Tetrahedron 71 (2015) 8535–8543

Contents lists available at ScienceDirect

Tetrahedron

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

Synthesis of 5-aryl-2-hydroxy-2-(trifluoromethyl)furan-3(2*H*)-ones and their reactions with aromatic 1,2-diamines, hydrazine and hydroxylamine

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ARTICLE INFO

Article history:
Received 16 July 2015
Received in revised form 1 September 2015
Accepted 14 September 2015
Available online 15 September 2015

Keywords:
2-(Trifluoromethyl)furanones
Nitrogen nucleophiles
Quinoxalines
Pyridazines
Pyrazoles
Isoxazoles

ABSTRACT

2-(Trifluoromethyl)furanones were obtained in good yields via the Claisen condensation of acetophenones with methyl 2-methoxytetrafluoropropionate, followed by sulfuric acid-mediated deprotection of the reaction products. These compounds react with 2,3-diaminopyridine, *o*-phenylenediamine and 2,3-diaminonaphthalene in refluxing acetic acid to give the corresponding quinoxaline derivatives, the regioisomeric and tautomeric composition of which was investigated. Reactions of 2-(trifluoromethyl) furanones with hydrazines and hydroxylamine proceeded regioselectively and gave pyridazine, pyrazole and isoxazole derivatives in high yields. Their regiochemistry was established by X-ray diffraction analysis.

1. Introduction

The synthesis of specifically trifluoromethylated molecules has remarkable interest due to the unique physical and biological properties imparted by the CF_3 group.[1] Therefore, the development of a simple method for the preparation of trifluoromethylated building blocks and their further utilization for the synthesis of desired CF_3-containing heterocycles are essential to organic chemistry. In recent years, considerable attention has been given to the development of new procedures for the synthesis of CF_3-containing synthons such as β-chloro-, β-alkoxy and β-aminovinyl trifluoromethyl ketones **1**.[2] These compounds readily react with a wide range of nucleophiles and they are extensively used for the synthesis of various trifluoromethylated heterocycles, which may be of interest in both medicine and agricultural chemistry.[2,3] Generally, nucleophiles initially attack their β-carbon atom with elimination of the leaving group (chloro, alkoxy or amino). On the other hand, the reactions of 1-trifluoromethyl-1,3-diketones **2** with the same nucleophiles usually start with an attack at the carbonyl carbon atom connected to the CF_3 group to give regioisomeric products.[4] Particularly interesting synthons, prepared in this series of trifluoromethylated building blocks, are 2-(trifluoroacetyl)chromones **3**, which can serve as versatile 1,2-dielectrophiles for the double nucleophilic addition of aliphatic and aromatic 1,2-diamines to produce pyrazine and quinoxaline derivatives. In this case, the first step of the reaction involves an attack of the more nucleophilic amino group at C-2 with concomitant opening of the pyrone ring; subsequent intramolecular attack of the second amino group at the trifluoroacetyl group leads to the heterocyclic products.[5]

Although the reactivity of a wide range of CF_3-containing diketones has been studied intensively over the last years,[6] to our knowledge, there are only two communications about the preparation of the CF_3-containing triketones **4**[7a] and **5**,[8] existing in a cyclic furanone form. Due to the concentration of electron-deficient groups in a small carbon skeleton, these compounds are potent trielectrophiles (Fig. 1). Very recently,[7b] it has been found that the methoxy derivative of furanone **4** is a valuable building block for the preparation of a wide range of trifluoromethylated *N*-heterocycles. In connection with our interest in the synthesis of simple and accessible fluoroorganic synthons,[9] we now report on the

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http://dx.doi.org/10.1016/j.tet.2015.09.035
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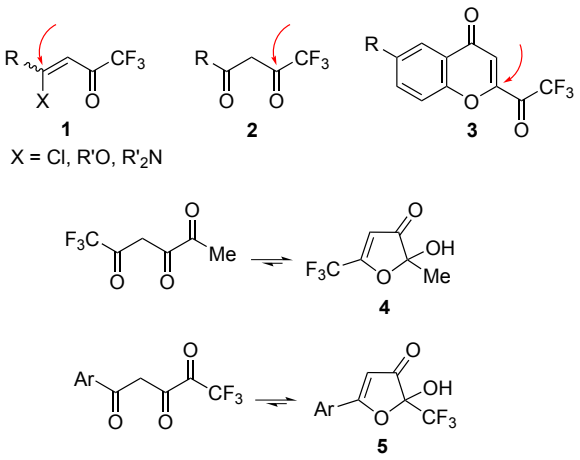


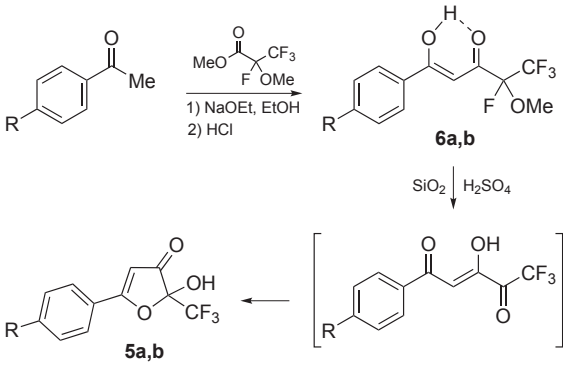
Fig. 1. Trifluoromethylated building blocks **1**–**5** (red arrows indicate the site of the initial attack).

synthesis of furanones **5**, which contain two masked carbonyl groups, and their facile conversion into various five- and six-membered nitrogenated heterocycles bearing a CF_3 group, including quinoxaline derivatives that will be of interest to synthetic and medicinal chemists.

2. Results and discussion

Despite the unique biological and physical properties imparted by the CF_3 group, and the obvious versatility of tricarbonyls as valuable scaffolds for heterocyclic chemistry, 1-trifluoromethyl-1,2,4-triketones have not received much attention, probably owing to the lack of general methods for their synthesis. Our approach to these compounds involves a Claisen condensation of methyl ketones with methyl 2-methoxy-2,3,3,3-tetrafluoropropionate, prepared from hexafluoropropene epoxide. It is known that methanol readily attacks the central carbon atom of hexafluoropropene epoxide, resulting in the formation of 2-methoxytetrafluoropropionyl fluoride, which further reacts with an additional molecule of methanol, forming methyl 2-methoxytetrafluoropropionate.[10] We reasoned that the use of this ester in the Claisen condensation, which represents a readily available starting fluorinated material, would be extremely advantageous, particularly on a preparative multigram scale. To the best of our knowledge, little is known about the Claisen-type preparation of 1,3-diketones from methyl 2-methoxytetrafluoropropionate and their deprotection to trifluoromethylated 1,2,4-triketones, which we deemed suitable for the synthesis of more complex CF_3-containing molecules. Indeed, apart from two our communications,[5,8] there is only one report, in which this ester was used as a carbonyl component in the condensation with cyclohexanone without deprotection.[11]

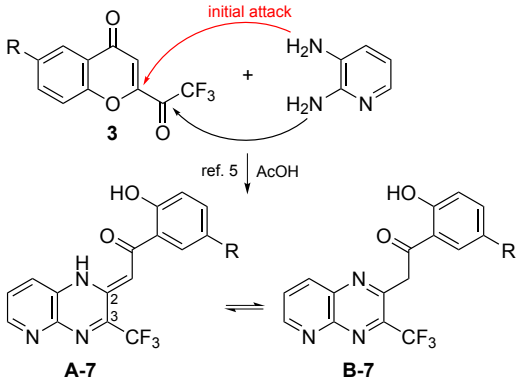
We found that methyl 2-methoxytetrafluoropropionate reacted with acetophenone and *p*-chloroacetophenone under Claisen reaction conditions (refluxing ethanol and NaOEt as a base) affording, after hydrochloric acid hydrolysis, 1,3-diketones **6a**,**b** in high yield (73–79%). Note that in refluxing THF in the presence of LiH the yield of compounds **6a**,**b** was only 33–35%. Deprotection of these diketones, which were fully enolic in $CDCl_3$ (δ_{OH}=15.5–15.6 ppm), was carried out using 96% H_2SO_4 and SiO_2[10b] to afford the corresponding 1,2,4-triketones. The latter underwent spontaneous intramolecular cyclization at the $COCF_3$ group to give 5-aryl-2-hydroxy-2-(trifluoromethyl)furan-3(2*H*)-ones **5a**,**b** in 61–64% yield. These compounds contain three carbonyl groups, with two of them masked in enol ether and ketal forms, i.e., with the two carbonyl groups differently masked (Scheme 1). The structures of 1,3-diketones **6** and furanones **5** were confirmed by elemental analysis, ^1H, ^{19}F, ^{13}C NMR, and IR spectroscopies. Recently, this very practical and convenient approach has been applied by us to the synthesis of 2-(trifluoroacetyl)chromones **3**.[5]



Ar	6	Yield (%)	5	Yield (%)
Ph	**a**	79	**a**	64
4-ClC_6H_4	**b**	73	**b**	61

Scheme 1. Synthesis of compounds **5a**,**b** and **6a**,**b**.

