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# Clean Procedure for Synthesis of Chromeno[4,3-*b*]benzo [*f* ]quinolin-6-one Derivatives: Reaction of *N*-arylidenenaphthalen-2-amine with 4-Hydroxycoumarin in Aqueous Media

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**Abstract:** A short and simple synthesis of chromeno[4,3-*b*]benzo[*f* ]quinolin-6-one derivatives was accomplished in good to high yields via the reaction of *N*-arylidene-naphthalen-2-amine with 4-hydroxycoumarin in aqueous media catalyzed by TEBAC. The structures were established by spectroscopic data and further confirmed by X-ray analysis. In addition, water was chosen as a green solvent.

**Keywords:** Aqueous medium, chromene, quinoline, Schiff base, TEBAC

Heteroaromatic rings containing nitrogen atoms often play important roles as the scaffolds of bioactive substances. Quinoline is one of the most popular

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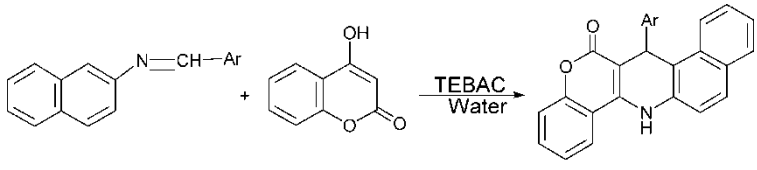
*N*-heteroaromatics incorporated into the structure of many pharmaceuticals. It is known that many quinoline-containing compounds exhibit a wide spectrum of pharmacological activities such as antiasthmatic, antiinflammatory, and antimalarial activities.[1] In addition, it was reported that chromenes and their derivatives are also important compounds, which are found to possess antiestrogenic activity and are devoid of any agonistic activity,[2] and are evaluated for potassium channel opening and hypotensive activities,[3] vasodilator and antihypertensive activies,[4] $\beta$-adrenolytic activity,[5] antimicrobial activity,[6] and biological activity of high-affinity retinoic acid receptor antagonist.[7] To the best of our knowledge, only a few examples of heteroaromatic rings containing quinoline and chromene at the same time have been mentioned in the literature.[8] Because of the toxic and volatile nature of many organic solvents, water as reaction medium was considered a very promising and attractive substitute for volatile organic solvents and was widely used in the green chemistry area since Breslow,[9] who showed that hydrophobic effects could strongly enhance the rate of several organic reactions, rediscovered the use of water as a solvent in organic chemistry in 1980s. There has been growing recognition that water is an attractive medium for many organic reactions resulting in less expensive, less dangerous, and environmentally friendly reactions, such as Diels–Alder reactions,[10] Claisen rearrangement reactions,[11] Reformatsky reactions,[12] and pinacol-coupling reactions.[13] As part of our current studies on the development of new routes to heterocyclic systems,[14] we now report an efficient and clean synthetic route to 7-aryl-7,14-dihydro-6*H*-benzo[*f*]chromeno[4,3-*b*]quinolin-6-one derivatives in aqueous medium catalyzed by TEBAC (triethylbenzyl ammonium chloride) by the reaction of *N*-arylidenenaphthalen-2-amine with 4-hydroxycoumarin.

When the reaction of *N*-arylidenenaphthalen-2-amine **1** and 4-hydroxycoumarin **2** was performed in water in the presence of TEBAC at 100°C, high yields of 7-aryl-7,14-dihydro-6*H*-benzo[*f*]chromeno[4,3-*b*]quinolin-6-one derivatives were obtained (Scheme 1).

To apply this reaction to a library synthesis, various kinds of *N*-arylidenenaphthalen-2-amine and 4-hydroxycoumarins were subjected to give the corresponding 7-aryl-7,14-dihydro-6*H*-benzo[*f*]chromeno[4,3-*b*]quinolin-6-one derivatives **3**, and representative examples are shown in Table 1. All of




**1** **2** **3**

***Scheme 1.***

***Table 1.*** Results of the reaction of **1** and **2** in water at 100°C[a]

| Entry | Ar | Products | Time (h) | Yields (%)[b] |
|---|---|---|---|---|
| **1** | 4-$BrC_6H_4$ | **3a** | 8 | 93.3 |
| **2** | 2-$ClC_6H_4$ | **3b** | 12 | 94.0 |
| **3** | 3-$ClC_6H_4$ | **3c** | 12 | 90.2 |
| **4** | 4-$ClC_6H_4$ | **3d** | 12 | 87.8 |
| **5** | 2,4-$Cl_2C_6H_3$ | **3e** | 10 | 90.9 |
| **6** | 3,4-$Cl_2C_6H_3$ | **3f** | 10 | 95.0 |
| **7** | 4-$OHC_6H_4$ | **3g** | 12 | 92.3 |
| **8** | 4-$(CH_3)_2NC_6H_4$ | **3h** | 12 | 95.2 |
| **9** | 2-$NO_2C_6H_4$ | **3i** | 8 | 90.5 |
| **10** | 4-$CH_3OC_6H_4$ | **3j** | 10 | 92.7 |
| **11** | 3,4-$(CH_3)_2C_6H_3$ | **3k** | 10 | 95.0 |
| **12** | 3,4-$(CH_3O)_2C_6H_3$ | **3l** | 8 | 88.9 |
| **13** | 3-OH-4-$CH_3OC_6H_3$ | **3m** | 12 | 92.8 |

