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The unexpected cyclization routes of *N,N′*-bis(oxotrifluoroalkenyl)-1,3-phenylenediamines in polyphosphoric acid medium

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ABSTRACT

The unexpected results of the cyclization reactions of *N,N′*-bis(oxotrifluoroalkenyl)-1,3-phenylenediamines [1,3-C_6H_4-(NHCR=CHC(O)CF_3)$_2$], where R = H, Me, and Ph, in a strongly acidic medium (PPA), allowing the synthesis of new trifluoromethylated heterocycles containing the 1,7-phenanthroline nucleus in 32–40% yields and 7-aminoquinolines (38–40% yields), is reported. The bis-enaminoketone intermediates were easily isolated from the reactions of 4-alkoxy-4-alkyl(aryl)-1,1,1-trifluoroalk-3-en-2-ones with 1,3-phenylenediamine in ethanol under mild conditions (68–86% yields).

Phenanthrolines have been prepared from aminoquinolines[1] or phenylenediamines.[2] From a synthetic point of view, those obtained from phenylenediamines are of particular advantage since both rings can be constructed simultaneously.[2] In addition, it has been observed that the replacement of a hydrogen or halogen atom or of an amino, alkoxy, or alkyl group by a CF_3 group can modulate the physical, chemical, and biological properties.[3] The attachment of a trifluoromethyl entity to a carbon skeleton can be accomplished in several ways.[3,4] One the most satisfactory methods of introducing a CF_3 group into heterocycles is via the trifluoromethylated building block approach.[5–11]

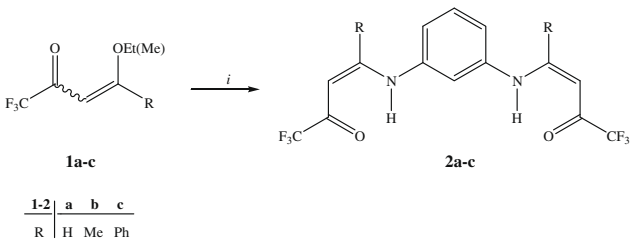
Similarly, enaminones like **2** are versatile readily obtainable reagents and their chemistry has received considerable attention in recent years.[12–18] These enamino-carbonyl compounds represent versatile synthetic precursors that combine the ambident nucleophilicity of enamines with the ambident electrophilicity of enones presenting three nucleophilic and two electrophilic sites.

Herein, we present a general method for the synthesis of enaminones **2a–c** from the reaction of enones **1a–c** with 1,3-phenylenediamine (Scheme 1), as well as a new application of the method previously described by us for the preparation of some trifluoromethyl-substituted benzo[*h*]quinolines,[13] dihydrobenzo[*c*]acridines,[14] cycloalka[*b*]quinolines,[15] and 1,2,3,4-tetrahydroacridines,[16] now applied successfully in the synthesis of bis-trifluoromethylated 1,7-phenanthrolines (**3a–c**) and 7-aminoquinolines (**4b–c**). We also report two interesting intramolecular cyclization routes when enaminones **2a–c** were heated in polyphosphoric acid medium.

Scheme 1 outlines the synthesis of a new series of three trifluoromethylated 1,3-phenylene-bis-enaminone intermediates (**2a–c**) isolated in satisfactory yield (68–86%) from the reaction of 4-alkoxy-4-alkyl(aryl)-1,1,1-trifluoroalk-3-en-2-ones (**1a–c**) with 1,3-phenylenediamine in a molar ratio of 2:1, respectively, when the reactions were carried out in ethanol at 40 °C for 2 h.[26]

4-Alkoxy-4-alkyl(aryl)-1,1,1-trifluoroalk-3-en-2-ones (**1a–c**) are readily available *CCC* synthetic blocks and were prepared from trifluoroacetylation reactions of enol ethers commercially available (for **1a–b**) or generated in situ from the respective acetophenone dimethyl acetal (for **1c**) with trifluoroacetic anhydride, respectively, in the presence of pyridine, as described in the literature.[19]

The structures of compounds **2a–c** were easily established on the basis of ^{1}H and ^{13}C NMR spectroscopy.[27] In order to obtain structural information about the configuration of the compounds **2a–c** we have performed an ^{1}H NMR study on *N,N′*-bis(3-oxo-4,4,4-trifluorobut-1-en-1-yl)-1,3-phenylenediamine (**2a**). The ^{1}H NMR spectrum of **2a** in $CDCl_3$ showed a *cis* coupling constant for the vicinal olefin protons with J ~8 Hz, which is consistent with a *Z*-configuration as the *E*- and *Z*-forms can be easily distinguished by their ^{1}H NMR spectra because the N–H signals of the *E*-form (in 4– 8 ppm) appear at a much higher field than those of the *Z*-form (in 9–13 ppm), indicating the presence of an intramolecular hydrogen bonding in the latter.[20] The ^{1}H NMR chemical shift of the



Scheme 1. Reagents and conditions: (i) = *m*-$(NH_2)_2C_6H_4$ (0.5 equiv), ethanol, 40 °C, 2 h (68–86%).

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enamino hydrogens (NH) for **2a–c** were observed on average at 12.18 ppm, allowing one to assume that the enaminones **2a–c** exist in the *Z,Z*-configuration in $CDCl_3$, which is stabilized by an intramolecular hydrogen bond (N–H···O=C) in each enaminone moiety.

In a second reaction step, the acyclic compounds **2a–c** were subjected to reactions carried out in the presence of a strongly acidic medium (polyphosphoric acid, PPA), in the absence of solvent. For all reactions, initially, PPA ($P_2O_5 + H_3PO_4$) was prepared at 90 °C and the compounds **2a–c** were added to the acid mixture. The cyclization of **2a–c** showed that the best results were at 165 °C for 36 h, affording the corresponding angular new series of bis-trifluoromethyl-substituted 1,7-phenanthrolines (**3a–c)** in 32–40% yields and 7-aminoquinolines (**4b–c)** in 38–40% yields (Schemes 2 and 3).[28]

The structures of **3a–c** were established on the basis of ^1H, ^{13}C NMR spectroscopy[29] and the literature data for similar compounds.[13–16,21] According to the results of the presented synthesis, we found two different mechanisms involved to obtain the phenanthrolines **3a–c**.

The structure pattern of the compound **3a** is different from that of **3b–c**,[29] although obtained under similar reaction conditions. For the 2,8-bis-trifluoromethyl-1,7-phenanthroline **(3a)** the two CF_3 groups occupy the nitrogen-adjacent positions, suggesting the occurrence of two retro 1,4-cyclocondensations (hydrolysis and recombination) at the same molecule **2a** during the closure of the two pyridine rings and following a mechanism already described in the literature for a single cyclocondensation reaction, which allowed the isolation of 2-trifluoromethyl-substituted quinolines[12,17,18,21–24] and benzo[*h*]quinolines.[23,24]

Gerus[12] employed the β-ethoxyvinyl trifluoromethyl ketone **1a** in reaction with aniline to promote the synthesis of the respective quinoline, obtaining the 2-(trifluoromethyl) quinoline isomer, in 30% yield, as the only product by heating the respective enaminone in acidic medium (PPA).

Linderman and Kirollos[21] reported the synthesis of 2-CF_3-substituted quinolines and assigned the chemical shift for the CF_3 group of the ^{13}C NMR spectra as quartets at δ 122.3 ppm (CF_3, $^1J_{CF}$ = 275 Hz) and at δ 148.5 ppm (C2, $^2J_{CF}$ = 34 Hz). In the same Letter, another intramolecular cyclization route was also described, which allowed the synthesis of the 4-(trifluoromethyl)quinoline isomer. With the synthesis of 4-CF_3 quinolines, they reported the ^{13}C NMR spectral data and assigned the chemical shift for the CF_3 group for this regioisomer as quartets at δ 124.2 ppm (CF_3, $^1J_{CF}$ = 275 Hz) and δ 134.8 ppm (C4, $^2J_{CF}$ = 31 Hz), respectively. In some cases, as described by the same authors, the reactions resulted in mixtures of 2- and 4-CF_3 quinolines.

Schlosser et al.[17,18] have investigated in details the synthesis of 2- and 4-(trifluoromethyl)quinolines and quinolinones and determined that some perfluoroalkyl-substituted 3-aminoenones when heated in the presence of phosphoryl chloride cleaved hydrolytically setting free the substituted anilines and the 1,3-dicarbonyl compounds. A proved recombination of these subunits furnished unexpected 2-$(CF_2)_nCF_3$-quinolines. We think that the mechanism suggested by Schlosser may also explain the unexpected findings of our work.

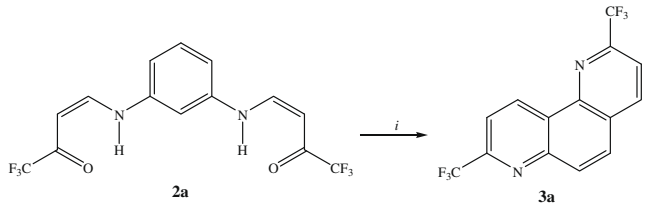
Surprisingly, these two cyclization routes that so far have only been observed separately in some molecules[12,17,18,21,22,24] here occurred for the symmetrical enaminones **2b–c** (R ≠ H) without any isomeric mixture, but also with the isolation of 7-aminoquinolines **4b–c** (Scheme 3).

From the analysis of NMR data we observed that one ring closure occurred by a 1,2-cyclocondensation reaction, while the other occurred by a retro 1,4-cyclocondensation. Thus, one CF_3 group is attached at the nitrogen-remote position (4-CF_3) and in the second ring the CF_3 group is occupying the nitrogen-adjacent position (8-CF_3). These two different mechanisms are involved in the synthesis of a series of 4,8-bis(trifluoromethyl)-1,7-phenanthrolines (**3b–c**). Compounds **3** were separated from the reaction mixture by a sublimation process during the heating of the pure enaminone precursors **2b–c**, in PPA medium.

The 2-alkyl(aryl/heteroaryl)-7-amino-4-(trifluoromethyl) quinolines (**4b–c**) were obtained in 38–40% yields, as by-products, from the reported cyclization reactions and were isolated by recrystallization after the work-up of residual reaction mixtures according to the procedure described.[28] The isolation of **4b–c** suggests also that a hydrolysis reaction occurred in **2b–c**, and the expected recombination of the precursors to allow the synthesis of **3b–c**, due to the high reaction temperature, did not occur totally and probably because the dicarbonyl compounds evaporated from the hot reaction mixtures.

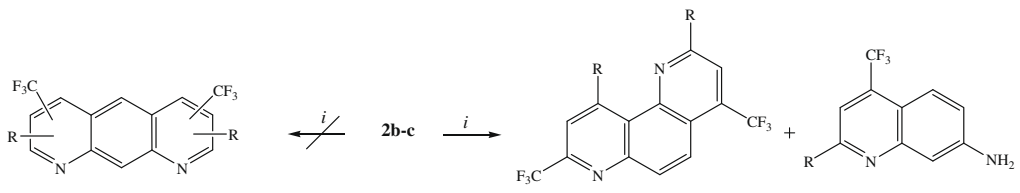
The structures of **4b–c** were established on the basis of ^1H and ^{13}C NMR spectroscopy[30] and the literature data for similar compounds.[21,22,24,25] It is interesting that according to the results observed for cyclization of *N,N′*-bis[3-oxo-4,4,4-trifluorobut-1-en-1-yl]-1,3-phenylenediamine (**2a**) in PPA the respective 7-amino-4-(trifluoromethyl)quinoline (**4a**) or any other quinoline analog was not isolated or observed by NMR experiments.

The possible formation of the 2,10-bis(trifluoromethyl)-1,7-phenanthroline isomer was also excluded because the 5-amino-4-(trifluoromethyl)quinolines were not detected in the cyclization reactions from **2b–c**. The possible formation of the 4,10-bis(trifluo-



2a 3a

Scheme 2. Reagents and conditions: (i) = PPA, 165 °C, 36 h (32%).



5 **3b-c** (38 - 40 %) **4b-c** (38 - 40 %)

2-5	b	c
R	Me	Ph

Scheme 3. Reagents and conditions: (i) = PPA, 165 °C, 36 h.

romethyl)-1,7-phenanthroline isomer was also excluded because the CF-coupling should be present on the NMR spectra as one quartet signal for the CF_3 group and two identical quartets for C-4 and C-10 in the narrow range of δ 147–150 ppm and no quartet signals should be expected in the region of δ 134–135 ppm.

On the other hand, the cyclization reactions of the enaminones **2** by heating in acidic medium (PPA) could result in the synthesis of the linear bis-trifluoromethyl pyrido[*g*]quinolines (**5**), as reported in the literature (Scheme 3).[23] However, the NMR spectrum should show four singlets for H-3, H-5, H-7, and H-10, which were not observed, thus excluding the formation of a linear isomer (pyrido[*g*]quinoline). In our case, all spectroscopic data were consistent with the angular proposed structures for phenanthrolines **3a–c**, which are preferably obtained according to the literature.[2]

Depending on the structure of the *N*,*N*′-bis(oxotrifluoroalkenyl)-1,3-phenylenediamines (**2**), 2,8-bis-(trifluoromethyl)-1,7-phenanthroline or a mixture of separable 4,8-bis-(trifluoromethyl)-1,7-phenanthrolines and 4-(trifluoromethyl)-7-aminoquinolines was obtained. The initial results reported here showed an interesting chemical behavior for the mechanism of cyclization of these new enamino ketones **2**, showing selective routes of ring closure including direct cyclocondensations, hydrolyses, and recombinations, which furnished new fused bis-(trifluoromethyl)-diazatricycles.

Unless otherwise indicated all common reagents and solvents were used as obtained from commercial suppliers without further purification. The melting points were determined using Kofler Reichert-Thermovar and Electrothermal Mel-Temp 3.0 apparatus. ^{1}H, ^{13}C, and ^{19}F NMR spectra were acquired on a Bruker DPX 200 spectrometer (^{1}H at 200.13 MHz) and Bruker DPX 400 (^{1}H at 400.13 MHz, ^{13}C at 100.32 MHz, and ^{19}F at 376.3 MHz) spectrometer, 5 mm sample tubes, 298 K, digital resolution ±0.01 ppm, in $CDCl_3$ for **1**, **2**, **3a–c** and in DMSO-d_6 for **4b–c**, using TMS as internal reference (^{1}H and ^{13}C) or fluorobenzene as external reference (^{19}F). Mass spectra were registered in a HP 6890 GC connected to a HP 5973 MSD and interfaced by a Pentium PC. The GC was equipped with a split–splitless injector, autosampler, cross-linked HP-5 capillary column (30 m, 0.32 mm of internal diameter), and helium was used as the carrier gas. The CHN elemental analyses were performed on a Perkin–Elmer 2400 CHN elemental analyzer (São Paulo University, USP/Brazil).

