Tetrahedron Letters 52 (2011) 6271–6274

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Reactions of 2-(trifluoromethyl)chromones with cyanoacetamides, ethyl cyanoacetate and diethyl malonate. Unexpected synthesis of benzo[*c*]coumarin derivatives

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ARTICLE INFO

Article history:
Received 19 July 2011
Revised 31 August 2011
Accepted 16 September 2011
Available online 29 September 2011

Keywords:
Chromones
Active methylene compounds
2-Pyridones
6*H*-Benzo[*c*]chromen-6-one
Trifluoromethylated heterocycles

ABSTRACT

While 2-(trifluoromethyl)chromones react with cyanoacetamides in the presence of sodium ethoxide to produce 6-(2-hydroxyaryl)-4-(trifluoromethyl)-2-oxo-1,2-dihydropyridine-3-carbonitriles, their reactions with ethyl cyanoacetate and diethyl malonate under the same conditions took an entirely different course and gave novel functionalized derivatives of 6*H*-benzo[*c*]chromen-6-one.

Chromones (4*H*-chromen-4-ones, 4*H*-1-benzopyran-4-ones) are naturally occurring oxygen-containing heterocyclic compounds which perform important biological functions in nature.[1] Many natural and synthetic chromone derivatives, including 2-methylchromones, exhibit various types of biological activities (antiviral, antiallergic, neuroleptic, anti-inflammatory, and antitumor)[2] and find use as valuable synthetic intermediates in the preparation of pharmacologically relevant products and new heterocyclic systems.[3] These compounds possess two strong electrophilic centers (carbon atoms C-2 and C-4 of the chromone system) and their reactions with dinucleophiles start predominantly with an attack of the C-2 atom (1,4-addition) and are accompanied by pyrone ring-opening to form an intermediate capable of undergoing intramolecular heterocyclizations.[4] Alternatively, the initial attack can also occur at C-4 (1,2-addition).[5]

Most pertinent to the present research are the reactions involving the addition of active methylene compounds to 2-alkylchromones. However, to the best of our knowledge, very little is known on this topic. In almost all cases, the reactions proceeded without cleavage of the pyrone ring and only 1,2-addition (Knoevenagel condensation) at the carbonyl group took place to give the corresponding methylidene derivatives.[5] There are only two reports on the reactions of 2-methylchromones (**1**) with malononitrile, cyanoacetamide, and ethyl cyanoacetate leading to products which can result from the initial nucleophilic 1,2- or 1,4-additions. Zeid et al.[6] investigated the addition of malononitrile (sodium ethoxide, ethanol) and ethyl cyanoacetate (piperidine, benzene) to the carbonyl group of **1** (R = H) and obtained the methylidene derivatives **2**. Recently,[7] the reaction of **1** with malononitrile, cyanoacetamide, and ethyl cyanoacetate in the presence of sodium ethoxide, leading to the isolation of 2-pyridones **3** and 2-pyrones **4**, was reported. In this case, the reaction proceeded via nucleophilic 1,4-addition with concomitant opening of the pyrone ring and subsequent intramolecular cyclization (Scheme 1).

It is known that 2-alkylchromones are less reactive than 2-unsubstituted chromones due to steric and electronic factors, however, the introduction of electron-withdrawing R^F groups at the 2-position of the chromone system significantly changes the reactivity of the pyrone ring with respect to nucleophiles, and provides broad synthetic potential for 2-(polyfluoroalkyl)chromones.[8] In recent years, these compounds have attracted considerable attention as highly reactive substrates, which can serve as the starting materials in the synthesis of various partially fluorinated heterocycles with useful properties due to the enhanced electrophilicity of the C-2 atom, which is usually attacked first in reactions with *N*-, *S*-, and *C*-nucleophiles.[9] Among the diverse

