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Dedicated to Professor Andrzej Rykowski on the occasion of his 77th birthday

Reinvestigation of the reaction of 3-substituted 1,2,4-triazines with nitronate anions: unexpected behavior of 3-(2-ethoxyphenyl)-1,2,4-triazine in the reaction with anions of nitroalkanes

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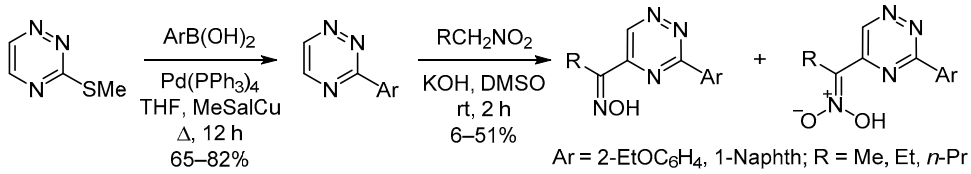


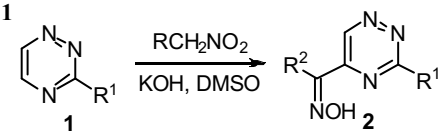
Ar = 2-EtOC$_6$H$_4$, 1-Naphth; R = Me, Et, *n*-Pr

3-Substituted 1,2,4-triazines easily react with nitronate anions to replace hydrogen atom in the position C-5 according to nucleophilic substitution mechanism and form appropriate oximes of 5-formyl- or 5-acyl-1,2,4-triazines. Present study has shown that the course of the reaction strongly depends on the structure of the substituent in the position C-3 of 1,2,4-triazine ring. Thus, 2-ethoxyphenyl substituent in 1,2,4-triazine allowed to form, besides appropriate oximes, also new nitronic acid derivatives stabilized by intramolecular hydrogen bonds. The synthesis pathway and molecular structures of oximes were confirmed by X-ray analysis performed for model compound 1-[3-(2-ethoxyphenyl)-1,2,4-triazin-5-yl]ethanone oxime. The presence of the new nitronic acid derivatives in the reaction mixture and the theoretical calculations at DFT/B3LYP/6-311++G(d,p) level strongly suggest that intermediate stabilized by bifurcated intramolecular hydrogen bond is a common intermediate for the construction of appropriate oximes.

Keywords: nitroalkanes, nitronate anions, oximes, 1,2,4-triazine, nucleophilic substitution reaction.

Hydrogen nucleophilic substitution reactions are excellent tools for the synthesis and functionalization of heterocyclic systems.[1] Due to the strong electron-deficient nature, 1,2,4-triazine derivatives readily undergo addition of nucleophilic agents. These processes may also include the reaction of 1,2,4-triazine with nitronate discovered by Rykowski and Mąkosza, in the mid 80's.[2] This reaction leads to the substitution of hydrogen atom at the C-5 position of 1,2,4-triazine by hydroxyiminoalkyl group (Scheme 1).

Scheme 1



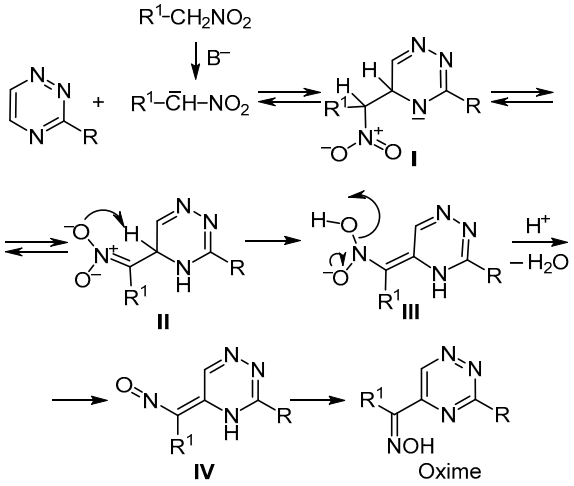
R^1 = H, Me, OMe, SMe, S*i*-Pr, Ph
R^2 = H, Me, Et, *n*-Pr, *n*-Bu

In this process, nitroalkanes play a role of masked acylating agents giving in a first stage oximes of 5-formyl- or 5-acyl-1,2,4-triazines.[2,3] Oximes of 5-formyl- and 5-acyl-1,2,4-triazines obtained in this way are used widely in the synthesis of new heterocyclic derivatives. They have been used in the preparation of 5-acyl-1,2,4-triazines,[2,3] chiral 1,2,4-triazine alcohols,[4] 2-acylpyridines,[5] cyanotriazines,[6] pyrazolo[4,3-*e*][1,2,4]triazines,[7] and 3-aryl-5,6,7,8-tetrahydroisoquinolines which are valuable precursors for the synthesis of alkaloid sempervirine and its analogs.[8]

Due to the fact that the synthesis of oximes has a wide range of applications in organic chemistry, it became of interest to reinvestigate their formation mechanism proposed for the first time by Rykowski and Mąkosza[2] (Scheme 2).

The proposed mechanism involves the attachment of carbanion to the carbon atom at the position C-5 of 1,2,4-triazine ring to form the anionic σ^H-adduct **I**. This adduct is in equilibrium with the *aci*-nitro form **II**, wherein the proton of the methine group is transferred to the nitrogen atom N-2 of 1,2,4-triazine ring. Detachment of proton from the position C-5 of 1,2,4-triazine ring through an oxygen atom of the nitro group followed by elimination of OH group (compound **III**) gives nitroso compound **IV**. Isomerization of the latter leads to the corresponding oxime. This scheme

Scheme 2



is only a hypothetical assumption because so far it has not been possible to prove the formation of intermediate products, except for the σ^H-adduct which is formed in the first step, and its presence was documented by spectroscopic methods.[9]

In this work, we have attempted to obtain and identify the intermediates proposed by Rykowski and Mąkosza using specific 3-substituted 1,2,4-triazines in the reaction with carbanions generated from nitroalkanes.

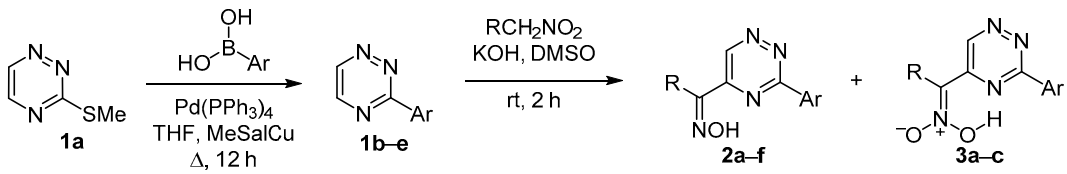
Recently, oximes of 5-acyl-1,2,4-triazine were used in the synthesis of sildenafil analogs with pyrazolo[4,3-*e*]-[1,2,4]triazine core.[10] A key feature of this synthesis was introduction of the 2-ethoxyphenyl substituent into the heterocyclic system in the place of the methylsulfanyl group.[10,11] This may be achieved in two ways. One way involved Suzuki coupling reaction of the appropriate derivatives of the pyrazolo[4,3-*e*][1,2,4]triazine with 2-ethoxyphenylboronic acid.[11] The second synthesis method of sildenafil analogs could be initiated by reaction of 3-methylsulfanyl-1,2,4-triazine (**1a**) with 2-ethoxyphenylboronic acid which leads to 3-(2-ethoxyphenyl)-1,2,4-triazine (**1b**) in 65% yield. The latter can easily react with nitronate anions generated from nitroethane, nitropropane, or nitrobutane (Scheme 3). However, besides of the expected oximes **2a**–**c**, byproducts **3a**–**c** were found in the reaction mixture, which so far have not been observed in the reaction of 3-phenyl-, 3-methyl, 3-methoxy-1,2,4-triazines, etc. with nitroalkanes.[2]

In all cases, the TLC control of the reactions of compound **1b** with nitronate anions revealed the presence in the reaction mixture of expected oximes **2a**–**c** and byproducts **3a**–**c** which did not precipitate after pouring the reaction mixture into ice water and acidification with AcOH. The latter compounds were isolated by extraction with Et_2O from the filtrate after separation of the oximes. The R_f value of compounds **3a**–**c** were always higher than the R_f value of the corresponding oximes. Products **3a**–**c** were purified by column chromatography using a mixture of CH_2Cl_2–EtOH, 50:1. The structures of the obtained new oximes **2a**–**c** and compounds **3a**–**c** were established by ^1H and ^{13}C NMR spectroscopy, elemental analysis, and mass spectrometry. In the ^1H NMR spectra for compounds **2a**–**c**, we could see characteristic signals in the range of 7.06–7.86 ppm corresponding to the protons of the aromatic ring in the C-3 position of 1,2,4-triazine and coupled signals for the ethoxy group as a triplet at 1.38 ppm and quartet at 4.15 ppm. The NMR spectra for derivatives **3a**–**c** were very similar to the spectra of the corresponding oximes **2a**–**c**. There was only a small difference in the chemical shifts of the corresponding signals.