[a]Reaction condition: 10 mL water and 0.1 g TEBAC, 2 mmol **1** and 2 mmol **2**.

the *N*-arylidenenaphthalen-2-amine gave expected products in excellent yields and purity. The isolated 7-aryl-7,14-dihydro-6*H*-benzo[*f*]chromeno[4,3-*b*] quinolin-6-one derivatives **3** were completely characterized by IR, $^1$H NMR, and elemental analyses. The analyses were in agreement with their structures. The IR spectra for **3a** exhibited sharp bands at 3310 $cm^{-1}$ (NH), 1657 $cm^{-1}$ (C═O). The $^1$H NMR spectrum of **3a** exhibited a singlet identified methine (5.91) and multiplets (7.28–8.40) for aromatic protons. The NH proton resonance at 10.18 disappeared after addition of $D_2O$ to the DMSO-$d_6$ solution of **3a**. To further confirm the structure of the product, the X-ray analysis (Crystal data for **3a**: $C_{26}H_{16}BrNO_2$; M = 454.31, orange-yellow block crystals, 0.59 × 0.34 × 0.15 mm, monoclinic, space group P 21/c, $a = 7.3681(8)$, $b = 13.5483(14)$, $c = 19.662(3)$ Å, $\beta = 100.372(4)^\circ$, $V = 1930.7(4)^3$, $Z = 4$, $D_c = 1.563\ g \cdot cm^{-3}$. $F(000) = 920$, $\mu(MoK\alpha) = 2.153\ mm^{-1}$. Intensity data were collected on Rigaku Mercury diffractometer with graphite monochromated Mo$K\alpha$ radiation ($\lambda = 0.71070$ Å) using $\omega$ scan mode with $3.01^\circ < \theta < 27.48^\circ$. 4412 unique reflections were measured and 3827 reflections with $I > 2\sigma(I)$ were used in the refinement. Structure was solved by direct methods and expanded using Fourier techniques. The final cycle of full-matrix least squares technique was done to $R = 0.0446$ and $wR = 0.0968$.) of **3a** was carried out. The selected bond lengths and bond angles are given in Table 2. The structure of **3a** and packing arrangement in a unit cell of **3a** along *a* are shown in Figs. 1 and 2. The X-ray crystal structure determination indicates the atoms C(1), C(2), C(3), C(4), C(5), and N(1) form a six-membered ring, with the interatomic distances 1.368(3) Å for C(1)-C(2) and 1.377(3) Å for C(4)-C(5), which are near to that of the typical C═C double bond (1.34 Å). The bond angles of

*Table 2.* Selected bond lengths (Å) and selected bond angles (°) for **3a**

| Bond | Distances | Distances | Distances |
|---|---|---|---|
| Bond distances for compound **3a** | | | |
| Br(1)-C(24) | 1.900(2) | C(2)-C(6) | 1.432(3) |
| O(1)-C(6) | 1.223(3) | C(2)-C(3) | 1.509(3) |
| O(2)-C(6) | 1.370(2) | C(3)-C(4) | 1.517(3) |
| O(2)-C(7) | 1.376(2) | C(3)-C(21) | 1.531(3) |
| N(1)-C(1) | 1.362(3) | C(4)-C(5) | 1.377(3) |
| N(1)-C(5) | 1.403(3) | C(4)-C(20) | 1.426(3) |
| C(1)-C(2) | 1.368(3) | C(5)-C(13) | 1.418(3) |
| C(1)-C(12) | 1.449(3) | | |
| Bond angles | Degree | Bond angles | Degree |
| Bond angles for compound **3a** | | | |
| C(6)-O(2)-C(7) | 121.09(16) | N(1)-C(5)-C(13) | 117.88(18) |
| C(1)-N(1)-C(5) | 121.46(17) | O(1)-C(6)-O(2) | 116.08(18) |
| N(1)-C(1)-C(2) | 119.83(18) | O(1)-C(6)-C(2) | 124.95(19) |
| N(1)-C(1)-C(12) | 120.11(18) | O(2)-C(6)-C(2) | 118.97(18) |
| C(2)-C(1)-C(12) | 120.06(18) | O(2)-C(7)-C(8) | 116.11(19) |
| C(1)-C(2)-C(6) | 120.29(19) | O(2)-C(7)-C(12) | 121.85(18) |
| C(1)-C(2)-C(3) | 122.73(18) | C(7)-C(12)-C(1) | 117.25(18) |
| C(6)-C(2)-C(3) | 116.97(17) | C(11)-C(12)-C(1) | 124.99(19) |
| C(2)-C(3)-C(4) | 110.53(16) | C(14)-C(13)-C(5) | 120.1(2) |
| C(2)-C(3)-C(21) | 110.09(16) | C(19)-C(20)-C(4) | 122.09(19) |
| C(4)-C(3)-C(21) | 111.29(16) | C(15)-C(20)-C(4) | 119.61(19) |
| C(5)-C(4)-C(20) | 119.36(19) | C(22)-C(21)-C(3) | 120.92(19) |
| C(5)-C(4)-C(3) | 120.19(18) | C(26)-C(21)-C(3) | 120.83(19) |
| C(20)-C(4)-C(3) | 120.26(18) | C(23)-C(24)-Br(1) | 119.59(19) |
| C(4)-C(5)-N(1) | 121.16(18) | C(25)-C(24)-Br(1) | 119.13(19) |
| C(4)-C(5)-C(13) | 120.95(19) | | |

