_6 as solvent. Its investigation appeared interesting as the following reactions were also done with these (**3** and **4**) compounds. This was because compound **3** has a reactive methylene group at position **3** while **4** has a 3-chloro group that could be substituted by various nucleophiles. Various substitution reactions of acidic hydrogen on nitrogen (>NH) were also carried out.

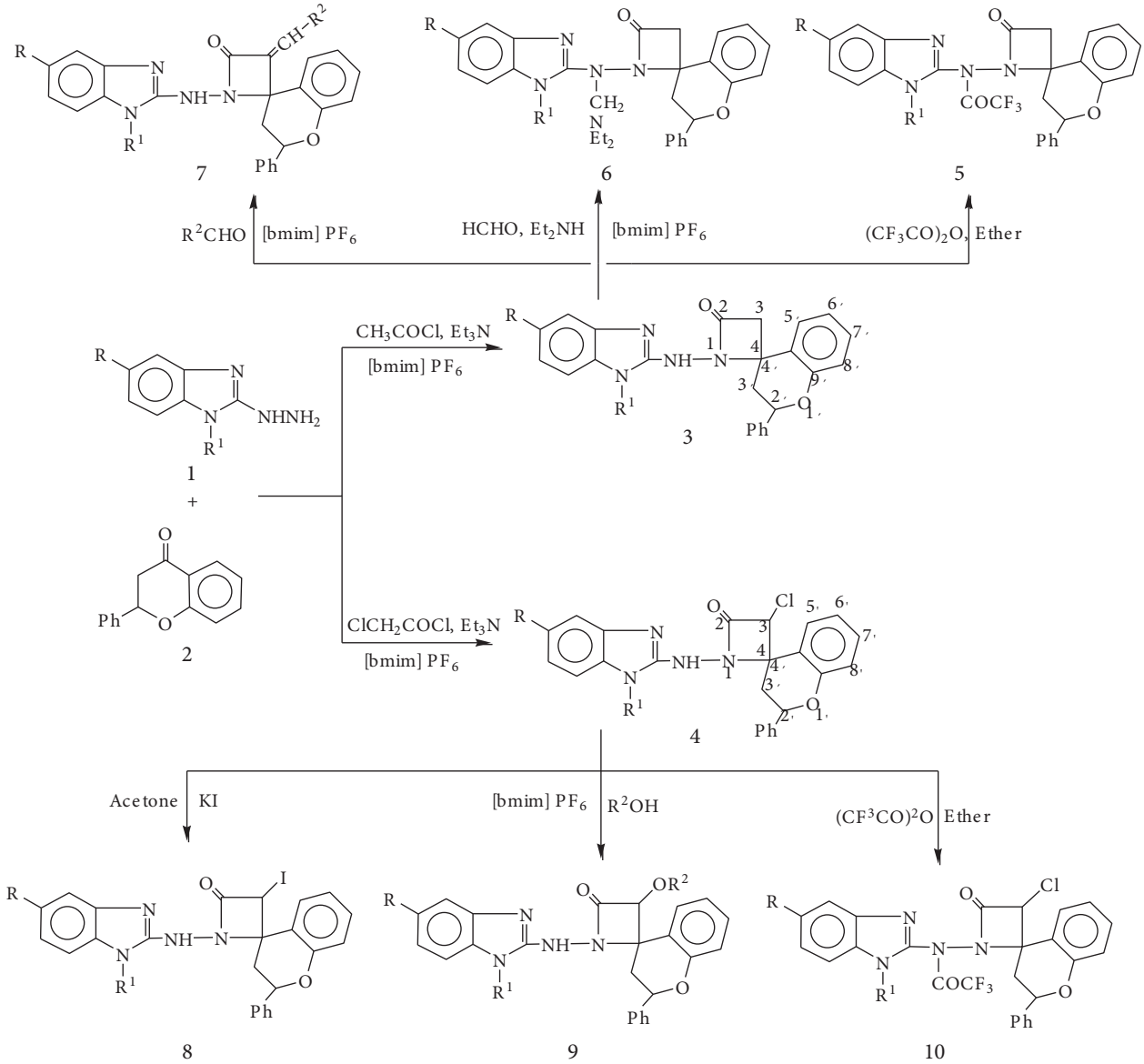
Treatment of **3** and **4** with trifluoroacetic anhydride[23] resulted in acylation of all the -NH groups present, affording 1-[trifluroacetyl-(1*H*-benzoimidazol-2-yl)amino]-2′-phenyl-spiro [azetidine-4,4′-[4′*H*]chroman]-2-ones (**5**) and 3-chloro-1-[trifluroacetyl-(1H-benzoimidazol-2-yl)amino]-2′-phenyl-spiro [azetidine-4,4′-[4′*H*] chroman]-2-ones (**10**).

Reaction with HCHO and diethylamine gave Mannich bases: 1-[diethylaminomethyl-(1*H*-benzoimidazol-2-yl) amino]-2′-phenyl spiro [azetidine-4, 4′-[4′*H*] chroman]-2-ones (**6**). 1-[(1*H*-Benzoimidazol-2-yl)amino]-3-arylidene-2′-phenyl-spiro[azetidine-4,4′-[4′*H*]chroman]-2-ones (**7**) were obtained by reacting **3** with aromatic aldehydes.

Nucleophilic substitution reaction of 3-chloroazetidinone (**4**) with (i) KI, i.e. Finkelstein reaction, gave iodo derivative 1-[(1*H*-benzoimidazol-2-yl)amino]-3-iodo-2′-phenyl-spiro [azetidine-4,4′-[4′*H*]chroman]-2-ones (**8**), and with (ii) phenols[31] the corresponding phenoxy derivative 1-[(1*H*-benzoimidazol-2-yl)amino]-3-phenoxy-2′-phenyl-spiro[azetidine-4,4′[4′*H*] chroman]-2-ones (**9**) were obtained (Scheme).

2. Experimental

Melting points are uncorrected and were obtained in open glass capillaries using a Gallenkamp melting point apparatus. The IR spectra were recorded on an 8400S Shimadzu IR spectrometer in KBr pellets and band positions are reported in wave numbers (cm^{-1}). ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL 300 MHz using $CDCl_3$ at 300.15 and 74.46 MHz, respectively, and chemical shifts (δ) are given in ppm. TMS was used as internal reference. The mass spectra were recorded on a XeVO, Q-TOF(ASAP) mass spectrometer. Elemental analyses were performed at the Central Drug Research Institute, Lucknow, India. All the chemicals used in the synthesis were purchased from ACROS ORGANICS and used as received.