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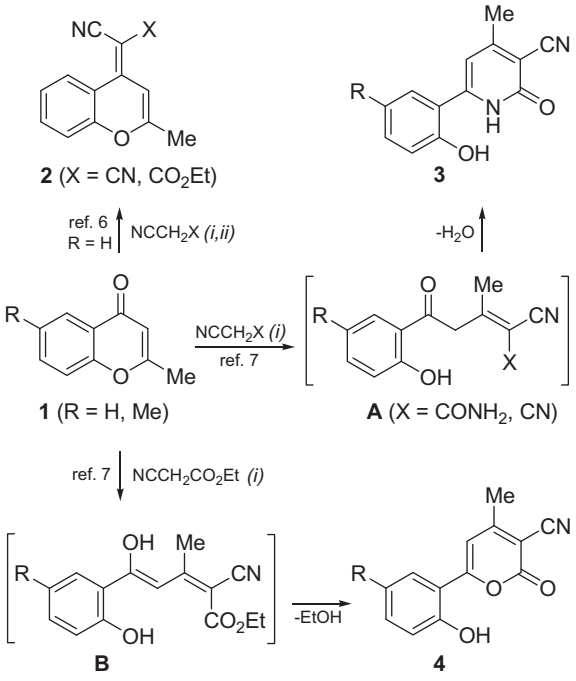
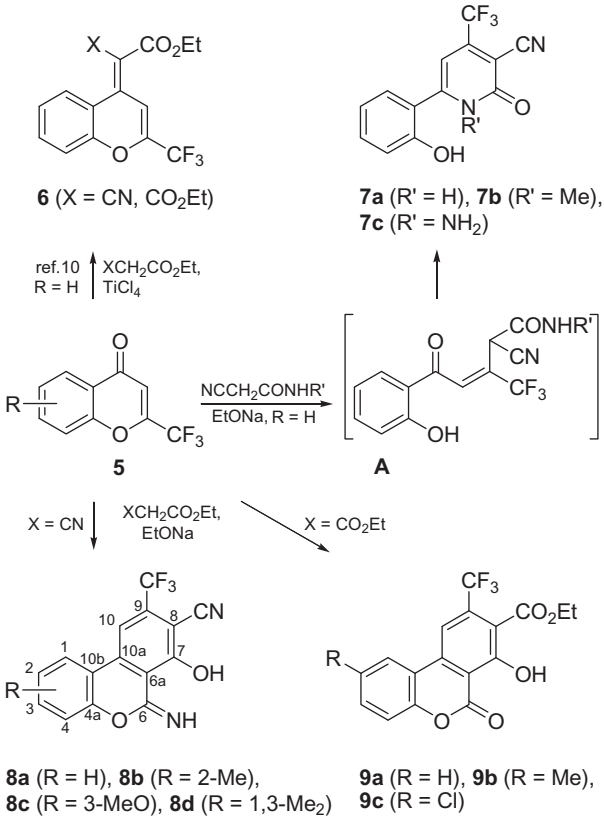
doi:10.1016/j.tetlet.2011.09.082



Scheme 1. Reagents and conditions: (i) EtONa, EtOH, reflux;[6,7] (ii) piperidine, benzene, reflux (X = CO_2Et).[6]



Scheme 2. Synthesis of compounds **7**–**9**.

transformations of 2-(trifluoromethyl)chromone (**5**, R = H), one of the most interesting is its $TiCl_4$-mediated Knoevenagel condensation with ethyl cyanoacetate and diethyl malonate to give methylidene derivatives of 4*H*-chromene **6** in good yields (Scheme 2).[10]

