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Graphical Abstract

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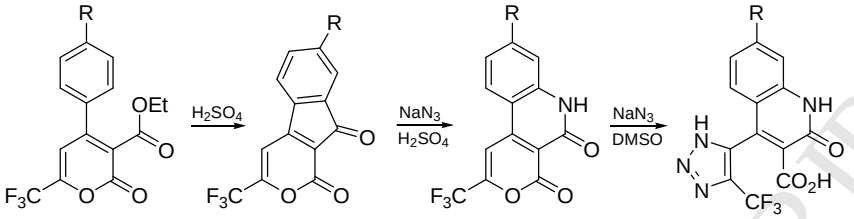

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A B S T R A C T

Treatment of ethyl 4-aryl-6-(trifluoromethyl)-2-oxo-2*H*-pyran-3-carboxylates, prepared from 4,4,4-trifluorobutane-1,3-diones, PCl_5, and sodium diethyl malonate, with sulfuric acid afforded the intramolecular Friedel-Crafts acylation products, 3-(trifluoromethyl)indeno[2,1-*c*]pyran-1,9-diones, from which 2-(trifluoromethyl)-6*H*-pyrano[3,4-*c*]quinoline-4,5-diones were obtained via the Schmidt reaction in moderate yields. The latter reacted with sodium azide to give 2-oxo-4-(5-trifluoromethyl-1,2,3-triazol-4-yl)-1,2-dihydroquinoline-3-carboxylic acids in good yields.

Keywords: 2-Pyrones; Friedel-Crafts acylation; Indeno[2,1-*c*]pyran-1,9-diones; Schmidt reaction; Pyrano[3,4-*c*]quinoline-4,5-diones; Triazoles; Trifluoromethylated heterocycles.

1. Introduction

Much attention has been given to trifluoromethylated heterocyclic compounds because they often show unique biological and physiological activities.[1] In particular, trifluoromethyl-substituted chromones[2] and other six-membered oxygen-containing heterocycles[3] have drawn considerable attention. The search for a simple and efficient access to such compounds with a CF_3 group at a specific position is one of the important goals in this area. However, there are a limited number of regioselective syntheses of CF_3-containing 2*H*-pyran derivatives, including 3,4-fused 6-trifluoromethyl-2-pyrones, that proceed in good yields.[4]

Most reports concerning 2*H*-pyran-2-ones (2-pyrones, α-pyrones) involve non-fluorinated derivatives, which perform important biological functions in nature and have great synthetic

potential for the construction of a variety of arenes and heteroarenes.[5] It is evident that their C-2, C-4 and C-6 positions are electrophilic in nature and prone to nucleophilic attack. Activation of 2-pyrones by the introduction of the electron-withdrawing CF_3 group at the 6-position makes this heterocyclic system more electrophilic and enables a diverse range of productive chemistry, with or without ring opening.[6,7]

Only a few methods for the preparation of 6-(trifluoromethyl)-2-pyrones have been reported to date. Most of them typically suffer from a narrow scope of substrates, long reaction time, tedious synthetic routes, drastic reaction conditions, low yields, as well as a very limited variety of substituents. The parent 6-(trifluoromethyl)-2-pyrone (**1**) has been synthesized by the reaction of 2-pyrone-6-carboxylic acid with SF_4–HF at 100 °C in 65% yield.[8] The ethyl 6-(trifluoromethyl)-2-pyrone-3-carboxylate (**2**) was prepared by condensation of trifluoroacetone with diethyl ethoxymethylenemalonate, followed by cyclization of intermediate diethyl (trifluoroacetonyl)methylenemalonate; this pyrone was used for the preparation of cage derivatives to explore their usefulness as antiviral agents.[9] A three-step formation of ethyl 6-(trifluoromethyl)-2-pyrone-4-carboxylate (**3**) in 28% overall yield was achieved by Cu-catalysed addition of 1,1,1-trichloro-2,2,2-trifluoroethane to methyl itaconate, followed by double HCl elimination with triethylamine and subsequent thermal elimination reaction of MeCl.[10] Dealkoxylation of trifluoroacetoacetic ester by P_2O_5 leads to trifluoroacetylketene, which quickly dimerizes to hexafluorodehydroacetic acid (**4**).[11] Moreover, Gerus et al. reported that heating of trifluoromethylated β-alkoxyvinyl ketones and *N*-acylglycines in acetic anhydride gave the corresponding 3-acylamino-6-(trifluoromethyl)-2-pyrones (**5**), the chemical properties of which were investigated in detail.[12] Apart from these approaches towards the synthesis of 6-CF_3-2-pyrones, a simple procedure for the preparation of pyrones **6** and **7** bearing an aryl substituent at the 4-position and a carbethoxy group or hydrogen at the position 3 from commercial 1-aryl-4,4,4-trifluorobutane-1,3-diones **8**, PCl_5, and sodium diethyl malonate, has been developed by us

recently.[6] This promising reaction deserves further investigations in order to expand the scope of its possible applications.

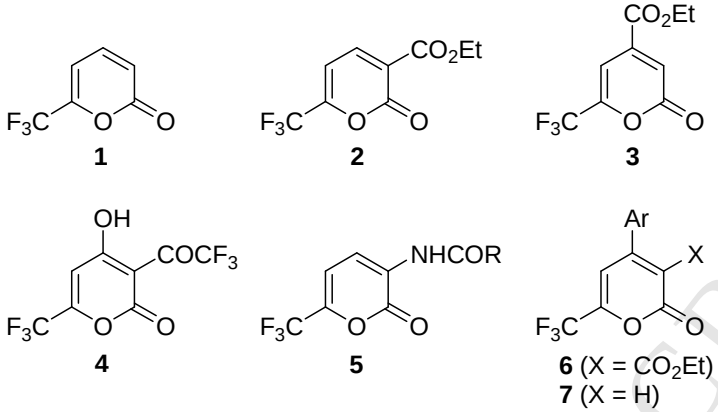


Figure 1. Known 6-trifluoromethyl-2-pyrone derivatives.

Herein we wish to demonstrate utility of readily available ethyl 4-aryl-6-(trifluoromethyl)-2-oxo-2*H*-pyran-3-carboxylates **6** as valuable building blocks for the construction of 3-(trifluoromethyl)indeno[2,1-*c*]pyran-1,9-diones **9** via an intramolecular Friedel-Crafts acylation. On the basis of these compounds, 2-(trifluoromethyl)-6*H*-pyrano[3,4-*c*]quinoline-4,5-diones **10** and 2-oxo-4-(5-trifluoromethyl-1,2,3-triazol-4-yl)-1,2-dihydroquinoline-3-carboxylic acids **12** were prepared by reactions with sodium azide. Moreover, in addition to our preliminary communication,[6] full experimental details concerning the synthesis of pyrones **6** and **7** are also reported.

