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Synthesis of 4-Trifluoromethyl-3,4-dihydro-1,3,5-triazino-[2,1-*a*]isoindol-2-ones by Cyclocondensation of 1-Aryl-1-chloro-2,2,2-trifluoroethyl Isocyanates with 3-Amino-1-arylimino-1*H*-isoindoles

A. V. Biitseva[a], O. V. Gordienko[a], M. Yu. Kornilov[a], V. A. Sukach[b], M. V. Vovk[b], O. V. Shishkin[c], and V. V. D'yakonenko[c]

[a]*Taras Shevchenko Kiev National University, Kiev, 01033 Ukraine*
e-mail: gel@univ.kiev.ua
[b]*Institute of Organic Chemistry, National Academy of Sciences of the Ukraine, Kiev, Ukraine*
[c]*Research and Technology Enterprise "Institute of Single Crystals", National Academy of Sciences of the Ukraine, Kiev, Ukraine*

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Abstract—4-Trifluoromethyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]isoindol-2-ones were prepared by reaction of 1-aryl-1-chloro-2,2,2-trifluoroethyl isocyanates with 3-amino-1-arylimino-1*H*-isoindoles in the presence of triethylamine. In some events alongside the main product isomeric 2-trifluoromethyl-2,3-dihydro-1,3,5-triazino[2,1-a]isoindol-4-ones were obtained. The regioselectivity of the reaction is affected by sterical and electronic characteristics of substituents and by temperature.

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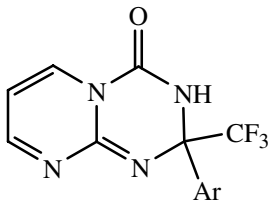
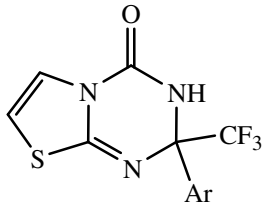
1-Chloroethyl isocyanates are highly reactive bielectrophilic reagents widely used in syntheses of versatile heterocyclic systems [1, 2]. For instance, their reactions with ambident nucleophiles like ureas [3], amidines [4], and 2-azahetarylamines [5] led to the formation of a series of 1,3,5-triazines derivatives and their pyrido, pyrimido, and triazolo fuzed analogs. Triazine derivatives, also those containing a CF_3 group, exhibit high biological activity. Among these compounds were found herbicides [6–8], insecticides, fungicides [9, 10], and also compounds with anticonvulsant [11], antiphlogistic, and analgesic action [12].

Derivatives of 3-amino-1*H*-isoindole were established [13–17] to be important initial compounds for the synthesis of fused isoindoles; however, among the latter only some triazinoisoindole derivatives were described [18, 19]. Taking into account the "amidine" character of the aminoisoindole structures their involvement into condensations with 1-chloro-2,2,2-trifluoroethyl isocyanates may constitute a preparatively convenient approach to CF_3-containing triazinoisoindoles, biologically promising substances.

It was shown formerly [5] that 1-aryl-1-chloro-2,2,2-trifluoroethyl isocyanates **Ia–Ic** reacted with 2-aminopyridine and 2-aminothiazole via alkylating the exocyclic nitrogen and acylating endocyclic nitrogen providing derivatives of 3,4-dihydropyrido[1,2-*a*]-1,3,5-triazin-4-ones **A** and 3,4-dihydro-1,3,5-triazino[2,1-*b*]thiazol-4-ones **B**.

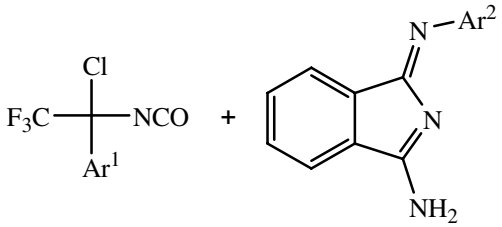


A

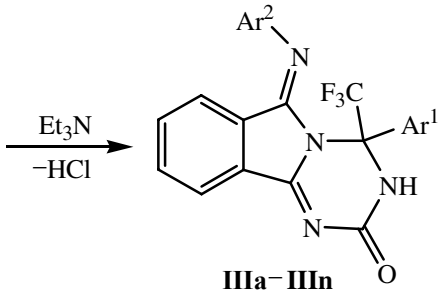


B

We investigated the reaction of isocyanates **Ia–Ic** with a series of 3-amino-1-arylimino-1*H*-isoindoles **IIa–IIg** that contained substituents Ar^2 with different sterical parameters. We established that isocyanates **Ia–Ic** notwithstanding the character of substituent Ar^1 reacted with *ortho*-substituted 3-amino-1-arylimino-1*H*-isoindoles **IIa–IId** in toluene at room temperature in the presence