C(2)-C(1)-N(1), C(1)-C(2)-C(3), C(3)-C(4)-C(5), and C(4)-C(5)-O(1) are 119.83(18), 122.73(18), 120.19(18) and 121.16(18)° respectively, which also illustrates that C(1), C(2), C(4), and C(5) all adopt $sp^2$ hybrid orbit to form C—C double bonds. The bond angle of C(1)-N(1)-C(5) [121.46(17)°] is near to 120°, which indicates that the atom N(1) adopts $sp^2$ hybrid orbit to conjugate to the intercyclic C=C double bonds C(1)—C(2) and C(4)—C(5). The X-ray crystal structure determination indicates the 1,4-dihydropyridine ring of the chromenopyridine moiety is slightly distorted and adopts a boat conformation. The atoms C(3) and N(1) deviate from the basal plane defined by the atoms C(1)/C(2)/C(4)/C(5)/by 0.254 (2) and 0.095 (2) Å, respectively. The 1,4-dihydropyridine is nearly parallel to the phenyl ring [C(4)/C(5)/C(13)/C(14)/C(15)/C(20)], phenyl ring [C(15)∼C(20)], phenyl ring [C(7)∼C(12)], and pyran ring [C(1)/C(2)/C(6)/C(7)/C(12)/O(2)],

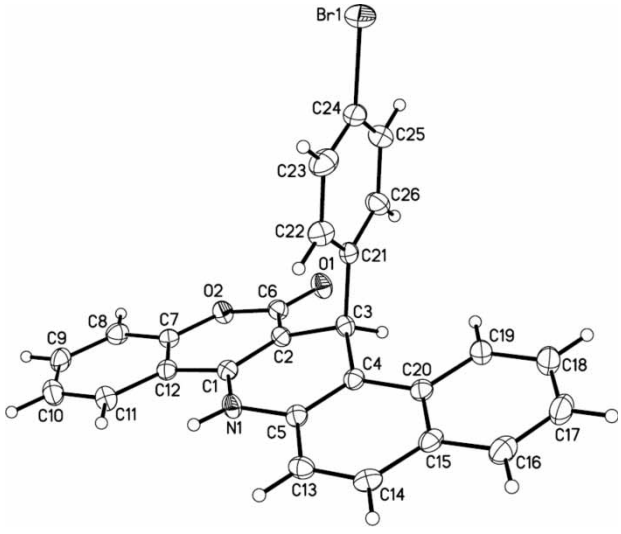



***Figure 1.*** Crystal structure of the product **3a**.

forming the dihedral angles of 5.2(1), 4.2(2), 6.7(1), and 7.9(1)°, respectively, and nearly perpendicular to phenyl ring [C(21)∼C(26)], forming a dihedral angles of 82.2(2)°. The dihedral angle between the phenyl ring [C(7)∼C(12)] and phenyl ring [C(15)∼C(20)] is 10.8(1)°.

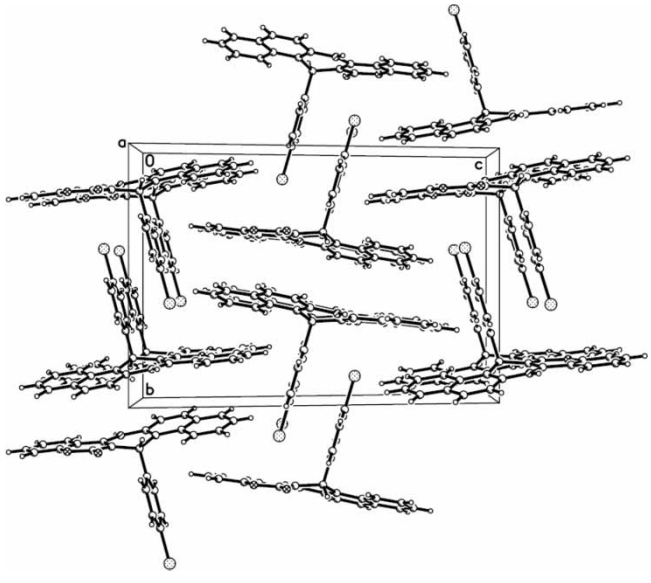
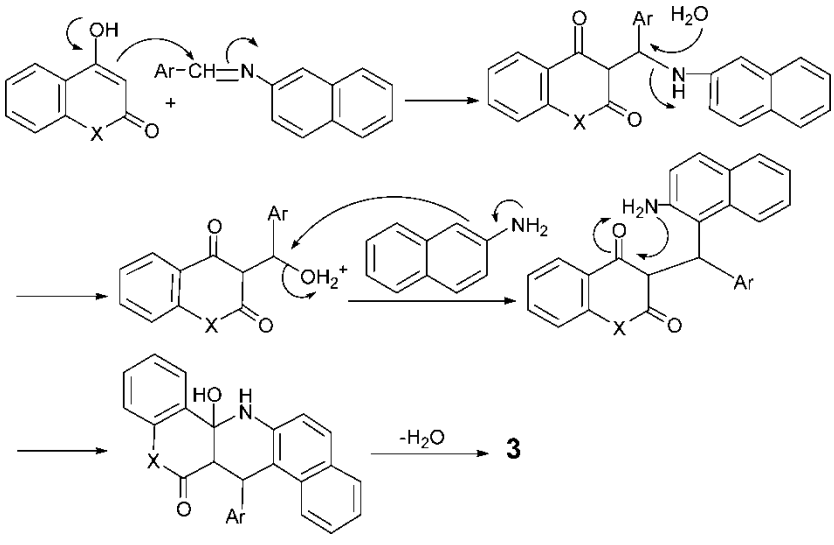