Compound	R	R^1	Compound	R	R^1	R^2
3[a]	H	H	**6a**	H	CH_2NEt_2	-
3b	CH_3	H	**6b**	CH_3	CH_2NEt_2	-
3c	H	CH_3	**6c**	H	CH_3	-
3d	H	CH_2Ph	**6d**	H	CH_2Ph	-
4[a]	H	H	**7a**	H	H	C_6H_5
4b	CH_3	H	**7b**	H	H	p-$OMeC_6H_4$
4c	H	CH_3	**8a**	H	H	-
4d	H	CH_2Ph	**8b**	CH_3	H	-
5[a]	H	$COCF_3$	**9a**	H	H	p-$NO_2C_6H_4$
5b	CH_3	$COCF_3$	**9b**	H	H	β−naphthyl
5c	H	CH_3	**10a**	H	$COCF_3$	-
5d	H	CH_2Ph	**10b**	CH_3	$COCF_3$	-

Scheme. Synthesis of benzimidazol-amino-spiro[azetidine-4,4′-[4′*H*]chroman]-2-ones.

2.1. 2-Hydrazinobenzimidazoles (1)

These were prepared according to the published method.[32]

2.2. General procedure for compounds 3a–d

A mixture of 2-hydrazinobenzimidazole (0.01 mol), flavanone (0.01 mol) and ionic liquid, [bmim]PF_6 (5.0 mL), was taken in a round bottom flask and heated at 60–70 °C under N_2 protection for 1 h. On cooling at room temperature (after 15 min) acetyl chloride (0.01 mol) and triethylamine (0.01 mol) were injected and stirred further for 15 min at room temperature; after that the temperature was increased to 60 °C. The mixture was stirred for 2 h. The progress of the reaction was monitored by TLC. After completion of the reaction the mixture was extracted with ether (6 × 10 mL). The organic extract was washed with 5% Na_2CO_3 (40 mL) and water (40 mL), dried with anhydrous magnesium sulfate, and evaporated in a vacuum. The residual product was purified by recrystallization from AcOEt/cyclohexane or by column chromatography (silica gel, 60–120 mesh, eluent cyclohexane/AcOEt = 4:1) to give **3a–d**.

2.3. Recovery of the ionic liquid

After completion of the reaction, the reaction mixture was poured into water containing crushed ice, and the product was filtered off. The filtrate was extracted with ethyl acetate to recover unreacted reactants, and the aqueous layer was subjected to evaporation of water to get viscous liquid, which on cooling gave the ionic liquid. The recovered ionic liquid was reused for 2 more cycles of the same cyclocondensation and found to act satisfactorily.

1-[(1*H*-Benzoimidazol-2-yl)amino]-2′-phenyl-spiro[azetidine-4,4′-[4′*H*]chroman]-2-one (3a): Yield 3.76 g (95%); mp, 208–210 °C; IR (KBr, cm^{-1}) υ_{max}: 3200 (-NHN-), 3000 (-NH), 1700 (CO, azetidine); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.85 (dd, 1H, J = 16.8, 2.8 Hz, H_{eq}. C-3′), 3.11 (dd, 1H, J = 16.8, 12.9 Hz, H_{ax} C-3′), 3.20 (s, 2H, CH_2CO), 5.58 (dd, 1H, J = 12.9, 2.8 Hz, C-2′H_{ax}), 6.86–7.38 (m, 13H, Ar-H), 9.44 (s, 1H, -NH) and 10.32 (s, 1H, -NHN); ^{13}C NMR (74 MHz, $CDCl_3$) δ: 44.8 (C-3′), 46.2 (C-3), 80.3 (C-2′), 100.8 (spiro C-4), 115.9-138.5 (19C, Ar-C), 165.8 (C-2); HRMS: m/z $(M+H)^+$ Calcd. for $C_{24}H_{21}N_4O_2$: 397.1664. found: 397.1701; Anal. calcd. for $C_{24}H_{20}N_4O_2$: C, 72.71; H, 5.08; N, 14.13, found: C, 72.73; H, 5.06; N, 14.17.

1-[(5-Methyl-1*H*-benzoimidazol-2-yl)amino]-2′-phenyl-spiro [azetidine-4,4′-[4′*H*] chroman]-2-one (3b): Yield 3.81 g (93%); mp 175–177 °C; IR (KBr, cm^{-1}) υ_{max}: 3200 (-NHN-), 3000 (-NH), 1705 (CO); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.52 (s, 3H, Ar- CH_3), 2.86 (dd, 1H, J = 16.9, 2.7 Hz, H_{eq} C-3′), 3.15 (dd, 1H, J = 16.9, 12.8 Hz, H_{ax} C-3′), 3.21 (s, 2H, CH_2CO), 5.56 (dd, 1H, J = 12.8, 2.7 Hz, H_{ax} C-2′) 6.85–7.3 5 (m, 12H, Ar-H), 9.42 (s, 1H, -NH), 10.35 (s, 1H, -NHN); ^{13}C NMR (74 MHz, $CDCl_3$) δ: 28.4(Ar-CH_3), 44.8 (C-3′), 46.3 (C-3), 80.3 (C-2′), 100.2 (C-4), 116.2–137.9 (19C, Ar-C), 166.5 (C-2); HRMS: m/z $(M+H)^+$ Calcd. for $C_{25}H_{23}N_4O_2$: 411.1821. found: 411.1840; Anal. calcd. for $C_{25}H_{22}N_4O_2$: C, 73.15; H, 5.40; N, 13.65; found: C, 73.13; H, 5.36 N, 13.66.

1-[(1-Methyl-1*H*-benzoimidazol-2-yl)amino]-2′-phenyl-spiro [azetidine-4,4′-[4′*H*] chroman]-2-one (3c): Yield 3.78 g (92%); mp 180–182 °C; IR (KBr, cm^{-1}) υ_{max}: 3200 (-NHN-), 1690 (CO); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.85 (dd, 1H, J = 16.8, 2.8 Hz, H_{eq}, C-3′), 3.15 (dd, 1H, J = 16.8, 12.9 Hz, H_{ax} C-3′), 3.20 (s, 2H, CH_2CO), 3.52 (s, 3H, -NCH_3), 5.53 (dd, 1H, J = 12.9, 2.8 Hz, H_{ax} C-2′), 6.89–7.31 (m,

13H, Ar-H), 10.26 (s, 1H, -NHN); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 33.8 (-NCH_3), 44.6 (C-3′), 46.2 (C-3), 86.4 (C-2′), 100.1 (C-4), 115.3–136.8 (19C, Ar-C), 168.2 (C-2); HRMS: m/z (M+ H)$^+$ Calcd for $C_{25}H_{23}N_4O_2$: 411.1821. found: 411.1825; Anal. calcd. for $C_{25}H_{22}N_4O_2$: C, 73.15; H, 5.40; N, 13.65. found: C, 73.14, H, 5.36; N, 13.64.