The presence of compounds **3a**–**c** in the reaction mixtures encouraged us to investigate the conditions of their formation and the possibility of transformation into the corresponding oximes **2a**–**c**. Thus, the first problem that had to be solved was determination of influence of the substituent structure present in the position C-3 of the 1,2,4-triazine ring on the course of the reaction. Therefore, in the next step of our study, we have prepared 3-aryl-1,2,4-triazines **1c**–**e** in the Suzuki reaction of compound **1a** with appropriate available arylboronic acids using procedure described in the literature (Scheme 3).[11] 3-Aryl-1,2,4-triazines **1c**–**e** were obtained in good yields. The chemical structures of the obtained 3-aryl-1,2,4-triazines were confirmed by ^1H and ^{13}C NMR spectra.

Next, we have decided to react obtained 3-aryl-1,2,4-triazine derivatives **1c**–**e** with nitroethane using literature procedure (Scheme 3).[2] In all performed reactions, only oximes **2d**–**f** were isolated and no corresponding structures similar to derivatives **3a**–**c** were observed. The structures of oximes **2d**–**f** were confirmed by ^1H and ^{13}C NMR spectra. These experiments show that the formation of derivatives **3a**–**c** strongly depends on the presence of the alkoxy group in position C-2' of the phenyl ring attached to the carbon C-3 of 1,2,4-triazine. This can probably be explained by the possibility of hydrogen bond formation between the OH group of *aci*-nitro group and triazine nitrogen atom N-4 (O–H···N(4)) (Fig. 1, structure **A**). It could be facilitated by the presence of electron-donating alkoxy group at the *ortho* position of the phenyl ring which can increase the electron density on the triazine nitrogen

Scheme 3



1 b Ar = 2-EtOC$_6$H$_4$ (65%), **c** Ar = 4-EtOC$_6$H$_4$ (80%), **d** Ar = Ph (82%), **e** Ar = 1-Naphth (70%)
2 a Ar = 2-EtOC$_6$H$_4$, R = Me (47%); **b** Ar = 2-EtOC$_6$H$_4$, R = Et (37%); **c** Ar = 2-EtOC$_6$H$_4$, R = *n*-Pr (45%);
d Ar = 4-EtOC$_6$H$_4$, R = Me (14%); **e** Ar = Ph, R = Me (41%); **f** Ar = 1-Naphth, R = Me (51%)
3 a Ar = 2-EtOC$_6$H$_4$, R = Me (6%); **b** Ar = 2-EtOC$_6$H$_4$, R = Et (10%); **c** Ar = 2-EtOC$_6$H$_4$, R = *n*-Pr (13%)

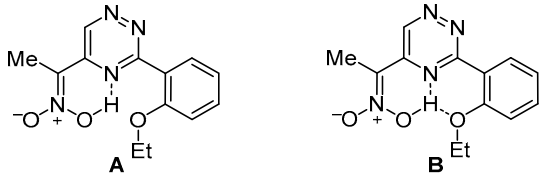


Figure 1. Plausible intramolecular hydrogen bonds in the structure of compounds **3a**–**c**.

atom N-4. Moreover, it should be mentioned that the basicity of the nitrogen atoms in the 1,2,4-triazine and its 3-substituted derivatives decrease in the order of N-4 > N-2 > N-1, which means that electron density in the 1,2,4-triazine molecule is the highest around nitrogen atom N-4 and the atom readily accepts electrons.[12] On the other hand, the formation of another hydrogen bond between the OH group and an ethoxy substituent is also possible (O–H···O–Et) giving structure **B** (Fig. 1) stabilized by a double intramolecular interaction.

The lack of appropriate nitronic acid form **3** in the reaction of triazines **1c**–**e** with nitroethane may confirm the occurrence of intramolecular hydrogen bonds in derivatives **3a**–**c**. These bonds have a significant effect on the stability of structures **3a**–**c** and allow their isolation from the reaction mixture, while in the reaction of triazines **1c**–**e** with nitromethane the less stable nitronic acid forms without additional O–H···O intramolecular hydrogen bond probably are completely transformed into final oximes **2d**–**f**.

As can be seen in Scheme 2, the reaction of 1,2,4-triazine with nitronate anions involves in the first step the addition of a nucleophilic agent and formation of σ^H-adduct which undergoes dehydration to yield final oxime. Detection of the σ^H-adducts as key intermediates in the nucleophilic substitution reaction is possible by nuclear magnetic resonance methods.[13] In the adduct, signals of hydrogen attached to carbon atom C-5 are shifted (Fig. 2). The chemical shift of the proton in the range of 3.5–4.0 ppm is a result of a change of hybridization of the C-5 carbon atom from sp^2 to sp^3. The formation of the σ^H-adduct is a very fast process, and the adduct has the highest stability due to energetically preferred *p*-quinone structure[12] with negative charge on the nitrogen atom N-2 (Fig. 2).

In order to investigate chemical transformations of the σ^H-adduct we have performed its synthesis starting from 1,2,4-triazine **1b** and nitroethane in the presence of K_2CO_3 in DMSO according to the method described previously (Scheme 4).[9] The reaction was carried out at room temperature for 2.5 h. After this time, the reaction mixture was poured into ice water. Diastereoisomers **4a** were extracted with Et_2O and then purified by column chromatography using EtOAc–hexane, 1:1 mixture to give products in 32% total yield. To increase the yield, the reaction time was prolonged to 3.5 h. In this case compounds **4a** were obtained in 69% total yield. Since the stereochemistry of the adduct does not affect subsequent steps in the synthesis of oximes, exact configuration of diastereoisomers was not determined. The structure of the major and minor adducts was confirmed using NMR spectroscopy and mass spectrometry.

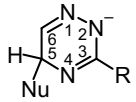
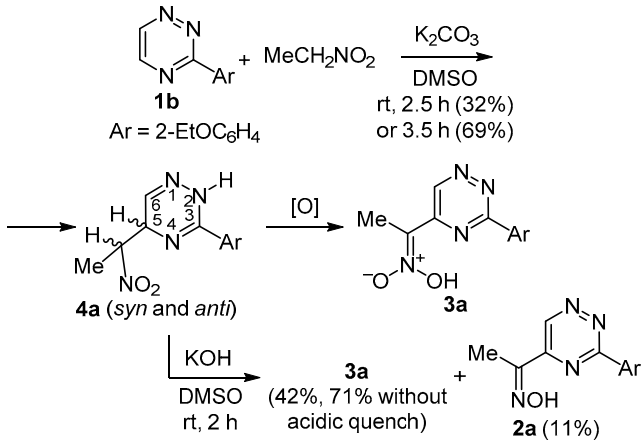


Figure 2. Structure of the σ^H-adduct.

Scheme 4



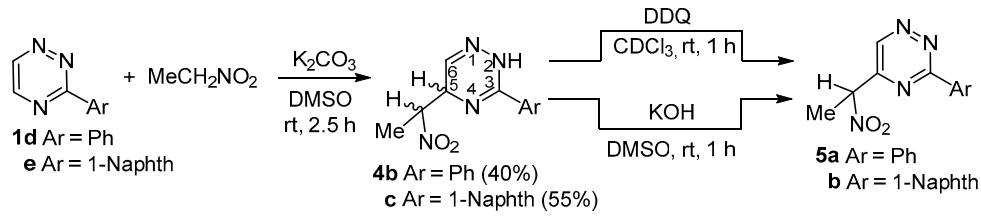
^{1}H NMR spectra of compound **4a** (major diastereomer) showed the characteristic doublet of doublet for the proton at C-5 in the range of 4.00–4.02 ppm while the proton in 3-(2-ethoxyphenyl)-1,2,4-triazine (**1b**) was observed with the chemical shift of 8.67 ppm. Moreover, the proton in the C-6 position of triazine **4a** was observed as doublet at 6.82 ppm while in the NMR spectra of compound **1b** the proton was present as doublet at 9.14 ppm. Signal at 10.69 ppm in the ^{1}H NMR spectra for compound **4a** is derived from the N(2)–H proton whereas signals in the range of 6.90–7.40 ppm belong to the ethoxyphenyl ring. Characteristic doublet of quartets in the range of 4.90–4.94 ppm derived from the proton linked to the carbon with nitro group NO_2 ($CH_3C\underline{H}NO_2$). Quartet at 4.07 and triplet at 1.32 ppm were provided by ethoxy group. Doublet present at 1.61 ppm derived from the methyl group of $C\underline{H}_3CHNO_2$ moiety. Continuing our research the obtained adduct **4a** was subjected to oxidation at room temperature using a variety of oxidizing agents, namely, DDQ, *p*-chloranil, $KMnO_4$, Br_2, O_2 (Scheme 4, Table 1).

