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CF_3-substituted 1,3-dicarbonyl compounds in the Biginelli reaction promoted by chlorotrimethylsilane

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ABSTRACT

Trifluoromethyl-1,3-diones were investigated as reactants in the Biginelli reaction promoted by Me_3SiCl. The dependence of the reaction pathway on the nature of substituent at the α-position to the carbonyl group was established. A set of new CF_3-containing dihydropyrimidine(thi)one derivatives was obtained. A number of novel 5-CF_3CO dihydropyrimidine(thi)ones were synthesized.

1. Introduction

Recently, we became interested in derivatives of dihydropyrimidones (DHPMs), which have diverse pharmacological activities. They are classified as one of the most important groups of drug-like scaffolds [1a]. The Biginelli reaction is a powerful tool for the facile synthesis of these scaffolds [1b,c]. It was shown that the use of TMSCl in this reaction allowed extending its scope [2]. Continuing our research on DMF/TMSCl condensing system we wished to use CF_3-substituted 1,3-dicarbonyl compounds as the reactants in the mentioned reaction. Before the trifluoromethyl-β-diketones and ethyl 4,4,4-trifluoro-3-oxobutanoate were subjected to Biginelli reaction with unsubstituted (thio)urea [3,4], guanidine [5a], aminotetrazole and amino-1,2,4-triazole [5b]. In this paper we compare the procedure employing DMF/TMSCl with the literature data on unsubstituted urea **5a** and thiourea **5e**, and report the results of extending the mentioned reaction to their substituted analogues **5b–d** and **5f–h** (Fig. 1). Benzaldehyde **6** was chosen as model aldehyde for this investigation.

2. Results and discussion

First, we subjected the unsubstituted urea **5a** and thiourea **5e**, to the Biginelli reaction. These building-blocks reacted accordingly to the established procedure, taking 1:1:1:4 molar ratio of (thio)urea, aldehyde, CF_3-β-diketones and Me_3SiCl in DMF solution (Scheme 1) [2a]. The reactions came to completion in 24–48 h at room temperature afford compounds **7–10a**, **7–10e**, which is in agreement with the literature data [3]. In our case, stereoselectivity observed leading to exclusive formation of the diastereoisomers shown in Scheme 2. The spectroscopic data for products **7a** and **8a** are similar to compounds, which structure has been previously determined by X-ray diffraction [3b,h].

With the substituted ureas and thioureas, which have never been subjected to Biginelli reaction with trifluoromethyl-β-diketones, an interesting dependence of chemical behavior of diketones **1–4** on the substituent R was disclosed. For R = Ph, OEt, CF_3 and R_2 = H the formation of expected products **7**, **9**, **10 (b,f,h)** was observed (Scheme 2). As for compounds **7–10a**, the same relative configuration of the stereocenters was observed, which was confirmed by NOESY experiments for the compounds **9b**, **9f** and **8a** (Fig. 2). The most convincing evidence of this is the observation of NOE correlation between H4 and (C6)-OH group marked in red.

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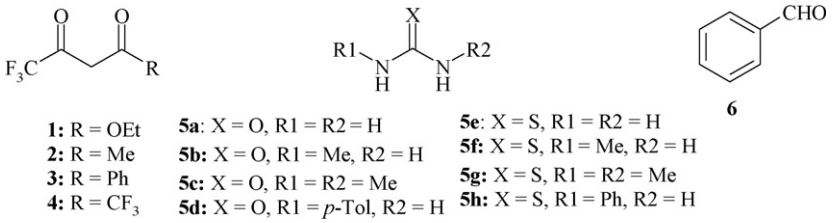
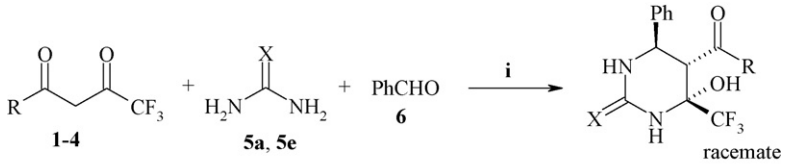
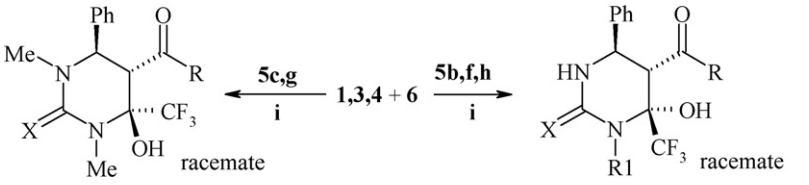


Fig. 1. The structures of model starting compounds for Biginelli reaction.



7a: R = OEt, X = O (75%); **7e**: R = OEt, X = S (79%)
8a: R = Me, X = O (69%); **8e**: R = Me, X = S (68%)
9a: R = Ph, X = O (85%); **9e**: R = Ph, X = S (82%)
10a: R = CF_3, X = O (71%); **10e**: R = CF_3, X = S (65%)

Scheme 1. *Reagents and conditions:* i, 4 eq. Me3SiCl, DMF, rt, 24–48 h.



7c: R = OEt, X = O (52%)
7g: R = OEt, X = S (48%)
9c: R = Ph, X = O (56%)
9g: R = Ph, X = S (51%)
10c: R = CF_3, X = O (41%)

7b: R = OEt, X = O, R1 = Me (73%)
7f: R = OEt, X = S, R1 = Me (60%)
7h: R = OEt, X = S, R1 = Ph (56%)
9b: R = Ph, X = O, R1 = Me (74%)
9f: R = Ph, X = S, R1 = Me (57%)
10b: R = CF_3, X = O, R1 = Me (57%)

Scheme 2. *Reagents and conditions:* i, 4 eq. Me_3SiCl, DMF, rt, 48–72 h.

In the case of *N*,*N*′-dimethyl(thio)urea **5c**,**g** and diketones **1**, **3**, **4** formation of diastereomers **7, 9, 10(c,g)**, possessing other relative configuration of the stereocenters, occurred. The stereochemistry of the products was also confirmed by NOE-experiments for compounds **9c** and **9g** (Fig. 3). In this case, instead of correlation between H4 and (C6)-OH group, correlation between H5 and (C6)-OH group was observed. Correlation between (C6)-OH group and *ortho*-protons of (C5)-COPh groups is an additional evidence for the relative configuration. Finally the structure of compound **9c** was unambiguously determined by single crystal X-ray diffraction study (Fig. 4).

At the same time, for the diketone **2** (R = Me), the cyclization leads to compounds **11**. These data are in agreement with the results obtained previously for the Friedländer reaction [6] and can be explained by the bulkiness of TMSCl. Some parallels with reaction of trifluoromethyl-β-diketones with hydrazines can be outlined [7] (Scheme 3).

To the best of our knowledge, compounds **11** are the first examples of DHPMs with the CF_3CO groups at the 5th positions [8].