1-[(1-Benzyl-1*H*-benzoimidazol-2-yl)amino]-2′-phenyl Spiro [azetidine-4,4′-[4′*H*] chroman]-2-one (3d): Yield 4.37 g (90%); mp 158–160 °C; IR (KBr, cm^{-1}) υ_{max}: 3205 (-NHN-), 1695 (CO); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.83 (dd, 1H, J = 16.7, 2.6 Hz, H_{eq} C-3′), 3.12 (dd, 1H, J = 16.7, 12.7 Hz H_{ax} C-3′), 3.20 (s, 1H, CH_2CO), 3.34 (s, 2H, CH_2Ph), 5.55 (dd, 1H J = 12.7, 2.6 Hz, H_{ax} C-2′), 6.78–7.36 (m, 18H, Ar-H), 10.18 (s, 1H, -NHN); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 43.2 (CH_2Ph), 44.5 (C-3′), 46.3 (C-3), 79.8 (C-2′), 99.9 (C-4), 115.8–137.2 (25C, Ar-C), 167.8 (C-2); HRMS: m/z (M+H)$^+$ Calcd. for $C_{31}H_{27}N_4O_2$: 487.2134. found: 487.2132; Anal. calcd. for $C_{31}H_{26}N_4O_2$: C, 76.54; H, 5.34; N, 11.52. found: C, 76.56; H, 5.38; N, 11.55.

2.4. General procedure for compounds 4a–d

These were prepared similarly to **3a–d** except for taking chloroacetyl chloride instead of acetyl chloride and gave **4a–d.**

1-[(1*H*-Benzoimidazol-2-yl)amino]-3-chloro-2′-phenyl-spiro[azetidine-4,4′-[4′*H*]chroman]-2-one (4a): Yield 4.05 g (94%); mp 183–185 °C; IR (KBr, cm^{-1}) υ_{max}: 3208 (-NHN-), 3010 (-NH), 1720 (CO), 750 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.84 (dd, 1H, J = 16.8, 2.6 Hz, H_{eq} C-3′), 3.15 (dd, 1H, J = 16.8, 12.8 Hz, H_{ax} C-3′), 4.12 (s, 1H, CHCl), 5.57 (dd, 1H, J = 12.8, 2.6 Hz, H_{ax} C-2′), 6.85–7.35 (m, 13H, Ar-H), 9.52 (s, 1H, -NH), 10.23 (s, 1H -NHN); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 44.2 (C-3′), 80.1 (C-2′), 100.2 (spiro C-4), 115.6–137.8 (19C, Ar-C), 127.2 (C-3) and 167.2 (C-2); HRMS: m/z (M+H)$^+$ Calcd. for $C_{24}H_{20}N_4O_2Cl$: 431.1275. found: 431.1265; Anal. calcd. for $C_{24}H_{19}N_4O_2Cl$: C, 66.90; H, 4.44; N, 13.00. found: C, 66.86; H, 4.43; N, 13.03.

3-Chloro-1-[(5-methtyl-1*H*-benzoimidazol-2-yl)amino]-2′-phenyl-spiro [azetidine-4,4′-[4′*H*] chroman]-2-one (4b): Yield 4.09 g (92%); mp 160–162 °C; IR (KBr, cm^{-1}) υ_{max}: 3210 (-NHN-), 3010 (-NH), 1710 (CO), 760 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.80 (s, 3H, Ar-CH_3) 2.82 (dd, 1H, J = 16.9, 2.8 Hz, H_{eq}. C-3′), 3.18 (dd, 1H, J = 16.9, 12.8 Hz, H_{ax} C-3′), 4.14 (s, 1H, -CHCl), 5.53 (dd, 1H, J = 12.8, 2.8 Hz, H_{ax} C-2′) 6.85–7.36 (m, 12H, Ar-H), 9.38 (s, 1H, -NH), 10.23 (s, 1H, -NHN-); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 28.6 (Ar-CH_3), 44.6 (C-3′), 80.2 (C-2′), 100.1 (C-4), 115.6-137.6 (19C, Ar-C), 127.3 (C-3), 167.6 (C-2); HRMS: m/z (M+H)$^+$ Calcd. for $C_{25}H_{22}N_4O_2Cl$: 445.1431. found: 445.1428; Anal. calcd. for $C_{25}H_{21}N_4O_2Cl$: C, 67.49; H, 4.76; N, 12.59 found: C, 67.46; H, 4.78; N, 12.62.

3-Chloro-1-[(1-methyl-1*H*-benzoimidazol-2-yl)amino]-2′-phenyl-spiro [azetidine-4,4′-[4′*H*] chroman]-2-one (4c): Yield 4.05 g (91%); mp 155–157 °C; IR (KBr, cm^{-1}) υ_{max}: 3190 (-NHN-), 1695 (CO), 755 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.81 (dd, 1H, J = 16.7, 2.6 Hz, H_{eq} C-3′), 3.15 (dd, 1H, J = 16.7, 12.6 Hz, H_{ax} C-3′), 3.57 (s, 3H, -NCH_3), 4.18 (s, 1H, -CHCl), 5.54 (dd, 1H, J = 12.6, 2.6 Hz, H_{ax} C-2′), 6.83–7.3 5 (m, 13H, Ar-H), 10.23 (s, 1H, -NHN-); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 33.6 (-NCH_3), 44.5 (C-3′), 80.6 (C-2′), 100.2 (C-4), 115.8-137.8 (19C, Ar-C), 127.5 (C-3), 167.6 (C-2); HRMS: m/z (M+H)$^+$ Calcd. for $C_{25}H_{22}N_4O_2Cl$: 445.1431. found. 445.1338; Anal. calcd. for $C_{25}H_{21}N_4O_2Cl$: C, 67.49; H, 4.76; N, 12.59; found: C, 67.46; H, 4.72; N, 12.57.

1-[(1-Benzyl-1*H*-benzoimidazol-2-yl)amino]-3-chloro-2′-phenyl spiro[azetidine-4,4′-[4′*H*] chroman]-2-one (4d): Yield 4.84 g (93%); mp 120–122 °C; IR (KBr, cm^{-1}) υ_{max}: 3200 (-NHN-), 1705 (CO), 760 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.86 (dd, 1H, J = 16.9, 2.8 Hz, H_{eq} C-3′), 3.17 (dd, 1H, J = 16.9, 12.8 Hz, H_{ax} C-3′), 3.36 (s, 2H, -CH_2Ph), 4.17 (s, 1H, -CHCl), 5.57 (dd, 1H, J = 12.8, 2.8 Hz, H_{ax} C-2′), 6.79–7.32 (m, 18H, Ar-H), 10.26 (s, 1H -NHN-); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 43.3 (CH_2Ph), 44.6 (C-3′), 80.4 (C-2′), 100.1 (C-4), 115.6–138.2 (25C, Ar-C), 127.8 (C-3), 168.2 (C-2); HRMS: m/z $(M+H)^+$ Calcd. for $C_{31}H_{26}N_4O_2Cl$: 521.1744. found: 521.1750; Anal. calcd. for $C_{31}H_{25}N_4O_2Cl$: C, 71.46; H, 4.84; N, 10.75. found: C, 71.50; H, 4.83; N, 10.78.

2.5. General procedure for compounds 5a–d, 10a, and 10b

Spiro[azetidine-4,4′[4′H]chroman-2-ones **(3a-d/4a and 4b)** (0.001 mol) was dissolved in dry ether (10.0 mL) and trifluoroacetic anhydride (0.002 mol) in dry ether (5.0 mL) was added with stirring at 0–5 °C. It was further stirred for 15 min. The ether was distilled under reduced pressure and water (10.0 mL) was added to it. The solid obtained was filtered after some time and recrystallized from ethanol to give **5a–d**, **10a**, and **10b**.