***Figure 2.*** Packing arrangement in a unit cell of **3a** along *a*.




***Scheme 2.***

Though the detailed mechanism of this reaction has not been clarified yet, the formation of **3** can be explained by the possible mechanism presented in Scheme 2.

Finally the reuse of the water and TEBAC was studied. At completion, monitored by TLC, the reaction mixture was allowed to cool to room temperature, the solid of the products was isolated by filtration, and the filtrate of the water together with TEBAC could be reused directly. **Investigations by using 1a and 2 as model substrates showed that successive reuse of the recovery water and TEBAC was feasible**. A summary of the reuse of water and TEBAC is shown in Table 3. Even in the fourth round the yield of the product **3** is fairly high.

In conclusion, an efficient green chemistry method for the synthesis of chromeno[4,3-*b*]benzo[*f*]quinolin-6-one derivatives by condensation of 4-hydroxycoumarin and *N*-arylidenenaphthalen-2-amine was successfully established. In this method, the potential active compounds containing quinoline as well as chromene heteroaromatic rings can be synthesized easily by a one-step reaction. Compared to other methods,[8] this new method has the advantage of good yields, mild reaction conditions, easy workup, inexpensive reagents, and environmentally friendly procedure.

## EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a Tensor 27 spectrometer in KBr. $^1$H NMR

*Table 3.* Study on the reuse of water and TEBAC[a]

| Entry | Temperature/°C | Reaction time/h | Yields (%)[b] |
|---|---|---|---|
| **1** | 100 | 12 | 93 |
| **2** | 100 | 12 | 93 |
| **3** | 100 | 12 | 95 |
| **4** | 100 | 12 | 92 |

[a]Reaction condition: 10 mL of water and TEBAC, 2 mmol of **1a**, and 2 mmol of **2**.
[b]Isolated yields.



spectra were obtained for solution in DMSO-$d_6$ with $Me_4Si$ as internal standard using a Bruker-400 spectrometer. Elemental analyses were carried out using a Carlo Erba 1110 analyzer. X-ray diffraction was measured on a Rigaku Mercury diffractometer.

## General Procedure

A suspension of a mixture of *N*-arylidenenaphthalen-2-amine **1** (2 mmol), 4-hydroxycoumarin **2** (2 mmol), and TEBAC (0.1 g) was stirred in water (10 mL) at 100°C for 8–12 h. The crystalline powder formed was collected by filtration, washed with water, and recrystallized from DMF and water to give pure 4-arylchromeno[4,3-*b*] benzo[*f*]quinoline derivatives **3**.

## Data

**3a**: mp >300°C (lit.[8a] 378–380°C). IR (KBr, $\nu$, $cm^{-1}$): 3310, 3056, 1657, 1621, 1588, 1570, 1527, 1511, 1478, 1430, 1404, 1321, 1251, 1203, 1185, 1089, 1056, 1010, 835, 757, 742; $^1$H NMR (DMSO-$d_6$, $\delta$, ppm): 5.91 (s, 1H, CH), 7.30 (d, $J = 8.8$ Hz, 2H, ArH), 7.37–7.40 (m, 4H, ArH), 7.46–7.50 (m, 2H, ArH), 7.64–7.68 (m, 1H, ArH), 7.73 (d, $J = 8.8$ Hz, 2H, ArH), 7.88 (d, $J = 7.6$ Hz, 1H, ArH), 7.91–7.98 (m, 2H, ArH), 8.39 (d, $J = 7.2$ Hz, 1H, ArH), 10.18 (s, 1H, NH).

**3b**: mp >300°C (lit.[8a], 409–410°C). IR (KBr, $\nu$, $cm^{-1}$): 3297, 3056, 1673, 1622, 1589, 1569, 1528, 1509, 1474, 1407, 1254, 1206, 1049, 760, 701; $^1$H NMR (DMSO-$d_6$, $\delta$, ppm): 6.21 (s, 1H, CH), 7.06–7.16 (m, 2H, ArH), 7.31 (dd, $J = 7.6$ Hz, $J' = 1.2$ Hz, 1H, ArH), 7.35–7.52 (m, 5H, ArH), 7.64–7.68 (m, 1H, ArH), 7.72 (d, $J = 8.8$ Hz, 1H, ArH), 7.85 (d, $J = 8.0$ Hz, 1H, ArH), 7.89 (d, $J = 8.8$ Hz, 1H, ArH), 8.18 (d, $J = 8.0$ Hz, 1H, ArH), 8.43 (d, $J = 8.0$ Hz, 1H, ArH), 10.18 (s, 1H, NH).

**3c**: mp >300°C. IR (KBr, $\nu$, $cm^{-1}$): 3305, 3065, 1656, 1620, 1589, 1510, 1475, 1430, 1405, 1251, 1205, 1184, 1055, 815, 754, 741, 709; $^1$H NMR

(DMSO-$d_6$, $\delta$, ppm): 5.96 (s, 1H, CH), 7.14 (d, $J = 8.8$ Hz, 1H, ArH), 7.22 (t, $J = 7.6$ Hz, 1H, ArH), 7.29 (d, $J = 7.6$ Hz, 1H, ArH), 7.38–7.41 (m, 3H, ArH), 7.46–7.51 (m, 2H, ArH), 7.64–7.68 (m, 1H, ArH), 7.74 (d, $J = 8.8$ Hz, 1H, ArH), 7.89 (d, $J = 8.0$ Hz, 1H, ArH), 7.94 (d, $J = 8.4$ Hz, 1H, ArH), 8.00 (d, $J = 8.4$ Hz, 1H, ArH), 8.39 (d, $J = 8.0$ Hz, 1H, ArH), 8.20 (s, 1H, NH). Anal. calcd. for $C_{26}H_{16}ClNO_2$: C, 76.19; H, 3.93; N, 3.42; found C, 76.28; H, 3.91; N, 3.49.

**3d**: mp >300°C. IR (KBr, $\nu$, $cm^{-1}$): 3310, 3055, 1659, 1621, 1588, 1569, 1527, 1510, 1477, 1430, 1404, 1321, 1250, 1204, 1187, 1089, 1053, 1015, 918, 834, 813, 782, 756, 711, 697; $^1$H NMR (DMSO-$d_6$, $\delta$, ppm): 5.93 (s, 1H, CH), 7.24 (d, $J = 8.4$ Hz, 2H, ArH), 7.36 (d, $J = 8.4$ Hz, 2H, ArH), 7.39 (d, $J = 8.0$ Hz, 2H, ArH), 7.48 (t, $J = 7.6$ Hz, 2H, ArH), 7.64–7.68 (m, 1H, ArH), 7.73 (d, $J = 8.8$ Hz, 1H, ArH), 7.88 (d, $J = 8.0$ Hz, 1H, ArH), 7.92 (d, $J = 8.8$ Hz, 1H, ArH), 7.97 (d, $J = 8.8$ Hz, 1H, ArH), 8.39 (d, $J = 7.6$ Hz, 1H, ArH), 10.18 (s, 1H, NH). Anal. calcd. for $C_{26}H_{16}ClNO_2$: C, 76.19; H, 3.93; N, 3.42; found C, 76.31; H, 3.87; N, 3.56.

**3e**: mp >300°C. IR (KBr, $\nu$, $cm^{-1}$): 3297, 3052, 1656, 1618, 1589, 1529, 1474, 1407, 1320, 1252, 1205, 1107, 1046, 863, 818, 758, 741; $^1$H NMR (DMSO-$d_6$, $\delta$, ppm): 6.20 (s, 1H, CH), 7.23 (dd, $J = 8.4$ Hz, $J' = 2.4$ Hz, 1H, ArH), 7.37–7.52 (m, 6H, ArH), 7.65–7.69 (m, 1H, ArH), 7.72 (d, $J = 8.8$ Hz, 1H, ArH), 7.87 (d, $J = 8.0$ Hz, 1H, ArH), 7.91 (d, $J = 8.8$ Hz, 1H, ArH), 8.10 (d, $J = 8.4$ Hz, 1H, ArH), 8.43 (d, $J = 8.0$ Hz, 1H, ArH), 10.21 (s, 1H, NH). Anal. calcd. for $C_{26}H_{15}Cl_2NO_2$: C, 70.28; H, 3.40; N, 3.15; found C, 70.42; H, 3.47; N, 3.28.

**3f:** mp >300°C. IR (KBr, $\nu$, $cm^{-1}$): 3300, 3067, 1657, 1621, 1588, 1528, 1512, 1476, 1404, 1251, 1206, 1059, 1031, 815, 754, 741, 708; $^1$H NMR (DMSO-$d_6$, $\delta$, ppm): 5.97 (s, 1H, CH), 7.26 (dd, $J = 8.4$ Hz, $J' = 1.6$ Hz, 1H, ArH), 7.39–7.50 (m, 5H, ArH), 7.61 (d, $J = 1.6$ Hz, 1H, ArH), 7.65–7.69 (m, 1H, ArH), 7.74 (d, $J = 8.4$ Hz, 1H, ArH), 7.89 (d, $J = 8.4$ Hz, 1H, ArH), 7.95 (d, $J = 8.4$ Hz, 1H, ArH), 7.99 (d, $J = 8.4$ Hz, 1H, ArH), 8.40 (d, $J = 8.0$ Hz, 1H, ArH), 10.23 (s, 1H, NH). Anal. calcd. for $C_{26}H_{15}Cl_2NO_2$: C, 70.28; H, 3.40; N, 3.15; found C, 70.33; H, 3.54; N, 3.18.

**3g**: mp >300°C. IR (KBr, $\nu$, $cm^{-1}$): 3300 (b), 1656, 1620, 1589, 1528, 1510, 1476, 1405, 1252, 1214, 1101, 1056, 1006, 836, 819, 755; $^1$H NMR (DMSO-$d_6$, $\delta$, ppm): 5.80 (s, 1H, CH), 6.55 (d, $J = 8.4$ Hz, 2H, ArH), 7.12 (d, $J = 8.4$ Hz, 2H, ArH), 7.35–7.39 (m, 2H, ArH), 7.45–7.49 (m, 2H, ArH), 7.63–7.66 (m, 1H, ArH), 7.70 (d, $J = 8.4$ Hz, 1H, ArH), 7.85–7.90 (m, 2H, ArH), 7.99 (d, $J = 8.0$ Hz, 1H, ArH), 8.38 (d, $J = 8.0$ Hz, 1H, ArH), 9.20 (b, 1H, OH), 10.08 (s, 1H, OH). Anal. calcd. for $C_{26}H_{17}NO_3$: C, 79.78; H, 4.38; N, 3.58; found C, 79.65; H, 4.44; N, 3.62.

**3h**: mp >300°C. IR (KBr, $\nu$, $cm^{-1}$): 3308, 3066, 2885, 1667, 1615, 1589, 1526, 1478, 1431, 1405, 1357, 1254, 1201, 1185, 1162, 1112, 1054, 947,

813, 782, 763, 744, 722; $^1$H NMR (DMSO-$d_6$, $\delta$, ppm): 2.74 (s, 6H, 2NCH$_3$), 5.77 (s, 1H, CH), 6.52 (d, $J = 8.8$ Hz, 2H, ArH), 7.13 (d, $J = 8.8$ Hz, 2H, ArH), 7.35–7.39 (m, 2H, ArH), 7.45–7.49 (m, 2H, ArH), 7.62–7.66 (m, 1H, ArH), 7.70 (d, $J = 8.8$ Hz, 1H, ArH), 7.84–7.89 (m, 2H, ArH), 8.00 (d, $J = 8.4$ Hz, 1H, ArH), 8.37 (d, $J = 8.0$ Hz, 1H, ArH), 10.07 (s, 1H, NH). Anal. calcd. for $C_{28}H_{22}N_2O_2$: C, 80.36; H, 5.30; N, 6.69; found C, 80.52; H, 5.40; N, 6.64.

**3i**: mp >300°C. IR (KBr, $\nu$, cm$^{-1}$): 3290, 3059, 1693, 1657, 1636, 1590, 1531, 1410, 1386, 1354, 1251, 1204, 1099, 1046, 1002, 827, 810, 756, 745, 716; $^1$H NMR (DMSO-$d_6$, $\delta$, ppm): 6.74 (s, 1H, CH), 7.21 (dd, $J = 7.6$ Hz, $J' = 1.2$ Hz, 1H, ArH), 7.30–7.50 (m, 7H, ArH), 7.63–7.67 (m, 1H, ArH), 7.78 (d, $J = 8.8$ Hz, 1H, ArH), 7.88–7.91 (m, 1H, ArH), 7.99(d, $J = 8.8$ Hz, 1H, ArH), 8.41 (d, $J = 8.0$ Hz, 1H, ArH), 8.49 (d, $J = 8.8$ Hz, 1H, ArH), 10.24 (s, 1H, NH). Anal. calcd. for $C_{26}H_{16}N_2O_4$: C, 74.28; H, 3.84; N, 6.66; found C, 74.13; H, 3.91; N, 6.70.

**3j**: mp >300°C (lit.[8a], 373–375°C). IR (KBr, $\nu$, cm$^{-1}$): 3302, 3052, 1658, 1621, 1589, 1538, 1476, 1428, 1405, 1321, 1301, 1251, 1207, 1178, 1108, 1057, 1031, 833, 814, 743; $^1$H NMR (DMSO-$d_6$, $\delta$, ppm): 3.61 (s, 3H, CH$_3$O), 5.85 (s, 1H, CH), 6.73 (d, $J = 8.8$ Hz, 2H, ArH), 7.24 (d, $J = 8.8$ Hz, 2H, ArH), 7.36–7.39 (m, 2H, ArH), 7.45–7.49 (m, 2H, ArH), 7.63–7.67 (m, 1H, ArH), 7.71 (d, $J = 8.0$ Hz, 1H, ArH), 7.86 (d, $J = 8.4$ Hz, 1H, ArH), 7.89 (d, $J = 8.0$ Hz, 1H, ArH), 8.00 (d, $J = 8.4$ Hz, 1H, ArH), 8.38 (d, $J = 8.0$ Hz, 1H, ArH), 10.12 (s, 1H, NH).

