Synthesis and Characterization Of “6-[2-Hydroxy-3(Substituted Amino)Propoxy]-2-Phenyl-4H-Chromen-4-One”

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Abstract. Polyphenolic compounds have recently attracted considerable interest in the field of nutrition, health and medicine. Our efforts are focused on the introduction of chemical diversity in the molecular frame work in order to synthesizing pharmacologically interesting compounds of widely different composition. Here we have reported the synthesis of flavonoid derivatives starting from commercially available material 6-hydroxyflavone based on beta-blocker and characterized by elemental analysis FTIR 8201 using KBr pallet method, ¹H NMR techniques.

INTRODUCTION

Flavonoids are a very large and important group of plant metabolites, present in all parts of plant, above and below ground, in vegetative and generative organs: stem, leaves, buds, bark, heartwood, thorns, roots, rhizomes, flowers, farina, fruits, seed, and also in root and leaf exudates or resin. In addition to various vegetables and fruits, flavonoids are found in nuts, grains, spices, and different medicinal plants as well as beverages, such as wine, tea, and beer. Flavonoids are responsible for the vividness in fruits and vegetables many have shown significant health beneficial activities in the prevention coronary heart diseases, bone loss, antioxidant, anti-microbial, anti-inflammatory, vasculo-protective effects and other age-related diseases [1-6]. Some factors like their structural class, degree of hydroxylation, other substitutions, conjugations, and degree of polymerization are responsible for their chemical nature. The activities of flavonoids are structure dependent. Although some flavonoids are readily available from plants, more derivatives have been accessed through chemical synthesis [4, 5].

EXPERIMENTAL

Material and Method

The chemical used for the synthesis of products were purchased from sigma-aldrich and used without further purifications. Melting points were recorded by open capillary method and are uncorrected. Infrared spectra were recorded on Shimadzu FT IR-8201 using KBr pallet method. Spectra were calibrated against the polystyrene absorption at 1610 cm⁻¹. Mass spectra were recorded on Shimadzu GC/MSQP 2000 spectrometer operating using direct injection probe technique. ¹H NMR spectra were recorded on Bruker Avance 400 spectrometer by making a solution of sample in DMSO d6 and CDCl3 solvents using tetramethylsilane (TMS) as the internal standard unless otherwise mentioned and are given in the δ scale. Analytical thin layer chromatography (TLC) was performed on Merck precoated silica gel-G F254 aluminium plated. Visualization of the spots on TLC plates was achieved either by exposure to iodine vapor or UV light. All evaporation of solvents was carried out under reduced pressure on Rota
Vapour. % yield reported are isolated yields of material judged homogeneous by TLC and before recrystallization. Elemental analysis was carried out on Elementar III Vario EL Carlo Erba 1108.

**Synthesis**

Compounds were synthesized following the procedure as shown in following scheme 1: To a solution of 6-hydroxyflavone (4a) (5g, 21mmol) in DMF (60 ml), potassium carbonate (8.6g, 63mmol) was added, and solution was stirred for 10 min. Then epichlorohydrin (3.8 g, 42mmol) was added and the mixture was stirred at 80°C for 7h and give product 4b. Scheme 2: Isopropylamine (5 eq) was added to a solution of 4b in ethanol and stirred at 70°C for 7h and give 6-[2-hydroxy-3(substituted amino)propoxy]-2-phenyl-4H-chromen-4-one as a product (4c). After the completion of reaction in each step as monitored by the TLC, it was then extracted with ethyl acetate and washed with water, brine solution and dried over anhydrous Na₂SO₄. The combined organic layer was concentrated under reduced pressure to give the product in good yield which was pure enough to use as such for the next step. Similarly, we have carried this reaction for different kind of amines to give good result.