In the continuation of our studies on the chemical properties of chromones **5**,[8,9] we investigated their reactions with active methylene compounds, such as cyanoacetamides, ethyl cyanoacetate, and diethyl malonate, under classical conditions (sodium ethoxide, ethanol, reflux). Herein, we report that, in contrast to 2-methylchromones, condensation of 2-(trifluoromethyl)chromones with ethyl cyanoacetate and diethyl malonate represents a one-pot, multistep transformation and can be employed to obtain the functionalized 6*H*-benzo[*c*]chromen-6-ones (benzo[*c*]coumarins). Recently reported syntheses of this skeleton, which are present in a number of pharmacologically relevant natural products, such as autumnariol,[11] autumnariniol,[12] alternariol,[13] and altenuisol,[14] rely on sequential [3+3]-cycloaddition–Suzuki cross-coupling reactions,[15] Me_3SiOTf-mediated condensation of 1,3-bis(silyl enol ethers) with chromones followed by domino retro-Michael-aldol-lactonization reactions,[16] reactions of chromones with dimethyl 1,3-acetonedicarboxylate,[17] and 4-chloro-3-formylcoumarin with 1,3-bis(silyl enol ethers)[18] and 1,3-dicarbonyl compounds.[19] However, the substitution pattern present in our products is, to the best of our knowledge, not available via these transformations.

We found that 2-(trifluoromethyl)chromone (**5**, R = H) reacts with cyanoacetamide, *N*-methyl cyanoacetamide, and cyanoacetohydrazide on refluxing in absolute ethanol in the presence of sodium ethoxide, affording novel 6-(2-hydroxyphenyl)-2-oxo-4-(trifluoromethyl)-1,2-dihydropyridine-3-carbonitriles **7a**–**c** in 55–74% yields. This reaction is an earlier known transformation of 2-methylchromones (Scheme 1),[7] which can be regarded as nucleophilic 1,4-addition of cyanoacetamides with the formation of a new C–C bond (intermediate **A**) followed by cyclodehydration to the products **7** (Scheme 2). It is worth noting that compound **7a** can also be obtained from **5** and malononitrile in 81% yield.

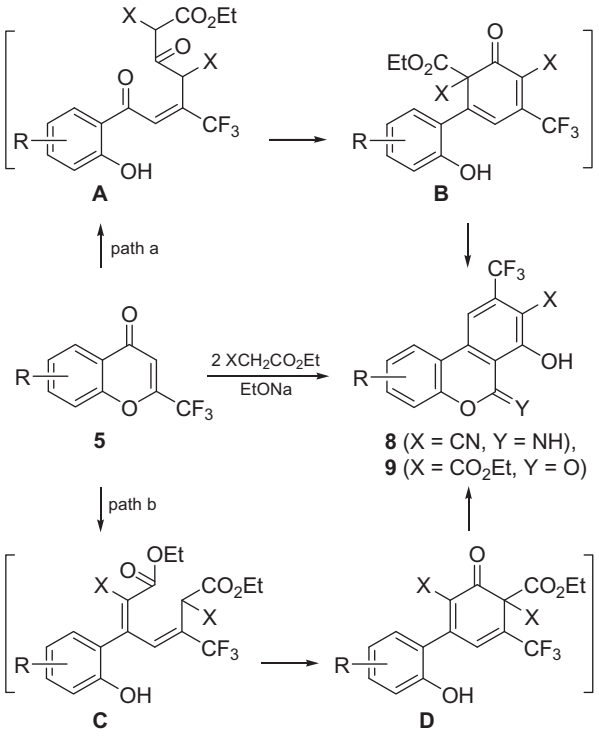
In this context, two Letters are of interest when trifluoromethylated 1,3-diketones are reacted with cyanoacetamide[20] and *N*-methyl cyanoacetamide[21] to give, regioselectively, one isomer, that is, 3-cyano-4-(trifluoromethyl)-6-substituted 2-pyridones. In our case, the choice between 4-CF_3- and 6-CF_3-2-pyridones was made in favor of the former on the basis of the ^{13}C NMR spectrum of **7b** (C-3: 97.0 ppm, q, $^3J_{C,F}$ = 2.2 Hz; C-5: 103.8 ppm, q, $^3J_{C,F}$ = 4.4 Hz; C-4: 143.9 ppm, q, $^2J_{C,F}$ = 33.0 Hz). The assignment of all the signals was achieved using 2D ^1H–^{13}C HSQC, and HMBC experiments.[22]

