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Cascade Heterocyclization of 2-Naphthylamine with Substituted Benzaldehydes and Acetophenones

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Abstract — Cascade heterocyclization of 2-naphthylamine with substituted benzaldehydes and acetophenones gave 1,3-diarylbenzo[*f*]quinoline derivatives in which the aldehyde fragment resides on C^1, and acetophenone fragment, on C^3.
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Benzo[*f*]quinoline derivatives containing aryl groups with various substituents are used in medical practice as antitumor [1] and antimicrobial drugs [2]. Furthermore, they are structural analogs of some alkaloids [3] and antibiotics [4].

The present communication reports on the synthesis of new benzo[*f*]quinoline derivatives via catalytic condensation of 2-naphthylamine (**I**) with substituted benzaldehydes **IIa**–**IIe** and acetophenone (**IIIa**) or its derivatives **IIIb**–**IIIe**. Variation of substituents in benzaldehyde and acetophenone molecules could give rise to benzo[*f*]quinolines containing a broad spectrum of pharmacophoric groups. The reactions were carried out by heating the initial reactants in butanol for 6–10 h in the presence of concentrated hydrochloric acid.

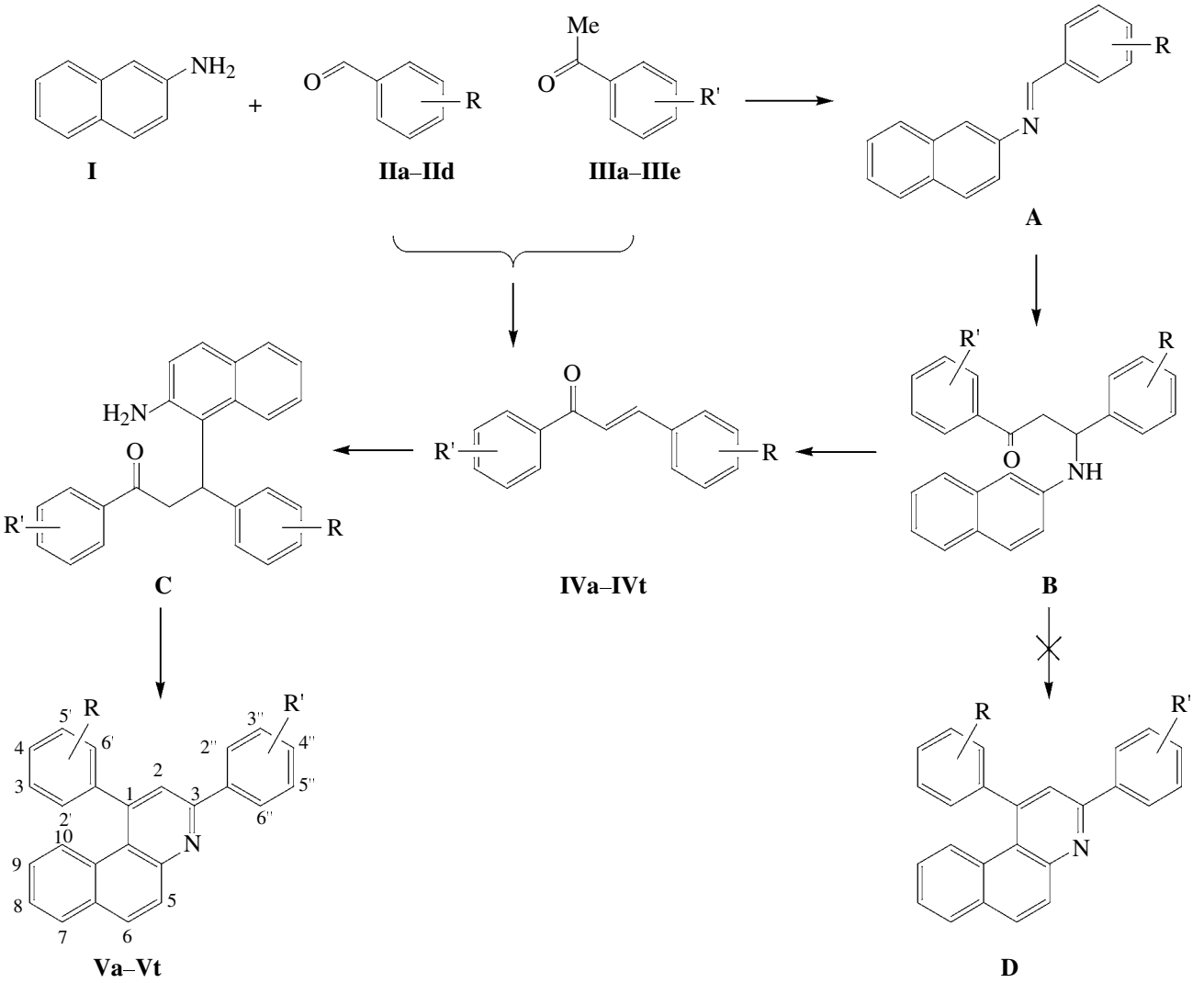
We previously showed [5] that Schiff bases derived from 2-naphthylamine react with acetophenone to give initially the corresponding amino ketone, β-phenyl-β-2-naphthylaminopropiophenone, which then undergoes intramolecular ring closure to benzo[*f*]quinoline. Intermediate amino ketones were isolated only under mild conditions (heating in ethanol for 15–20 min in the presence of a small amount of catalyst). Under the conditions of cascade heterocyclization, no amino ketones were isolated, but the formation of α,β-unsaturated ketones **IVu**–**IVw** was established; therefore, we presumed intermediacy of α,β-enones in the cascade heterocyclization under study.