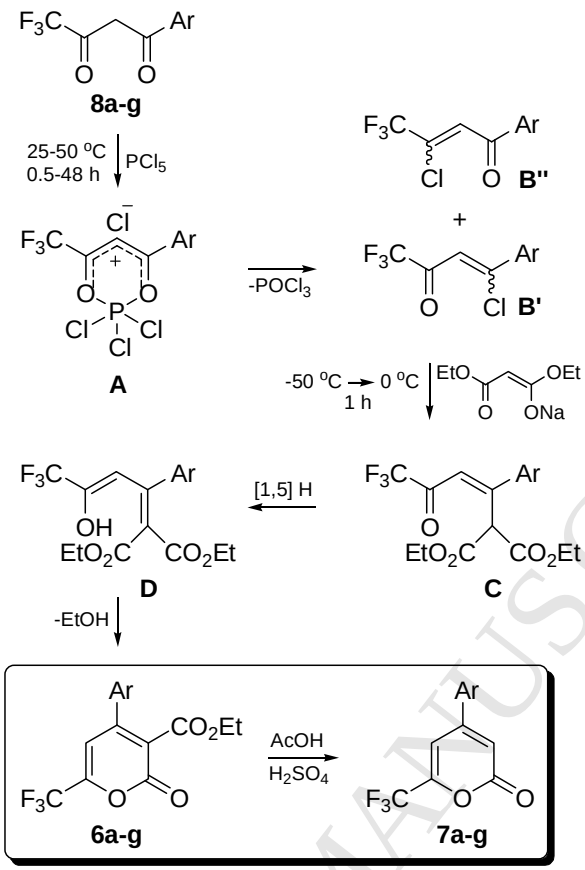
2. Results and discussion

We found that the reaction of 1-aryl-4,4,4-trifluorobutane-1,3-diones **8** with PCl_5 (the first stage) and sodium diethyl malonate (the second stage) can be employed to generate ethyl 4-aryl-6-(trifluoromethyl)-2-oxo-2*H*-pyran-3-carboxylates **6**. After several trials, it became clear that the first stage is a slow reaction while the second stage is fast. In our initial studies, we optimized the reaction conditions by using 1-phenyl-4,4,4-trifluorobutane-1,3-dione (**8a**) and monitored the reaction progress using ^{19}F NMR. To subsequently design a preparative procedure and determine the scope of the reaction, products of the first stage were not isolated but were observed by ^{19}F

NMR spectroscopy. When 1-phenyl-4,4,4-trifluorobutane-1,3-dione was treated with 1.1 equiv of PCl_5 for 30 hours at room temperatures, ^{19}F NMR analysis of the reaction mixture showed formation of a mixture of products containing a major intermediate. Thus, four signals corresponding to the CF_3-bearing intermediates were observed in C_6D_6: δ –79.8 (3%), δ –70.5 (8%), δ –70.0 (80%, major intermediate), δ –63.5 (3%). The reaction mixture also contained 6% of the starting diketone **8a** (δ –77.4). The ^{19}F NMR spectral data for the mixtures prepared from the other diketones **8** and PCl_5 were similar to those observed for the mixture of **8a** and PCl_5.

Probably, the major intermediates **A** with the signal at about δ –70 ppm are responsible for the formation of the intermediate α,β-unsaturated chloro ketones **B'** and **B''**, from which ketones **B'** then react with sodium diethyl malonate to produce 2-pyrones **6** through intermediates **C** and **D**. The reaction time of the first stage depends strongly on the nature of the aryl substituent. An electron-withdrawing substituent (F, Cl, NO_2) at the para position of the aromatic ring retards the reaction (24–48 h), whereas an electron-donating aromatic moiety (*p*-tolyl, 2-naphthyl, 2-thienyl) greatly accelerates it (0.5–7 h). The temperature level of the reactions should be as low as possible (25–35 °C). Prolonged heating at higher temperatures resulted in a more complex mixture of intermediates and decrease in the yields of **6**. Nevertheless, in order to reduce the reaction time as much as possible, in the case of diketone **8e** the reaction was carried out at 45–50 °C to give pyrone **6e** in 18% yield.

The reaction mixture was then treated with sodium diethyl malonate at –50 to 0 °C within 1 h (the second stage). After some optimization, we were pleased to find that with the use of 4.5 equiv of sodium diethyl malonate relative to starting diketones **8**, the maximum yield of the desired products **6** was reached. No pyrone **6a** was obtained, when the same reaction was conducted using 1.1 or 9.5 equiv of sodium diethyl malonate. A plausible pathway leading to the formation of compounds **6a–g** via intermediates **A**, **B**, **C**, and **D** is outlined in Scheme 1.



Ar	**6**	Yield (%)	**7**	Yield (%)
Ph	**a**	24	**a**	83
4-ClC_6H_4	**b**	29	**b**	90
4-FC_6H_4	**c**	39	**c**	87
4-MeC_6H_4	**d**	39	**d**	74
4-$NO_2C_6H_4$	**e**	18	**e**	69
2-$C_{10}H_7$	**f**	45	**f**	70
2-C_4H_3S	**g**	22	**g**	64

Scheme 1. Synthesis of 6-CF_3-2-pyrones **6a–g** and **7a–g**.

It was also found that ethyl 4-aryl-6-(trifluoromethyl)-2-oxo-2*H*-pyran-3-carboxylates **6** are convenient precursors of 4-aryl-6-(trifluoromethyl)-2*H*-pyran-2-ones **7** because of their ability to undergo easy decarbethoxylation. Thus, when pyrones **6a–g** were refluxed in aqueous acetic acid with addition of H_2SO_4, compounds **7a–g** were isolated in high yields (Scheme 1). The structure of the synthesized 6-CF_3-2*H*-pyran-2-ones **6** and **7** was confirmed by NMR, EI-MS, HRMS, IR spectra, and elemental analysis. The H-5 proton of **6** appeared as a singlet at δ 6.75–6.92 ppm, while H-3 and H-5 of **7** appeared as doublets with ^4J = 0.8–1.1 Hz at δ 6.60–6.79 and 6.92–7.12 ppm, respectively; their CF_3 group manifests itself as a singlet at about δ –72.4 ppm. In the ^{13}C

NMR spectrum of compound **6a**, the characteristic quartets of the CF_3 group at δ 117.7 ($^1J_{C,F}$ = 273.2 Hz), C-6 at δ 148.0 ($^2J_{C,F}$ = 39.7 Hz), and C-5 at δ 107.1 ($^3J_{C,F}$ = 3.6 Hz) were observed. In the EI-MS spectra, fragmentation of pyrones **6** was presented by intense ion peaks $[M]^+$, $[M–28]^+$, $[M–45]^+$, $[M–28–69]^+$, and by ion peak $[CF_3]^+$ (~30%).

Taking into account the arrangement of the aryl moiety and carbethoxy group in pyrones **6** to each other, we envisaged that the reaction of **6** with sulfuric acid would produce the corresponding fused indone derivatives **9** as a result of intramolecular Friedel-Crafts acylation. Indeed, we found that treatment of **6a** with H_2SO_4 at 110–125 °C for 10 min afforded 3-(trifluoromethyl)indeno[2,1-*c*]pyran-1,9-dione (**9a**) (yield 41%), the first representative of a novel polynuclear fused heterocyclic system. The more reactive pyrone **6d** gave indone **9d** in 61% yield under the same conditions, whereas the less reactive pyrones **6b**,**c** bearing Cl and F atoms in the benzene ring required a longer period of time and only partial hydrolysis followed by decarboxylation had occurred. Since the protocol for **6b**,**c** requires anhydrous conditions and to avoid the formation of pyrones **7**, the reaction was carried out in the presence of P_2O_5 to remove traces of water and compounds **9b** and **9c** were obtained in 47% and 65% yield, respectively.