As 2-methylchromones have been shown[7] to react with ethyl cyanoacetate in the presence of sodium ethoxide to give 6-(2-hydroxyaryl)-4-methyl-2-oxo-2*H*-pyran-3-carbonitriles **4** (Scheme 1), it was expected that Michael addition of ethyl cyanoacetate to chromones **5**, followed by a ring-opening–ring-closure sequence would provide a direct route to the hitherto unknown 6-(2-hydroxyaryl)-4-(trifluoromethyl)-2-oxo-2*H*-pyran-3-carbonitriles (**4** with a CF_3 group at the 4-position instead of a methyl group). However, it turned out that under these conditions (EtONa, EtOH, reflux, 12 h), chromones **5** reacted with two molecules of ethyl cyanoacetate, yielding 7-hydroxy-6-imino-9-(trifluoromethyl)-6*H*-benzo[*c*]chromene-8-carbonitriles **8a**–**d** as the only isolated products in 35–66% yields (reaction conditions were not optimized).[23] This outcome was rather unexpected and indicated that the reaction of **5** with ethyl cyanoacetate took an entirely different course compared with the reaction of **1**. In this process ethyl cyanoacetate may be regarded as a synthetic equivalent of 1,3-dicyanoacetone, which is not a readily available compound.

A similar base-mediated reaction of **5** with diethyl malonate followed the same 1:2 stoichiometry and gave 7-hydroxy-6-oxo-9-(trifluoromethyl)-6*H*-benzo[*c*]chromene-8-carboxylates **9a**–**c** in 37–62% yields (Scheme 2).[24] Note that coumarin **9a** was also obtained from **5** and diethyl 1,3-acetonedicarboxylate, albeit in a lower yield. These results are of particular interest because the formation of 6*H*-benzo[*c*]chromen-6-one derivatives, also known as benzo[*c*]coumarins or dibenzo-α-pyrones,[25] from 2-substituted chromones has not been reported to date.

The structures of compounds **8** and **9** were confirmed by spectroscopic data, including IR, NMR (^{1}H, ^{19}F, and ^{13}C), and elemental analysis; assignment of all the signals was accomplished based on results from 2D ^{1}H–^{13}C, HSQC, and HMBC experiments. In the ^{1}H NMR spectra of compounds **8a–d** and **9a–c** in DMSO-d_6, the most downfield shifted signals were assigned to the OH proton (δ 8.0–8.3 for **8** and 11.6–11.8 for **9**), H-1 (δ 8.21–8.38 for **8** and 8.29–8.54 for **9**), and H-10 (δ 7.73–7.80 for **8** and 7.99–8.17 for **9**). The position of the OH signal can be explained by the intramolecular hydrogen bond present in **9**. In the ^{19}F NMR spectra the CF_3 group manifests itself at −63.1 to −63.5 ppm for **8a–d** and −60.0 ppm for **9a–c**. The most informative and strong cross-peaks in the 2D HMBC spectra for **9a** are as follows: H-10/C-6a, H-10/C-10b, H-10/C-8, H-10/CF_3, H-10/C-6, H-10/CO_2Et, H-1/C-3, H-1/C-10a, H-1/C-4a. In the IR spectra of compounds **8** and **9**, a highly characteristic nitrile absorption at 2220–2225 cm^{-1} and carbonyl bonds at 1720–1741 and 1679–1682 cm^{-1}, respectively, were observed.