1-[Trifluroacetyl-(1-trifluroacetyl-1*H*-benzoimidazol-2-yl)amino]-2′-phenyl-spiro[azetidine-4,4′-[4′*H*]chroman]-2-one (5a): Yield 0.564 g (96%); mp 230–232 °C; IR (KBr, cm^{-1}) υ_{max}: 1710 (CO, azetidine), 1800 ($COCF_3$), 1755 ($COCF_3$), ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.87 (dd, 1H, J = 16.9, 2.7 Hz, H_{eq} C-3′), 3.15 (dd, lH, J = 16.9, 12.8 Hz, H_{ax} C-3′), 3.20 (s, 2H, CH_2CO), 5.60 (dd, 1H, J = 12.8, 2.7 Hz, H_{ax} C-2′), 6.85–7.35 (m, 13H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 44.7 (C-3′), 46.8 (C-3), 80.7 (C-2′), 100.9 (C-4), 115.2 (2C, CF_3), 118–138.5 (19C, Ar-C), 168.5 (C-2), 188.5 (**C**OCF_3), 190.1 (**C**OCF_3); HRMS: m/z $(M+H)^+$ Calcd. for $C_{28}H_{19}N_4O_4F_6$: 589.1310. found: 589.1319; Anal. calcd. for $C_{28}H_{18}N_4O_4F_6$: C, 57.15; H, 3.08; N, 9.52, found C, 57.17; H, 3.04: N, 9.54.

1-[Trifluroacetyl-(5-Methyl-1-trifluoroacetyl-1*H*-benzoimidazol-2-yl)amino]-2′-phenyl-spiro [azetidine-4,4′-[4′*H*]chroman]-2-one (5b): Yield 0.566 g (94%); mp 224–226 °C; IR (KBr, cm^{-1}) υ_{max}: 1805 ($COCF_3$), 1770 ($COCF_3$), 1710 (CO); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.68 (s, 3H, Ar-CH_3), 2.84 (dd, 1H, J = 16.6, 2.6 Hz, H_{eq} C-3′), 3.16 (dd, 1H, J = 16.6, 12.7 Hz H_{ax} C-3′), 3.21 (s, 2H, CH_2CO), 5.58 (dd, 1H, J = 12.7, 2.6 Hz, H_{ax} C-2′), 6.82–7.56 (m, 12H, Ar-H), ^{13}C NMR (75 MHz, $CDCl_3$) δ: 28.6 (Ar-CH_3), 44.6 (C-3′), 46.9 (C-3) 80.5 (C-2′), 100.2 (C-4), 115.5 (2C, CF_3), 117–137.8 (19C, Ar-C), 168.6 (C-2), 188.6 ($COCF_3$), 190.3 (**C**OCF_3); HRMS: m/z $(M+H)^+$ Calcd. for $C_{29}H_{21}N_4O_4F_6$: 603.1467. found: 603.1471; Anal. calcd. for $C_{29}H_{20}N_4O_4F_6$, C, 57.81; H, 3.35; N, 9.30, found: C, 57.84; H, 3.34; N, 9.31.

1-[Trifluroacetyl-(1-Methyl-1*H*-benzoimidazol-2-yl)amino]-2′-phenyl-spiro[azetidine-4,4-[4′*H*]chroman]-2-one (5c): Yield 0.481 g (95%); mp 235–237 °C; IR (KBr, cm^{-1}) υ_{max}: 1810 ($COCF_3$), 1690 (CO); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.80 (dd, 1H, J = 16.8, 2.8 Hz, H_{eq}. C-3′), 3.16 (dd, 1H, J = 16.8, 12.7 Hz, H_{ax} C-3′) 3.21 (s, 2H, CH_2CO), 3.58 (s, 3H, -NCH_3), 5.58 (dd, 1H, J = 12.7, 2.8 Hz, H_{ax} C-2′) 6.78–7.3 2 (m, 13H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 33.6 (-NCH_3), 44.5 (C-3′), 46.4 (C-3), 80.5 (C-2′), 99.8 (C-4), 115.2 (CF_3), 117.2–138.3 (19C, Ar-C) 167.9 (C-2), 188.8 (**C**OCF_3); HRMS: m/z $(M+H)^+$ Calcd. for $C_{27}H_{22}N_4O_3F_3$: 507.1644. found: 507.1649; Anal. calcd. for $C_{27}H_{21}N_4O_3F_3$: C, 64.03; H, 4.18; N, 11.06; found: C, 64.06; H, 4.18; N, 11.09.

1-[Trifluroacetyl-(1-benzyl-1*H*-benzoimidazol-2-yl)amino]-2′-phenyl-spiro [azetidine-4,4′-[4′*H*]chroman]-2-one (5d): Yield 0.535 g (92%); mp 218–220 °C; IR (KBr, cm^{-1}) υ_{max}: 1800 ($COCF_3$),

1680 (CO); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.81 (dd, 1H, J = 16.9, 2.9 Hz, H_{eq} C-3′), 3.15 (dd, 1H, J = 16.9, 12.8 Hz, H_{ax} C-3′), 3.20 (s, 2H, CH_2CO), 3.36 (s, 2H, -CH_2Ph), 5.53 (dd, 1H, J = 12.8, 2.9 Hz, H_{ax} C-2′), 6.79–7.35 (m, 18H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 43.4 (**C**H_2Ph), 44.5 (C-3′), 46.7 (C-3), 80.2 (C-2′), 100.2 (C-4), 115.4 (CF_3), 116.8–137.6 (25c, Ar-C), 167.6 (C-2), 188.6 (**C**OCF_3); HRMS: m/z $(M+H)^+$ Calcd. for $C_{33}H_{26}N_4O_3F_3$: 583.1957. found: 583.1961 (M+H); Anal. calcd. for $C_{33}H_{25}N_4O_3F_3$: C, 68.04; H, 4.33; N, 9.62, found: C, 68.07; H, 4.31; N, 9.64.

2.6. General procedure for compounds 6a–d

Compound **3a–d** (0.001 mol) was taken in R. B. F. with [bmim]PF_6 (5.0 mL). To it HCHO (0.002 mol) and diethylamine (0.002 mol) were added and heated for 1 h. It was worked up further as for **3** to give **6a–d**.