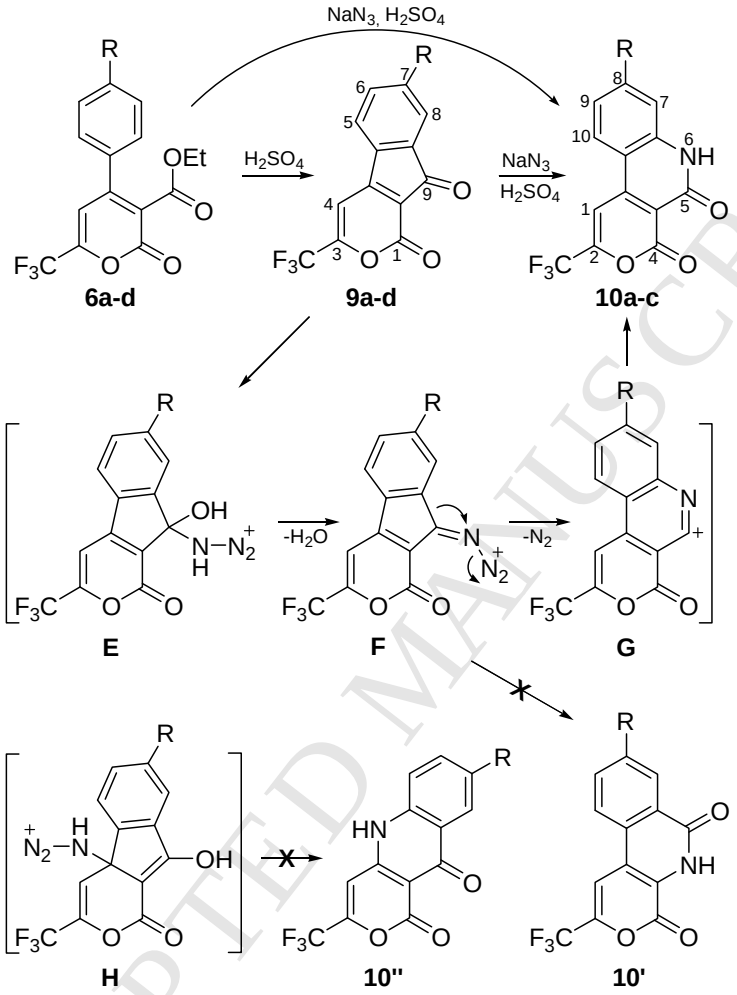
We next investigated the reaction of indones **9** with sodium azide in concentrated H_2SO_4 with the intention of forming the 3,4-fused 2-quinolone (carbostyril) derivatives **10** via the Schmidt reaction. The carbostyril system constitutes the skeleton of a number of physiologically active natural products and drugs and its derivatives have attracted strong interest due to their useful biological and pharmacological properties.[13] In contrast to the various classical approaches towards the synthesis of carbostyrils, such as Vilsmeier–Haack, Knorr, and Friedlander reactions,[14] azido-Schmidt reaction has not drawn much attention, probably due to the use of strong protic acids (H_2SO_4, CCl_3CO_2H), which result in a large number of side-products. Most pertinent to the present research are the reactions involving the additions of azide to 2,3-disubstituted indone derivatives.[15,16]

To optimize the Schmidt reaction conditions, we investigated the transformation of indone **9b** as a model substrate. The reaction of **9b** with sodium azide was examined in concentrated sulfuric acid at heating for several hours (the progress of the reaction was monitored by TLC, eluent – chloroform). The desired product, 8-chloro-2-(trifluoromethyl)-4*H*-pyrano[3,4-*c*]quinoline-4,5(6*H*)-dione (**10b**), was obtained at 90 °C for 3 hours in 56% yield. This compound has fused cyclic structure, which is difficult synthesize using other methods.[17] A similar reaction, when performed in the presence of $MeSO_3H$ at 70 °C for 6 hours, provided **10b** only in 21% yield. In contrast, the use of such catalysts as PPA,[18] CF_3SO_3H/CH_2Cl_2,[19] $AlCl_3$ or $FeCl_3$ in 1,2-dichloroethane[20] for the preparation of quinolone **10b** was not satisfactory.

With optimized reaction conditions established, the substrate scope was briefly studied. Indone **9c** with a fluorine atom on the benzene ring reacted smoothly under the same conditions to give quinolone **10c** in 47% yield. However, substrates **9a,d** (R = H, Me) were too active to the reaction, leading to a complicated mixture of products. The use of a mixture of H_2SO_4, P_2O_5, and CCl_3CO_2H allowed us to prepare carbostyril **10a** albeit in only 23% yield and we could not improve the yield significantly. It was also found that pyrones **6a–c** could be employed directly under similar conditions to give carbostyrils **10a–c** in 39–56%. It is important that a higher yield and easier purification of products was possible if the transformation was performed by using a one-pot approach. Thus, compounds **9** and **10** could be synthesized from the same starting material **6** simply by the choice of the reaction conditions.

The structure of the quinolone product merits some comment. In accord with the previously reported mechanism,[15,16,20] the Schmidt reaction involves acid activation of the indone keto group followed by the addition of hydrazoic acid (intermediate **E**). After the elimination of water the iminodiazonium ion **F** is formed, which by loss of nitrogen and migration of the *anti*-substituent to the electron deficient nitrogen (intermediate **G**) can give either carbostyril **10** or isocarbostyril **10'** derivatives. It is known that 2,3-diphenylindone can be converted into 3,4-diphenylcarbostyril and 3,4-diphenylisocarbostyril derivatives by the Schmidt reaction (the former in greater amount).[15] In

some cases, a conjugate addition of hydrazoic acid to C-3 of indones was observed to give 4-quinolones.[16] Thus, the formation of intermediate **H** leading to 4-quinolone **10''** could not be ruled out (Scheme 2).



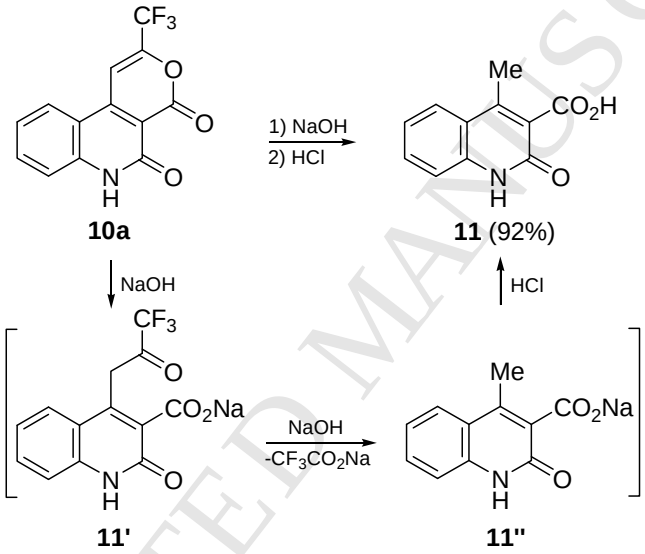
R		9	Yield (%)		10	Yield (%)[a]	Yield (%)[b]
H		**a**	41		**a**	23	39
Cl		**b**	47		**b**	56	49
F		**c**	65		**c**	47	43
Me		**d**	61			–	–

[a] From **9**.
[b] From **6**.

Scheme 2. Synthesis of compounds **9a–d** and **10a–c**.

The choice between the isomeric quinolones **10**, **10'**, and **10''** (the latter can be explained in terms of the rearrangement of an intermediate originated from a conjugate addition of the reagent) was made in favor of the former on the basis of degradation of compound **10a** at refluxing in

ethanol solution in the presence of base. We found that **10a** is opened to the intermediate salt **11'**, which could not be isolated and underwent spontaneous detrifluoroacetylation to give via acidification of **11''** known 4-methylcarbostyril-3-carboxylic acid **11** in 92% yield (Scheme 3).[21] Comparison of the melting point and ^{1}H NMR spectrum of acid **11** prepared by us with the data reported for this compound in the literature[21] indicates that they are identical and, hence, the carbostyril structure **10** is proved. Thus, the reactions of compounds **6** and **9** with sodium azide lead to the successful synthesis of fused carbostyrils **10** containing a CF_3 group in the pyran ring, a previously unknown group of 2-quinolone derivatives.