For the formation of products **8** and **9** a plausible mechanism is depicted in Scheme 3. There are two possible routes to these compounds. In the first (path a), initial nucleophilic attack of the base-activated methylene compound at C-2 followed by Claisen condensation (intermediate **A**, the initial Claisen self-condensation of the starting ester could not be excluded), intramolecular cyclization, and dehydration (intermediate **B**), and then by aromatization (after hydrolysis and decarboxylation) leads to compounds **8** or **9** through the involvement of phenolic hydroxy group. The second route (path b) implies initial double nucleophilic attack at the electrophilic C-2 and C-4 atoms (intermediate **C**) followed by intramolecular cyclization (intermediate **D**), aromatization, and lactonization (Scheme 3). As diethyl 1,3-acetonedicarboxylate can be used in this multi-step transformation, we believe that 'path a' is more preferred. The formation of 3,4-benzoannulated coumarins **8** and **9** is strictly linked to their high thermodynamic stability which represents the driving force of the process. Clearly, the most significant difference between the reactions of chromones **5** with cyanoacetamides, and related reactions with the other compounds containing an active methylene group, such as ethyl cyanoacetate and diethyl malonate, is the failure of cyanoacetamides to form 1:2 adducts. This failure may be attributed to the readiness with which 1:1 adducts undergo ring closure involving the amide group to form 2-pyridones **7**.



Scheme 3. Possible mechanism for the formation of products **8** and **9**.

In conclusion, we have shown, for the first time, that the condensation of 2-(trifluoromethyl)chromones with active methylene compounds in the presence of sodium ethoxide affords two types of products: 6-(2-hydroxyaryl)-3-cyano-4-(trifluoromethyl)-2-pyridones with cyanoacetamides and 7-hydroxy-9-(trifluoromethyl)-6*H*-benzo[*c*]chromen-6-ones with ethyl cyanoacetate and diethyl malonate. The latter reaction is a straightforward and convenient route to functionalized benzo[*c*]coumarins and has advantages with regard to ease of operation and the ready availability of starting materials.

Acknowledgment

This work was supported financially by the Russian Foundation for Basic Research (Grant 11-03-00126).