1-[Diethylaminomethyl-(1-diethylaminomethyl-1*H*-benzoimidazol-2-yl)amino]-2′-phenyl-spiro[azetidine-4,4′-[4′*H*]chroman]-2-one (6a): Yield 0.509 g (90%); mp 150–152 °C; IR (KBr, cm^{-1}) υ_{max}: 1700 (CO); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.25 [t, 12H, J = 7.0 Hz, 2×-N($CH_2C\mathbf{H}_3)_2$], 2.85 (dd, 1H, J = 16.6, 2.6 Hz H_{eq} C-3′), 3.15 (dd, 1H, J = 16.6, 12.6 Hz, H_{ax} C-3′), 3.20 (s, 2H, CH_2CO), 3.52 [q, 8H, J = 7.0 Hz, 2×N($C\mathbf{H}_2CH_3)_2$] 4.36 (s, 4H, 2×-NCH_2N-), 5.61(dd, 1H, J = 12.6, 2.6 Hz, H_{ax} C-2′), 6.81–7.35 (m, 13H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 26.5 (4C, [N($CH_2\mathbf{C}H_3)_2$]), 44.8 (C-3′), 46.8 (C-3), 80.9 (C-2′), 100.2 (C-4), 118.1–139 (19C, Ar-C), 130.8 (4C, [N(**C**$H_2CH_3)_2$]), 171.2 (2C, -NCH_2N-), 173.5 (C-2); HRMS: m/z $(M+H)^+$ Calcd. for $C_{34}H_{43}N_6O_2$: 567.3447. found: 567.3450; Anal. calcd. for $C_{34}H_{42}N_6O_2$: C, 72.06; H, 7.47; N, 14.83; found: C, 72.05; H, 7.48; N, 14.85.

1-[Diethylaminomethyl(1-diethylaminomethyl-5-methyl-1*H*-benzoimidazol-2-yl)amino]-2′-phenyl-spiro[azetidine4,4′[4′*H*]chroman]2one (6b): Yield 0.522 g (90%); mp 146–148 °C; IR (KBr, cm^{-1})υ_{max}: 1710 (CO); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.25 [t, 12H, J = 7.1 Hz, 2×N($CH_2C\mathbf{H}_3)_2$], 1.86 (s, 3H, Ar-CH_3), 2.84 (dd, 1H, J = 16.8, 2.8 Hz, H_{eq} C-3′), 3.15 (dd, 1H, J = 16.8, 12.7 Hz, H_{ax} C-3′), 3.21 (s, 2H, CH_2CO), 3.54 [q, 8H, J = 7.1 Hz, 2×N($C\mathbf{H}_2CH_3)_2$], 4.38 (s, 4H, 2×-NCH_2N-), 5.65 (dd, 1H, J = 12.7, 2.8 Hz H_{ax} C-2′), 6.78–7.36 (m, 12H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 26.5 (4C, [N($CH_2\mathbf{C}H_3)_2$]), 28.7 (Ar-CH_3), 44.9 (C-3′), 46.6 (C-3), 80.5 (C-2′), 100.3 (C-4), 127.6 (4C, [N(**C**$H_2CH_3)_2$]), 116.2–137.6 (19C, Ar-C), 171 (2C, -NCH_2N-), 173.4 (C-2); HRMS: m/z $(M+H)^+$ Calcd. for $C_{35}H_{45}N_6O_2$: 581.3604. found: 581.3610; Anal. calcd. for $C_{35}H_{44}N_6O_2$: C, 72.38; H, 7.64; N, 14.47, found C, 72.42; H, 7.60; N, 14.44.

1-[Diethylaminomethyl(1-methyl-1*H*-benzoimidazol-2-yl)amino]-2′-phenyl-spiro [azetidine-4,4′-[4′*H*]chroman]-2-one (6c): Yield 0.460 g (93%); mp 160–162 °C; IR (KBr cm^{-1}) υ_{max}: 1700 (CO); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.23 [t, 6H, J = 6.9 Hz, N($CH_2C\mathbf{H}_3)_2$], 2.83 (dd, 1H, J = 16.9, 2.9 Hz H_{eq}. C-3′), 3.14 (dd, 1H, J = 16.9, 12.8 Hz, H_{ax} C-3′), 3.20 (s, 2H, CH_2CO), 3.50 [q, 4H, J = 6.9 Hz, N($C\mathbf{H}_2CH_3)_2$], 3.62 (s, 3H, -NCH_3), 4.40 (s, 2H, -NCH_2N-), 5.67 (dd, 1H, J = 12.8, 2.9 Hz H_{ax} C-2′), 6.75–7.32 (m, 13H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 26.8 (2C,[N($CH_2\mathbf{C}H_3)_2$]), 33.8 (-NCH_3), 44.5 (C-3′), 46.8 (C-3), 80.2 (C-2′), 100.2 (C-4), 126.5 (2C, [N(**C**$H_2CH_3)_2$]), 116.3–137.2 (19C, Ar-C), 170 (-NCH_2N-), 172.2 (C-2); HRMS: m/z $(M+H)^+$ Calcd. for $C_{30}H_{34}N_5O_2$: 496.2712. found: 496.2719; Anal. calcd. for $C_{30}H_{33}N_5O_2$: C, 72.70; H, 6.71; N, 14.13; found C, 72.72; H, 6.68; N, 14.17.

1-[Diethylaminomethyl(1-benzyl-1*H*-benzoimidazol-2-yl)amino]-2′-phenyl-spiro [azetidine-4,4′[4′*H*]chroman]-2-one (6d): Yield 0.520 g (91%); mp 135–136 °C; IR (KBr, cm^{-1}) υ_{max}: 1705 (CO); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.26 [t, 6H, J = 7.2 Hz, ($CH_2C\mathbf{H}_3)_2$], 2.80 (dd, 1H, J = 16.8, 2.6 Hz H_{eq}

C-3′), 3.13 (dd, 1H, J = 16.8, 12.6 Hz, H_{ax} C-3′), 3.20 (s, 2H, CH_2CO), 3.37 (s, 2H, -CH_2Ph), 3.50 [q, 4H, J = 7.2 Hz, N(C**H**$_2$ $CH_3)_2$], 4.42 (s, 2H, -NCH_2N-), 5.65 (dd, 1H, J = 12.6, 2.6 Hz, H_{ax} C-2′), 6.79–7.87 (m, 18H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 26.6 (2C, [N(CH_2**C**$H_3)_2$]), 43.3 (CH_2Ph), 44.7 (C-3′), 46.5 (C-3), 80.5 (C-2′) 100.2 (C-4), 126.2 (2C, [N(**C**H_2 $CH_3)_2$]), 116.5–138.4 (25C, Ar-C), 169.9 (-NCH_2N-), 173.1 (C-2); HRMS: m/z (M+H)$^+$ Calcd. for $C_{36}H_{38}N_5O_2$: 572.3025. found: 572.3020; Anal. calcd. for $C_{36}H_{37}N_5O_2$: C, 75.65; H, 6.47; N, 12.25; found: C, 75.69; H, 6.43; N, 12.22.

2.7. General procedure for compounds 7a and 7b

To **3a** (0.001 mol) in ionic liquid, [bmim]PF_6 (5.0 mL), aromatic aldehyde (0.001 mol) was added and heated for 1 h. The progress of the reaction was monitored by TLC using silica gel 60F 254 aluminum sheets in pet ether/EtOA 7:3. Upon completion of the reaction water (10.0 mL) was added to it. The organic compound was then extracted with EtOAc (2 × 15 mL). The combined organic layer was distilled under reduced pressure (10 mmHg) at 50 °C to afford compounds **7a** and **7b**. These compounds were further purified by column chromatography on silica gel 60–120 mesh by eluting with pet-ether/EtOAc (7:3).