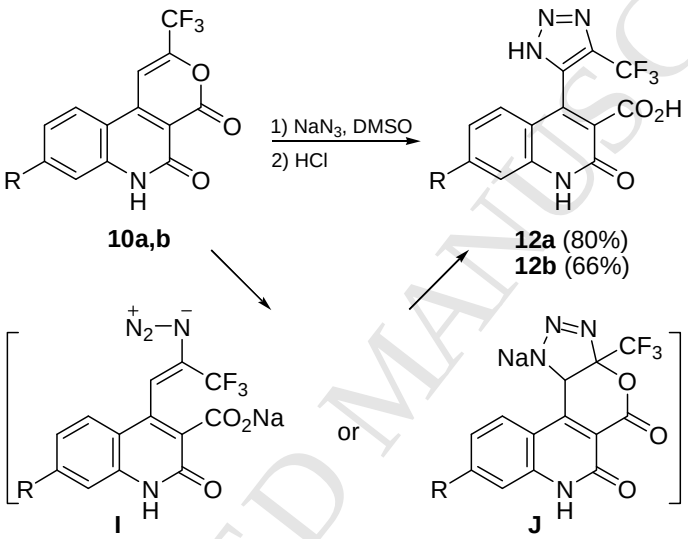


Scheme 3. Synthesis of known acid **11**.

Recently, we reported that pyrones **6** and **7** react with sodium azide to produce highly functionalized triazolyl derivatives of cinnamic acid.[7] Bearing this in mind, we envisaged that pyranocarbostyrils **10** could be converted into previously unknown 4-triazolylcarbostyrils **12** by their reaction with sodium azide. In fact, we found that when pyranocarbostyrils **10a,b** were heated in DMSO with NaN_3 (2 equiv) at 120 °C for 3 h, the desired products **12a,b** were obtained in good yields and presumably arise via intermediate vinyl azide **I** or ring-opening of the initially formed fused intermediate **J** (Scheme 4). In case of pyranocarbostyril **10c** this reaction failed presumably

due to facile nucleophilic aromatic substitution of a fluorine in the quinolone moiety and further degradation of formed arylazide.

The structures of compounds **9–12** were confirmed by elemental analysis, ^{1}H, ^{19}F, ^{13}C NMR, and IR spectroscopy. In the ^{19}F NMR spectra, the trifluoromethyl group appeared as a singlet at δ –71.4 for **9** ($CDCl_3$), –70.6 for **10** (DMSO-d_6), and –59.5 ppm for **12** (DMSO-d_6). The ^{13}C NMR spectrum of **9a** showed that the C-4 atom at δ 99.8 ppm was coupled with the fluorine atoms of the trifluoromethyl group with $^{3}J_{C,F}$ = 3.5 Hz and the C-3 atom at δ 156.1 ppm with $^{2}J_{C,F}$ = 39.6 Hz.



Scheme 4. Synthesis of 4-triazolylcarbostyrils **12a,b**.

3. Conclusion

In conclusion, we have shown that the synthesized 6-CF_3-2*H*-pyran-2-ones can be used as perspective building blocks for the preparation of novel trifluoromethylated heterocycles, which are not readily available by other methods. In particular, a series of indone and carbostyril derivatives were obtained in moderate to good yields. These products constitute an important structural subunit of a variety of biologically active compounds and could be serve as useful substrates in the construction of more complex heterocyclic systems.

4. Experimental

4.1. General

NMR spectra were recorded on Bruker DRX-400 and Bruker Avance II spectrometers (^{1}H – 400 MHz, ^{19}F – 376 MHz, and ^{13}C – 100 MHz) in DMSO-d_6 and $CDCl_3$ with TMS, $CFCl_3$, and C_6F_6 as internal standards. IR spectra were recorded on a Perkin–Elmer Spectrum BX-II and Nicolet 6700 instruments (KBr pellets, FTIR mode). Elemental analyses were performed at the Microanalysis Services of the Institute of Organic Synthesis, Ural Branch, Russian Academy of Sciences. All solvents used were dried and distilled per standard procedures. The starting 1-aryl-4,4,4-trifluorobutane-1,3-diones **8** were prepared according to described procedure.[22]

4.2. General procedure for the synthesis of compounds (6a–g)

A mixture of the corresponding 1-aryl-4,4,4-trifluorobutane-1,3-dione **8** (0.16 mol), PCl_5 (37.1 g, 0.18 mol), and CCl_4 (10 mL) was stirred at 25–35 °C for several hours. After complete conversion as indicated by ^{19}F NMR, volatile components were removed under reduced pressure. The residue was diluted with dry CH_2Cl_2 (100 mL), cooled to –50 °C and quenched with a cooled to –50 °C suspension of sodium diethyl malonate (0.72 mol) in absolute ethanol (450 mL). After achieving 0 °C, the reaction was left under stirring for 1 h at this temperature. The dark red reaction mixture was quenched with 10% H_2SO_4 (1.5 L) and the organic layer was washed once with water, distilled under reduced pressure and crystallized from ethanol (cooling to –30 °C) to afford pure **6**.

*4.2.1. Ethyl 2-oxo-4-phenyl-6-(trifluoromethyl)-2H-pyran-3-carboxylate (**6a**).* Yield 24% (30 h), colourless crystals, mp 90 °C. IR (ATR): 1758, 1714, 1667, 1581, 1559, 1494, 1471 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (t, J = 7.1 Hz, 3H, Me), 4.21 (q, J = 7.1 Hz, 2H, CH_2O), 6.80 (s, 1H, H-5), 7.42–7.55 (m, 5H, Ph); ^{1}H NMR (200 MHz, C_6D_6) δ 0.75 (t, J = 7.0 Hz, 3H, Me), 3.90 (q, J = 7.0 Hz, 2H, CH_2O), 5.89 (s, 1H, H-5), 7.00 (s, 5H, Ph); ^{19}F NMR (188 MHz, C_6D_6) δ –72.3 (s, CF_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 62.4, 107.1 (q, $^3J_{C,F}$ = 3.6 Hz, C-5), 117.7 (q, $^1J_{C,F}$ = 273.2 Hz, CF_3), 121.9, 127.3, 129.2, 131.0, 134.4, 148.0 (q, $^2J_{C,F}$ = 39.7 Hz, C-6), 152.1, 156.5, 163.4; MS (EI, 70 eV) *m/z* (%) 312 (100, $[M]^+$), 284 (72), 267 (75), 215 (69); HRMS (ESI): calcd for $C_{15}H_{11}F_3O_4$ $[M]^+$ 312.06094, found 312.05989. Anal. Calcd for $C_{15}H_{11}F_3O_4$: C, 57.70; H, 3.55. Found: C, 57.77; H, 3.53.

*4.2.2. Ethyl 4-(4-chlorophenyl)-2-oxo-6-(trifluoromethyl)-2H-pyran-3-carboxylate (**6b**).* Yield 29% (24 h), colourless crystals, mp 78 °C. IR (ATR): 1760, 1709, 1663, 1595 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.17 (t, J = 7.1 Hz, 3H, Me), 4.24 (q, J = 7.1 Hz, 2H, CH_2O), 6.77 (s, 1H, H-5), 7.36–7.52 (m, 4H, arom.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.06 (t, J = 7.1 Hz, 3H, Me), 4.17 (q, J = 7.1 Hz, 2H, CH_2O), 7.42 (s, 1H, H-5), 7.55 (d, J = 8.6 Hz, 2H, arom.), 7.64 (d, J = 8.6 Hz, 2H, arom.); ^{19}F NMR (188 MHz, $CDCl_3$) δ –72.4 (s, CF_3); ^{19}F NMR (376 MHz, DMSO-d_6) δ –70.3 (s, CF_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 13.9, 62.8, 106.8 (q, $^3J_{C,F}$ = 3.5 Hz, C-5), 117.8 (q, $^1J_{C,F}$ = 273.4 Hz, CF_3), 122.3, 128.9, 129.7, 132.9, 137.7, 148.5 (q, $^2J_{C,F}$ = 39.9

Hz, C-6), 150.9, 156.4, 163.4; MS (EI, 70 eV) *m/z* (%) 346 (79, $[M]^+$), 318 (87), 301 (67), 249 (100), 183 (39); HRMS (ESI): calcd for $C_{15}H_{10}ClF_3O_4$ $[M]^+$ 346.02197, found 346.02203.