All the derivatives were derived from their parent compound. The chemical structures, spectral and elemental analysis data are for individual compounds synthesized are mentioned as follows:

**FB1:** 6-[[3-di(propan-2-yl)amino]-2-hydroxypropoxy]-2-phenyl-4H-chromen-4-one. Yield: 57% (4.72g), Brown powder; IR: (KBr, cm⁻¹) 3,423, 6403; ¹H NMR (CDCl₃): δ= 7.95-7.93 (m, 2H, Ar-H), 7.59-7.52 (m, 5H, Ar-H), 6.81 (s, 1H); 1H NMR (CDCl₃): δ= 7.95-7.92 (m, 2H, Ar-H), 7.61 (s, 1H); 1H NMR (CDCl₃): δ= 7.95-7.92 (m, 2H, Ar-H), 7.61-7.36 (m, 1H); 6.81 (s, 1H); 4.11-4.10 (d, J=4, 2H), 4.07-4.06 (m, 1H), 3.24 (br. s, 1H), 3.12-3.08 (d, J=16, 2H), 2.71 (s, 1H), 2.55 (s, 1H), 1.25 (s, 12H); Elemental analysis: Calculated for C₂₄H₂₉NO₄: C=72.89, H=7.39, N=3.54; Found: C=71.82, H=7.99, N=3.83

**FB2:** 6-[[3,4-difluorophenyl]amino]-2-hydroxypropoxy]-2-phenyl-4H-chromen-4-one. Yield: 62% (5.50g), Yellow powder; IR: (KBr, cm⁻¹) 3,422, 2,958, 1,639; ¹H NMR (CDCl₃): δ= 7.95-7.92 (m, 2H, Ar-H), 7.61-7.35 (m, 6H, Ar-H), 6.94-6.92 (m, 1H, Ar-H), 6.8 (s, 1H, Ar-H), 6.35-6.34 (m, 2H, Ar-H), 4.8-4.6 (m, 3H), 4.6-4.1 (m, 2H), 3.4-3.2 (m, 2H); Elemental analysis: Calculated for C₂₄H₁₉F₂NO₄: C=68.08, H=4.52, F=8.97, N=3.31; Found: C=67.82, H=8.09, F=8.59, N=4.03.
Table 1: Physical data of 6-hydroxyflavone derivatives.

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<th>MP(°C)</th>
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FB3: 6-{3-[(4-fluorophenyl)amino]-2-hydroxypropoxy]-2-phenyl-4H-chromen-4-one. Yield: 61% (5.18g), Yellow powder; IR: (KBr, cm⁻¹) 3,536, 3,359, 1,624 ¹H NMR (DMSO): δ= 8.12-8.10 (d, J=8, 2H, Ar-H), 7.78-7.76 (d, J=8, 1H), 7.61-7.59 (d, J=8, 1H), 7.49-7.46 (m, 3H, Ar-H), 7.03 (s, 1H), 6.92-6.89 (t, 2H, Ar-H), 6.63-6.62 (d, J=4, 2H, Ar-H), 5.53 (s, 1H), 5.25 (s, 1H), 4.15-4.14 (d, J=4, 2H), 4.07-4.06 (m, 1H), 3.27-3.10 (m, 2H); Elemental analysis: Calculated for C₂₅H₂₅FNO₄: C=71.10, H=4.97, F=4.69, N=3.45; Found: C=69.82, H=8.29, F=4.09, N=4.03

FB4: 6-{2-hydroxy-3-[(3-trifluoromethyl)phenyl]amino]propoxy]-2-phenyl-4H-chromen-4-one. Yield: 65% (6.20g), Brown powder; IR: (KBr, cm⁻¹) 3,467, 3,382, 1,637; ¹H NMR (CDCl₃): δ= 7.91 (s, 1H), 7.58-7.27 (m, 10H, Ar-H), 6.81-6.73 (m, 5H, Ar-H), 4.41-4.41 (d, 2H), 4.39 (s, 2H), 4.20 (s, 1H), 3.40-3.41 (d, J=4, 2H); Elemental analysis: Calculated for C₂₅H₂₅FNO₄: C=65.93, H=4.43, F=12.51, N=3.08; Found: C=64.12, H=4.09, F=12.97, N=3.83

FB5: 6-{2-hydroxy-3-(phenylamino)propoxy]-2-phenyl-4H-chromen-4-one. Yield: 59% (4.79g), Cream powder; IR: (KBr, cm⁻¹) 3,332, 3,231, 1,638; ¹H NMR (CDCl₃): δ= 7.94-7.91 (d, J=12, 2H, Ar-H), 7.61-7.47 (m, 5H, Ar-H), 7.38-7.34 (m, 1H), 7.17-7.13 (m, 2H), 6.80 (s, 1H), 6.69-6.65 (m, 3H), 4.77 (s, 1H, NH), 4.54 (s, 1H, OH), 4.26-4.18 (m, 1H, CH), 4.17-4.16 (d, J=4, 2H, OCH₂), 3.43-3.26 (d, 2H, CH₂N); Elemental analysis: Calculated for C₂₅H₂₅NO₅: C=74.40, H=5.46, N=3.6; Found: C=73.82, H=5.99, N=3.83