1-[(1*H*-Benzoimidazol-2-yl)amino]-3-benzylidene-2′-phenyl-spiro[azetidine-4,4′-[4′*H*]chroman]-2-one (7a): Yield 0.436 g (90%); mp 230–232 °C; IR (KBr, cm^{-1}) v_{max}: 3200 (-NHNC-), 3020 (-NH), 1700 (CO); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.83 (dd, 1H, J = 16.6, 2.6 Hz H_{eq} C-3′), 3.16 (dd, 1H, J = 16.6, 12.8 Hz, H_{ax} C-3′), 5.68 (dd, 1H, J = 16.6, 2.6 Hz, H_{ax} C-2′), 6.75–7.31 (m, 18H, Ar-H), 8.25 (s, 1H, =CH), 9.48 (s, 1H, -NH), 10.15 (s, 1H, -NHN); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 44.8 (C-3′), 80.5 (C-2′), 101.2 (C-4), 102.4 (C-3) 115.9–139.6 (25C, Ar-C), 148.2 (=CH), 168.5 (C-2); HRMS: m/z (M+H)$^+$ Calcd. for $C_{31}H_{25}N_4O_2$: 485.1977. found: 485.1981; Anal. calcd. for $C_{31}H_{24}N_4O_2$: C, 76.84; H, 4.99; N, 11.56, found C, 77.86, H, 4.95; N, 11.60.

1-[1*H*-Benzoimidazol-2-yl)amino]-3-p-methoxybenzylidene-2′-phenyl-spiro [azetidine-4,4′-[4′*H*]chroman]-2-one (7b): Yield 0.463 g (90%); mp 215–217 °C; (KBr, cm^{-1}) $v_{\max}$: 3200 (-NHN-), 3025 (-NH), 1708 (CO), ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.84 (dd, 1H, J = 16.9, 2.8 Hz, H_{eq} C-3′), 3.16 (dd, 1H, J = 16.9, 12.9 Hz, H_{ax} C-2′), 3.80 (s, 3H, p-OC**H**$_3$Ph), 5.65 (dd, 1H, J = 16.9, 2.8 Hz, H_{ax} C-2′), 6.70–7.35 (m, 17H, Ar-H), 8.23 (s, 1H, =CH), 9.35 (s, 1H, -NH), 10.20 (s, 1H, -NHN); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 44.0 (p-O**C**H_3Ph), 44.8 (C-3′), 80.5 (C-2′), 100.3 (C-4), 101.2 (C-3) 116.2–138.9 (25C, Ar-C), 148.6 (=CH), 168.9 (C-2); HRMS: m/z (M+H)$^+$ Calcd. for $C_{32}H_{27}N_4O_3$: 515.2083. found: 515.2086; Anal. calcd. for $C_{32}H_{26}N_4O_3$: C, 74.69; H, 5.09; N, 10.89, found: C, 74.71; H, 5.09; N, 10.91.

2.8. General procedure for compounds 8a and 8b (Finkelstein reaction)

3-Chloro-2′-phenyl spiro[azetidine-4,4′-[4′*H*] chroman] **4a/4b** (0.001 mol) and KI (0.002 mol) in acetone (10.0 mL) were stirred for 2 h. After that the solid obtained was filtered, washed with water, and recrystallized from acetone to give **8a** and **8b**.

1-[(1*H*-Benzoimidazol-2-yl)amino]-3-iodo-2′-phenyl spiro [azetidine-4,4′-[4′*H*] chroman]-2-one (8a): Yield 0.491 g (94%); mp 320–322 °C; IR (KBr, cm^{-1}) $v_{\max}$: 3220 (-NHN-), 3005 (-NH), 1720 (CO), 570 (C-I); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.85 (dd, 1H, J = 16.9, 2.7 Hz, H_{eq} C-3′), 3.25 (dd, 1H, J = 16.9, 12.8 Hz, H_{ax} C-3′), 4.35 (s, 1H, CH-I), 5.58 (dd, 1H, J = 12.8, 2.7 Hz, H_{ax} C-2′), 6.75-7.39 (m, 13H, Ar-H), 9.54 (s, 1H, -NH), 10.25 (s, H, -NHN-); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 44.8 (C-3′), 80.5 (C-2′), 101.2 (C-4),

117 (C-3), 118.2–141.2 (19C, Ar-C), 168.2 (C-2); HRMS: m/z (M+ H)$^+$ Calcd. for $C_{24}H_{20}N_4O_2I$: 523.0631. found: 523.0639; Anal. calcd. for $C_{24}H_{19}N_4O_2I$: C, 55.19; H, 3.67; N, 10.73, found: C, 55.20, H, 3.65; N, 10.70.

1-[(5-Methyl-1*H*-benzoimidazol-2-yl)amino]-3-iodo-2′-phenyl spiro[azetidine-4,4′-[4′*H*] chroman]-2-one (8b): Yield 0.488 g (91%); mp 341–343 °C; IR (KBr, cm^{-1}) υ_{max}: 3210 (-NHN-), 3010 (-NH), 1705 (CO), 575 (C-I); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.70 (s, 3H, Ar-CH_3), 2.84 (dd, 1H, J = 16.8, 2.8 Hz C-3′), 3.20 (dd, 1H, J = 16.8, 12.7 Hz H_{ax} C-3′), 4.36 (s, 1H, CH-I), 5.56 (dd, 1H, J = 12.7, 2.8 Hz, H_{ax} C-2′), 6.75, 7.30 (m, 12H, Ar-H), 9.50 (s, 1H, -NH), 10.23 (s, 1H, -NHN-); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 28.8 (**C**H_3Ph), 44.6 (C-3′), 80.4 (C-2′), 100.8 (C-4), 117.2 (C-3), 117.9-140 (19C, Ar-C), 168.6 (C-2); HRMS: m/z (M+ H)$^+$ Calcd. for $C_{25}H_{22}N_4O_2I$: 537.0787. found: 537.0790; Anal. calcd. for $C_{25}H_{21}N_4O_2I$: C, 55.98; H, 3.95; N, 10.45; found: C, 56.00, H, 3.94; N, 10.47.

2.9. General procedure for compounds 9a and 9b

An equimolar (0.002 mol) mixture of **4a** and phenol in ionic liquid, [bmim]PF_6 (5.0 mL), containing Et_3N (0.003 mol) was refluxed for 2 h. The progress of the reaction was checked by TLC. After completion of the reaction it was worked up as described for **3**, affording **9a** and **9b**.