Judging by the structure of the final products, which were identified as 1-alkoxyphenyl-3-arylbenzo[*f*]quinoline derivatives on the basis of spectral data, we propose the following reaction scheme (Scheme 1).

2-Naphthylamine reacts with benzaldehyde to give Schiff base **A** which takes up a proton in the presence of acid and adopts a planar conformation; as a result, its electrophilicity increases [6]. Moreover, acid medium enhances the nucleophilicity of the carbon atom neighboring to the carbonyl group in acetophenone molecule. Thus favorable conditions are created for the addition of acetophenone to Schiff base with formation of a new bond between the C=N carbon atom and methyl carbon atom of acetophenone. Unstable arylamino ketone **B** decomposes into 2-naphthylamine (**I**) and α,β-unsaturated ketone **IV**. The β-carbon atom in the latter has a considerable positive charge; therefore, its electrophilicity is sufficient to form a new bond with the α-carbon atom (with respect to the amino group) in 2-naphthylamine. Proton addition at the neighboring carbon atom gives saturated ketone **C** which undergoes heterocyclization with selective formation of 1,3-diarylbenzo[*f*]quinolines **Va**–**Vt**. In the reactions of acetophenones **IIIa**, **IIIb**, and **IIId** with 2-naphthylamine and 3-*p*-fluorophenyl-1*H*-pyrazole-4-carbaldehyde (**IIe**), the formation of chalcones **IVu**–**IVw** is the terminal stage; presumably, the positive charge on the carbon atom in unsaturated ketone is reduced due to effect of the heterocyclic substituent (Scheme 2).

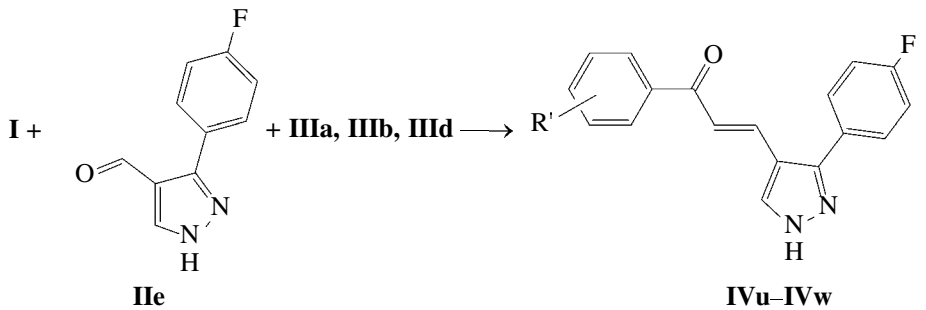
α,β-Unsaturated ketones **IVa**–**IVt** were synthesized previously by aldol condensation of acetophenones with benzaldehydes; their reaction with 2-naphthylamine in boiling gave the same benzo[*f*]quinoline derivatives **Va**–**Vf** as those obtained by three-component condensation. Thus there are grounds to believe that the scheme of synthesis of benzo[*f*]quinolines includes preliminary formation of α,β-unsaturated ketones and their subsequent reaction with 2-naphthylamine, which is consistent with the data of [7, 8].

Scheme 1.



II, R = 4-EtO (**a**), 4-PrO (**b**), 3-Br-4-HO-5-EtO (**c**), 2-$FC_6H_4CH_2O$ (**d**); **III**, R' = H (**a**), 4-Cl (**b**), 4-Br (**c**), 4-HO (d), 2-HO (**e**); **IV, V**, R = 4-EtO, R' = H (**a**), 4-Cl (**b**), 4-Br (**c**), 4-HO (**d**), 2-HO (**e**); R = 4-PrO, R' = H (**f**), 4-Cl (**g**), 4-Br (**h**), 4-HO (**i**), 2-HO (**j**), R = 3-Br-4-HO-5-EtO, R' = H (**k**), 4-Cl (**l**), 4-Br (**m**), 4-HO (**n**), 2-HO (**o**), R = 2-$FC_6H_4CH_2O$, R' = H (**p**), 4-Cl (**q**), 4-Br (**r**), 4-HO (**s**), 2-HO (**t**).

Scheme 2.



IV, R' = H (**u**), 4-Cl (**v**), 4-HO (**w**).

As shown in [9, 10], reactions of α,β-unsaturated ketones with amines could give rise to structures like **D** which correspond to a different cyclocondensation pathway. Compounds **Va**–**Vt** and **D** are regioisomers, and they are very difficult to distinguish. In the present study we applied two-dimensional COSY, HSQC, and HMBC techniques to assign proton signals, signals from carbon atoms attached to protons, and signals from quaternary carbon atoms, respectively; in addition, the NOESY spectrum of compound **Vo** was recorded. As a result, we were able to unambiguously determine the product structure and assign all proton signals in their NMR spectra.

The chemical shifts of the key protons 2-H, 2'-H, 5-H, 6'-H', 6''-H, and 10-H in molecule **Vo** are equal to δ 7.94, 8.12, 8.02, 7.89, 7.33, and 7.98 ppm. 1-[(3-Bromo-5-ethoxy-4-hydroxyphenyl)-3-(2-hydroxyphenyl)benzo[*f*]quinoline (**Vo**) was selected taking into account that one phenyl group in its molecule has no protons in the *meta* positions, in contrast to the acetophenone fragment. According to our previous data [11], protons in the *meta* positions of the benzene ring attached to C^1 should give cross-peaks with the 10-H protons in the two-dimensional NOESY spectrum due to spatial interaction. The absence of such peaks in the NOESY spectrum of **Vo** indicates that the 3,4,5-trisubstituted benzene ring is attached to C^1. The ^{13}C NMR spectrum of **Vo** (see Experimental) confirms the assumed structure.