The first experiment was conducted for 1 h at room temperature in $CDCl_3$ using DDQ as an oxidant (Table 1, entry 1). The use of the deuterated solvent enabled the control of the reaction progress by NMR. As a result of this transformation, compound **3a** was obtained with 50% yield. Its structure was established by ^{1}H NMR spectrum

Table 1. Conditions and yields of the oxidation of compound **4a**

Entry	Oxidant	Product	Yield, %
1	DDQ	**3a**	50
2	*p*-Chloranil	**3a**	71
3	$KMnO_4$	–	Decomposition of the adduct
4	Br_2	–	Decomposition of the adduct
5	O_2	**4a**	Only adduct recovered

Scheme 5



and was compared with the spectrum obtained for compound **3a** from the reaction of triazine **1b** with nitroethane in suspension of KOH in DMSO (Scheme 3). The comparison of ^{1}H NMR and mass spectra confirmed that compound **3a** can form upon oxidation of adduct **4a**. The next oxidation process was performed at room temperature in $CDCl_3$ in the presence of *p*-chloranil as the oxidizing agent (Table 1, entry 2). In this case, after 1 h product **3a** was obtained in 71% yield, and its ^{1}H NMR spectrum was identical with the spectrum of product obtained in the reaction with DDQ. Oxidation of adduct **4a** in the presence of $KMnO_4$, Br_2, and O_2 failed (Table 1, entries 3–5).

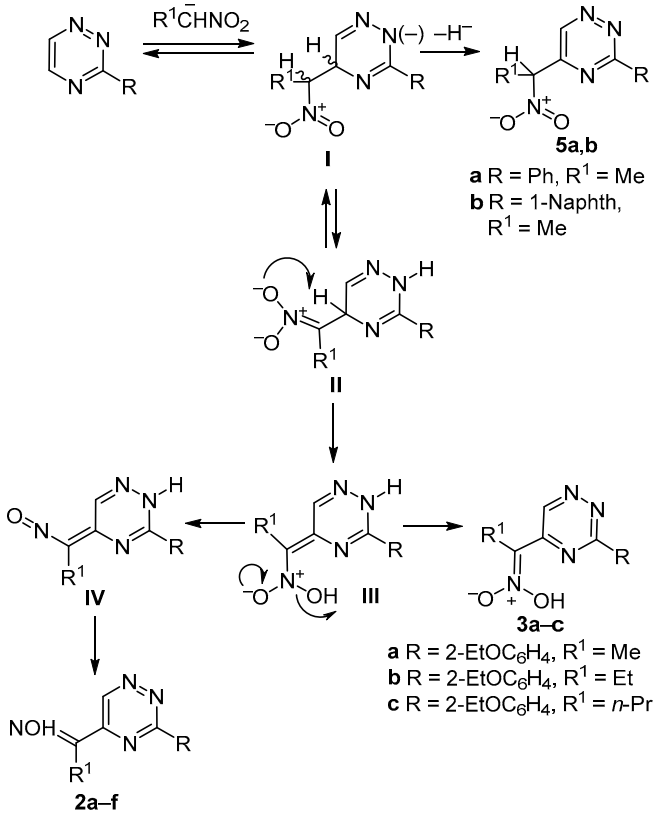
Considering the experimental results and the fact that adduct **4a** is intermediate in the synthesis of the corresponding oxime **2a**, derivative **4a** was mixed in suspension of KOH in DMSO (Scheme 4) under typical reaction conditions used for preparation of oxime. The reaction mixture was stirred at room temperature for 2 h till substrate **4a** disappeared. After that, the reaction mixture was poured into ice water and neutralize with AcOH to pH 7. Two products were formed and isolated by extraction with Et_2O from an aqueous solution followed by column chromatography. Product **3a** was formed in 42% yield, and oxime **2a** was isolated in 11% yield. The reaction was repeated under the same conditions, but the reaction mixture was poured into ice water without neutralization with AcOH. As a result of this change, only one product **3a** was obtained in 71% yield.

These results prompted us to synthesize other adducts with different substituents at the C-3 position of the 1,2,4-triazine ring. Therefore, 3-phenyl- and 3-(1-naphthyl)-1,2,4-triazines were reacted with nitroethane in the presence of K_2CO_3 in DMSO at room temperature. The reactions were carried out for 2.5 h (Scheme 5). Adducts **4b**,**c** were isolated in the same way as diastereomers **4a**, and NMR spectra were recorded. It should be noted that it is not possible to prepare the appropriate σ^H-adduct of 3-methylsulfanyl-1,2,4-triazine (**1a**) in this way. The adduct with methylsulfanyl group could be only obtained in the presence of KOH in liquid ammonia.[9]

In the next stage of our study, the obtained adducts **4b**,**c** were subjected to oxidation using DDQ in $CDCl_3$. The oxidation process was carried out in a small scale (0.1 mmol) at room temperature for 1 h. The NMR spectra performed for the reaction mixtures confirmed structures **5a**,**b**. We have also investigated transformation of adducts **4b**,**c** in a suspension of KOH in DMSO. As a result of these transformations we have obtained respective products **5a**,**b**. Their structures were different from compound **3a** obtained from compound **4a** under KOH/DMSO conditions or using DDQ in $CDCl_3$.

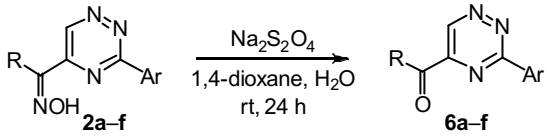
Taking into account that the reaction of nitroalkanes with 1,2,4-triazines can be considered as nucleophilic substitution reaction of hydrogen and in part as Nef-type reaction, the formation of structures **3a**–**c** is reasonable and could be a result of two mentioned above reaction mechanisms. Therefore a plausible mechanism for the formation of triazines **3a**–**c** is presented in Scheme 6. However, it should be noted that nitronic acid forms **3a**–**c** were not observed so far and not isolated from reactions of 3-methyl-, 3-phenyl-, 3-methylsulfanyl-, or 3-methoxy-1,2,4-triazine with nitroalkanes. This result can confirm our previous suggestion that 2-ethoxyphenyl substituent in 1,2,4-triazine allows to form nitronic acids **3a**–**c** stabilized by intramolecular hydrogen bonds.

Scheme 6



Oximes of 5-acyl-1,2,4-triazine **2a**–**f** are valuable starting materials for the synthesis of carbonyl compounds useful in organic synthesis.[3,4,8,10,14,15] Therefore, using Pojer's method[16] for reduction of oximes to the corresponding carbonyl compounds, we have converted

Scheme 7



6 a Ar = 2-EtOC$_6$H$_4$, R = Me (52%); **b** Ar = 2-EtOC$_6$H$_4$, R = Et (58%); **c** Ar = 2-EtOC$_6$H$_4$, R = *n*-Pr (52%); **d** Ar = 4-EtOC$_6$H$_4$, R = Me (56%); **e** Ar = Ph, R = Me (64%); **f** Ar = 1-Naphth, R = Me (53%)

oximes **2a**–**f** into corresponding ketones **6a**–**f** (Scheme 7). The structures of the obtained compounds **6a**–**f** were established by NMR spectroscopy.

In order to confirm the synthesis pathway, the proposed molecular structures, and conformational preferences associated with the possible formation of intramolecular hydrogen bonds, the X-ray analysis of triazine **2a** as the model compound was performed. View of molecule **2a** in conformation observed in crystal with numbering of atoms is shown in Figure 3.

The oxime substituent adopts the *trans-trans* conformation in relation to the 1,2,4-triazine ring with the methyl group in the *cis* position with respect to N(4)–C(5) bond, which is confirmed by the torsion angles N(4)–C(5)–C(7)–N(8), C(5)–C(7)–N(8)–O(9) and N(4)–C(5)–C(7)–C(10) of –173.0(3), 179.1(3) and 5.3(4)°, respectively. This conformation is stabilized by C(10)–H(102)···N(4) intramolecular hydrogen bond (Table 2), but in this conformation the intramolecular hydrogen bond between O–H group and N-4 atom of the 1,2,4-triazine ring is not observed. The same conformation of the oxime group with respect to the triazine and pyridine rings is observed in closely related structure of (*E*)-1-(3-methylsulfanyl-1,2,4-triazin-5-yl)-ethanone *O*-acryloyl oxime[17] and (*E*)-1-(pyridin-2-yl)-ethanone *O*-acryloyl oxime,[18] respectively. The theoretical calculations at DFT/B3LYP/6-311++G(d,p) level showed, that the alternative *cis–cis* conformation of the oxime group with calculated torsion angles N(4)–C(5)–C(7)–N(8) of 3.28° and C(5)–C(7)–N(8)–O(9) of –0.11° and the possibility to form O(9)–H(9)···N(4) intramolecular hydrogen bond (Table 2; Supplementary information file, Table S1, Fig. S1) is less energetically stable than that observed in the crystal with the difference of energy of 2.399 kcal/mol. This value of energy does not exclude the coexistence of these two conformations with the population of 0.98:0.02 in favor of that observed in the crystal at room temperature calculated from non-degenerate Boltzmann distribution. It should be noted, that this calculation was performed for isolated molecule (gaseous phase), while the X-ray analysis unambiguously showed that compound **2a** occurs in one *trans–trans* conformation in the crystalline state.