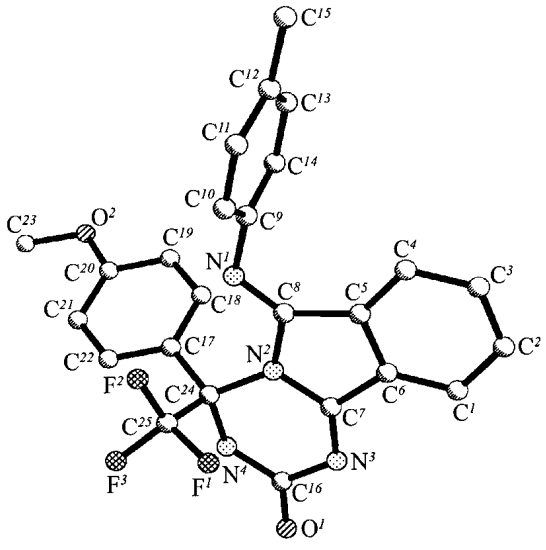
Ia–Ic **IIa–IIg**



IIIa–IIIn

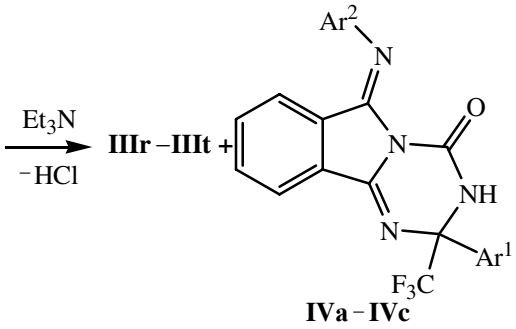
I, Ar^1 = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**); **II**, Ar^2 = 2-MeC_6H_4 (**a**), 2-$MeOC_6H_4$ (**b**), 2,4-$Me_2C_6H_3$ (**c**), 2,6-$Me_2C_6H_3$ (**d**), 4-BrC_6H_4 (**e**), 4-MeC_6H_4 (**f**), 4-$MeOC_6H_4$ (**g**); **III**, Ar^1 = Ph, Ar^2 = 2-MeC_6H_4 (**a**), 2-$MeOC_6H_4$ (**b**), 2,4-$Me_2C_6H_3$ (**c**), 2,6-$Me_2C_6H_3$ (**d**); Ar^1 = 4-MeC_6H_4, Ar^2 = 2,4-$Me_2C_6H_3$ (**e**), 4-BrC_6H_4 (**f**), 4-MeC_6H_4 (**g**), Ar^1= 4-$MeOC_6H_4$, Ar^2 = 2-MeC_6H_4 (**h**), 2-$MeOC_6H_4$ (**i**), 2,4-$Me_2C_6H_3$ (**j**), 2,6-$Me_2C_6H_3$ (**k**), 4-BrC_6H_4 (**l**), 4-MeC_6H_4 (**m**), 4-$MeOC_6H_4$ (**n**).

of triethylamine to give a single type of compounds from the series of 4-trifluoromethyl-3,4-dihydro-1,3,5-triazino-[2,1-*a*]isoindol-2-one (**III**). Triazinone fragment in these compounds is structurally isomeric to the previously



General view of a molecule of 6-(4-methylphenyl)imino-4-(4-methoxyphenyl)-4-trifluoromethyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]isoindol-2-one (**IIIm**).

Ia + IIe–IIg



IIIr–IIIt **IVa–IVc**

III, Ar^1 = Ph, Ar^2 = 4-BrC_6H_4 (**o**), 4-MeC_6H_4 (**p**), 4-$MeOC_6H_4$ (**q**); **IV**, Ar^1 = Ph, Ar^2 = 4-BrC_6H_4 (**a**), 4-MeC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**).

synthesized compounds of the **A** and **B** type. When the Ar^2 of isoindole has no *ortho*-substituents (**IIe–IIg**) analogous cyclocondensation giving compounds **IIIf, IIIg, IIIl–IIIn** occurred only with isocyanates with the more pronounced donor substituents in Ar^1 (**Ib** and **Ic**).

The reaction of isocyanate **I**a with 3-aminoisoindoles **IIe–IIg** under the conditions described above alongside compounds **IIIo–IIIq**, as show ^{19}F NMR spectra, gave rise also in lesser quantity (12–17%) isomeric 2,6-dihydro--1,3,5-triazino[2,1-*a*]-isoindol-4-ones **IVa–IVc** that we failed to separate by recrystallization.

We demonstrated by an example of reaction between isocyanate **Ia** and 3-aminoisoindole **IIf** that the ratio of regioisomers **IIIp** and **IVb** depended on the reaction conditions, in particular, on the temperature. The reaction carried out in toluene at 60–65°C gave predominantly isomer **IIIp** (97%). Raising temperature further we obtained more complex mixture of reaction products as showed the ^{19}F NMR spectra. In ethyl ether at –78°C the relative amount of compound **IIIp** decreased, and compounds **IIIp** and **IVb** formed in a ratio 0.6:0.4. Regioisomers **IIIp** and **IVb** were successfully separated by column chromatography.

The unambiguous assignment of the structure of isomeric compounds was based on the X-ray diffraction analysis of a single crystal of compound **IIIm**.

It was established that the repulsion between tolyl substituent and isoindole moiety {shortened intramolecular contacts $C^4\cdots C^9$ 3.15 A (sum of van der Waals radii 3.42 Å[20]), $H^4\cdots C^9$ 2.67 Å(2.87 Å), and $C^{14}\cdots H^4$ 2.68 Å(2.87 Å)} resulted in some twisting of the double bond $N^1{=}C^8$ [torsion angle $C^9N^1C^8C^5$ 4.5(4)°]. The tolyl substituent is located virtually normal to the plane of the isoindole fragment [torsion angle $C^{10}C^9N^1C^8$ 106.1(3)°]