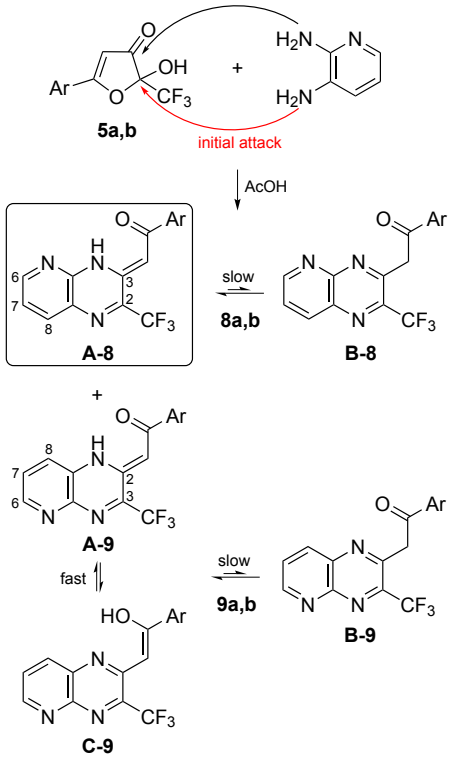
To demonstrate the ability of furanones **5** to undergo regioselective heterocyclization reactions and to determine the site of the initial nucleophilic attack, they were treated with 2,3-diaminopyridine, having two amino groups with different nucleophilicity. In connection with this, it should be noted that when 2-(trifluoroacetyl)chromones **3** were reacted with 2,3-diaminopyridine in acetic acid at room temperature within one week, only 3-CF_3-isomers as a mixture of tautomers **A**-**7** and **B**-**7** precipitated from the reaction mixture[5] (Scheme 2).



Scheme 2. Synthesis of 3-CF_3-pyrido[2,3-*b*]pyrazines **7** (red arrow indicates the site of the initial attack).

In contrast to these results, furanones **5a**,**b** have now been shown to react under the same conditions with 2,3-diaminopyridine to form 2-CF_3-isomers **8a**,**b**, existing principally as the enamine tautomeric form **A**-**8** in 88–94% yield. This reaction proceeds very cleanly without any undesirable side-products. Pyrido[2,3-*b*]pyrazines **8a**,**b** (structure assignment see below) precipitated from the reaction mixture and a simple filtration provides analytically pure products in both cases. However, the reaction conditions were important for the regioselectivity and tautomeric composition. Thus, when furanones **5a**,**b** were reacted with 2,3-diaminopyridine in refluxing AcOH for 4 h, apart from 2-CF_3-isomers **A**-**8** 3-CF_3-isomers **9** as a tautomic mixture and imine tautomers **B**-**8** were observed in a small amount (4–13% for tautomers **9** and 4–6% for **B**-**8**, see experimental part). The

proportions of these tautomers were determined by integration of the CF_3 signals in the ^{19}F NMR spectra. Note that in the case of regioisomers **9a**,**b**, regardless of the reaction conditions, tautomers **B**-**9a**,**b** were found in the crude reaction mixture in only very small amounts (ca. 1%). The first step of the reaction leading to major products **8a**,**b** apparently involves an attack of the more nucleophilic 3-NH_2 group at C-2 of compounds **5** with concomitant opening of the furanone ring. Subsequent intramolecular attack of the less nucleophilic 2-NH_2 group at the carbonyl group leads to pyrido[2,3-*b*]pyrazines **8** (Scheme 3).



Ar	8+9[a]	A-8/B-8	A,C-9/B-9	Yield (%)
Ph	**a**	90:6	3:1	88
4-ClC_6H_4	**b**	83:4	12.5:0.5	94

[a] At reflux in AcOH for 4 h.

Scheme 3. Synthesis and composition of compounds **8** and **9** (red arrow indicates the site of the initial attack).

The structure of the major products **A**-**8a**,**b** was established by the usual spectroscopic analyses. A characteristic feature of their ^1H NMR spectra in a $CDCl_3$ solution is the appearance of a quartet at δ 6.46–6.52 ($^5J_{H,F}$=1.7 Hz) and a singlet at δ 15.1 ppm for the =CH and NH protons, respectively. The CF_3 group in the ^{19}F NMR spectra manifests itself as a doublet at δ 93.4 ppm due to coupling with the =CH proton, in good accordance with the given structure. The assignment of structure **8** to the 2-CF_3-regioisomer is based on the ^1H NMR chemical shifts of the pyridine protons H-6, H-7 and H-8 in its enamine tautomeric form **A**-**8**. A comparison of these chemical shifts in **8a** with the values reported[5] for 2-CF_3-regioisomer **A**-**10** confirms the validity of the structure and shows that 2-CF_3-isomer **8a** exists as a single tautomer **A** with the aminoenone fragment. In the case of 3-CF_3-pyrido[2,3-*b*]pyrazine **9a**, the observed chemical shift of the same pyridine protons is a weighted average of the contributions from **A**-**7** and **B**-**7**[5] indicating an approximately 1:1 mixture of the tautomers **A**-**9a** and **C**-**9a** (Scheme 3). This suggested that in a $CDCl_3$ solution of compound **9a** the proton exchange between the ketoenamine (**A**-**9**) and iminoenol (**C**-**9**) tautomeric forms is too fast and only average signals were observed. The signal of the CF_3 group in **8a** and **9a** as well as the ^1H and ^{19}F NMR spectra of **8b** and **9b** are in accordance with this conclusion. At the same time, the enamine form **A**-**8a** is stable and interconversion of type **A**⇆**C** does not occur, probably because the prototropic shift proceeds very slowly as a result of interaction between the *N*-5 lone pair and NH proton (Scheme 3, Fig. 2).

Obviously, the observed differences in regioselectivity of chromones **3** and furanones **5** is a result of different directions of the initial nucleophilic attack (addition of the more nucleophilic 3-NH_2 group to C-2 of **3**, the former carbonyl adjacent to the CF_3CO group, and to C-2 of **4**, the former carbonyl connected to the CF_3 group) with the formation of 3-CF_3-quinoxalines **7** from **3** and 2-CF_3-quinoxalines **8** from **5**. The regiochemical outcome of the reaction reveals that 2,3-diaminopyridine is a useful dinucleophile for evaluation of the site of the initial nucleophilic attack.

We also found that furanones **5a**,**b** reacted with *o*-phenylenediamine in refluxing acetic acid for 4 h to give products **11a**,**b** as a mixture of enamine and imine tautomers **A** and **B** in 68–87% yield (Scheme 4). In the ^{19}F NMR spectra of **11a**,**b**, the CF_3 group of tautomer **A** appeared as a doublet ($^5J_{F,H}$=1.7–1.9 Hz) at 96.8–96.9 ppm and the CF_3 group of **B** appeared as a triplet ($^5J_{F,H}$=1.6 Hz) or a broadened singlet at 98.9–99.0 ppm (DMSO-d_6, C_6F_6). Thus, this reaction afforded a mixture of two tautomeric forms (ca. 1:1) as was observed previously for their analogues prepared from chromones **3**.[5]

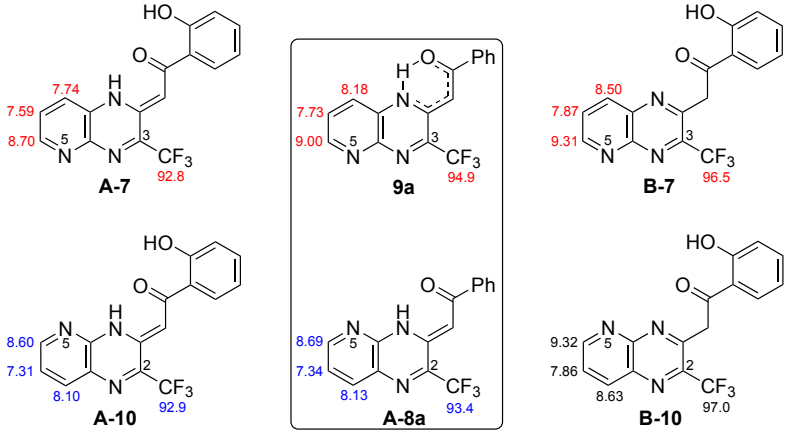
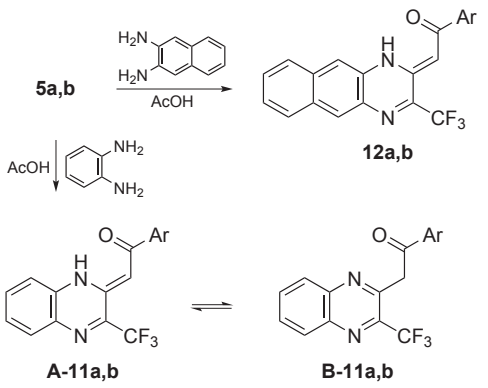


Fig. 2. Diagnostic ^1H and ^{19}F NMR signals (δ, ppm, $CDCl_3$) of compounds **7**–**10**.



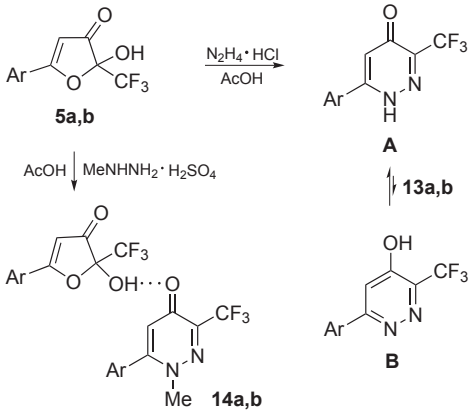
Ar	11	A:B	Yield (%)	12	Yield (%)
Ph	**a**	45:55	68	**a**	84
4-ClC_6H_4	**b**	51:49	87	**b**	97

Scheme 4. Synthesis of compounds **11a**,**b** and **12a**,**b**.