*4.2.3. Ethyl 4-(4-fluorophenyl)-2-oxo-6-(trifluoromethyl)-2H-pyran-3-carboxylate (**6c**).* Yield 39% (36 h), colourless crystals, mp 121–123 °C. IR (ATR): 1755, 1708, 1663, 1601, 1560, 1510 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.15 (t, J = 7.1 Hz, 3H, Me), 4.23 (q, J = 7.1 Hz, 2H, CH_2O), 6.78 (s, 1H, H-5), 7.14–7.24 (m, 2H, arom.), 7.41–7.51 (m, 2H, arom.); ^{19}F NMR (188 MHz, $CDCl_3$) δ –109.0 (m, F), –72.5 (s, CF_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 13.8, 62.6, 106.9 (q, $^3J_{C,F}$ = 3.6 Hz, C-5), 116.6 (d, $^2J_{C,F}$ = 22.1 Hz, C-3′, C-5′), 117.7 (q, $^1J_{C,F}$ = 273.4 Hz, CF_3), 122.1, 129.7 (d, $^3J_{C,F}$ = 8.8 Hz, C-2′, C-6′), 130.5 (d, $^4J_{C,F}$ = 3.4 Hz, C-1′), 148.2 (q, $^2J_{C,F}$ = 39.9 Hz, C-6), 150.9, 156.4, 163.4, 164.3 (d, $^1J_{C,F}$ = 253.4 Hz, C-4′); MS (EI, 70 eV) *m/z* (%) 330 (41, $[M]^+$), 302 (50), 285 (46), 261 (25), 233 (100), 167 (46); HRMS (ESI): calcd for $C_{15}H_{10}F_4O_4$ $[M]^+$ 330.05152, found 330.05168.

*4.2.4. Ethyl 4-(4-tolyl)-2-oxo-6-(trifluoromethyl)-2H-pyran-3-carboxylate (**6d**).* Yield 39% (7 h), colourless crystals, mp 60 °C. IR (ATR): 1769, 1740, 1716, 1663, 1610 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.16 (t, J = 7.1 Hz, 3H, Me), 2.42 (s, 3H, Me), 4.23 (q, J = 7.1 Hz, 2H, CH_2O), 6.80 (s, 1H, H-5), 7.27–7.36 (m, 4H, arom.); MS (EI, 70 eV) *m/z* (%) 326 (100, $[M]^+$), 298 (93), 281 (69), 257 (29), 229 (62). Anal. Calcd for $C_{16}H_{13}F_3O_4$: C, 58.90; H, 4.02. Found: C, 58.77; H, 3.90.

*4.2.5. Ethyl 4-(4-nitrophenyl)-2-oxo-6-(trifluoromethyl)-2H-pyran-3-carboxylate (**6e**).* Yield 18% (45–50 °C, 48 h), light yellow crystals, mp 134–136 °C. IR (ATR): 1758, 1714, 1667, 1581, 1559, 1494, 1471 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.16 (t, J = 7.1 Hz, 3H, Me), 4.23 (q, J = 7.1 Hz, 2H, CH_2O), 6.75 (s, 1H, H-5), 7.63 (dd, J = 9.0, 2.2 Hz, 2H, arom.), 8.35 (dd, J = 9.0, 2.2 Hz, 2H, arom.); MS (EI, 70 eV) *m/z* (%) 357 (48, $[M]^+$), 329 (47), 312 (53), 288 (27), 260 (100); HRMS (ESI): calcd for $C_{15}H_{10}F_3NO_6$ $[M]^+$ 357.04602, found 357.04674.

*4.2.6. Ethyl 4-(2-naphthyl)-2-oxo-6-(trifluoromethyl)-2H-pyran-3-carboxylate (**6f**).* Yield 45% (6 h), yellow powder, mp 108–110 °C. IR (ATR): 1762, 1714, 1663, 1627, 1548 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.07 (t, J = 7.1 Hz, 3H, Me), 4.21 (q, J = 7.1 Hz, 2H, CH_2O), 6.92 (s, 1H, H-5), 7.49 (dd, J = 8.5, 1.8 Hz, 1H, arom.), 7.56–7.64 (m, 2H, arom.), 7.90 (dd, J = 8.3, 1.0 Hz, 2H, arom.), 7.94–7.97 (m, 2H, arom.); ^{19}F NMR (471 MHz, $CDCl_3$) δ –72.3 (s, CF_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 13.7, 62.5, 107.2 (q, $^3J_{C,F}$ = 3.6 Hz, C-5), 117.8 (q, $^1J_{C,F}$ = 273.3 Hz, CF_3), 122.0, 123.7, 127.5, 127.90, 127.91, 128.2, 128.7, 129.3, 131.6, 132.8, 134.0, 148.1 (q, $^2J_{C,F}$ = 39.8 Hz, C-6), 152.1, 156.6, 163.6; MS (EI, 70 eV) *m/z* (%) 362 (100, $[M]^+$), 334 (35), 317 (29), 247 (39); HRMS (ESI): calcd for $C_{19}H_{13}F_3O_4$ $[M]^+$ 362.07659, found 362.07727.

*4.2.7. Ethyl 4-(2-thienyl)-2-oxo-6-(trifluoromethyl)-2H-pyran-3-carboxylate (**6g**).* Yield 22% (0.5 h), light yellow crystals, mp 112–113 °C. IR (ATR): 1747, 1712, 1671, 1557, 1476 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, J = 7.2 Hz, 3H, Me), 4.40 (q, J = 7.2 Hz, 2H, CH_2O), 6.92 (s, 1H, H-5), 7.20 (dd, J = 5.0, 3.9 Hz, 1H, H-4′), 7.53 (dd, J = 3.9, 1.1 Hz, 1H, H-3′), 7.68 (dd, J = 5.0, 1.1 Hz, 1H, H-5′); ^{13}C NMR (126

MHz, $CDCl_3$) δ 13.8, 62.9, 106.0 (q, $^3J_{C,F}$ = 3.7 Hz, C-5), 117.7 (q, $^1J_{C,F}$ = 273.3 Hz, CF_3), 118.7, 129.0, 131.3, 132.3, 135.2, 142.6, 147.6 (q, $^2J_{C,F}$ = 39.7 Hz, C-6), 156.9, 164.0; MS (EI, 70 eV) *m/z* (%) 318 (100, $[M]^+$), 290 (69), 273 (55), 262 (30), 221 (55). Anal. Calcd for $C_{13}H_9F_3O_4S$: C, 49.06; H, 2.85. Found: C, 48.98; H, 2.79.

4.3. General procedure for the synthesis of compounds (7a–g)

A solution of the corresponding pyrone **6** (32 mmol) in AcOH–H_2O–H_2SO_4 (4:2:1, 100 mL) was refluxed for 4 h. When the reaction was complete, the reaction mixture was allowed to cool to room temperature and then diluted with water (100 mL). The solid that formed was filtered and recrystallized from hexane.