and has *E*-orientation. Triazine ring is present in a *sofa* conformation (folding parameters [21] *S* 0.29, θ 46.6°, ψ 14.0°). Deviation of C^{24} from the least-mean square plane of the other atoms in the ring amounts to 0.27 Å. The trifluoromethyl substituent at C^{24} is axially oriented [torsion angle $C^{25}C^{24}N^{2}C^{7}$ 96.2(2)°] and is so located that F^{1} atom is in the +*sc* position with respect to N^{2}–C^{24} bond [torsion angle $F^{1}C^{25}C^{24}N^{2}$ 47.3(2)°]. This orientation of the trifluoromethyl substituent results in appearance of shortened intramolecular contacts $F^{2}\cdots N^{1}$ 2.79 Å (2.90 Å), $F^{1}\cdots C^{7}$ 3.01 Å(3.11 Å), $F^{3}\cdots C^{22}$ 2.94 Å(3.11 Å), and $F^{3}\cdots H^{22}$ 2.30 A (2.56 Å). Anisyl substituent at C^{24} atom is oriented equatorially [torsion angle $C^{17}C^{24}N^{2}C^{7}$ 138.1(2)°] and is somewhat turned with respect to N^{2}–C^{24} bond [torsion angle $C^{18}C^{17}C^{24}N^{2}$ 15.9(3)°]. Methoxy group is coplanar with the benzene ring $C^{17}\cdots C^{22}$ [torsion angle $C^{23}O^{2}C^{20}C^{21}$ 2.3(4)°] notwithstanding the shortened intramolecular contacts $C^{21}\cdots H^{23C}$ 2.74 Å(2.87 Å), $C^{21}\cdots H^{23B}$ 2.76 A (2.87 Å). In the crystal the molecules form centrosymmetrical dimers owing to intermolecular hydrogen bond N^{4}–$H^{4N}\cdots O^{1}$ (H···O 1.99 Å, N–H···O 168.8°).

We developed a simple and at the same time reliable method of structural identification of the compounds synthesized by means of ^{19}F NMR spectroscopy based on the structure of compound **IIIm** established by X-ray diffraction analysis. Thus compounds of **III** type are characterized by the chemical shift of CF_3 group equal to –74 ppm [22], and in the alternative structures of **IV** type the chemical shift of the corresponding signal is –80 ppm in keeping with the published data for previously obtained fused CF_3-containing 1,3,5-triazin-4-ones **A** and **B** [5].

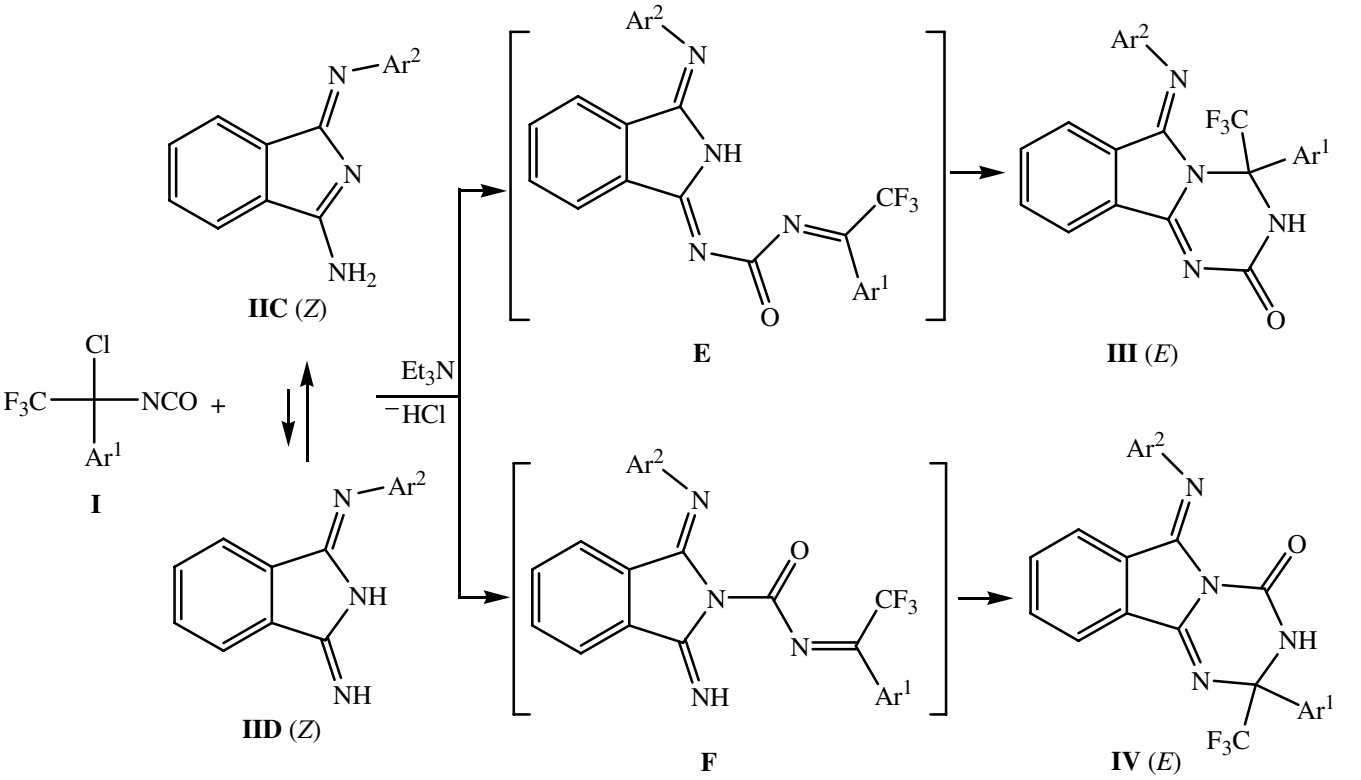
IR spectra of compounds **III** contain characteristic strong absorption bands of stretching vibrations of C=O groups from the triazinone fragment in the region 1640–1645 cm^{-1}. In contrast, in the IR spectrum of compound **IVb** the vibrations of the carbonyl group are observed at higher frequencies (1740 cm^{-1})characteristic of the structurally related derivatives of **A**, **B** type [5]. This difference may be attributed to involvement of the carbonyl group in compounds **III** into a conjugation system which results in the shift of the absorption bands to lower frequencies [23]. The vibrations of NH groups of compounds under study appear as two wide absorption bands in the region 3085–3220 cm^{-1} (isomers **III**) and 3165–3260 cm^{-1} (isomers **IV**) indicating associates formation through intermolecular hydrogen bonds between the amide moieties of the molecules; these findings are consistent with the X-ray crystallography of compound **IIIm**.