FB6: 6-{3-[(3-fluorophenyl)amino]propoxy]-2-phenyl-4H-chromen-4-one. Yield: 67% (5.69g), Yellow powder; IR: (KBr, cm⁻¹) 3,344, 2,876, 1,621 ¹H NMR (CDCl₃): δ= 7.91-7.89 (dd, 2H, Ar-H), 7.60-7.59 (d, J=4, 1H, Ar-H), 7.54-7.49 (m, 1H, Ar-H), 7.32-7.29 (m, 1H), 7.26 (s, 1H, Ar-H), 7.10-7.05 (m, 3H, Ar-H), 6.8 (s, 1H, Ar-H), 6.45-6.35 (m, 3H, Ar-H), 4.35-4.29 (d, 2H), 4.19-4.13 (m, 1H), 3.78 (s, 2H), 3.44-3.28 (d, 2H); Elemental analysis: Calculated for C₂₅H₂₅FNO₄: C=71.10, H=4.97, F=4.69, N=3.45; Found: C=70.22, H=5.69, F=4.98, N=3.23

FB7: 6-{2-hydroxy-3-[(4-trifluoromethyl)phenyl]amino]propoxy]-2-phenyl-4H-chromen-4-one. Yield: 63% (6.01g), Brown powder; IR: (KBr, cm⁻¹) 3,478, 3,319, 1,647; ¹H NMR (CDCl₃): δ= 7.92-7.91 (d, J=4, 2H), 7.65-7.26 (m, 8H, Ar-H), 6.81 (s, 1H), 6.69-6.67 (d, J=8, 2H), 4.50 (s, 2H), 4.22-4.15 (m, 2H), 3.98 (m, 1H), 3.94 (m, 1H), 3.58 (s, 1H), 3.35 (d, 2H); Elemental analysis: Calculated for C₂₅H₂₅FNO₄: C=65.93, H=4.43, F=12.51, N=3.08; Found: C=65.02, H=4.99, F=13.11, N=3.19

FB8: 6-{2-hydroxy-3-(morpholin-4-yl)propoxy]-2-phenyl-4H-chromen-4-one. Yield: 68% (5.44g), Brown powder; IR: (KBr, cm⁻¹) 3,359, 3,072, 2,924, 1,637 ¹H NMR (CDCl₃): δ= 8.06 (s, 1H), 7.94-7.92 (d, J=8, 2H), 7.61-7.37 (m, 4H, Ar-H), 7.37-7.27 (d, 1H), 6.83 (s, 1H), 5.47 (s, 1H), 3.81-4.17 (m, 3H), 3.75-3.58 (m, 8H), 3.41-3.40 (d, J=4, 2H); Elemental analysis: Calculated for C₂₅H₂₃NO₅: C=69.28, H=6.08, N=3.67; Found: C=68.82, H=6.99, N=4.23

FB9: 6-{2-hydroxy-3-(benzylamino)propoxy]-2-phenyl-4H-chromen-4-one. Yield: 70% (5.89g), Brown powder; IR: (KBr, cm⁻¹) 3,450, 3,032, 2,802, 1,627 ¹H NMR (CDCl₃): δ= 8.40 (s, 1H), 7.53-7.26 (m, 12H, Ar-H), 6.8 (s, 1H), 4.83 (s, 2H), 4.12-4.07 (m, 4H), 3.87-3.86 (m, 3H); Elemental analysis: Calculated for C₂₅H₂₃NO₄: C=74.79, H=5.77, N=3.49; Found: C=73.82, H=6.19, N=3.87

CONCLUSION

In summary, new class of 6-Hydroxyflavone derivatives containing an organochalcogen group in their structure were synthesized. The product was easily obtained in good to excellent yield and in relative short period of time using mild reaction conditions.

REFERENCES: