JOC*Note*

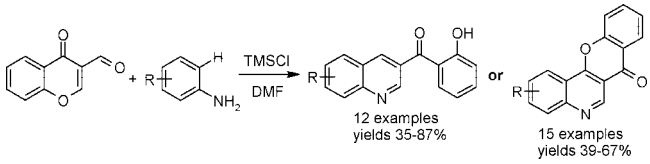
Synthesis of Quinolines from 3-Formylchromone

Andrey S. Plaskon,[†,‡] Sergey V. Ryabukhin,*[,†,‡] Dmitriy M. Volochnyuk,[†,§] Konstantin S. Gavrilenko,[†,‡] Alexander N. Shivanyuk,[†,‡] and Andrey A. Tolmachev[‡]

Enamine Ltd., 23 A. Matrosova st., Kyiv 01103, Ukraine, National Taras Shevchenko University, 62 Volodymyrska st., Kyiv 01033, Ukraine, and Institute of Organic Chemistry, National Academy of Sciences of Ukraine, 5 Murmanska st., Kyiv 02094, Ukraine

ryabukhin@mail.enamine.net

Received May 2, 2008



A facile and versatile procedure for the synthesis of 3-(2-hydroxybenzoyl)quinolines and 7*H*-chromeno[3,2-*c*]quinolin-7-ones was elaborated on the basis of TMSCl-mediated recyclization of 3-formylchromone with various anilines. Limitations and scope of this methodology were established, and a possible mechanism for the heterocyclizations was proposed.

The functionalized quinolines are attractive compounds for drug discovery since many of them have been shown to exhibit excellent biological activities.[1] Therefore, the development of facile methodologies for the synthesis of highly functionalized quinoline derivatives represents a challenge in medicinal chemistry.[2,3] For example oxoindeno[1,2-*b*]quinolines have shown strong binding to DNA and efficient inhibition DNA topoisomerase 1 that were associated with their well pronounced anticancer activities.[4] 3-Benzoylquinolines[5,6] are inhibitors of HIV-1 replication[7a] and cathepsin D[7b] and possess antianaphylactic activity.[7c] The Combes synthesis is one of the most efficient approaches to the quinolines. It occurs through condensation of 1,3-dicarbonyl compounds with primary anilines followed by acid-catalyzed ring closure of the intermediate Schiff bases.[8–11] 3-Fomylchromone **1** is a latent 1,3-dialdehyde bearing a masked 2-hydroxybenzoyl fragment at the *meso*-position.[12,13] Recently we have shown that the recyclization and [3 + 3] cyclocondensation of 3-formylchromones with CH-active compounds such as cyanoacetamides,[14a] amino heterocycles,[5a] and benzimidazoles[14b] readily gives functionally diverse sub-

[†] Enamine Ltd.
[‡] National Taras Shevchenko University.
[§] National Academy of Sciences of Ukraine.

(1) (a) Balasubramanian, M.; Keay, J. G. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., ; Rees, C. W., ; Scriven, E. F. V., Eds.; Pergamon Press: Oxford, 1996; Vol. 5, pp 245−300. (b) Catoen-Chackal, S.; Facompre, M.; Houssin, R.; Pommery, N.; Goossens, J.-F.; Colson, P.; Bailly, C.; Henichart, J.-P. *J. Med. Chem.* **2004**, *47*, 3665–3673. (c) Vazquez, M. T.; Romero, M.; Pujol, M. D. *Bioorg. Med. Chem.* **2004**, *12*, 949–956. (d) Chen, Y.-L.; Chen, I.-L.; Lu, C.-M.; Tzeng, C.-C.; Tsao, L.-T.; Wang, J.-P. *Bioorg. Med. Chem.* **2004**, *12*, 387–392. (e) Chen, Y. J.; Fang, K. C.; Sheu, J.-Y.; Hsu, S. L.; Tzeng, C. C. *J. Med. Chem.* **2001**, *44*, 2374–2377.

(2) (a) Gilchrist, T. L. *Heterocyclic Chemistry*, 3rd ed.; Adison-Wesley Longman: Essex, 1997; pp 158−164. (b) Jones, G. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R.; Rees, A. R., Eds.; Pergamon: Oxford, 1984; Vol. 2, p 395. (c) Jones, G. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon Press: Oxford, 1996; Vol. 5, pp 167−243.

(3) (a) Kouznetsov, V. V.; Vargaz Mendez, L. Y.; Melendez Gomez, C. M. *Curr. Org. Chem.* **2005**, *9*, 141–161. (b) Ishkawa, T.; Manabe, S.; Aikawa, T.; Kudo, T.; Saito, S. *Org. Lett.* **2004**, *6*, 2361–2364. (c) Sangu, K.; Fuchibe, K.; Akiyama, T. *Org. Lett.* **2004**, *6*, 353–355. (d) Kobayashi, K.; Yoneda, K.; Miyamoto, K.; Morikawa, O.; Konishi, H. *Tetrahedron* **2004**, *60*, 11639–11645. (e) Wang, J.; Fan, X.; Zhang, X.; Han, L. *Can. J. Chem.* **2004**, *82*, 1192–1196. (f) Palimkar, S. S.; Siddiqui, S. A.; Daniel, T.; Lahoti, R. J.; Srinivasan, K. V. *J. Org. Chem.* **2003**, *68*, 9371–9378. (g) Du, W.; Curran, D. P. *Org. Lett.* **2003**, *5*, 1765–1768. (h) Jiang, B.; Yui-Gui, S. *J. Org. Chem.* **2002**, *67*, 9449–9451. (i) Amii, H.; Kishikawa, Y.; Uneyama, K. *Org. Lett.* **2001**, *3*, 1109–1112.

(4) (a) Deady, L. W.; Desneves, J.; Kaye, A. J.; Finlay, G. J.; Baguley, B. C.; Denny, W. A. *Bioorg. Med. Chem.* **2001**, *9*, 445–452. (b) Chen, J.; Deady, L. W.; Desneves, J.; Kaye, A. J.; Finlay, G. J.; Baguley, B. C.; Denny, W. A. *Bioorg. Med. Chem.* **2000**, *8*, 2461–2466. (c) Deady, L. W.; Desneves, J.; Kaye, A. J.; Finlay, G. J.; Baguley, B. C.; Denny, W. A. *Bioorg. Med. Chem.* **2000**, *8*, 977–984. (d) Deady, L. W.; Kaye, A. J.; Finlay, G. J.; Baguley, B. C.; Denny, W. A. *J. Med. Chem.* **1997**, *40*, 2040–2046.

(5) For the synthesis of 3-(2-hydroxybenzoyl)quinoline, see:(a) Ryabukhin, S. V.; Plaskon, A. S.; Volochnyuk, D. M.; Tolmachev, A. A. *Synthesis* **2007**, 1861–1871. (b) Basavaiah, D.; Reddy, R. J.; Rao, J. S. *Tetrahedron Lett.* **2006**, *47*, 73–77.

(6) For recent syntheses of 3-benzoylquinoline derivatives, see:(a) Yoon, K.; Ha, S. M.; Kim, K. *J. Org. Chem.* **2005**, *70*, 5741–5744. (b) Patteux, C.; Levacher, V.; Dupas, G. *Org. Lett.* **2003**, *5*, 3061–3063. (c) Mahata, P. K.; Venkatesh, C.; Syam Kumar, U. K.; Ila, H.; Junjappa, H. *J. Org. Chem.* **2003**, *68*, 3966–3975. (d) Singh, G.; Singh, L.; Ishar, M. P. S. *Tetrahedron* **2002**, *58*, 7883–7890. (e) Singh, G.; Singh, R.; Girdhar, N. K.; Ishar, M. P. S. *Tetrahedron* **2002**, *58*, 2471–2480. (f) Harrowven, D. C.; Sutton, B. J.; Coulton, S. *Tetrahedron Lett.* **2001**, *42*, 2907–2910. (g) Ishar, M. P. S.; Kumar, K.; Singh, R. *Tetrahedron Lett.* **1998**, *39*, 6547–6550.

(7) (a) Normand-Bayle, M.; Benard, C.; Zouhiri, F.; Mouscadet, J.-F.; Leh, H.; Thomas, C.-M.; Mbemba, G.; Desmaele, D.; d'Angelo, J. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 4019–4022. (b) Whitesitt, C. A.; Simon, R. L.; Reel, J. K.; Sigmund, S. K.; Phillips, M. L.; Shadle, J. K.; Heinz, L. J.; Koppel, G. A.; Hunden, D. C.; Lifer, S. L.; Berry, D.; Ray, J.; Little, S. P.; Liu, X.; Marshall, W. S.; Panetta, J. A. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 2157–2162. (c) Evans, D.; Cracknell, M. E.; Saunders, J. C.; Smith, C. E.; Williamson, W. R. N.; Dawson, W.; Sweatman, W. J. F. *J. Med. Chem.* **1987**, *30*, 1321–1327.

(8) (a) Combes, A. *Bull. Soc. Chim. Fr.* **1888**, *49*, 89. (b) Bergstrom, F. W. *Chem. Rev.* **1944**, *35*, 77–277.

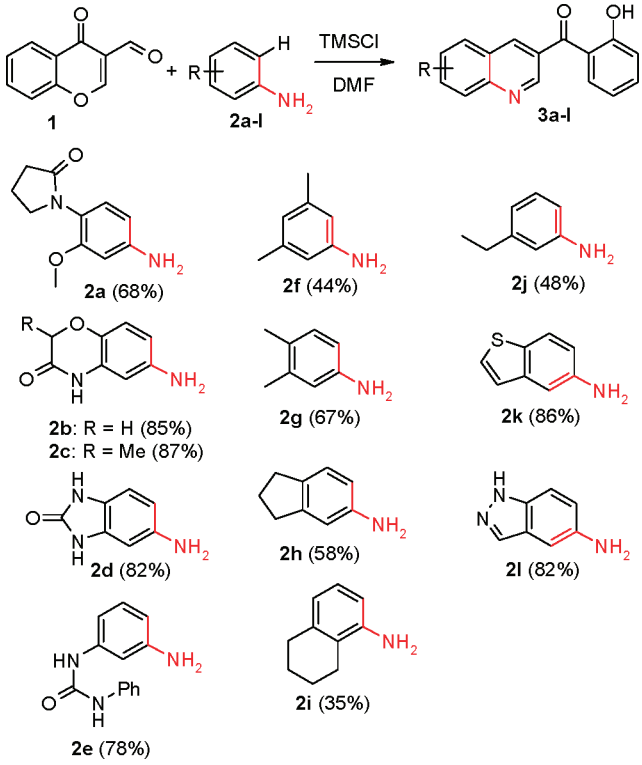
(9) For using 1,3-dialdehydes in Combes synthesis, see:(a) Gaillard, S.; Papamicael, C.; Marsais, F.; Dupas, G.; Levacher, V. *Synlett* **2005**, 441–444. (b) Nair, J. S.; Rajasekharan, K. N. *Indian J. Chem. Sect. B* **2004**, *43*, 1944–1949. (c) Takeuchi, I.; Ushida, M.; Hamada, Y.; Yuzuri, T.; Suezawa, H.; Hirota, M. *Heterocycles* **1995**, *41*, 2221–2231. (d) Magnus, P. D.; Iliadis, T.; Eisenbeis, S. A.; Fairhurst, R. A. U.S. Patent 5442065, 1995; *Chem. Abstr. 123*, 313637. (e) Sequeria, S.; Seshadri, S. *Indian J. Chem. Sect. B* **1987**, *26*, 436–439.

(10) For using 1,3-ketoaldehydes in Combes synthesis, see:(a) Sharma, K. S.; Singh, S. P.; Kumari, S. *Indian J. Chem. Sect. B* **1994**, *33*, 1191–1192. (b) Acheson, R. M.; Birtwistle, D. H.; Constable, E. C.; Tester, G. G.; Whitehead, J. W. F.; Wyatt, P. B. *J. Chem. Res. Synop.* **1986**, 269. (c) Kessar, S. V.; Singh, I.; Kumar, A. *Tetrahedron Lett.* **1965**, *7*, 2207–2209.

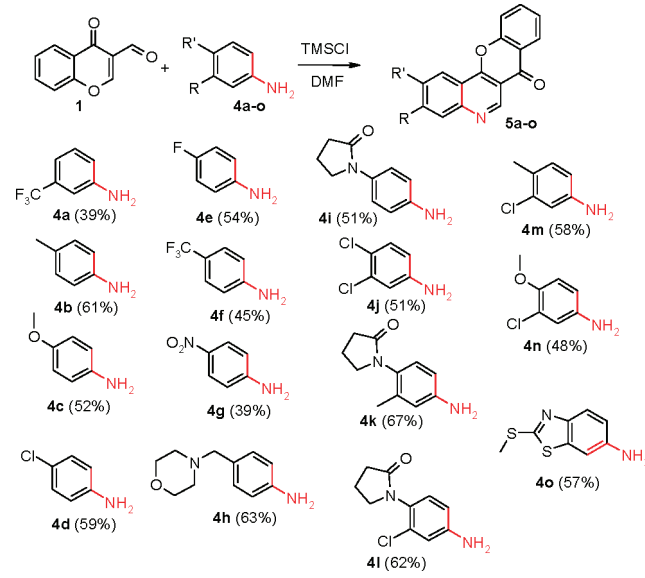
(11) For using 1,3-diketones in Combes synthesis, see:(a) Hungarian Patent Appl. HU 200401607, 2006; *Chem. Abstr.* **2007**, *147*, 385856. (b) Yamashkin, S. A.; Oreshkina, E. A.; Romanova, I. S.; Yurovskaya, M. A. *Chem. Heterocycl. Compd. (Engl.Transl.)* **2005**, *41*, 1280–1289. (c) Boltacheva, N. S.; Filyakova, V. I.; Charushin, V. N. *Russ. J. Org. Chem.* **2005**, *41*, 1452–1457. (d) Singh, B. K. N.; Fernandes, P. S. *Indian J. Heterocycl. Chem.* **2003**, *13*, 19–24. (e) Volochnyuk, D. M.; Pushecnikov, A. O.; Krotko, D. G.; Sibgatulin, D. A.; Kovaleva, S. A.; Tolmachev, A. A. *Synthesis* **2003**, 1531–1540. (f) Karpenko, N. S.; Filyakova, V. I.; Matochkina, E. G.; Kodess, M. I.; Pashkevich, K. I. *Russ. Chem. Bull.* **2003**, *52*, 1215–1216. (g) Aly, A. A. *Tetrahedron* **2003**, *59*, 1739–1747. (h) Sanna, P.; Carta, A.; Paglietti, G. *Heterocycles* **1999**, *51*, 2171–2181. (i) El ouar, M.; Knouzi, N.; El kihel, A.; Essassi, E. M.; Benchidmi, M.; Hamelin, J.; Carrier, R.; Danion-Bougot, R. *Synth. Commun.* **1995**, *25*, 1601–1604.

10.1021/jo800950y CCC: $40.75
Published on Web 07/02/2008

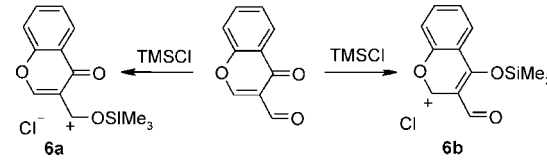
SCHEME 1



SCHEME 2



SCHEME 3



stituted pyridines. The present study was undertaken in order to develop a facile method for the synthesis of 3-(2-hydroxybenzoyl)quinolines through the coupling of 3-formylchromone **1** with anilines.

On the basis of our previous studies,[5a,14] we considered TMSCl as a potential promoter and water scavenger for the reaction of 3-formylchromone with anilines unsubstituted at the *ortho*-position that might result in various *o*-hydroxybenzoyl quinolines. The present research was undertaken in order to determine limitation and establish the scope of this reaction with various substituted anilines. The reaction of substituted anilines **2a**−**l** with 3-formylchromone gave quinolines **3a**−**l** in 35−87% yield. (Scheme 1). It seems likely that the reactivity of the *ortho*-position in substituted anilines is influenced by +M and sterical effect of the functional groups in *meta*- and *para*-positions. This indicates that on the first bimolecular step of the reaction anilines **2** react as C-nucleophiles. The reactions of the *ortho*-substituted anilines with formylchromone resulted in multicomponent mixtures, which according to LCMS contain less than 20% of the corresponding quinolines **3**.

Surprisingly, the reactions of anilines **4a**−**i** with 3-formylchromone (TMSCl, DMF) led to 7*H*-chromeno[3,2-*c*]quinolin-7-ones[15] **5a**−**i** (Scheme 2) in 39−63% yield. No quinolines of type **3** were detected in the reaction mixtures by LCMS. The fact that the substituents in molecules **4** withdraw electrons from the *ortho*-positions to the amino group or increase the electron density on the nitrogen atom indicate that anilines **4** react as N-nucleophiles. The reaction of 3-chloroaniline with 3-formylchromone gave a multicomponent mixture containing the corresponding compounds **3** (33%) and **5** (14%) and three unidentified products. 3,4-Dichloroaniline **4j** whose C-nucleophilicity is decreased by the presence of a chlorine atom at the *meta*-position to the amino group reacted with **1** to give chromenoquinolin-7-one **5j** in 51% yield.

TMSCl can activate 3-formylchromone **1** through addition to aldehyde or ketone C=O bonds to give intermediates **6a** and **6b**, respectively[16] (Scheme 3).

Apparently intermediate **6a** is more electrophilic and more reactive than resonance-stabilized *O*-trimethylsilyl-3-formylchromone chloride **6b**. Scheme 4 outlines possible mechanisms for the formation of quinolines **3** and **6** starting from activated 3-formylchromone **6a**. Amines **2** are likely to react with **6a** as C-nucleophiles to give intermediate **7**, which after activation of the keto group and double bond of chromone undergoes intramolecular N-arylation to give intermediate **8**. Elimination of HMDS from **8** can result in N-silylated quinolyl chromone **9**, which can be transformed into trimethylsiloxybenzoyl quino-

(12) Reviews:(a) Ghosh, C. K. *J. Heterocycl. Chem.* **1983**, *20*, 1437–1445. (b) Sabitha, G. *Aldrichimica Acta* **1996**, *29*, 15–25. (c) Ghosh, C. K. *Indian J. Chem. Sect. B* **1997**, *36*, 968–980. (d) Ghosh, C. K. *Heterocycles* **2004**, *63*, 2875–2898.

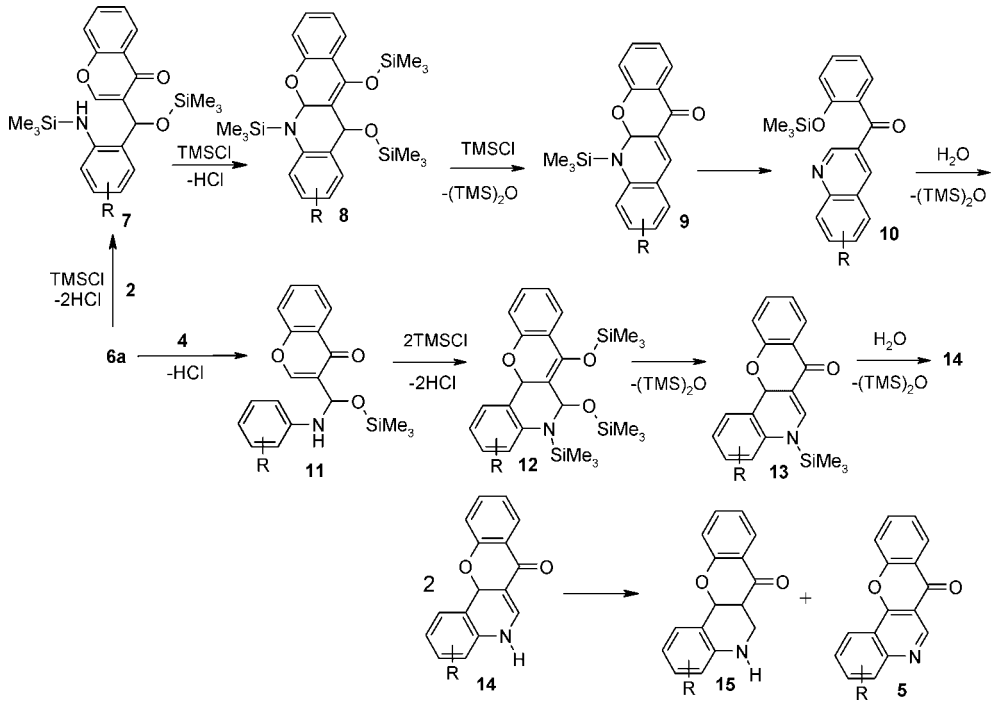
(13) Recent publications:(a) Chovancová, J.; Stankovièová, H.; Gáplovský, A.; Lácová, M.; Puchala, A. *J. Heterocycl. Chem.* **2006**, *43*, 843–848. (b) Ghosh, T.; Bandyopadhyay, C. *J. Heterocycl. Chem.* **2006**, *43*, 1431–1434. (c) Iaroshenko, V. O.; Groth, U.; Kryvokhyzha, N. V.; Obeid, S.; Tolmachev, A. A.; Wesch, T. *Synlett* **2008**, 343–346. (d) Figueiredo, A. G. P. R.; Tome, A. C.; Silva, A. M. S.; Cavaleiro, J. A. S. *Tetrahedron* **2007**, *63*, 910–917.

(14) (a) Ryabukhin, S. V.; Plaskon, A. S.; Volochnyuk, D. M.; Tolmachev, A. A. *Synlett* **2004**, 2287–2290. (b) Ryabukhin, S. V.; Plaskon, A. S.; Volochnyuk, D. M.; Tolmachev, A. A. *Synthesis* **2007**, 3155–3162. (c) Ryabukhin, S. V.; Plaskon, A. S.; Volochnyuk, D. M.; Pipko, S. E.; Tolmachev, A. A. *Heterocycles* **2008**, *75*, 583–597. (d) Plaskon, A. S.; Ryabukhin, S. V.; Volochnyuk, D. M.; Tolmachev, A. A. *Synthesis* **2008**, 1069–1077. (e) Plaskon, A. S.; Ryabukhin, S. V.; Volochnyuk, D. M.; Shivanyuk, A. N.; Tolmachev, A. A. *Tetrahedron* **2008**, *64*, 5933–5943.

(15) Some compounds of type **5** have been previously prepared via complicated multistep procedures: (a) Partridge, M. W.; Bloomfield, D. G.; Vipond, H. J. *J. Chem. Soc. C* **1970**, 2647–2653. (b) Khodair, A. I.; Abbasi, M. M. A.; Ibrahim, El-Sayed I.; Soliman, A. H.; ElAshry, El-Sayed H. *Heterocycl. Commun.* **1999**, *5*, 577–584.

(16) Iwasaki, H.; Kume, T.; Yamamoto, Y.; Akiba, K. *Heterocycles* **1988**, *27*, 1599–1602.

SCHEME 4



line **10** through intramolecular migration of the trimethylsilyl group from the nitrogen to oxygen atom and breaking the C−O bond.

The reaction of N-nucleophilic amine **4** with intermediate **6a** seems likely to give intermediate **11**, which after activation of the keto group and the adjacent double bond of chromone undergoes intramolecular cyclization through electrophilic substitution at the *ortho*-position to the aniline nitrogen atom. The intramolecular elimination of HMDS is likely to result in the silylated dihydroquinoline **13** intermediate, which can be transformed into compound **5** through the loss of hydride and hydrolysis. It seems plausible that the long distance between the silicon and oxygen atom at position 4 makes impossible the intramolecular migration of the trimethylsilyl group resulting in the opening of the pyrone ring. After quenching of the reaction mixture, dihydroquinoline **14** seems likely to disproportionate into final product **5** and tetrahydroquinoline **15**. Accordingly, the LCMS studies of the reaction mixtures revealed the presence of tetrahydroquinolines **15** as a byproduct of quinolines **5**. Unfortunately the preparative HPLC failed to isolate individual compounds **15**.

Similar considerations indicate that the reaction of intermediate **6b** with C-nucleophilic anilines **2** and N-nucleophilic anilines **4** should give quinolines **5** and **3**, respectively (see Scheme 1 in Supporting Information). This provides an additional argument in favor of the mechanism shown in Scheme 4.

The composition and structure of all the compounds obtained were determined by LC/MS, elemental analysis, and ^{1}H and ^{13}C NMR and IR spectroscopy. The signals in the ^{1}H and ^{13}C NMR spectra were assigned on the basis of 2D NMR techniques (COSY, NOESY, HMBC, HMQC) of representative compounds. The typical ^{1}H NMR spectrum of quinolines **3** contains a characteristic set of signals for the protons of *ortho*-acylated phenol ring, and two doublets ($^4J_{HH} \approx 2.0$ Hz) or broadened singlets for the protons of the pyridine fragment. The signal of the OH group appears in the range of 10.4−10.6 ppm (DMSO-d_6) and is deshielded as a result of the formation of the stable intramolecular bond to the adjacent carbonyl group. The typical ^{13}C NMR spectrum of quinolines **3** contains the signal of a carbonyl carbon atom at $\delta \approx 193.1-196.6$ ppm and a characteristic set of signals for the carbons of *ortho*-acylated phenol ring and for the carbons of the pyridine fragment. In the typical IR spectra of quinolines **3**, a wide absorption band at 3650−3300 cm^{-1} corresponding to valence vibrations of the hydroxyl group, and an intensive peak at 1622−1639 cm^{-1} corresponding to valence vibrations of carbonyl group is present. The ^{1}H NMR spectra of compounds **5** contains a set of signals for the *ortho*-substituted aryl ring of the chromone residue and a singlet for the methine proton of the quinoline fragment (9.3−9.6 ppm in DMSO-d_6 or 9.9−10.2 in CF_3COOD), whereas no signal was detected for the phenolic OH group. The ^{13}C NMR spectra of compounds **5** contains the signal of carbonyl carbon atom at $\delta \approx 175.5-175.8$ ppm (DMSO-d_6) or $\delta \approx 175.8-185.5$ ppm (CF_3COOD), a set of signals for the *ortho*-substituted aryl ring of the chromone residue, and a signal for the C-2 of the quinoline fragment (145.5−148.7 ppm in DMSO-d_6 or 145.2−148.1 in CF_3COOD).

The structure of compound **5k** was unambiguously determined by single crystal X-ray analysis[17] (see Figure 1, X-ray crystal structure determination, in Supporting Information). In the crystalline state plane molecules of **5k** are involved in stacking interactions to give infinite columns in the crystal.

In conclusion, we have elaborated efficient synthetic procedures for the preparation of functionalized quinolines from 3-formylchromone and substituted anilines using TMSCl as a promoter and water scavenger. The reaction of 3-formylchromone with C-nucleophilic anilines **2** or N-nucleophilic anilines **4** leads to 3-(2-hydroxybenzoyl)quinolines and 7*H*-chromeno[3,2-*c*]quinolin-7-ones, respectively. Apparently the

(17) Sheldrick, G. M. *SHELXTL PLUS, Rev. 5.1*; 1998. PC Version. A system of computer programs for the determination of crystal structure from X-ray diffraction data.

developed procedure can be applied for the synthesis of diverse sets of functional drug-like quinolines.

Experimental Section

Preparation of 3-(2-Hydroxyphenyl)quinolines 3a−l and 7*H*-Chromeno[3,2-*c*]quinolin-7-ones 5a−o from Anilines 2a−l or 4a−o and 3-formylchromone 1. General Procedure. Anilines **2a−l** or **4a−o** (2 mmol) and 3-formylchromone **1** (348 mg, 2 mmol) were placed in a 15-mL pressure tube and dissolved in DMF (2−4 mL). Chlorotrimethylsilane (652 mg, 3 mmol) was added dropwise to the solution. The tube was thoroughly sealed and heated on a water bath (100 °C) for 12−24 h. After cooling the flask was opened (*Caution! Excessive pressure inside*), and the reaction mixture was poured into water (15 mL) and allowed to stand at 20 °C in an ultrasonic bath for 1 h. The precipitate formed was filtered and washed with a small amount of *i*-PrOH. Recrystallization from an appropriate solvent yielded targeted compounds **3a−l** and **5a−o**. Compounds **3i** and **5g** were purified by preparative HPLC.

8-(2-Hydroxybenzoyl)-2-methyl-2*H*-[1,4]oxazino[2,3-*g*]quinolin-3(4*H*)-one (3c). Yield 87%; mp 272−273 °C (EtOH−DMF). ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.50 (d, $^3J_{H,H}$ = 6.6 Hz, 3H, CHC$\underline{H}_3$), 4.92 (q, $^3J_{H,H}$ = 6.6 Hz, 1H, C$\underline{H}$CH$_3$), 6.98 (t, $^3J_{H,H}$ = 8.1 Hz, 1H, 5-H$_{Ar}$), 7.02 (d, $^3J_{H,H}$ = 8.1 Hz, 1H, 3-H$_{Ar}$), 7.40−7.51 (m, 3H, 4,6-H$_{Ar}$, 5-H$_{Qn}$), 7.53 (s, 1H, 8-H$_{Qn}$), 8.53 (s, 1H, 4-H$_{Qn}$), 8.93 (s, 1H, 2-H$_{Qn}$), 10.38 (br. s, 1H, OH), 11.27 (br. s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 17.0 (qd, $^1J_{CH}$ = 129.2 Hz, $^2J_{CH}$ = 3.7 Hz, CH$_3$), 73.6 (dq, $^1J_{CH}$ = 151.2 Hz, $^2J_{CH}$ = 4.2 Hz, $\underline{C}$HCH$_3$), 112.6 (dd, $^1J_{CH}$ = 164.5 Hz, $^3J_{CH}$ = 5.0 Hz, 5-C$_{Qn}$), 113.6 (d, $^1J_{CH}$ = 164.1 Hz, 8-C$_{Qn}$), 117.6 (dd, $^1J_{CH}$ = 161.8 Hz, $^2J_{CH}$ = 7.4 Hz, 3-C$_{Ar}$), 119.8 (dd, $^1J_{CH}$ = 129.2 Hz, $^2J_{CH}$ = 7.6 Hz, 5-C$_{Ar}$), 123.3 (d, $^2J_{CH}$ = 5.0 Hz, 3-C$_{Qn}$), 124.7 (m, 1-C$_{Ar}$), 129.7 (d, $^2J_{CH}$ = 7.3 Hz, 4a-C$_{Qn}$), 130.0 (d, $^2J_{CH}$ = 6.8 Hz, 7-C$_{Qn}$), 131.4 (ddd, $^1J_{CH}$ = 160.3 Hz, $^2J_{CH}$ = 7.4 Hz, $^3J_{CH}$ = 1.8 Hz, 6-C$_{Ar}$), 134.4 (dd, $^1J_{CH}$ = 160.4 Hz, $^2J_{CH}$ = 8.7 Hz, 4-C$_{Ar}$), 137.2 (dt, $^1J_{CH}$ = 165.0 Hz, $^3J_{CH}$ = 5.0 Hz, 4-C$_{Qn}$), 147.1 (m, 6-C$_{Qn}$), 148.4 (m, 8a-C$_{Qn}$), 148.8 (dd, $^1J_{CH}$ = 181.9 Hz, $^3J_{CH}$ = 6.0 Hz, 2-C$_{Qn}$), 158.0 (m, 2-C$_{Ar}$), 167.5 (t, $^2J_{CH}$ = 3.7 Hz, CONH), 196.4 (m, C=O). IR (KBr), ν_{max} (cm^{-1}): 3650−3300 (br, OH, NH), 3049, 2995, 2951, 1704 (C=O$_{amide}$), 1624 (C=O), 1593, 1512, 1462, 1377, 1348, 1304, 1248, 1219, 1159, 1097, 1041, 920, 759. APSI MS: M$^+$ + 1 = 335. Anal. Calcd for $C_{19}H_{14}N_2O_4$: C, 68.26; H, 4.22; N, 8.38. Found: C, 68.42; H, 4.09; N, 8.31.

3-Methyl-2-(2-oxopyrrolidin-1-yl)-7*H*-chromeno[3,2-*c*]quinolin-7-one (5k). Yield 67%; mp 281−282 °C (MeCN). ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.24 (quintet, $^3J_{H,H}$ = 6.9 Hz, 2H, NCH$_2$C$\underline{H}_2$), 2.42 (s, 3H, CH$_3$), 2.43 (t, $^3J_{H,H}$ = 6.9 Hz, 2H, COCH$_2$), 3.90 (t, $^3J_{H,H}$ = 6.9 Hz, 2H, NCH$_2$), 7.57 (t, $^3J_{H,H}$ = 8.2 Hz, 1H, 6-H$_{Chr}$), 7.89 (d, $^3J_{H,H}$ = 8.2 Hz, 1H, 8-H$_{Chr}$), 7.96 (t, $^3J_{H,H}$ = 8.2 Hz, 1H, 7-H$_{Chr}$), 8.04 (s, 1H, 8-H$_{Qn}$), 8.23 (d, $^3J_{H,H}$ = 8.2 Hz, 1H, 5-H$_{Chr}$), 8.46 (s, 1H, 5-H$_{Qn}$), 9.37 (s, 1H, 2-H$_{Qn}$). ^{13}C NMR (125 MHz, DMSO-d_6): δ 18.9 (CH$_3$), 19.4 (NCH$_2$$\underline{C}H_2$), 31.3 (CO$\underline{C}H_2$), 50.9 (NCH$_2$), 112.6 (3-C$_{Chr}$), 117.2 (4a-C$_{Chr}$), 119.1 (8-C$_{Chr}$), 120.8 (8-C$_{Qn}$), 123.4 (4a-C$_{Qn}$), 126.1 (6-C$_{Chr}$), 126.3 (5-C$_{Chr}$), 131.0 (5-C$_{Qn}$), 136.2 (7-C$_{Chr}$), 139.3 (6-C$_{Qn}$), 142.5 (7-C$_{Qn}$), 148.7 (2-C$_{Qn}$), 149.2 (8a-C$_{Qn}$), 155.8 (2-C$_{Chr}$), 158.6 (8a-C$_{Chr}$), 174.6 ($\underline{C}OCH_2$), 175.6 (C=O). IR (KBr), ν_{max} (cm^{-1}): 3070, 3041, 2962, 2920, 1682 (C=O$_{amide}$), 1662 (C=O), 1628, 1614, 1495, 1470, 1446, 1414, 1362, 1294, 1223, 899, 827, 756. APSI MS: M$^+$ + 1 = 345. Anal. Calcd for $C_{21}H_{16}N_2O_3$: C, 73.24; H, 4.68; N, 8.13. Found: C, 73.08; H, 4.82; N, 8.21.

Acknowledgment. The authors acknowledge Mr. V. V. Polovinko ("Enamine Ltd.") and Dr. S. A. Alekseev (Kyiv National Taras Shevchenko University) for spectral measurements.

Supporting Information Available: Details of the experimental procedures, spectroscopic data of the products, and X-ray data for the compound **5k** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

JO800950Y