1-[1*H*-Benzoimidazol-2-yl)amino)]-3-p-nitrophenoxy-2′-phenylspiro[azetidine-4,4′-[4′*H*] chroman]-2-ones (9a): Yield 0.496 g (93%); mp 240–242 °C; IR (KBr, cm^{-1}), υ_{max}: 3200 (-NHN-), 3005 (-NH), 1700 (CO), 1355 (NO_2 of phenol), 1255 (C-O-C asymmetrical stretching), 1075 (C-O-C symmetrical stretching); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.86 (dd, 1H, J = 16.9, 2.8 Hz, H_{eq} C-3′), 3.23 (dd, 1H, J = 16.9, 12.6 Hz, H_{ax} C-3′), 5.50 (dd, 1H, J = 12.6, 2.8 Hz, H_{ax} C-2′), 4.81 (s, 1H, –**C**H-$OC_6H_4NO_2$), 6.86–7.35 (m, 17H, Ar-H), 9.50 (s, 1H, -NH), 10.20 (s, 1H, -NHN); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.9 (C-3′), 80.6 (C-2′), 99.8 (C-4), 116–138.9 (25C, Ar-C), 158.9 (**C**H-O-C_6H_4p-NO_2); 168.8 (C-2); HRMS: m/z (M+H)$^+$ calcd. for $C_{30}H_{24}N_5O_5$: 534.1777. found: 534.1772; Anal. calcd. for $C_{30}H_{23}N_5O_5$: C, 67.53; H, 4.35; N, 13.13 found: C, 67.57; H, 4.35; N, 13.15.

1-[(1*H*-Benzoimidazol-2-yl)amino]-3-(β-naphthoxy)-2′-phenylspiro[azetidine-4,4′-[4′*H*] chroman]-2-one (9b): Yield 0.495 g (92%); mp 253–255 °C; IR (KBr cm^{-1}) υ_{max}: 3205 (-NHN-), 3000 (-NH), 1700 (CO), 1255 (C-O-C asymmetrical stretching), 1075 (C-O-C), symmetrical stretching); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.84 (dd, 1H, J = 16.9, 2.8 Hz, H_{eq} C-3′), 3.19, (dd, 1H, J = 16.9, 12.7 Hz, H_{ax} C-3′), 5.53 (dd, 1H, J = 12.7, 2.8 Hz, H_{ax} C-2′), 4.80 (s, 1H, -C**H**-O-β-naphthyl), 6.84–7.31 (m, 20H, Ar-H), 9.45 (s, 1H, -NH), 10.25 (s, 1H, -NHN-); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 44.6 (C-3′), 80.3 (C-2′), 100.1 (C-4), 116.2–138.6 (29C, Ar-C), 158.8 (-**C**H-O-naphthyl), 168.9 (C-2); HRMS: m/z (M+H)$^+$ Calcd. for $C_{34}H_{27}N_4O_3$: 539.2077. found: 539.2071; Anal. calcd. for $C_{34}H_{26}N_4O_3$: C, 75.83; H, 4.83; N, 10.40. found: C, 75.86; H, 4.80; N, 10.43.

3-Chloro-1-[trifluoroacetyl-(1-trifluoroacetyl-1*H*-benzoimidazol-2-yl)amino]-2′-phenyl-spiro [azetidine-4,4′-[4′*H*]chroman]-2-one (10a): Yield 0.585 g (94%); mp 246–248 °C; IR (KBr, cm^{-1}) υ_{max}: 1805 ($COCF_3$), 1760 ($COCF_3$), 1700 (CO, azetidine), 760 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.88 (dd, 1H, J = 16.9, 2.8 Hz, H_{eq} C-3′), 3.18 (dd, 1H, J = 16.9, 12.7 Hz, H_{ax} C-3′), 4.16 (s, 1H, CH-Cl), 5.61 (dd, 1H, J = 12.7, 2.8 Hz, H_{ax} C-2′), 6.84–7.39 (m, 13H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 45.1 (C-3′), 80.6 (C-2′), 101 (C-4), 115.6 (2C, CF_3), 118–136.8 (19C, Ar-C), 128 (C-3), 168. 8. (C-2), 188.8 (**C**OCF_3), 190.4

(**C**OCF$_3$); HRMS: m/z (M+H)$^+$ Calcd. for $C_{28}H_{18}N_4O_4ClF_6$: 623.0921. found: 623.0926; Anal. calcd. for $C_{28}H_{17}N_4O_4ClF_6$: C, 53.99; H, 2.75; N, 8.99, found: C, 54.01; H, 2.75; N, 8.96.

3-Chloro-1-[trifluoroacetyl(5-methyl-1-trifluoroacetyl-1*H*-benzoimidazol-2-yl) amino]2′-phenyl spiro [azetidine-4,4′[4′*H*]chroman]-2-one (10b): Yield 0.499 g (93%); mp 238–240 °C; IR (KBr, cm^{-1}) υ_{max}: 1820 (COCF$_3$), 1750 (COCF$_3$), 1710 (CO, azetidine), 765 (C-Cl); ^{1}H NMR (300 MHz, CDCl$_3$) δ: 1.65 (s, 3H, Ar-CH$_3$), 2.86 (dd, 1H, J = 16.8, 2.6 Hz, H$_{eq}$ C-3′), 3.13 (dd, 1H, J = 16.8, 12.7 Hz, H$_{ax}$ C-3′), 3.13 (dd, 1H, J = 16.8, 12.7 Hz, H$_{ax}$ C-3′), 3.13 (dd, 1H, J = 16.8, 12.7 Hz, H$_{ax}$ C-3′), 4.20 (s, 1H, CH–Cl), 5.52 (dd, 1H, J = 12.7, 2.6 Hz, H$_{ax}$ C-2′), 6.84–7.46 (m, 12H, Ar-H); ^{13}C NMR (75 MHz, CDCl$_3$) δ: 28.8 (**C**H$_3$–Ph), 45.4 (C-3′), 80.4 (C-2′), 100.2 (C-4), 116 (2C, CF$_3$), 117.1–135.5 (19C, Ar-C), 127 (C-3), 167.9 (C-2), 187.8 (**C**OCF$_3$), 190.2 (**C**OCF$_3$); HRMS: m/z (M+H)$^+$ Calcd. for $C_{29}H_{20}N_4O_4ClF_6$: 637.1077. found: 637.1080; Anal. calcd. for $C_{29}H_{19}N_4O_4ClF_6$: calcd. for C, 54.69; H, 3.01; N, 8.80; found: C, 54.63; H, 3.04; N; 8.84.

3. Results and discussion

In 1-pot 3-component synthesis, 2-hydrazinobenzimidazole derivatives, flavanone, and acetyl chloride/chloroacetyl chloride were heated in ionic liquid [bmim] PF$_6$ for 2 h with or without using the catalyst Et$_3$N to give **3** and **4.** The yield is much better (90%–95%) when catalyst is used during the reaction than without using catalyst (80%–85%).