**3k**: mp >300°C. IR (KBr, $\nu$, cm$^{-1}$): 3304, 3050, 2916, 1659, 1621, 1588, 1527, 1510, 1474, 1404, 1319, 1252, 1211, 1183, 1057, 817, 759, 740, 723; $^{11}$H NMR (DMSO-$d_6$, $\delta$, ppm): 2.04 (s, 3H, CH$_3$), 2.06 (s, 3H, CH$_3$), 5.83 (s, 1H, CH), 6.92 (d, $J = 8.0$ Hz, 1H, ArH), 7.03 (d, $J = 8.0$ Hz, 1H, ArH), 7.10 (s, 1H, ArH), 7.38 (d, $J = 8.0$ Hz, 2H, ArH), 7.45–7.49 (m, 2H, ArH), 7.62–7.66 (m, 1H, ArH), 7.72 (d, $J = 8.8$ Hz, 1H, ArH), 7.86 (d, $J = 8.4$ Hz, 1H, ArH), 7.90 (d, $J = 8.8$ Hz, 1H, ArH), 7.99 (d, $J = 8.8$ Hz, 1H, ArH), 8.38 (d, $J = 8.0$ Hz, 1H, ArH), 10.12 (s, 1H, NH). Anal. calcd. for $C_{28}H_{21}NO_2$: C, 83.35; H, 5.25; N, 3.47; found C, 83.19; H, 5.31; N, 3.56.

**3l**: mp >300°C. IR (KBr, $\nu$, cm$^{-1}$): 3312, 2927, 2833, 1657, 1636, 1622, 1589, 1528, 1477, 1406, 1265, 1252, 1185, 1137, 1058, 1026, 820, 807, 757, 742; $^1$H NMR (DMSO-$d_6$, $\delta$, ppm): 3.59 (s, 3H, CH$_3$O), 3.65 (s, 3H, CH$_3$O), 5.87 (s, 1H, CH), 6.66 (d, $J = 8.4$ Hz, 1H, ArH), 6.72 (d, $J = 8.4$ Hz, 1H, ArH), 7.08 (d, $J = 1.2$ Hz, 1H, ArH), 7.36–7.40 (m, 2H, ArH), 7.45–7.50 (m, 2H, ArH), 7.65 (t, $J = 8.0$ Hz, 1H, ArH), 7.72 (d, $J = 8.8$ Hz, 1H, ArH), 7.87 (d, $J = 8.0$ Hz, 1H, ArH), 7.90 (d, $J = 8.8$ Hz, 1H, ArH), 8.03 (d, $J = 8.4$ Hz, 1H, ArH), 8.38 (d, $J = 8.0$ Hz, 1H, ArH), 10.14 (s, 1H, NH). Anal. calcd. for $C_{28}H_{21}NO_4$: C, 77.23; H, 4.86; N, 3.22; found C, 77.16; H, 4.92; N, 3.40.

**3n**: mp >300°C. IR (KBr, $\nu$, $cm^{-1}$): 3312, 2928, 1656, 1618, 1590, 1528, 1476, 1448, 1430, 1407, 1382, 1281, 1253, 1225, 1183, 1146, 1125, 1103, 1055, 1033, 1007, 823, 759, 749, 706; $^1$H NMR (DMSO-$d_6$, $\delta$, ppm): 3.66 (s, 3H, $CH_3$), 5.82 (s, 1H, CH), 6.51–6.54 (m, 2H, ArH), 7.03 (s, 1H, ArH), 7.36–7.39 (m, 2H, ArH), 7.44–7.48 (m, 2H, ArH), 7.62–7.66 (m, 1H, ArH), 7.71 (d, $J = 8.8$ Hz, 1H, ArH), 7.87 (d, $J = 8.0$ Hz, 1H, ArH), 7.89 (d, $J = 8.8$ Hz, 1H, ArH), 8.03 (d, $J = 8.4$ Hz, 1H, ArH), 8.37 (d, $J = 8.0$ Hz, 1H, ArH), 8.78 (b, 1H, OH), 10.12 (s, 1H, NH). Anal. calcd. for $C_{27}H_{19}NO_4$: C, 76.95; H, 4.54; N, 3.32; found C, 77.05; H, 4.61; N, 3.37.



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## REFERENCES

1. Arcadi, A.; Chiarini, M.; Giuseppe, S. D.; Marinelli, F. A new green approach to the Friedlaender synthesis of quinolines. *Synlett.* **2003**, 203.
2. Hajela, K.; Kapil, R. S. Synthesis and post-coital contraceptive activity of a new series of substituted 2,3-diaryl-2H-1-benzopyrans. *Euro. J. Med. Chem.* **1997**, *32*, 135.
3. (a) Horino, H.; Mimura, T.; Kagechika, K.; Ohta, M.; Kubo, H.; Kitagawa, M. Synthesis and antihypertensive activity of 4-(diazabicyclo[4.1.0]heptenyloxy) benzopyran derivatives and their analogs. *Chem. Pharm. Bull.* **1998**, *46*, 602; (b) Mannhold, R.; Cruciani, G.; Weber, H.; Lemoine, H.; Derix, A.; Weichel, C.; Clementi, M. 6-Substituted benzopyrans as potassium channel activators: synthesis, vasodilator properties, and multivariate analysis. *J. Med. Chem.* **1999**, *42*, 981; (c) Rovnyak, G. C.; Ahmed, S. Z.; Baird, A. J.; Ding, C. Z.; Dzwonczyk, S.; Ferrata, F. N.; Humphreys, W. G. Cardioselective antiischemic ATP-sensitive Potassium channel ($K_{ATP}$) openers. 5. Identification of 4-(*N*-aryl)-substituted benzopyran derivatives with high selectivity. *J. Med. Chem.* **1997**, *40*, 24.
4. Sun, H. B.; Chen, W. Y.; Peng, S. X.; Wang, T.; Liu, G. Q. Study on Potassium channel openers (I): Synthesis and cardiovascular activity of substituted trans-4-amino-3,4-dihydro-2,2-dimethyl-2*H*-1- benzopyran-3-ol. *Gaodeng Xuexiao Huaxue Xuebao* **1997**, *18*, 730.
5. Kossakowski, J.; Jerzy, Z. T.; Suski, S. Synthesis of aminopropanol derivatives of 7-ethoxyl-8-hydroxy- and 6,7-diethoxyl-8-hydroxy-2*H*-1-benzopyran-2-one with an expected $\beta$–adrenolytic activity. *Acta Poloniae Pharmaceutica* **1998**, *55*, 77.
6. El-Shaaer, H. M.; Foltinova, P.; Lacova, M.; Chovancova, J.; Stankovicova, H. Synthesis, antimicrobial activity and bleaching effect of some reaction products of 4-oxo-4H-benzopyran-3-carboxaldehydes with aminobenzothiazoles and hydrazides. *Farmaco* **1998**, *53*, 224.
7. Johnson, A. T.; Wang, L.; Standeven, A. M.; Escobar, M.; Chandraratna, R. A. S. Synthesis and biological activity of high-affinity retinoic acid receptor antagonists. *Bioorg. Med. Chem* **1999**, *7*, 1321.