*4.3.1. 4-Phenyl-6-(trifluoromethyl)-2H-pyran-2-one (**7a**).* Yield 83%, colourless crystals, mp 60 °C. IR (ATR): 1744, 1698, 1666, 1560 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.67 (d, *J* = 0.9 Hz, 1H, H-3), 6.97 (d, *J* = 0.9 Hz, 1H, H-5), 7.50–7.62 (m, 5H, Ph); ^{19}F NMR (188 MHz, C_6D_6) δ –72.4 (s, CF_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 104.8 (q, $^3J_{C,F}$ = 3.8 Hz, C-5), 113.8, 118.0 (q, $^1J_{C,F}$ = 272.9 Hz, CF_3), 126.6, 129.5, 131.5, 134.1, 148.5 (q, $^2J_{C,F}$ = 39.2 Hz, C-6), 153.3, 159.3; MS (EI, 70 eV) *m/z* (%) 240 (100, $[M]^+$), 212 (92), 171 (58), 115 (80); HRMS (ESI): calcd for $C_{12}H_7F_3O_2$ $[M]^+$ 240.03981, found 240.03995. Anal. Calcd for $C_{12}H_7F_3O_2$: C, 60.01; H, 2.94. Found: C, 59.85; H, 3.00.

*4.3.2. 4-(4-Chlorophenyl)-6-(trifluoromethyl)-2H-pyran-2-one (**7b**).* Yield 90%, colourless crystals, mp 101–102 °C. IR (ATR): 1741, 1670, 1590 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.64 (d, *J* = 0.9 Hz, 1H, H-3), 6.92 (d, *J* = 0.9 Hz, 1H, H-5), 7.49–7.57 (m, 4H, arom.); ^{19}F NMR (471 MHz, $CDCl_3$) δ –72.4 (s, CF_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 104.4 (q, $^3J_{C,F}$ = 3.7 Hz, C-5), 113.9, 118.0 (q, $^1J_{C,F}$ = 273.0 Hz, CF_3), 128.0, 129.9, 132.6, 138.1, 148.8 (q, $^2J_{C,F}$ = 39.3 Hz, C-6), 152.1, 159.1; MS (EI, 70 eV) *m/z* (%) 274 (52, $[M]^+$), 246 (79), 205 (59), 149 (100); HRMS (ESI): calcd for $C_{12}H_6ClF_3O_2$ $[M]^+$ 274.00084, found 274.00052.

*4.3.3. 4-(4-Fluorophenyl)-6-(trifluoromethyl)-2H-pyran-2-one (**7c**).* Yield 87%, colourless crystals, mp 60 °C. IR (ATR): 1740, 1669, 1597, 1566, 1515 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.63 (s, 1H, H-3), 6.94 (s, 1H, H-5), 7.18–7.30 (m, 2H, arom.), 7.57–7.67 (m, 2H, arom.); ^{19}F NMR (188 MHz, $CDCl_3$) δ –108.7 (m, 1F), –72.4 (s, CF_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 104.5 (q, $^3J_{C,F}$ = 3.7 Hz, C-5), 113.6, 116.9 (d, $^2J_{C,F}$ = 22.1 Hz, C-3′, C-5′), 118.1 (q, $^1J_{C,F}$ = 273.0 Hz, CF_3), 128.9 (d, $^3J_{C,F}$ = 8.8 Hz, C-2′, C-6′), 130.4 (d, $^4J_{C,F}$ = 3.3 Hz, C-1′), 148.8 (q, $^2J_{C,F}$ = 39.3 Hz, C-6), 152.2, 159.1, 164.8 (d, $^1J_{C,F}$ = 253.8 Hz, C-4′); MS (EI, 70 eV) *m/z* (%) 258 (17, $[M]^+$), 230 (33), 189 (29), 133 (100); HRMS (ESI): calcd for $C_{12}H_6F_4O_2$ $[M]^+$ 258.03039, found 258.03052.

*4.3.4. 4-(4-Tolyl)-6-(trifluoromethyl)-2H-pyran-2-one (**7d**).* Yield 74%, colourless crystals, mp 114–115 °C. IR (ATR): 1737, 1666, 1609, 1578, 1557 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H, Me), 6.64 (d, *J* = 0.8 Hz, 1H, H-3), 6.97 (d, *J* = 0.8 Hz, 1H, H-5), 7.33 (d, *J* = 8.2 Hz, 2H, arom.), 7.51 (d, *J* = 8.2 Hz, 2H,

arom.); MS (EI, 70 eV) *m/z* (%) 254 (100, $[M]^+$), 226 (87), 185 (46), 129 (50); HRMS (ESI): calcd for $C_{13}H_9F_3O_2$ $[M]^+$ 254.05546, found 254.05500.

*4.3.5. 4-(4-Nitrophenyl)-6-(trifluoromethyl)-2H-pyran-2-one (**7e**).* Yield 69%, colourless crystals, mp 178–180 °C. IR (ATR): 1741, 1667, 1520 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.73 (d, J = 1.0 Hz, 1H, H-3), 6.95 (d, J = 1.0 Hz, 1H, H-5), 7.78 (dd, J = 9.0, 2.3, 2H, arom.), 8.39 (dd, J = 9.0, 2.3 Hz, 2H, arom.); ^{13}C NMR (126 MHz, $CDCl_3$) δ 103.7 (q, $^3J_{C,F}$ = 3.7 Hz, C-5), 110.2, 118.0 (q, $^1J_{C,F}$ = 273.1 Hz, CF_3), 129.1, 129.2, 131.2, 137.4, 146.0, 148.5 (q, $^2J_{C,F}$ = 39.2 Hz, C-6), 159.2; MS (EI, 70 eV) *m/z* (%) 285 (100, $[M]^+$), 257 (86), 216 (80), 160 (36); HRMS (ESI): calcd for $C_{12}H_6F_3NO_4$ $[M]^+$ 285.02489, found 285.02490.

*4.3.6. 4-(2-Naphthyl)-6-(trifluoromethyl)-2H-pyran-2-one (**7f**).* Yield 74%, colourless crystals, mp 114–115 °C. IR (ATR): 1736, 1669, 1629, 1553 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.79 (d, J = 1.1 Hz, 1H, H-3), 7.12 (q, J = 1.1 Hz, 1H, H-5), 7.58–7.68 (m, 3H, arom.), 7.88–8.00 (m, 3H, arom.), 8.10 (d, J = 1.7 Hz, 1H, arom.); ^{19}F NMR (471 MHz, $CDCl_3$) δ –72.3 (s, CF_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 104.8 (q, $^3J_{C,F}$ = 3.7 Hz, C-5), 113.8, 118.1 (q, $^1J_{C,F}$ = 273.0 Hz, CF_3), 123.0, 127.3, 127.4, 127.9, 128.3, 128.9, 129.6, 131.2, 133.0, 134.5, 148.5 (q, $^2J_{C,F}$ = 39.1 Hz, C-6), 153.1, 159.4; MS (EI, 70 eV) *m/z* (%) 290 (100, $[M]^+$), 262 (71), 221 (39), 165 (55); HRMS (ESI): calcd for $C_{16}H_9F_3O_2$ $[M]^+$ 290.05546, found 290.05519.

*4.3.7. 4-(2-Thienyl)-6-(trifluoromethyl)-2H-pyran-2-one (**7g**).* Yield 64%, colourless crystals, mp 141–143 °C. IR (ATR): 1733, 1668, 1560, 1508 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.60 (d, J = 1.1 Hz, 1H, H-3), 6.93 (d, J = 1.1 Hz, 1H, H-5), 7.21 (dd, J = 5.0, 3.8 Hz, 1H, H-4′), 7.57 (dd, J = 3.8, 1.1 Hz, 1H, H-3′), 7.61 (dd, J = 5.0, 1.1 Hz, 1H, H-5′); ^{13}C NMR (126 MHz, $CDCl_3$) δ 104.2 (q, $^3J_{C,F}$ = 3.7 Hz, C-5), 116.1, 117.9 (q, $^1J_{C,F}$ = 273.4 Hz, CF_3), 124.2, 127.9, 140.2, 149.3 (q, $^2J_{C,F}$ = 39.7 Hz, C-6), 149.5, 151.1, 158.4; MS (EI, 70 eV) *m/z* (%) 246 (100, $[M]^+$), 218 (69), 177 (36); HRMS (ESI): calcd for $C_{10}H_5F_3O_2S$ $[M]^+$ 245.99624, found 245.99670.