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References and notes

1. Liska, K. J. *J. Med. Chem.* **1972**, *15*, 1177.
2. Graf, G. I.; Hastreiter, D.; da Silva, L. E.; Rebelo, R. A.; Montalbanb, A. G.; McKillop, A. *Tetrahedron* **2002**, *58*, 9095.
3. Schlosser, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 5432.
4. Schlosser, M. *Synlett* **2007**, 3096.
5. Bonacorso, H. B.; Bittencourt, S. R. T.; Lourega, R. V.; Flores, A. F. C.; Zanatta, N.; Martins, M. A. P. *Synthesis* **2000**, 1431.
6. Cottet, F.; Marull, M.; Lefebvre, O.; Schlosser, M. *Eur. J. Org. Chem.* **2003**, 1559.
7. Marull, M.; Schlosser, M. *Eur. J. Org. Chem.* **2003**, 1576.
8. Ondi, L.; Lefebvre, O.; Schlosser, M. *Eur. J. Org. Chem.* **2004**, 3714.
9. Dubinina, G. G.; Furutachi, H.; Vicic, D. A. *J. Am. Chem. Soc.* **2008**, *130*, 8600.
10. Martins, M. A. P.; Machado, P.; Rosa, F. A.; Cunico, W.; Bonacorso, H. G.; Zanatta, N. *Mini-Rev. Org. Chem.* **2008**, *5*, 53.
11. Bonacorso, H. G.; Porte, L. M. F.; Cechinel, C. A.; Paim, G. R.; Deon, E. D.; Zanatta, N.; Martins, M. A. P. *Tetrahedron Lett.* **2009**, *50*, 1392.
12. Gerus, I. I.; Gorbunova, M. G.; Kukhar, V. P. *J. Fluorine Chem.* **1994**, *69*, 195.
13. Bonacorso, H. B.; Duarte, S. H. G.; Zanatta, N.; Martins, M. A. P. *Synthesis* **2002**, 1037.
14. Bonacorso, H. G.; Drekener, R. L.; Rodrigues, I. R.; Vezzosi, R. P.; Costa, M. B.; Martins, M. A. P.; Zanatta, N. *J. Fluorine Chem.* **2005**, *126*, 1384.
15. Bonacorso, H. G.; Moraes, T. S.; Zanatta, N.; Martins, M. A. P.; Flores, A. F. C. *ARKIVOC* **2008**, *xvi*, 75.
16. Bonacorso, H. G.; Moraes, T. S.; Zanatta, N.; Martins, M. A. P. *Synth. Commun.* **2009**, *39*, 3677.
17. Schlosser, M.; Keller, H.; Sumida, S.-I.; Yang, J. *Tetrahedron Lett.* **1997**, *38*, 8523.
18. Marull, M.; Lefebvre, O.; Schlosser, M. *Eur. J. Org. Chem.* **2004**, 54.
19. (a) Hojo, M.; Masuda, R.; Kokuryo, Y.; Shioda, H.; Matsuo, S. *Chem. Lett.* **1976**, 499; (b) Effenberger, F.; Maier, R.; Schonwalder, K. H.; Ziegler, T. *Chem. Ber.* **1982**, *115*, 2766; (c) Effenberger, F.; Schonwalder, K. H. *Chem. Ber.* **1984**, *117*, 3270; (d) Kamitori, Y.; Hojo, M.; Masuda, R.; Fujitani, T.; Kobuchi, T.; Nishigaki, T. *Synthesis* **1986**, 340; (e) Hojo, M.; Masuda, R.; Okada, E. *Synthesis* **1986**, 1013; (f) Hojo, M.; Masuda, R.; Sakaguchi, S.; Takagawa, M. *Synthesis* **1986**, 1016; (g) Colla, A.; Martins, M. A. P.; Clar, G.; Krimmer, S.; Fischer, P. *Synthesis* **1991**, 483; (h) Martins, M. A. P.; Emmerich, D. J.; Pereira, C. M. P.; Cunico, W.; Rossato, M.; Zanatta, N.; Bonacorso, H. G. *Tetrahedron Lett.* **2004**, *45*, 4935.
20. Zhuo, J.-C. *Magn. Reson. Chem.* **1997**, *35*, 21.
21. Linderman, R. J.; Kirollos, K. S. *Tetrahedron Lett.* **1990**, *31*, 2689.
22. Keller, H.; Schlosser, M. *Tetrahedron* **1996**, *52*, 4637.
23. Riedel, D.; Feindt, A.; Pulst, M. *J. Prakt. Chem.* **1995**, *337*, 34.
24. Sloop, J. C.; Bumgardner, C. L.; Loehle, W. D. *J. Fluorine Chem.* **2002**, *118*, 135.
25. Panda, K.; Siddiqui, I.; Mahata, P. K.; Junjappa, H. *Synlett* **2004**, 449.
26. Synthesis of *N*,*N*′-bis(oxotrifluoroalkenyl)-1,3-phenylenediamines (**2a–c**). General procedure: To a stirred solution of 1,3-phenylenediamine (0.54 g, 5 mmol) in ethanol (10 mL), **1a–c** (10 mmol) was added at room temperature. The mixture was stirred for 2 h at 40 °C. After the end of the reaction (TLC), the resulting solid products **2a–c** were isolated by filtration (1st fraction—80%). Subsequently, the filtrates were evaporated under reduced pressure and the residues were dissolved in hot chloroform and stirred with activated charcoal. After filtration, the filtrates were evaporated under reduced pressure. Then, the crude oily products **2** were dissolved in hot ethanol and subsequently cooled (4–8 °C, 48 h) to give **2** as powders (2nd fraction—20%). Finally, both fractions were gathered and recrystallized from chloroform (68–86% yields).
27. Compounds **2a–c** were characterized by ^{1}H and ^{13}C NMR. Spectral data of compound **2a**: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 11.74 (d, J = 12 Hz, 2H, NH), 7.63 (dd, J_1 = 8, J_2 = 12 Hz, 2H, H-1), 7.41 (t, J = 8 Hz, 1H, H-9), 6.95 (dd, J_1 = 2, J_2 = 8 Hz, 2H, H-8, H-10), 6.86 (t, J = 2 Hz, 1H, H-6), 5.71 (d, J = 8 Hz, 2H, H-2). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.3 (q, ^2J = 34 Hz, 2 C-3), 149.3 (2 C-1), 140.3 (2C, C-5, C-7), 131.3 (C-6), 116.5 (q, ^1J = 289 Hz, $2CF_3$), 113.8 (2C, C-8, C-10), 105.7 (C-9), 90.3 (2 C-2). GC–MS (EI, 70 eV): *m*/*z* (%) = 352 (M^+, 100), 283 (55), 213 (23), 185 (33), 107 (24), 263 (11), 69 (5). ^{19}F NMR (376 MHz, $CDCl_3$): δ = −75.35 (2-CF_3). Anal. Calcd. For $C_{14}H_{10}F_6N_2O_2$ (352.06): C, 47.74; H, 2.86; N, 7.95. Found: C, 48.03; H, 2.96; N, 7.85. Melting points and yields of new compounds 2: Compound [mp (°C), yield (%)]: **2a** [171–173, 68]; **2b** [126–128 °C, 86]; **2c** [190–192, 80].
28. Synthesis of 2,8-bis(trifluoromethyl)-1,7-phenantroline (**3a**) and 2,10-substituted-4,8-bis(trifluoromethyl)-1,7-phenanthrolines (**3b–c**) and 7-aminoquinolines (**4b–c**). General procedure: To a stirred mixture of H_3PO_4 (2 mL) and P_2O_5 (3 g) (PPA) at 90°, **2a–c** (2 mmol) were added. Using a 10 cm length glass adapter connecting the reaction flask and the condenser, the mixture was stirred for 36 h at 165 °C. After this time, the sublimated products **3a–c** were recovered from the adapter using chloroform and the remaining amounts of **3** in the reaction flask were also extracted with chloroform. Both organic fractions were recrystallized from chloroform (32–40% yields). To the dark residue remainder in the reaction flask were added 20 g of crushed ice and ethyl acetate (20 mL). After stirring, the 7-aminoquinolines (**4b–c**) were isolated when the aqueous phase was extracted with ethyl acetate (6 × 20 mL) combined with NaOH solution 40% (5 mL). The organic layer was washed with distilled water (3 × 15 mL) and dried over sodium sulfate. After filtration, the liquid phase was stirred and heated in the presence of activated charcoal, filtered again, and the solvent was removed under reduced pressure. The resulting powders (**4b–c**) were recrystallized from a mixture of ethyl acetate/hexane (3:1 v/v) (38–40% yields).
29. Compounds **3a–c** were characterized by ^{1}H and ^{13}C NMR. Spectral data of compound **3a**: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.79 (d, J = 9 Hz, 1H, H-10), 8.48 (d, J = 8 Hz, 1H, H-4), 8.27 (d, J = 9 Hz, 1H, H-3), 8.11 (d, J = 9 Hz, 1H, H-9), 8.03 (d, J = 8 Hz, 1H, H-5), 8.01 (d, J = 8 Hz, 1H, H-6). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.6 (q, ^2J = 35 Hz, C-2), 149.0 (C-10b), 147.6 (q, ^2J = 35 Hz, C-8), 144.6 (C-6a), 137.8 (C-10), 135.2 (C-4), 130.9 (C-6), 129.7 (C-5), 128.0 (C-10a), 127.9 (C-4a), 121.5 (q, ^1J = 275 Hz, CF_3), 119.2 (C-3), 118.4 (C-9). ^{19}F NMR (376 MHz, $CDCl_3$): δ = −67.12, −67.26 (CF_3-2, CF_3-8). GC–MS (EI, 70 eV): *m*/*z* (%) = 316 (M^+, 100); 297 (16); 247 (77); 227 (17); 177 (28); 69 (5). Anal. Calcd for $C_{14}H_6F_6N_2$ (316.20): C, 53.18; H, 1.91; N, 8.86. Found: C, 53.34; H 2.01; N, 8.91. Spectral data of compound **3b**: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.23 (dq, J_1 = 2, J_2 = 8 Hz, 1H, H-5), 8.15 (d, J = 8 Hz, 1H, H-6), 7.74 (s, 1H, H-3), 7.70 (s, 1H, H-9), 3.33 (s, 3H, CH_3), 2.86 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.1 (C-10), 151.5 (C-2), 149.6 (C-10b), 148.0 (C-6a), 147.6 (q, ^2J = 34 Hz, C-8), 134.3 (q, ^2J = 31 Hz, C-4), 130.5 (C-10a), 126.5 (C-6), 125.2 (q, ^4J = 3 Hz, C-5), 121.6 (q, ^3J = 5 Hz, C-3), 120.0 (C-4a), 124.0 (q, ^1J = 275 Hz, CF_3), 123.4 (q, ^1J = 275 Hz, CF_3), 118.5 (q, ^3J = 5 Hz, C-9), 27.2 (CH_3), 25.1 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ = −60.46 (CF_3-4), −67.36 (CF_3-8). GC–MS (EI, 70 eV): *m*/*z* (%) = 344 (M^+, 100); 325 (19); 275 (19); 172 (8); 69 (6). Anal. Calcd for $C_{16}H_{10}F_6N_2$ (344.25): C, 55.77; H, 2.90; N, 8.13. Found: C, 55.48; H, 3.14; N, 8.03. Melting points and yields of new compounds **3**: Compound [mp (°C), yield (%)]: **3a** [131–133, 32]; **3b** [147–149 °C, 38]; **3c** [226–228, 40].
30. Compounds **4b–c** were characterized by ^{1}H and ^{13}C NMR. Spectral data of compound **4b**: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.87 (dq, J_1 = 2, J_2 = 9 Hz, 1H, H-

5), 7.30 (s, 1H, H-3), 7.21 (d, J = 2 Hz, 1H, H-8), 7.02 (dd, J_1 = 2, J_2 = 9 Hz, 1H, H-6), 4.18 (s, 2H, NH), 2.72 (s, 3H, 2 CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.1 (C-2), 150.7 (C-8a), 150.6 (C-7), 132.2 (q, ^2J = 30 Hz, C-4), 123.6 (C-5), 119.5 (C-6), 118.3 (q, ^1J = 275 Hz, CF_3), 113.5 (q, ^3J = 5 Hz, C-3), 112.2 (C-4a), 106.8 (C-8), 24.7 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ = −61.25 (CF_3-4). GC–MS (EI, 70 eV): m/z (%) = 226 (M^+, 100); 210 (7), 199 (31); 157 (8); 142 (7); 69 (6). Anal. Calcd for $C_{11}H_9F_3N_2$ (226.07): C, 58.41; H, 4.01; N, 12.38. Found: C, 58.04; H, 4.01; N, 12.01. Melting points and yields of new compounds **4**: Compound [mp (°C), yield (%)]: **4b** [174–176, 40]; **4c** [139–141 °C, 38].