Table 2. The hydrogen bond lengths (Å) observed in crystal and obtained using DFT/B3LYP/6-311++G(d,p) calculations for compound **2a**

D–H···A	D–H	H···A	D···A	D–H···A
		2a (X-ray)		
C(10)–H(102)···O(9)	0.96	2.25	2.664(4)	105
O(9)–H(9)···N(1)*	0.96(4)	2.45(3)	3.152(3)	130(3)
O(9)–H(9)···N(2)*	0.96(4)	1.86(4)	2.797(4)	163(3)
		2a (DFT)		
O(9)–H(9)···N(4)	0.995	1.704	2.590	146.0
O(9)–H(9)···O(17)	0.995	2.515	3.261	131.5
		3a (DFT)		
O–H···N(4)	1.030	1.547	2.497	150.7
O–H···O(Et)	1.030	2.461	3.140	122.7
		3d (DFT)		
O–H···N(4)	1.024	1.553	2.508	152.9
		3e (DFT)		
O–H···N(4)	1.020	1.568	2.519	152.9
		3f (DFT)		
O–H···N(4)	1.019	1.581	2.522	151.2

* Symmetry code $i = 1 - x, 1/2 + y, 1/2 - z$.

The benzene ring of the ethoxyphenyl substituent is twisted with respect to 1,2,4-triazine ring with the torsion angle N(2)–C(3)–C(11)–C(16) of –30.3(4)°. This mutual position of the rings is forced by the electrostatic repulsion of the lone pairs of N-4 and O-17 atoms. The 2-ethoxy group in the phenyl substituent lies practically in the plane of the benzene ring with the *trans-trans* conformation as shown by the torsion angles C(11)–C(12)–O(17)–C(18) of –174.5(3)° and C(12)–O(17)–C(18)–C(19) of 177.0(3)°.

In the crystal structure, the molecules related by 2_1 axes are linked into chains parallel to Y direction *via* bifurcated intermolecular O–H···N hydrogen bonds (Fig. 4, Table 2). It should be noted that the *trans–trans* conformation of the oxime group with respect to 1,2,4-triazine ring favors the formation of structural motif observed in crystal of triazine **2a**.

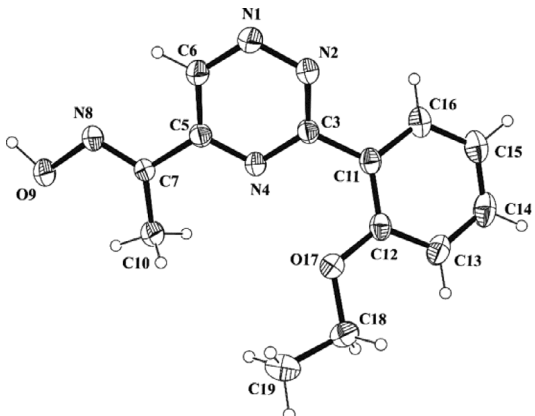


Figure 3. Molecular structure of compound **2a** with atoms represented as thermal vibration ellipsoids of 30% probability.

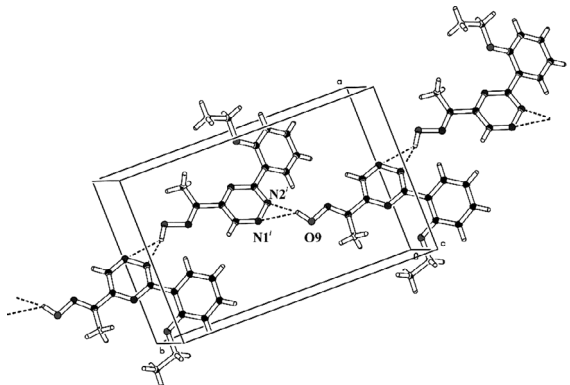


Figure 4. The molecular motif formed by molecules *via* O–H···N intermolecular hydrogen bonds (symmetry code $i = 1 - x, 1/2 + y, 1/2 - z$) in crystal of compound **2a**.

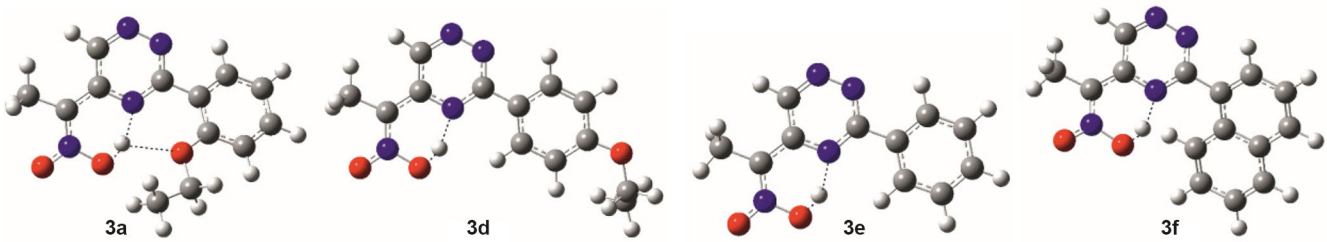


Figure 5. The structure of compound **3a** and hypothetical structures of compounds **3d**–**f** obtained after theoretical calculations at DFT/B3LYP/6-311++G(d,p) level.

Moreover, the 1,2,4-triazine rings belonging to the inversion-related molecules overlap each other with a centroid-to-centroid separation of 4.0016(19) Å (1 – *x*, –*y*, 1 – *z*) and the slippage of 1.156 Å.

As mentioned earlier, the experiments carried out suggest that the formation of derivatives **3a**–**c** strongly depends on the presence of the alkoxy group in position 2' of the phenyl ring attached to the carbon C-3 of 1,2,4-triazine ring. This may be due to the occurrence of O–H···N(4) hydrogen bond between the OH group of *aci*-nitro group and triazine nitrogen atom N(4) (Fig. 1, structure **A**) or O–H···N(4) and O–H···O hydrogen bonds, where the atom O from ethoxy substituent is additional acceptor of proton (Fig. 1, structure **B**). It could be facilitated by presence of electron-donating alkoxy group at the *ortho* position of the phenyl ring which may increase the electron density on the triazine nitrogen atom N-4. Unfortunately, attempts to crystallize compounds **3a**–**c** with nitro-*aci* group and adducts **4a**–**c** from different solvents were unsuccessful giving residues unsuitable for X-ray analysis. However, theoretical calculations at DFT/B3LYP/6-311++G(d,p) level performed for compound **3a** and hypothetical structures **3d**–**f** do not confirm correlation between the possibility to formation of derivatives **3a**–**c** and **3d**–**f** and the net charge on N-4 atom of the 1,2,4-triazine ring. The geometry and conformation calculated using DFT method for molecules **3a**,**d**–**f** are presented in Figure 5.

One can see the strong intramolecular hydrogen bond O–H···N(4) with the clear shift of the H atom from O atom in the direction of N-4 atom; the respective O···H and H···N distances are 1.030 and 1.547 Å in compound **3a**, 1.024 and 1.553 Å in compound **3d**, 1.020 and 1.568 Å in compound **3e**, and 1.019 and 1.581 Å in compound **3f** (Table 2). Moreover, the weak intramolecular hydrogen bond O–H···O between O atoms of *aci*-nitro and ethoxy groups in compound **3a** is observed with H···O distance of 2.461 Å (Table 2) being shorter than the sum of van der Waals radii of H (1.20 Å) and O (1.52 Å) atoms. It is also noted, that the calculated NBO net charge on N-4 atom is –0.534 *e* for compound **3a** and –0.554 *e*, –0.551 *e*, and –0.555 *e* for compounds **3d**, **3e**, and **3f**, respectively, and this charge does not depend on the presence of additional proton acceptor atom in the *ortho*-substituent of the phenyl group (Supplementary information file, Table S2).

Theoretical calculations show, that the electronic nature of the substituent in position 2' of the phenyl ring is probably not associated with the formation of derivatives **3a**–**c**. The impossibility of isolation of appropriate nitronic acid form **3** in the reaction of triazines **1c**–**e** with nitroethane may be due to the lack of intramolecular O–H···O hydrogen bond stabilizing molecular structures of triazines **3a**–**c**.

The results presented in this paper indicate that 3-methylsulfanyl-1,2,4-triazine easily react with various boronic acids according to methodology of Suzuki-type reaction and provided 3-aryl-1,2,4-triazines in very good yield. 3-(2-Ethoxyphenyl)-1,2,4-triazine in the reaction with nitroalkanes yielded appropriate oximes and new nitronic acid forms stabilized by intramolecular hydrogen bonds. Reaction of 3-aryl derivatives of 1,2,4-triazine with nitroalkanes in a suspension of K_2CO_3 in DMSO leads to the corresponding σ^H-adducts isolated in good yield. The structures of the σ^H-adducts were clearly confirmed by spectroscopic methods. Adducts can be oxidized, and the course of these reactions depends on their structures. If the adduct contained 2-ethoxyphenyl substituent at the C-3 position of the 1,2,4-triazine ring we have observed only 3-(2-etoxyphenyl)-5-(1-*aci*-nitroethyl)-1,2,4-triazine intermediate identical to the product of the reaction with KOH in DMSO. However, if at the C-3 position of the adduct, an aryl substituent is other than 2-ethoxyphenyl, only nitro product was obtained. Introduction of 2-ethoxyphenyl moiety in the C-3 position of the 1,2,4-triazine ring allows to form compounds with nitronic acid structure which have never been observed during the synthesis of oximes starting from 3-methyl-, 3-phenyl, 3-methylsulfanyl-, or 3-methoxy-1,2,4-triazine and applying described herein procedure. We have not obtained or have not even detected by spectroscopic methods the presence of other intermediates proposed by Rykowski and Mąkosza in the mechanism of the synthesis of oximes from 1,2,4-triazines and nitroalkanes. However, our studies can indirectly confirm the formation of key structure as essential intermediate for the construction of both oximes and new nitronic acid forms.

Experimental

IR spectra were recorded in CCl_4 on a Nicolet Magna 760 FTIR spectrometer in thin films. ^{1}H and ^{13}C NMR spectra were recorded on a Varian 400 MR spectrometer (400 and 100 MHz, respectively), TMS used as internal standard. Mass spectra were recorded on an Agilent Technologies 6538 UHD Accurate Mass Q-TOF LC/MS spectrometer with electrospray ionization (ESI/MS). Mass spectra of compounds **3**, **4 a** were recorded on a DFS High Resolution GC/MS spectrometer (EI, 70 eV). Elemental

analysis was performed on a LECO 628 series elemental analyzer. Melting points were determined on a Mel-Temp apparatus and are uncorrected.

Triazine **1a**[19] and Cu(I) 3-methylsalicylate (MeSalCu)[20] were prepared by methods described in the literature.

Synthesis of 3-aryl-1,2,4-triazines 1b–e (General method). $Pd(PPh_3)_4$ (1.15 g, 1 mmol, 0.1 equiv) was added to a mixture of 3-methylsulfanyl-1,2,4-triazine (**1a**) (1.27 g, 10 mmol, 1.0 equiv), MeSalCu (4.7 g, 22 mmol, 2.2 equiv), arylboronic acid (22 mmol, 2.2 eqiuv) in dry THF (50 ml) under argon atmosphere. The reaction mixture was stirred overnight at reflux. The reaction was quenched with a saturated Na_2CO_3 solution and extracted with CH_2Cl_2. The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. After purification by column chromatography on silica gel, eluent hexane–CH_2Cl_2, 3:1, the desired products were obtained.

3-(2-Ethoxyphenyl)-1,2,4-triazine (1b).[21] Yield 1.96 g (98%), yellowish oil. IR spectrum, ν, cm^{-1}: 2927, 1600, 1452, 1236, 1037, 750. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.31 (3H, t, *J* = 5.8, CH_3); 4.10 (2H, q, *J* = 5.8, CH_2); 7.02–7.09 (2H, m, H Ar); 7.42–7.46 (1H, m, H Ar); 7.75 (1H, dd, ^1J = 7.6, ^2J = 2.0, H Ar); 8.67 (1H, d, *J* = 2.0, H Ar); 9.14 (1H, d, *J* = 2.0, H Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.5; 64.5; 113.2; 120.6; 125.6; 131.6; 131.9; 147.0; 148.0; 157.3; 165.9.

3-(4-Ethoxyphenyl)-1,2,4-triazine (1c). Yield 1.60 g (80%), yellow solid, mp 104–105°C. IR spectrum, ν, cm^{-1}: 2983, 1608, 1517, 1402, 1390, 1354, 1257, 1174, 1116, 1041, 844, 792. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.45 (3H, t, *J* = 7.0, CH_3), 4.13 (q, 2H, *J* = 7.0, CH_2); 7.01–7.03 (2H, m, H Ar); 8.46–8.49 (2H, m, H Ar); 8.59 (1H, s, H triazine); 9.07 (1H, s, H triazine). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.7; 63.6; 114.7; 126.9; 130.0; 146.9; 148.5; 162.1; 164.0. Found, %: C 65.70; H 5.64; N 20.64. $C_{11}H_{11}N_3O$. Calculated, %: C 65.66; H 5.51; N 20.88.

3-Phenyl-1,2,4-triazine (1d). Yield 1.28 g (82%), yellow solid, mp 35–38°C. IR spectrum, ν, cm^{-1}: 1523, 1398, 1355, 748, 686. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 7.51–7.57 (3H, m, H Ph); 8.51 (2H, d, *J* = 1.6, H Ph); 8.68 (1H, s, H triazine); 9.17 (1H, s, H triazine). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 115.4; 128.1; 128.7; 129.4; 131.7; 134.5; 147.6. Found, %: C 68.90; H 4.60; N 26.49. $C_9H_7N_3$. Calculated, %: C 68.78; H 4.49; N 26.73.

3-(Naphthalen-1-yl)-1,2,4-triazine (1e). Yield 1.45 g (70%), yellow solid, mp 53–55°C. IR spectrum, ν, cm^{-1}: 1506, 1338, 1305, 1041, 767. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 7.52–7.63 (2H, m, H Ar); 7.93 (2H, d, *J* = 7.6, H Ar); 8.02 (1H, d, *J* = 8.4, H Ar); 8.20 (1H, d, *J* = 7.2, H Ar); 8.70 (1H, d, *J* = 8.0, H Ar); 8.70 (1H, d, *J* = 1.6, H Ar); 9.20 (1H, d, *J* = 1.6, H Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 125.0; 125.2; 126.1; 127.3; 128.5; 130.2; 130.7; 131.6; 132.5; 133.9; 147.1; 148.3; 166.9. Found, %: C 75.39; H 4.51; N 20.08. $C_{13}H_9N_3$. Calculated, %: C 75.35; H 4.38; N 20.28.

Reaction of 3-aryl-1,2,4-triazines with nitroalkanes (General method). A solution of the appropriate 1,2,4-triazine **1b–e** (10 mmol) and nitroalkane (25 mmol) in DMSO (2 ml) was added in one portion to a stirred suspension of powdered KOH (8.0 g, 0.14 mol) in dry DMSO (20 ml) at room temperature. The mixture was stirred at room temperature for 2 h, then poured into ice water (200 ml) and neutralized with AcOH to pH 7.0. The precipitated oxime was filtered off and washed with H_2O. The crude oxime was purified by chromatography on silica gel, eluent CH_2Cl_2–EtOH, 50:1, to afford products **2a–f** as yellowish powders. After filtration of the oxime, the solution was extracted with Et_2O. After evaporation of the Et_2O, the residue was purified by column chromatography using silica gel and CH_2Cl_2–EtOH, 50:1, to yield byproducts **3a–c** as yellow solids.

1-[3-(2-Ethoxyphenyl)-1,2,4-triazin-5-yl]ethanone oxime (2a). Yield 1.21 g (47%), mp 154–156°C. IR spectrum, ν, cm^{-1}: 3120, 2937, 1583, 1274, 751. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.38 (3H, t, *J* = 6.8, CH_3); 2.37 (3H, s, CH_3); 4.15 (2H, q, *J* = 6.8, CH_2); 7.06–7.13 (2H, m, H Ar); 7.46–7.49 (1H, m, H Ar); 7.87 (1H, dd, *J* = 7.6, *J* = 1.6, H Ar); 9.66 (1H, s, H triazine); 10.20 (1H, br. s, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 9.0; 14.7; 64.4; 113.2; 120.7; 125.0; 131.9; 132.2; 143.2; 153.7; 154.1; 157.7; 164.9. Found, *m*/*z*: 259.1188 $[M+H]^+$. $C_{13}H_{14}N_4O_2$. Calculated, *m*/*z*: 259.1190.. Found, %: C 60.51; H 5.63; N 21.55. $C_{13}H_{14}N_4O_2$. Calculated, %: C 60.46; H 5.46; N 21.69.

1-[3-(2-Ethoxyphenyl)-1,2,4-triazin-5-yl]propanone oxime (2b). Yield 1.0 g (37%), mp 121°C. IR spectrum, ν, cm^{-1}: 3123, 2940, 1589, 1268, 755. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.19 (3H, t, *J* = 7.6, CH_3); 1.38 (3H, t, *J* = 7.2, CH_3); 2.97 (2H, q, *J* = 7.6, CH_2); 4.16 (2H, q, *J* = 6.8, CH_2); 7.06–7.13 (2H, m, H Ar); 7.47–7.49 (1H, m, H Ar); 7.49–7.87 (1H, m, H Ar); 9.64 (1H, s, H triazine). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 10.4; 14.6; 16.6; 64.4; 113.0; 120.6; 125.0; 131.9; 132.2; 143.5; 157.6; 158.7; 166.1. Found, *m*/*z*: 273.1346 $[M+H]^+$. $C_{14}H_{17}N_4O_2$. Calculated, *m*/*z*: 273.1268. Found, %: C 61.53; H 6.03; N 20.48. $C_{14}H_{16}N_4O_2$. Calculated, %: C 61.75; H 5.92; N 20.57.

1-[3-(2-Ethoxyphenyl)-1,2,4-triazin-5-yl]butan-1-one oxime (2c). Yield 1.28 g (45%), mp 124–126°C. IR spectrum, ν, cm^{-1}: 3130, 2947, 1571, 1260, 752. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.98 (3H, t, *J* = 7.2, CH_3); 1.38 (3H, t, *J* = 6.8, CH_3); 1.63–1.70 (2H, m, CH_2); 2.94 (2H, t, *J* = 7.2, CH_2); 4.15 (2H, q, *J* = 6.8, CH_2); 7.06–7.12 (2H, m, H Ar); 7.48 (1H, t, *J* = 7.2, H Ar); 7.82 (1H, d, *J* = 7.2, H Ar); 9.65 (1H, s, H triazine); 9.84 (1H, br. s, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.4; 14.8; 19.5; 25.2; 64.5; 113.3; 120.7; 125.6; 132.1; 132.2; 143.7; 153.4; 157.8; 157.9; 165.2. Found, *m*/*z*: 287.1502 $[M+H]^+$. $C_{15}H_{19}N_4O_2$. Calculated, *m*/*z*: 287.1503. Found, %: C 62.88; H 6.40; N 19.40. $C_{15}H_{18}N_4O_2$. Calculated, %: C 62.92; H 6.34; N 19.57.

1-[3-(4-Ethoxyphenyl)-1,2,4-triazin-5-yl]ethanone oxime (2d). Yield 0.36 g (14%), mp 228–229°C. IR spectrum, ν, cm^{-1}: 3211, 2943, 1543, 1354, 1257, 844, 792. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.36 (3H, t, *J* = 6.8, CH_3); 2.25 (3H, s, CH_3); 4.11 (2H, q, *J* = 6.8, CH_2); 7.08 (2H, d, *J* = 8.8, H Ar); 8.37 (2H, d, *J* = 8.8, H Ar); 9.51 (1H, s, H triazine); 12.61 (1H, s, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 8.9; 14.5; 63.3; 114.8; 126.6; 129.4;

143.1; 152.5; 153.1; 157.5; 161.5. Found, *m/z*: 259.1190 $[M+H]^+$. $C_{13}H_{15}N_4O_2$. Calculated, *m/z*: 259.1190. Found, %: C 60.38; H 5.80; N 21.49. $C_{13}H_{14}N_4O_2$. Calculated, %: C 60.46; H 5.46; N 21.69.

1-(3-Phenyl-1,2,4-triazin-5-yl)ethanone oxime (2e). Yield 0.87 g (41%), mp 198°C. IR spectrum, ν, cm^{-1}: 3145, 2827, 1539, 1517, 1363, 1354, 1029, 756, 686. ^1H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 2.30 (3H, s, CH_3); 7.60–7.62 (3H, m, H Ph); 8.48 (2H, d, *J* = 8.0, H Ph); 9.62 (1H, s, H triazine); 12.67 (1H, s, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 9.0; 127.7; 129.0; 131.8; 134.5; 143.9; 152.5; 153.4; 162.1. Found, *m/z*: 215.2747 $[M+H]^+$. $C_{12}H_{14}N_4O$. Calculated, *m/z*: 214.2749. Found, %: C 61.51; H 4.80; N 26.29. $C_{11}H_{10}N_4O$. Calculated, %: C 61.67; H 4.71; N 26.15.

1-[3-(Naphthalen-1-yl)-1,2,4-triazin-5-yl]ethanone oxime (2f). Yield 1.34 g (51%), mp 196°C. IR spectrum, ν, cm^{-1}: 3134, 3053, 2812, 1506, 1338, 1305, 1041, 1028, 767. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.42 (3H, s, CH_3); 7.52 –7.67 (3H, m, H Ar); 7.95–7.97 (1H, m, H Ar); 8.05–8.08 (1H, t, *J* = 7.2, H Ar); 8.24 (1H, d, *J* = 7.2, H Ar); 8.71 (1H, d, *J* = 8.0, H Ar); 9.80 (1H, s, H triazine). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 25.5; 124.8; 125.1; 125.2; 126.4; 127.6; 128.0; 128.8; 128.9; 130.8; 131.8; 132.3; 133.0; 134.1; 169.4. Found, *m/z*: 264.3310 $[M+H]^+$. $C_{15}H_{12}N_4O$. Calculated, *m/z*: 264.3306. Found, %: C 68.42; H 5.71; N 21.00. $C_{15}H_{12}N_4O$. Calculated, %: C 68.17; H 4.58; N 21.20.

1-[3-(2-Ethoxyphenyl)-1,2,4-triazin-5-yl]-*N*-hydroxyethanimine oxide (3a). Yield 0.16 g (6%), mp 138–140°C. IR spectrum, ν, cm^{-1}: 3331, 2981, 1587, 1537, 1463, 1222, 1029, 734, 682. ^1H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.27 (3H, t, *J* = 6.8, CH_3); 3.30 (3H, s, CH_3); 4.13 (2H, q, ^1J = 6.8, CH_2); 7.14–7.26 (2H, m, H Ar); 7.54–7.56 (1H, m, H Ar); 7.76–7.86 (1H, m, H Ar); 9.62 (1H, s, H triazine). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 14.5; 25.3; 64.0; 113.7; 120.5; 124.8; 131.5; 132.3; 142.9; 148.3; 157.1; 164.9; 199.2. Mass spectrum, *m/z* (I_{rel}, %): 274 $[M]^+$ (4), 228 (8), 200 (5), 148 (13), 119 (100), 53 (16).

1-[3-(2-Ethoxyphenyl)-1,2,4-triazin-5-yl]-*N*-hydroxypropanimine oxide (3b). Yield 0.29 g (10%), mp 130–132°C. IR spectrum, ν, cm^{-1}: 3278, 2956, 1583, 1465, 1230, 1029, 750. ^1H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.02 (3H, t, *J* = 7.6, CH_3); 1.34 (3H, t, *J* = 6.8, CH_3); 2.81 (2H, q, *J* = 7.6, CH_2); 4.15 (2H, q, *J* = 6.8, CH_2); 7.12 (1H, t, *J* = 7.6, H Ar); 7.21 (1H, d, *J* = 8.0, H Ar); 7.57 (1H, td, ^1J = 8.0, ^2J = 1.6, H Ar); 7.69 (1H, t, *J* = 7.2, H Ar); 9.19 (1H, s, H triazine); 13.30 (1H, s, OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 14.4; 16.2; 30.6; 64.0; 113.4; 120.5; 124.8; 130.7; 131.5; 132.3; 143.2; 156.9; 157.1. Found, *m/z*: 289.1295 [M–H]. $C_{14}H_{18}N_4O_3$. Calculated, *m/z*: 289.1217.

1-[3-(2-Ethoxyphenyl)-1,2,4-triazin-5-yl]-*N*-hydroxybutanimine oxide (3c). Yield 0.39 g (13%), mp 85–86°C. IR spectrum, ν, cm^{-1}: 3315, 2920, 1436, 1234, 1375, 750. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.88 (3H, t, *J* = 7.2, CH_3); 1.34 (3H, t, *J* = 6.8, CH_3); 1.47 (2H, dq, *J* = 7.2, CH_2); 2.78 (2H, t, *J* = 7.2, CH_2); 4.15 (2H, q, *J* = 7.2, CH_2); 7.12 (1H, t, *J* = 7.6, H Ar); 7.21 (1H, d, *J* = 8.4, H Ar); 7.57 (1H, td, ^1J = 8.4, ^2J = 1.6, H Ar); 7.63 (1H, dd, ^1J = 8.0, ^2J = 1.6, H Ar); 9.19 (1H, s, H triazine). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.4; 15.4; 19.7; 25.5; 65.0; 114.5; 121.4; 125.7; 132.4; 133.3; 143.9; 149.1; 158.1; 165.8; 202.1. Found, *m/z*: 303.1451 [M–H]. $C_{15}H_{20}N_4O_3$. Calculated, *m/z*: 303.1452.

Synthesis of σ^H-adducts (General method). A solution of the appropriate 1,2,4-triazine **1b**,**d**,**e** (1 mmol) and nitroethane (0.225 g, 3 mmol) in DMSO (1 ml) was added in one portion to a vigorously stirred suspension of powdered K_2CO_3 (0.414 g, 3 mmol) in dry DMSO (1 ml) at room temperature. The mixture was stirred at room temperature for 2.5 h, then poured into ice water (20 ml) and extracted with Et_2O. After evaporation of the solvent, the residue was purified by column chromatography on silica gel, eluent EtOAc–hexane, 1:1, to yield product as yellow crystals.

3-(2-Ethoxyphenyl)-5-(1-nitroethyl)-2,5-dihydro-1,2,4-triazine (4a), mixture of diastereomers 1.3:1. Yield 0.19 g (69%). **Major diastereomer**: R_f 0.78. IR spectrum, ν, cm^{-1}: 3407, 2926, 1600, 1544, 1454, 1236, 1033, 750. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.32 (3H, t, *J* = 7.2, CH_3); 1.61 (3H, d, *J* = 6.8, CH_3); 4.01 (1H, dd, ^1J = 7.2, ^2J = 2.0, CH); 4.07 (2H, q, *J* = 7.2, CH_2); 4.92 (1H, p, *J* = 6.8, CH); 6.82 (1H, d, *J* = 2.0, H triazine); 6.98 (1H, t, *J* = 8.0, H Ar); 7.08 (1H, d, *J* = 8.0, H Ar); 7.36–7.44 (2H, m, H Ar); 10.69 (1H, br. s, NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 15.3; 55.5; 83.1; 112.6; 119.8; 121.5; 131.4; 132.4; 133.7; 154.5; 156.9. Mass spectrum, *m/z* (I_{rel}, %): 276 $[M]^+$ (1), 229 (48), 202 (100), 174 (44), 148 (6), 120 (28), 91 (10), 39 (5). **Minor diastereomer**: R_f 0.69. IR spectrum, ν, cm^{-1}: 3409, 2920, 1602, 1546, 1451, 1230, 1028, 758. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.32 (3H, t, *J* = 7.2, CH_3); 1.54 (3H, d, *J* = 6.8, CH_3); 4.07 (2H, q, *J* = 7.2, CH_2); 4.20 (1H, dd, ^1J = 3.6, ^2J = 2.0, CH); 5.00 (1H, p, *J* = 5.6, CH); 6.78 (1H, d, *J* = 1.6, H triazine); 6.98 (1H, t, *J* = 8.0, H Ar); 7.08 (1H, d, *J* = 8.0, H Ar); 7.36–7.44 (2H, m, H Ar); 10.60 (1H, br. s, NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 15.5; 55.3; 82.9; 112.7; 119.8; 121.4; 131.2; 132.4; 134.3; 154.5; 156.9. Mass spectrum (EI, 70 eV) *m/z* (I_{rel}, %): 276 $[M]^+$ (1), 229 (38), 202 (100), 174 (55), 148 (8), 120 (25), 91 (16), 39 (8).

5-(1-Nitroethyl)-3-phenyl-2,5-dihydro-1,2,4-triazine (4b), mixture of diastereomers 1.5:1. Yield 0.09 g (40%). **Major diastereomer**: R_f 0.70. IR spectrum, ν, cm^{-1}: 3390, 2937, 1602, 1548, 1355, 692. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.70 (3H, d, *J* = 6.8, CH_3); 4.31 (1H, dd, ^1J = 6.4, ^2J = 2.4, CH); 4.90 (1H, q, *J* = 6.8, CH); 6.82 (1H, d, *J* = 1.6, H triazine); 7.43–7.51 (4H, m, H Ph); 7.71 (1H, t, *J* = 7.2, H Ph); 8.71 (1H, br. s, NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 15.3; 55.4; 83.0; 126.5; 128.4; 131.4; 131.8; 132.0; 134.8. **Minor diastereomer**: R_f 0.62. IR spectrum, ν, cm^{-1}: 3396, 2933, 1610, 1552, 1356, 700. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.77 (3H, d, *J* = 6.8, CH_3); 4.22 (1H, dd, ^1J = 6.4, ^2J = 2.4, CH); 4.86 (1H, p, *J* = 6.8, CH); 6.77 (1H, d, *J* = 1.2, H triazine); 7.43–7.51 (4H, m, H Ph); 7.71 (1H, t, *J* = 7.2, H Ph); 8.71 (1H, br. s, NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 15.6; 55.4; 83.2; 126.4; 128.5; 131.4; 131.9; 132.1; 134.8.

3-(Naphthalen-1-yl)-5-(1-nitroethyl)-2,5-dihydro-1,2,4-triazine (4c), mixture of diastereomers 4:1. Yield 0.16 g

(55%), mp 126–127°C. **Major diastereomer**: R_f 0.72. IR spectrum, ν, cm^{-1}: 3380, 2920, 1587, 1537, 1463, 1228, 1031, 754, 738, 690. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.77 (3H, d, *J* = 6.8, CH_3); 4.40 (1H, dd, ^1J = 6.0, ^2J = 2.0, CH); 5.03 (1H, p, *J* = 6.8, CH); 6.90 (1H, d, ^1J = 2.0, H triazine); 7.40–7.62 (4H, m, H Ar); 7.89 (1H, d, *J* = 7.6, H Ar); 7.96 (1H, d, *J* = 8.4, H Ar); 8.00 (1H, d, *J* = 7.6, H Ar); 8.66 (1H, br. s, NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 15.8; 55.5; 83.3; 124.2; 125.0; 126.5; 126.8; 126.9; 127.3; 128.5; 130.1; 130.4; 130.9; 133.6; 134.6. **Minor diastereomer**: R_f 0.65. IR spectrum, ν, cm^{-1}: 3387, 2927, 1582, 1542, 1469, 1219, 1037, 759, 732, 698. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.84 (3H, d, *J* = 6.8, CH_3); 4.23 (1H, dd, ^1J = 6.4, ^2J = 1.6, CH); 4.99 (1H, p, *J* = 6.8, CH); 6.87 (1H, d, ^1J = 1.2, H triazine); 7.40–7.62 (4H, m, H Ar); 7.89 (1H, d, *J* = 7.6, H Ar); 7.96 (1H, d, *J* = 8.4, H Ar); 8.00 (1H, d, *J* = 7.6, H Ar); 8.63 (1H, br. s, NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 15.3; 55.4; 82.8; 124.3; 124.9; 126.5; 126.8; 126.9; 127.3; 128.5; 130.2; 130.3; 130.9; 133.7; 134.9.

Conversion of adducts 4a–c. **Oxidation**. Adduct **4a**–**c** (0.1 mmol) was dissolved in $CDCl_3$ (2 ml), and DDQ (56 mg, 0.25 mmol) was added. The reaction mixture was stirred at room temperature for 1 h, then quenched with brine (NaCl in D_2O, 1 ml). The organic layer was separated, dried with anhydrous $MgSO_4$, and filtered. The resultant organic solution containing crude product was used to run NMR spectra.

Transformation in KOH–DMSO. Appropriate adduct **4b**,**c** (0.1 mmol) was added in one portion to a stirred suspension of powdered KOH (80 mg, 1.4 mmol) in dry DMSO (1 ml) at room temperature. The mixture was stirred at room temperature for 1 h, then poured into ice water and neutralized with AcOH to pH 7.0. The precipitated product was filtered off and washed with H_2O. The crude product was investigated by NMR.

5-(1-Nitroethyl)-3-phenyl-1,2,4-triazine (5a). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.07 (3H, d, *J* = 6.8, CH_3); 5.79 (1H, q, *J* = 6.8, CH); 8.08 (2H, s, H Ph); 8.56 (2H, d, *J* = 7.2, H Ph); 8.62 (1H, d, *J* = 6.4, H Ph); 9.32 (1H, s, H triazine).

3-(Naphthalen-1-yl)-5-(1-nitroethyl)-1,2,4-triazine (5b). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.09 (3H, d, *J* = 6.8, CH_3); 5.85 (1H, q, ^1J = 6.8, CH); 7.66–7.49 (3H, m, H Ar); 7.96 (1H, d, *J* = 7.6, H Ar); 8.07 (1H, d, *J* = 7.6, H Ar); 8.25 (1H, d, *J* = 7.2, H Ar); 8.68 (1H, d, *J* = 8.0, H Ar); 9.42 (1H, s, H triazine).

Synthesis of ketones 6a–**f** (General method). The corresponding oxime **2a**–**f** (10 mmol) was dissolved in 1,4-dioxane (40 ml) and treated with a solution of $Na_2S_2O_4$ (4.6 g, 26.4 mmol) in H_2O (40 ml). The resulting mixture was stirred at room temperature for 24 h. 1,4-Dioxane was removed under reduced pressure, and the residue was treated with 10% HCl (pH ~3) and bubbled by air for 10 min. Then the mixture was made neutral (pH ~7.0) by addition of solid $NaHCO_3$ and extracted with CH_2Cl_2. Evaporation of the organic solvent gave a crude product, which was purified by chromatography on silica gel, eluent CH_2Cl_2–hexane, 1:2.