References and notes

1. Ellis, G. P. Chromenes, Chromanones and Chromones In *The Chemistry of Heterocyclic Compounds*; Wiley: New York, 1977; Vol. 31.
2. (a) Horton, D. A.; Bourne, G. T.; Smythe, M. L. *Chem. Rev.* **2003**, *103*, 893–930; (b) De Meyer, N.; Haemers, A.; Mishra, L.; Pandey, H.-K.; Pieters, L. A. C.; Van den Berghe, D. A.; Vlietinck, A. J. *J. Med. Chem.* **1991**, *34*, 736–746; (c) Nohara, A.; Kuriki, H.; Saijo, T.; Ukawa, K.; Murata, T.; Kanno, M.; Sanno, Y. *J. Med. Chem.* **1975**, *18*, 34–37; (d) Nohara, A.; Kuriki, H.; Saijo, T.; Sugihara, H.; Kanno, M.; Sanno, Y. *J. Med. Chem.* **1977**, *20*, 141–145; (e) Ellis, G. P.; Becket, G. J. P.; Shaw, D.; Wilson, N. K.; Vardey, C. J.; Skidmore, I. F. *J. Med. Chem.* **1978**, *21*, 1120–1126; (f) Bolos, J.; Gubert, S.; Anglada, L.; Planas, J. M.; Burgarolas, C.; Castello, J. M.; Sacristán, A.; Ortiz, J. A. *J. Med. Chem.* **1996**, *39*, 2962–2970.
3. (a) Langer, P. *Synlett* **2007**, 1016–1025; (b) Sabitha, G. *Aldrichim. Acta* **1996**, *29*, 15–25; (c) Ghosh, C. K.; Patra, A. *J. Heterocycl. Chem.* **2008**, *45*, 1529–1547; (d) Nohara, A.; Umetani, T.; Ukawa, K.; Sanno, Y. *Chem. Pharm. Bull.* **1974**, *22*, 2959–2965; (e) Ukawa, K.; Ishiguro, T.; Wada, Y.; Nohara, A. *Heterocycles* **1986**, *24*, 1931–1941; (f) Hsung, R. P. *J. Org. Chem.* **1997**, *62*, 7904–7905.
4. (a) Ghosh, C. K. *J. Heterocycl. Chem.* **1983**, *20*, 1437–1445; (b) Morin, C.; Beugelmans, R. *Tetrahedron* **1977**, *33*, 3183–3192; (c) Ibrahim, M. A.; Ali, T. E.; Alnamer, Y. A.; Gabr, Y. A. *Arkivoc* **2010**, *i*, 98–135; (d) Chosh, C. K. *J. Heterocycl. Chem.* **2006**, *43*, 813–820.
5. (a) Eiden, F.; Engelhardt, A. *Arch. Pharm.* **1967**, *300*, 211–225; (b) Mahmoud, M. R.; Amine, M. S.; Guirgius, D. B. *Indian J. Chem.* **1993**, *32B*, 427–430; (c) Al Naimi, I. S.; Hussain, B. A. *Qatar. Univ. Sci. J.* **1992**, *12*, 73–79.
6. Zeid, I.; El-Bary, H. A.; Yassin, S.; Zahran, M. *Liebigs Ann. Chem.* **1984**, 186–190.
7. Ibrahim, S. S.; El-Shaaer, H. M.; Hassan, A. *Phosphorus, Sulfur, Silicon* **2002**, *177*, 151–172.
8. Sosnovskikh, V. Y. *Uspekhi Khim.* **2003**, *72*, 550–578. *(Russ. Chem. Rev.* **2003**, *72*, 489–516).