Under similar conditions, 2,3-diaminonaphthalene gave benzo[*g*]quinoxalines **12a**,**b** in excellent yields (84–97%). According to the ^{1}H, ^{19}F and ^{13}C NMR spectra, these compounds are predominantly in the form of enamine tautomer, probably because of the additional benzene ring (Scheme 4). In the ^{19}F NMR spectra of **12a**,**b**, the CF_3 group appeared as a broadened singlet at δ 93.8–93.9 ppm ($CDCl_3$). Since only one structural isomer can be produced in reactions involving the symmetrical diamines such as *o*-phenylenediamine and 2,3-diaminonaphthalene, the structures of the products **11** and **12** require no special discussion. Thus, our results showed that trifluoromethylated 1,2,4-triketones, existing principally as the furanones **5**, behave as a latent 1-trifluoromethyl-1,2-diketone and react with aromatic 1,2-diamines to give various quinoxaline derivatives in high yields. Attempts to prepare the corresponding pyrazine derivative from furanone **5a** and ethylenediamine under various conditions were fruitless due to the more nucleophilic character of this diamine, leading to cleavage of the starting material.

Our next concern was focused on the reactions of furanones **5** with other dinucleophiles, such as hydrazines and hydroxylamine. We found that treatment of compounds **5a** in refluxing AcOH for 8 h with $N_2H_4\cdot 2HCl$ (2 equiv) resulted in the formation of 6-aryl-3-(trifluoromethyl)pyridazin-4(1*H*)-ones **13a**,**b** (yield 81–88%), which exist as a mixture of two tautomeric forms (**A**/**B**=95:5 and 80:20, respectively) in DMSO-d_6 solution (Scheme 5). It should be noted that isomeric 6-phenyl-4-(trifluoromethyl)pyridazin-3(2*H*)-one can be prepared from acetophenone, methyl trifluoropyruvate, and hydrazine hydrate.[12] Interestingly, the reaction of methoxy derivative of furanone **4** with hydrazine hydrate in methanol gave pyrazole derivative as a sole product;[7b] a similar pyrazole formation was observed in the reaction of nonfluorinated furanones.[13]

Several competing pathways in both the initial step of nucleophilic attack and the subsequent heterocyclization would have been expected for the reaction of furanones **5** with methylhydrazine. However, we found that the principal direction of the reaction of $MeNHNH_2\cdot H_2SO_4$ with **5a**,**b** in refluxing AcOH for 12 h is the formation of pyridazin-4-ones **14a**,**b**, which were isolated in 39–45% yield as a 1:1 complex with a furanone molecule (Scheme 5). The crystal structure of complex with **14a** was confirmed by XRD analysis. In according to XRD data, molecules **14a** and **5a** have standard bonds lengths and angles. The furanone ring is planar in limits of 0.015 Å and due to the OH group forms strong intermolecular hydrogen bond OH···O with the carbonyl oxygen atom of **14a** with parameters d(O(2)···O(4) [1−x, 2−y, 1−z])=2.634(2) Å, d(O(2)–H(2))=0.87(3) Å, d(H(2)···O(4) [1−x, 2−y, 1−z])=1.77(3) Å, angle O(2)H(2)O(4) [1−x, 2−y, 1−z] 172(3)°. No any significantly shortened contacts in the crystal packing are observed (Fig. 3).



Ar	13	A:B	Yield (%)	14	Yield (%)
Ph	**a**	95:5	81	**a**	39
4-ClC_6H_4	**b**	80:20	88	**b**	45

Scheme 5. Synthesis of compounds **13a**,**b** and **14a**,**b**.

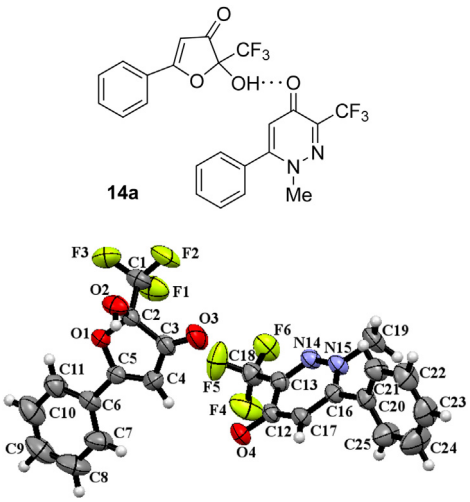
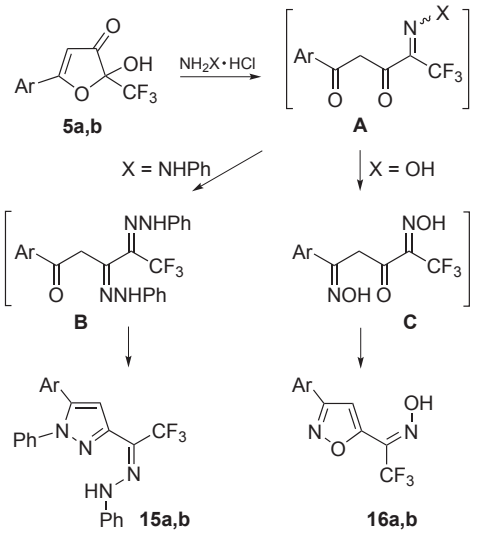


Fig. 3. ORTEP view of compound **14a** according to XRD data (thermal ellipsoids at 50% probability).

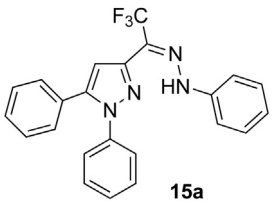
Another reaction route was observed for the reaction of furanones **5a**,**b** with phenylhydrazine hydrochloride (3.5 equiv) under the same conditions (AcOH, reflux, 8 h). In this case, the only isolated products were pyrazoles **15a**,**b** (25–33% yields), which resulted from the double nucleophilic addition of two phenylhydrazine molecules at the C-1 and C-2 atoms of the 1,2,4-tricarbonyl system. The alternative addition of the second phenylhydrazine molecule, involving the C-4 atom, does not occur, and no formation of the regioisomeric pyrazole was detected (Scheme 6). The regiochemistry and *E*-configuration at the C=N double bond of pyrazole **15a** was confirmed by X-ray single crystal analysis (Fig. 4).

When compounds **5a**,**b** were treated with $NH_2OH\cdot HCl$ (2 equiv, AcOH, reflux, 8 h), isoxazoles **16a**,**b** were isolated in 71–74% yield as beige crystals. The regiochemistry of **16b** was unambiguously confirmed by X-ray single crystal analysis (Fig. 5). The difference in behaviour between the hydrochlorides of hydroxylamine and phenylhydrazine in the reaction with furanones **5** is remarkable. In this case, the double nucleophilic addition of two hydroxylamine molecules occurs at the C-1 and C-4 atoms of the 1,2,4-tricarbonyl system. Obviously, the change in the reaction course is a result of the replacement of the phenylamino group by hydroxy group in the binucleophilic agent (Scheme 6).



Ar	15	Yield (%)	16	Yield (%)
Ph	**a**	25	**a**	74
4-ClC$_6$H$_4$	**b**	33	**b**	71

Scheme 6. Synthesis of compounds **15a**,**b** and **16a**,**b**.



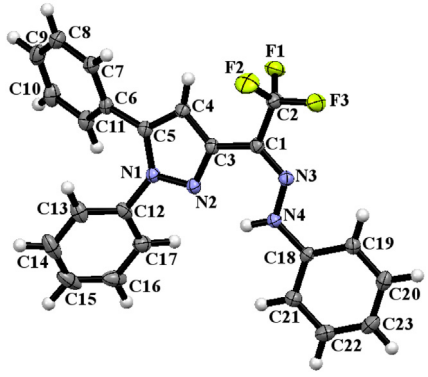
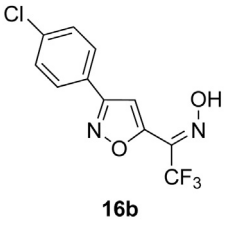


Fig. 4. ORTEP view of compound **15a** according to XRD data (thermal ellipsoids at 50% probability).

Finally, we found that 2-(trifluoroacetyl)chromones **3**[5] react with $NH_2OH\cdot HCl$ (2 equiv) under the same conditions for 4 h to give *E*-oximes **17a**,**b** in excellent yield (Scheme 7). Their configuration was deduced from the chemical shift of the CF_3 group (δ_{CF3}=97.9 ppm for **16a**,**b** and δ_{CF3}=98.4–98.5 ppm for **17a**,**b**).