The formation of structures **11** is fully confirmed by analysis of the corresponding spectral data, e.g. the signal of CF_3 group in ^{19}F

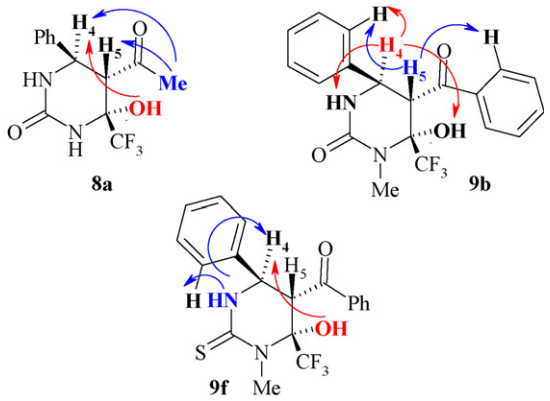


Fig. 2. Significant NOE-correlations for compounds **8a**, **9b** and **9f**. (For interpretation of the references to colour in the text regarding this figure, the reader is referred to the web version of the article.)

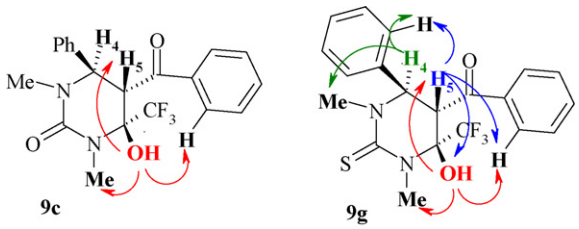


Fig. 3. Significant NOE-correlations for compounds **9c** and **9g**.

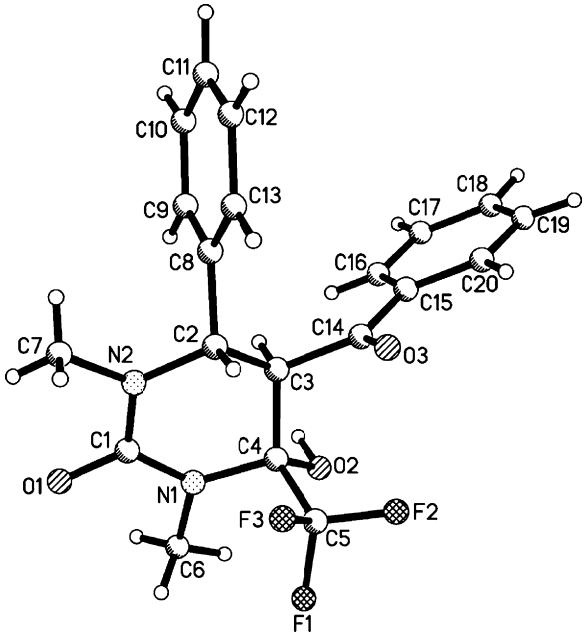
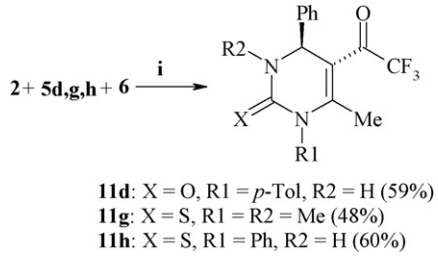


Fig. 4. Single crystal X-ray structure of **9c**.



Scheme 3. *Reagents and conditions:* i, 4 eq. Me_3SiCl, DMF, rt, 48–72 h.

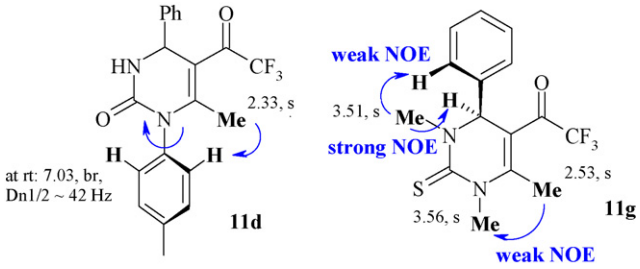
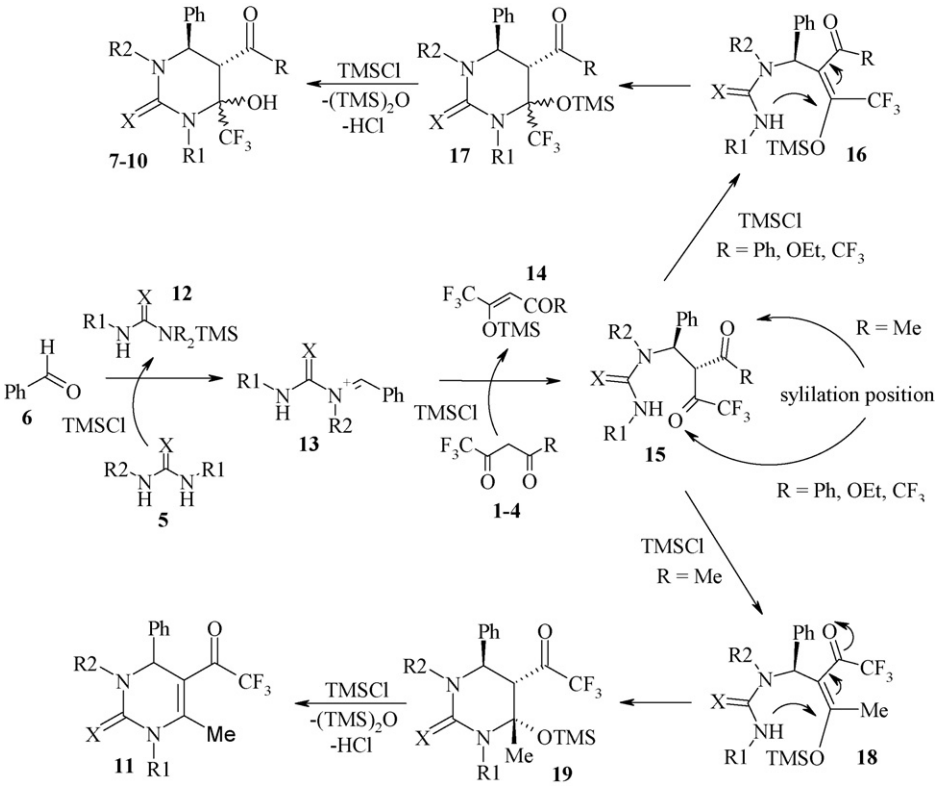


Fig. 5. Some ^1H NMR data for compounds **11d** and **11g**.

spectra of ketones **11** is shifted to the lower field in comparison to compounds **8a** and **8e** (~−72 ppm for **11**, ~−80 ppm for **8**); the presence of a doublet (or a singlet in the case of **11g**) in ^1H spectra at ~5.3 ppm with $^3J_{HH}$ ~5 Hz which corresponds to the proton at C-4, unlike the compounds **7–10** where two doublets are observed; the presence of a quartet in ^{13}C spectra at ~177 ppm with $^2J_{CF}$ ~33 Hz which corresponds to the carbon of C=O group, unlike the singlet at ~204 ppm in the compounds **8a** and **8e**; the absence of a quartet in ^{13}C spectra of CF_3-ketones **11** at ~81 ppm with $^2J_{CF}$ ~31 Hz which is characteristic for C-4 of tetrahydropyrimidine cycle of compounds **8a** and **8e**; the presence of a wide singlet of two protons in the spectrum of compound **11d** at 7.03 ppm with $\Delta\nu_{1/2}$ = 42 Hz which corresponds to two benzene core *ortho*-protons; NOE is observed for the compound **11g** (Fig. 5).

We suggest that the reaction proceeds by the mechanism which is generally accepted for the Biginelli-type reactions in the presence of Me_3SiCl [2]. The first key step is the formation of iminium intermediate **13** (Scheme 4) [9]. The next step is addition



Scheme 4. Proposed mechanism for the formation of compounds **7–11** promoted by chlorotrimethylsilane.

of silylated ketones **14** [10] to the imine **13** affording intermediate **15**. There are two possible positions for silylation of the intermediate product **15**. In the case of methyl, which is less hindered than the CF_3 group, silylation of carbonyl group adjacent to methyl leads to compounds **18**. Intermediates **18** undergo 6-*exo-trig* cyclization followed by elimination of TMS_2O giving **19**. In the case of the substituents more hindered than the methyl group, silylation of $COCF_3$ groups afford intermediates **16** which cyclized to intermediate **17**. The hydrolysis of **17** gives final products **7–10.** Meanwhile, intermediates **19** converts into compounds **11**.

3. Conclusions

The chemical behavior of various trifluoromethyl-1,3-diones such as 1,1,1-trifluoropentane-2,4-dione, 4,4,4-trifluoro-1-phenylbutane-1,3-dione, ethyl 4,4,4-trifluoro-3-oxobutanoate and 1,1,1,5,5,5-hexafluoropentane-2,4-dione in classical Biginelli reaction using DMF/TMSCl was investigated. We demonstrated the possibility to use CF_3-β-diketones and substituted (thio)ureas in this reaction. We established that regioselectivity of the conversion is controlled by sterical factors and depends on the nature of substituent at α-position to carbonyl group of trifluoromethyl-1,3-diones. In the case of 1,1,1-trifluoropentane-2,4-dione and substituted (thio)ureas unexpected cyclization route was disclosed. The derivatives of dihydropyrimid(thi)ones containing $COCF_3$ group at 5-position were obtained for the first time.

4. Experimental

4.1. General

All chemicals were obtained from commercially available sources and used without further purification (Aldrich, Fluka, "Enamine LTD"). DMF for the reactions was freshly distilled and dried by standard methods, monitoring of water content in solvents (all solvents have <0.05%, usually 0.02% of water) was performed using Mettler Toledo DL31 KF Titrator. All solvents for the crystallizations were used without additional purification.

Melting points were measured with a Buchi melting points apparatus and are uncorrected. The ^1H spectra (400 and 500 MHz) were recorded on a Varian Mercury-400 spectrometer and Bruker Avance DRX 500 spectrometer with TMS as an internal standard. ^{13}C spectra (125 MHz) were recorded on a Bruker Avance DRX 500 spectrometer with TMS as an internal standard. ^{19}F NMR (470 MHz) were recorded on a Bruker Avance DRX 500 spectrometer with $CFCl_3$ as an internal standard. NMR experiments (NOE, NOESY) were recorded on a Bruker Avance drx 500 spectrometer. LC/MS spectra were recorded using chromatography/mass spectrometric system that consists of high-performance liquid chromatograph "Agilent 1100 Series" equipped with diode-matrix and mass-selective detector "Agilent LC\MSD SL". According to HPLC MS and ^1H NMR data all the synthesized compounds have purity 95%. IR spectra were recorded on a Nexus-470 spectrometer for samples in KBr discs. Microanalyses were performed in the Microanalytical Laboratory of the Institute of Organic Chemistry, National Academy of Sciences of Ukraine.

4.2. X-ray crystallography

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC 686176 and can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: (international) +44 1223/336 033; E-mail: deposit@ccdc.cam.ac.uk).

4.3. General procedures

Trifluoromethyl-1,3-dione **1–4** (2 mmol), an appropriate urea **5a–d** or thiourea **5e–h** (2 mmol) and benzaldehyde **6** (2 mmol) were placed in 15 mL pressure tube and dissolved in DMF (10 mL). Chlorotrimethylsilane (869 mg, 8 mmol) was added dropwise to the solution. The tube was thoroughly sealed and allowed to stand at 20 °C in ultrasonic bath for 1 h and then allowed to stand at 20 °C for 24–72 h (by TLC). The reaction mixture was poured into water (15–20 mL) and allowed to stand at 20 °C in ultrasonic bath for 1 h. The precipitate formed was filtered and washed with small amount of *i*-PrOH or diethyl ether. First filtrate was evaporated under reduced pressure and the residue was treated with small amount of *i*-PrOH or diethyl ether. Recrystallization of both parts from an appropriate solvent yielded target compounds.

4.3.1. Ethyl rel-(4S,5R,6S)-4-hydroxy-2-oxo-6-phenyl-4-(trifluoromethyl)hexahydropyrimidine-5-carboxylate (7a)

White solid (498 mg, 75%); mp 163 °C (Et_2O-*i*-PrOH), (Lit.: 162 °C [3b]). ^{19}F NNR (470 MHz, DMSO-d_6): δ = −81.9. APSI MS: $M^+ + 1 = 333$. ^1H NMR, ^{13}C NMR, and IR spectroscopic data agree with published ones [3b].

4.3.2. Ethyl rel-(4S,5R,6S)-6-hydroxy-1-methyl-2-oxo-4-phenyl-6-(trifluoromethyl)hexahydropyrimidine-5-carboxylate (7b)

White solid (506 mg, 73%); mp 190 °C (hexane-*i*-PrOH). ^1H NMR (500 MHz, DMSO-d_6): δ = 0.74 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_2CH_3), 2.86 (s, 3H, NCH_3), 3.11 (d, $^3J_{HH}$ = 11.5 Hz, 1H, 5-H_{THPM}), 3.73 (m, 2H, CH_2CH_3), 4.66 (d, $^3J_{HH}$ = 11.5 Hz, 1H, 4-H_{THPM}), 7.32 (m, 5H, H_{Ph}), 7.43 (s, 1H, NH), 7.75 (s, 1H, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.9, 29.0, 53.2, 54.7, 60.6, 84.1 (q, $^2J_{CF}$ = 29.5 Hz), 124.1 (q, $^1J_{CF}$ = 291.3 Hz), 128.5, 128.8, 129.0, 138.0, 155.8, 167.1. ^{19}F NMR (470 MHz, DMSO-d_6): δ = −76.8. IR (KBr), ν_{max} (cm^{-1}): 3280 (br, NH), 3201 (br, OH), 3053, 3003, 2987, 2929, 2904, 1740 ($C{=}O_{ester}$), 1641 (C=O), 1504, 1402, 1348, 1255 (C–F), 1192, 1049, 949, 769, 704, 661. APSI MS: $M^+ + 1 = 347$. Analysis calc. for $C_{15}H_{17}F_3N_2O_4$: C, 52.03; H, 4.95; F, 16.46; N, 8.09; O, 18.48. Found: C, 52.09; H, 4.88; N, 8.12.

4.3.3. Ethyl rel-(4R,5R,6S)-4-hydroxy-1,3-dimethyl-2-oxo-6-phenyl-4-(trifluoromethyl)hexahydropyrimidine-5-carboxylate (7c)

Colourless crystals (375 mg, 52%); mp 188 °C (Et_2O). ^1H NMR (500 MHz, DMSO-d_6): δ = 0.98 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_2CH_3), 2.47 (s, 3H, NCH_3), 2.88 (s, 3H, NCH_3), 3.33 (d, $^3J_{HH}$ = 12.0 Hz, 1H, 5-H_{THPM}), 3.95 (m, 2H, CH_2CH_3), 4.63 (d, $^3J_{HH}$ = 12.0 Hz, 1H, 4-H_{THPM}), 7.23 (d, $^3J_{HH}$ = 7.6 Hz, 2H, 2,6-H_{Ph}), 7.32 (t, $^3J_{HH}$ = 7.6 Hz, 1H, 4-H_{Ph}), 7.38 (t, $^3J_{HH}$ = 7.6 Hz, 2H, 3,5-H_{Ph}), 8.04 (s, 1H, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 14.1, 28.7, 33.7, 55.9, 59.0, 61.5, 82.4 (q, $^2J_{CF}$ = 30.5 Hz), 124.3 (q, $^1J_{CF}$ = 292.2 Hz), 128.0, 129.0, 129.3, 139.5, 154.4, 166.9. ^{19}F NMR (470 MHz, DMSO-d_6): δ = −76.6. IR (KBr), ν_{max} (cm^{-1}): 3157 (br, OH), 3032, 2991, 2947, 2922, 1734 ($C{=}O_{ester}$), 1626 (C=O), 1606 (OH), 1498, 1400, 1323, 1252 (C–F), 1234, 1186, 1090, 1030, 727, 700. APSI MS: $M^+ + 1 = 361$. Analysis calc. for $C_{16}H_{19}F_3N_2O_4$: C, 53.33; H, 5.31; F, 15.82; N, 7.77; O, 17.76. Found: C, 53.39; H, 5.23; N, 7.84.

4.3.4. Ethyl rel-(4S,5R,6S)-4-hydroxy-6-phenyl-2-thioxo-4-(trifluoromethyl)hexahydropyrimidine-5-carboxylate (7e)

White solid (550 mg, 79%); mp 195 °C (*i*-PrOH-hexane), (Lit.: 191–192 °C [3c,d]). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 14.0, 49.9, 54.8, 60.9, 80.1 (q, $^2J_{CF}$ = 31.3 Hz), 123.3 (q, $^1J_{CF}$ = 286.9 Hz), 128.7, 128.9, 129.1, 137.4, 167.0, 177.6. APSI MS: $M^+ + 1 = 349$. ^1H NMR, ^{19}F NMR and IR spectroscopic data agree with published ones [3c].

*4.3.5. Ethyl rel-(4S,5R,6S)-6-hydroxy-1-methyl-4-phenyl-2-thioxo-6-(trifluoromethyl)hexahydropyrimidine-5-carboxylate (**7f**)*

Colourless crystals (435 mg, 60%); mp 195 °C (hexane-Et_2O). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.76 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_2CH_3), 3.26 (s, 3H, NCH_3), 3.32 (d, $^3J_{HH}$ = 11.2 Hz, 1H, 5-H_{THPM}), 3.77 (m, 2H, CH_2CH_3), 4.64 (d, $^3J_{HH}$ = 11.2 Hz, 1H, 4-H_{THPM}), 7.34 (m, 5H, H_{Ph}), 8.34 (s, 1H, OH), 9.25 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.9, 35.5, 54.1, 54.9, 60.8, 84.2 (q, $^2J_{CF}$ = 30.5 Hz), 123.8 (q, $^1J_{CF}$ = 291.7 Hz), 128.8, 129.07, 129.14, 136.5, 166.6, 182.5. ^{19}F NMR (470 MHz, DMSO-d_6): δ = −76.5. IR (KBr), ν_{max} (cm^{-1}): 3213 (br, NH, OH), 3045, 3003, 2983, 2954, 2908, 1736 (C=O_{ester}), 1537, 1489, 1373, 1344, 1279 (C–F), 1242, 1188, 1119, 1043, 1016, 970, 766, 729, 702. APSI MS: M^+ + 1 = 363. Analysis calc. for $C_{15}H_{17}F_3N_2O_3S$: C, 49.72; H, 4.73; F, 15.73; N, 7.73; O, 13.25; S, 8.85. Found: C, 49.79; H, 4.69; N, 7.75; S, 8.81.

*4.3.6. Ethyl rel-(4R,5R,6S)-4-hydroxy-1,3-dimethyl-6-phenyl-2-thioxo-4-(trifluoromethyl)hexahydropyrimidine-5-carboxylate (**7g**)*

Colourless crystals (361 mg, 48%); mp 147 °C (Et_2O). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.02 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_2CH_3), 2.91 (s, 3H, NCH_3), 3.34 (s, 3H, NCH_3), 3.43 (d, $^3J_{HH}$ = 12.3 Hz, 1H, 5-H_{THPM}), 4.01 (q, $^3J_{HH}$ = 7.1 Hz, 2H, CH_2CH_3), 4.88 (d, $^3J_{HH}$ = 12.3 Hz, 1H, 4-H_{THPM}), 7.17 (d, $^3J_{HH}$ = 7.6 Hz, 2H, 2,6-H_{Ph}), 7.35 (t, $^3J_{HH}$ = 7.6 Hz, 1H, 4-H_{Ph}), 7.40 (t, $^3J_{HH}$ = 7.6 Hz, 2H, 3,5-H_{Ph}), 8.49 (s, 1H, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.7, 35.0, 41.7, 55.1, 61.2, 61.4, 81.9 (q, $^2J_{CF}$ = 30.6 Hz), 123.3 (q, $^1J_{CF}$ = 291.3 Hz), 127.2, 128.7, 129.1, 138.7, 166.2, 180.6. ^{19}F NMR (470 MHz, DMSO-d_6): δ = −76.4. IR (KBr), ν_{max} (cm^{-1}): 3157 (br, OH), 3032, 2989, 2943, 1738 (C=O_{ester}), 1498, 1454, 1396, 1329, 1252 (C–F), 1225, 1190, 1082, 1003, 762, 698. APSI MS: M^+ + 1 = 377. Analysis calc. for $C_{16}H_{19}F_3N_2O_3S$: C, 51.06; H, 5.09; F, 15.14; N, 7.44; O, 12.75; S, 8.52. Found: C, 51.15; H, 5.01; N, 7.48; S, 8.49.

*4.3.7. Ethyl rel-(4S,5R,6S)-6-hydroxy-1,4-diphenyl-2-thioxo-6-(trifluoromethyl)hexahydropyrimidine-5-carboxylate (**7h**)*

White solid (475 mg, 56%); mp 180 °C (EtOH). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.74 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_2CH_3), 3.50 (d, $^3J_{HH}$ = 11.8 Hz, 1H, 5-H_{THPM}), 3.76 (m, 2H, CH_2CH_3), 4.99 (d, $^3J_{HH}$ = 11.8 Hz, 1H, 4-H_{THPM}), 7.19 (m, 1H, 4-H_{Ph}), 7.27–7.42 (m, 9H, 2,3,5,6-H_{Ph} + 2,3,4,5,6-H_{Ph}), 8.37 (s, 1H, OH), 9.46 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.9, 52.1, 54.6, 60.8, 84.0 (q, $^2J_{CF}$ = 30.5 Hz), 124.1 (q, $^1J_{CF}$ = 286.8 Hz), 127.4, 127.9, 128.2, 128.7, 129.0, 132.4, 137.3, 141.3, 166.6, 181.2. ^{19}F NMR (470 MHz, DMSO-d_6): δ = −77.2. IR (KBr), ν_{max} (cm^{-1}): 3385 (br, NH), 3180 (br, OH), 3061, 2981, 2939, 1738 (C=O_{ester}), 1535, 1462, 1342, 1257 (C–F), 1217, 1173, 1103, 1011, 754, 723, 696. APSI MS: M^+ + 1 = 425. Analysis calc. for $C_{20}H_{19}F_3N_2O_3S$: C, 56.60; H, 4.51; F, 13.43; N, 6.60; O, 11.31; S, 7.55. Found: C, 56.71; H, 4.42; N, 6.67; S, 7.61.

*4.3.8. rel-(4S,5R,6S)-5-Acetyl-4-hydroxy-6-phenyl-4-(trifluoromethyl)tetrahydropyrimidin-2(1H)-one (**8a**)*

White solid (417 mg, 69%); mp 172 °C (Et_2O-*i*-PrOH), (Lit.: 180–182 °C [3c,d]). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 31.1, 53.7, 57.8, 81.2 (q, $^2J_{CF}$ = 31.3 Hz), 123.7 (q, $^1J_{CF}$ = 287.7 Hz), 128.5, 128.95, 129.02, 138.6, 154.1, 204.4. APSI MS: M^+ + 1 = 303. ^{1}H NMR, ^{19}F NMR and IR spectroscopic data agree with published ones [3c].

*4.3.9. 1-[rel-(4S,5R,6S)-4-Hydroxy-6-phenyl-2-thioxo-4-(trifluoromethyl)hexahydropyrimidin-5-yl]ethanone (**8e**)*

White solid (433 mg, 68%); mp 210 °C (Et_2O-*i*-PrOH), (Lit.: 211–212 °C [3c,d]). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 31.1, 54.7, 56.0, 80.3 (q, $^2J_{CF}$ = 31.3 Hz), 123.4 (q, $^1J_{CF}$ = 287.6 Hz), 128.7, 129.0, 129.1, 137.2, 177.3, 203.7. APSI MS: M^+ + 1 = 319. ^{1}H NMR, ^{19}F NMR and IR spectroscopic data agree with published ones [3c].

*4.3.10. rel-(4S,5R,6S)-5-Benzoyl-4-hydroxy-6-phenyl-4-(trifluoromethyl)tetrahydropyrimidin-2(1H)-one (**9a**)*

White solid (619 mg, 85%); mp 206 °C (EtOH), (Lit.: 204–205 °C [3c,d]). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 48.6, 55.2, 81.9 (q, $^2J_{CF}$ = 31.3 Hz), 123.7 (q, $^1J_{CF}$ = 286.9 Hz), 128.2, 128.5, 128.6, 128.7, 128.9, 133.7, 137.8, 138.8, 154.3, 196.3. APSI MS: M^+ + 1 = 365. ^{1}H NMR, ^{19}F NMR and IR spectroscopic data agree with published ones [3c].

*4.3.11. rel-(4S,5R,6S)-5-Benzoyl-6-hydroxy-1-methyl-4-phenyl-6-(trifluoromethyl)tetrahydropyrimidin-2(1H)-one (**9b**)*

White solid (560 mg, 74%); mp 225 °C (EtOH). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.91 (s, 3H, NCH_3), 4.50 (d, $^3J_{HH}$ = 11.1 Hz, 1H, 5-H_{THPM}), 4.84 (d, $^3J_{HH}$ = 11.1 Hz, 1H, 4-H_{THPM}), 7.08 (t, $^3J_{HH}$ = 7.8 Hz, 1H, 4-H_{Ph}), 7.14 (t, $^3J_{HH}$ = 7.8 Hz, 2H, 3,5-H_{Ph}), 7.29–7.36 (m, 4H, 2,6-H_{Ph} + 3,5-$H_{Ph'}$), 7.46 (m, 2H, 4-$H_{Ph'}$ + NH), 7.64 (d, $^3J_{HH}$ = 7.4 Hz, 2H, 2,6-$H_{Ph'}$), 7.65 (s, 1H, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 29.0, 51.2, 54.4, 85.2 (q, $^2J_{CF}$ = 30.0 Hz), 124.2 (q, $^1J_{CF}$ = 291.8 Hz), 128.2, 128.56, 128.59, 128.77, 128.83, 133.5, 137.7, 138.0, 155.7, 195.7. ^{19}F NMR (470 MHz, DMSO-d_6): δ = −76.0. IR (KBr), ν_{max} (cm^{-1}): 3280 (br, NH), 3190 (br, OH), 3059, 3003, 2972, 2927, 2900, 1682 (C=O_{COPh}), 1643 (C=O), 1599 (OH, NH), 1497, 1448, 1404, 1344, 1252 (C–F), 1194, 1149, 1043, 955, 768, 700, 685, 631. APSI MS: M^+ + 1 = 379. Analysis calc. for $C_{19}H_{17}F_3N_2O_3$: C, 60.32; H, 4.53; F, 15.06; N, 7.40; O, 12.69. Found: C, 60.39; H, 4.45; N, 7.46.

*4.3.12. rel-(4R,5R,6S)-5-Benzoyl-4-hydroxy-1,3-dimethyl-6-phenyl-4-(trifluoromethyl)tetrahydropyrimidin-2(1H)-one (**9c**)*

White solid (439 mg, 56%); mp 215 °C (*i*-PrOH-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.58 (s, 3H, NCH_3), 2.93 (s, 3H, NCH_3), 4.33 (d, $^3J_{HH}$ = 11.7 Hz, 1H, 5-H_{THPM}), 4.84 (d, $^3J_{HH}$ = 11.7 Hz, 1H, 4-H_{THPM}), 7.14 (m, 1H, 4-H_{Ph}), 7.23 (m, 4H, 2,3,5,6-H_{Ph}), 7.32 (t, $^3J_{HH}$ = 8.0 Hz, 2H, 3,5-H_{Ph}), 7.45 (t, $^3J_{HH}$ = 8.0 Hz, 1H, 4-H_{Ph}), 7.52 (s, 1H, OH), 7.68 (d, $^3J_{HH}$ = 8.0 Hz, 1H, 2,6-H_{Ph}). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 29.1, 33.7, 55.4, 59.6, 83.1 (q, $^2J_{CF}$ = 30.1 Hz), 124.4 (q, $^1J_{CF}$ = 292.7 Hz), 128.1, 128.7, 128.85, 128.88, 129.3, 133.9, 138.4, 139.6, 154.5, 196.0. ^{19}F NMR (470 MHz, DMSO-d_6): δ = −75.0. IR (KBr), ν_{max} (cm^{-1}): 3111 (br, OH), 2987, 2964, 2924, 1682 (C=O_{COPh}), 1620 (C=O), 1597 (OH), 1491, 1448, 1396, 1354, 1286, 1250 (C–F), 1200, 1147, 1086, 1036, 771, 725, 702, 660. APSI MS: M^+ + 1 = 393. Analysis calc. for $C_{20}H_{19}F_3N_2O_3$: C, 61.22; H, 4.88; F, 14.53, N, 7.14; O, 12.23. Found: C, 61.30; H, 4.78; N, 7.19.

*4.3.13. [rel-(4S,5R,6S)-4-Hydroxy-6-phenyl-2-thioxo-4-(trifluoromethyl)hexahydropyrimidin-5-yl](phenyl)methanone (**9e**)*

White solid (624 mg, 82%); mp 230 °C (EtOH), (Lit.: 229–230 °C [3c,d]). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 47.0, 56.2, 81.1 (q, $^2J_{CF}$ = 31.0 Hz), 123.3 (q, $^1J_{CF}$ = 288.8 Hz), 128.3, 128.7, 128.8, 128.98, 129.01, 133.8, 137.5, 137.7, 177.4, 195.4. APSI MS: M^+ + 1 = 381. ^{1}H NMR, ^{19}F NMR and IR spectroscopic data agree with published ones [3c].

*4.3.14. [rel-(4S,5R,6S)-4-Hydroxy-6-phenyl-2-thioxo-4-(trifluoromethyl)hexahydropyrimidin-5-yl](phenyl)methanone (**9f**)*

White solid (450 mg, 57%); mp 200 °C (*i*-PrOH-hexane). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 3.30 (s, 3H, NCH_3), 4.70 (d, $^3J_{HH}$ = 10.5 Hz, 1H, 5-H_{THPM}), 4.81 (d, $^3J_{HH}$ = 10.5 Hz, 1H, 4-H_{THPM}), 7.11 (t, $^3J_{HH}$ = 7.4 Hz, 1H, 4-H_{Ph}), 7.16 (t, $^3J_{HH}$ = 7.4 Hz, 2H, 3,5-H_{Ph}), 7.32–7.39 (m, 4H, 2,6-H_{Ph} + 3,5-$H_{Ph'}$), 7.49 (t, $^3J_{HH}$ = 7.5 Hz, 1H, 4-$H_{Ph'}$), 7.73 (d, $^3J_{HH}$ = 7.5 Hz, 2H, 2,6-$H_{Ph'}$), 8.17 (s, 1H, OH), 9.27 (s, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 35.6, 51.2, 55.2, 85.2 (q, $^2J_{CF}$ = 30.1), 123.8 (q, $^1J_{CF}$ = 291.8), 128.5, 128.6, 128.7, 128.9, 129.0, 133.7, 136.7, 137.6, 181.9, 195.0. ^{19}F NMR (470 MHz, DMSO-d_6): δ = −74.7. IR (KBr), ν_{max} (cm^{-1}): 3650–3300 (br, NH), 3205 (br,

OH), 3043, 3007, 2960, 2920, 1682 (C=O), 1541, 1493, 1448, 1342, 1240 (C–F), 1196, 1117, 1030, 957, 764, 685. APSI MS: $M^+ + 1 = 395$. Analysis calc. for $C_{19}H_{17}F_3N_2O_2S$ C, 57.86; H, 4.34; F, 14.45; N, 7.10; O, 8.11; S, 8.13. Found: C, 57.80; H, 4.25; N, 7.17; S, 8.12.

4.3.15. [rel-(4R,5R,6S)-4-Hydroxy-1,3-dimethyl-6-phenyl-2-thioxo-4-(trifluoromethyl)hexahydropyrimidin-5-yl](phenyl)methanone (9g)

White solid (417 mg, 51%); mp 182 °C (hexane-*i*-PrOH). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 3.03 (s, 3H, NCH_3), 3.31 (s, 3H, NCH_3), 4.97 (d, $^3J_{HH}$ = 10.0 Hz, 1H, 5-H_{THPM}), 5.05 (d, $^3J_{HH}$ = 10.0 Hz, 1H, 4-H_{THPM}), 7.18 (t, $^3J_{HH}$ = 7.6 Hz, 1H, 4-H_{Ph}), 7.24 (t, $^3J_{HH}$ = 7.6 Hz, 2H, 3,5-H_{Ph}), 7.38 (d, $^3J_{HH}$ = 7.6 Hz, 2H, 2,6-H_{Ph}), 7.42 (t, $^3J_{HH}$ = 7.6 Hz, 2H, 3,5-H_{Ph}), 7.55 (t, $^3J_{HH}$ = 7.6 Hz, 1H, 4-H_{Ph}), 7.86 (d, $^3J_{HH}$ = 7.6 Hz, 1H, 2,6-H_{Ph}), 8.19 (br. s, 1H, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 36.9, 41.6, 50.3, 61.2, 84.7 (q, $^2J_{CF}$ = 30.7 Hz), 123.8 (q, $^1J_{CF}$ = 292.5 Hz), 128.8, 128.9, 128.97, 129.02, 129.2, 133.8, 136.6, 137.6, 183.3, 195.2. ^{19}F NMR (470 MHz, DMSO-d_6): δ = −74.6. IR (KBr), ν_{max} (cm^{-1}): 3196 (br, OH), 3003, 2924, 1682 (C=O), 1497, 1451, 1241 (C–F), 1198, 765. APSI MS: $M^+ + 1 = 409$. Analysis calc. for $C_{20}H_{19}F_3N_2O_2S$ C, 58.81; H, 4.69; F, 13.95; N, 6.86; O, 7.83; S, 7.85. Found: C, 58.89; H, 4.61; N, 6.90; S, 7.81.

4.3.16. rel-(4R,5S,6R)-4-Hydroxy-6-phenyl-5-(trifluoroacetyl)-4-(trifluoromethyl)tetrahydropyrimidin-2(1H)-one (10a)

White solid (506 mg, 71%); mp 196 °C (hexane-*i*-PrOH), (Lit.: 200–201 °C [3d]). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 50.9, 54.9, 81.7 (q, $^2J_{CF}$ = 31.4 Hz), 114.2 (q, $^1J_{CF}$ = 292.9 Hz), 123.3 (q, $^1J_{CF}$ = 286.1 Hz), 128.7, 129.1, 129.4, 137.5, 153.8, 187.6 (q, $^2J_{CF}$ = 36.0 Hz). APSI MS: $M^+ + 1 = 357$. ^{1}H NMR, ^{19}F NMR and IR spectroscopic data agree with published ones [3d].

4.3.17. rel-(4R,5S,6R)-6-Hydroxy-1-methyl-4-phenyl-5-(trifluoroacetyl)-6-(trifluoromethyl)tetrahydropyrimidin-2(1H)-one (10b)

White solid (422 mg, 57%); mp 190 °C (hexane-*i*-PrOH). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.90 (s, 3H, NCH_3), 4.04 (d, $^3J_{HH}$ = 10.8 Hz, 1H, 5-H_{THPM}), 4.78 (d, $^3J_{HH}$ = 10.8 Hz, 1H, 4-H_{THPM}), 7.34 (m, 4H, H_{Ph}), 7.66 (s, 1H, NH), 8.28 (s, 1H, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 28.9, 53.8, 56.0, 84.1 ($^2J_{CF}$ = 31.0 Hz), 115.3 (q, $^1J_{CF}$ = 291.7 Hz), 123.7 (q, $^1J_{CF}$ = 286.1 Hz), 128.0, 128.6, 129.2, 136.9, 154.7, 187.3 ($^2J_{CF}$ = 36.0 Hz). ^{19}F NMR (470 MHz, DMSO-d_6): δ = −76.4, −78.2. IR (KBr), ν_{max} (cm^{-1}): 3277 (br, NH), 3197 (br, OH), 3051, 2985, 2929, 2897, 1759 (C=O_{COCF3}), 1637 (C=O), 1504, 1406, 1352, 1292, 1246 (C–F), 1213, 1165, 1147, 1047, 769, 702, 652. APSI MS: $M^+ + 1 = 371$. Analysis calc. for $C_{14}H_{12}F_6N_2O_3$: C, 45.42; H, 3.27; F, 30.79; N, 7.57; O, 12.96. Found: C, 45.49; H, 3.22; N, 7.60.

4.3.18. rel-(4S,5S,6R)-4-Hydroxy-1,3-dimethyl-6-phenyl-5-(trifluoroacetyl)-4-(trifluoromethyl)tetrahydropyrimidin-2(1H)-one (10c)

Colourless crystals (315 mg, 41%); mp 179 °C (hexane-Et_2O). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.52 (s, 3H, NCH_3), 2.93 (s, 3H, NCH_3), 4.19 (d, $^3J_{HH}$ = 11.9 Hz, 1H, 5-H_{THPM}), 4.75 (d, $^3J_{HH}$ = 11.9 Hz, 1H, 4-H_{THPM}), 7.23 (d, $^3J_{HH}$ = 8.1 Hz, 2H, 2,6-H_{Ph}), 7.36 (t, $^3J_{HH}$ = 8.1 Hz, 1H, 4-H_{Ph}), 7.41 (t, $^3J_{HH}$ = 8.1 Hz, 2H, 3,5-H_{Ph}), 8.60 (s, 1H, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 28.9, 33.6, 56.4, 58.5, 82.9 (q, $^2J_{CF}$ = 31.0 Hz), 114.5 (q, $^1J_{CF}$ = 291.7 Hz), 123.9 (q, $^1J_{CF}$ = 292.7 Hz), 128.0, 129.5, 129.6, 138.0, 154.1, 188.5 (q, $^2J_{CF}$ = 37.0 Hz). ^{19}F NMR (470 MHz, DMSO-d_6): δ = −75.6, −78.1. IR (KBr), ν_{max} (cm^{-1}): 3152 (br, OH), 2988, 2927, 1759 (C=O_{COCF3}), 1625 (C=O), 1502, 1403, 1241 (C–F), 1196, 1145, 766, 703. APSI MS: $M^+ + 1 = 385$. Analysis calc. for $C_{15}H_{14}F_6N_2O_3$: C, 46.88; H, 3.67; F, 29.66; N, 7.29; O, 12.49. Found: C, 46.95; H, 3.60; N, 7.23.

4.3.19. 2,2,2-Trifluoro-1-[rel-(4R,5S,6R)-4-hydroxy-6-phenyl-2-thioxo-4-(trifluoromethyl)hexahydropyrimidin-5-yl]ethanone (10e)

White solid (484 mg, 65%); mp 211 °C (hexane-*i*-PrOH), (Lit.: 215–216 °C [3c,d]). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 49.2, 55.8, 80.8 (q, $^2J_{CF}$ = 32.8 Hz), 114.2 (q, $^1J_{CF}$ = 293.0 Hz), 123.0 (q, $^1J_{CF}$ = 286.1 Hz), 128.9, 129.1, 129.5, 136.2, 177.5, 187.6 (q, $^2J_{CF}$ = 33.9 Hz). APSI MS: $M^+ + 1 = 373$. ^{1}H NMR, ^{19}F NMR and IR spectroscopic data agree with published ones [3c].

4.3.20. 6-Methyl-1-(4-methylphenyl)-4-phenyl-5-(trifluoroacetyl)-3,4-dihydropyrimidin-2(1H)-one (11d)

White solid (442 mg, 59%); mp 180 °C (*i*-PrOH-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.16 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 5.28 (d, $^3J_{HH}$ = 4.7 Hz, 1H, 4-H_{DHPM}), 7.03 (br. s, $\Delta\nu_{1/2}$ ~42 Hz, 2H, 2,6-H_{Ar}), 7.25 (d, $^3J_{HH}$ = 8.0 Hz, 2H, 3,5-H_{Ar}), 7.34 (t, $^3J_{HH}$ = 7.2 Hz, 1H, 4-H_{Ph}), 7.37–7.46 (m, 4H, 2,3,5,6-H_{Ph}), 8.75 (d, $^3J_{HH}$ = 4.7 Hz, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 20.5, 21.2, 51.4, 105.0, 117.1 (q, $^1J_{CF}$ = 293.0 Hz), 118.6, 126.6, 128.5, 129.4, 130.1, 134.7, 138.7, 142.6, 151.6, 160.6, 176.9 (q, $^2J_{CF}$ = 32.8 Hz). ^{19}F NMR (470 MHz, DMSO-d_6): δ = −71.9. IR (KBr), ν_{max} (cm^{-1}): 3242 (br, NH), 3126, 3032, 2927, 1716 (C=O_{COCF3}), 1684 (C=O), 1568 (NH), 1512, 1448, 1394, 1242 (C–F), 1201, 1171, 1138, 1101, 1022, 935, 721, 696. APSI MS: $M^+ + 1 = 375$. Analysis calc. for $C_{20}H_{17}F_3N_2O_2$: C, 64.17; H, 4.58; F, 15.22; N, 7.48; O, 8.55. Found: C, 64.23; H, 4.51; N, 7.52.

4.3.21. 2,2,2-Trifluoro-1-(1,3,6-trimethyl-4-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone (11g)

Colourless crystals (315 mg, 48%); mp 171 °C (hexane-Et_2O). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.53 (s, 3H, CH_3), 3.51 (s, 3H, NCH_3), 3.56 (s, 3H, NCH_3), 5.55 (s, 1H, 4-H_{DHPM}), 7.07 (d, $^3J_{HH}$ = 7.4 Hz, 2H, 2,6-H_{Ph}), 7.24–7.36 (m, 3H, 3,4,5-H_{Ph}). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 18.5, 38.7, 43.7, 59.7, 106.4, 117.0 ($^1J_{CF}$ = 292.3 Hz), 126.5, 128.9, 129.4, 138.7, 156.9, 177.2 (q, $^2J_{CF}$ = 33.2 Hz), 178.2. ^{19}F NMR (470 MHz, DMSO-d_6): δ = −71.5. IR (KBr), ν_{max} (cm^{-1}): 3035, 2926, 1698 (C=O), 1489, 1389, 1218 (C–F), 1150, 960, 696. APSI MS: $M^+ + 1 = 329$. Analysis calc. for $C_{15}H_{15}F_3N_2OS$: C, 54.87; H, 4.60; F, 17.36; N, 8.53; O, 4.87; S, 9.76. Found: C, 54.92; H, 4.55; N, 8.56; S, 9.71.

4.3.22. 2,2,2-Trifluoro-1-(6-methyl-1,4-diphenyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone (11h)

White solid (452 mg, 60%); mp 188 °C (*i*-PrOH-hexane). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.16 (s, 3H, CH_3), 5.35 (d, $^3J_{HH}$ = 5.4 Hz, 1H, 4-H_{DHPM}), 7.28–7.48 (m, 10H, H_{Ph}), 10.56 (d, $^3J_{HH}$ = 5.4 Hz, 1H, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 20.4, 51.8, 106.5, 116.9 (q, $^1J_{CF}$ = 293.2 Hz), 123.5, 126.7, 128.8, 129.1, 129.3, 129.5, 140.1, 141.4, 155.9, 177.5, 177.9 (q, $^2J_{CF}$ = 33.9 Hz). ^{19}F NMR (470 MHz, DMSO-d_6): δ = −72.0. IR (KBr), ν_{max} (cm^{-1}): 3650–3320 (br, NH), 3169, 3037, 2926, 1689 (C=O), 1578 (NH), 1493, 1387, 1252, 1213 (C–F), 1151, 1113, 962, 696. APSI MS: $M^+ + 1 = 377$. Analysis calc. for $C_{19}H_{15}F_3N_2OS$: C, 60.63; H, 4.02; F, 15.14; N, 7.44; O, 4.25; S, 8.52. Found: C, 60.64; H, 3.98; N, 7.45; S, 8.49.

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References

[1] (a) C.O. Kappe, Eur. J. Med. Chem. 35 (2000) 1043–1052;
(b) C.O. Kappe, Tetrahedron 49 (1993) 6937–6963;
(c) C.O. Kappe, Acc. Chem. Res. 33 (2000) 879–888.

[2] (a) S.V. Ryabukhin, A.S. Plaskon, E.N. Ostapchuk, D.M. Volochnyuk, A.A. Tolmachev, Synthesis (2007) 417–427;
(b) S.V. Ryabukhin, A.S. Plaskon, E.N. Ostapchuk, D.M. Volochnyuk, A.N. Shivanyuk, A.A. Tolmachev, Orglett 9 (2007) 4215–4218;
(c) Y.-L. Zhu, Y.-J. Pan, S.-L. Huang, Synth. Commun. 34 (2004) 3167–3174;
(d) Y.-L. Zhu, S.-L. Huang, Y.-J. Pan, Eur. J. Org. Chem. (2005) 2354–2367.
[3] (a) C.O. Kappe, S.F. Falsone, Synlett (1998) 718–720;
(b) C.O. Kappe, S.F. Falsone, W.M.F. Fabian, F. Belaj, Heterocycles 51 (1999) 77–84;
(c) V.I. Saloutin, Ya.V. Burgart, O.G. Kuzueva, C.O. Kappe, O.N. Chupakhin, J. Fluorine Chem. 103 (2000) 17–24;
(d) Ya.V. Burgart, O.G. Kuzueva, M.V. Pryadeina, C.O. Kappe, V.I. Saloutin, Russ. J. Org. Chem. 37 (2001) 869–880;
(e) Ch.V. Reddy, M. Mahesh, P.V.K. Raju, T.R. Babu, V.V.N. Reddy, Tetrahedron Lett. 43 (2002) 2657–2660;
(f) A. Manjula, B.V. Rao, P. Neelakantan, Synth. Commun. 34 (2004) 2665–2672;
(g) Y. Ma, C. Qian, L. Wang, M. Yang, J. Org. Chem. 65 (2000) 3864–3868;
(h) X. Han, F. Xu, Y. Luo, Q. Shen, Eur. J. Org. Chem. (2005) 1500–1504;
(i) E.S. Putilova, N.A. Troitskii, S.G. Zlotin, O.G. Khudina, Ya.V. Burgart, V.I. Saloutin, O.N. Chupakhin, Russ. J. Org. Chem. 42 (2006) 1392–1395;
(j) D.S. Bose, M.V. Chary, H.B. Mereyala, Heterocycles 68 (2006) 1217–1224.
[4] (a) J.C. Barrow, P.G. Nantermet, H.G. Selnick, K.L. Glass, K.E. Rittle, K.F. Gilbert, T.G. Steele, C.F. Homnick, R.M. Freidinger, R.W. Ransom, P. Kling, D. Reiss, T.P. Broten, T.W. Schorn, R.S.L. Chang, S.S. O'Malley, T.V. Olah, J.D. Ellis, A. Barrish, K. Kassahun, P. Leppert, D. Nagarathnam, C. Forray, J. Med. Chem. 43 (2000) 2703–2718;
(b) J.S. Yadav, B.V.S. Reddy, K.B. Reddy, K.S. Raj, A.R. Prasad, J. Chem. Soc. Perkin Trans. 1 (2001) 1939–1941;
(c) M. Shailaja, A. Manjula, B.V. Rao, N. Parvathi, Synth. Commun. 34 (2004) 1559–1564;
(d) R. Varala, M.M. Alam, S.R. Adapa, Synlett (2003) 67–70;
(e) M.S. Akhtar, M. Seth, A.P. Bhaduri, Indian J. Chem. Sect. B 26 (1987) 556–561.
[5] (a) M.V. Pryadeina, Ya.V. Burgart, M.I. Kodess, V.I. Saloutin, O.N. Chupakhin, Russ. Chem. Bull. 53 (2004) 1261–1266;
(b) M.V. Pryadeina, Ya.V. Burgart, V.I. Saloutin, M.I. Kodess, E.N. Ulomskii, V.L. Rusinov, Russ. J. Org. Chem. 40 (2004) 902–907.
[6] S.V. Ryabukhin, D.M. Volochnyuk, A.S. Plaskon, V.S. Naumchik, A.A. Tolmachev, Synthesis (2007) 1214–1224.
[7] (a) J.C. Sloop, C.L. Bumgardner, W.D. Loehle, J. Fluorine Chem. 118 (2002) 135–148;
(b) S.P. Singh, D. Kumar, H. Batra, I. Rozas, J. Elguero, Can. J. Chem. 78 (2000) 1109–1120;
(c) S.P. Singh, J.K. Kapoor, D. Kumar, M.D. Threadgill, J. Fluorine Chem. 83 (1997) 73–80.
[8] SciFinder search find 1 Hit, but detailed analysis of paper: A. Shaabani, A. Bazgir, F. Teimouri, Tetrahedron Lett. 44 (2003) 857–859, shown that this structure is mistake.
[9] [a] L. Ciszewski, D. Xu, T. Li, O. Repic, T.J. Blacklock, Tetrahedron Lett. 39 (1998) 1107–1110;
(b) D. Xu, L. Ciszewski, T. Li, O. Repic, T.J. Blacklock, Tetrahedron Lett. 45 (2004) 8091–8093;
(c) U. Jahn, W. Schroth, Tetrahedron Lett. 34 (1993) 5863–5866;
(d) W. Schroth, U. Jahn, D. Stroehl, Chem. Ber. 127 (1994) 2013–2022.
[10] (a) J.A. Mcclarin, A. Schwartz, T.J.J. Pinnavaia, Organomet. Chem. 188 (1980) 129–140;
(b) C. Mamat, T. Pundt, A. Schmidt, P. Langer, Tetrahedron Lett. 47 (2006) 2183–2185;
(c) B.-L. Wang, F. Yu, X.-L. Qiu, Z.-X. Jiang, F.-L. Qing, J. Fluorine Chem. 127 (2006) 580–587;
(d) D.M. Volochnyuk, A.N. Kostyuk, D.A. Sibgatulin, A.N. Chernega, Tetrahedron 61 (2005) 2839–2847.