The HMBC spectrum contained correlation peaks between the 10-H and 5-H protons and carbon nucleus resonating at δ_C 145.5 ppm; therefore, the latter was identified as C^1. The presence of 2'-H/C^1 and 6'-H/C^1 correlation peaks unambiguously indicates that the benzene ring with Br, OH, and OEt groups is located at C^1, whereas correlation between 2''-H and C^3 suggests localization of the ortho-hydroxyphenyl substituent on C^3 (δ_C 146.5) ppm. These data confirm the structure of the final products as 1-alkoxyphenyl-3-arylbenzo[*f*]quinolines.

The structure of 1,3-diarylbenzo[*f*]quinolines **Va**–**Vt** was also supported by the IR and GC–MS data. In the IR spectra of **Va**–**Vt**, stretching vibrations of aromatic C–H bonds appear at 3060–3030 cm^{-1}. Absorption bands at 725–715 and 860–859 cm^{-1}, which are insensitive to substituent effects, correspond to out-of-plane bending vibrations of two neighboring C–H bonds [12]. The mass spectra of 1,3-diarylbenzo[*f*]quinolines **Va**–**Vt** characteristically contain a small number of fragment ion peaks. The most abundant ion (I_{rel} 100%) is $[C_6H_4]^+$, the molecular ion peaks have a relative intensity of 70–80%, and medium-intensity peaks (48–64%) belonging to $[M - C_2H_5]^+$ (**Va**–**Ve**) and $[M - C_3H_7]^+$+ (**Vf**–**Vj**) are present.

EXPERIMENTAL

The IR spectra were recorded on a Nicolet Protege-460 spectrometer with Fourier transform. The ^1H and ^{13}C NMR spectra were measured on Tesla BS-567A (100 MHz) and Bruker AC-500 spectrometers (500 MHz) from 2–5% solutions in DMSO-d_6; the chemical shifts were determined relative to tetramethylsilane as internal reference. The mass spectra (electron impact, 70 eV) were obtained on a Hewlett–Packard 5890/5972 GC/MS instrument (HP-5MS column; samples were injected as solutions in methylene chloride).

α,β-Unsaturated ketones **IVa**–**IVt** were synthesized by aldol condensation of acetophenones **IIIa**–**IIIe** with benzaldehydes **IIa**–**IId** according to the standard procedure [13]. Their physical constants coincided with those reported in [8, 14, 15].

1-Aryl-3-[3-(4-fluorophenyl)-1*H*-pyrazol-4-yl]-prop-2-en-1-ones IVu–**IVw** *(general procedure).* A mixture of 0.01 mol of 3-(4-fluorophenyl)-1*H*-pyrazole-4-carbaldehyde (**IIe**), 0.01 mol of 2-naphthylamine, 0.01 mol of acetophenone **IIIa**–**IIId**, and 5–8 drops of hydrochloric acid in 60 ml of butanol was heated for 4–5 h on a water bath. The precipitate was filtered off and recrystallized from ethanol.

3-[3-(4-Fluorophenyl)-1*H*-pyrazol-4-yl]-1-phenylprop-2-en-1-one (IVu). Yield 54%, colorless crystalline substance, mp 256–257°C. IR spectrum, ν, cm^{-1}: 3060, 2920, 1650, 1527, 1519, 1400, 1433, 1382, 1305, 1271, 1109, 1033, 920, 835, 759, 704. ^1H NMR spectrum, δ, ppm: 7.75–8.00 m and 8.10–8.35 m (9H, H_{arom}), 9.30– 9.50 m (3H, CH=CH, =CHN), 10.70 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 279 (100) $[M]^+$, 184 (40), 186 (37), 95 (50). Found, %: F 6.79; N 10.25. $C_{17}H_{12}FN_2O$. Calculated, %: F 6.81; N 10.40.

1-(4-Chlorophenyl)-3-[3-(4-fluorophenyl)-1*H*-pyrazol-4-yl]prop-2-en-1-one (IVv). Yield 58%, colorless crystalline substance, mp 273–274°C. IR spectrum, ν, cm^{-1}: 3030, 3010, 2970, 1640, 1542, 1437, 1385, 1298, 1264, 1100, 910, 850, 754, 700. ^1H NMR spectrum, δ, ppm: 7.70–8.00 m and 8.10–8.30 m (8H, H_{arom}), 9.35–9.50 m (3H, CH=CH, =CHN), 10.75 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 314 (20) $[M + 1]^+$, 313 (100) $[M]^+$, 218 (33), 217 (28). Found, %: Cl 11.19; F 6.04; N 8.93. $C_{17}H_{11}ClFN_2O$. Calculated, %: Cl 11.18; F 6.07; N 8.95.

3-[3-(4-Fluorophenyl)-1*H*-pyrazol-4-yl]-1-(4-hydroxyphenyl)prop-2-en-1-one (IVw). Yield 42%, colorless crystalline substance, mp 298–300°C. IR spectrum, ν, cm^{-1}: 3530, 3100, 2965, 2800, 1570,

1430, 1367, 1250, 1090, 830. ^{1}H NMR spectrum, δ, ppm: 7.65–7.90 m and 8.00–8.40 m (8H, H_{arom}, 1H, OH), 9.27–9.42 m (3H, CH=CH, =CHN), 10.70 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 295 (100) $[M]^+$, 200 (37), 203 (18), 95 (42). Found, %: F 6.46; N 9.47. $C_{17}H_{12}FN_2O_2$. Calculated, %: F 6.44; N 9.49.

1,3-Diarylbenzo[*f*]quinolines Va–Vt *(general procedure).* A mixture of 0.01 of substituted benzaldehyde **IIa**–**IIe**, 0.01 mol of 2-naphthylamine (**I**), 0.01 mol of acetophenone **IIIa**–**IIIe**, and 5–8 drops of hydrochloric acid in 60 ml of butanol was heated for 6–10 h on a water bath. The resulting tarry material was treated with diethyl ether under stirring. After 24 h or more, a solid precipitated from the ether solution and was filtered off, washed with warm (30–40°C) 25% aqueous ammonia, and repeatedly recrystallized from butanol, benzene, or toluene until a purity of no less than 95% was attained. If no solid precipitated upon treatment of the tarry material with ether, it was treated with ammonia (see above), stirred for 3 h, and the precipitate was filtered off recrystallized. Compounds **Vp**–**Vs** were isolated in such a way.

1-(4-Ethoxyphenyl)-3-phenylbenzo[*f*]quinoline (Va). Yield 48%, colorless crystalline substance, mp 152°C. IR spectrum, ν, cm^{-1}: 3442, 2973, 1605, 1577, 1541, 1524, 1509, 1473, 1451, 1388, 1357, 1307, 1288, 1236, 1177, 1115, 1039, 923, 835, 805, 757, 704, 661, 594. ^{1}H NMR spectrum, δ, ppm: 1.42 t (3H, OCH_2*Me*), 4.10 q (2H, OCH_2Me), 7.00–7.20 m (3H, H_{arom}), 7.48–7.62 m (7H, H_{arom}), 7.80–8.10 m (4H, H_{arom}), 8.20 d (1H, H_{arom}, J = 8.0 Hz), 8.30 d (1H, H_{arom}, J = 7.6 Hz). Mass spectrum, *m/z* (I_{rel}, %): 376 (40) $[M + 1]^+$, 375 (100) $[M]^+$, 346 (42) $[M - C_2H_5]^+$. Found, %: C 86.44; H 5.57; N 3.70. $C_{27}H_{21}$·NO. Calculated, %: C 86.40; H 5.60; N 3.73.

3-(4-Chlorophenyl)-1-(4-ethoxyphenyl)benzo[*f*]quinoline (Vb). Yield 68%, yellow crystalline substance, mp 210–212°C. IR spectrum, ν, cm^{-1}: 3440, 2970, 1603, 1574, 1547, 1513, 1509, 1470, 1452, 1386, 1351, 1300, 1232, 1176, 1046, 931, 852, 750, 700, 663, 592. ^{1}H NMR spectrum, δ, ppm: 1.40 t (3H, OCH_2*Me*), 4.07 q (2H, OCH_2Me), 7.03–7.15 m (3H, H_{arom}), 7.45–7.58 m (6H, H_{arom}), 7.90–8.10 m (4H, H_{arom}), 8.18 d (1H, H_{arom}, J = 7.7 Hz), 8.34 d (1H, H_{arom}, J = 7.9 Hz). Mass spectrum, *m/z* (I_{rel}, %): 410 (40) $[M + 1]^+$, 409 (100) $[M]^+$, 382 (13) $[M - C2H5]^+$, 380 (38), 352 (12), 346 (14), 315 (12). Found, %: C 79.24; H 4.90; Cl 8.53; N 3.44. $C_{27}H_{20}ClNO$. Calculated, %: C 79.22; H 4.89; Cl 8.56; N 3.42.

3-(4-Bromophenyl)-1-(4-ethoxyphenyl)benzo[*f*]quinoline (Vc). Yield 72%, colorless crystalline substance, mp 216°C. IR spectrum, ν, cm^{-1}: 3431, 2968, 1614, 1578, 1509, 1464, 1387, 1308, 1230, 1174, 1038, 930, 751, 702, 664, 569. ^{1}H NMR spectrum, δ, ppm: 1.37 t (3H, OCH_2*Me*), 4.00 q (2H, OCH_2Me), 7.00–7.18 m (3H, H_{arom}), 7.40–7.50 m (6H, H_{arom}), 7.90–8.15 m (4H, H_{arom}), 8.24 d (1H, H_{arom}, J = 7.9 Hz), 8.40 d (1H, H_{arom}, J = 8.0 Hz). Mass spectrum, *m/z* (I_{rel}, %): 455 (10) $[M + 1]^+$, 454 (100) $[M]^+$, 427 (11) $[M - C_2H_5]^+$, 425 (42), 397 (12). Found, %: C 71.32; H 4.43; Br 17.60; N 3.10. $C_{27}N_{20}BrNO$. Calculated, %: C 71.36; H 4.40; Br 17.62; N 3.08.

1-(4-Ethoxyphenyl)-3-(4-hydroxyphenyl)benzo[*f*]quinoline (Vd). Yield 53%, colorless crystalline substance, mp 217–218°C. IR spectrum, ν, cm^{-1}: 3445, 3327, 2978, 1601, 1572, 1539, 1517, 1477, 1458, 1381, 1359, 1303, 1286, 1234, 1176, 1115, 1039, 925, 831, 803, 759, 701, 668. ^{1}H NMR spectrum, δ, ppm: 1.09 t (3H, OCH_2*Me*), 3.49 q (2H, OCH_2Me), 6.60–6.72 m (2H, H_{arom}), 6.80–6.90 m (2H, H_{arom}), 7.05–7.15 m (6H, H_{arom}), 7.30–7.50 m (3H, H_{arom}), 7.90–8.10 m (2H, H_{arom}), 8.20 s (1H, OH). Mass spectrum, *m/z* (I_{rel}, %): 392 (48) $[M + 1]^+$, 391 (100) $[M]^+$, 362 (45) $[M - C_2H_5]^+$, 353 (38), 143 (84), 115 (62). Found, %: C 82.84; H 5.39; N 3.60. $C_{27}H_{21}NO_2$. Calculated, %: C 82.87; H 5.37; N 3.58.

1-(4-Ethoxyphenyl)-3-(2-hydroxyphenyl)benzo[*f*]quinoline (Ve). Yield 53%, colorless crystalline substance, mp 210°C. IR spectrum, ν, cm^{-1}: 3442, 3321, 2973, 1600, 1572, 1534, 1522, 1471, 1455, 1379, 1352, 1288, 1239, 1176, 1113, 1037, 922, 834, 806, 759, 668. ^{1}H NMR spectrum, δ, ppm: 1.06 t (3H, OCH_2*Me*), 3.42 q (2H, OCH_2Me), 6.68–6.79 m (2H, H_{arom}), 6.84–6.97 m (2H, H_{arom}), 7.10–7.23 m (6H, H_{arom}), 7.32–7.52 m (3H, H_{arom}), 8.00–8.16 m (2H, H_{arom}), 8.27 s (1H, OH). Mass spectrum, *m/z* (I_{rel}, %): 392 (43) $[M + 1]^+$, 391 (100) $[M]^+$, 362 (34) $[M - C_2H_5]^+$, 353 (27), 143 (76), 115 (52). Found, %: C 82.90; H 5.34; N 3.57. $C_{27}H_{21}NO_2$. Calculated, %: C 82.87; H 5.37; N 3.58.

3-Phenyl-1-(4-propoxyphenyl)benzo[*f*]quinoline (Vf). Yield 32%, colorless crystalline substance, mp 138°C. IR spectrum, ν, cm^{-1}: 3440, 2975, 1627, 1544, 1472, 1436, 1379, 1323, 1300, 1288, 1231, 1172, 1110, 1041, 923, 835, 801, 762, 704, 669. ^{1}H NMR spectrum, δ, ppm: 0.80 t (3H, OCH_2CH_2*Me*), 1.50 t (2H, OCH_2CH_2Me), 3.50 t (2H, OCH_2CH_2Me), 7.06–7.18 m (3H, H_{arom}), 7.42–7.60 m (7H, H_{arom}), 7.85–8.12 m (4H, H_{arom}), 8.18 d (1H, H_{arom}, J = 8.0 Hz), 8.27 d (1H, H_{arom}, J = 7.9 Hz). Mass spectrum, *m/z* (I_{rel}, %): 390 (16) $[M + 1]^+$, 389 (100) $[M]^+$, 347 (63) $[M - C_2H_5]^+$, 346 (84), 252 (13). Found, %: C 86.41; H 6.02; N 3.57. $C_{28}H_{23}NO$. Calculated, %: C 86.37; H 5.91; N 3.60.

3-(4-Chlorophenyl)-1-(4-propoxyphenyl)benzo[*f*]quinoline (Vg). Yield 90%, yellow crystalline

substance, mp 176°C. IR spectrum, ν, cm^{-1}: 3444, 2961, 2922, 2545, 1598, 1573, 1516, 1450, 1367, 1320, 1301, 1257, 1197, 1159, 1014, 971, 847, 750, 738, 588. ^1H NMR spectrum, δ, ppm: 0.85 t (3H, OCH_2CH_2*Me*), 1.47 t (2H, OCH_2CH_2Me), 3.46 t (2H, OCH_2CH_2Me), 7.06–7.20 m (3H, H_{arom}), 7.42–7.60 m (6H, H_{arom}), 7.80–8.14 m (4H, H_{arom}), 8.20 d (1H, H_{arom}, J = 7.6 Hz), 8.33 d (1H, H_{arom}, J = 7.6 Hz). Mass spectrum, *m/z* (I_{rel}, %): 424 (33) $[M + 1]^+$, 423 (100) $[M]^+$, 380 (65) $[M - C_2H_5]^+$, 291 (63), 149 (84), 107 (85). Found, %: C 79.40; H 5.18; Cl 8.25; N 3.37. $C_{28}H_{22}ClNO$. Calculated, %: C 79.43; H 5.20; Cl 8.27; N 3.30.

3-(4-Bromophenyl)-1-(4-propoxyphenyl)benzo[*f*]quinoline (Vh). Yield 76%, colorless crystalline substance, mp 183°C. IR spectrum, ν, cm^{-1}: 3440, 2960, 2921, 2543, 1592, 1500, 1457, 1362, 1318, 1254, 1191, 1157, 1014, 970, 823, 750, 736, 579. ^1H NMR spectrum, δ, ppm: 0.87 t (3H, OCH_2CH_2*Me*), 1.46 t (2H, OCH_2CH_2Me), 3.49 t (2H, OCH_2CH_2Me), 7.06–7.20 m (3H, H_{arom}), 7.46–7.59 m (6H, H_{arom}), 7.94–8.19 m (4H, H_{arom}), 8.24 d (1H, H_{arom}, J = 7.6 Hz), 8.38 d (1H, H_{arom}, J = 7.9 Hz). Mass spectrum, *m/z* (I_{rel}, %): 469 (40) $[M + 1]^+$, 468 (100) $[M]^+$, 425 (59) $[M - C_3H_7]^+$, 345 (30), 108 (27). Found, %: C 71.81; H 4.69; Br 17.01; N 2.98. $C_{28}H_{22}BrNO$. Calculated, %: C 71.79; H 4.70; Br 17.05; N 2.99.

3-(4-Hydroxyphenyl)-1-(4-propoxyphenyl)benzo[*f*]quinoline (Vi). Yield 94%, yellow crystalline substance, mp 199–200°C. IR spectrum, ν, cm^{-1}: 3442, 3104, 2923, 1611, 1587, 1516, 1446, 1363, 1320, 1250, 1190, 1156, 1069, 1012, 975, 881, 848, 830, 758, 736, 518, 480. ^1H NMR spectrum, δ, ppm: 0.88 t (3H, OCH_2CH_2*Me*), 1.49 t (2H, OCH_2CH_2Me), 3.45 t (2H, OCH_2CH_2Me), 6.64–6.78 m (2H, H_{arom}), 6.82–6.94 m (2H, H_{arom}), 7.00–7.22 m (6H, H_{arom}), 7.32–7.48 m (3H, H_{arom}), 7.82–8.05 m (2H, H_{arom}), 8.20 s (1H, OH). Mass spectrum, *m/z* (I_{rel}, %): 406 (14) $[M + 1]^+$, 405 (100) $[M]^+$, 363 (51) $[M - C_3H_7]^+$, 362 (61), 107 (15), 143 (98), 115 (48), 107 (19). Found, %: C 82.95; H 5.67; N 3.44. $C_{28}H_{23}NO_2$. Calculated, %: C 82.96; H 5.67; N 3.46.

3-(2-Hydroxyphenyl)-1-(4-propoxyphenyl)benzo[*f*]quinoline (Vj). Yield 84%, colorless crystalline substance, mp 200°C. IR spectrum, ν, cm^{-1}: 3439, 3101, 2927, 1611, 1593, 1484, 1375, 1324, 1266, 1190, 1163, 1068, 1017, 970, 874, 832, 750, 732, 522, 484. ^1H NMR spectrum, δ, ppm: 0.90 t (3H, OCH_2CH_2*Me*), 1.45 t (2H, OCH_2CH_2Me), 3.48 t (2H, OCH_2CH_2Me), 6.65–6.72 m (2H, H_{arom}), 6.86–6.98 m (2H, H_{arom}), 7.05–7.19 m (6H, H_{arom}), 7.37–7.53 m (3H, H_{arom}), 7.82–8.07 m (2H, H_{arom}), 8.26 s (1H, OH). Mass spectrum, *m/z* (I_{rel}, %): 406 (22) $[M + 1]^+$, 405(100) $[M]^+$, 363 (57) $[M - C_3H_7]^+$, 362 (54), 107 (23), 143 (51), 115 (34), 107 (25). Found, %: C 82.94; H 5.68; N 3.42. $C_{28}H_{23}NO_2$. Calculated, %: C 82.96; H 5.67; N 3.46.

1-(3-Bromo-5-ethoxy-4-hydroxyphenyl)-3-phenylbenzo[*f*]quinoline (Vk). Yield 42%, light brown substance, mp 229–230°C. IR spectrum, ν, cm^{-1}: 3452, 3446, 3323, 2971, 1594, 1526, 1478, 1459, 1384, 1363, 1301, 1287, 1232, 1178, 1110, 1043, 938, 843, 762, 571. ^1H NMR spectrum, δ, ppm: 1.40 t (3H, OCH_2Me), 4.25 q (2H, OCH_2Me), 7.20 m (1H, H_{arom}), 7.40–7.68 m (7H, H_{arom}), 7.85–8.18 m (6H, H_{arom}), 9.70 s (1H, OH). Mass spectrum, *m/z* (I_{rel}, %): 470 (100) $[M]^+$, 441 (57), 425 (15), 390 (23). Found, %: C 68.95; H 4.27; Br 17.02; N 2.96. $C_{27}H_{20}NO_2Br$. Calculated, %: C 68.93; H 4.25; Br 17.02; N 2.98.

1-(3-Bromo-5-ethoxy-4-hydroxyphenyl)-3-(4-chlorophenyl)benzo[*f*]quinoline (Vl). Yield 20%, colorless crystalline substance, mp 230–231°C. IR spectrum, ν, cm^{-1}: 3338, 2985, 1607, 1572, 1529, 1474, 1448, 1381, 1352, 1307, 1238, 1174, 1043, 929, 848, 741, 725, 572. ^1H NMR spectrum, δ, ppm: 1.43 t (3H, OCH_2Me), 4.23 q (2H, OCH_2Me), 7.25 m (1H, H_{arom}), 7.36–7.54 m (7H, H_{arom}), 7.63–7.72 m (3H, H_{arom}), 7.79 d (1H, H_{arom}, J = 7.6 Hz), 8.06 d (1H, H_{arom}, J = 7.9 Hz), 9.65 s (1H, OH). Mass spectrum, *m/z* (I_{rel}, %): 504 (100) $[M]^+$, 475 (53), 463 (20), 459 (17). Found, %: C 65.23; H 3.76; Cl 6.92; Br 15.79; N 2.75. $C_{27}H_{19}ClBrNO_2$. Calculated, %: C 65.28; H 3.77; Cl 6.94; Br 15.87; N 2.78.

1-(3-Bromo-5-ethoxy-4-hydroxyphenyl)-3-(4-bromophenyl)benzo[*f*]quinoline (Vm). Yield 40%, light brown substance, mp 235–236°C. IR spectrum, ν, cm^{-1}: 3341, 3328, 2963, 1604, 1568, 1514, 1472, 1443, 1376, 1342, 1301, 1235, 1170, 1039, 930, 740, 720, 569. ^1H NMR spectrum, δ, ppm: 1.40 t (3H, OCH_2Me), 4.37 q (2H, OCH_2Me), 7.34 m (1H, H_{arom}), 7.39–7.52 m (7H, H_{arom}), 7.60–7.70 m (3H, H_{arom}), 7.82 d (1H, H_{arom}, J = 8.2 Hz), 8.03 d (1H, H_{arom}, J = 8.0 Hz), 9.68 s (1H, OH). Mass spectrum, *m/z* (I_{rel}, %): 549 (100) $[M]^+$, 520 (53), 504 (27), 424 (16). Found, %: C 59.00; H 3.47; Br 29.08; N 2.58. $C_{27}H_{19}Br_2NO_2$. Calculated, %: C 59.02; H 3.16; Br 29.14; N 2.55.

1-(3-Bromo-5-ethoxy-4-hydroxyphenyl)-3-(4-hydroxyphenyl)benzo[*f*]quinoline (Vn). Yield 23%, colorless crystalline substance, mp 257–258°C. IR spectrum, ν, cm^{-1}: 3341, 3333, 2970, 2815, 1612, 1573, 1509, 1467, 1441, 1358, 1311, 1234, 1162, 1031, 928, 713, 563. ^1H NMR spectrum, δ, ppm: 1.40 t (3H, OCH_2Me), 4.25 q (2H, OCH_2Me), 7.00–7.60 m (6H, H_{arom}), 7.70–8.20 m (7H, H_{arom}), 9.45 s (1H, OH), 9.68 s (1H, OH). Mass spectrum, *m/z* (I_{rel}, %):

486 (100) $[M]^+$, 457 (41), 440 (25), 360 (11). Found, %: C 66.63; H 4.06; Br 16.50; N 2.88. $C_{27}H_{20}BrNO_3$. Calculated, %: C 66.66; H 4.11; Br 16.46; N 2.88.

1-(3-Bromo-5-ethoxy-4-hydroxyphenyl)-3-(2-hydroxyphenyl)benzo[*f*]quinoline (Vo). Yield 16%, colorless crystalline substance, mp 256–258°C. IR spectrum, ν, cm^{-1}: 3339, 2992, 2823, 1618, 1574, 1509, 1468, 1443, 1361, 1321, 1239, 1167, 1026, 924, 717, 560. ^1H NMR spectrum, δ, ppm: 1.35 t (3H, OCH_2*Me*), 4.20 q (2H, OCH_2Me), 7.02 d (1H, 3''-H, $J_{3',4''}$ = 8 Hz), 7.05 d.d (1H, 5''-H, $J_{4'',5''}$ = 8, $J_{5'',6''}$ = 7 Hz), 7.22 t (1H, 8-H, $J_{8,9}$ = 7 Hz), 7.33 d (1H, 6''-H, $J_{6'',5''}$ = 8 Hz), 7.41 d.d (1H, 4''-H, $J_{3'',4''}$ = 7, $J_{4'',5''}$ = 8 Hz), 7.52 t (1H, 9-H, $J_{9,10}$ = 8 Hz), 7.81 d (1H, 7-H, $J_{7,8}$ = 7 Hz), 7.89 s (1H, 6'-H), 7.94 s (1H, 2-H), 7.98 d (1H, 10-H, $J_{10,9}$ = 8 Hz), 8.02 d (1H, 5-H, $J_{5,6}$ = 9 Hz), 8.09 d (1H, 6-H, $J_{5,6}$ = 9 Hz), 8.12 s (1H, 2'-H), 9.30 s (1H, OH), 9.45 s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 145.5 (C^1), 121.2 (C^2), 146.5 (C^3), 148.5 (C^{4a}), 128.7 (C^5), 131.2 (C^6), 130.0 (C^{6a}), 125.9 (C^7), 126.1 (C^8), 126.4 (C^9), 128.6 (C^{10}), 131.9 (C^{10a}), 130.3 (C^{10b}), 129.5 ($C^{1'}$), 123.2 ($C^{2'}$), 122.8 ($C^{3'}$), 147.7 ($C^{4'}$), 124.2 ($C^{5'}$), 110.8 ($C^{6'}$), 122.8 ($C^{1''}$), 153.9 ($C^{2''}$), 115.8 ($C^{3''}$), 129.7 ($C^{4''}$), 119.9 ($C^{5''}$), 129.5 ($C^{6''}$). Mass spectrum, *m/z* (I_{rel}, %): 486 (100) $[M]^+$, 457 (43), 440 (29), 360 (17). Found, %: C 66.62; H 4.07; Br 16.47; N 2.87. $C_{27}H_{20}BrNO_3$. Calculated, %: C 66.66; H 4.11; Br 16.46; N 2.88.

1-[4-(2-Fluorophenylmethoxy)phenyl]-3-phenylbenzo[*f*]quinoline (Vp). Yield 29%, colorless crystalline substance, mp 176°C. IR spectrum, ν, cm^{-1}: 3305, 2954, 2807, 1594, 1568, 1514, 1462, 1352, 1237, 1160, 1153, 1035, 936, 918, 725. ^1H NMR spectrum, δ, ppm: 5.20 s (2H, OCH_2), 7.05–7.25 m (7H, H_{arom}), 7.38–7.50 m (6H, H_{arom}), 7.80–7.94 m (3H, H_{arom}), 8.05 s (1H, H_{arom}), 8.24 s (1H, H_{arom}), 8.37 d (1H, H_{arom}, *J* = 7.8 Hz), 8.50 d (1H, H_{arom}, *J* = 7.8 Hz). Mass spectrum, *m/z* (I_{rel}, %): 456 (12) $[M + 1]^+$, 455 (100) $[M]^+$, 356 (36), 330 (28). Found, %: C 84.35; H 4.80; N 3.10. $C_{32}H_{22}FNO$. Calculated, %: C 84.39; H 4.83; N 3.08.

3-(4-Chlorophenyl)-1-[4-(2-fluorophenylmethoxy)phenyl]benzo[*f*]quinoline (Vq). Yield 27%, colorless crystalline substance, mp 196–198°C. IR spectrum, ν, cm^{-1}: 3328, 3306, 2953, 2810, 1597, 1576, 1508, 1464, 1350, 1232, 1164, 1150, 1031, 934, 848. ^1H NMR spectrum, δ, ppm: 5.20 s (2H, OCH_2), 7.10–7.50 m (11H, H_{arom}), 7.70–7.90 m (3H, H_{arom}), 8.00 s (1H, H_{arom}), 8.30–8.40 m (2H, H_{arom}), 8.54 d (1H, H_{arom}, *J* = 7.7 Hz). Mass spectrum, *m/z* (I_{rel}, %): 490 (15) $[M + 1]^+$, 489 (100) $[M]^+$, 364 (44), 269 (13). Found, %: C 78.59; H 4.31; Cl 7.18; N 2.87. $C_{32}H_{21}$·ClFNO. Calculated, %: C 78.52; H 4.29; Cl 7.18; N 2.86.

3-(4-Bromophenyl)-1-[4-(2-fluorophenylmethoxy)phenyl]benzo[*f*]quinoline (Vr). Yield 82%, colorless crystalline substance, mp 210–212°C. IR spectrum, ν, cm^{-1}: 3334, 2967, 2820, 1604, 1581, 1510, 1468, 1353, 1236, 1167, 1158, 1024, 930, 564. ^1H NMR spectrum, δ, ppm: 5.40 s (2H, OCH_2), 7.10–7.75 m (14H, H_{arom}), 7.85 d (1H, H_{arom}, *J* = 8.5 Hz), 7.90–8.05 m (2H, H_{arom}), 8.10–8.20 m (2H, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 535 (9) $[M + 1]^+$, 534 (100) $[M]^+$, 409 (53), 314 (15), 126 (23). Found, %: C 71.91; H 3.96; Br 14.94; N 2.60. $C_{32}H_{21}BrFNO$. Calculated, %: C 71.91; H 3.93; Br 14.98; N 2.62.

1-[4-(2-Fluorophenylmethoxy)phenyl]-3-(4-hydroxyphenyl)benzo[*f*]quinoline (Vs). Yield 51%, colorless crystalline substance, mp 229–230°C. IR spectrum, ν, cm^{-1}: 3330, 3324, 3010, 2971, 2818, 1599, 1573, 1512, 1463, 1358, 1234, 1179, 1150, 1016, 929, 831, 646, 512. ^1H NMR spectrum, δ, ppm: 5.25 s (2H, OCH_2), 7.10–7.60 m (12H, H_{arom}), 7.80–8.10 m (5H, H_{arom}), 8.25 d (1H, H_{arom}, *J* = 7.6 Hz), 8.38 d (1H, H_{arom}, *J* = 7.9 Hz), 9.40 s (1H, OH). Mass spectrum, *m/z* (I_{rel}, %): 472 (22) $[M + 1]^+$, 471 (100) $[M]^+$, 346 (65), 251 (18), 234 (15), 233 (21), 232 (11). Found, %: C 81.55; H 4.63; N 3.00. $C_{32}H_{22}FNO_2$. Calculated, %: C 81.53; H 4.67; N 2.97.

1-[4-(2-Fluorophenylmethoxy)phenyl]-3-(2-hydroxyphenyl)benzo[*f*]quinoline (Vt). Yield 47%, colorless crystalline substance, mp 224–225°C. IR spectrum, ν, cm^{-1}: 3328, 3318, 3007, 2976, 2823, 1592, 1569, 1514, 1462, 1358, 1231, 1179, 1156, 1012, 927, 832, 646, 521. ^1H NMR spectrum, δ, ppm: 5.19 s (2H, OCH_2), 7.00– 7.40 m (12H, H_{arom}), 7.64–8.00 m (5H, H_{arom}), 8.28 d (1H, H_{arom}, *J* = 7.9 Hz), 8.43 d (1H, H_{arom}, *J* = 8.0 Hz), 9.36 s (1H, OH). Mass spectrum, *m/z* (I_{rel}, %): 472 (12) $[M + 1]^+$, 471 (100) $[M]^+$, 346 (61), 251 (25), 234 (11), 233 (29), 232 (9). Found, %: C 81.54; H 4.68; N 2.99. $C_{32}H_{22}FNO_2$. Calculated, %: C 81.53; H 4.67; N 2.97.

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