It is evident from the reactions of furanones **5** with a number of dinucleophiles that the C-2 atom, due to the electron-withdrawing effect of the CF_3 group, is very susceptible to nucleophilic attack, which makes them useful for constructing biologically and medicinally important products. Since many natural products are based on the quinoxaline, pyridazine, pyrazole and isoxazole structures, this



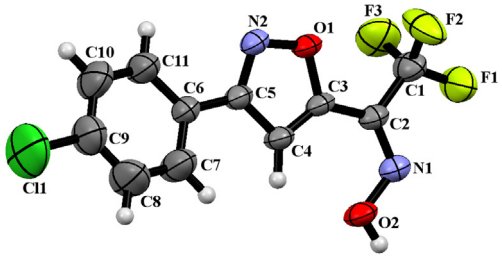
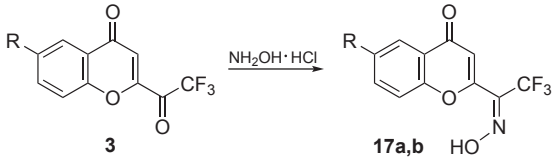


Fig. 5. ORTEP view of compound **16b** according to XRD data (thermal ellipsoids at 50% probability).



Ar	17	Yield (%)
Ph	**a**	83
4-ClC$_6$H$_4$	**b**	90

Scheme 7. Synthesis of compounds **17a**,**b**.

furanone system offers the potential as an entry to the synthesis of trifluoromethylated analogues of these compounds.

3. Conclusion

In summary, we have developed a simple and convenient two-step synthesis of 5-aryl-2-hydroxy-2-(trifluoromethyl)furan-3(2*H*)-ones starting from commercially available acetophenones and hexafluoropropene epoxide via introduction of a CF_3COCO moiety into a ketone methyl group. The compounds obtained, which contain two masked carbonyl groups due to the cyclic furanone form, are of interest as precursors for the synthesis of various trifluoromethylated nitrogenated heterocycles. The latter result from the initial addition of the more nucleophilic centre to the C-2 atom of 2-(trifluoromethyl)furanones.

4. Experimental

4.1. General

^{1}H, ^{19}F and ^{13}C NMR spectra were recorded on Bruker DRX-400 (400, 376, 100 MHz) and AVANCE-500 (500, 470.5, 126 MHz) spectrometers in $CDCl_3$ or DMSO-d_6 with TMS and C_6F_6 as internal standards. IR spectra were recorded on a Perkin–Elmer Spectrum BX-II as KBr discs and Nicolet 6700 instruments (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.

4.2. Synthesis of diketones 6a,b

*4.2.1. (Z)-4,5,5,5-Tetrafluoro-3-hydroxy-4-methoxy-1-phenylpent-2-en-1-one (**6a**)*

4.2.1.1. Method A. A mixture of methyl 2-methoxy-2,3,3,3-tetrafluoropropionate (9.5 g, 50.0 mmol) and acetophenone (5.0 g, 42.0 mmol) was added dropwise to an alcoholic solution of NaOEt obtained by dissolution of sodium (2.9 g, 126.1 mmol) in anhydrous EtOH (50 mL). The resulting reaction mixture was heated at reflux with stirring for 5 h and allowed to stand overnight. Concentrated HCl (20 mL) and water (175 mL) were added to the disodium salt, and the oily product was extracted with ether (3×65 mL). The combined extracts were washed with water (50 mL), dried over anhydrous Na_2SO_4 and evaporated to afford a colourless solid. The solid was recrystallized from petroleum ether (40–70 °C) to give **6a** in 79% yield, beige crystals, mp 56–57 °C. IR (KBr): 1620, 1600, 1573 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.61 (d, $^4J_{H,F}$=0.9 Hz, 3H, MeO), 6.70 (d, $^4J_{H,F}$=2.1 Hz, 1H, =CH), 7.48–7.53 (m, 2H, H-3′, H-5′), 7.62 (tt, J=7.4, 1.3 Hz, 1H, H-4′), 7.95–7.99 (m, 2H, H-2′, H-6′), 15.62 (br s, 1H, OH); ^{19}F NMR (376 MHz, $CDCl_3$) δ 22.8 (q, $^3J_{F,F}$=3.5 Hz, F), 80.6 (d, $^3J_{F,F}$=3.5 Hz, CF_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 53.3 (d, $^3J_{C,F}$=3.1 Hz), 95.4 (d, $^3J_{C,F}$=3.6 Hz), 105.7 (dq, $^1J_{C,F}$=241.2 Hz, $^2J_{C,F}$=34.9 Hz), 119.5 (qd, $^1J_{C,F}$=287.0 Hz, $^2J_{C,F}$=35.1 Hz), 127.6, 129.0, 133.4, 133.8, 182.1 (d, $^2J_{C,F}$=35.0 Hz), 185.7 (d, $^4J_{C,F}$=0.8 Hz); MS (EI, 29 °C): *m/z* (%) 278 $[M]^+$ (5), 147 $[M-C(F)(OMe)CF_3]^+$ (100), 105 $[C_6H_5CO]^+$ (19), 77 $[C_6H_5]^+$ (14), 69 $[CF_3]^+$ (60); MS (EI, 239 °C): *m/z* (%) 228 $[M-F-OMe]^+$ (32), 147 $[M-C(F)(OMe)CF_3]^+$ (58), 105 $[C_6H_5CO]^+$ (49), 102 (100), 77 $[C_6H_5]^+$ (30), 69 $[CF_3]^+$ (44), 44 (50). Anal. Calcd for $C_{12}H_{10}F_4O_3$: C, 51.81; H, 3.62. Found: C, 52.16; H, 3.45.

4.2.1.2. Method B. A mixture of methyl 2-methoxy-2,3,3,3-tetrafluoropropionate (9.5 g, 50.0 mmol) and acetophenone (5.0 g, 42.0 mmol) was added dropwise to a suspension of LiH (0.67 g, 83.8 mmol) in anhydrous THF (40 mL). The resulting reaction mixture was heated at reflux with stirring for 6 h. After that, the mixture was concentrated under reduced pressure, the residue was washed with ether (50 mL), filtered and quenched by addition of 20% H_2SO_4 (100 mL). The oily product obtained was extracted with ether (3×65 mL) and dried over anhydrous Na_2SO_4. After evaporation of the solvent the solid was recrystallized from petroleum ether (40–70 °C) to give **6a** in 35% yield.

*4.2.2. (Z)-1-(4-Chlorophenyl)-4,5,5,5-tetrafluoro-3-hydroxy-4-methoxypent-2-en-1-one (**6b**).* This compound was prepared by the procedure described for **6a**. Yield 73% (method *A*), yield 33% (method *B*), beige crystals, mp 65–66 °C. IR (ATR): 3119, 3064, 3001, 2958, 2858, 1594, 1557, 1486 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.61 (d, $^4J_{H,F}$=0.8 Hz, 3H, MeO), 6.65 (d, $^4J_{H,F}$=2.1 Hz, 1H, =CH), 7.48 (dt, J=8.7, 2.2 Hz, 2H, H-3′, H-5′), 7.90 (dt, J=8.7, 2.2 Hz, 1H, H-2′, H-6′), 15.54 (br s, 1H, OH); ^{19}F NMR (376 MHz, $CDCl_3$) δ 22.9 (q, $^3J_{F,F}$=3.4 Hz, F), 80.7 (d, $^3J_{F,F}$=3.4 Hz, CF_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 53.3 (d, $^3J_{C,F}$=3.1 Hz), 95.3 (d, $^3J_{C,F}$=4.1 Hz), 105.7 (dq, $^1J_{C,F}$=241.2 Hz, $^2J_{C,F}$=35.0 Hz), 119.4 (qd, $^1J_{C,F}$=287.1 Hz, $^2J_{C,F}$=35.1 Hz), 128.9, 129.3, 131.8, 140.3, 182.2 (d, $^2J_{C,F}$=35.1 Hz), 184.4 (d, $^4J_{C,F}$=0.9 Hz). Anal. Calcd for $C_{12}H_9ClF_4O_3$: C, 46.10; H, 2.90. Found: C, 46.24; H, 2.75.

4.3. Synthesis of furanones 5a,b

*4.3.1. 2-Hydroxy-5-phenyl-2-(trifluoromethyl)furan-3(2H)-one (**5a**).* To a suspension of SiO_2 (480 mg, 8.0 mmol) in concentrated sulfuric acid (15 mL), diketone **6a** (6.7 g, 24 mmol) was added in small portions with stirring. The resulting solution was slowly heated with stirring to 90–95 °C for 45 min and allowed to stand for 1 h at this temperature. The cooled mixture was poured on crushed ice (125 g) and extracted with ethyl acetate (3×40 mL). The combined extracts were washed with brine (3×50 mL), dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The solid that formed was recrystallized from cyclohexane/methyl *tert*-butyl ether (10:1) to give **5a** in 64% yield, beige crystals, mp 143–144 °C. IR (KBr): 3066, 1696, 1600, 1588, 1567, 1489 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.0–5.8 (br s, 1H, OH), 6.12 (s, 1H, H-4), 7.52–7.57 (m, 2H, H-3′, H-5′), 7.66 (tt, J=7.6, 1.2 Hz, 1H, H-4′), 7.88–7.91 (m, 2H, H-2′, H-6′); ^1H NMR (500 MHz, DMSO-d_6) δ 6.70 (s, 1H, H-4), 7.63 (t, J=7.6 Hz, 2H, H-3′, H-5′), 7.73 (tt, J=7.4, 1.1 Hz, 1H, H-4′), 7.99–8.03 (m, 2H, H-2′, H-6′), 9.79 (s, 1H, OH); ^{19}F NMR (376 MHz, $CDCl_3$) δ 79.4 (s, CF_3); ^{19}F NMR (376 MHz, DMSO-d_6) δ 81.2 (s, CF_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 97.3 (q, $^2J_{C,F}$=34.8 Hz), 99.3, 120.3 (q, $^1J_{C,F}$=285.9 Hz), 127.1, 127.9, 129.2, 134.4, 186.8, 194.7; ^{13}C NMR (126 MHz, DMSO-d_6) δ 97.7 (q, $^2J_{C,F}$=32.8 Hz), 99.9, 120.7 (q, $^1J_{C,F}$=285.8 Hz), 127.2, 127.4, 129.4, 134.1, 184.2, 194.0; MS (EI): *m/z* (%) 244 $[M]^+$ (48), 216 $[M-CO]^+$ (20), 147 $[M-COCF_3]^+$ (16), 105 $[C_6H_5CO]^+$ (11), 102 (100), 77 $[C_6H_5]^+$ (11), 69 $[CF_3]^+$ (16), 51 (16). Anal. Calcd for $C_{11}H_7F_3O_3$: C, 54.11; H, 2.89. Found: C, 53.99; H, 2.50.