8. (a) Martinez, R.; Cortes, E.; Toscano, R. A.; Alfaro, L. J. Reaction of $\beta$-arylidennaphthylamines with 4-hydroxycoumarin: A correction in structural assignment of the product, III. *J. Heterocycl. Chem.* **1990**, *27*, 1273; (b) Bandyopadhyay, C.; Ranabir, S. K.; Partra, R.; Banerjee, S. One-pot synthesis of 2-alkyl/arylamino-4-oxo-4*H*-1-benzopyran-3-carboxaldehyde from 4-oxo-4*H*-1- benzopyran-3-carboxaldehyde. *J. Chem. Res.* **2003** (8), 459; (c) Hafez, E. B. A.; Elnagdi, M. H.; Elagamey, A. G. A.; El-Taweel, F. M. A. A. Nitriles in heterocyclic synthesis: novel synthesis of benzo[*c*]coumarin and of benzo[*c*]pyrano[3,2-*c*]quinoline derivatives. *Heterocycles* **1987**, *26*, 903.
9. (a) Breslow, R.; Rideout, D. C. Hydrophobic acceleration of Diels–Alder reactions. *J. Am. Chem. Soc.* **1980**, *102*, 7816; (b) Breslow, R. Hydrophobic effects on simple organic reactions in water. *Acc. Chem. Res.* **1991**, *24*, 159.
10. (a) Breslow, R.; Maitra, U.; Rideout, D. C. Selective Diels–Alder reactions in aqueous solutions and suspensions. *Tetrahedron Lett.* **1983**, *24*, 1901; (b) Breslow, R.; Maitra, U. On the origin of product selectivity in aqueous Diels–Alder reactions. *Tetrahedron Lett.* **1984**, *25*, 1239.
11. (a) Ponaras, A. A. A new variant of the Claisen rearrangement capable of creating the bond between two quaternary centers. *J. Org. Chem* **1983**, *48*, 3866; (b) Coates, R. M.; Rogers, B. D.; Hobbs, S. J.; Peck, D. R.; Curran, D. P. Synthesis and Claisen rearrangement of alkoxyallyl enol ethers: Evidence for a dipolar transition state. *J. Am. Chem. Soc.* **1987**, *109*, 1160.
12. (a) Mattes, H.; Benezra, C. Reformatsky-type reactions in aqueous media use of bromomethyl-acrylic acid for the synthesis of $\alpha$-methylene-$\gamma$-butyrolactones. *Tetrahedron Lett.* **1985**, *26*, 5697; (b) Zhou, J. Y.; Lu, G. D.; Wu, S. H. A new approach for the synthesis of $\alpha$-methylene-$\gamma$-butyrolactones from $\alpha$-bromomethylacrylic acid (or esters). *Synth. Commun.* **1992**, *22*, 481.
13. Delair, P.; Luche, J. L. A new sonochemical carbonyl cross-coupling reaction. *J. Chem. Soc. Chem. Commun.* **1989**, 398.
14. (a) Wang, X. S.; Shi, D. Q.; Li, Y. L.; Chen, H.; Wei, X. Y.; Zong, Z. M. A clean synthesis of 1-oxo-hexahydroxanthene derivatives in aqueous media catalyzed by TEBA. *Synth. Commun.* **2005**, *35*, 97; (b) Wang, J.; Shi, D. Q.; Zhuang, Q. Y.; Wang, X. S.; Hu, H. W. Synthesis of 4*H*,5*H*-pyrano[3,2-*c*][1]benzopyran-5-ones in aqueous media. *J. Chem. Res. Synop.* **2004**, 818; (c) Wang, X. S.; Shi, D. Q.; Zhang, Y. F.; Wang, S. H.; Tu, S. J. Synthesis of 9-arylpolyhydroacridine in water catalyzed by triethylbenzylammonium chloride (TEBA). *Chin. J. Org. Chem.* **2004**, *24*, 430.