1-[3-(2-Ethoxyphenyl)-1,2,4-triazin-5-yl]ethan-1-one (6a). Yield 1.26 g (52%), yellow solid, mp 65°C. IR spectrum, ν, cm^{-1}: 2981, 1705, 1600, 1516, 1454, 1386, 1276, 1246, 1037, 754. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.27 (3H, t, *J* = 6.8, CH_3); 2.68 (3H, s, CH_3); 4.14 (2H, q, *J* = 6.8, CH_2); 7.15 (2H, t, *J* = 7.6, H Ar); 7.25 (1H, d, *J* = 8.8, H Ar); 7.55–7.57 (1H, m, H Ar); 7.78 (1H, dd, ^1J = 7.6, ^2J = 1.6, H Ar); 9.62 (1H, s, H triazine). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.8; 25.4; 64.4; 113.2; 120.8; 124.7; 132.1; 132.6; 142.3; 147.7; 157.8; 165.9; 199.7. Found, *m*/*z*: 244.0925 $[M+H]^+$. $C_{13}H_{14}N_3O_2$. Calculated, *m*/*z*: 244.1003. Found, %: C 64.13; H 5.53; N 17.20. $C_{13}H_{13}N_3O_2$. Calculated, %: C 64.19; H 5.39; N 17.27.

1-[3-(2-Ethoxyphenyl)-1,2,4-triazin-5-yl]propan-1-one (6b). Yield 1.49 g (58%), yellow solid, mp 65°C. IR spectrum, ν, cm^{-1}: 2982, 1714, 1603, 1510, 1460, 1391, 1268, 1245, 1039, 750. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.17 (3H, t, *J* = 7.6, CH_3); 1.38 (3H, t, *J* = 7.2, CH_3); 3.00 (2H, q, *J* = 7.6, CH_2); 4.16 (2H, q, *J* = 7.2, CH_2); 7.07 (1H, d, *J* = 7.6, H Ar); 7.10 (1H, td, ^1J = 7.2, ^2J = 0.8, H Ar); 7.47–7.51 (1H, m, H Ar); 7.86 (1H, dd, ^1J = 7.6, ^2J = 1.6, H Ar); 9.64 (1H, s, H triazine). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.3; 15.0; 16.9; 64.4; 113.1; 120.6; 124.9; 132.0; 132.5; 142.5; 147.6; 157.9; 164.8; 199.8. Found, *m*/*z*: 258.2821 $[M+H]^+$. $C_{14}H_{16}N_3O_2$. Calculated, *m*/*z*: 258.2802. Found, %: C 65.43; H 6.03; N 16.21. $C_{14}H_{15}N_3O_2$. Calculated, %: C 65.36; H 5.88; N 16.33.

1-[3-(2-Ethoxyphenyl)-1,2,4-triazin-5-yl]butan-1-one (6c). Yield 1.40 g (52%), yellow oil. IR spectrum, ν, cm^{-1}: 2962, 1707, 1597, 1510, 1454, 1382, 1246, 1016, 752. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.02 (3H, t, *J* = 7.6, CH_3); 1.38 (3H, t, *J* = 6.8, CH_3); 1.77–1.84 (2H, m, CH_2); 3.23 (2H, t, *J* = 7.2, CH_2); 4.16 (2H, q, *J* = 6.8, CH_2); 7.08–7.15 (2H, m, H Ar); 7.49–7.54 (1H, m, H Ar); 7.91 (1H, dd, ^1J = 7.6, ^2J = 2.0, H Ar); 9.62 (1H, s, H triazine). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.7; 14.7; 16.9; 39.6; 64.4; 113.2; 120.7; 124.8; 132.0; 132.5; 142.4; 147.7; 157.8; 165.8; 201.8. Found, *m*/*z*: 272.1394 $[M+H]^+$. $C_{15}H_{18}N_3O_2$. Calculated, *m*/*z*: 272.1399. Found, %: C 66.45; H 6.44; N 15.30. $C_{15}H_{17}N_3O_2$. Calculated, %: C 66.40; H 6.32; N 15.49.

1-[3-(4-Ethoxyphenyl)-1,2,4-triazin-5-yl]ethan-1-one (6d). Yield 1.36 g (56%), yellow oil. IR spectrum, ν, cm^{-1}: 2981, 2941, 1707, 1604, 1516, 1361, 1251, 1174, 1116, 1039, 850, 796. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.47 (3H, t, *J* = 6.8, CH_3); 2.82 (3H, s, CH_3); 4.15 (2H, q, *J* = 6.8, CH_2); 7.05 (2H, d, *J* = 8.8, H Ar); 8.54 (2H, d, *J* = 8.8, H Ar); 9.53 (1H, s, H triazine). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.7; 25.3; 63.7; 114.9; 126.2; 130.2; 142.2; 148.0; 162.5; 163.9; 199.6. Found, %: C 63.98; H 5.60; N 17.10. $C_{13}H_{13}N_3O_2$. Calculated, %: C 64.19; H 5.39; N 17.27.

1-(3-Phenyl-1,2,4-triazin-5-yl)ethan-1-one (6e). Yield 1.27 g (64%), yellow solid, mp 133–134°C. IR spectrum, ν, cm^{-1}: 3068, 1707, 1531, 1350, 1122, 761, 698. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.85 (3H, s, CH_3); 7.55–7.61 (3H, m, H Ar); 8.60–8.62 (2H, m, H Ar); 9.63 (1H, s, H triazine). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 25.3; 128.4; 129.0; 132.3; 133.9; 143.0; 148.1; 164.1; 199.4.

Found, %: C 66.22; H 4.68; N 20.92. $C_{11}H_9N_3O$. Calculated, %: C 66.32; H 4.55; N 21.09.

1-[3-(Naphthalen-1-yl)-1,2,4-triazin-5-yl]ethan-1-one (6f). Yield 1.32 g (53%), yellow solid, mp 192–195°C. IR spectrum, ν, cm^{-1}: 3049, 2922, 1708, 1525, 1508, 1367, 1346, 783. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.84 (3H, s, CH_3); 7.56–7.63 (2H, m, H Ar); 7.67 (1H, t, *J* = 8.0, H Ar); 7.98 (1H, d, *J* = 7.2, H Ar); 8.09 (1H, d, *J* = 8.4, H Ar); 8.29 (1H, d, *J* = 7.2, H Ar); 8.73 (1H, d, *J* = 8.0, H Ar); 9.74 (1H, s, H triazine). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 25.5; 125.1; 125.2; 126.4; 127.6; 128.8; 130.8; 131.8; 132.3; 134.1; 142.6; 147.8; 166.8; 199.3. Found, %: C 72.39; H 4.53; N 16.64. $C_{15}H_{11}N_3O$. Calculated, %: C 72.28; H 4.45; N 16.86.

X-ray analysis of compound 2a was performed on a Kuma KM4 diffractometer; crystal size 0.50 × 0.15 × 0.10 mm, MoKα (λ 0.71073 Å) radiation, ω-2θ scans, 293(2) K, absorption correction: refdelf,[22] T_{min}/T_{max} = 0.416/0.677. The structure was solved by direct methods using SHELXS97[22] program and refined by full-matrix least-squares method with SHELXL-2014/7 program.[23] The O-bound H atom was located by difference Fourier synthesis and refined freely. The remaining H atoms were positioned geometrically and treated as riding on their parent C atoms with C–H distances of 0.97 Å (CH_2), 0.96 Å (CH_3), and 0.93 Å (Ar). All H atoms were refined with isotropic displacement parameters taken as 1.5 times those of the respective parent atoms. All calculations were performed using the WINGX version 2014.1 package.[24] Crystal data of compound **2a** ($C_{13}H_{14}N_4O_2$, *M* 258.28): monoclinic; space group $P2_1/c$; *a* 10.281(2), *b* 16.098(3), *c* 7.914(2) Å; β 100.38(3)°; *V* 1288.3(5) $Å^3$; *Z* 4; d_{calc} 1.332 $g \cdot cm^{-3}$; *F*(000) 544; μ(Ko*K*α) 0.094 mm^{-1}; 4632 measured reflections (θ range 2.01–30.08°), 3783 unique reflections, final *R* 0.059, *wR* 0.182, *S* 0.824 for 1060 reflections with $I > 2\sigma(I)$. Crystallographic data of compound **2a** was deposited at the Cambridge Crystallographic Data Center (deposit CCDC 1877568).

Theoretical calculations at the DFT/B3LYP level with 6-311++G(d,p) basis set implemented in GAUSSIAN 03[25] were carried out to investigate the conformational preferences of compounds **2a**, **3a**–**c** and hypothetical structures of compounds **3d**–**f**. All structures were fully optimized without any symmetry constraint and the initial geometries were built from crystallographic data of compound **2a**.

Supplementary information file containing crystallographic data of compound **2a** and DFT calculations of compounds **2a**, **3a**,**d**–**f** is available at the journal website at http://link.springer.com/journal/10593.

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