As shown by the X-ray crystallography of compound **IIIm** the Ar^2 substituent has *E*-orientation with respect to the exocyclic C=N bond unlike the initial 3-amino-1-(4-methylphenyl)imino-1*H*-isoindole (**IIf**) [24]. Analogous pattern was observed in solutions and was reflected in the ^1H NMR spectra. For instance, solutions of compounds **IIIa–IIIn** and **IVb** in DMSO-d_6 give rise in the ^1H NMR spectra to one-proton doublet in the region 6.4–6.7 ppm belonging to the proton at C^7 atom of the triazinoisoindole fragment. This upfield shift by 2 ppm compared to initial compounds **IIa–IIg** can be ascribed to the shielding effect of the ring current in the Ar^2 substituent that in its turn can occur only at the *E*-orientation of the substituent.

In the ^1H NMR spectra of compounds **IIIa–IIIe**, **IIIh–IIIk** containing an *ortho*-substituent (CH_3, OCH_3) in Ar^2 a notably broadened singlet is observed corresponding to the protons of methyl or methoxy group; this fact may be ascribed to the hindered rotation of Ar^2 owing to sterical hindrances from the substituent in the *ortho*-position. The signal from proton H^6 in Ar^2 is also considerably broadened.

Introduction of a second *ortho*-substituent into Ar^2 hindered its rotation with respect to C–N bond to such extent that in the ^1H NMR spectra of compounds **IIId** and **IIIk** appeared two narrow singlets from magnetically nonequivalent methyl groups at 1.3 and 1.9 ppm. Therewith one of the methyl groups occurred in the range of shielding by ring currents from the substituent Ar^1 of the triazinone ring resulting in the upfield shift of this methyl protons by 0.6 ppm compared with the signal from the second methyl group. The magnitude of the diamagnetic shift is in agreement with that calculated by procedure [25].

Taking into account the ambident character of 3-aminoisoindoles **II**, the possible tautomeric equilibrium between amino-imino **IIC** and diimino form **IID** [24], and also published data [26] on acylation of 2-azahetarylamins the scheme of their reaction with 1-chloroethyl isocyanates **I** may be represented as follows. For compounds **IIa–IId** the most probable primary pathway of reaction independent of the nature of isocyanate **Ia–Ic** is the carbamoylation of the exocyclic nitrogen followed by HCl elimination giving intermediates **E**. The alternative carbamoylation of the endocyclic nitrogen by isocyanates **I** that should lead to the formation of intermediates **F** is prevented by the sterical effect of the *ortho*-substituted phenylimino group. Isocyanates **Ib** and **Ic** due to electro-



philicity decreased by the effect of substituent Ar^1 in reaction with less sterically hindered 3-aminoisoindoles **IIe–IIg** also led to carbomoylation of the exocyclic nitrogen. With isocyanate **Ia** possessing enhanced electrophilicity of the heterocumulene group both alternatives of the primary reaction may occur resulting in formation alongside intermediates **E** also intermediates **F** that further undergo cyclization into compounds **IVa–IVc**. The experiments carried out at various temperature suggest that intermediate **E** resulted from the thermodynamical control, and intermediate **F**, from kinetic control.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer UR-20 from KBr pellets. ^1H, ^{13}C, and ^{19}F NMR spectra taken from solutions in DMSO-d_6 were registered on a spectrometer Varian Mercury (400.39, 100.69, 376.71 MHz respectively), internal refernces TMC (^1H, ^{13}C), C_6F_6 (^{19}F).

Compound **IIIm** exists in the crystal as a solvate with ethanol. Crystals of compound **IIIm** triclinic, $C_{25}H_{19}F_3N_4O_2 \cdot C_2H_5OH$, at 20°C *a* 9.975(2), *b* 10.244(2), *c* 14.224(3) Å, α 103.12(6), β 101.11(3), γ 112.39(3), *V* 1244.4(5) Å^3, M_r 510.51, *Z* 2, space group *Püÿ*, d_{calc} 1.362 g/cm^3, μ(MoK_α) 0.106 mm^{-1}, *F*(000) 532. The unit cell parameters and intensities of 4526 reflections (4270 independent, R_{int} 0.039) were measured on an automatic four-circle diffractometer Siemens P3/PC (MoK_α, graphite monochromator, 2θ/θ-scanning, $2\theta_{max}$ 50°). The structure was solves by the direct method using software package SHELX97 [27]. The hydrogen atoms positions were revealed from the difference synthesis of the electron density and refined in *rider* model with $U_{iso} = nU_{eq}$ of the nonhydrogen atom linked to the given hydrogen (n = 1.5 for methyl, 1.2 for the other hydrogen atoms). The ethanol molecule is disordered by two positions with occupancies 59:41% as refined by putting constrains on the length of C–C bonds [1.513(3) Å] and C–O [1.426(3) Å]. The structure was refined with respect to F^2 by the full-matrix least-mean-squares method in anisotropic approximation for nonhydrogen atoms till wR_2 0.135 for 4229 reflections [R_1 0.051 for 2691 reflections with $F > 4\sigma(F)$, *S* 1.007]. Crystallographic parameters, atomic coordinates, and geometrical parameters of molecules are deposited in Cambridge Structural Database (no. CCDC 287905).