4.4. Compounds 9a–d

*4.4.1. 3-(Trifluoromethyl)indeno[2,1-c]pyran-1,9-dione (**9a**).* A solution of **6a** (200 mg, 0.64 mmol) in 96% H_2SO_4 (2.0 mL) was heated at 110–125 °C for 10 min. The reaction mixture was cooled to 0 °C and diluted with H_2O (100 mL). The solid that formed was filtered and recrystallized from toluene to give 0.07 g (41%) of **9a**, yellow crystals, mp 244–245 °C. IR (KBr) 1776, 1698, 1633, 1599, 1550 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.14 (s, 1H, H-4), 7.56–7.60 (m, 1H), 7.62–7.66 (m, 2H), 7.74–7.78 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ –72.5 (s, CF_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.8 (q, $^3J_{C,F}$ = 3.5 Hz, C-4), 114.6, 123.1, 125.0, 132.5, 134.4, 134.7, 137.4, 152.7, 156.1 (q, $^2J_{C,F}$ = 39.6 Hz, C-3), 164.8, 188.2 (the quartet of the CF_3 carbon atom was not observed due to its intensity being too low). Anal. Calcd for $C_{13}H_5F_3O_3$: C, 58.66; H, 1.89. Found: C, 58.31; H, 1.76.

*4.4.2. 7-Chloro-3-(trifluoromethyl)indeno[2,1-c]pyran-1,9-dione (**9b**).* A mixture of **6b** (200 mg, 0.58 mmol), 96% H_2SO_4 (1.0 mL), and P_2O_5 (1.0 g, 7.0 mmol) was heated at 120–125 °C for 1–1.5 h. The reaction mixture was cooled to 0 °C and diluted with H_2O (70 mL). The solid that formed was filtered and recrystallized from *p*-xylene to give 80 mg (47%) of **9b** as orange crystals, mp 255–257 °C. IR (ATR): 1778, 1764, 1716, 1630, 1608, 1582, 1573, 1548 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.13 (s, 1H, H-4), 7.53 (d, J = 7.8 Hz, 1H, H-5), 7.62 (dd, J = 7.8, 1.7 Hz, 1H, H-6), 7.74 (d, J = 1.7 Hz, 1H, H-8); ^{19}F NMR (376 MHz, $CDCl_3$): δ –71.4 (s, CF_3). Anal. Calcd for $C_{13}H_4ClF_3O_3$: C, 51.94; H, 1.34. Found: C, 52.13; H, 1.36.

*4.4.3. 7-Fluoro-3-(trifluoromethyl)indeno[2,1-c]pyran-1,9-dione (**9c**).* This product was prepared according to the procedure described for compound **9b**. Yield 110 mg (65%), orange crystals, mp 232–234 °C. IR (ATR): 1771, 1700, 1632, 1596, 1548 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.13 (s, 1H, H-4), 7.31 (td, J = 8.3, 2.3 Hz, 1H, H-6), 7.47 (dd, J = 6.7, 2.3 Hz, 1H, H-8), 7.59 (dd, J = 8.0, 4.2 Hz, 1H, H-5). Anal. Calcd for $C_{13}H_4F_4O_3$: C, 54.95; H, 1.42. Found: C, 54.94; H, 1.33.

*4.4.4. 7-Methyl-3-(trifluoromethyl)indeno[2,1-c]pyran-1,9-dione (**9d**).* This product was prepared according to the procedure described for compound **9a**. Yield 79 mg (61%), orange crystals from petroleum ether/toluene (2:1), mp 210–220 °C (subl.). IR (KBr): 1778, 1698, 1632, 1599, 1550 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.47 (s, 3H, Me), 7.10 (s, 1H, H-4), 7.41 (d, J = 7.6 Hz, 1H, H-6), 7.45 (d, J = 7.6 Hz, 1H, H-5), 7.57 (s, 1H, H-8); ^{19}F NMR (376 MHz, DMSO-d_6): δ –71.4 (s, CF_3). Anal. Calcd for $C_{14}H_7F_3O_3$: C, 60.01; H, 2.52. Found: C, 59.84; H, 2.53.

4.5. Compounds 10a–c

*4.5.1. 2-(Trifluoromethyl)-6H-pyrano[3,4-c]quinoline-4,5-dione (**10a**).* **From 9a**. A mixture of 96% H_2SO_4 (0.13 g), P_2O_5 (0.07 g), and CCl_3CO_2H (1.0 g) was heated until complete melting and **9a** (50 mg, 0.19 mmol) was added. After that, carefully milled NaN_3 (25 mg, 0.38 mmol) in five equal portions was added during 1 h. The reaction mixture was heated at 65 °C for 1.5 h and then diluted with ice H_2O (15 mL). The solid that formed was filtered and recrystallized from ethyl acetate to give 12 mg (23%) of **10a** as light yellow crystals, mp 250 °C (subl.). **From 6a**. A mixture of 96% H_2SO_4 (0.27 g), P_2O_5 (0.13 g), and **6a** (0.20 g, 0.64 mmol) was heated with stirring at 110 °C over 10 min. After that, CCl_3CO_2H (2.0 g) was added, the reaction mixture was heated to 60 °C, and NaN_3 (84 mg, 1.29 mmol) in several small portions over 0.5 h was added. The reaction mixture was heated at 65 °C for 1.5 h and then diluted with ice H_2O (15 mL), the solid that formed was filtered, washed with water, and recrystallized from ethyl acetate (the mother liquor was evaporated and crystallized again) to give 70 mg (39%) of **10a** as light yellow crystals, mp 250 °C (subl.). IR (ATR): 1770, 1651, 1616, 1596, 1538, 1504, 1475 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 7.33 (t, J = 7.6 Hz, 1H, H-9), 7.38 (d, J = 8.2 Hz, 1H, H-7), 7.75 (t, 1H, J = 7.6 Hz, H-8), 8.08 (s, 1H, H-1), 8.46 (d, J = 8.3 Hz, 1H, H-10), 12.25 (s, 1H, NH); ^{19}F NMR (376 MHz, DMSO-d_6): δ –70.6 (s, CF_3); ^{13}C NMR (126 MHz,

DMSO-d_6) δ 101.6, 110.8, 114.1, 115.8, 118.0 (q, $^1J_{C,F}$ = 273.3 Hz, CF_3), 122.6, 126.6, 134.8, 141.1, 147.5 (q, $^2J_{C,F}$ = 38.4 Hz, C-2), 149.1, 154.3, 157.2. Anal. Calcd for $C_{13}H_6F_3NO_3$: C, 55.53; H, 2.15; N, 4.98. Found: C, 55.32; H, 2.29; N, 4.90.