Formation of azetidine derivatives by CH$_3$COCl was characterized by IR absorption bands at 3200 cm^{-1}, 3000 cm^{-1}, and 1700 cm^{-1} due to -NHN$^-$, -NH, and **CO**CH$_2$ of monocyclic β-lactam ring with disappearance of the band at 1680 cm^{-1} due to flavanone. In ^{1}H NMR it showed a peak at δ 3.11 ppm (s, 2H, -CH$_2$CO) due to –CH$_2$ of the azetidinone ring, at 2.85 (dd, 1H, J = 16.8, 2.6 Hz) for H$_{eq}$, and at 3.11 (dd, 1H, J = 16.8, 12.9 Hz) for H$_{ax}$ at C-3′; peaks at δ 5.58 (dd, 1H, J = 12.9, 2.6 Hz) appeared for C-2′H$_{ax}$ proton. A multiplet at δ 6.86–7.38 appeared for aromatic protons. Singlets appearing at δ 9.44 ppm and 10.32 ppm, which disappeared on deuteration, were assigned to -NHN- and –NH protons respectively. ^{13}C NMR showed peaks at δ 46.0 and 165.6 ppm for **C**H$_2$CO and **C**O of the azetidine ring with disappearance of the peak at δ 180.2 ppm due to flavanoyl CO.

Formation of azetidine derivative by ClCH$_2$COCl was characterized by IR absorption bands at 1720 cm^{-1} (CO monocyclic β-lactam ring), 750–780 cm^{-1} (C-Cl group), and 3110 cm^{-1} due to –NHN- with the disappearance of the band at 1680 cm^{-1} due to flavanone. In ^{1}H NMR it showed peaks at δ 4.12 ppm (s, 1H, CHCl), δ 2.84 (dd, 1H, J = 16.8, 2.6 Hz) for H$_{eq}$ and 3.15 (dd, 1H, J = 16.8, 12.8 Hz) for H$_{ax}$ at C-3′. Peaks at δ 5.57 (dd, 1H, J = 12.8, 2.6 Hz) appeared for C-2′H$_{ax}$ protons. A multiplet at δ 6.85–7.35 and a singlet at δ 10.23 ppm also appeared for aromatic protons and -NHN-. ^{13}C NMR showed peaks at δ 167.2 ppm and 127.2 ppm for -CO and -CH-Cl of the azetidinone ring with disappearance of the peak at δ 180 ppm due to flavanoyl CO.

Acylation of **3** and **4** by trifluoroacetic anhydride to give **5** and **10** (-NCOCF$_3$ derivative) was confirmed by disappearance of the peak due to -NH in both IR and ^{1}H NMR spectra and appearance of the peaks in ^{13}C NMR at δ 115.6 and 188.4 ppm due to –**C**F$_3$ and -**C**OCF$_3$, respectively.

The formation of Mannich bases from **3** to give **6** was characterized by the disappearance of the peak at 3100 cm^{-1} due to -NH in the IR spectrum. In the ^{1}H NMR it showed disappearance of the peak at δ 10.32 ppm (-NHN) along with appearance of a peak due to -NCH$_2$N- at δ 4.36 ppm (s, 2H, CH$_2$). In the ^{13}C

NMR characteristic -NCH_2N- signals belonging to Mannich bases were observed at δ 171.2 ppm. Formation of 3-arylidene derivatives **7** from **3** were confirmed by ^{1}H NMR spectra in which a peak appeared at δ 8.25 ppm due to =CH instead of at δ 3.21 ppm (due to –CH_2-). In the ^{13}C NMR a peak appeared at δ 148.0 ppm due to =CH-.

Further, the -Cl group attached to the azetidine ring (**4**) is very reactive and on reacting with (i) KI in acetone/ionic liquid due to the Finkelstein reaction gave iodo derivative **8**. Formation of **8** was confirmed by IR spectra in which a band appeared at 570–600 cm^{-1} due to CH-I instead of at 750–780 cm^{-1} due to CH-Cl. In the ^{1}H NMR spectra a peak appeared at δ 4.35 ppm due to CH-I more downfield than CHCl (δ 4.12 in **3a**). It gave a purple layer in the chloroform layer test, which confirms displacement of –Cl by –I group; (ii) on reacting **4** with phenols it gave phenoxy derivatives (**9**), which were confirmed by IR spectra in which the peak at 750–780 cm^{-1} (for C-Cl group) disappeared and a band at 1225–1200 cm^{-1} appeared for C-O-C asymmetrical stretching and a band at 1075–1020 cm^{-1} appeared for symmetrical stretching. In the ^{1}H NMR it gave a signal at δ 4.81 ppm due to -C**H**OR more downfield than CH-Cl (4.12 ppm). ^{13}C NMR showed a peak at δ 158.9 ppm for -**C**HOR.

The high resolution mass spectrum gave good values for M+H, which corresponded well to the calculated value for their molecular formula for all benzimidazol-amino spiro[azetidine-4,4′[4′*H*]chroman]-2-ones, **3**–**10**.

Table. Insecticidal activity of the synthesized compounds against *Periplaneta americana*[a].

Compound	Time (min)	
	1% conc.	2% conc.
3a	5	3
3b	5	3
3c	6	4
3d	7	5
4a	4	2
4b	5	3
4c	5	3
4d	5	4
5a	3	2
5b	4	2
5c	4	3
5d	5	4
6a	6	5
6b	6	4
6c	7	5
6d	8	6
7a	9	5
7b	8	6
8a	7	5
8b	8	6
9a	8	6
9b	9	6
10a	3	2
10b	3	2
DMF	15	10
Cypermethrin	7	5

[a](KD value in min)

3.1. Insecticidal activity

For insecticidal activity,[33,34] *Periplaneta americana* was used due to its easy availability and wide use in such studies. Consequently, 1% and 2% solutions in DMF of the prepared compounds were injected into the abdominal region of the cockroach with the help of a microsyringe. At the time of death the antennae became motionless, the appendages shrank and folded towards the central side, and the cockroach lay dorsally,[35] which was noted as the KD (knock-down) value. The KD values of synthesized heterocyclic derivatives were compared with that of the control drug (cypermethrin). The results are shown in the Table.

It was observed that compounds having chloro and $-COCF_3$ groups exhibited better insecticidal activity (KD value 2–5 min) in comparison to the standard drug (KD value 5–7 min). The rest of the compounds had high to moderate activity (KD value 6–9 min).

4. Conclusion

The 1-pot multicomponent condensation of 2-hydrazino benzimidazoles **1**, flavanone **2**, and acetyl chloride/chloroacetyl chloride in the presence of Et_3N and $[bmim]PF_6$ afforded the novel system benzoimidazolyl spiro[azetidine-chroman] **3** and a chloro derivative **4** has been reported for the first time by us. Ionic liquids are environmentally friendly, efficient, and convenient for synthesis compared to the other, hazardous solvents and they are recycled indefinitely for further use. Further, compounds **3** and **4** were acylated with trifluoroacetic anhydride yielding **5** and **10.** Mannich bases **6** and 3-arylidene derivatives **7** were also prepared from **3**. Compounds **4** due to the 3-chloro group on nucleophilic substitution with potassium iodide and phenols gave the corresponding iodo **8** and phenoxy **9** derivatives. The synthesized compounds were evaluated for insecticidal activity and showed good results. Therefore, these compounds may act as potential insecticidal agents.

Acknowledgments

One of the authors (KS) is grateful to UGC New Delhi, India, for granting the Research Award. We are also thankful to the Central Drug Research Institute, Lucknow, India, for elemental analyses and mass spectral measurements.

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