3-Amino-1-arylimino-1*H*-isoindoles were synthesized from phthalonitrile and the corresponding amines along the known method [24]. 1-Chloroalkyl isocyanates were prepared by procedure [28].

4-Aryl-6-arylimino-4-trifluoromethyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]isoindol-2-ones IIIa–

IIIn. To a dispersion of 3 mmol of 3-amino-1-arylimino-1*H*-isoindole **IIa–IIg** in 10 ml of anhydrous toluene was added 3.6 mmol of triethylamine. Then at stirring was added dropwise a solution of 3 mmol of isocyanate **Ia–Ic** in 5 ml of toluene. The reaction mixture was stirred for 2 h at room temperature. The separated precipitate was filtered off, washed with water to remove triethylamine hydrochloride, and recrystallized from 60% aqueous ethanol.

6-(2-Methylphenyl)imino-4-trifluoromethyl-4-phenyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]isoindol-2-one (IIIa). Yield 89%, mp 180–182°C. IR spectrum, ν, cm^{-1}: 1645 (C=O), 3105, 3220 (N–H). ^{1}H NMR spectrum, δ, ppm: 1.50 br.s (3H, CH_3), 6.46–6.53 m (2H), 7.01–7.13 m (3H), 7.42–7.50 m (4H), 7.69–7.76 m (3H), 8.09 d (1H, *J* 7.6 Hz), 9.17 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 17.39 (CH_3), 118.25, 123.71, 124.44, 124.92, 125.33, 126.64, 127.34, 127.95, 128.06, 128.79, 129.79, 131.06, 132.80, 133.68, 134.81, 135.01, 146.29, 147.41, 154.22, 160.50 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.13. Found, %: C 66.22; H 4.11; N 12.83. $C_{24}H_{17}F_3N_4O_3$. Bû ×θCλε-νO, %: C 66.36; H 3.94; N 12.90.

6-(2-Methoxyphenyl)imino-4-trifluoromethyl-4-phenyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]isoindol-2-one (IIIb). Yield 79%, mp 230–231°C. IR spectrum, ν, cm^{-1}: 1640 (C=O), 3100, 3220 (N–H). ^{1}H NMR spectrum, δ, ppm: 3.52 br.s (3H, OCH_3), 6.39 br.s (1H), 6.70 d (1H, *J* 7.6 Hz), 6.84 t (1H, *J* 8 Hz), 6.92 d (1H, *J* 8.4 Hz), 7.06 t (1H, *J* 8 Hz), 7.38–7.42 m (3H), 7.50 t (1H, *J* 7.6 Hz), 7.65 br.s (2H), 7.72 t (1H, *J* 7.6 Hz), 8.07 d (1H, *J* 7.6 Hz), 9.11 C (1H, NH). ^{13}C NMR spectrum, δ, ppm: 56.23 (OCH_3), 113.18, 119.91, 121.64, 123.68, 124.27, 125.29, 125.83, 126.60, 127.82, 128.43, 128.62, 129.68, 132.48, 133.60, 134.69, 135.08, 136.37, 148.19, 148.78, 154.23, 160.54 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.17. Found, %: C 63.82; H 4.00; N 12.39. $C_{24}H_{17}F_3N_4O_2$. Calculated, %: C 64.00; H 3.80; N 12.44.

6-(2,4-Dimethylphenyl)imino-4-trifluoromethyl-4-phenyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]isoindol-2-one (IIIc). Yield 74%, mp 138–140°C. IR spectrum, ν, cm^{-1}: 1640 (C=O), 3100, 3205 (N–H). ^{1}H NMR spectrum, δ, ppm: 1.50 br.s (3H, CH_3), 2.24 s (3H, CH_3), 6.41 br.s (1H), 6.60 d (1H, *J* 7.6 Hz), 6.93 d (1H, *J* 8 Hz), 6.98 s (1H), 7.43–7.54 m (3H), 7.59 t (1H, *J* 7.6 Hz), 7.73–7.78 m (3H), 8.09 d (1H, *J* 7.6 Hz), 9.27 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 17.38 (CH_3), 20.97 (CH_3), 118.15, 123.72, 124.38, 125.37, 126.63, 126.86, 127.71, 127.91, 128.03, 128.76, 129.75, 131.67, 132.77, 133.60, 133.85, 134.82, 135.02, 143.76, 147.41, 154.24, 160.53 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.17. Found, %: C 67.22; H 4.38; N 12.50. $C_{25}H_{19}F_3N_4O$. Calculated, %: C 66.96; H 4.27; N 12.49.

6-(2,6-Dimethylphenyl)imino-4-trifluoromethyl-4-phenyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]isoindol-2-one (IIId). Yield 94%, mp 225–227°C. IR spectrum, ν, cm^{-1}: 1645 (C=O), 3085, 3215 (N–H). ^{1}H NMR spectrum, δ, ppm: 1.29 s (3H, CH_3), 1.89 s (3H, CH_3), 6.38 d (1H, *J* 7.6 Hz), 6.89–7.00 m (3H), 7.41–7.48 m (4H), 7.72–7.76 m (3H), 8.08 d (1H, *J* 7.6 Hz), 9.18 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 17.68 (CH_3), 17.90 (CH_3), 123.69, 124.28, 124.32, 124.40, 125.17, 126.21, 126.60, 128.15, 128.38, 128.61, 128.75, 128.84, 129.85, 132.32, 133.89, 134.92, 135.46, 145.27, 147.89, 154.19, 160.41 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.17. Found, %: C 66.80; H 4.15; N 12.19. $C_{25}H_{19}F_3N_4O$. Calculated, %: C 66.96; H 4.27; N 12.49.

4-(4-Methylphenyl)-6-(2,4-dimethylphenyl)-imino-4-trifluoromethyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]-isoindol-2-one (IIIe). Yield 80%, mp 230–231°C. IR spectrum, ν, cm^{-1}: 1640 (C=O), 3100, 3220 (N–H). ^{1}H NMR spectrum, δ, ppm: 1.53 br.s (3H, CH_3), 2.28 s (3H, CH_3), 2.37 s (3H, CH_3), 6.36 br.s (1H), 6.60 d (1H, *J* 7.6 Hz), 6.88 d (1H, *J* 7.6 Hz), 6.92 C (1H, *J* 7.6 Hz), 7.20 d (2H, *J* 8 Hz), 7.47 t (1H, *J* 7.6 Hz), 7.54 d (2H, *J* 8 Hz), 7.72 t (1H, *J* 7.6 Hz), 8.07 d (1H, *J* 7.6 Hz), 9.07 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 19.73 (CH_3), 20.98 (CH_3), 21.21 (CH_3), 118.16, 123.75, 124.36, 125.36, 126.68, 126.87, 127.72, 127.83, 128.07, 129.21, 131.69, 131.94, 132.75, 133.56, 133.82, 135.00, 139.23, 143.82, 147.45, 154.31, 160.52 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.21. Found, %: C 67.59; H 4.69; N 12.29. $C_{26}H_{21}F_3N_4O$. Calculated, %: C 67.52; H 4.58; N 12.11.

6-(4-Bromophenyl)imino-4-(4-methylphenyl)-4-trifluoromethyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]-isoindol-2-one (IIIf). Yield 78%, mp 195–197°C. IR spectrum, ν, cm^{-1}: 1640 (C=O), 3100, 3215 (N–H). ^{1}H NMR spectrum, δ, ppm: 2.37 s (3H, CH_3), 6.48 d (2H, *J* 8.8 Hz), 6.73 d (1H, *J* 7.6 Hz), 7.19 d (2H, *J* 8.4 Hz), 7.42 d (2H, *J* 8.4 Hz), 7.51–7.56 m (3H), 7.75 t (1H, *J* 7.6 Hz), 8.08 d (1H, *J* 7.6 Hz), 9.10 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 21.27 (CH_3), 116.94, 121.21, 123.72, 124.54, 125.88, 126.57, 126.64, 127.73, 127.84, 129.16, 129.58, 130.07, 131.44, 131.54, 132.94, 132.97, 133.76, 134.98, 139.21, 146.60, 147.84, 154.16, 160.50 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.45. Found, %: C 55.96; H 3.29; N 11.11. $C_{24}H_{16}BrF_3N_4O$. Calculated, %: C 56.16; H 3.14; N 10.91.

4-(4-Methylphenyl)-6-(4-methylphenyl)imino-4-trifluoromethyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]-isoindol-2-one (IIIg). Yield 82%, mp 158–160°C. IR spectrum, ν, cm^{-1}: 1640 (C=O), 3095, 3200 (N–H). ^{1}H NMR spectrum, δ, ppm: 2.32 s (3H, CH_3), 2.38 s (3H, CH_3), 6.42 d (2H, *J* 8 Hz), 6.69 d (1H, *J* 7.6 Hz), 7.07 d (2H, *J* 8 Hz), 7.20 d (2H, *J* 8 Hz), 7.48 t (1H, *J* 7.6 Hz), 7.53 d (2H, *J* 8 Hz), 7.72 t (1H, *J* 7.6 Hz), 8.07 d (1H, *J* 7.6 Hz), 9.05 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 21.01 (CH_3), 21.26 (CH_3), 118.78, 123.78, 124.39, 125.81, 126.68, 127.71, 127.87, 129.12, 130.46, 131.77, 132.95, 133.52, 133.84, 134.78, 139.11, 144.95, 147.60, 154.27, 160.61 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.47. Found, %: C 66.99; H 4.35; N 12.22. $C_{25}H_{19}F_3N_4O$. Calculated, %: C 66.96; H 4.27; N 12.49.

6-(2-Methylphenyl)imino-4-(4-methoxyphenyl)-4-trifluoromethyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]-isoindol-2-one (IIIh). Yield 82%, mp 182–183°C. IR spectrum, ν, cm^{-1}: 1645 (C=O), 3100, 3210 (N–H). ^{1}H NMR spectrum, δ, ppm: 1.52 br.s (3H, CH_3), 3.79 s (3H, OCH_3), 6.45–6.52 m (2 H), 6.92 d (2H, *J* 8.4 Hz), 7.01–7.13 m (3H), 7.46 t (1H, *J* 7.2 Hz), 7.59 d (2H, *J* 8.4 Hz), 7.73 t (1H, *J* 7.2 Hz), 8.07 d (1H, *J* 7.2 Hz), 9.08 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 17.44 (CH_3), 55.84 (OCH_3), 114.02, 118.25, 123.79, 124.41, 124.88, 125.31, 126.62, 126.71, 126.91, 127.38, 128.12, 129.54, 131.10, 132.78, 133.62, 134.95, 146.42, 147.51, 154.70, 160.30, 160.48 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.42. Found, %: C 64.69; H 4.19; N 11.97. $C_{25}H_{19}F_3N_4O_2$. Calculated, % C 64.65; H 4.12; N 12.06.