9. (a) Sosnovskikh, V. Y.; Sevenard, D. V.; Usachev, B. I.; Röschenthaler, G.-V. *Tetrahedron Lett.* **2003**, *44*, 2097–2099; (b) Sosnovskikh, V. Y.; Usachev, B. I.; Sevenard, D. V.; Röschenthaler, G.-V. *J. Org. Chem.* **2003**, *68*, 7747–7754; (c) Sosnovskikh, V. Y.; Usachev, B. I.; Sizov, A. Y.; Barabanov, M. A. *Synthesis* **2004**, 942–948; (d) Sosnovskikh, V. Y.; Usachev, B. I.; Sizov, A. Y.; Kodess, M. I. *Tetrahedron Lett.* **2004**, *45*, 7351–7354; (e) Sosnovskikh, V. Y.; Usachev, B. I.; Sevenard, D. V.; Röschenthaler, G.-V. *Tetrahedron* **2003**, *59*, 2625–2630; (f) Castaneda, I. C. H.; Ulic, S. E.; Védova, C. O. D.; Metzler-Nolte, N.; Jios, J. L. *Tetrahedron Lett.* **2011**, *52*, 1436–1440.
10. Sosnovskikh, V. Y.; Usachev, B. I.; Permyakov, M. N.; Sevenard, D. V.; Röschenthaler, G.-V. *Izv. Akad Nauk, Ser. Khim.* **2006**, 1628–1630 (*Russ. Chem. Bull., Int. Ed*. **2006**, *55*, 1687–1689).
11. Sidwell, W. T. L.; Fritz, H.; Tamm, C. *Helv. Chim. Acta* **1971**, *54*, 207–215.
12. Tamm, C. *Arzneim. -Forsch.* **1972**, *22*, 1776–1784.
13. Raistrick, H.; Stickings, C. E.; Thomas, R. *Biochem. J.* **1953**, *55*, 421–433.
14. Pero, R. W.; Harvan, D.; Blois, M. C. *Tetrahedron Lett.* **1973**, *14*, 945–948.
15. (a) Hussain, I.; Nguyen, V. T. H.; Yawer, M. A.; Dang, T. T.; Fischer, C.; Reinke, H.; Langer, P. *J. Org. Chem.* **2007**, *72*, 6255–6258; (b) Nguyen, V. T. H.; Langer, P. *Tetrahedron Lett.* **2005**, *46*, 1013–1015.
16. (a) Appel, B.; Saleh, N. N. R.; Langer, P. *Chem. Eur. J.* **2006**, *12*, 1221–1236; (b) Ullah, E.; Appel, B.; Fischer, C.; Langer, P. *Tetrahedron* **2006**, *62*, 9694–9700; (c) Lubbe, M.; Appel, B.; Flemming, A.; Fischer, C.; Langer, P. *Tetrahedron* **2006**, *62*, 11755–11759; (d) Langer, P.; Appel, B. *Tetrahedron Lett.* **2003**, *44*, 5133–5135.
17. Terzidis, M. A.; Tsoleridis, C. A.; Stephanidou-Stephanatou, J.; Terzis, A.; Raptopoulou, C. P.; Psycharis, V. *Tetrahedron* **2008**, *64*, 11611–11617.
18. Fatunsin, O.; Iaroshenko, V. O.; Dudkin, S.; Mkrtchyan, S.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2010**, *51*, 4693–4695.
19. Iaroshenko, V. O.; Abbasi, M. S. A.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2011**, *52*. doi:10.1016/j.tetlet.2011.07.140.
20. Portnoy, S. *J. Org. Chem.* **1965**, *30*, 3377–3380.