*4.3.2. 5-(4-Chlorophenyl)-2-hydroxy-2-(trifluoromethyl)furan-3(2H)-one (**5b**).* This compound was prepared by the procedure described for **5a**. Yield 61%, beige crystals, mp 146–147 °C. IR (ATR): 3285, 3101, 1700, 1598, 1584, 1558, 1487 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.10 (s, 1H, H-4), 6.3–6.7 (br s, 1H, OH), 7.53 (d, J=8.6 Hz, 2H, H-3′, H-5′), 7.84 (d, J=8.6 Hz, 2H, H-2′, H-6′); ^1H NMR (500 MHz, DMSO-d_6) δ 6.74 (s, 1H, H-4), 7.71 (m, 2H, H-3′, H-5′), 8.02 (m, 2H, H-2′, H-6′), 9.82 (s, 1H, OH); ^{19}F NMR (376 MHz, $CDCl_3$) δ 79.4 (s, CF_3); ^{19}F NMR (376 MHz, DMSO-d_6) δ 81.3 (s, CF_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ 97.8 (q, $^2J_{C,F}$=32.6 Hz), 100.4, 120.6 (q, $^1J_{C,F}$=286.0 Hz), 126.0, 129.1, 129.6, 138.9, 183.0, 194.0. Anal. Calcd for $C_{11}H_6ClF_3O_3$: C, 47.42; H, 2.17. Found: C, 47.40; H, 2.12.

4.4. Synthesis of pyrido[2,3-*b*]pyrazines 8

*4.4.1. (Z)-1-Phenyl-2-(2-(trifluoromethyl)pyrido[2,3-b]pyrazin-3(4H)-ylidene)ethanone (**8a**).* A solution of furanone **5a** (244 mg, 1.0 mmol) and 2,3-diaminopyridine (131 mg, 1.2 mmol) in AcOH (5 mL) was heated at reflux for 4 h and allowed to stand at room temperature overnight. The solid that formed was filtered and washed with cooled ethanol. Yield 88%, red crystals, mp 195–196 °C. IR (ATR): 1620, 1575, 1539 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (**A-8a**, 90%) 6.53 (q, J=1.7 Hz, 1H, =CH), 7.34 (dd, J=8.0, 4.6 Hz, 1H, H-7), 7.45–7.55 (m, 3H, Ph), 7.92–7.97 (m, 2H, Ph), 8.13 (dd, J=8.0, 1.7 Hz, 1H, H-8), 8.70 (dd, J=4.6, 1.7 Hz, 1H, H-6), 15.09 (s, 1H, NH); (**B-8a**, 6%) 5.04 (q, J=1.3 Hz, 2H, CH_2), 7.45–7.55 (m, 2H, Ph), 7.64 (m, 1H, Ph), 7.83 (dd, J=8.4, 4.2 Hz, 1H, H-7), 8.02–8.06 (m, 2H, Ph), 8.60 (dd, J=8.4, 1.8 Hz, 1H, H-8), 9.30 (dd, J=4.1, 1.8 Hz, 1H, H-6); *(Z)-1-phenyl-2-(3-(trifluoromethyl)pyrido[2,3-b]pyrazin-2(1H)-ylidene)ethanone (**9a**)* (**A-9a**, 3%) 6.63 (q, J=1.7 Hz, 1H, =CH), 7.45–7.55 (m, 3H, Ph), 7.73 (dd, J=8.4, 4.1 Hz, 1H, H-7), 7.92–7.97 (m, 2H, Ph), 8.18 (dd, J=8.4, 1.7 Hz, 1H, H-8), 9.00 (dd, J=4.1, 1.7 Hz, 1H, H-6), 15.31 (s, 1H, NH); (**B-9a**, 1%) 4.99 (br q, J=1.3 Hz, 2H, CH_2), 7.45–7.55 (m, 2H, Ph), 7.64 (m, 1H, Ph), 7.83 (dd, J=8.4, 4.1 Hz, 1H, H-7), 8.02–8.06 (m, 2H, Ph), 8.48 (dd, J=8.5, 1.9 Hz, 1H, H-8), 9.30 (m, 1H, H-6); ^{19}F NMR (376 MHz, $CDCl_3$) δ (**A-8a**, 90%) 93.4 (d, $^5J_{F,H}$=1.7 Hz, CF_3), (**B-8a**, 6%) 97.0 (t, $^5J_{F,H}$=1.2 Hz, CF_3), (**A-9a**, 3%) 94.9 (d, $^5J_{F,H}$=1.7 Hz, CF_3), (**B-9a**, 1%) 96.5 (t, $^5J_{F,H}$=1.2 Hz, CF_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ (**A-8a**) 90.2 (q, $^4J_{C,F}$=3.2 Hz), 120.0 (q, $^1J_{C,F}$=276.6 Hz), 121.4, 127.2, 128.7, 129.1, 132.0, 137.9, 138.0, 143.9, 144.0, 144.6 (q, $^2J_{C,F}$=35.6 Hz), 154.5, 186.3. Anal. Calcd for $C_{16}H_{10}F_3N_3O$: C, 60.57; H, 3.18; N, 13.24. Found: C, 60.31; H, 3.17; N, 13.10. Signals for **A-9a** and **B-9a** were abstracted from the spectra of products, isolated from the mother liquor. When the reaction was

conducted in AcOH at room temperature within one week, only 2-CF_3-isomer **A-8a** was obtained in 90% yield.

*4.4.2. (Z)-1-(4-Chlorophenyl)-2-(2-(trifluoromethyl)pyrido[2,3-b]pyrazin-3(4H)-ylidene)ethanone (**8b**).* This compound was prepared by the procedure described for **8a**. Yield 94%, orange crystals, mp 223–224 °C. IR (ATR): 1615, 1574, 1536, 1489 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (**A-8b**, 83%) 6.47 (q, J=1.7 Hz, 1H, =CH), 7.37 (dd, J=8.0, 4.6 Hz, 1H, H-7), 7.45 (d, J=8.6 Hz, 2H, Ar), 7.89 (d, J=8.6 Hz, 2H, Ar), 8.15 (dd, J=8.0, 1.7 Hz, 1H, H-8), 8.71 (dd, J=4.6, 1.7 Hz, 1H, H-6), 15.09 (s, 1H, NH); (**B-8b**, 4%) 4.99 (q, J=1.2 Hz, 2H, CH_2), 7.51 (d, J=8.5 Hz, 2H, Ar), 7.83–7.92 (m, 1H, H-7), 7.99 (d, J=8.6 Hz, 2H, Ar), 8.61 (dd, J=8.4, 1.8 Hz, 1H, H-8), 9.31 (dd, J=4.0, 1.8 Hz, 1H, H-6); *(Z)-1-(4-chlorophenyl)-2-(3-(trifluoromethyl)pyrido[2,3-b]pyrazin-2(1H)-ylidene)ethanone (**9b**)* (**A-9b**, 12.5%) 6.58 (q, J=1.7 Hz, 1H, =CH), 7.46 (d, J=8.7 Hz, 2H, Ar), 7.75 (dd, J=8.4, 4.2 Hz, 1H, H-7), 7.86 (d, J=8.7 Hz, 2H, Ar), 8.20 (dd, J=8.4, 1.7 Hz, 1H, H-8), 9.02 (dd, J=4.2, 1.7 Hz, 1H, H-6), 15.29 (s, 1H, NH); (**B-9b**, 0.5%) 4.95 (br q, J=1.2 Hz, 2H, CH_2), 7.51 (d, J=8.5 Hz, 2H, Ar), 7.83–7.92 (m, 1H, H-7), 7.99 (d, J=8.6 Hz, 2H, Ar), 8.48 (dd, J=8.4, 1.7 Hz, 1H, H-8), 9.30 (m, 1H, H-6); ^{19}F NMR (376 MHz, $CDCl_3$) δ (**A-8b**, 83%) 93.4 (d, $^5J_{F,H}$=1.7 Hz, CF_3), (**B-8b**, 4%) 97.0 (t, $^5J_{F,H}$=1.2 Hz, CF_3), (**A-9b**, 12.5%) 95.0 (d, $^5J_{F,H}$=1.7 Hz, CF_3), (**B-9b**, 0.5%) 96.5 (t, $^5J_{F,H}$=1.2 Hz, CF_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ (**A-8b**) 89.8 (q, $^4J_{C,F}$=3.4 Hz), 120.0 (q, $^1J_{C,F}$=276.5 Hz), 121.6, 128.6, 128.9, 129.2, 136.4, 137.9, 138.3, 143.8, 144.0, 144.5 (q, $^2J_{C,F}$=35.6 Hz), 154.7, 185.0. Anal. Calcd for $C_{16}H_9ClF_3N_3O$: C, 54.64; H, 2.58; N, 11.95. Found: C, 54.37; H, 2.46; N, 11.86. Signals for **A-9b** and **B-9b** were abstracted from the spectra of products, isolated from the mother liquor. When the reaction was conducted in AcOH at room temperature within one week, only 2-CF_3-isomer **A-8b** was obtained in 90% yield.

4.5. General procedure for the synthesis of quinoxalines 11 and 12

A solution of the corresponding furanone **5** (1.0 mmol) and *o*-phenylenediamine or 2,3-diaminonaphthalene (1.2 mmol) in AcOH (5 mL) was heated at reflux for 4 h and allowed to stand at room temperature overnight. The solid that formed was filtered and washed with cooled ethanol to give compounds **11** or **12** as red or orange crystals.

*4.5.1. (Z)-1-Phenyl-2-(3-(trifluoromethyl)quinoxalin-2(1H)-ylidene)ethanone (**11a**).* Yield 68%, red crystals, mp 150–151 °C. IR (ATR): 3064, 1617, 1593, 1572, 1532, 1493 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ (**A**, 45%) 6.45 (q, J=1.9 Hz, 1H, =CH), 7.54–7.64 (m, 2H, Ar), 7.71–7.76 (m, 2H, Ar), 7.90–7.95 (m, 3H, Ar), 8.02–8.14 (m, 2H, Ar), 15.51 (br s, 1H, NH); (**B**, 55%) 5.10 (q, J=1.6 Hz, 2H, CH_2), 7.54–7.64 (m, 3H, Ar), 8.02–8.14 (m, 4H, Ar), 8.20 (dd, J=8.3, 1.3 Hz, 1H, H-8), 8.30 (dd, J=8.3, 1.3 Hz, 1H, H-5); ^{19}F NMR (376 MHz, DMSO-d_6) δ (**A**, 45%) 96.8 (d, $^5J_{F,H}$=1.9 Hz, CF_3), (**B**, 55%) 98.9 (t, $^5J_{F,H}$=1.6 Hz, CF_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ (**A**+**B**) 45.9 (q, $^4J_{C,F}$=2.3 Hz), 88.5 (q, $^4J_{C,F}$=3.1 Hz), 120.8 (q, $^1J_{C,F}$=276.2 Hz), 121.3 (q, $^1J_{C,F}$=276.0 Hz), 123.1, 126.0, 128.2, 128.4, 128.5, 128.94, 129.0, 129.4, 129.6, 131.4, 131.7, 133.3, 133.9, 134.0, 135.5, 135.6, 135.7, 135.9, 138.5, 140.1 (q, $^2J_{C,F}$=34.2 Hz), 141.1 (q, $^2J_{C,F}$=33.9 Hz), 142.3, 146.7, 148.8, 174.3, 196.2. Anal. Calcd for $C_{17}H_{11}F_3N_2O$: C, 64.56; H, 3.51; N, 8.86. Found: C, 64.29; H, 3.51; N, 8.74.

*4.5.2. (Z)-1-(4-Chlorophenyl)-2-(3-(trifluoromethyl)quinoxalin-2(1H)-ylidene)ethanone (**11b**).* Yield 87%, orange crystals, mp 182–183 °C. IR (ATR): 3062, 1618, 1591, 1531, 1487, 1470 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ (**A**, 51%) 6.44 (br q, J=1.7 Hz, 1H, =CH), 7.62 (d, J=8.6 Hz, 2H, Ar), 7.74 (ddd, J=8.1, 7.0, 1.1 Hz, 1H, H-6), 7.93 (ddd, J=8.1, 7.0, 1.1 Hz, 1H, H-7), 7.95 (d, J=8.6 Hz, 2H, Ar), 8.05–8.11 (m, 2H, H-5, H-8), 15.56 (s, 1H, NH); (**B**, 49%) 5.09 (br q, J=1.3 Hz, 2H, CH_2), 7.68 (d, J=8.6 Hz, 2H, Ar), 8.01–8.11 (m, 2H, H-6, H-7), 8.13 (d, J=8.6 Hz, 2H, Ar), 8.19 (dd, J=8.1, 1.4 Hz, 1H, H-8), 8.30 (dd, J=8.1, 1.4 Hz, 1H, H-5); ^{19}F NMR (376 MHz, DMSO-d_6) δ (**A**, 51%) 96.9 (d, $^5J_{F,H}$=1.7 Hz, CF_3), (**B**, 49%) 99.0 (br s, CF_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ (**A**+**B**) 45.8 (q, $^4J_{C,F}$=1.8 Hz), 88.6 (q, $^4J_{C,F}$=3.4 Hz), 120.7 (q, $^1J_{C,F}$=277.2 Hz), 121.3 (q, $^1J_{C,F}$=276.2 Hz), 122.9, 127.9, 128.5, 128.98, 129.03, 129.3, 129.5, 130.2, 131.7, 133.3, 134.0, 134.4, 134.5, 135.5, 135.6, 136.1, 138.5, 138.8, 140.1 (q, $^2J_{C,F}$=33.8 Hz), 141.0 (q, $^2J_{C,F}$=33.8 Hz), 142.2, 146.4, 148.5, 173.4, 195.2. Anal. Calcd for $C_{17}H_{10}F_3ClN_2O$: C, 58.22; H, 2.87; N, 7.99. Found: C, 57.93; H, 2.82; N, 7.96.

*4.5.3. (Z)-1-Phenyl-2-(3-(trifluoromethyl)benzo[g]quinoxalin-2(1H)-ylidene)ethanone (**12a**).* Yield 84%, vinous crystals, mp 196–197 °C. IR (ATR): 3049, 1587, 1543, 1460 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.52 (q, J=1.8 Hz, 1H, =CH), 7.45 (ddd, J=8.2, 6.9, 1.2 Hz, 1H, H-8), 7.46–7.55 (m, 3H, Ph), 7.56 (ddd, J=8.2, 6.9, 1.2 Hz, 1H, H-7), 7.69 (s, 1H, H-10), 7.84 (d, J=8.3 Hz, 1H, H-9), 7.92 (d, J=8.3 Hz, 1H, H-6), 7.95 (m, 2H, Ph), 8.36 (s, 1H, H-5), 15.19 (s, 1H, NH); ^{19}F NMR (376 MHz, $CDCl_3$) δ 93.8 (s, CF_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 90.1 (q, $^3J_{C,F}$=3.3 Hz), 113.3, 120.2 (q, $^1J_{C,F}$=276.5 Hz), 125.8, 127.1, 127.2, 128.7 (2C), 129.1 (2C), 130.2, 131.0, 131.9, 132.4, 135.9, 138.6, 141.5, 144.7 (q, $^2J_{C,F}$=35.1 Hz), 188.0. Anal. Calcd for $C_{21}H_{13}F_3N_2O$: C, 68.85; H, 3.58; N, 7.65. Found: C, 68.70; H, 3.56; N, 7.61.

*4.5.4. (Z)-1-(4-Chlorophenyl)-2-(3-(trifluoromethyl)benzo[g]quinoxalin-2(1H)-ylidene)ethanone (**12b**).* Yield 97%, vinous crystals, mp 244–245 °C. IR (ATR): 3098, 3044, 1589, 1539, 1487 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.48 (q, J=1.8 Hz, 1H, =CH), 7.49 (d, J=8.7 Hz, 2H, Ar), 7.49 (ddd, J=8.2, 6.8, 1.1 Hz, 1H, H-8), 7.60 (ddd, J=8.2, 6.8, 1.1 Hz, 1H, H-7), 7.76 (s, 1H, H-10), 7.88 (d, J=8.2 Hz, 1H, H-9), 7.90 (d, J=8.7 Hz, 2H, Ar), 7.97 (d, J=8.1 Hz, 1H, H-6), 8.42 (s, 1H, H-5), 15.26 (s, 1H, NH); ^{19}F NMR (376 MHz, $CDCl_3$) δ 93.9 (s, CF_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 89.8 (q, $^3J_{C,F}$=3.3 Hz), 113.5, 120.2 (q, $^1J_{C,F}$=276.4 Hz), 125.9, 127.1, 128.4, 128.5, 128.9, 129.1, 129.2, 130.3, 131.1, 132.4, 136.0, 136.9, 138.1, 141.6, 144.5 (q, $^2J_{C,F}$=35.1 Hz), 186.6. Anal. Calcd for $C_{21}H_{12}ClF_3N_2O$: C, 62.93; H, 3.02; N, 6.99. Found: C, 63.06; H, 3.02; N, 6.92.