4-(4-Methoxyphenyl)-6-(2-methoxyphenyl)-imino-4-trifluoromethyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]-isoindol-2-one (IIIi). Yield 88%, mp 207–208°C. IR spectrum, ν, cm^{-1}: 1645 (C=O), 3090, 3200 (N–H). ^{1}H NMR spectrum, δ, ppm: 3.53 br.s (3H, OCH_3), 3.80 s (3H, OCH_3), 6.44 br.s (1H), 6.69 d (1H, *J* 7.6 Hz), 7.82–7.94 m (4H), 7.05 t (1H, *J* 8 Hz), 7.49 t (1H, *J* 7.6 Hz), 7.56 d (2H, *J* 8.8 Hz), 7.71 t (1H, *J* 7.6 Hz), 8.05 d (1H, *J* 7.6 Hz), 9.01 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 55.77 (OCH_3), 56.20 (OCH_3), 113.18, 113.84, 119.88, 121.67, 123.75, 124.24, 125.27, 125.79, 126.55, 126.67, 128.45, 129.43, 132.48, 133.54, 135.02, 136.53, 148.27, 148.81, 154.39, 160.13, 160.49 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.34. Found, %: C 62.59; H 4.17; N 11.60. $C_{25}H_{19}F_3N_4O_3$. Calculated, %: C 62.50; H 3.99; N 11.66.

6-(2,4-Dimethylphenyl)imino-4-(4-methoxyphenyl)-4-trifluoromethyl-3,4-dihydro-1,3,5-triazino-[2,1-*a*]isoindol-2-one (IIIj). Yield 78%, mp 230–232°C. IR spectrum, ν, cm^{-1}: 1640 (C=O), 3085, 3205 (N–H). ^{1}H NMR spectrum, δ, ppm: 1.56 br.s (3H, CH_3), 2.29 s (3H, CH_3), 3.80 s (3H, OCH_3), 6.37 br.s (1H), 6.58 d (1H, *J* 8.0 Hz), 6.87–6.93 m (4H), 7.47 t (1H, *J* 7.6 Hz), 7.58 d (2H, *J* 8.4 Hz), 7.72 t (1H, *J* 7.6 Hz), 8.06 d (1H, *J* 7.6 Hz), 9.04 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 17.38 (CH_3), 20.97 (CH_3), 55.83 (OCH_3), 113.99, 118.25, 123.80, 124.34, 125.34, 126.69, 126.79, 127.75, 128.09, 129.49, 131.69, 132.75, 133.54, 133.80, 134.96, 143.89, 147.52, 154.43, 160.27, 160.49 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.47. Found, %: C 65.31; H 4.50; N 11.79. $C_{26}H_{21}F_3N_4O_2$. Calculated, %: C 65.27; H 4.42; N 11.71.

6-(2,6-Dimethylphenyl)imino-4-(4-methoxyphenyl)-4-trifluoromethyl-3,4-dihydro-1,3,5-triazino-[2,1-*a*]isoindol-2-one (IIIk). Yield 89%, mp 218–220°C. IR spectrum, ν, cm^{-1}: 1640 (C=O), 3090, 3200 (N–H). ^{1}H NMR spectrum, δ, ppm: 1.36 s (3H, CH_3), 1.89 s (3H, CH_3), 3.80 s (3H, OCH_3), 6.37 d (1H, *J* 7.6 Hz), 6.89–7.01 m (5H), 7.46 t (1H, *J* 7.6 Hz), 7.63 d (2H, *J* 8.8 Hz), 7.73 t (1H, *J* 7.6 Hz), 8.07 d (1H, *J* 7.6 Hz), 9.10 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 17.71 (CH_3), 17.89 (CH_3), 55.86 (OCH_3), 114.07, 123.76, 124.26, 124.28, 124.35, 125.17, 126.14, 126.69, 128.43, 128.64, 128.75, 129.73, 132.30, 133.83, 135.42, 145.37, 147.94, 154.32, 160.38 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.21. Found, %: C 65.38; H 4.35; N 12.10. $C_{26}H_{21}F_3N_4O_2$. Calculated, %: C 65.27; H 4.42; N 11.71.

6-(4-Bromophenyl)imino-4-(4-methoxyphenyl)-4-trifluoromethyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]-isoindol-2-one (IIIl). Yield 91%, mp 202–203°C. IR spectrum, ν, cm^{-1}: 1645 (C=O), 3100, 3215 (N–H). ^{1}H NMR spectrum, δ, ppm: 3.81 s (3H, OCH_3), 6.51 d (2H, *J* 8 Hz), 6.73 d (1H, *J* 7.6 Hz), 6.90 d (2H, *J* 8.4 Hz), 7.43 d (2H, *J* 8 Hz), 7.51–7.58 m (3H), 7.75 t (1H, *J* 7.6 Hz), 8.08 d (1H, *J* 7.6 Hz), 9.08 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 55.79 (OCH_3), 113.87, 116.91, 121.21, 123.77, 124.53, 125.88, 126.31, 126.69, 127.85, 129.44, 132.85, 132.98, 133.72, 134.95, 146.68, 147.88, 154.30, 160.15, 160.44 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.46. Found, %: C 54.53; H 3.19; N 10.77. $C_{24}H_{16}BrF_3N_4O_2$. Calculated, %: C 54.46; H 3.05; N 10.58.