21. Krishnaiah, A.; Narsaiah, B. *J. Fluorine Chem.* **2002**, *113*, 133–137.
22. *6-(2-Hydroxyphenyl)-1-methyl-2-oxo-4-(trifluoromethyl)-1,2-dihydropyridine-3-carbonitrile* (**7b**). Yield 74%, light brown crystals, mp 221–222 °C (EtOH); IR (ATR) 3151, 2232, 1634, 1601, 1571, 1557 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 3.38 (s, 3H, Me), 6.67 (s, 1H, H-5), 6.99 (t, 1H, H-5′, J = 7.5 Hz), 7.02 (d, 1H, H-3′, J = 8.3 Hz), 7.32 (dd, 1H, H-6′, J = 7.5, 1.6 Hz), 7.43 (ddd, 1H, H-4′, J = 8.3, 7.5, 1.6 Hz), 10.48 (s, 1H, OH); ^{19}F NMR (376 MHz, DMSO-d_6) δ −64.6 (s, CF_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 34.8 (Me), 97.0 (q, C-3, $^3J_{C,F}$ = 2.2 Hz), 103.8 (q, C-5, $^3J_{C,F}$ = 4.4 Hz), 113.4 (CN), 116.0 (C-3′), 119.7 (C-5′), 120.7 (C-1′), 121.1 (q, CF_3, $^1J_{C,F}$ = 275.8 Hz), 129.8 (C-6′), 132.5 (C-4′), 143.9 (q, C-4, $^2J_{C,F}$ = 33.0 Hz), 154.3 (C-2′), 156.7 (C-6), 160.1 (C-2). Anal. Calcd for $C_{14}H_9F_3N_2O_2$: C, 57.15; H, 3.08; N, 9.52. Found: C, 57.02; H, 3.43; N, 9.50.
23. *7-Hydroxy-6-imino-9-(trifluoromethyl)-6H-benzo[c]chromene-8-carbonitrile* (**8a**). Yield 66%, yellow crystals, mp 303–305 °C (DMF); IR (ATR) 3403, 3296, 2225, 1695, 1620, 1601, 1591 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.41 (d, 1H, H-4, J = 8.0 Hz), 7.43 (t, 1H, H-2, J = 7.6 Hz), 7.67 (td, 1H, H-3, J = 7.8, 1.3 Hz), 7.78 (s, 1H, H-10), 8.02–8.32 (br s, 1.7H, NH, OH), 8.16 (s, 0.3H, NH), 8.38 (d, 1H, H-1, J = 8.0 Hz); ^{19}F NMR (376 MHz, DMSO-d_6) δ −63.1 (s, CF_3). Anal. Calcd for $C_{15}H_7F_3N_2O_2$: C, 59.22; H, 2.32; N, 9.21. Found: C, 59.62; H, 2.51; N, 9.43.
7-Hydroxy-6-imino-3-methoxy-9-(trifluoromethyl)-6H-benzo[c]chromene-8-carbonitrile (**8c**). Yield 42%, light brown crystals, mp 259–260 °C (DMF); IR (ATR) 3403, 3294, 2222, 1696, 1610, 1598, 1548, 1519, 1478 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 3.88 (s, 3H, MeO), 6.99 (dd, 1H, H-2, J = 9.0, 2.5 Hz), 7.01 (d, 1H, H-4, J = 2.5 Hz), 7.73 (s, 1H, H-10), 8.10 (br s, 2H, NH, OH), 8.35 (d, 1H, H-1, J = 9.0 Hz); ^{19}F NMR (376 MHz, DMSO-d_6) δ −63.2 (s, CF_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 56.1 (MeO), 88.3 (q, C-8, $^3J_{C,F}$ = 1.5 Hz), 101.0 (C-4), 104.9 (C-6a), 106.1 (q, C-10, $^3J_{C,F}$ = 5.1 Hz), 109.6 (C-10b), 113.2 (C-2), 114.1 (CN), 122.2 (q, CF_3, $^1J_{C,F}$ = 275.0 Hz), 126.8 (C-1), 136.6 (q, C-9, $^2J_{C,F}$ = 31.5 Hz), 141.4 (C-10a), 153.2 (C-4a), 154.8 (C-7), 160.8 (C-6), 163.2 (C-3). Anal. Calcd for $C_{16}H_9F_3N_2O_3$: C, 57.49; H, 2.71; N, 8.38. Found: C, 57.33; H, 2.64; N, 8.33.
24. *Ethyl 7-hydroxy-6-oxo-9-(trifluoromethyl)-6H-benzo[c]chromene-8-carboxylate* (**9a**). Yield 62%, colorless crystals, mp 139–140 °C (EtOH); IR (ATR) 1737, 1682, 1627, 1608, 1562 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.36 (t, 3H, Me, J = 7.0 Hz), 4.38 (q, 2H, CH_2O, J = 7.0 Hz), 7.48 (ddd, 1H, H-2, J = 8.3, 7.3, 1.0 Hz), 7.48 (dd, 1H, H-4, J = 8.3, 1.0 Hz), 7.67 (ddd, 1H, H-3, J = 8.3, 7.3, 1.3 Hz), 8.17 (s, 1H, H-10), 8.47 (dd, 1H, H-1, J = 8.3, 1.3 Hz), 11.76 (s, 1H, OH); ^{19}F NMR (376 MHz, DMSO-d_6) δ −60.0 (s, CF_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.2 (Me), 62.5 (CH_2), 110.1 (C-6a), 110.7 (q, C-10, $^3J_{C,F}$ = 4.4 Hz), 117.2 (C-10b), 117.8 (C-4), 119.7 (q, C-8, $^3J_{C,F}$ = 2.2 Hz), 123.0 (q, CF_3, $^1J_{C,F}$ = 275.1 Hz), 125.3 (C-1), 126.0 (C-2), 132.8 (C-3), 132.9 (q, C-9, $^2J_{C,F}$ = 32.3 Hz), 137.3 (C-10a), 151.0 (C-4a), 158.7 (C-6), 164.1 (C-7), 164.3 (C=O). Anal. Calcd for $C_{17}H_{11}F_3O_5 \cdot 0.5H_2O$: C, 56.52; H, 3.35. Found: C, 56.69; H, 3.22.
25. Darbarwar, M.; Sundaramurthy, V. *Synthesis* **1982**, 337–388.