4.6. Reactions with hydrazines

*4.6.1. 6-Phenyl-3-(trifluoromethyl)pyridazin-4(1H)-one (**13a**).* A solution of furanone **5a** (244 mg, 1.0 mmol) and $N_2H_4 \cdot 2HCl$ (210 mg, 2.0 mmol) in AcOH (5 mL) was heated at reflux for 8 h. The cooled mixture was quenched by addition of water (15 mL) and the solid that formed was filtered, washed with water and recrystallized from ethanol. Yield 81%, beige crystals, mp 291–292 °C. IR (ATR): 3154, 3117, 3078, 3014, 2755, 2361, 1697, 1673, 1627, 1603, 1574, 1552, 1538, 1498, 1471 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ (**A**, 95%) 6.96 (s, 1H, H-5), 7.57–7.66 (m, 3H, Ph), 7.78–7.84 (m, 2H, Ph), 14.07 (br s, 1H, NH); (**B**, 5%) 7.08 (s, 1H, H-5), 7.43–7.55 (m, 3H, Ph), 7.87–7.90 (m, 2H, Ph), 14.48 (br s, 1H, OH); ^{19}F NMR (376 MHz, DMSO-d_6) δ (**A**, 95%) 95.2 (s, CF_3); (**B**, 5%) 97.3 (s, CF_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 117.5, 121.1 (q, $^1J_{C,F}$=274.8 Hz), 127.5, 129.2, 130.2, 131.4, 142.7 (q, $^2J_{C,F}$=30.6 Hz), 152.4, 167.0; MS (EI): *m/z* (%) 240 $[M]^+$ (100), 212 $[M-N_2]^+$ (23), 164 $[M+H-Ph]^+$ (22), 145 $[M-CF_3C{=}N]^+$ (38), 117 $[PhC(NH){=}CH]^+$ (25), 104 $[PhC(NH)]^+$ (85), 89 $[PhC]^+$ (11), 77 $[Ph]^+$ (28), 68 (13), 51 $[CHF_2]^+$ (17). Anal. Calcd for $C_{11}H_7F_3N_2O$: C, 55.01; H, 2.94; N, 11.66. Found: C, 54.77; H, 2.94; N, 12.06.

*4.6.2. 6-(4-Chlorophenyl)-3-(trifluoromethyl)pyridazin-4(1H)-one (**13b**).* This compound was prepared by the procedure described for **13a**. Yield 88%, beige crystals, mp>300 °C. IR (ATR): 3224, 3106, 2680, 1673, 1634, 1601, 1573, 1531, 1496, 1466 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ (**A**, 80%) 6.98 (s, 1H, H-5), 7.68 (d, J=8.5 Hz,

2H, Ar), 7.84 (d, *J*=8.5 Hz, 2H, Ar), 14.09 (br s, 1H, NH); (**B**, 20%) 7.14 (s, 1H, H-5), 7.60 (d, *J*=8.5 Hz, 2H, Ar), 7.92 (d, *J*=8.5 Hz, 2H, Ar), 14.53 (br s, 1H, OH); ^{19}F NMR (376 MHz, DMSO-d_6) δ (**A**, 80%) 95.4 (s, CF_3); (**B**, 20%) 97.5 (s, CF_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ 117.6, 119.9, 122.1, 125.4 (q, $^1J_{C,F}$=273.7 Hz), 127.6, 129.2, 129.4, 136.3, 142.7 (q, $^2J_{C,F}$=30.9 Hz), 151.4, 166.8. Anal. Calcd for $C_{11}H_6ClF_3N_2O$: C, 48.11; H, 2.20; N, 10.20. Found: C, 48.27; H, 2.41; N, 10.56.

*4.6.3. 1-Methyl-6-phenyl-3-(trifluoromethyl)pyridazin-4(1H)-one as complex with 2-hydroxy-5-phenyl-2-(trifluoromethyl)furan-3(2H)-one (**14a**).* A solution of furanone **5a** (244 mg, 1.0 mmol) and $MeNHNH_2 \cdot H_2SO_4$ (290 mg, 2.0 mmol) in AcOH (5 mL) was heated at reflux for 12 h. The cooled mixture was quenched by addition of water (15 mL), kept at room temperature for 24 h and the solid that formed was filtered and washed with water. Yield 39%, colourless crystals, mp 126–127 °C. IR (ATR): 3125, 3073, 2967, 2823, 2688, 2616, 2458, 1719, 1604, 1572, 1540, 1492, 1463 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ (pyridazine part) 3.71 (s, 3H, Me), 6.60 (s, 1H, H-5), 7.53–7.66 (m, 5H, Ph); (furan part) 6.70 (s, 1H, H-4), 7.63 (t, *J*=7.6 Hz, 2H, H-3′, H-5′), 7.73 (tt, *J*=7.4, 1.1 Hz, 1H, H-4′), 7.99–8.03 (m, 2H, H-2′, H-6′), 9.78 (s, 1H, OH); ^{19}F NMR (376 MHz, DMSO-d_6) δ (pyridazine part) 95.3 (s, CF_3); (furan part) 81.2 (s, CF_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ (pyridazine part) 46.0, 120.8 (q, $^1J_{C,F}$=275.2 Hz), 122.0, 128.4, 128.8, 130.4, 132.0, 142.2 (q, $^2J_{C,F}$=30.6 Hz), 155.2, 166.0; (furan part) 97.7 (q, $^2J_{C,F}$=32.8 Hz), 99.9, 120.7 (q, $^1J_{C,F}$=285.8 Hz), 127.1, 127.3, 129.3, 134.0, 184.2, 194.0. Anal. Calcd for $C_{12}H_9F_3N_2O \cdot C_{11}H_7F_3O_3$: C, 55.43; H, 3.24; N, 5.62. Found: C, 55.25; H, 2.91; N, 5.66.

*4.6.4. 1-Methyl-6-(4-chlorophenyl)-3-(trifluoromethyl)pyridazin-4(1H)-one as complex with 2-hydroxy-5-(4-chlorophenyl)-2-(trifluoromethyl)furan-3(2H)-one (**14b**).* This complex was prepared by the procedure described for **14a**. Yield 45%, colourless crystals, mp 130–131 °C. IR (ATR): 3130, 3059, 2997, 2853, 2689, 2624, 2469, 1717, 1603, 1563, 1547, 1486, 1460 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ (pyridazine part) 3.70 (s, 3H, Me), 6.63 (s, 1H, H-5), 7.60–7.68 (m, 5H, Ph); (furan part) 6.74 (s, 1H, H-4), 7.71 (m, 2H, H-3′, H-5′), 8.02 (m, 2H, H-2′, H-6′), 9.84 (s, 1H, OH); ^{19}F NMR (376 MHz, DMSO-d_6) δ (pyridazine part) 95.3 (s, CF_3); (furan part) 81.3 (s, CF_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ (pyridazine part) 46.1, 120.7 (q, $^1J_{C,F}$=275.2 Hz), 122.2, 128.9, 130.5, 130.8, 135.4, 142.2 (q, $^2J_{C,F}$=30.7 Hz), 154.2, 166.0; (furan part) 97.8 (q, $^2J_{C,F}$=32.6 Hz), 100.4, 120.6 (q, $^1J_{C,F}$=286.0 Hz), 126.0, 129.1, 129.6, 138.9, 183.0, 194.0. Anal. Calcd for $C_{12}H_8ClF_3N_2O \cdot C_{11}H_6ClF_3O_3$: C, 48.70; H, 2.49; N, 4.94. Found: C, 48.76; H, 2.37; N, 4.94.

*4.6.5. (E)-1,5-Diphenyl-3-(2,2,2-trifluoro-1-(2-phenylhydrazono) ethyl)-1H-pyrazole (**15a**).* A solution of furanone **5a** (244 mg, 1.0 mmol) and $PhNHNH_2 \cdot HCl$ (505 mg, 3.5 mmol) in AcOH (5 mL) was heated at reflux for 8 h. The resulting mixture was evaporated and the solid that formed was washed with ethanol (2 mL) and recrystallized from ethanol. Yield 25%, light yellow crystals, mp 161–162 °C. IR (ATR): 3203, 3134, 3060, 3027, 1583, 1540, 1525, 1496, 1452 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 6.90 (br q, *J*=1.5 Hz, 1H, H-4), 7.01 (br t, *J*=7.3 Hz, 1H, H-4′), 7.23 (d, *J*=7.9 Hz, 2H, Ph), 7.31–7.38 (m, 4H, Ph), 7.38–7.43 (m, 3H, Ph), 7.45–7.54 (m, 5H, Ph), 12.22 (br s, 1H, NH); ^{19}F NMR (470.5 MHz, DMSO-d_6) δ 99.0 (d, $^5J_{F,H}$=1.3 Hz, CF_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ 106.6 (q, *J*=2.3 Hz), 113.9, 119.6 (q, $^2J_{C,F}$=33.7 Hz), 122.2 (q, $^1J_{C,F}$=272.2 Hz), 122.4, 125.2, 128.5, 128.6, 128.7, 128.8, 129.2, 129.4, 129.5, 138.8, 142.6, 142.7, 143.8. Anal. Calcd for $C_{23}H_{17}F_3N_4$: C, 67.97; H, 4.22; N, 13.79. Found: C, 67.75; H, 4.16; N, 13.69.