*4.5.2. 8-Chloro-2-(trifluoromethyl)-6H-pyrano[3,4-c]quinoline-4,5-dione (**10b**).* **From 9b**. A solution of **9b** (100 mg, 0.33 mmol) in 96% H_2SO_4 (2.75 g) was heated to 90 °C and NaN_3 (28 mg, 0.43 mmol) was added in several small portions during 0.5 h. Then the reaction mixture was heated at the same temperature for 2.5 h and diluted with ice H_2O (10 mL). The solid that formed was filtered, washed with water, and recrystallized from ethyl acetate to give 59 mg (56%) of **10b** as light yellow crystals, mp 280 °C (subl.). **From 6b**. A mixture of 96% H_2SO_4 (9.0 g), P_2O_5 (5.0 g), and **6b** (0.50 g, 1.44 mmol) was heated with stirring at 110 °C over 1 h. The resulting mixture was cooled to room temperature and NaN_3 (187 mg, 2.87 mmol) was added with vigorous stirring. Then the reaction mixture was heated at 90 °C for 2 h and diluted with ice H_2O (20 mL). The solid that formed was filtered, washed with water, and recrystallized from ethyl acetate (the mother liquor was evaporated and crystallized again) to give 210 mg (49%) of **10b** as light yellow crystals, mp 280 °C (subl.). IR (ATR): 1754, 1651, 1614, 1587, 1471 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.37 (d, J = 8.6 Hz, 1H, H-9), 7.39 (s, 1H, H-7), 8.08 (s, 1H, H-1), 8.51 (d, J = 8.6 Hz, 1H, H-10), 12.30 (s, 1H, NH); ^{19}F NMR (376 MHz, DMSO-d_6): δ –70.6 (s, CF_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 102.2, 111.4, 113.6, 115.5, 118.5 (q, $^1J_{C,F}$ = 273.8 Hz, CF_3), 123.3, 129.3, 140.0, 142.3, 148.3 (q, $^2J_{C,F}$ = 38.6 Hz, C-2), 149.2, 154.7, 157.6. Anal. Calcd for $C_{13}H_5ClF_3NO_3$: C, 49.47; H, 1.60; N, 4.44. Found: C, 49.35; H, 1.56; N, 4.48.

*4.5.3. 8-Fluoro-2-(trifluoromethyl)-6H-pyrano[3,4-c]quinoline-4,5-dione (**10c**).* This product was prepared from **9c** (yield 47%) and from **6c** (yield 43%) according to the procedures described for compound **10b**, white crystals, mp 295–297 °C. IR (ATR): 1774, 1678, 1664, 1624, 1603, 1515, 1465, 1428 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.10 (dd, $^3J_{H,F}$ = 9.8 Hz, $^4J_{H,H}$ = 2.4 Hz, 1H, H-7), 7.22 (td, $^3J_{H,F}$ = $^3J_{H,H}$ = 8.7 Hz, $^4J_{H,H}$ = 2.4 Hz, 1H, H-9), 8.06 (s, 1H, H-1), 8.57 (dd, $^3J_{H,H}$ = 9.0 Hz, $^4J_{H,F}$ = 5.8 Hz, 1H, H-10), 12.31 (s, 1H, NH); ^{19}F NMR (376 MHz, DMSO-d_6): δ –102.8 (td, J = 9.0, 6.0 Hz, F), –70.6 (s, CF_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ 101.4 (d, $^2J_{C,F}$ = 25.5 Hz), 101.6 (q, $^3J_{C,F}$ = 3.4 Hz, C-1), 109.9, 111.1, 111.3, 117.9 (q, $^1J_{C,F}$ = 273.5 Hz, CF_3), 130.0 (d, $^3J_{C,F}$ = 11.1 Hz), 143.0 (d, $^3J_{C,F}$ = 13.2 Hz), 147.6 (q, $^2J_{C,F}$ = 38.4 Hz, C-2), 148.7, 154.1, 157.2, 165.5 (d, $^1J_{C,F}$ = 253.6 Hz, C-4′). Anal. Calcd for $C_{13}H_5F_4NO_3$: C, 52.19; H, 1.68; N, 4.68. Found: C, 51.95; H, 1.48; N, 4.69.

*4.5.4. 4-Methyl-2-oxo-1,2-dihydroquinoline-3-carboxylic acid (4-methylcarbostyril-3-carboxylic acid) (**11**).* A solution of **10a** (18 mg, 0.06 mmol) and NaOH (40 mg, 1.0 mmol) in 70% ethanol (1 mL) was heated to reflux with stirring for 1.5 h. Then the reaction mixture was diluted with HCl (1:2, 5 mL) and the formed precipitate was filtered and recrystallized from 70% ethanol to give 12 mg (92%) of **11** as colourless crystals, mp 273–274 °C (lit.[21] 274–276 °C). ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.56 (s, 3H, Me), 7.29 (ddd, J = 8.2,

7.3, 1.0 Hz, 1H, H-6), 7.37 (dd, *J* = 8.2, 1.0 Hz, 1H, H-8), 7.60 (ddd, *J* = 8.2, 7.3, 1.0 Hz, 1H, H-7), 7.88 (dd, *J* = 8.2, 1.0 Hz, 1H, H-5), 12.20 (br s, 1H, NH), 13.77 (br s, 1H, OH).

4.6. Compounds 12a,b

*4.6.1. 2-Oxo-4-(5-trifluoromethyl-1,2,3-triazol-4-yl)-1,2-dihydroquinoline-3-carboxylic acid (**12a**).* A mixture of **10a** (50 mg, 0.18 mmol) and NaN_3 (23 mg, 0.35 mmol) in DMSO (1 mL) was heated at 120 °C for 3 h. Then the reaction mixture was diluted with HCl (1:2, 8 mL), the formed precipitate was filtered, washed with water, and recrystallized from 50% ethanol to give 46 mg (80%) of **12a** as white crystals, mp 280 °C (decomp.). IR (ATR): 1721, 1623, 1598, 1551, 1523, 1472, 1453 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 6.96 (d, *J* = 7.7 Hz, 1H, H-8), 7.24 (t, *J* = 7.4 Hz, 1H, H-6), 7.51 (d, *J* = 8.0 Hz, 1H, H-5), 7.69 (t, *J* = 7.5 Hz, 1H, H-7), 12.85 (s, 1H, CO_2H), 13.93 (br s, 1H, NH), 16.47 (br s, 1H, NH triaz.); ^{19}F NMR (376 MHz, DMSO-d_6): δ –59.5 (s, CF_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ 116.1, 118.3, 120.8 (q, $^1J_{C,F}$ = 268.4 Hz, CF_3), 123.4, 126.3, 126.4, 132.8, 135.2 (q, $^2J_{C,F}$ = 36.6 Hz, C-5′), 138.2, 159.7, 164.5 (two carbon atoms were not observed due to their intensity being too low). Anal. Calcd for $C_{13}H_7F_3N_4O_3$: C, 48.16; H, 2.18; N, 17.28. Found: C, 48.30; H, 1.90; N, 17.04.

*4.6.2. 7-Chloro-2-oxo-4-(5-trifluoromethyl-1,2,3-triazol-4-yl)-1,2-dihydroquinoline-3-carboxylic acid (**12b**).* This product was prepared according to the procedure described for compound **12a**. Yield 66%, light yellow crystals, mp 286–288 °C (decomp.). IR (ATR): 1705, 1614, 1595, 1494, 1474 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 7.01 (d, *J* = 8.6 Hz, 1H, H-6), 7.26 (d, *J* = 8.6 Hz, 1H, H-5), 7.49 (s, 1H, H-8), 11.0–15.0 (br s, 2H, NH, OH), 15.0–17.5 (br s, 1H, NH triaz.); ^{19}F NMR (376 MHz, DMSO-d_6): δ –59.4 (s, CF_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ 115.2, 117.0, 120.7 (q, $^1J_{C,F}$ = 268.5 Hz, CF_3), 123.4, 128.1, 128.3, 135.3 (q, $^2J_{C,F}$ = 38.0 Hz, C-5′), 137.0, 139.1, 158.9, 164.5 (two carbon atoms were not observed due to their intensity being too low). Anal. Calcd for $C_{13}H_6ClF_3N_4O_3$: C, 43.53; H, 1.69; N, 15.62. Found: C, 43.16; H, 1.52; N, 15.57.

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