6-(4-Methylphenyl)imino-4-(4-methoxyphenyl)-4-trifluoromethyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]-isoindol-2-one (IIIm). Yield 85%, mp 210–212°C. IR spectrum, ν, cm^{-1}: 1640 (C=O), 3080, 3210 (N–H). ^{1}H NMR spectrum, δ, ppm: 2.33 s (3H, CH_3), 3.81 s (3H, OCH_3), 6.44 d (2H, *J* 7.6 Hz), 6.68 d (1H, *J* 7.6 Hz),

6.91 d (2H, *J* 8.4 Hz), 7.08 d (2H, *J* 7.6 Hz), 7.47 t (1H, *J* 7.6 Hz), 7.56 d (2H, *J* 8.4 Hz), 7.71 t (1H, *J* 7.6 Hz), 8.06 d (1H, *J* 7.6 Hz), 9.02 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 21.02 (CH_3), 55.78 (OCH_3), 113.84, 118.77, 123.81, 124.38, 125.81, 126.54, 126.89, 127.88, 129.41, 130.48, 132.95, 133.49, 133.83, 134.76, 145.02, 147.64, 154.40, 160.11, 160.56 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.43. Found, %: C 64.76; H 4.25; N 12.19. $C_{25}H_{19}F_3N_4O_2$. Calculated, %: C 64.65; H 4.12; N 12.06.

4-(4-Methoxyphenyl)-6-(4-methoxyphenyl)-imino-4-trifluoromethyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]-isoindol-2-one (IIIn). Yield 79%, mp 223–224°C. IR spectrum, ν, cm^{-1}: 1640 (C=O), 3085, 3215 (N–H). ^{1}H NMR spectrum, δ, ppm: 7.76 s (3H, OCH_3), 3.80 s (3H, OCH_3), 6.48 d (2H, *J* 8.8 Hz), 6.76 d (1H, *J* 7.6 Hz), 6.83 d (2H, *J* 8.8 Hz), 6.91 d (2H, *J* 8.4 Hz), 7.50 t (1H, *J* 7.6 Hz), 7.56 d (2H, *J* 8.4 Hz), 7.71 t (1H, *J* 7.6 Hz), 8.06 d (1H, *J* 7.6 Hz), 9.14 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 55.76 (OCH_3), 55.78 (OCH_3), 113.82, 115.25, 120.15, 123.81, 124.34, 125.77, 126.64, 126.72, 127.80, 129.41, 132.94, 133.34, 134.80, 140.54, 147.93, 154.45, 156.83, 160.09, 160.60 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.37. Found, %: C 62.59; H 4.15; N 11.67. $C_{25}H_{19}F_3N_4O_3$. Calculated, % C 62.50; H 3.99; N 11.66.

6-(4-Methylphenyl)imino-2-trifluoromethyl-2-phenyl-2,3-dihydro-1,3,5-triazino[2,1-*a*]isoindol-4-one (IVb) was obtained in a mixture with **6-(4-methylphenyl)imino-4-trifluoromethyl-4-phenyl-3,4-dihydro-1,3,5-triazino[2,1-*a*]isoindol-2-one (IIIp)** by a similar procedure. Yield of isomers mixture 90%. The isomers were separated by column chromatography (silica gel, dichloromethane–acetone, 8:2).

Compound IVb. mp 262–263°C. IR spectrum, ν, cm^{-1}: 1740 (C=O), 3165, 3260 (N–H). ^{1}H NMR spectrum, δ, ppm: 2.40 s (3H, CH_3), 6.63 d (1H, *J* 7.6 Hz), 6.78 d (2H, *J* 8.4 Hz), 7.20 d (2H, *J* 8.4 Hz), 7.41–7.55 m (4H), 7.70 t (1H, *J* 7.6 Hz), 7.88 d (2H, *J* 7.6 Hz), 8.12 d (1H, *J* 7.6 Hz), 9.58 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 21.11 (CH_3), 119.02, 123.91, 125.42, 126.13, 127.38, 129.05, 129.32, 130.06, 130.10, 131.81, 133.41, 134.02, 137.84, 146.21, 146.27, 147.57, 152.19 (C=O). ^{19}F NMR spectrum, δ, ppm: –80.73. Found, %: C 66.57; H 3.90; N 12.77. $C_{24}H_{17}F_3N_4O$. Calculated, %: C 66.36; H 3.94; N 12.90.

Compound IIIp. Mp 262–263°C. IR spectrum, ν, cm^{-1}: 1645 (C=O), 3085, 3190 (N–H). ^{1}H NMR spectrum, δ, ppm: 2.32 s (3H, CH_3), 6.39 d (2H, *J* 8 Hz), 6.70 d (1H, *J* 7.6 Hz), 7.06 d (2H, *J* 8 Hz), 7.40–7.43 m (3H), 7.48 t (1H, *J* 7.6 Hz), 7.64–7.71 m (2H), 7.73 t (1H, *J* 7.6 Hz), 8.07 d (1H, *J* 7.6 Hz), 9.23 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 21.02 (CH_3), 118.74, 123.68, 124.42, 125.80, 126.67, 127.80, 128.62, 129.73, 130.44, 132.94, 133.55, 133.88, 134.68, 134.81, 144.81, 147.46, 154.25, 160.59 (C=O). ^{19}F NMR spectrum, δ, ppm: –74.14. Found, %: C 66.49; H 3.81; N 12.92. $C_{24}H_{17}F_3N_4O$. Calculated, %: C 66.36; H 3.94; N 12.90.

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