*4.6.6. (E)-5-(4-Chlorophenyl)-1-phenyl-3-(2,2,2-trifluoro-1-(2-phenylhydrazono)ethyl)-1H-pyrazole (**15b**).* This compound was prepared by the procedure described for **15a**. Yield 33%, light yellow crystals, mp 174–175 °C. IR (ATR): 3211, 3154, 3102, 3069, 3033, 1714, 1581, 1528, 1498, 1487, 1453 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 6.95 (br q, *J*=1.8 Hz, 1H, H-4), 7.01 (br t, *J*=7.2 Hz, 1H, H-4′), 7.23 (d, *J*=7.6 Hz, 2H, Ar), 7.33–7.39 (m, 4H, Ar), 7.46–7.56 (m, 7H, Ar), 12.18 (br s, 1H, NH); ^{19}F NMR (376 MHz, DMSO-d_6) δ 99.0 (d, *J*=1.8 Hz, CF_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ 106.7 (q, *J*=2.4 Hz), 113.8 (2C), 119.5 (q, $^2J_{C,F}$=33.9 Hz), 122.2 (q, $^1J_{C,F}$=272.2 Hz), 122.3, 125.2 (2C), 127.4, 128.7, 129.4, 129.5, 130.6, 134.0, 138.6, 142.6, 142.7. Anal. Calcd for $C_{23}H_{16}ClF_3N_4$: C, 62.66; H, 3.66; N, 12.71. Found: C, 62.27; H, 3.54; N, 12.68.

4.7. Reactions with hydroxylamine

*4.7.1. (E)-2,2,2-Trifluoro-1-(3-phenylisoxazol-5-yl)ethanone oxime (**16a**).* A solution of furanone **5a** (244 mg, 1.0 mmol) and $NH_2OH \cdot HCl$ (140 mg, 2.0 mmol) in AcOH (5 mL) was heated at reflux for 8 h. The cooled mixture was quenched by addition of water (15 mL), the solid that formed was filtered and washed with water. Yield 74%, beige crystals, mp 209–210 °C. IR (ATR): 3146, 3032, 2861, 2807, 1609, 1594, 1577, 1486, 1468, 1446 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.53–7.57 (m, 3H, Ph), 7.98–8.02 (m, 2H, Ph), 7.99 (s, 1H, H-5), 14.41 (s, 1H, OH); ^{19}F NMR (470.5 MHz, DMSO-d_6) δ 97.9 (s, CF_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ 109.0, 120.3 (q, $^1J_{C,F}$=273.6 Hz), 126.9, 127.4, 129.2, 130.7, 133.5 (q, $^2J_{C,F}$=33.1 Hz), 155.5, 162.4; MS (EI): *m/z* (%) 256 $[M]^+$ (75), 144 $[M-CF_3C{=}NOH]^+$ (91), 116 $[PhC(=N)CH]^+$ (39), 104 $[PhC{=}NH]^+$ (47), 89 $[PhC]^+$ (17), 77 $[Ph]^+$ (100), 69 $[CF3]^+$ (11), 51 $[CHF_2]^+$ (35). Anal. Calcd for $C_{11}H_7F_3N_2O_2$: C, 51.57; H, 2.75; N, 10.94. Found: C, 51.17; H, 2.83; N, 10.74.

*4.7.2. (E)-1-(3-(4-Chlorophenyl)isoxazol-5-yl)-2,2,2-trifluoroethanone oxime (**16b**).* This compound was prepared by the procedure described for **16a**. Yield 71%, beige crystals, mp 220–221 °C. IR (ATR): 3147, 3038, 2865, 2809, 1604, 1588, 1567, 1489 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.62 (d, *J*=8.5 Hz, 2H, Ar), 8.03 (s, 1H, H-5), 8.04 (d, *J*=8.5 Hz, 2H, Ar), 14.43 (s, 1H, OH); ^{19}F NMR (376 MHz, DMSO-d_6) δ 97.9 (s, CF_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ 109.1, 120.3 (q, $^1J_{C,F}$=273.3 Hz), 126.3, 128.8, 129.3, 133.4 (q, $^2J_{C,F}$=33.1 Hz), 135.5, 155.6, 161.5. Anal. Calcd for $C_{11}H_6ClF_3N_2O_2$: C, 45.46; H, 2.08; N, 9.64. Found: C, 45.43; H, 2.12; N, 9.61.

*4.7.3. (E)-2-(2,2,2-Trifluoro-1-(hydroxyimino)ethyl)-4H-chromen-4-one (**17a**).* A solution of chromone **3** (R=H, 300 mg, 1.15 mmol) and $NH_2OH \cdot HCl$ (160 mg, 2.3 mmol) in AcOH (5 mL) was heated at reflux for 4 h. The resulting mixture was allowed to stand at room temperature overnight and the solid that formed was filtered and washed with cooled ethanol. Yield 83%, colourless crystals, mp 218–219 °C. IR (ATR): 3112, 2992, 2724, 1633, 1606, 1590, 1567, 1486 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.02 (s, 1H, H-3), 7.56 (ddd, *J*=7.9, 7.2, 0.7 Hz, 1H, H-6), 7.67 (d, *J*=8.5 Hz, 1H, H-8), 7.88 (ddd, *J*=8.5, 7.2, 1.7 Hz, 1H, H-7), 8.07 (dd, *J*=8.0, 1.7 Hz, 1H, H-5), 14.28 (s, 1H, OH); ^{19}F NMR (470.5 MHz, DMSO-d_6) δ 98.4 (s, CF_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ 115.2, 118.5, 120.1 (q, $^1J_{C,F}$=273.9 Hz), 123.3, 125.0, 126.2, 135.2, 137.5 (q, $^2J_{C,F}$=32.9 Hz), 149.8, 155.3, 176.3. Anal. Calcd for $C_{11}H_6F_3NO_3$: C, 51.37; H, 2.35; N, 5.45. Found: C, 51.23; H, 2.33; N, 5.27.

*4.7.4. (E)-6-Chloro-2-(2,2,2-trifluoro-1-(hydroxyimino)ethyl)-4H-chromen-4-one (**17b**).* This compound was prepared by the procedure described for **17a**. Yield 90%, colourless crystals, mp 231–232 °C. IR (ATR): 3143, 3094, 3011, 2732, 1612, 1591, 1564, 1490, 1466 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.06 (s, 1H, H-3), 7.74 (d, *J*=9.0 Hz, 1H, H-8), 7.91 (dd, *J*=9.0, 2.7 Hz, 1H, H-7), 7.99 (d, *J*=2.6 Hz, 1H, H-5), 14.34 (s, 1H, OH); ^{19}F NMR (470.5 MHz, DMSO-d_6) δ 98.5 (s, CF_3); ^{13}C NMR (126 MHz, DMSO-d_6) δ 115.1, 120.0 (q, $^1J_{C,F}$=274.0 Hz), 121.0, 123.9, 124.4, 130.7, 135.0, 137.2 (q, *J*=33.0 Hz),

150.0, 153.9, 175.3. Anal. Calcd for $C_{11}H_5ClF_3NO_3$: C, 45.31; H, 1.73; N, 4.80. Found: C, 45.14; H, 1.83; N, 5.00.

4.8. Crystallographic data for compounds 14a, 15a, and 16b

XRD experiments were accomplished on 'Xcalibur E' diffractometer with CCD detector on standard procedure (Mo Kα irradiation, graphite monochromator, ω-scans with step 1°). The crystals of compounds **14a** and **16b** were analysed at T=295(2) K, compound **15a** was analysed at T=150.0(1) K; empirical absorption correction was applied. Using Olex2,[14] the structures **14a**, **15a**, and **16b** were solved with the ShelXS structure solution program using direct methods and refined in anisotropic approximation for non-H atoms with the ShelXL refinement package using least-squares minimisation.[15]

4.8.1. Crystal data for ***14a****.* $C_{23}H_{16}F_6N_2O_4$, M=498.38, triclinic, a=9.9966(7) Å, b=10.8579(4) Å, c=11.6639(10) Å, α=102.076(5)°, β=94.618(6)°, γ=111.803(5)°, V=1131.85(13) Å^3, space group P-1 (no. 2), Z=2, μ(Mo Kα)=0.133 mm^{-1}, 9943 reflections measured, 5617 unique (R_{int}=0.0300), which were used in all calculations. The final wR_2 was 0.1850 (all data) and R_1 was 0.0580 (I>2σ(I)). Deposition number CCDC 1412562.

4.8.2. Crystal data for ***15a****.* $C_{23}H_{17}F_3N_4$, M=406.41, monoclinic, a=12.9413(3) Å, b=11.2241(3) Å, c=13.3660(3) Å, β=92.110(2)°, V=1940.16(8) Å^3, space group P2$_1$/n (no. 14), Z=4, μ(Mo Kα)=0.105 mm^{-1}, 10,684 reflections measured, 5304 unique (R_{int}=0.0200), which were used in all calculations. The final wR_2 was 0.1437 (all data) and R_1 was 0.0437 (I>2σ(I)). Deposition number CCDC 1412561.

4.8.3. Crystal data for ***16b****.* $C_{11}H_6ClF_3N_2O_2$, M=290.63, monoclinic, a=4.8234(4) Å, b=27.103(5) Å, c=9.576(2) Å, β=99.320(13)°, V=1235.3(4) Å^3, space group P2$_1$/c, Z=4, μ(Mo Kα)=0.345 mm^{-1}, 7309 reflections measured, 3061 unique (R_{int}=0.0316), which were used in all calculations. The final wR_2 was 0.1201 (all data) and R_1 was 0.0458 (I>2σ(I)). Deposition number CCDC 1412560.

Acknowledgements

This work was financially supported by the Russian Foundation for Basic Research (Grant 14-03-00179) and performed within the State Task from the Ministry of Education and Science of Russian Federation.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2015.09.035.

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